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**Title: Using dynamic programming to optimise First In Human trial designs**

**Abstract:**
First in Human trials investigate whether a potential new medicine is safe for human use. The aim of the trial is typically to find the maximum tolerated dose of the potential new medicine. The trial design must specify the dose escalation scheme, a rule that states which dose to give to which subjects at which point in the trial. It is important to allocate doses in such a way that avoids exposing subjects in the trial to unacceptable risk and also provides information on the relationship between dose and toxicity.
If we define the aims of the trial using a loss function we can use dynamic programming to obtain the optimal dose escalation scheme for a First in Human trial with respect to that loss function. Different loss functions lead to different schemes. Thus, this work provides a flexible framework that can be used to compare different trial designs.
Dynamic programming requires a set of calculations to be performed for every possible data set at each stage of the trial. Even with a small trial this state space is large. We consider reformulating the state space as the space of posterior density functions for the dose-response model parameter. We employ generalised additive models to adapt the dynamic programming algorithm to a sample of this space. This produces a dose escalation scheme that is an approximation to the optimal rule produced by performing dynamic programming on the space of all possible data sets. With this approximate version of the algorithm, we extend the methodology to find an optimal dose escalation scheme for a First in Human trial with both a binary efficacy endpoint and a binary safety endpoint.