SEQUENTIAL MEDICAL TRIALS WITH DATA DEPENDENT TREATMENT ALLOCATION

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1. Introduction

This paper is concerned with clinical trials intended to determine which, if either, of two treatments for a disease is the superior. The experimental situation is one in which patients arrive for treatment sequentially over some period of time. When a patient is admitted to the trial, he is immediately administered one of the two treatments. The effect of the treatment on the patient may be measured, either immediately, or after some delay. After a certain amount of data is collected, the trial is terminated with the conclusion that one of the two methods is superior or that there is no significant difference between them.

Emphasis in this study is on a search for protocols which assign fewer patients to the inferior treatment as compared to classical statistical methods, while retaining the error probabilities associated with these methods. In these protocols, the assignment of a patient to one of the two treatments being compared is determined by data about patients previously treated. The statistical properties (error probabilities, expected sample sizes, expected number to inferior treatment) of a variety of protocols have been explored by computer simulation, and it has been demonstrated that Wald type sequential procedures can be combined with data dependent assignment rules to reduce the expected number assigned to the inferior treatment. The Neyman-Pearson measures of significance and power remain unchanged.

2. Definition of a protocol

Treatments 1 and 2 are to be compared. The effect on the jth patient assigned to treatment i is assumed to be a random variable X_{ij} with density f_i which

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