Fitting Emax Models to Clinical Trial Dose-Response Data

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It has become of greater interest recently to model the dose-response relationship for a new drug which is typically explored in Phase II clinical trials. A key model because of its Clinical Pharmacology rationale is the so-called Emax model. In its 4 parameter form this model is usually written as

\[ E(Y) = E_0 + \frac{E_{\text{max}} \cdot Dose^b}{ED_{50}^b + Dose^b} \]

where \( Y \) is the response of interest, \( E_0 \) is the placebo response, \( E_{\text{max}} \) is the maximum achievable increase above the placebo response and \( ED_{50} \) is the dose which produces 50% of the \( E_{\text{max}} \) effect. Setting \( B = 1 \) gives the 3 parameter Emax model.

Two distinct features of clinical trial dose-response data mean that it can be difficult to fit either the 3-parameter or 4-parameter Emax model. One feature is that dose-response clinical trials typically only use relatively few doses, and the other is that it may not be possible to study the effect of large doses.

We consider how the difficulty in fitting the 4-parameter Emax model as written above and the corresponding 3-parameter model obtained by setting \( B = 1 \) can be dealt with and some of the properties of the resulting methods.