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Authors' reply

EDITOR,—M J Shield and S V Morant agree with us about the usefulness of deriving values for the number of patients needed to be treated with misoprostol to prevent serious upper gastrointestinal complications associated with non-steroidal anti-inflammatory drugs. We disagree, however, with their criticism of our exclusion of gastrointestinal haemorrhage from the number needed to treat analysis in our editorial. This approach was justified as misoprostol does not significantly reduce the incidence of gastrointestinal bleeding.¹ Data so far presented support the application of the number needed to treat calculation to only the less common complications of perforation and gastric outlet obstruction.

Furthermore, halving the derived value for the number needed to treat for the six month data to obtain an annualised figure seems inappropriate. To extend the data beyond their validity in this way is misleading. Similarly, the calculated annualised rate of serious gastrointestinal complications induced by non-steroidal anti-inflammatory drugs may also be inaccurate.

The additional data provided by Shield and Morant—the number needed to treat in two age groups—are useful. As Silverstein *et al* do not indicate that the misoprostol and placebo groups had been stratified with regard to cardiovascular disease,¹ we are uncertain about the accuracy of the number of patients with prior cardiovascular disease who need to be treated to prevent one serious event.

Since misoprostol prevents only perforation and gastric outlet obstruction it would be useful to identify risk factors for these events in isolation from gastrointestinal bleeding to define the subgroups of users of non-steroidal anti-inflammatory drugs who are most likely to benefit from misoprostol.

Finally, prophylactic treatments that are routinely used are on the whole well tolerated, and it must be remembered that 42% of patients stopped taking misoprostol because of side effects.¹

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- 1 Silverstein FE, Graham DY, Senior JR, Davies HW, Struthers BJ, Bittman RM, *et al*. Misoprostol reduces serious gastrointestinal complications in patients with rheumatoid arthritis receiving non-steroidal anti-inflammatory drugs. *Ann Intern Med* 1995;123:241-9.

Patients' understanding of consent form should be checked before participation in trial

EDITOR,—In their article on getting patients' consent to enter clinical trials Elizabeth Wager and colleagues emphasise the need for care in obtaining informed consent.¹ In our psychopharmacology research laboratory we routinely obtain informed consent from heroin and cocaine users for participation in clinical trials. More than a clearly written, concise consent form is needed with these potential subjects, since they vary greatly in education and reading ability.

To ensure informed consent and to confirm the

subject's ability to understand potential risks and benefits of participation we administer a brief questionnaire after the prospective subject has read the consent form. The questionnaire allows us to confirm that the subject is literate and understands the information in the consent document. Knowledge of the purpose of the trial, procedures, drug treatments, devices used, amounts of biological fluids to be collected, time required for participation, and potential risks is confirmed by a member of the research team. Responses to the questionnaire help us pinpoint parts of the consent form that may be unclear. Subjects who are unable to comprehend the consent form or who have an unrealistic understanding of participation in research do not participate.

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AIDS associated with blood transfusion and haemophilia in Europe

EDITOR,—S Franceschi and colleagues report the incidence of AIDS associated with blood transfusion and haemophilia in Europe and the United States.¹ However, they provide little information to help us understand these epidemics and erroneously suggest that the higher incidence in France than in other western European countries could be attributed to a delay in screening blood donations for HIV.

Rates of AIDS associated with blood transfusion and haemophilia depend on the use of blood and blood products, the general prevalence of HIV infection, and measures to ensure the safety of blood and blood products. These factors have differentially influenced the patterns of the two epidemics, which differ among and within countries (fig 1).

