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A QUASILINEAR REGRESSION MODEL FOR CROSS-OVER TRIALS

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A quasilinear regression model for the analysis of data from a two-period, two-treatment cross-over trial is proposed. In a way similar to Fang, Mao and Jones (1990), the response (or output) is modelled as a function of the inputs, i.e. treatments, periods and residual effects. The model is such that the output at any particular time depends on the history of the inputs up to and including that particular time. The parameters in the model account for the treatment effects, the period effects and the decay rate of the residual effects. The method of statistical inference used is based on the likelihood function and the analysis of variance. Computer simulations show that the parameters are estimated satisfactorily. Finally, the model is illustrated by fitting it to two real data sets.

1. Introduction. When comparing the efficacy of two treatments in a clinical trial the classical approach is based on the parallel group design. In this design the patients are randomly divided into two groups and every patient in the first group receives treatment A and every patient in the second group receives treatment B. A major disadvantage of such a design is that, as patients vary greatly in their initial disease state and their response to therapy, the test for a treatment difference lacks power. The loss of power results from comparing treatments using between-subject information. An alternative, more powerful design, is the cross-over trial which uses within-subject information to compare the treatments. In the cross-over trial the patients are randomly divided into two groups. Each patient in the first group receives treatment A for a given period of time, then 'crosses over' to receive treatment B for a further equal period of time. Each patient in the second group receives B first, then crosses over to A. In such a design each patient serves as his or her own control and as such is very appealing to clinicians and pharmacologists.

A potential disadvantage of the cross-over trial is that the effect of the first treatment a patient receives might still be retained by the patient when the second treatment is administered. If this is the case then the effect seen

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