so; however, the evidence supporting such a practice is no better than that supporting the other treatments reviewed. The two studies cited are both retrospective surveys without randomised controls.[3,4] There really is insufficient evidence on the dose-response relation of inhaled steroids in terms of either wanted or unwanted side effects to allow a firm statement in the context of patients taking oral steroids. We do not know whether 5 mg of oral prednisolone is more than 2 mg of inhaled beclomethasone in terms of osteoporosis or other serious systemic side effects. It is worth remembering that beclomethasone is many times more potent dose for dose than prednisolone and that most of the inhaled drug is swallowed.

We agree with Dr Wilkinson that treating psychological factors may have a role in managing this type of patient. However, in a disease such as asthma, which is associated with such a strong placebo effect, only rigidly controlled prospective studies can prove the efficacy of a particular approach to treatment. Sadly, these trials are lacking.

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Psychiatric aspects of Parkinson's disease

SIR,—We would like to take issue with Drs R C Baldwin's and E J Byrne's suggestion in their review of the psychiatric aspects of Parkinson's disease that dementia affects only about a tenth of patients whereas up to two thirds suffer from a frontal-subcortical dysfunction.[1] Our results suggest that such conclusions might be premature. In a whole population study of the city of Aberdeen we identified 157 patients who were suffering from idiopathic Parkinson's disease. Our procedure for finding cases included screening general practice lists and old people's homes as well as hospitals and was identical with that employed by Mutch *et al*, who had clinically examined the larger part of our cohort three and a half years earlier.[2]

We found a prevalence of dementia, as defined by *Diagnostic and Statistical Manual of Mental Disorders III* criteria, of 24·3% (95% confidence interval 17·1 to 32·4%). Of the two studies quoted by Drs Baldwin and Byrne, one was based on a small sample drawn from attenders at a regional neurological centre[3] and the other employed a retrospective analysis of case notes.[4] Both studies would be expected to underestimate the true prevalence of dementia. A number of particularly elderly parkinsonian patients tend to be seen only by their general practitioners or by old age doctors or occasionally are not followed up at all.[2] These patients, who are unlikely to be seen in tertiary neurological referral centres, were included in our sample and might be responsible for the higher prevalence of dementia in our study compared with other studies.[5]

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The Bamako initiative

SIR,—We are prompted to respond to Dr Paul Garner's editorial on the Bamako initiative,[1] as we work in a rural district hospital in northern Ghana that charges for medicines. We observe that most patients expect drug treatment and are able to pay and that charging emphasises the importance of prescriptions and thereby improves compliance. Patients willingly spend far greater sums on "native" remedies; but a farmer may be reluctant to sell capital for the health needs of his wife and children. Undoubtedly some people are unable to pay, and it is essential to identify these and ensure the efficient running of a "poor and sick fund." Patients need protection from "invisible" costs on visiting health institutions—for example, illicit payment for consultation, investigation, and treatment—which act as a powerful deterrent to utilising health services.

Poor prescribing habits are an important contribution to drug bills. The reasons for these include poor training of staff, lack of prescribing policy, blanket treatment rather than investigation, and patient pressure. Overprescribing is a great problem. Much can be achieved by appropriate training and rationalising treatment regimens. For instance, the high priority placed on treating hypertension rather than diarrhoeal illness reflects Western style training.

An essential drug list for each tier of health care is of utmost importance. But how true it is that the necessary management skills are often lacking, so that forward planning, store keeping, ordering, and bulk buying are haphazard. The result is repeated shortages and expensive emergency purchases. Statistical analysis of morbidity data is also essential if annual and seasonal drug consumption is to be rationalised.[2] Certain drugs will be available within the country concerned, while bulk buying reduces transportation costs. The Bamako initiative will incur additional costs for Unicef if all of its drugs are supplied from overseas. People should, however, be aware of cheap, fake generic drugs. We encounter concern amounting to mild hysteria over expired drugs, and though one must endeavour to use drugs within the expiry period, most drugs remain safe and active for longer. Considerable savings are possible if infusions,[3] drops, syrups, and ointments are manufactured locally. Certain treatments, however, will always remain expensive—for example, some antibiotics and ketamine—but their costs can be offset by modest mark ups on cheaper, commonly used treatments. Occasionally more expensive drugs prove more cost effective than less potent cheap alternatives. Certain treatment regimens should remain free, such as treatment for tuberculosis and family planning. We find that many drugs are prescribed free for health service personnel and their families such that up to 50% of the drug budget is lost to revolving drug funds. Are the health services for staff or patients?

