DESIGNING CLINICAL TRIALS TO REDUCE SUBJECTS' INCONVENIENCE AND TO ALLOW FLEXIBLE SAMPLING

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In this presentation, a new approach to designing clinical trials with time-dependent models is proposed. Within a standard framework, an individual design $\xi = (t_1, \ldots, t_s)$ with s sampling times t_i can be found by maximizing the D-optimality criterion $\Psi(\xi)$, say. This solution, however, disregards the inconvenience caused to trial patients waiting between samples. To reduce the inconvenience and to achieve the study goals, it is proposed to use a design minimizing $\phi(\xi) = \sum_{i=1}^{s} \alpha_i t_i$ subject to $\Psi(\xi) \geq e$. Here, $\alpha_i \in R$ reflects the inconvenience due to sampling at t_i, and e fixes the required design efficiency. With s samples per clinical visit and a self-administered drug, patients' waiting time is minimized by $\xi^* = \arg\min t_s - t_1$. For the model considered, the individual waiting time was 5.6 hrs for a D-optimal design compared to 3.4 hrs for a design with 90% efficiency. Alternatively, $\phi(\xi) = \sum_{i=1}^{s} \alpha_i (u_i - l_i)$ can be maximized under $\Psi(\xi) \geq e$ to obtain a sampling interval $[l_i, u_i]$ for each sample i. Such interval designs can provide the flexibility required, for example, for conducting therapeutic procedures concurrent with the trial. Simple methods of convex optimization with linear objectives apply in both cases. The new method can be useful for balancing statistical goals with the costs and practical requirements of clinical and other trials.