to women. Although the numbers quoted are "rounded" for simplicity, it is clear that in the clinic there are many factors simultaneously influencing cardiovascular deaths. Several of these have greater or equal effect on the cardiovascular death rate compared to the effect of tolbutamide. As a result, it would be difficult for a clinician to perceive an elevated cardiovascular death rate associated with tolbutamide. Such an effect would be almost completely obscured by these other important factors. Only if there is careful and structured record keeping on a large number of patients would a changed cardiovascular death rate of 2-3 be detected. The analysis of such multi-faceted data requires more sophisticated data analytic methods than those in common usage by clinicians.

Next, I wish to discuss some features of the Biometrics Society report. A criticism of the original UGDP analysis is that it failed to explore the effects of several factors acting simultaneously on the cardiovascular mortality. Our Committee did in fact consider this matter very carefully. We found that when one examines the group of older women (age greater than 53) the tolbutamide cardiovascular death rate is almost five times that of the placebo group. It is in this group of older women where the tolbutamide excess cardiovascular mortality is most dramatically shown.

Finally, I wish to comment on the problem of planning and analyzing clinical investigations in which patients are