Estimating Relative Potency Based on Multivariate Risk/Benefit Assessment

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Relative potency plays a key role in understanding the relationship between the doses of two treatments. Defined as the ratio of equally effective doses, it is central to communicating the relationship between a new drug entering the market and older medications. Because doses are tested and collected at discrete points in clinical trials, estimation in direct assays is hampered by the fact that clinical responses and tolerances are usually only available as grouped data which is frequently left- or right-censored information or both. This problem was considered in Bonzo, Friedman, and Laska (2004), which modeled premature discontinuation of treatment. However, further difficulties arise when the risk/benefit assessment is multivariate in dimension. This paper proposes an extension of the author's previous work for estimating relative potency in the multivariate setting utilizing dimension reduction and generalized mixed data model (GMDM) approaches. Large sample approximation and an analogue of Fieller's theorem are used to construct confidence interval estimates. Simulated data and data from a clinical trial are used to illustrate the methods' use.

Key Words: left-/right-censored information, grouped data, generalized mixed data model, fiducial limits