Comment

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I would like to congratulate Professor Breslow on his thought-provoking paper. The many and varied biostatistical problems discussed serve to illustrate the advantages, and sometimes the limitations, of the Bayesian approach. The paper is typical of recent trends in that it promotes Bayesian methods by demonstrating their application to real and often complex problems, a refreshing change from abstract justifications from first principles of the Bayesian paradigm. While I do not subscribe to an all-embracing Bayesian philosophy, I am happy to recognize the advantages of Bayesian methods in many specific instances. But, for readers like myself it is essential that the debate addresses real examples; we need to be able to compare other methods of analysis and to assess the suitability of assumed prior distributions. This latter point is of prime importance since doubt about the validity of an informative prior weakens the credibility of any analysis that depends strongly on its prior.

PROBLEMS WITH MANY PARAMETERS

The examples in Section 3 of the paper demonstrate that the Bayesian approach has much to offer in problems with many parameters, be they parameters of interest or nuisance parameters. Introducing a joint distribution for parameter values is a useful way of incorporating prior information or expectations, and the examples of Section 3 provide convincing illustrations of this technique. Nonetheless, I am pleased to see in the closing paragraph some healthy skepticism about the use of arbitrary priors and warnings about their possible ill-effects.

In some problems, similar models have been developed outside the Bayesian school, for example random effects models are commonly used in classical analysis of variance. However, the interpretations of such models that different people are willing to recognize can vary substantially. I am reminded of my own experience in connection with work on the estimation of treatment effects in agricultural field trials in the presence of fertility trends (Green, Jennison and Seheult, 1985). We proposed treatment estimates which could be derived either as least-squares estimates in the presence of a fixed but unknown smooth trend or as general least-squares estimates in the presence of a random trend; the random trend model has the advantage that it facilitates calculation of standard errors for estimates of treatment differences. My own view is that there is no real difference between an unknown fixed trend and an appropriately defined random trend, but these appear to be quite separate concepts to many agricultural statisticians. Unfortunately, the distinction is important, and the difficulty of calculating standard errors has been a major factor in the failure of "neighbour adjustment" methods to challenge classical randomization methods for the analysis of field trial data.

It is interesting to note the willingness of researchers working in problems with very many parameters to embrace the Bayesian approach. Prior distributions for regression functions have been proposed in the context of nonparametric regression (see, for example, Silverman, 1985); Bayesian models have been widely adopted in statistical image reconstruction (see Geman and Geman, 1984; Besag, 1986). In both these areas, the Bayesian paradigm appears to be alone in offering hope of progress toward formal inferences in the presence of so many related parameters.

BIOEQUIVALENCE

The issue of bioequivalence testing is clearly an important one with major financial implications for pharmaceutical companies. While not disputing the Bayesian approach to this problem (apart from possible doubts regarding the origins of prior distributions), I would challenge the suggestion that suitable "frequentist" procedures cannot be found. I believe the difficulties alluded to arise from unfortunate and rather confused early formulations of the problem.

The repeated-sampling requirements of a frequentist testing procedure are clear. It should accept bioequivalence with high probability when two compounds have the same response distribution, and it should reject bioequivalence with high probability when response distributions differ by some specified amount. For many types of response, standard methods are available to construct a test meeting such requirements. A problem that has arisen is a semantic one, concerning the naming of hypotheses. To protect the consumer, one must guard against wrongly accepting bioequivalence, and it is the probability of such an error that will be the main concern of a regulatory body. Under the usual convention, the "more serious" form of error is called *type I* and this

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