

tdm - A Tool of Therapeutic Drug Monitoring in R

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Introduction Therapeutic drug monitoring (TDM) aims to optimize individual patient's drug therapy through monitoring the plasma/serum concentrations of the target drug, as well as the observed clinical responses. However, there are usually only few blood samples that can be collected and analyzed. Usually there is even only one single blood sample available. Therefore, it becomes very important to accurately estimate individual pharmacokinetic (PK) parameters with limited observations. Bayesian estimation is a very suitable algorithm for this situation. In contrast to minimizing an objective function, Bayesian estimation with Markov-chain Monte-Carlo (MCMC) simulation (integration) using Gibbs sampler technique (BUGS) might be worth to implement and apply. Hence, the objective of this study was to develop a TDM tool using *BUGS* for R. **Methods and Materials** We chose *OpenBUGS*, an open-source version of BUGS for Windows (through its R interface package *BRugs*), to develop this tool under R. Each drug model was divided into two parts: the probability distribution of population PK parameter (as priors), and the probability distribution of observed drug serum/plasma concentration or observed clinical response (as the conditional probability or the likelihood function). This tool was validated with simulated data obtained from the published PK parameters within the range of 2*s.d.. And the accuracy of PK parameters was evaluated with percent prediction error (PE %). **Results and Discussion** We named this tool as *tdm*. Seventeen drug models including one PK/PD model (warfarin) and sixteen PK models were built in *tdm*. It can be used to estimate individual PK/PD parameters with one or more observations obtained from a single subject, as well as multiple subjects at the same time. Other than one drug, imatinib, PK or PD parameters of all other drugs are estimated at their steady-state. Furthermore, *tdm* also provides dosage adjustment function. Based on the results of estimation validation, we found PEs of PK parameters of built drugs were similar to those using nonlinear regression obtained from other computer software, *JPKD*. **Conclusion** *tdm* has been released on Nov. 2006 and can be downloaded and installed from R mirror websites. The latest version is 2.2.1. Currently *tdm* is only available for Windows, because *BRugs* has not been available for other platforms yet.