Statistical Methods for Composite Endpoints

Win Ratio and Beyond

Lu Mao

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Course Info

This is a companion site for the same-titled **workshop** at the 2024 Society for Clinical Trials (SCT) Annual Meeting given on May 19, 2024 at Boston Marriott Copley Place (map) in Boston, MA.

Time and Place

- Sun, May 19 | 8:00 AM - 12:00 PM
- Room: Suffolk (3rd Floor)

Instructor Profile

Lu Mao, PhD

- Associate Professor of Biostatistics at UW-Madison
- Methodologic research
  - R01HL149875: *Novel Statistical Methods for Complex Time-to-Event Data in Cardiovascular Clinical Trials* (12/01/2019 – 07/31/2028)
  - DMS2015526: *Randomized Trials with Non-Compliance* (07/01/2020 – 06/30/2024)
- Collaborative research
  - Cardiovascular disease, cancer, radiology, behavioral health interventions
- Teaching
  - Survival Analysis: Theory and Methods (UW; 2020 - 2024)
- Editorial service
  - Statistical Editor, *JACC Journals*
  - Associate Editor, *Statistics for Biopharmaceutical Research*

Learning Outcomes

- Understand the statistical and scientific challenges with composite endpoints as well as regulatory guidelines/requirements
- Learn the basics of statistical methodology, e.g., testing, power analysis, nonparametric estimation, and semiparametric regression to address these challenges
- Get hands-on experience with real data using publicly available R-packages

Syllabus

- **1. Introduction** (30 min)
  - 1.1 Examples & guidelines
  - 1.2 Traditional methods and limitations
  - 1.3 Win ratio methods and limitations
- **2. Hypothesis Testing** (40 min)
  - 2.1 Win ratio by Pocock et al. (2012)
  - 2.2 Statistical properties
  - 2.3 Handling recurrent events (R-package `WR`)
  - 2.4 Sample size calculation (R-package `WR`)
- **3. Nonparametric Estimation** (60 min)
  - 3.1 Restricted win ratio
  - 3.2 Average win time analysis (R-package `rmt`)
    - 3.1.1 Restricted mean time in favor of treatment
    - 3.1.2 Estimation, inference, and graphics
    - 3.1.3 Real Examples
  - 3.3 While-alive loss rate (R-package `WA`)
    - 3.2.1 Definition, interpretation, and estimation
    - 3.2.3 Real Examples
- **4. Semiparametric Regression** (30 min)
  - 4.1 Proportional win-fractions model (R-package `WR`)
    - 4.1.1 Model assumptions
    - 4.1.2 Estimation, inference, and model diagnostics
    - 4.1.3 Real Examples
  - 4.2 Generalized proportional odds model (tentative)
    - 4.2.1 Model specification and possible estimation
- **5. Discussions** (20 min)