

6.1.3 Multiple logistic model

We have used the same model as was employed by the UGDP investigators, in which the probability of death was expressed as a function of the treatment and of the base-line variables. We have, however, added additional variables, 1 to take account of the time between enrollment of the subject and completion of the study, and 11 to account for the influence of the clinics. The lengthy list of variables that was assembled in this way is shown in Table A.5. A brief account of the method of analysis based on the multiple logistic model is given in appendix A.(26). The analysis leads to the findings reported in Table A.6.1.

As shown in the upper portion of Table A.6.1, the potential length of follow-up, that is, the length of time from admission to the study to the time of analysis, proved, as one would expect, to be a highly significant predictor of cardiovascular death, the value of X^2 on 1 df being 23.56. This variable was not included in the analyses done by UGDP. Many of the demographic variables and risk factors studied by the UGDP were also highly significant predictors of cardiovascular death. After adjusting for the UGDP variables, treatments, and potential length of follow-up in the analysis, no additional significant improvement was made by adding the clinic effects; however, the UGDP base-line variables as a group still remained highly significant. It is worthy of note that the clinic effects remained significant after adjustment had been made for demographic variables and treatment. It was the additional adjustment by means of the variable length of follow-up that reduced the clinic effects to a nonsignificant level. Although the finding of clinic differences would not be surprising, since they might be due to differences in the patient populations or clinical practice, this indicates that most of the differences are explained by adjusting for the different length of follow-up.

The most important point in this analysis is whether or not the adjustments for covariables could be responsible for the treatment differences observed. Our analysis indicates that the treatment effects have been changed very little by this adjustment. Tolbutamide treatment vs. an average of other treatments, adjusted for a subset of the demographic variables and time of potential follow-up, showed a X^2 of 12.14 on 1 df. In comparing the tolbutamide treatment with the other treatments, it is apparent that this contrast accounts for almost the entire treatment effect, and thus there is no significant difference between the insulin treatments and placebo.

When the data are presented separately for males and females in the next two parts of Table A.6.1, the comparison of tolbutamide with the remaining treatments results in a X^2 of 2.56 on 1 df in the case of males and 9.06 on 1 df in the case of females. The effect of tolbutamide may further be compared with the placebo treatment alone in such a way that the insulin groups also supply information on the demographic variables. Under these circumstances, the X^2 that tests for the adjusted effect of the tolbutamide treatment is 0.35 for males and 11.70 for females. These results indicate that the effect of tolbutamide treatment is significant in females but not in males.

Table A.6.3 shows that the coefficient for the tolbutamide treatment effect is 2.1158 in females and 0.3528 in males, and that the standard errors are 0.7094 and 0.4983, respectively. This implies, as noted before, that the effect is significant only in females. The effect in females, however, is not significantly different from that in males.

The analysis by means of the multiple logistic model confirms the principal finding from the simpler study of failure rates, namely, that the cardiovascular death rate was higher in certain patients receiving tolbutamide than in those receiving placebo. This result was definite in the case of females; it may well be true also of males, but the evidence in that group is not statistically significant. The multiple logistic analysis indicates that the difference in death rates remains after adjustment has been made for the effect of various base-line variables and cardiovascular risk factors.

6.1.4 Analysis with respect to adherence to assigned treatment

The UGDP protocol specified fixed doses for the placebo, tolbutamide, and insulin standard treatments. Alterations were permitted only if the patient "could not be safely maintained on the assigned medication schedule." Modification of the dosage on the basis of elevated blood glucose levels alone was not permitted. Adjustments of the dose for the patients taking variable-dose insulin, however,