If a revolving drug fund is to work safeguards must exist to prevent money being sidetracked—for example, for the purchase of diesel. With the introduction of drug charges must come a global look at efficiency and management within health institutions, together with the pursuit of effective and realistic treatment aims. Governments must be concerned with improving management skills to enable them to come closer to the ultimate aim of independence in terms of running costs for health services.[4]

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Enteropathy induced by non-steroidal anti-inflammatory drugs

SIR,—In their letter Mr I Bjarnason and Professor J M Gumpel described the difficulty of diagnosing small bowel strictures not only from the results of barium studies but also at laparotomy.[1]

A mucosal stricture (and there may be several) may well be impossible to diagnose by either palpation or transillumination. Rather than use inflation with carbon dioxide as described I suggest a cheap and simple alternative for what I like to term "occult small bowel obstruction."

The upper jejunum is opened by a small transverse enterotomy and a marble is popped in. After closure of the jejunum the marble is gently milked down the small bowel, where it will impact at a mucosal web or stricture. Surgeons must appreciate that there need be no proximal dilatation and thus the unfortunate patient may have a negative exploration. When there is a high index of clinical suspicion this simple procedure can result in a more than grateful patient.

When no hold up occurs the marble is milked into the caecum and subsequently passed (it is as well to warn the patient of a possible unusual noise in the lavatory). No surgeon is likely to encounter many patients with this uncommon condition. It is 16 years since I paid nine pence for five marbles, and I still have one left.

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Myoclonus associated with high doses of morphine

SIR,—I would like to raise three points concerning the paper by Dr Julia M Potter and colleagues describing the role of supplemental drugs in "myoclonus" associated with treatment with high doses of morphine.[1]

Firstly, myoclonus consists of brief, shock like muscle jerks, classically lasting 25-200 ms, arising from the central nervous system. Yet in the patients described "the duration of the spasms was generally about one second." This is compatible with chorea or dystonia, or either combined with myoclonus, but not with myoclonus alone. A surface polyelectromyogram and videotape examination would help resolve the nature of the movements.

Secondly, although the possible role of concurrent electrolyte abnormalities is considered, no mention is made of urea or creatinine concentrations. Since uraemia may cause myoclonus, I presume this was excluded.

Thirdly, the (largely D_2) dopamine receptor blocking drugs haloperidol, chlorpromazine, and fluphenazine are grouped (and treated statistically)

together with doxepin and amitriptyline under the heading antipsychotics, whereas the (largely D_2) dopamine receptor blocking drugs thiethylperazine, metoclopramide, prochlorperazine, and domperidone appear under a separate heading of antinauseant drugs. This does not make pharmacological sense. As I see it, the point of this study is not that eight of 13 patients with side effects were taking antipsychotics and six of 13 were taking antiemetics, but rather that 12 of 12 patients with involuntary movements were taking dopamine receptor blocking drugs, which, unlike morphine, are widely recognised as a frequent cause of a wide variety of involuntary movements, including myoclonus.[2]

Rather than concluding that "myoclonus as a side effect of treatment with morphine is more likely to occur in patients taking antidepressants or antipsychotic drugs as antiemetics or as adjuvant agents," I would pose the question, Does morphine treatment increase the likelihood of neuroleptics causing certain involuntary movements?

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1 Potter JM, Reid DB, Shaw RJ, Hackett P, Hickman PE. Myoclonus associated with treatment with high doses of morphine: the role of supplemental drugs. *Br Med J* 1989;**299**: 150-3. (15 July.)
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SIR,—We are surprised at the suggestion that myoclonus is an important side effect of morphine treatment in patients with cancer and sceptical of the evidence produced to support it.[1]

In our experience myoclonic jerks are a relatively rare side effect of morphine and indicate either that the dose is too high or that it has been increased too quickly. The myoclonus is invariably transient and disappears on dose reduction. Our opinion would be that myoclonus is probably the least common and least important of all the side effects of morphine in patients with cancer receiving long term treatment with this drug.

The authors base their conclusions and speculation about the mechanisms underlying the myoclonus on observations of only 19 patients out of "about" 1100. Twelve patients had myoclonus and one hyperalgesia. These 13 patients were compared with an arbitrarily selected group of six patients taking "high" dose morphine who had neither of these problems. We do not understand the logic of this comparison or why another eight patients who had myoclonus were not included in this study or why the other 1075 patients without myoclonus were disregarded. The myoclonus was also little documented. We were not told if the myoclonus disappeared when the dose of morphine was reduced, which is what we would expect.

The common side effect of chronic opioid treatment is constipation; drowsiness and nausea may also trouble some patients. This study, which purports to examine the prevalence of important side effects, does not mention these problems. Are we to assume that none of these 1100 patients had constipation, or is constipation unimportant?

We found the interpretation of the plasma morphine concentrations unhelpful. The timing of the blood samples relative to morphine doses is mentioned only in the discussion, but there was no indication of the sample timing in relation to the myoclonus. The large variation between patients in the plasma concentrations of morphine and also in the ratio of plasma concentration to daily dose (from nearly seven to less than one) makes it highly unlikely that there would be any relation between the single estimations and any pharmacodynamic effect.

