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Methods for meta-analysis of EC50/IC50 curves: a valuable tool for decision making in pharmaceutical research

An important parameter in pharmacological research is the half-maximal inhibitory concentration (IC50/EC50), which quantifies the potency of a drug by measuring the concentration required to inhibit a biological process by 50%. The 4-parameter logistic (4PL) model is widely employed for estimating IC50/EC50 values, as it provides a flexible sigmoidal fit. Meta-analysis on the other hand, has become an indispensable tool for synthesizing the results of independent studies into a unified, statistically robust estimate and facilitates the decision making in various fields from medicine to economics. In this work, we discuss methods for meta-analysis of IC50/EC50 values arising from independent studies. We first show the application of standard summary data methods that pool IC50/EC50 estimates obtained from independent studies, and then we proceed with more advanced methods that allow the calculation of an entire pooled sigmoid curve, using multiple measurements per study and estimating all parameters of interest in a single step. We discuss non-linear estimation methods in Stata using the nl and menl commands for fixed and random effects, respectively. We also show that in some special cases, when the upper and lower asymptote of the sigmoid curve is 1 and 0, respectively, the model reduces to a two-parameter logistic (2PL) model. In this framework, variants of the generalized linear model, such as the fractional logistic regression model, fitted with specialized commands such as glm, fracreg, or gllamm, can be used to obtain the pooled sigmoid curve with all parameters of interest, either under fixed or random effects. We present examples of the methods and discuss details of the implementation.

Special/ Invited session

Classification

Mainly methodology

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