Bocconi
Università Commerciale Luigi Bocconi

Department of Decision Sciences

Statistics Seminar

Borrowing Strength with Nonexchangeable Priors over Subpopulations

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Abstract

We introduce a nonparametric Bayesian model for a phase II clinical trial with patients presenting different subtypes of the disease under study. The objective is to estimate the success probability of an experimental therapy for each subtype. We consider the case when small sample sizes require extensive borrowing of information across subtypes, but the subtypes are not a priori exchangeable. The lack of a priori exchangeability hinders the straightforward use of traditional hierarchical models to implement borrowing of strength across disease subtypes. We introduce instead a random partition model for the set of disease subtypes. This is a variation of the product partition model that allows us to model a nonexchangeable prior structure. Like a hierarchical model, the proposed clustering approach considers all observations, across all disease subtypes, to estimate individual success probabilities. But in contrast to standard hierarchical models, the model considers disease subtypes a priori nonexchangeable. This implies that when assessing the success probability for a particular type our model borrows more information from the outcome of the patients sharing the same prognosis than from the others. Our data arise from a phase II clinical trial of patients with sarcoma, a rare type of cancer affecting connective or supportive tissues and soft tissue (e.g., cartilage and fat). Each patient presents one subtype of the disease and subtypes are grouped by good, intermediate, and poor prognosis. The prior model should respect the varying prognosis across disease subtypes. The practical motivation for the proposed approach is that the number of accrued patients within each disease subtype is small. Thus it is not possible to carry out a clinical study of possible new therapies for rare conditions, because it would be impossible to plan for sufficiently large sample size to achieve the desired power. We carry out a simulation study to compare the proposed model with a model that assumes similar success probabilities for all subtypes with the same prognosis, i.e., a fixed partition of subtypes by prognosis. When the assumption is satisfied the two models perform comparably. But the proposed model outperforms the competing model when the assumption is incorrect.

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