ARVO EDUCATION COURSE

Saturday, April 27, 2019
8am-12pm
Vancouver Convention Centre
Vancouver, British Columbia, Canada

Statistical methods for correlated eye data

Course organizer

Maureen G Maguire, PhD, FARVO, University of Pennsylvania

Gui-shuang Ying, PhD, University of Pennsylvania

Presentations

Presenters and presentations may change.

8-8:05am

Welcome and Introductions

Maureen G Maguire, PhD, FARVO, University of Pennsylvania

A brief overview of the course presenters and their topics will be provided.

8:05-8:30am

Current approaches to the statistical analysis of correlated eye data and Discussion/Questions

Maureen G Maguire, PhD, FARVO, University of Pennsylvania

Examples of the degree of correlation in measures between eyes of the same person will be discussed. Historical and naive approaches to handling correlated eye data will be described and their shortcomings identified. Appropriate techniques for uncomplicated study designs will be presented.

8:30-9:10am

Analyses for continuous, correlated outcomes in cross-sectional studies and Discussion/Questions

Gui-shuang Ying, PhD, University of Pennsylvania

This presentation will start with the non-model-based analysis approaches (paired t-test, Wilcoxon signed rank test) for correlated continuous eye data under paired design (e.g., two eyes in two different comparison groups) and analysis approaches (e.g., clustered Wilcoxon rank test) for data from unpaired design (e.g., two eyes in the same comparison groups). The presentation will then describe several model-based analysis approaches for continuous correlated eye data from cross-sectional studies, including mixed effects models and marginal models under various covariance structures to account for inter-eye correlation and other covariates (person-specific or eye-specific). The presentation will demonstrate, with SAS statistical software, applications in a study comparing baseline refractive error between one eye with choroidal neovascularization and the unaffected fellow eye, and in a study determining factors associated with visual field in the elderly. The comparisons between these appropriate analysis approaches vs. the inappropriate yet commonly used analysis approaches (e.g., ignore inter-eye correlation, or one-eye analysis) will be made and discussed.

9:10-9:45am

Statistical analysis of binary, correlated outcomes in cross-sectional studies and Discussion/Questions

Robert Glynn, PhD, T.C. Channing School of Public Health, Harvard University

We discuss study designs giving rise to a dichotomous outcome measured in each eye of a study population (e.g. presence of cataract, glaucoma, or diabetic retinopathy), either in a cross-sectional prevalence study, or after follow-up of a fixed time period in a prospective cohort study or clinical trial. We first consider studies with a single, dichotomous predictor variable, such as treatment assignment in a randomized trial, and distinguish situations where the eye and the person are the unit of randomization. Next, we describe methods with multiple independent variables, possibly including both continuous and categorical characteristics. A main focus will be on fitting and interpretation of logistic regression models that appropriately account for the correlation between the outcome in the two eyes of the same person. Real data examples will consider both eye-specific and person-specific covariates as well as the situation when some subjects contribute information from a single eye.

9:45-10am - Morning Break

10-10:40 am

Analyses for continuous, correlated outcomes in longitudinal studies and Discussion/Questions

Bernard Rosner, PhD, T.C. Channing School of Public Health Harvard University

We will discuss the analysis of longitudinal ophthalmic continuous outcome data. There are several types of correlation that need to be taken into account including: (a) cross-sectional correlation between outcomes for fellow eyes at a specific visit; b) longitudinal correlation between outcomes for the same eye over time; (c) longitudinal correlation between outcomes for one eye at a specific visit and the fellow eye at different visits. Both fixed effects, mixed effects, and GEE methods of analysis will be considered for this type of data. Examples will be provided of change in visual acuity data from the CAPT study and the AREDS study, respectively.

10:40-11:15am

Analyses for correlated categorical outcomes in longitudinal studies and Discussion/Questions

Michele Melia, ScM, JAEB Center for Health Research

This module will expand upon the earlier presentation on use of linear mixed models and marginal models for analysis of binary correlated outcomes to longitudinal studies where a binary or categorical outcome is measured in one or both eyes over time. Topics to be covered include: advantages of longitudinal analysis over cross-sectional analysis focusing on a single key time point; exploring the longitudinal data structure; choosing a model; model assumptions; choosing a correlation structure; model fitting and checking; interpretation of results; non-convergence issues; and missing data. All concepts will be illustrated using examples of longitudinal analyses from clinical trials or longitudinal observational studies in ophthalmology.

11:15-11:50am

Survival analyses for time to event outcomes in longitudinal studies and Discussion/Questions

Xiangrong Kong, PhD, Wilmer Eye Institute, Johns Hopkins School of Medicine

The overarching goal of this presentation is to introduce the fundamental statistical concepts, methods and computational tools in analyzing survival (i.e. time-to-event) data in ophthalmological studies involving observations from both eyes of an individual. The presentation will start by reviewing the key terminologies in describing time-to-event data, such as censoring, survivor function and hazard function, as well as reviewing commonly used methods to summarize and analyze survival data (Kaplan-Meier method, logrank tests, and Cox proportional hazards models). The presentation will introduce extended Cox modeling for analysis of correlated time-to-event data (i.e. data available from both eyes). Real-world ophthalmological datasets will be used to illustrate the concepts and methods. Computational tools will also be introduced.

Participants are expected to fulfil the following learning objectives:

- To have a better understanding of situations when time-to-even data may arise in ophthalmological studies and what kinds of scientific interests may be addressed by analysis of time-to-event data.
- To be able to understand and interpret correctly key statistical concepts particularly relevant to time-to-event data analysis, such as censoring, truncation, survivor function, and hazard function.
- To have a basic knowledge of the statistical methods that can be used to analyze correlated time-to-event data.
- To have a basic knowledge of the statistical software tools that can be used for survival data analysis.

11:50 – 12pm - Final questions and answers - All speakers