one-stage prothrombin time test) had remained within a therapeutic range of 2·0-3·0. In both cases the dosage of warfarin had been unchanged for several months.

Case 1—A 55-year-old woman attended a routine postoperative follow-up appointment and complained that she had had a black tongue for three months. A fungal cause was suspected, and she was treated with a two-week course of miconazole gel 250 mg four times daily. She was also taking hydrochlorothiazide 100 mg daily, amiloride 10 mg daily, digoxin 250 μg daily, and warfarin 4 mg and 5 mg on alternate days. Twelve days after starting miconazole she reported that she had had numerous blood blisters and had bruised easily for two days. The prothrombin time ratio was 16·0. Miconazole and warfarin were withheld and the prothrombin time ratio returned towards the therapeutic range. Subsequently the prothrombin time ratio has remained within the therapeutic range on warfarin 4 mg daily.

Case 2—A 56-year-old man had had diarrhoea for seven months. A fungal cause was suspected, and he was treated with a five-day course of miconazole tablets 250 mg four times daily. He was also taking frusemide 40 mg daily, effervescent potassium two tablets daily, digoxin 125 μg daily, allopurinol 100 mg daily, and warfarin 6 mg and 7 mg on alternate days. Eleven days after starting miconazole he attended a routine anticoagulation clinic appointment, and the prothrombin time ratio was 23·4. There was no history or evidence of haemorrhagic complications. Miconazole and warfarin were withheld, and he developed two haematomas on his limbs as the prothrombin time ratio returned towards the therapeutic range. Subsequently the prothrombin time ratio has remained within the therapeutic range on warfarin 6 mg daily, and he has continued to have diarrhoea.

The second patient took allopurinol, which may potentiate warfarin (24 July, p 274), but the dosage of allopurinol had not been changed in the previous year and the prothrombin time ratio had been stable on this drug.

Miconazole is 91-93% bound to protein, mainly albumin,[1] and potentiates warfarin possibly by displacing it from its binding sites. There have been previous reports of miconazole potentiating treatment with oral anticoagulants,[2 3] but this interaction is not widely recognised and no warning against the combination is given either in the recent review or in the *British National Formulary*.[4] In the two cases that we describe the combination of warfarin and oral miconazole resulted in haemorrhagic complications and admission to hospital at a similar time after starting miconazole. We recommend that if miconazole is given to a patient on warfarin, the prothrombin time ratio should be monitored very closely.

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Non-drug treatments of hypertension

SIR,—The recent paper by Dr G Andrews and others (22 May, p 1523) presents a meta-analysis of the published reports on non-pharmacological interventions. There are several problems with the analysis, and these cast doubt on the conclusion that non-pharmacological treatments are markedly less effective than drugs.

The analysis is based on the calculation of effect sizes defined as: "The difference between mean blood pressures in treated and control groups standardised by the variability of blood pressures in the control group." The appropriateness of this measure depends on the availability and adequacy of control groups, but as the authors point out only 65% of the studies examined had any form of control group at all. We assume therefore that in most instances effect sizes were calculated by standardising the reduction of pressure within a treatment by the variability within that same treatment. Given the well known tendency for blood pressure to drop without active treatment, this results in the inflation of effect sizes in uncontrolled investigations compared with methodologically stronger studies. We do not consider that the authors' use of design quality ratings provides an adequate safeguard, since they appear to have been based on aspects of studies that will have had differing and unpredictable effects on blood pressure. There are no substitutes for control groups in studies of this problem.

