STATISTICAL ASPECTS OF CLINICAL TRIALS

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1. Introduction

My object in this lecture will be to give an overview of the statistical aspects of current clinical trial methodology, including a very brief history, my view of current practice, recent relevant statistical developments, and areas that need further statistical research.

My primary concern will be clinical experiments, though I will have some comments on other types of study of clinical data also.

Of course, the idea of trying out a new treatment and then comparing the results with past experience with other remedies is natural. Insistence on some systematic attempt to assure a *controlled* comparison of treatment effects is a recent development. Scattered reports of controlled studies have appeared in the literature only within the last few hundred years. The idea of *random* allocation of treatments to experimental units, in agricultural science, originated with Fisher [30] and gained acceptance in agriculture through the work of such men as Yates and Snedecor [51]. My impression is that agricultural scientists now accept the ideas of randomization, experimental design, and statistical evaluation as essential to sure and orderly scientific progress.

These experimental principles were introduced into clinical medicine in the post World War II period by Hill [36], [37] and taken up by Mainland [43], Lasagna [41], and others. In recent years Cornfield [18] and Armitage [4] have played important roles in encouraging further development of the methodology for planning and evaluating clinical experiments.

2. Present practice

Clinical trial methodology, employing concurrent controls, randomization, and the blindfold technique, has had a great impact on medical scientists. Hundreds of valid medical experiments have been completed and currently it can safely be said that the method is accepted and in use by at least some investigators in every medical specialty. However, it must be quickly added that in many fields, such as surgery, randomized clinical trials are still rare. In fact, there are influential and fluent clinical scientists who enthusiastically point out the difficulties and publicly ponder the usefulness of the experimental approach in clinical