Course Syllabus

Visiting Professor: David Wypij

Course	Biostatistics: Multicenter Clinical Trials		
Credit	1	Method of Teaching	Lecture

Objective

The objective of this course is on understanding basic concepts and methods of how to apply quantitative methods and how to collaborate effectively with clinical investigators in large multicenter clinical trials.

Outline

The emphasis of this course is on understanding basic concepts and methods in the running of large multicenter clinical trials, particularly quantitative issues in the design of the trials, conduct during the trials, and final trial analyses and publications. Specific topics include protocol development, sample size and power, randomization methods, the data analysis plan, trial registration, Data and Safety Monitoring Board interactions, potential early stopping of trials, and manuscript development including tables and figures. Other topics include meta-analysis, secondary data analysis, propensity score analysis, the impact of the COVID-19 pandemic, and specific issues arising from multinational trials and pediatric trials. The focus will be on the life cycle of several recent large trials, including the Safe Pediatric Euglycemia after Cardiac Surgery trial (SPECS; Agus et al., *NEJM*, 2012), the Heart and Lung Failure – Pediatric Insulin Titration trial (HALF-PINT; Agus et al., *NEJM*, 2017), and the Randomized Evaluation of Sedation Titration for Respiratory Failure trial (RESTORE; Curley et al., *JAMA*, 2015), as well as secondary analyses arising from these trials and other related trials. The course is intended for all students interested in epidemiology, biostatistics, and public health; the course assumes some basic background in biostatistics and clinical trials.

Class Schedule (90 minutes each)

Day 1 (January 4, 2027)

1. **Course Introduction; Glucose Management Trials, including the SPECS Trial** (9:00-10:30 am)
2. **The HALF-PINT Trial; SPIRIT Statement; Trial Registration; CONSORT Statement** (10:45 am-12:15 pm)

Day 2 (January 5, 2027)

3. **More Details on the HALF-PINT Trial; Subgroup Analysis** (9.00-10.30 am)
4. **Meta-Analysis of Glucose Management Trials; PRISMA Statement** (10:45 am-12:15 pm)

Day 3 (January 6, 2027)

5. **The RESTORE Trial; Cluster-Randomized Trials** (9:00-10:30 am)

6. **Secondary Data Analysis; Applications to RESTORE** (10:45 am-12:15 pm)

Day 4 (January 7, 2027)

7. **Propensity Score Analysis and RESTORE** (9:00-10:30 am)
8. **Issues Arising from the Ongoing SHIPSS and PROSpect Trials; Future Directions** (10:45 am-12:15 pm)

Written Exam (January 7, 2027): (13:30-15:00 pm)

We may add seminars by Japanese teachers for each to assist students with difficulty in language/background knowledge

Related readings

SPECS: Agus et al., Tight Glycemic Control versus Standard Care after Pediatric Cardiac Surgery, *New England Journal of Medicine*, 2012; 367:1208-1219. DOI: 10.1056/NEJMoa1206044

HALF-PINT: Agus et al., Tight Glycemic Control in Critically Ill Children, *New England Journal of Medicine*, 2017; 376:729-741. DOI: 10.1056/NEJMoa1612348

RESTORE: Curley et al., Protocolized Sedation vs Usual Care in Pediatric Patients Mechanically Ventilated for Acute Respiratory Failure: A Randomized Clinical Trial, *Journal of the American Medical Association*, 2015; 313:379-389. DOI: 10.1001/jama.2014.18399

Recommended Text: Friedman, Furberg, DeMets, Reboussin, and Granger. *Fundamentals of Clinical Trials*, 5th Edition, Springer, 2015.

Handout of lecture slides will be made available prior to the lectures.

Achievement evaluation

There will be a written final exam about the course content scheduled in the class upon completion of the course.