ADAPTIVE DESIGNS IN CLINICAL TRIALS: SOME ISSUES WITH EMPHASIS ON ASYMPTOTIC INFERENCE

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Abstract

Response-adaptive designs in clinical trials involve incorporating accruing information from patient responses to treatment into the randomization scheme in order to assign more patients to the treatment performing better thus far in the trial. While ethically attractive at first glance, these designs are rarely used in practice. A brief overview of the ethical and logistical concerns for this apparent paradox are given, focusing in particular on the randomized play-the-winner design of Wei and Durham. Some asymptotic results are then presented for adaptive strategies. A large-sample permutation test statistic is derived for the randomized play-the-winner design. The martingale central limit theorem is employed to show asymptotic normality under certain conditions on the sequence of responses. A new adaptive design is then proposed to handle cases where the responses are polychotomous or continuous. A large-sample test statistic is given. Although a rigorous proof of asymptotic normality has eluded us, simulation evidence is presented which strongly indicates asymptotic normality.