Letters

Phenformin Ban

Gina Bari Kolata (News and Comment, 16 Mar., p. 1094) describes the circumstances leading to removal from the market of phenformin as an "imminent hazard to the public health." What Kolata does not make clear and, indeed, perhaps only those directly involved with the phenformin decision would readily recognize, is that the Food and Drug Administration (FDA) felt that, regardless of the method chosen by Health, Education, and Welfare Secretary Califano to remove phenformin from the general market, the drug should continue to remain available for those few patients in whom the benefits would appear to outweigh the risks. In choosing the option to suspend approval of the applications *for general marketing* of phenformin on the basis that the drug is an "imminent hazard," Secretary Califano was not ruling out permanently all use of the drug. The imminent hazard provision of the law is simply a legal mechanism for suspending marketing while an ultimate solution to an important safety problem is arrived at through the usual processes of a hearing and subsequent court review.

Since the intent was always to permit the drug to be available to a limited population, it is not at all "ironic" that approximately 3000 patients have received phenformin under an ongoing investigational new drug application. It is noteworthy that this represents only 1 percent of the population that received phenformin during any 1 year when the drug was freely available on the market. We attribute this low figure to the fact that most maturity-onset diabetics can be treated successfully with other modes of therapy—diet, insulin, sulfonylureas—and that FDA has developed stringent criteria for patient eligibility to receive phenformin.

Kolata quotes me as stating that calling phenformin an investigatory drug is our way of restricting its distribution. The conditions under which the drug is permitted to be distributed do, of course, confine its use to a small number of individuals. The investigational drug application for phenformin, however, provides another useful purpose. Because one of the conditions under the application is that physicians are required to report instances of suspected or confirmed lactic acidosis, it permits us to assess the incidence of lactic acidosis when the drug is confined to patients who do not have certain risk factors for lactic acidosis and who receive the drug in dosages associated with a diminished risk for lactic acidosis.

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Statistical Quality

Utah State University offers a course entitled "Quantitative Methods of Natural Resource Management" for juniors in the College of Natural Resources. The take-home exam in this course requires that the student "find an article in your area of professional development in which the hypothesis H_0: $\mu = a$, σ unknown, is tested." These students have had a university statistics course which includes tests of hypotheses and the subject is reviewed in this methods course. Students seek these articles in range, wildlife, forestry, watershed management, outdoor recreation, science, and ecology journals.

The students often find one or more of the following problems:

- The hypothesis being tested is not stated (clearly).
- The test being applied is not identified (clearly). There are numerous tests based on the t-statistic.
- There are not enough data presented to check the application of the test.
- The assumptions that underlie the test are not mentioned, and the design does *not* make it clear that those assumptions are met.
- There are not enough intermediate results (standard deviations, standard errors, numbers of samples, and the like) to check the application of the test.
- The interpretation of the test results is inconsistent with their understanding of what the author did.
- The wrong test is used, the test is incorrectly applied, the calculated values do not follow from the data, and the results are incorrectly interpreted.

The last situation occurs in about 20 percent of the papers where enough information is presented for the student to repeat the test.

This is the first serious look that many students take at the literature in their field. They often tell me that they were afraid of those journals because they thought the material was too esoteric for them. Many are let down by the fact that the published material asks them to accept the conclusions on faith; an objective evaluation is impossible. Some students who have trouble with statistics take heart from the fact that apparently the professionals have not mastered it either; they even challenge my insistence that they learn it.

It is my humble opinion that a smaller number of publications done well would better support good science than this large number of papers done poorly. It also seems that a special class of reviewers (perhaps staff people) need to check quantitative results for assumptions, correct application, correct calculations, correct interpretations, and so forth.

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Burt's Tables

In "The Cyril Burt question: new findings" (29 Sept. 1978, p. 1177), D. D. Dorfman has analyzed an article by Burt and claims to have found evidence that he "fabricated data," that his frequency distributions were "systematic constructions." The article has in turn led to rather less charitable characterizations in newspaper headlines (often involving the word "fraud"). All of this is unfortunate, in that Dorfman is in error on two major points, and his other points are sufficiently open to reasonable doubt to call his conclusions into serious question.

First, I wish to call attention to a significant misrepresentation of Burt in Dorfman's section entitled "Burt's row totals." Dorfman writes, "The row totals of Burt's tables I to IV and the column totals of his tables III and IV would appear on the basis of Burt's descriptions and discussions to be simply totals per mille." He then goes on to show that