In comparing the effect sizes for pharmacological and non-pharmacological treatments, Dr Andrews and others do not make due allowance for the fact that in many instances behavioural and other non-pharmacological treatments are applied to patients who are already receiving antihypertensive drugs. It is incorrect to conclude from such a data base that drugs are more effective; this is equivalent to claiming that the final drug used in a stepped-care regimen is less effective than drugs used earlier because it produces a smaller decrease in blood pressure. On the contrary, we consider it powerful evidence in favour of non-pharmacological treatments that they add to the effects of drugs, as has been found in studies of relaxation and related procedures.[1 2] The effects of such treatments are not, of course, restricted to patients treated with drugs.[3 4]

An additional problem is the selection of inappropriate drug trials with which to compare non-drug treatments. It has been repeatedly observed in drug studies that the extent of change in blood pressure depends on the initial level; larger treatment responses are recorded among patients with high starting pressures. Non-drug studies have generally included patients with mild hypertension. For example, the mean pretreatment diastolic pressures in the investigations categorised as "yoga" by Dr Andrews and others were in the range 100-105 mm Hg,[1 4] but the drug trials used for comparison included patients with much higher pressures, incorrectly inflating the magnitude of effects. This is evident from breakdown of treatment response by initial value in the hypertension detection and follow-up programme.[5] The average reduction over five years from patients in stratum 1 (diastolic pressure 90-104 mm Hg) was 12·9 mm Hg compared with 24·6 mm Hg in stratum III (more than 115 mm Hg). Similarly, the authors selected results from the Veterans Administration study of patients in the 115-129 mm Hg range (average decrease in diastolic pressure of 29·7 mm Hg)[6] rather than data from the mild range (decrease of 17·9 mm Hg).[7] It is no wonder that the response to drugs appears superior in these comparisons. The high drop out rate in drug trials is not considered either: this varies between 22% and 42% in the investigations cited.

Finally, some comments on the purpose of such comparisons are pertinent. The authors make an implicit assumption by use of effect size statistics that the larger the change the better. The goal in the treatment of hypertension, however, is the control of blood pressure rather than the maximum reduction possible. Few investigators would claim that drugs should be withheld from individuals with severe hypertension, but when pressures are only moderately raised, immediate control is less pressing and the prospect of long-term treatment may lead many patients to welcome advice on self-management as an initial step. It is surely more relevant therefore to consider whether a particular intervention brings blood pressure under adequate control. Based on the currently popular criterion of a diastolic pressure under 90 mm Hg, it is apparent that many patients in the non-pharmacological treatment studies are successfully controlled. This is certainly the case for most participants in many of the weight loss, relaxation, and salt restriction programmes.[1 2 8 9]

Dr Andrews and others claim that the meta-analytic technique eliminates the need for reviewers of empirical work to exercise "the judgment of Solomon." While acknowledging that most reviewers fail to meet such exacting standards of wisdom, we believe that with most treatments informed if fallible judgment is preferable to quasi-statistical methods. If Solomon were available to judge non-drug treatment of hypertension, he would probably conclude that the evidence is encouraging and that such methods play a useful role. The issue cannot be resolved, however, without further, carefully conducted research.

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**We sent this letter to the authors, who reply below.—ED, *BMJ*.

SIR,—Dr Johnston and Mr Steptoe suggest that our analysis of drug and non-drug treatment outcome studies in hypertension (22 May, p 1523) contained three sources of bias: the use of studies that did not include a control group; the inclusion of studies of non-drug regimens in patients already receiving antihypertensive drugs; and the selection of inappropriate drug trials for comparison.

Two-thirds of studies reviewed in our analysis were pre-post, baseline controlled trials—that is, trials controlled for regression to the mean but not controlled for the effects of placebo. It is true that this may have resulted in the effect size being overestimated in these studies. Although randomised controlled trials provide a more accurate estimate of effect size it was felt, given the scarcity of such trials in non-drug techniques, that pre-post studies should also be included.

Studies of non-drug treatments in patients already receiving antihypertensive treatment were included because they too comprise a substantial proportion of the published reports, even though the magnitude of the effect size in these studies might be underestimated. We would agree that the results of some of these studies, particularly studies of weight reduction and yoga, are indeed suggestive of the power of certain non-drug regimens as adjunctive treatments for hypertension.

We dispute the suggestion that the drug studies chosen for comparative purposes were of persons with significantly higher blood