(1) the excess mortality in the tolbutamide group was due to the data obtained from just a few clinics:

(2) the studies of Keen et al and of Paasikivi contradict the U.G.D.P.

(3) the baseline differences among the treatment groups account for the finding of the adverse effects from tolbutamide. On this point I might remark that none of the critics, to my knowledge, has given serious consideration to the multiple logistic method that was used by the U.G.D.P. to take the effect of baseline risk factors into account. Until they do they have not carried out an adequate review of the U.G.D.P. analysis.

(4) the findings on the effect of tolbutamide are flawed by the failure to adapt dosage to individual need.

(5) the evidence was not adequate to justify the discontinuation of the oral drugs.

In our analysis of the U.G.D.P. data we have used the same multiple logistic model as was employed by the U.G.D.P. investigators, but have taken additional variables into account to allow for the time each subject was under study and for differences between clinics. We confirm the principal finding from the simpler study of failure rates, namely that the cardiovascular death rate was higher in patients receiving tolbutamide than in those receiving placebo. This difference remains after adjustment for the effect of baseline variables and cardiovascular risk factors.

We have also made an analysis in which the extent of adherence to assigned treatment was taken into account. The highest death rate was found in the tolbutamide group who adhered 100% to their treatment and who did not modify the dose.

In an analysis of the data from the Bedford trial we found no difference in death rate between the placebo and the tolbutamide group. As indicated