Covariate Model Building

Hands-On Session – SCM and linearized SCM

A. In this exercise we will build covariate models using regular and linearized SCM for phenobarbital dataset.

Files provided:

Data set:

Pheno.dta

Model files:

run100.mod = one compartment IV bolus model parameterized in terms of CL and V.
This is the base model i.e. no covariates.

SCM configuration file:

run100.scm and run101.scm

Tasks:

1. The continuous covariates included in the dataset are weight and APGR score. You need to test them on CL and V.

(i). Using the provided SCM configuration file (run100.scm and run101.scm) run both non-linear and linearized SCM.

scm run100.scm -dir=run100_nl
scm run101.scm -dir=run101_lin

(ii). Note ΔOFV's (covariate-base) of the univariate models from non-linear and linear method (obtained after the first step of the scm). Do you see any major differences in ΔOFV's between non-linear and linear?

Univariate results	ΔOFV (covariate-base)	
	Non-linear	Linear
Wt on CL		
APGR on CL		
Wt on V		
APGR on V		

(iii) Compare the final models obtained from non-linear and linearized SCM. Comment if there are any differences in the final model. (Note: the final models are in final_models directory)

B. In this exercise we will build covariate models using regular and linearized SCM for moxonidine dataset.

Data set:

mx19.csv

Model files:

run1.mod = one compartment model parameterized in CL, V and Ka with inter-individual variability (IIV) and inter-occasion variability (IOV). The model includes CRCL on CL and WT on V.

run2.mod= This is same as above but without CRCL on CL and WT on V.

SCM configuration file:

run1.scm and run1_lin.scm

Tasks:

1. The provided dataset contains 5 continuous and 5 dichotomous covariates. The dichotomous covariates are concomitant medications (digoxin, diuretic and ace inhibitors) NYHA, and sex. Continuous covariates are AGE, WT, CRCL, SCR, and NEUY. Originally, NYHA score had 4 different categories but for the purpose of this exercise NYHA has been dichotomized. In this exercise we will test concomitant medications, NYHA, sex and age on CL and V.

(i). Using the provided SCM configuration file (run1.scm and run1_lin.scm) run both non-linear and linearized SCM.

scm run1.scm -dir=run1_nl
scm run1_lin.scm -dir=run1_lin

(ii). Note ΔOFV's (covariate-base) of the univariate models from non-linear and linear method from the first, univariate, step of the scm. Do you see any major differences in ΔOFV's between two methods?

Covariate on parameter	ΔOFV (covariate-base)	
	Non-linear	Linear

(iii) Compare the final model models obtained from non-linear and linearized SCM. Comment if there are any differences between the final models. (Note: Final models are in final_models directory)

Extra Credit

These tasks allow you to practise different parameterizations for inclusion in the scm.

Task 1

(i) Start with run2.mod. Modify the provided SCM configuration file so that age is included as hockey-stick model on CL and V, Weight on V linearly, CRCL on CL linearly, and dichotomous covariates on both CL and V.

(a) Run both linear and regular SCM.
(b) Compare the final models obtained from linear and regular SCM. Comment
(c) Is the final models obtained here different from (iii). Comment

Task 2

(i) Start with run2.mod. Modify the provided SCM configuration file so that age is included as exponential model on CL and V, Weight on V as linear, CRCL on CL as linear, and dichotomous covariates on both CL and V.

(a) Run both linear and regular SCM.
(b) Compare the final models obtained from linear and regular SCM. Comment
(c) Is the final models obtained here different from (iii). Comment

Task 3

(i) Start with run2.mod. Modify the provided SCM configuration file so that CRCL is included as hockey-stick model on CL, Weight on V as linear, age on CL and V as linear, and dichotomous covariates on both CL and V.

(a) Run both linear and regular SCM.
(b) Compare the final models obtained from linear and regular SCM. Comment
(c) Is the final models obtained here different from (iii). Comment

Task 4

(i) Start with run2.mod. Modify the provided SCM configuration file so that CRCL is included as hockey-stick model on CL, Weight on V as power, age on CL and V as linear, and dichotomous covariates on both CL and V.

(a) Run both linear and regular SCM.
(b) Compare the final models obtained from linear and regular SCM. Comment
(c) Is the final models obtained here different from (iii). Comment