

Title: Dose-response curves

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Abstract: In this thesis, we deal with the process of research and development of new medical substances with a focus on statistical methods used to determine appropriate doses. For this purpose, we examine the dose-response relationship.

First, we describe a typical procedure for the development of a new drug. Second, we focus in detail on the MCP-Mod method. Third, we propose a new method based on the theory of gradual change models. This approach tests whether the administration of the drug has a significant effect. If so, the dose with desired effect is estimated using an appropriate model. Specifically, we provide an estimate using linear, quadratic and Emax gradual change models. We also describe a construction of a confidence interval for the point of change and also for the dose with the desired effect. The advantage of the proposed method over the MCP-Mod is the determination of the confidence intervals.

Finally, we apply the above mentioned methods to data from the U.S. Tox21 research program and compare the results based on several tested substances and clearly demonstrate the application and advantages of each method.

Keywords: dose; response; curves; MED; MCP-Mod; gradual; change; model; drug; development; Tox21