We believe that this paper is misleading in suggesting that myoclonus is an important side effect of long term morphine treatment.

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AUTHORS' REPLY,—Dr Quinn raises several important points. It must be kept in mind that this paper considers the treatment of the terminally ill, and it is in this context that the comments in our paper were made.

Firstly, the myoclonus was extremely brief muscle contraction, the duration of which was given by patients as "generally about one second." Medical staff who observed the contractions described them as myoclonic individual jerks shorter than one second.

Secondly, no patient with myoclonus had a plasma creatinine concentration of greater than 0·26 mmol/l. One had a plasma potassium concentration of 2·6 mmol/l and creatinine of 0·23 mmol/l. Therefore while uraemia per se was unlikely to have caused the myoclonus, deteriorating renal function may have contributed, with the electrolyte abnormality, to its occurrence.

Thirdly, concerning the strict pharmacological classification of drugs, all identified compounds do have dopamine receptor blocking activity. However, in the context of treatment, palliative care approaches these drug groups in a practical, symptom based way; hence, the antinauseant compounds were subdivided from the antipsychotic drugs, even though the latter are also useful as antinauseants.

Fine control of neuromuscular function is complex. Both opioids and neuroleptic compounds have an important effect on the fine modulatory and feedback control of skeletal muscle, that of the opioids being less well understood than many other pharmacological agents. Which is the background drug and which the added and therefore "interfering" agent will depend on the perspective of the observer. Our observations relate to palliative care and the appropriate use of analgesics, most frequently opioids. Relatively high doses of opioids may be necessary in many of these patients. Clarifying the possible source of side effects such as we have described is valuable information in the management of sometimes difficult clinical conditions.

Dr H J McQuay and colleagues take us to task for not considering constipation. Our object was not to examine all side effects of high dose morphine, but rather to investigate the incidence of myoclonus and its relation to medications and other factors. Our concern before starting the study was that, contrary to our own experience, myoclonus was infrequently reported and therefore was perhaps not often recognised as an important side effect of high dose opiates. We had observed that myoclonus diminished when the morphine dose was reduced and therefore had assumed that myoclonus was dose related. Our subsequent observations (as documented) suggest the importance of supplementary drugs in the causation of myoclonus.

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SIR,—In their carefully presented study Dr Julia M Potter and colleagues highlight the prevalence of myoclonus in patients with malignant disease who were receiving high doses of morphine as part of their palliative treatment.[1] They were, however, incorrect in citing a recent case report of myoclonic spasms after intrathecal morphine[2] as evidence that "in palliative care, particularly with opiates administered epidurally, local cerebrospinal fluid concentrations are high, and myoclonus is not uncommon." Although their conclusion may be true, the reference they quote does not support it.

It is important to distinguish between the two sites of administration of morphine. The pharmacokinetic behaviour of most drugs, especially relatively water soluble (hydrophilic) molecules such as morphine, is quite different when they are introduced into the predominantly lipid surrounded epidural space, with its many traversing blood vessels, from their behaviour when they are introduced directly into cerebrospinal fluid. Thus it has been for different reasons for the two sites that doubt has been expressed over recent years on whether "spinal" opiates do indeed provide analgesia at the spinal level.

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Patient preferences and randomised clinical trials

SIR,—Drs C R Brewin and C Bradley[1] are concerned about the difficulties of translating the methods of randomised controlled trials from drug trials to programme evaluations, especially when such programmes entail establishing personal therapeutic relationships. We share their concern, but nothing in their paper convinces us that there is any merit in abandoning the randomised controlled trial as the model evaluative tool towards which all should aspire.

We find it difficult to locate Drs Brewin and Bradley's views in the range of attitudes towards randomised controlled trials, which extends from unyielding advocacy at one extreme[2] to scepticism at the other.[3] They seem initially to be highly sceptical of the whole technique of randomisation; they later claim to advocate a pragmatic approach to study design. The pragmatic approach entails evaluating whole programmes (non-compliance, treatment modification, warts and all) as totalities without attempting to tease out the contribution of each individual component. Given that, you would expect Drs Brewin and Bradley to accept the indivisible nature of treatment programmes and their associated motivational requirements. But paradoxically, despite their espousal of pragmatism, they seem anxious to adopt an explanatory approach in that they are concerned that non-compliance and analysis on an "intention to treat" basis may disguise the benefits of effective procedures. This is the classic and elusive "explanatory" goal.[4,5]

This problem is not solved by arguing that we should reduce our commitment to randomisation. To do so would merely substitute one set of unwanted confounding influences for another. Other strategies are available that should overcome some of these difficulties. One of these is the exclusion of obviously poorly motivated patients before randomisation, which Drs Brewin and Bradley seem too ready to dismiss. This reduces