CORRESPONDENCE

- *All letters must be typed with double spacing and signed by all authors.*
- *No letter should be more than 400 words.*
- *For letters on scientific subjects we normally reserve our correspondence columns for those relating to issues discussed recently (within six weeks) in the BMJ.*
- *We do not routinely acknowledge letters. Please send a stamped addressed envelope if you would like an acknowledgment.*
- *Because we receive many more letters than we can publish we may shorten those we do print, particularly when we receive several on the same subject.*

Surely a natural cancer remedy can't be dangerous

SIR,—Dr Jeffrey Tobias is understandably irritated by the dismissive response of the workers at the Bristol Cancer Help Centre to the adverse result of the recent breast cancer trial.[1] I was equally disappointed by their reaction but for a somewhat different reason.

Instead of trying to explain the result away they should have been, if not jumping for joy, at least making the best of a bad job. Before this report most people scoffed at the idea that diet and psychological factors could have any significant effect on cancer, but here is an impeccably conducted clinical trial showing an effect of considerable magnitude. Granted, it was in the wrong direction, but so what?

Imagine for a moment that the investigators had been studying the relative effectiveness of a new drug and radiotherapy and the drug treated group had had a higher relapse and death rate. Clearly, no one would be likely to go on using that particular drug, but I doubt if anyone would declare that all drug treatment of cancer should be abandoned. We also know that any effective treatment is likely to carry the potential for harm if used in the wrong way, and so had the trial shown no difference between the two groups (the outcome apparently expected by most of the researchers) it would have been far more discouraging for practitioners of complementary medicine. Dr Michael Wetzler's protestation that nothing they do at Bristol could conceivably harm patients is not only complacent but comes close to saying that their methods are unlikely to have any effect, for good or ill.

So what should the Bristol group do next? They were brave to put themselves to the test and naive to expect to avoid the disappointments that most conventional medical researchers have learnt to accept, but I hope that they will now put this episode behind them. They need to go on to isolate the variables in their regimen, discover which techniques are helpful, and discard those which are harmful. The worst thing they could do would be to continue on their present course in the face of all the evidence, but nearly as bad would be to throw in the towel: if they are sincere in their desire to help patients with cancer they have the same duty we all have—to keep trying.

BOB BURY

Oakwood, Leeds LS8 2JX

1 Tobias J. Surely a natural cancer remedy can't be dangerous—can it? *Br Med J* 1990;**301**:613. (22 September.)

Lowering cholesterol concentrations and mortality

SIR,—Dr Matthew F Muldoon and colleagues use four criteria to decide whether a study should be included in the analysis.[1] The first criterion is that the trial should be in a patient population without evidence of heart disease—that is, a primary prevention trial.

The Los Angeles Veterans Administration study included patients with pre-existing complications of atherosclerosis and, as its authors accept, is "... thus a combined study of primary and secondary prevention."[2] The Minnesota coronary survey also included patients with electrocardiographic evidence of prior myocardial infarction.[3] Approximately 30% of the population in the colestipol-Upjohn study had evidence of coronary heart disease.[4] Thus, according to the rules set out by Dr Muldoon and colleagues, these three studies should not have been included in the meta-analysis. Alternatively if the rules are so loosely followed other studies were wrongly excluded. These three studies found mortalities from all causes of 5·19%, 6·44%, and 2·11% a year compared with 0·38%, 0·49%, and 0·43% a year in the remaining three studies, which are genuine primary prevention trials.

The authors do not address the appropriateness of the length of follow up in the studies included in the analysis. Data from the Framingham heart study[5] and the long term follow up of the coronary drug project[6] indicate that the difference in total mortality in groups with differing plasma cholesterol concentrations did not emerge until 10-15 years of follow up. The mean follow up periods in the six studies range from only 1·1 to 8 years.

The argument that these trials contain 120 000 patient years of observation is of little value when the trials have not continued long enough to observe the natural course of the disease.

