vascular). In group 2 only one of the 13 patients had a complication (retinopathy) and none had hypertension for which they were receiving treatment. The addition of an angiotensin converting enzyme inhibitor significantly reduced the blood pressure without a significant progression in albumin excretion rate (table 1). In group 2 there was no significant change in blood pressure but the albumin excretion rate increased significantly. The albumin excretion rate correlated with blood pressure (systolic, $r=0\cdot33$, $P<0\cdot05$; diastolic, $r=0\cdot39$, $P<0\cdot02$) but not with haemoglobin A_{1c} concentration.

Hence effective control of blood pressure rather than glycaemic control seems to be a major determinant for preventing progression of microalbuminuria in patients with non-insulin dependent as well as insulin dependent diabetes mellitus.

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1 Microalbuminuria Collaborative Study Group, United Kingdom. Intensive therapy and progression to clinical albuminuria in patients with insulin dependent diabetes mellitus and microalbuminuria. *BMJ* 1995;311:973-7. (14 October.)

Interpretation of study's results is open to criticism

EDITOR,—The Microalbuminuria Collaborative Study Group concludes that intensive insulin treatment had no impact on the progression of nephropathy in insulin dependent diabetic patients with microalbuminuria.[1] The analysis, presentation, and interpretation of their data, however, are open to criticism.

The main conclusion is based on a non-significant difference in the slopes of albumin excretion between the two groups. However, only the P value and a confidence interval for the overall mean slope are given, without descriptive information. The authors do not give the mean slopes for each group, standard deviations, and a confidence interval for interpretation.[2] If we assume that standard methods were used to calculate confidence intervals then an estimate of the mean slope is 3 (SE 7·86) μg/min. With the sample size n=70 the SD is 65·76 μg/min. As the effect size is not presented, we calculated the power in an exemplary manner. Given a decrease in albumin excretion in the intervention group of 20% (−9·52 μg/min) and an increase in the control group of 20% (9·64 μg/min) on average, then owing to high variation the power to get a significant result is only 0·22. Hence no valid conclusions can be drawn from a non-significant result.

In addition, blood pressure decreased in the control group and increased slightly in the intervention group (authors' fig 3). Therefore the beneficial effect of improved metabolic control in the intervention group was probably associated with poorer control of blood pressure. The positive effect of intensive insulin treatment on diabetic complications is due to long term improved glycaemic control. During two thirds of the study, however, glycaemic control did not differ between the groups. During the first 36 months, when there was a relative difference in the glycated haemoglobin concentrations between the groups, two patients in the intervention group and three in the control group progressed to overt diabetic nephropathy. Clearly, no valid conclusions can be drawn from these few events.

Several additional issues remain unclear. The results section lacks sufficient follow up data and does not state which test was used for the P values presented. The authors do not show that the slopes are adequate measures of the change in albumin excretion—which is not the case if the curves are non-linear. The data were analysed on an intention to treat basis, which may cause bias because the authors tried to draw conclusions from a non-significant result. As only three quarters of the patients remained in their assigned groups actual differences may be blurred.[3]

In summary, the interpretation of this study is inconclusive as non-significant results were caused by high variation, low power, confounding, and inadequate application of the intention to treat principle.

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1 Microalbuminuria Collaborative Study Group, United Kingdom. Intensive therapy and progression to clinical albuminuria in patients with insulin dependent diabetes mellitus and microalbuminuria. *BMJ* 1995;311:973-7. (14 October.)
2 Altman DG, Bland JM. Absence of evidence is not evidence of absence. *BMJ* 1995;311:485. (19 August.)
3 Gillings DB, Koch GG. The application of the principle of intention-to-treat to the analysis of clinical trials. *Drug Information Journal* 1991;25:411-24.

Authors' reply

EDITOR,—Nish Chaturvedi and John H Fuller point to a limitation of our study—the sample size—which we acknowledged in our paper. A larger sample size was planned, but screening yielded fewer suitable patients than expected. Nevertheless, this is the largest study of the kind published to date, and its size in combination with that of the subgroup with microalbuminuria in the diabetes control and complications trial[1] could detect a reduction in the risk of progression to clinical albuminuria of 33% or more. Neither study showed any effect of intensive treatment on the categorical change from microalbuminuria to clinical albuminuria.

In the 73 patients with insulin dependent diabetes mellitus and baseline microalbuminuria in the diabetes control and complications trial the difference in the rate of change in albumin excretion rate between the two treatment groups was far from significant (P=0·09). Chaturvedi and Fuller assume that a larger sample would have shown a significant difference between the two groups. The direction of change in a "next lot" of similar patients, however, is unpredictable. Indeed, in the next lot in our study the difference in the rate of change in albumin excretion rate was less than 1% (P=0·31). Moreover, whether the non-significant difference in the mean slope of the albumin excretion rate in the diabetes control and complications trial can be ascribed to glycaemic differences is unknown as the data for the subset of patients with microalbuminuria are unpublished.

The only study comparable to ours that showed a significant reduction in the risk of development of persistent albuminuria in the intensive treatment group was half the size of ours[2]; we agree with Chaturvedi and Fuller that this result is most likely to have been due to a type I error.

We accept that results, particularly if controversial and contrary to expectation, should be challenged, but such challenges should preferably be based on factual data, which Chaturvedi and Fuller do not provide. Whether strict glycaemic control delays the progression of microalbuminuria remains to be proved.

Our study was not designed to test the effect of intensive treatment on retinopathy, and 67% of subjects already had moderate to severe retinopathy, confirming previous reports[3] and making them unsuitable for this type of study.

Like R Davison and colleagues, we found blood pressure to be a more significant predictor of progression of microalbuminuria. We do not, however, advocate replacing optimised diabetes care with antihypertensive treatment in these subjects. Rather, we believe that these two approaches should go together, though we would advise doctors of their relative importance and impact in different phases of the evolution of diabetic renal complications.

Ralf Bender and Peter T Sawicki have misread our paper. Our conclusions were based mainly on the categorical change from microalbuminuria to clinical albuminuria; no differences between the two groups were found. Detailed analysis of the rate of change in the slopes of albumin excretion rate (which we did not present because of space restrictions) again showed no differences between the two groups. The direction of change was the same in the two groups. The question of the duration of glycaemic separation is discussed in our paper.

We disagree with Bender and Sawicki that analysis on an intention to treat basis was inappropriate. However, even when we analysed the data on the basis of attained glycaemia and compared the groups with better and worse blood glucose control (haemoglobin A_{1c} concentrations below and above the median, respectively) no differences were found in albumin excretion rate as either a categorical or a continuous variable.

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1 Diabetes Control and Complications (DCCT) Research Group. Effect of intensive therapy on the development and progression of diabetic nephropathy in the diabetes control and complications trial. *Kidney Int* 1995;47:1703-20.
2 Feldt-Rasmussen B, Mathiesen ER, Deckert T. Effects of two years of strict metabolic control on progression of incipient nephropathy in insulin-dependent diabetes. *Lancet* 1986;ii: 1300-4.
3 Parving H-H, Hammon E, Skiott P, Edsberg P, Bahnsen M, Launtzen M, *et al.* Prevalence of microalbuminuria, retinopathy, and neuropathy in patients with insulin-dependent diabetes. *BMJ* 1988;296:156-60.

Electronic mail may infect computers with viruses

EDITOR,—In their article on using computers in general practice Andrew Millman and colleagues state that the Internet does not pose an important threat with regard to infection with viruses unless programs are downloaded and not screened for viruses.[1] This has been the case until relatively recently, but it is now becoming apparent that electronic mail is another important potential source of infection. Plain text files cannot carry viruses, but anything more complex—such as formatted documents and database or spreadsheet files, which must be encoded for transmission by electronic mail—can potentially carry viruses, which are activated when the encoded file is decoded in the appropriate application on the recipient's computer.

Software to detect viruses struggles to deal with this problem as the virus cannot be recognised for what it is until the file has been decoded and opened, by which time the damage may already have been done.

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1 Millman A, Lee N, Brooke A. Computers in general practice. II. *BMJ* 1995;311:864-7. (30 September.)