Recipients of transfusions were mostly infected by unscreened blood collected locally. Thus the

incidence of AIDS associated with transfusion depends largely on the prevalence of HIV in local blood supplies. The more rapid spread of HIV in France in the early 1980s than in most other European countries (France accounts for one third of all cases of AIDS diagnosed in Europe by 1984²) may have contributed to, though cannot fully explain, the higher rate of AIDS associated with transfusion in France. In 1985 screening of blood donations for HIV was introduced in the United States (in March) followed by the Federal Republic of Germany (April) and became systematic in the Netherlands and Sweden (June); Italy (July); Belgium, Finland, France, Greece, and Norway (August); Denmark and Portugal (September); Britain (October); and Switzerland (November).³ Thus France was not among the last to screen donations systematically and the higher rate of AIDS associated with transfusion cannot be attributed to a delay in the implementation of screening. More relevant is the implementation of recommendations to exclude people at risk of HIV infection from donating blood, which in many countries predated screening for HIV by about two years.³ In France, despite the existence of such recommendations since 1983, some centres continued collecting blood from prisoners—a population at increased risk of HIV infection—until 1990.⁴

Haemophilic patients were primarily infected by clotting factor concentrates from the United States that had not been heat treated. Thus the incidence of AIDS associated with haemophilia essentially reflects the use of these concentrates. In Spain, Britain, and the former Federal Republic of Germany, where imported concentrates were used extensively,⁵ the incidence associated with haemophilia is among the highest, while in Belgium, Finland, and Norway, where treatment of haemophilia was largely based on cryoprecipitates,⁶ the incidence is the lowest. In France, despite relative self sufficiency in the production of concentrates,⁷ the incidence associated with haemophilia is relatively high, partly because the prevalence of HIV in blood donations was high.

In eastern Europe, where the epidemic of HIV infection is relatively recent and imported concentrates were almost unavailable, AIDS among recipients of transfusions and haemophilic patients has been rare. The exception is in Romania, where thousands of children were infected by routine microtransfusion.

Thus, to understand the different dynamics of AIDS associated with transfusion and haemophilia by country, several factors should be considered, among which the timing of the implementation of

Fig 1—Cumulative incidence of AIDS associated with blood transfusion and haemophilia to end of 1994 (adjusted for delay in reporting) per million total population in western Europe
Data sources: European Centre for Epidemiological Monitoring of AIDS and Robert Koch Institute (for Germany)
*Excluding former German Democratic Republic.

screening of blood seems to have had a very limited role.

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Effects of fundholding on prescribing habits

Results of similar study in Mersey were different

EDITOR,—In their study into the effects of fundholding on prescribing Sarah Stewart-Brown and colleagues found that although fundholders initially contained prescribing costs more effectively than non-fundholders, this effect was not maintained and was even reversed.¹

Our studies of prescribing in fundholding practices show that similar patterns of cost containment occurred in the first year of fundholding in the first three waves² but that the effect was not maintained.³ Stewart-Brown and colleagues suggest several possible explanations: these include deliberate inflation of prescribing costs in the pre-fundholding year to increase the budget for the next year (on the basis of our data² we thought it unlikely that such an approach was widespread, but it might be a factor in some practices); that all reasonable savings were achieved early on; and that the comparator group of non-fundholders was also trying to contain costs as a result of new prescribing incentive schemes, minimising differences between the groups. We favour this last explanation and in support of this show a dramatic rise in the rate of generic prescribing among all non-fundholders in Mersey region in 1993-4 (fig 1). We believe that this was the result of incentive schemes and a local requirement that the rate of generic prescribing among prospective fourth wave fundholders should be 50%.

Stewart-Brown and colleagues point out an apparent reversal of the pattern of cost containment between fundholders and non-fundholders by the end of the study. We found no such reversal in our study of almost an entire population of fundholders and non-fundholders in Mersey,³ and we suggest that it is the result of the small number of practices studied, as the authors considered. The fact that two of the five non-fundholding practices were

studied in a year in which they were preparing for fundholding may also be important. We question the authors' assertion that their "results are highly significant" because of the large numbers of prescriptions studied, since their unit of study was the practice, not the prescription. We consider it inappropriate to report the mean difference and parametric 95% confidence interval when n is 3 or 5, as this makes interpretation of the results difficult and even the existence of any (statistically or practically) significant difference between the different types of practice studied uncertain. We agree with the primary conclusion of the authors' paper—that the rate of increase in prescribing costs after the first fundholding year is similar to that among non-fundholding practices—but disagree that a reversal in cost containment patterns occurs later.

