

An Introductory Workshop in Population PK Data Analysis with NONMEM®

July 12th - 16th, 2021

Workshop Synopsis

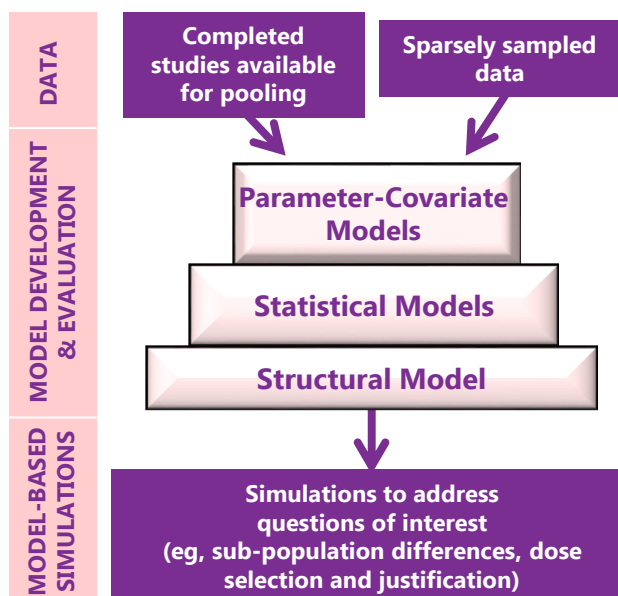
This introductory population PK training workshop has been designed to provide the necessary information to successfully implement population pharmacokinetic methodology in a drug development program and to provide foundational understanding of the basics of NONMEM coding and interpretation of NONMEM output. The material is structured to impart both the theoretical and practical aspects of the population approach and is versatile so that participants with diverse backgrounds and areas of expertise may benefit. No prior experience with NONMEM is assumed or required. Examples of the use of population PK studies in drug development programs will be presented to provide specific details of various implementations and better illustrate essential aspects of population PK methods. Participants will gain an appreciation for the essentials of accurate and sufficient data collection and learn how to proactively plan in order to maximize study effectiveness. Throughout the workshop, the presenters will provide examples from their experience to inform best practices for implementation and avoiding problems. Emphasis will be placed on compliance with the FDA's Guidance for Industry on Population PK and the EMA's Guideline on Reporting the Results of Population PK Analyses.

The workshop content will be provided as a combination of live lectures, review of data, code, and modeling results, plus hands-on individual and small group exercises. Participants will be able to practice coding control streams, running various models, and evaluating the results. A thorough examination of an example dataset, from development of the structural and statistical models through covariate analysis will be covered. To ease the learning curve and ensure that participants are up and running with NONMEM very quickly, the KIWI™ Pharmacometric Communication Platform will be used in conjunction with NONMEM. KIWI is useful in facilitating code writing, finding errors, comparing output from different models, and generating point-and-click model diagnostics.

Learning Objectives

Following the workshop, the participant should be able to:

1. Understand the conceptual basis and rationale for the population approach to data analysis, its benefits and advantages, including where and when population methods may be optimally applied during drug development
2. Write, execute, and de-bug basic NONMEM® control streams for structural PK models
3. Outline the requirements and understand the format for basic NONMEM® datasets
4. Understand the importance of exploratory data analysis (EDA) and the interpretation of standard goodness-of-fit diagnostic plots
5. Perform covariate analyses to evaluate determinants of variability by understanding, identifying, and coding basic functional forms for covariate-parameter relationships
6. Understand the basis for model selection strategies and discriminate between candidate models on the basis of both quantitative and qualitative factors
7. Understand and interpret NONMEM® output, including error messages, and have insight into model refinement issues



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Course Instruction

The workshop is organized and taught by experienced pharmacometricians from Cognigen Corporation, also affiliated with the University at Buffalo and Union University Departments of Pharmaceutical Sciences. Cognigen Corporation, a wholly owned subsidiary of Simulations Plus, Inc., has been providing clinical pharmacology and pharmacometric consulting services, including population PK/PD modeling and simulation to the global pharmaceutical industry for over 25 years to generate and communicate the knowledge required for time-sensitive decision-making and regulatory review. The workshop will be primarily taught by Jill Fiedler-Kelly and Joel Owen, co-authors of *Introduction to Population Pharmacokinetic/Pharmacodynamic Analysis with Nonlinear Mixed Effects Models* (John Wiley & Sons Inc., 2014), with support from other expert pharmacometricians on the Cognigen team.



