

**Tasks---Topic Parameter Estimation –Influenza dynamics after oseltamivir (tamiflu) treatment.**

- 1) Read in the data from the file and separate by virus type:
  - i. influenza A/H1N1(2009) sensitive
  - ii. influenza A/H1N1(2009) resistant
  - iii. influenza B sensitive
- 2) Pool the data and compute the mean/median virus load  $\mu_i$  for each time-point  $t = 0, 3, 5, \dots$  [days]:
  - a. for each virus type separately,...

....and perform a maximum likelihood parameter estimation using the model depicted in Rath et al (2012), eq.(2) [estimate the initial virus load  $V_0$  and the virus clearance  $CL_V$ ], with weights for each time-point  $t$  according to a

- additive (Gaussian) error
- proportional (Gaussian) error

with the variance to be estimated from the data. Store your estimates of  $V_0$  and  $CL_V$  for these scenarios

- 3) Estimate parameters  $V_0(i)$  and  $CL_V(i)$  for each individual  $i$  separately assuming a
  - additive (Gaussian) error (as done in Rath et al. (2012), eq(2))
  - proportional (Gaussian) error

and compute the median  $CL_V$  and  $V_0$  of all individual estimates.

- 4) Use a non-linear mixed effect modelling approach (Matlab or R) to compute population parameters and random effects on these parameters. Using an
  - i. additive (Gaussian) error
  - ii. proportional (Gaussian) errorand putting random effects on a) both parameters b)  $CL_V$  c)  $V_0$ , d) none of the parameters. Perform model checking using AIC/BIC.

Discuss the different scenarios (i.e. in the talk).

**Original Literature:**

1. Rath, M. von Kleist, F. Tief, K. Karsch, E. Türk, S. Mühlhans, F. Louis, H. Skopnik, B. Schweiger and S. Duwe. *Pediatr Infect Dis J.* 31, 9, 2012
2. S. Duwal, M. von Kleist, *Eur J Pharm Sci*, 94, 72, 2016 (Supplementary Material)

## **Review**

- 1. PharmatrX Module on Pop PK (the be added later)**
- 2. Pharmacometrics Book 265pp**