Randomised trial of prophylactic daily aspirin in British male doctors

SIR,—There can be no doubt that the British trial (30 January, p 313) has made a great contribution to research into the effect of aspirin on the frequency of primary infarction and stroke. Both the extent and the duration of this study deserve peer recognition, and these results, acknowledged the world over, are of great scientific interest.

In contrast to the results obtained by the British research group, those produced by the American group clearly show a significant reduction in the rate of infarction in doctors who took aspirin, a result which ultimately led to the premature termination of the study.¹

An attempt to explain these discrepancies reveals fundamental differences in the way in which these two major studies were carried out. The American study featured not only a considerably larger number of volunteers but also a true control group which took placebos according to a double blind study design. The British control group was merely recommended to avoid taking aspirin. Furthermore, during the six year study about 12% of the British control group changed over to the group taking aspirin, while 30% of the aspirin group stopped taking it. Also, part of the aspirin group transferred to a different formulation during the study and reduced the dose from 500 to 300 mg, thus destroying the comparability of the two groups. Moreover, the results of the study were projected arbitrarily on to a reference value of 10 000 man years.

It is at this point, if not sooner, that we must question the binding nature of a scientific study protocol. What is the claim to validity of a scientific study which is carried out according to criteria that change so frequently? The authors themselves are apparently aware of the shortcomings of their study and in their discussion readily refer to their American colleagues, whose results they consider more significant.

They observe that an unbiased and qualified evaluation of the side effects can be carried out only on the basis of a placebo group. Why did the British research group pass up the opportunity of gaining such important results? It is regrettable that the necessary further scientific analysis of the range of activity of aspirin in the primary prevention of infarction should be endangered so easily by a study protocol which is equivocal to say the least. This is all the more tragic if we consider the pioneering character of this British study in the discussion surrounding the use of aspirin in the primary prophylaxis of myocardial infarction.

ELLEN WEBER

D-6900 Heidelberg,
Federal Republic of Germany

¹ Steering Committee of the Physicians' Health Study Research Group. Preliminary report: findings from the aspirin component of the ongoing physicians' health study. *N Engl J Med* 1988;318:262-4.

AUTHORS' REPLY.—There were, as Dr Weber points out, major differences between the British and the United States studies of the prophylactic value of aspirin; but we do not need to look to these to account for the different results.

The main difference in the results (the apparent effect on the incidence of non-fatal myocardial infarction) can be attributed to chance. The results of both studies are statistically compatible with the idea that doses of aspirin of the order prescribed reduce the risk of non-fatal myocardial infarction by a third, which is close to the 32% recorded in a review of 31 randomised trials of aspirin and other antiplatelet drugs in the treatment of patients with

a history of transient ischaemic attack, occlusive stroke, unstable angina, or myocardial infarction (30 January, p 320). We conclude, therefore, that aspirin has about the same relative effect irrespective of whether it is used prophylactically or therapeutically. Whether it reduces the overall mortality from vascular disease in people not at high risk of a myocardial infarction is another matter. Neither of the prophylactic trials suggests that it does, and it may be that the benefit in healthy people, who will have a relatively low risk of thrombosis, is partly counteracted by an increased risk of cerebral haemorrhage. It is, however, only reasonable to suppose that a reduction in non-fatal myocardial infarction is accompanied by some reduction in fatal myocardial infarction, as occurred in the treatment trials.

We are sorry that Dr Weber regards our study protocol as equivocal. The protocol may be open to criticism, but not, we think, because we failed to make it double blind. The nature and extent of the non-fatal side effects of aspirin have been shown by the double blind trials of aspirin in the treatment of myocardial infarction, and we saw no need to seek information about them. Our study was designed to see if aspirin given prophylactically would reduce the risk of death from vascular disease in people who had never previously had a myocardial infarct. We believed we could record death from vascular disease objectively and for this purpose it was not necessary to try to hold several thousand doctors to the daily use of a placebo. If we were to repeat the study we would again do it openly. What we would not do, however, would be to give aspirin to thousands of men without first finding out whether it caused them dyspepsia. The experience of the first six months of our trial showed that so many men reacted unfavourably within a matter of months that Hennekens (who had been working with us when the trial started and is a joint author of both papers) sensibly gave all the American volunteers a trial of aspirin before allocating them to aspirin or placebo. As a result a high proportion of non-compliers were weeded out before the study began.