Jill Fiedler-Kelly



Joel Owen

Agenda

Monday

- 09:00 - 09:10 **Welcome and Introduction to the Workshop**
- 09:10 - 10:10 **The Population Approach in Drug Development**
- 10:10 - 10:45 **Population Modeling Basics**
- 10:45 - 11:00 **Break**
- 11:00 - 12:00 **NONMEM® Terminology**
- 12:00 - 12:00 **Estimation Methods in NONMEM®**

Tuesday

- 09:00 - 09:10 **Brief Overview of the NONMEM® Program**
- 09:10 - 10:30 **Writing an NM-TRAN Control Stream**
- 10:30 - 10:45 **Break**
- 10:45 - 11:45 **NONMEM® Dataset Structure**
- 11:45 - 12:05 **Exercise: Writing Control Streams and Diagnosing Dataset Problems**
- 12:05 - 12:30 **Review Control Stream & Dataset Exercise**
- 12:30 - 13:00 **Exploratory Data Analysis**

Wednesday

- 09:00 - 09:40 **Running NONMEM® and Interpreting the Output**
- 09:40 - 10:10 **Exercise: Introduction to KIWI**
- 10:10 - 10:30 **Data Review: Introduction to the Example Dataset and Exploratory Data Analysis**
- 10:30 - 10:45 **Break**
- 10:45 - 11:45 **Exercise: Developing a Base Structural Model**

Wednesday (cont'd)

- 11:45 - 12:00 **Data Review: Base Model**
- 12:10 - 12:30 **Model Diagnostic Plots**
- 12:30 - 13:00 **Model Selection and Covariate Evaluation – Part 1: The Covariate Assessment Process**

Thursday

- 09:00 - 09:45 **Covariate Evaluation – Part 2: Functional Forms**
- 09:45 - 10:00 **Data Review: Introduction to Covariate Analysis and Coding Issues**
- 10:00 - 11:15 **Exercise: Forward Selection of Covariate Effects, incl Break**
- 11:15 - 12:00 **Data Review: Forward Selection Results and Multivariable Model Checking**
- 12:00 - 12:30 **Exercise: Backward Elimination of Covariate Effects**
- 12:30 - 13:00 **Applications of Bayesian Parameter Estimation**

Friday

- 09:00 - 10:30 **Diagnosing Errors, Model Checking, Model Refinement, and Model Evaluation Techniques**
- 10:30 - 10:45 **Break**
- 10:45 - 11:00 **Data Review: Backward Elimination and Model Refinement**
- 11:00 - 12:15 **Pharmacometric Analysis Planning and Population PK/PD Modeling and Simulation**
- 12:15 - 13:00 **Wrap-up and Final Q & A**

Registration Details

Virtual platform: The course will be held via Zoom, including live lectures and Q&A discussions and will utilize breakout rooms to facilitate hands-on sessions in small groups. All participants will be requested to attend via computer with camera and microphone switched on for interactive discussion sessions.

Requirements: Laptop computers equipped with Internet access, functional cameras and microphones, and Google Chrome with Flash 9+ plugins are required to fully participate in hands-on exercises. Access to NONMEM and KIWI will be provided for the duration of the course and do NOT need to be installed prior to the workshop.



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Title: Professor Dr. Mr. Mrs. Miss Ms. **Industry**
Graduate Student

First name:

Last name: Company:

Position: Department:

Address:

Telephone: Email:

Purchase Order No. (if applicable):

FeeIndustry: **\$2,800**Graduate Student: **\$1,400** (available for up to 3 participants)**Method of payment (Please check one)**

- Payment by check (you will be invoiced upon receipt of your completed registration form)
- Payment online (you will be redirected to the payment portal when registering online at www.simulations-plus.com/workshops)

Terms and Conditions

Registration: The course is limited to the capacity of 30 participants. Confirmation email of registration will be returned upon successful registration at the following web site: www.simulations-plus.com/workshops

Cancellations: Cancellations with a refund minus 4% credit card fees may be made until July 5th, 2021. No refunds will be given for cancellations received after this date. Substitutions may be made at any time.

Payment Terms: Following completion and return of the registration form, the total fee must be paid within 30 days of receipt of invoice. All fees must be paid in full prior to the start of the workshop.