

**MI260: Bayesian Model-Based Meta-Analysis to Support Decision Making in Drug Development (2 CR)**

MI260 provides an introduction to model-based meta-analysis of summary data or a combination of summary and individual data from clinical trials to support decision-making in clinical drug development. Upon completion of the course, participants will be able to design a model-based meta-analysis of clinical trial data to address strategic decisions in a clinical drug development program and implement it using a Bayesian approach executed with WinBUGS and R. The course includes hands-on experience in constructing models for the relationship between an efficacy- or safety-related clinical outcome and independent variables such as dose, time and patient characteristics by analysis of summary data from multiple studies, e.g., treatment means and standard deviations, as well as by analysis of a combination of summary and individual data. In addition participants will learn to execute and interpret population simulations to support decision-making in clinical drug development. Participants may apply the 2 credit hours from this course to the Metrum Institute Certificate Program in Pharmacometrics.

**Instructors**

Bill Gillespie and Metrum Institute staff

**Prerequisites**

Experience with PK-PD modeling and some familiarity and hands-on experience with nonlinear regression, mixed-effects modeling, Bayesian modeling using WinBUGS, and use of R (or S-PLUS). Applicable MI courses include: MI200, MI205 (formerly MI220) and MI250, or contact us, [info@metruminstitute.org](mailto:info@metruminstitute.org).

**Computer Hardware/Software**

This course requires a Windows laptop computer with an available USB 2.0 port. All required software used for hands-on examples will be freeware/open-source software and simple instructions will be provided for users to configure their computers before the course.

**Summer 2010 Schedule**

Thursday, August 19 8:30am-4:30pm  
Friday, August 20 8:30am-4:30pm

**Location**

College of the Atlantic  
105 Eden Street  
Bar Harbor, ME 04609

**Accommodations**

Metrum Institute does not provide hotel accommodations for students. All travel accommodations must be arranged independently.

**Fees**

Regular registration: \$2000 USD / Academic & government registration: \$1000 USD

**Course Outline**

1. Introduction
  - Rationale and role of model-based meta-analysis in clinical drug development
    - Why do it?
    - What decisions benefit from model-based meta-analysis?
  - Motivating examples
  - Why Bayesian? / Why BUGS?
2. Overview of the model-based meta-analysis process
  - Types of data and data sources
  - The process

- Plan your modeling strategy
  - Identify key information you want to collect
  - Construct a database
  - Construct the modeling and simulation work plan
  - Implementation and application
    - Model development
    - Model application, e.g., simulations to support decision-making
3. Database construction
    - Data sources
    - Data types, e.g., mean, mean change from baseline, percent change from baseline, standard deviation, standard error..
  4. Modeling sample mean data
  5. Hands-On Problem 1: Dose response model based on sample means
  6. Modeling sample standard deviations: why and how
  7. Population stimulations
    - Simulating probable ranges of population estimands, e.g., population mean, probability of an event, etc.
    - Using simulation results to support decision-making in a competitive market environment
  8. Hands-On Problem 2: Population stimulations
  9. Issues arising from analysis of summary data
    - Applying models developed to describe responses in individuals to summary data
    - Analysis of longitudinal data
      - Pitfalls of treating treatment arms as "super-patients"
      - Within-arm correlation
      - Approaches for addressing these issues
  10. Modeling other types of summary statistics
    - Number or fraction of patients with a particular outcome or that experience an event
    - Number or fraction of patients within each level of an ordinal scale
    - Number of events per patient
    - Summary statistics for time-to-event measurements
  11. Hands-On Problem 3: Longitudinal dose-response model based on longitudinal summary data
  12. Publication bias
  13. Issues arising from use of LOCF and OC data
  14. Combining summary and individual data
  15. Hands-on Problem 4: Longitudinal dose-response model based on a combination of summary and individual data
  16. Incorporating a broader range of data and knowledge
    - Leveraging the Bayesian framework to incorporate additional quantitative knowledge via informative prior distributions
    - Integrating preclinical, biomarker and clinical outcome data to improve prediction and decision-making in early clinical development
  17. Closing discussion