get treatment of the highest surgical and ethical standard: the interests of parents and patients may, we fear, be suffering as a result.

In the past two months both the Cleft Lip and Palate Association and the charity Changing Faces have received calls from anxious and confused parents and patients who have been told categorically that one course of surgery is preferable or, worse, that their surgery to date has been poor and needs revision. In our view, this is an unacceptable and unprofessional way for patients to be treated.

Our response to such distressing calls is to emphasise the importance of a multidisciplinary approach to the management of cleft lip and palate so that specialists, including psychologists, speech therapists, and paediatricians, together agree the priorities and objectives for surgery and therefore the most appropriate procedures in consultation with fully informed parents and patients. This is almost impossible at present because plastic surgeons and oral surgeons do not seem to be collaborating in clinical practice; rather, they seem to be in open competition.

As lay people we are unable to judge the strength of the arguments on both sides, and more research over 10-20 years may well be called for. Meanwhile, patients should not be pawns in a professional (unprofessional) feud. The Royal College of Surgeons or some other powerful agency urgently needs to organise discussion in camera before more distress is caused.

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Risk of breast cancer is also increased among Danish female airline cabin attendants

EDITOR,—Eero Pukkala and colleagues report the incidence of cancer among a cohort of Finnish airline cabin attendants.[1] Women made up the overwhelming majority of the cohort, and they were found to have an excess risk of cancer of the breast (number of cases observed, 20; standardised incidence ratio 1·87 (95% confidence interval 1·15 to 2·23)). Excess risks were also found for cancer of the bone and leukaemia, on the basis of only two cases of each of these diseases.

In Denmark the incidence of cancer has been monitored for 17 years for the cohort of participants in the 1970 census.[2] The standardised incidence ratio was calculated for each occupational group on the basis of the incidence for all economically active people. In 1970, 915 women were registered as airline cabin attendants in Denmark, while 362 men were registered as cabin attendants and 620 men as pilots. Table I shows the Danish data for the three types of cancer found in excess among the Finnish workers. The standardised incidence ratio for breast cancer in the Danish female cabin attendants is 1·61 (0·9 to 2·7), while that in all women in social class I is 1·40. The Danish data thus support the Finnish observation that the risk of breast cancer in female airline cabin attendants is higher than that for their social class.

Table 1—*Observed and expected numbers of cases of breast and bone cancer and leukaemia among Danish female and male airline crews*

	Breast		Bone		Leukaemia	
	Observed	Expected	Observed	Expected	Observed	Expected
Women:						
Cabin attendants	14	8·67	0	0·04	0	0·56
Men:						
Cabin attendants	0	0·02	0	0·04	1	0·38
Pilots	0	0·04	0	0·07	0	0·69

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Effect of intensive treatment in insulin dependent diabetes mellitus with microalbuminuria

Sample size was too small

EDITOR,—The Microalbuminuria Collaborative Study Group concludes that intensive glycaemic control has no effect on the progression of albuminuria in people with insulin dependent diabetes mellitus who already have microalbuminuria.[1] These conclusions have important implications for the care of diabetic patients and should not go unchallenged.

The main problem with this study, as the authors admit, is the sample size. If we assume that 21% of patients with microalbuminuria will progress to overt albuminuria, as shown in this and other studies, and we wish to show a reduction in progression by 50% in the intensively treated group (that is, a rate of progression of 10.5%) with 80% power and a significance level of 5%, we would need 412 participants (206 in each group). A more modest reduction in risk would require a larger sample. Thus the inclusion of just 70 patients is not enough, even if the risk of progression in the intensively treated group was close to zero.

The authors quote earlier studies showing significant reductions in risk associated with intensive treatment, which had similar sample sizes to theirs. But these results could partly have been due to a type I error. The authors also quote findings from the diabetes control and complications trial in support of their conclusions. In this trial the difference in the rate of change in albumin excretion rate in the group given intensive treatment compared with the group given conventional treatment was similar in patients with normal albumin excretion to that in patients with microalbuminuria at baseline.[2] But this difference was significant only in those with normal albumin excretion rates as the number of participants with microalbuminuria was too small to provide adequate power.

The authors' study had two main outcome measures—progression to clinical albuminuria and rate of change in the albumin excretion rate. Only detailed results for the former are presented, and we are not shown how the rate of change in the albumin excretion rate differed between the two groups. Simply stating that these differences were not significant is inadequate: rates of change for each group, with confidence intervals, should be presented.

Little mention is made of retinopathy in this paper, but the EURODIAB insulin dependent diabetes mellitus complications study has shown that about half the patients with microalbuminuria have some degree of retinopathy,[3] the progression of which is slowed by improved glycaemic control.[4]

We believe that this study has important methodological limitations and that the target of improving glycaemic control in patients with insulin dependent diabetes mellitus with microalbuminuria should not be abandoned.

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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.)
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Work in non-insulin diabetes corroborates study's findings

EDITOR,—The Microalbuminuria Collaborative Study Group suggests that arterial blood pressure rather than glycated haemoglobin concentration is the main predictor of progression from microalbuminuria to clinical albuminuria.[1] Our work in non-insulin dependent diabetes corroborates these findings.

We undertook a prospective five year study of 42 patients (median (range) age 62 (32-71)) with non-insulin dependent diabetes and microalbuminuria (albumin excretion rate >20 μg/min). They were divided into two groups on the basis of diastolic pressure. Those with a diastolic pressure >85 mm Hg on two occasions (group 1) were treated with an angiotensin converting enzyme inhibitor and the rest (group 2) were not. There was no significant difference in initial albumin excretion rate or haemoglobin A_{1c} concentration between the two groups. In group 1, 17 of the 29 patients were taking antihypertensive treatment before the addition of the angiotensin converting enzyme inhibitor and 11 had complications (all macro-

Table 1—*Blood pressure and albumin excretion rate (AER) at start and end of five year study in patients with non-insulin dependent diabetes and microalbuminura treated with angiotensin converting enzyme inhibitor (group 1) and serving as controls (group 2). Figures are medians (ranges)*

	Start of study	End of study	P value
Group 1			
Blood pressure (mm Hg):			
Systolic	170 (120-252)	146 (120-200)	<0·01
Diastolic	100 (80-105)	80 (70-100)	<0·001
AER (μg/min)	48 (20-282)	30 (7-200)	NS
Group 2			
Blood pressure (mm Hg):			
Systolic	162 (150-180)	158 (120-175)	NS
Diastolic	82 (70-84)	78 (65-84)	NS
AER (μg/min)	53 (20-115)	85 (7-227)	<0·03

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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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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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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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.)