RICHARD DOLL
RICHARD GRAY
KEITH WHEATLEY

Clinical Trial Service Unit,
Nuffield Department of Clinical Medicine,
Radcliffe Infirmary,
Oxford OX2 6HE

Audit of a surgical firm by microcomputer

SIR,—My friend Mr D C Dunn (5 March, p 687) has clearly made surgical audit his pastime. The vast number of figures produced reminds one of Lowry's paintings. What are the resultant alterations in his surgical practice? "The high incidence of chest and wound infections led us to put increased emphasis on measures that might reduce these problems. . . . Increased care was taken with wound haemostasis and remembering prophylactic antibiotics . . . complications were more likely to occur when many major operations were performed in a short space of time."

His enormous data input hardly justifies a need for such conclusions. Long before microcomputers wound infection rates were adequately reduced. Maybe his were unduly high in 1982?

But my main purpose in writing is to warn against the unlimited collection of figures. Limited resources are better directed into clinical work. The cult of numeracy in surgery has its serious limits. No two surgical units are alike. It is therefore not possible to argue from the figures of one to those of the other. Such a course is beset with pitfalls, not least illustrated by the occasion

some years ago when two professors of surgery argued about the validity of each other's statistical methods.

New knowledge does not consist in the production of figures. If surgical audit is meant to show outsiders that surgeons keep their houses in order how will they prove that their indications for operations were right? In Mr Dunn's paper I cannot see the wood for trees. The danger lies in our official bodies requiring similar analyses from elsewhere only to have shown to them after a lot of labour and time that the collection of figures over a broad canvas has little practical value.

FELIX WEALE

Shorne, Kent

AUTHOR'S REPLY.—I take it as a compliment to have my paper compared with the achievement of one of Lowry's paintings. Those who know me will be aware that my pastimes are quite different from that of "playing with audit." Nevertheless, I like to know what is going on in my unit. This has nothing to do with "official bodies." It is simply a question of taking a professional pride in what one is doing and making sure it is as good as possible. It is important that the machine is a microcomputer and is under our control. We forward what we choose to "outside bodies."

In retrospect our complication rates may have been slightly high in 1982. We found this out and we did something about it. Does Mr Weale know what his complication rates are? Can he be sure that there is nothing to be done to improve his practice? Possibly he is not interested in such questions, but I do not think he has any solid grounds for criticising others who are so interested.

When he states that "the enormous data input" is hardly justified by the results he has missed the point. No extra effort is now required to collect the data. We collect data to produce discharge summaries and have almost halved the time necessary for this exercise. The data are then easily available for any other purpose. We use them for monthly audit meetings, which I and my colleagues find useful and interesting. The computer reduces the time required to prepare for these meetings from several weeks to a few days. Can improving efficiency in our unit really be called a misuse of resources? Would the effort have been better spent producing more undetected complications? Mr Weale seems obsessed with "outsiders" and "official bodies," but we feel that our audit is something personal and private, which is of value to ourselves and makes life more interesting.

Mr Weale's worry about the unlimited collection of figures is nevertheless entirely in accordance with my own point of view. That is why I have taken the trouble to keep the data collected to a minimum and to develop a computer system which makes sure that less time is spent running the firm with it than without it. Mr Weale's fears about such efforts being wasteful were shared by us initially, but, after six years' experience, we have found the regular audit to be rewarding. None of our junior staff, secretaries, or consultants wish to return to the bad old days, with piles of notes lying around waiting for summaries to be written and no information available about the work we were doing.

D C DUNN

Cambridge CB2 2AJ

Reactions to contrast media

SIR,—Dr J F Reidy discusses the desirability of using the new low osmolar contrast media, which