The Statistical Analysis of Failure Time Data

### WILEY SERIES IN PROBABILITY AND STATISTICS

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## Second Edition

JOHN D. KALBFLEISCH ROSS L. PRENTICE



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To Sharon and Didi

## Contents

1.	Intr	oduction	1	
	1.1	Failure Time Data, 1		
	1.2	Failure Time Distributions, 6		
	1.3	Time Origins, Censoring, and Truncation, 12		
	1.4	Estimation of the Survivor Function, 14		
	1.5	Comparison of Survival Curves, 20		
	1.6	Generalizations to Accommodate Delayed Entry, 23		
	1.7	Counting Process Notation, 24		
	Bibliographic Notes, 26			
	Exercises and Complements, 28			
2.	Failure Time Models			
	2.1	Introduction, 31		
	2.2	Some Continuous Parametric Failure Time Models, 31		
	2.3	Regression Models, 40		
	2.4	Discrete Failure Time Models, 46		
	Bibliographic Notes, 49			
	Exe	rcises and Complements, 49		
3.	Inference in Parametric Models and Related Topics		52	
	3.1	Introduction, 52		
	3.2	Censoring Mechanisms, 52		
	3.3	Censored Samples from an Exponential Distribution, 54		
	3.4	Large-Sample Likelihood Theory, 57		
	3.5	Exponential Regression, 65		

xi

3.6	Estimation in Log-Linear Regression Models, 68					
3.7	Illustrations in More Complex Data Sets, 70					
3.8	Discrimination Among Parametric Models, 74					
3.9	Inference with Interval Censoring, 78					
3.10	Discussion, 83					
Biblic	ographic Notes, 85					
Exerc	ises and Complements, 87					
Relative Risk (Cox) Regression Models						
4.1	Introduction, 95					
4.2	Estimation of $\beta$ , 99					
4.3	Estimation of the Baseline Hazard or Survivor Function, 114					
4.4	Inclusion of Strata, 118					
4.5	Illustrations, 119					
4.6	Counting Process Formulas, 128					
4.7	Related Topics on the Cox Model, 130					
4.8	Sampling from Discrete Models, 135					
Biblio	ographic Notes, 142					
Exerc	tises and Complements, 144					
Cour	Counting Processes and Asymptotic Theory					
5.1	Introduction, 148					
5.2	Counting Processes and Intensity Functions, 149					
5.3	Martingales, 157					
5.4	Vector-Valued Martingales, 164					
5.5	Martingale Central Limit Theorem, 165					

- 5.6 Asymptotics Associated with Chapter 1, 167
- 5.7 Asymptotic Results for the Cox Model, 172
- 5.8 Asymptotic Results for Parametric Models, 178
- 5.9 Efficiency of the Cox Model Estimator, 181
- 5.10 Partial Likelihood Filtration, 188

Bibliographic Notes, 189

Exercises and Complements, 190

Likelihood Construction and Further Resul
---

- 6.1 Introduction, 193
- 6.2 Likelihood Construction in Parametric Models, 193
- 6.3 Time-Dependent Covariates and Further Remarks on Likelihood Construction, 196

4.

5.

