

# Probation review report

*Alessandro Gasparini*

*2017-08-01*



# Contents

<b>Introduction</b>	<b>5</b>
<b>1 Introduction to survival analysis</b>	<b>7</b>
<b>2 Survival models with random effects</b>	<b>9</b>
<b>3 Joint models for longitudinal and survival data</b>	<b>11</b>
<b>4 Computational challenges in survival models with random effects</b>	<b>13</b>
<b>5 Simulation study: accuracy of Gaussian quadrature</b>	<b>15</b>
<b>6 Simulation study: impact of misspecification in survival models with shared frailty terms</b>	<b>17</b>
<b>7 Exploring results from simulation studies interactively</b>	<b>19</b>
<b>8 Informative visiting process</b>	<b>21</b>
<b>9 Future research developments</b>	<b>23</b>
<b>10 Personal development</b>	<b>25</b>
10.1 Supervisory meetings . . . . .	25
10.2 Training and courses . . . . .	25
10.3 Conferences . . . . .	26
<b>A Slides</b>	<b>29</b>
<b>B Manuscript</b>	<b>31</b>



# Introduction

This report presents the work I have done during my first year as a PhD student at the Department of Health Sciences, University of Leicester, under the supervision of Dr. Michael Crowther and Prof. Keith Abrams.

I will begin by briefly introducing the topic of survival analysis in Chapter 1. Second, I will introduce survival models with random effects (e.g. frailties, in the simplest form) and joint models for longitudinal and time-to-event data in Chapters 2 and 3, respectively. Computational challenges that survival models with random effects and joint models pose are presented in Chapter 4. Third, I will present the results of two simulation studies in Chapters 5 and 6; the first simulation study investigates the accuracy of quadrature methods when approximating analytically intractable terms, while the second simulation study investigates the impact of model misspecification in survival models with shared frailty terms. Fourth, I will introduce an interactive tool I have been developing to aid the dissemination of results from simulation studies in Chapter 7. Then, I will introduce the problem of informative visiting process in clinical research using healthcare consumption data in Chapter 8, and how we aim to evaluate and compare the different approaches that have been proposed and utilised in literature to tackle such problem in Chapter 9. Finally, I will briefly summarise the training and personal development activities I have participated to during the first year of my PhD in Chapter 10.

This work is licensed under a Creative Commons Attribution-ShareAlike 4.0 International License, and can be accessed online at <https://ellessenne.github.io/prr/>.



## Chapter 1

# Introduction to survival analysis





## Chapter 2

# Survival models with random effects



## Chapter 3

# Joint models for longitudinal and survival data



## Chapter 4

# Computational challenges in survival models with random effects



## Chapter 5

# Simulation study: accuracy of Gaussian quadrature





## Chapter 6

# Simulation study: impact of misspecification in survival models with shared frailty terms



## Chapter 7

# Exploring results from simulation studies interactively



## Chapter 8

# Informative visiting process



## Chapter 9

# Future research developments





# Chapter 10

## Personal development

In this chapter I will introduce and briefly discuss the personal development activities I carried out during the first year of my PhD. In particular, I will present the supervisory meetings, training courses, and conferences I attended.

### 10.1 Supervisory meetings

I have been meeting my supervisors at least once a month for formal supervisory meetings, with summaries produced and shared between us; a comprehensive list of supervisory meetings is available on PROSE (<https://prose.le.ac.uk>). Additionally, we held informal meetings to discuss developments and more urgent matters more often, whenever it was needed and every week on average.

### 10.2 Training and courses

I have attended a wide variety of courses during my first year, both externally and internally to the University of Leicester. The external courses I attended are:

- *Efficient R Programming*, on November 8<sup>th</sup> 2016, organised by the Royal Statistical Society in London. The instructor was Dr. Colin Gillespie, from the University of Newcastle, United Kingdom, and Jumping Rivers. The course covered how to program efficiently with R; in particular, it covered common pitfalls when writing R code, code profiling, RCpp, and parallel programming. General hints and tips were provided.
- *Introduction to causal inference*, on April 25<sup>th</sup> and 26<sup>th</sup> 2017, organised by the Biostatistics Research Group at the University of Leicester and delivered by Dr. Arvid Sjölander from Karolinska Institutet, Stockholm, