with data bases: analyses of comprehensive data bases are not subject to publication biases.) Such a system is both ethically and scientifically sound.

CONCLUSIONS

1. Randomization is not essential for scientific inference.
2. Randomized clinical trials are inherently unethical. They are not appropriate for life-threatening conditions.
3. Clinical equipoise is an invention used to avoid difficult ethical questions.
4. Randomized consent is unethical by its nature.
5. It is possible to learn in a clinical setting and still deliver good medicine.
6. Analysis of clinical trials should use all available information, including historical controls.
7. Analysis of clinical trial data should use all available covariates, whether or not the trial was randomized.
8. Neyman-Pearson inference, in which the analysis is tied irrevocably to the design, is impractical and sometimes unworkable.
9. Bayesian inferences apply at any time during or after a study; the course of a study can be dictated by interim Bayesian calculations which weigh the costs and benefits (in terms of good medical treatment) of the various options.
10. Medical research should move away from randomized trials and toward establishing comprehensive patient registries.

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Comment: A Bayesian Perspective

Robert E. Kass and Joel B. Greenhouse

Ever since the first modern randomized clinical trial (RCT), clinicians and statisticians have struggled with the question of whether it is proper to deny a patient some possibly beneficial treatment for the sake of conducting an experiment. Even as Sir A. Bradford Hill made his influential arguments in favor of RCTs, he emphasized the importance of ethical considerations. They are, Hill (1951) said, ". . . paramount and must never, on any scientific grounds whatever, be lost sight of. If a treatment cannot ethically be withheld then clearly no controlled trial can be instituted." The problem, however, is to define the circumstances under which "a treatment cannot ethically be withheld." Hill (1951, 1953) distinguished the "dramatic" situations, in which a treatment might offer a cure for an otherwise invariably fatal disease, from the "more mundane" in which a treatment might produce a decline in mortality from, say, 15 to 10 per cent. The dramatic cases might not require a concurrent control group, but, he argued, the more common investigations could provide reliable information only through the use of RCTs.

As Professor Ware has clearly shown in the case of ECMO, the most difficult situation involves a disease that is not invariably fatal, yet the therapy is potentially of great benefit. The basic issue is whether such cases should be considered to be like the "dramatic" ones, or like the "more mundane," or whether, perhaps, there is an intermediate classification in which some third method of study, such as adaptive allocation, should be used.

In some respects, the trial Ware describes is like another that raised considerable debate by using an RCT to examine the effectiveness of Ara-A, an antiviral agent, in the treatment of herpes simplex viral encephalitis, a disease that had a historical fatality rate of around 70%. In that case, McCartney (1978) argued that none of the usual justifications for RCTs

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