193

	6.4	Time Dependence in the Relative Risk Model, 200		
	6.5	Nonnested Conditioning Events, 208		
	6.6	Residuals and Model Checking for the Cox Model, 210		
	Bibliographic Notes, 212			
	Exerc	ises and Complements, 214		
7.	Rank	Regression and the Accelerated Failure Time Model	218	
	7.1	Introduction, 218		
	7.2	Linear Rank Tests, 219		
	7.3	Development and Properties of Linear Rank Tests, 224		
	7.4	Estimation in the Accelerated Failure Time Model, 235		
	7.5	Some Related Regression Models, 241		
	Biblio	ographic Notes, 242		
	Exercises and Complements, 244			
8.	8. Competing Risks and Multistate Models		247	
	8.1	Introduction, 247		
	8.2	Competing Risks, 248		
	8.3	Life-History Processes, 266		
	Biblio	ographic Notes, 273		
	Exerc	ises and Complements, 275		
9. Modeling and Analysis of Recurrent Eve		ling and Analysis of Recurrent Event Data	278	
	9.1	Introduction, 278		
	9.2	Intensity Processes for Recurrent Events, 280		
	9.3	Overall Intensity Process Modeling and Estimation, 282		
	9.4	Mean Process Modeling and Estimation, 286		
	9.5	Conditioning on Aspects of the Counting Process History, 297		
	Bibliographic Notes, 299			
	Exerc	ises and Complements, 300		
10.	Analysis of Correlated Failure Time Data		302	
	10.1	Introduction, 302		
	10.2	Regression Models for Correlated Failure Time Data, 303		
	10.3	Representation and Estimation of the Bivariate Survivor Function, 308		
	10.4	Pairwise Dependency Estimation, 311		
	10.5	Illustration Australian Turin Data 212		

ix

	10.6	Approaches to Nonparametric Estimation of the Bivariate Survivor Function, 315			
	10.7	Survivor Function Estimation in Higher Dimensions, 322			
	Biblio	graphic Notes, 323			
		ises and Complements, 324			
11.	Additional Failure Time Data Topics		328		
	11.1	Introduction, 328			
	11.2	Stratified Bivariate Failure Time Analysis, 329			
	11.3	Fixed Study Period Survival Studies, 334			
	11.4	Cohort Sampling and Case-Control Studies, 337			
	11.5	Missing Covariate Data, 343			
	11.6	Mismeasured Covariate Data, 346			
	11.7	Sequential Testing with Failure Time Endpoints, 348			
	11.8	Bayesian Analysis of the Proportional Hazards Model, 352			
	11.9	Some Analyses of a Particular Data Set, 361			
	Biblic	graphic Notes, 369			
	Exerc	ises and Complements, 371			
Glo	Glossary of Notation				
App	ændix	A: Some Sets of Data	378		
Арр	endix	B: Supporting Technical Material	396		
Bib	Bibliography Author Index				
Aut					
Sub	Subject Index				

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## Preface

As in the first edition of this book, the purpose of this revision is the collection and unified presentation of statistical models and methods for the analysis of failure time data. The motivation for this effort continues to derive primarily from biomedical contexts and, to a lesser extent, industrial life-testing purposes.

A voluminous literature on failure time analysis and the closely related event history analysis has developed in the more than 20 years since the publication in 1980 of the first edition of this book. The theoretical underpinnings of the methods described previously have been strengthened in the interim, and many important generalizations and related developments have taken place. Counting process methods and related martingale convergence results have led to precise and general asymptotic results for tests and estimators under key classes of failure time models and important censoring and truncation mechanisms. These developments have also contributed to the formulation of broader classes of models and methods.

An important challenge in developing this revision was to preserve the feature of a fairly elementary and classical likelihood-based presentation of failure time models and methods while integrating the counting process notation and related theory. This we have done by using classical notation and descriptions throughout the first four chapters of the revision while introducing the reader to key estimating functions and estimators in notation involving counting processes and stochastic integration. These chapters deal with survivor function estimation and comparison of survival curves (Chapter 1); statistical models for failure time distributions, including parametric and semiparametric regression models (Chapter 2); testing and estimation in parametric regression models under right censoring and other selected censoring schemes (Chapter 3); and testing and estimation under the semiparametric Cox regression model (Chapter 4). These chapters, along with parts of Chapters 6 to 8, can form the basis for an introductory graduate-level biostatistics or statistics course. We have tried to keep a solid contact with the first edition in many places and, for example, have retained illustrations from that edition where they still seemed to make the relevant points well.

