ST 790 Longitudinal Data Analysis

Lecture Notes

M. Davidian

Department of Statistics

North Carolina State University

©2018 by Marie Davidian

Contents

| 1 | Intro | oduction and Motivation | 1 |
|---|-------|---|-----|
| | 1.1 | Objective of this course | 1 |
| | 1.2 | Examples | 2 |
| | 1.3 | Statistical models for longitudinal data | 16 |
| | 1.4 | Outline of the course | 19 |
| 2 | Mod | deling Longitudinal Data | 21 |
| | 2.1 | Introduction | 21 |
| | 2.2 | Data structure and notation | 21 |
| | 2.3 | Conceptual framework for continuous response | 26 |
| | 2.4 | Population-averaged versus subject-specific modeling | 37 |
| | 2.5 | Models for correlation structure | 44 |
| | 2.6 | Exploring mean and correlation structure | 50 |
| | 2.7 | Considerations for discrete response | 59 |
| 3 | Rep | peated Measures Analysis of Variance | 64 |
| | 3.1 | Introduction | 64 |
| | 3.2 | Univariate repeated measures analysis of variance | 66 |
| | 3.3 | Specialized within-individual hypotheses and tests | 83 |
| | 3.4 | Multivariate repeated measures analysis of variance | 94 |
| 4 | Mod | dern Methods: Preliminaries | 102 |
| | 4.1 | Introduction | 102 |
| | 4.2 | Drawbacks of classical methods | 102 |
| | 4.3 | Large sample theory and estimating equations | 105 |
| 5 | Рор | oulation-Averaged Linear Models for Continuous Response | 115 |
| | 5.1 | Introduction | 115 |
| | 5.2 | Model specification | 116 |
| | 5.3 | Maximum likelihood estimation under normality | 131 |
| | 5.4 | Restricted maximum likelihood | 135 |
| | 5.5 | Large sample inference | 142 |

| | 5.6 | Missing data | 157 | |
|---|-------------------------------|--|-----|--|
| 6 | 6 Linear Mixed Effects Models | | | |
| | 6.1 | Introduction | 169 | |
| | 6.2 | Model specification | 170 | |
| | 6.3 | Inference and considerations for missing data | 186 | |
| | 6.4 | Best linear unbiased prediction and empirical Bayes | 190 | |
| | 6.5 | Implementation via the EM algorithm | 198 | |
| | 6.6 | Testing variance components | 201 | |
| 7 | Gen | eralized and Nonlinear Models for Univariate Response | 207 | |
| | 7.1 | Introduction | 207 | |
| | 7.2 | Nonlinear mean-variance models | 208 | |
| | 7.3 | Estimation of mean and variance parameters | 215 | |
| | 7.4 | Large sample results | 221 | |
| 8 | Pop | ulation-Averaged Models and Generalized Estimating Equations | 229 | |
| | 8.1 | Introduction | 229 | |
| | 8.2 | Model specification | 230 | |
| | 8.3 | Linear estimating equations | 237 | |
| | 8.4 | Quadratic estimating equations | 248 | |
| | 8.5 | Large sample inference | 251 | |
| | 8.6 | Modeling issues | 255 | |
| | 8.7 | Missing data | 263 | |
| | 8.8 | Examples | 272 | |
| | 8.9 | Further results for quadratic equations | 276 | |
| 9 | Non | linear and Generalized Linear Mixed Effects Models | 280 | |
| | 9.1 | Introduction | 280 | |
| | 9.2 | Model specification | 281 | |
| | 9.3 | Maximum likelihood | 303 | |
| | 9.4 | Approximate inference based on individual estimates | 307 | |
| | 9.5 | Approximate inference based on linearization | 315 | |
| | 9.6 | "Exact" likelihood inference | 325 | |

| | 9.7 | Examples | 328 | | |
|----------------------|------------------------------|---|-----|--|--|
| 10 Additional Topics | | | | | |
| | 10.1 | Introduction | 333 | | |
| | 10.2 | Bayesian formulation of hierarchical models | 333 | | |
| | 10.3 | Complex nonlinear models | 340 | | |
| | 10.4 | Time-dependent covariates in nonlinear mixed effects models | 345 | | |
| | 10.5 | Multilevel models | 349 | | |
| | 10.6 | Distribution of random effects | 357 | | |
| Αŗ | Appendix A: Fun Matrix Facts | | | | |
| Αŗ | penc | lix B: Notation and Taylor Series | 368 | | |
| Αŗ | pend | lix B: Review of Large Sample Theory | 372 | | |
| Αŗ | pend | lix D: Brief Review of Monte Carlo Simulation | 384 | | |
| Αŗ | pend | lix E: PROC MIXED Syntax | 387 | | |
| Αŗ | pend | lix F: Writing a Data Analysis Report | 390 | | |
| Re | eferer | nces | 396 | | |