DAVID CANTER

Ann Arbor, MI 48105, United States

1 Muldoon MF, Manuck SB, Matthews KA. Lowering cholesterol concentrations and mortality: a quantitative review of primary prevention trials. *Br Med J* 1990;**301**:309-14. (11 August.)
2 Dayton S, Pearce ML, Hashimoto S, Dixon WJ, Tomiyasu U. A controlled clinical trial of a diet high in unsaturated fat in preventing complications of atherosclerosis. *Circulation* 1969;**40**(suppl II):1-63.
3 Frantz ID, Dawson EA, Ashman PL, *et al*. Test of effect of lipid lowering by diet on cardiovascular risk. *Arteriosclerosis* 1989;**8**:99-118.
4 Dorr AE, Gundersen K, Schneider JC, Spencer TW, Martin WB. Colestipol hydrochloride in hypercholesterolaemic patients—effect on serum cholesterol and mortality. *J Chronic Dis* 1978;**31**:5-14.
5 Anderson KM, Castelli WP, Levy D. Cholesterol and mortality: 30 years' follow-up from the Framingham study. *JAMA* 1989;**257**:2176-80.
6 Canner PL, Berge KG, Wenger NK, *et al*. Fifteen year mortality in coronary drug project patients: long-term benefit with niacin. *J Am Coll Cardiol* 1986;**8**:1245-55.

SIR,—Having reviewed six selected trials, Dr Matthew F Muldoon and colleagues claim that lowering cholesterol concentration in healthy people tends to decrease mortality from coronary heart disease and decreases it significantly if only drugs are used.[1] One of the criteria for a study to be included in their review was that it should be randomised. Two of the selected trials, however, did not meet this criterion.

In the Los Angeles Veterans Administration study heavy smokers were significantly overrepresented in the control group.[2] Even if this failure of randomisation was of no importance it remains to be proved that the insignificantly lower number of deaths from coronary heart disease in the intervention group was due to nothing but mere chance because although the serum cholesterol concentration of subjects in the intervention group was lowered, the cholesterol content of their coronary arteries did not differ from that of controls and in the aorta their cholesterol concentration was higher than that of the controls.

The colestipol-Upjohn study was not randomised for smoking habits at all.[3] Furthermore, a significantly lower serum triglyceride concentration was noted in the placebo group compared with the treated group (220 *v* 284 mg/dl). The difference was assumed to be due to an excess of control patients with familial hypercholesterolaemia as such patients usually have normal triglyceride values. This conclusion was probably right because the higher mortality from coronary heart disease was confined to the younger age groups, but the number of such patients was not given. That this bias was balanced by a non-significant 3·5% higher serum cholesterol concentration in the intervention group, as suggested, is questioned.

Excluding these two studies the difference in the numbers of deaths from coronary heart disease between the intervention and control groups disappears (1·04 *v* 1·09%). But although the randomisation failures are detrimental to the conclusions of the mentioned studies, they do not invalidate the message from Dr Muldoon and colleagues. Thus, lowering your serum cholesterol concentration does no good to your heart, and it may be dangerous to your mind.

UFFE RAVNSKOV

Råbygatan 2,
S-22360 Lund, Sweden

1 Muldoon MF, Manuck SB, Matthews KA. Lowering cholesterol concentrations and mortality: a quantitative review of primary prevention trials. *Br Med J* 1990;**301**:309-14. (11 August.)
2 Dayton S, Pearce ML, Hashimoto S, Dixon WJ, Tomiyasu U. A controlled clinical trial of a diet high in unsaturated fat in preventing complications of atherosclerosis. *Circulation* 1969;**40**(suppl II):1-63.
3 Dorr AE, Gundersen K, Schneider JC, Spencer TW, Martin WB. Colestipol hydrochloride in hypercholesterolaemic patients—effect on serum cholesterol and mortality. *J Chronic Dis* 1978;**31**:5-14.

SIR,—The meta-analysis of Dr Matthew F Muldoon and colleagues is restricted to mortality and fails to consider the important impact of cholesterol lowering on non-fatal coronary heart