EPID 766: Analysis of Longitudinal Data from Epidemiological Studies

Graduate Summer Session in Epidemiology

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COURSE DESCRIPTION

It has been popular in epidemiology to conduct longitudinal studies where study participants are followed over time and repeated measurements of interest are obtained. Compared to traditional cross-sectional or case-control studies, longitudinal studies can be more efficient to detect difference of interest, offer more evidence for possible causal inference, etc. However, longitudinal data are likely to be correlated, which presents substantial challenge in analyzing such data. This course will address 1) epidemiologic methods for the design and interpretation of longitudinal studies involving repeated measures and 2) statistical methods appropriate for longitudinal data including generalized estimating equations (GEEs), linear mixed models and generalized linear mixed models. A series of studies will be used to illustrate the major design issues and statistical approaches. Relevant procedures in statistical package SAS will be introduced and appropriate interpretation of results will be emphasized.

MAJOR COURSE OBJECTIVES

1. Realize the unique features of and the methodological implication of analyzing the data from longitudinal studies, as compared to the data from traditional studies.

2. Understand statistical methods/models, particularly linear/generalized linear mixed models and GEE approaches, for analyzing longitudinal data.

3. Master the proper implementation and interpretation of the statistical methods/models for analyzing longitudinal data using SAS.

COURSE COMPETENCIES:

1. Students will be able to identify the characteristics of a disease or a health outcome that warrant longitudinal investigation.

2. Students will be able to design a longitudinal study and to realize the advantages and disadvantages of various design alternatives based on the question of interest.

3. Students will be able to choose an appropriate statistical model and method for a longitudinal data set to conduct and interpret the statistical analysis.
Pre-Requisites: Students are expected to have one or two graduate biostatistics courses on (simple and multiple) linear regression models, categorical data analysis such as logistic regression models and experience of conducting data analysis using statistical software SAS.

GRADING: For those taking the course for a grade, grades will be based on the data analysis class project. Class will be divided to 4 to 5 groups depending on the class size. Each group will pick up a data set and 1) define a scientific question for a continuous and discrete outcome; 2) graph data; 3) conduct a linear mixed analysis and a GEE analysis; 4) present to the class. Students are encouraged to bring their own datasets.

TEXTBOOKS:

1. **Required:** No textbook is required. Lecture notes for this course can be downloaded from [http://www4.stat.ncsu.edu/ dzhang2/epid766/index.html](http://www4.stat.ncsu.edu/dzhang2/epid766/index.html). Other related materials such as SAS programs and data sets can be downloaded from this website too.

2. **Useful website:** The website [www.stat.ncsu.edu/people/davidian/courses/st732/](http://www.stat.ncsu.edu/people/davidian/courses/st732/) contains the lecture notes, examples, SAS programs, etc, from my colleague Prof. Marie Davidian’s course *Applied Longitudinal Data Analysis*. Take a look at this website and you may download the materials you find useful. This will be a very good source for your study and research.


SOFTWARE:


2. The other software *R* can also be downloaded for free.
<table>
<thead>
<tr>
<th>Date</th>
<th>Hour</th>
<th>Topic</th>
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<tbody>
<tr>
<td>Monday</td>
<td>8:30</td>
<td>Introduction and overview</td>
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<tr>
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<td>9:00</td>
<td>Review of studies: cross-sectional studies, prospective cohort studies, retrospective (case-control) studies; motivation of longitudinal studies; formulation of the scientific questions; examples; graphical descriptions; understanding patterns of variation in longitudinal data; within vs. between subject variation, etc.</td>
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<td>10:15</td>
<td>Features of longitudinal data; challenges in analyzing longitudinal data (issues in applying standard linear regression to longitudinal data); methods of analyzing continuous (normal) longitudinal data: two-stage, linear mixed model, generalized estimating equation (GEE).</td>
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<td>11:30</td>
<td>Data analysis projects – Assignment</td>
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<td>Tuesday</td>
<td>8:30</td>
<td>Analyzing continuous (normal) longitudinal data using linear mixed models (Fixed effects vs. random effects, Interpretation of linear mixed models, Issues in choosing random effects and its variance-covariance matrix, Time-varying covariates, Estimates and significance tests)</td>
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<td>9:45</td>
<td>Linear mixed models (continued)</td>
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<td>Break</td>
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<td>11:00</td>
<td>Linear mixed models (continued)</td>
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<td>Wednesday</td>
<td>8:30</td>
<td>Modeling issues: modeling raw data vs. modeling difference, use baseline outcome as a covariate, auto-regression type of modeling, etc.; what to do if mixed model fails: GEE as a rescue, missing data issue.</td>
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<td>9:45</td>
<td>Discussion I – HIV and CD4 paper, Hypertensive Kidney Disease paper (Linear Mixed Model)</td>
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<td>10:45</td>
<td>Break</td>
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<td>11:00</td>
<td>Design issues: recruitment and retention of participants, selection bias, sample size estimation (its relationship with within and between subject variations).</td>
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Thursday  8:30  Discrete data: problems of applying logistic regression to longitudinal binary (binomial) data or Poisson regression to longitudinal count data – GEEs and generalized linear mixed models (GLMMs)

9:30  Break

9:45  GEEs and GLMMs (continued)

10:45  Break

11:00  GEEs and GLMMs (continued)

Friday  8:30  Discussion – Menstrual cycle paper (GEE, linear mixed model) and vasomotor symptoms paper (GLMM)

9:30  Break

9:35  Class project presentations - 3 projects (20 minutes/project)

10:40  Break

10:50  Class project presentations - 2 projects

11:30  Summary and evaluations
DATA ANALYSIS ASSIGNMENT FOR EPID 766

REQUIREMENTS
All individuals taking this course for credit are required to perform the data analysis assignment and to present their results on the last day of the class. Course grades will be based on the this presentation. Individuals who are not taking the course for credit are encouraged but not required to participate.

The class will be divided into 4-5 groups, based on the availability of data sets and interests. To improve efficiency in working in U-M computer systems, UM students are encouraged to distribute themselves among the groups.

Analysis will be preferably be conducted in SAS using Proc Mixed, Proc Genmod, Proc Glimmix and Proc Nlmixed.

COMPUTER ACCESS
WEB site to download class data sets: http://www4.stat.ncsu.edu/~dzhang2/epid766

DATA SETS
Two data sets are available to the class in addition to the ones class participants may have brought with them. One data is from the Framingham study and the other is from a study on substance use and menstrual cycle function.

Please remember that all data sets are for use in this class only and should not be copied for personal use or for further analysis without explicit permission from the investigators.
ASSIGNMENT FOR EPID 766

Monday
1) Define a scientific question from your data set for both a continuous and binary outcome
2) Provide a description of the pattern of change in independent and dependent variables over time – use graphical representation of the data

Tue & Wed
3) Run a linear mixed model analysis on the continuous outcome

Thursday
4) Run a GEE model and GLMM model for the binary outcome

Friday
6) Present to the class