A new Chapter 5 provides a more systematic introduction to counting processes and martingale convergence results and describes how they can be applied to yield

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asymptotic results for many of the statistical methods discussed in the first four chapters. The treatment is somewhat less formal than in some more specialized books, but presents the reader with a development and summary of the main ideas and a good basis for further investigation and study.

The remainder of the book uses the notation from counting processes and stochastic integrals where it is helpful, but continues to emphasize the likelihood basis for testing and estimation procedures. Like Chapter 5 in the first edition, Chapter 6 is devoted to general concepts of likelihood and partial likelihood construction, especially in relation to time-dependent and evolving covariate histories. We also provide an example in which martingale methods do not allow the development of asymptotic results because the conditioning events are not nested in time. Like our previous Chapter 6, Chapter 7 is devoted to the semiparametric log-linear or accelerated failure time model. Over the past two decades much effort has been devoted to regression estimation under this model, to the point where it can provide a practical alternative to the Cox model. Like our previous Chapter 7, Chapters 8 through 10 are devoted to aspects of multivariate failure time data analysis, including competing risk and multistate failure time modeling and estimation (Chapter 8), recurrent event modeling and estimation (Chapter 9), and correlated failure time methods (Chapter 10). Aside from a part of Chapter 8, most of the material in these chapters reflects developments since the first edition was published. Martingale convergence results are applicable to some of the estimating functions considered in these chapters, but others rely on empirical process methods. The latter methods can largely subsume the martingale methods, but we have not attempted comprehensive coverage here. Chapter 11 is devoted to more specialized topics. We have retained some of the material from our original Chapter 8 while providing a description of methods for such topics as risk set sampling, missing covariate data, mismeasured covariate data, sequential testing and estimation, and Bayesian methods, mostly in the context of the Cox model. The revision as a whole can serve as the textbook for a more advanced graduate course in biostatistics or statistics.

With the vast literature that has developed on failure time analysis, we have had to be selective in both the scope and depth of our coverage. We have chosen not to provide in-depth coverage of probability theory that is relevant to the asymptotic methods and results discussed, nor, except for some general comments in Appendix B, have we attempted to include a description of how available statistical software packages can or cannot be used to implement the various methods. We have chosen to emphasize some statistical models and approaches that séem to us to be of particular importance, to stress the ideas behind their development and application, and to provide some worked examples that illustrate their use.

To augment the usefulness of this revision as a graduate text, we have included a set of exercises at the end of each chapter. A number of these problems introduce the reader to additional pertinent failure time literature. As before, we have used references sparingly, especially in the early chapters, and bibliographic notes are provided at the close of each chapter. For historical reasons we have retained most of bibliographic notes from the original version, but we have augmented them with important recent references for each failure time topic. PREFACE

There are a number of books on failure time methods that nicely complement this work and provide more comprehensive coverage of specific topics. For example, Lawless (1982) provides extensive coverage of parametric failure time models and estimation procedures; Cox and Oakes (1984) provide a concise and readable account of a range of failure time data topics; Fleming and Harrington (1991) provide a rigorous presentation of Cox regression methods and selected other failure time topics with considerable attention to model checking procedures; Andersen et al. (1993) give a comprehensive compendium of failure time and event history analysis methods with emphasis on counting processes. Andersen et al. (1993) provide additional material on a number of the topics discussed here. Books by Collett (1994) and Klein and Moeschberger (1997) provide relatively less technical accounts of the methods for key failure time topics. Collett includes a presentation of computer software options. Therneau and Grambsch (2000) discuss the implementation of failure time methods using SAS and S-Plus and provide a number of detailed illustrations with particular attention to model building and testing. Hougaard (2000) presents the first book dedicated to multivariate failure time methods. His book nicely complements our Chapters 8 through 10, with a greater emphasis on random effects or frailty models.

We would like to express our thanks to colleagues and to former and current students who have helped to shape our understanding of failure time analysis issues and methods. Their ideas and efforts have helped to inform this presentation.

> JOHN D. KALBFLEISCH ROSS L. PRENTICE

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