sumption; Adelstein and White (*6*) observed an excess of breast cancer mortality among female alcoholics; our group (7) again observed the association independently, and then replicated it in additional data. After making detailed analyses, we published "the hypothesis that alcohol consumption, or related dietary factors, increases the risk of breast cancer" (7). All of the early observations were based on multiple comparisons. Subsequently several studies have been published (*8*), some positive and some null. Whether or not alcohol increases the risk has by no means been established, and none of the investigators has suggested otherwise.

Feinstein is free to express any opinion he wishes, but I question his freedom to back his opinion by distortion or selective citation. The reader should note that, while he now says that the association between smoking and lung cancer is a "splendid achievement" of epidemiologic research, he at one time wrote that it should be regarded with suspicion and suggested that it might be accounted for by cough leading to preferential diagnosis among smokers, or by psychic stress (*9*).

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Response: I am grateful to my respected academic colleagues for making public a set of views that will be enlightening to contemporary nonepidemiologic scientists and perhaps to future historians.

The statements in these and in several unpublished letters are reminiscent of the response offered by members of the medical "establishment" in the mid-19th century (*1*), when Ignaz Semmelweis suggested that the unclean hands of doctors were sometimes giving women fatal infections (puerperal sepsis) after childbirth. The defenders of the status quo attacked Semmelweis for not emphasizing all the successful harm-free deliveries and denounced his scholarship as untrustworthy and perhaps mentally deranged; but they made no acknowledgement of the dirty-hands problem and of his plea for cleanliness.

The current letters are analogous to those responses. Some of the commentators took me to task for not giving suitable credit to the many things epidemiologists have successfully accomplished despite the faulty scientific methods. The published comments refer to my intellectual infirmities in allegedly distorting and inadequately reviewing the literature, and even doubting certain dogmas now regarded as established wisdom. And none of the comments acknowledges or calls for repairing any of the cited flaws in scientific methods.

As for my scholarly malefactions, let me immediately assure Shapiro that I am familiar with the "multiple comparison" problem in "statistical significance"; I used the word "calculations" because I thought it would be easier for nonstatisticians to understand. The term "artifact" seemed appropriate for a spurious finding that arose, as Shapiro says, by chance. I did not quote him as using the words "data dredging," and I am sorry he thinks it is a pejorative term for data dredging. Shapiro's principles for allowing an "association [to] be taken seriously" do not seem to have been applied to explain the sources of error in the two concomitantly published studies that "replicated" his original fallacious conclusion.

I assure Kass that I did not intend to demean either his investigative colleagues or their work. In an era when almost any feature of modern life has been accused of causing almost any selected disease, investigators having enough data can readily examine hundreds of hypotheses. Since tests of more than 13 different hypotheses have now been reported from that single project, I doubt that each of the individual hypotheses was specifically identified in the original research protocol. If so, I wonder how the investigators planned to deal statistically with the multiple comparison problem.

As for my heresies, they arise because my colleagues and I have given careful thought to the problems produced by absent or low scientific standards in epidemiologic studies of cause-effect relationships. We have developed new methods, using improved standards, that have been applied in our own research. Thus, we have now shown (*2*) that lung cancer is indeed underdiagnosed in noncoughers and nonsmokers. My remark about psychic stress, which Shapiro appears to have misunderstood, was intended to refer not to lung cancer, but to coronary disease, which has been inadequately investigated for the role of certain forms of psychic stress in possibly causing both smoking and coronary disease. Kass writes that the causal relationships between "exogenous estrogens and endometrial cancer" and between "diethylstilbestrol and vaginal carcinoma ... are now beyond doubt." My colleagues and I disagree; and we have recently (*3*) reviewed the evidence, stated the reasons for our disagreements, and indicated why the problems will not be solved without new studies, using better methods. As for the aspirin–Reyes syndrome relationship, we have now carried out a study (*4*) using improved scientific standards. In this instance, we confirmed the original statistical association.

The most remarkable feature of the letters to *Science* is the absence of concern for the fundamental scientific defects I cited in epidemiologic methods. After completing their attacks, the critics do not seem upset by investigators making changes in control groups after the results have been analyzed, by large numbers of studies with unresolved and unreconciled contradictions, by the infrequent precautions against ascertainment bias, by statistical maneuvers that are substituted for a true dose-response curve, or by the credulous acceptance of erroneous death-certificate diagnoses. No one seems troubled by the persistent scientific neglect of detection bias, which may also be responsible for yet another recently publicized "menace" of daily life: the relationship of breast cancer and oral contraceptive agents.

I hope my colleagues will forgive me, but I could not have asked for better illustrations of the type of scientific complacency I lamented.

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NOTICE

Because of a printer's error, some copies of the 17 February issue of *Science* contain duplicate pages. We will, of course, replace your defective issue with a good copy. If you received one of these copies, please return the entire copy to: Mary Curry, AAAS, 1333 H Street, NW, Washington, DC 20005.

Erratum: In line 7 of the caption for table 1 (p. 1682) of the report "Association of transfer RNA acceptor identity with a helical irregularity" by William H. McClain *et al.* (23 Dec., p. 1679), "≥20%" should have been "≤20%."