

6.2 *The Bedford trial*

The data supplied information on both cardiovascular events and mortality.

6.2.1 *Cardiovascular events*

In the analysis of the data from the Bedford study the authors devote major attention to "cardiovascular events." These have been described by Keen and Jarrett (6) as "a mixed bag" and indeed do raise problems of classification in that the events are not mutually exclusive and are ascertained partly by questionnaire, partly by electrocardiographic evidence, and partly from mortality data. They include reported episodes of angina and intermittent claudication, and this could cause ambiguity, since reports of pain may be greatly influenced by variations in the mood of the subject and in the style of inquiry. In view of the lack of a formal procedure to ensure blind evaluation, the results of such analyses do not lead to firm conclusions.

6.2.2 *Mortality data*

These will be examined by two methods: the estimation of failure rates and death rates, and the use of the multiple logistic model.

6.2.2.1 *Failure rates and death rates*

These two rates differ only in their denominator, which is person-periods in the first case and persons in the second. The numerator in each instance is the number of deaths. The two rates are highly correlated for this set of data, since there was little variation in the length of exposure to risk.

In Table A.8.1 the influence of binary background variables on the death rate is shown. The rate is increased by hypertension, hyperglycemia, and arterial disease. It is higher for females than for males and higher for those over 45 years of age than for younger patients.

In Table A.8.2, placebo and tolbutamide treatments are compared, taking into account the background variables one or two at a time. In no case is there adequate evidence of a difference between the two treatments.

In Table A.8.3, the death rates (by treatment group and sex) are given for more finely divided age groups. The reason for this is that as shown in Table 3, the proportion of older subjects is higher in the placebo groups, and age is therefore a potentially confounding variable in the comparison of treatment effects. Owing to the relatively small numbers of subjects in the individual age groups, the rates are somewhat irregular. The effect of age is marked, but there is no evidence of a difference between the treatment groups.

6.2.2.2 *Multiple logistic model*

In this trial, all the patients were entered into the study at essentially two different points in time and not over a period of time, as in the UGDP. This feature enables some simplification of the analysis of the data. To adjust for the differences in the length of follow-up, and possibly for other differences as well, between those who entered at the two different times, an indicator variable was included in the logistic analysis to distinguish the two groups of subjects. The variables included in the logistic analysis of these data are given in Table A.9.1.

The results of the analysis of the Bedford study deaths due to cardiovascular causes and deaths due to all causes are shown in Table A.9.2. The variances introduced in this analysis were significant in predicting death either from all causes ($X^2=81.02$ on 5 df) or from cardiovascular causes ($X^2=55.16$ on 5 df). Adjusting for these variables, however, did not change the basic conclusion reached from the unadjusted analysis that the death rates did not differ significantly according to treatment.

7. CONCLUSIONS

In this section we summarize our overall findings of the UGDP study with respect to the protocol, the conduct of the study, the methods of analysis, and the findings.

7.1 *Protocol*

Question. Was the target population for this study an appropriate one?

Answer. Critics have pointed out that certain patients were required to accept treatment that would not normally conform to clinical practice, and they

References at end of article.