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- 1 Stewart-Brown S, Surender R, Bradlow J, Coulter A, Doll H. The effects of fundholding in general practice on prescribing habits three years after introduction of the scheme. *BMJ* 1995;311:1543-7. (9 December.)
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Generic prescriptions are defined differently for dispensing practices

EDITOR,—Sarah Stewart-Brown and colleagues compare the rate of generic prescribing between dispensing and non-dispensing practices in their paper on fundholding and prescribing.¹ Are they aware that the Prescription Pricing Authority (which provided the data for the study) defines a generic prescription differently for dispensing practices? Few doctors are aware of this fact, which is not mentioned in the paper and may well explain the observed differences in the rate of generic prescribing. Any comparison of generic prescribing between dispensing and non-dispensing practices is therefore invalid, as are comparisons between areas with different proportions of dispensing practices.

If this was purely an academic matter it would be of minor importance. However, budget setting for districts and practices, and prescribing incentive schemes, include rates of generic prescribing in their criteria. This discriminates against dispensing practices and hence rural areas.

The fact that even researchers in health economics seem to be unaware of this important peculiarity prompts me to publicise it in the hope of reform.

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- 1 Stewart-Brown S, Surender R, Bradlow J, Coulter A, Doll H. The effects of fundholding in general practice on prescribing habits three years after introduction of the scheme. *BMJ* 1995;311:1543-7. (9 December.)

Authors' reply

EDITOR,—R Wilson and T Walley present some valuable data on rates of generic prescribing in the Mersey region. Their figures differ from ours only in that, in 1990, the rate of generic prescribing among non-fundholders in Mersey was much lower than that among non-fundholders in Oxford. The trends that we observed in our study mirror those observed throughout the Oxford region (T Jones, medical adviser to Oxfordshire Health,

personal communication), suggesting that our study practices were typical of the region. These data confirm what we already know: that there are some regional differences in prescribing practice. It is possibly more remarkable that data from fundholding practices in the two regions are so similar.

The rate of generic prescribing is only one of several factors that determine prescribing costs. Our argument that trends in prescribing costs had reversed between 1990-1 and 1993-4 was based on data which Wilson and Walley do not present.

We think that it is unhelpful for Wilson and Walley to use spurious statistical arguments and selective quotation from our paper to argue that their findings are more valid than ours. Both of our studies are valid, and instead of arguing about who is "more right" we would surely do better by trying to learn from the differences we observed.

The point that Ted Willis makes is important. He is right that we were unaware of the different ways in which generic rates used to be calculated for dispensing and non-dispensing practices. Changes in the presentation of PACT (prescribing analysis and cost) data in June 1994 enabled medical advisers to learn that earlier data on generic rates had been calculated on the basis of rates of generic prescriptions in non-dispensing practices and rates of generic dispensing in dispensing practices. The difference is of the order of 2-5% for dispensing practices. This means that the generic rate in dispensing practices in our paper is likely to underestimate the true rate by this amount. Adjusting for this difference reduces but does not eliminate the gap that we observed in generic rates between the different types of practice and does not affect the validity of the other prescribing data.

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Prescribing by general practitioner fundholders

Longer study shows that costs rise again after initial savings

EDITOR,—Two interesting papers have examined the effects of general practitioner fundholding on prescribing costs.^{1,2} Robert P H Wilson and colleagues conclude that fundholding affects prescribing costs,¹ but they examined only the first year after practices joined the scheme. Bradlow and Coulter, in their study of general practitioners' prescribing in Oxford, also found that fundholders' costs initially rose less steeply than non-fundholders',³ but further follow up of the practices showed that the fundholders were unable to sustain this advantage two years later.²

We have examined aggregated prescribing budgets for fundholders and non-fundholders in Nottingham and have found a pattern remarkably similar to that reported from Oxford by Sarah Stewart-Brown and colleagues³ (fig 1). Fundholders initially made savings, but their costs are now higher, and rising more rapidly, than those of non-fundholders. In compiling our figures we did not account for possible confounding variables,

Fig 1—Rates of generic prescribing among fundholding and non-fundholding practices, 1990-4