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MI250: Introduction to Bayesian PK-PD Modeling & Simulation

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   (b) Bayesian modeling & inference process
   (c) Likelihood principle
3. Computation for Bayesian modeling
   (a) Key challenge of Bayesian modeling and inference: high-dimensional multiple integration
   (b) General computational approach: posterior simulation
   (c) Brief intro to Markov chain Monte Carlo simulation
4. WinBUGS basics
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   (b) WinBUGS demo: Linear regression
5. Introduce PK/PD modeling case study to be used throughout the course
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   (b) R tools for running WinBUGS and analyzing MCMC simulations
   (c) Assessing convergence
   (d) Programming hierarchical models (aka mixed effect or population models)
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   (c) Dealing with censored data in WinBUGS
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    (a) Informative prior distributions in clinical pharmacology applications
    (b) Using the cut function in WinBUGS
    (c) Programming models in terms of differential equations
12. Hands-on example 4: Population PK-PD using an indirect action model

13. Additional topics & closing discussion

    (a) Selected published examples of Bayesian applications

    (b) Considerations in deciding whether to use:

        i. Bayesian or maximum likelihood methods

        ii. WinBUGS or NONMEM or ?

    (c) What didn't we cover?

MI255: Exposure-Response Modeling of Categorical, Count, and Time-to-Event Data

1. Some general theory/background:
   (a) Modeling from a probabilistic point of view: the likelihood function
   (b) Maximum likelihood for continuous data
   (c) Extending ML to odd-type data
   (d) Hierarchical (mixed effects) modeling of odd-type data
   (e) Bayesian modeling of odd-type data
2. Modeling binary data
   (a) Logistic regression models
   (b) Bernoulli model for individual binary data
   (c) Binomial model for summary data
   (d) Mixed effects modeling of binary data
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   (b) Modeling longitudinal ordinal data: Comparative performance of approximate ML (e.g., NONMEM) and MCMC (e.g., WinBUGS)
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   (b) Variations on the Poisson model to deal with over-dispersion or zero inflation
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    (a) Principles and methods of survival analysis for modeling censored data
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12. Models with time-varying hazard
13. Miscellaneous topics:
    (a) Modeling repeated time-to-event data
    (b) Modeling of inter-event time intervals
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MI260: Model-based Meta-analysis to Support Decision-Making in Clinical Drug Development

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   (a) Rationale and role of model-based meta-analysis in clinical drug development
   (b) Why do it?
   (c) What decisions benefit from meta-analysis and model-based meta-analysis in particular?
   (d) Motivating examples
2. The systematic review and planning your meta-analysis
   (a) Analysis plan
   (b) Database construction
      i. Data sources
      ii. Data types, e.g., mean, mean change from baseline, percent change from baseline, standard deviation, standard error
3. Traditional meta-analysis
   (a) What is it?
   (b) Fixed effects meta-analysis
4. Random effects meta-analysis and meta-regression
   (a) Measures of heterogeneity
   (b) What the traditional random effects model is and how it differs from fixed effects
   (c) Meta-regression
5. Selection bias and missing data
6. Combining different types of data
7. Network Meta-analysis
   (a) Relationship to random effects meta-analysis
   (b) Assumptions
   (c) Fitting the models
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   (a) What is it?
   (b) Role of MBMA: Objectives not adequately addressed by traditional meta-analysis
   (c) Why Bayesian? / Why BUGS?
9. Modeling sample mean data
10. Modeling sample standard deviations: why and how
11. Population simulations
    (a) Simulating probable ranges of population estimands, e.g., population mean, probability of an event, etc.

(b) Using simulation results to support decision-making in a competitive market environment

12. Issues arising from analysis of summary data
    (a) Applying models developed to describe responses in individuals to summary data
    (b) Analysis of longitudinal data
        i. Pitfalls of treating treatment arms as "super-patients"
        ii. Within-arm correlation
        iii. Approaches for addressing these issues
13. Modeling other types of summary statistics:
    (a) Number or fraction of patients with a particular outcome or that experience an event
    (b) Number or fraction of patients within each level of an ordinal scale
    (c) Number of events per patient
    (d) Summary statistics for time-to-event measurements
14. Issues arising from use of LOCF and OC data
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    (a) Leveraging the Bayesian framework to incorporate additional quantitative knowledge via informative prior distributions
    (b) Integrating preclinical, biomarker and clinical outcome data to improve prediction and decision-making in early clinical development
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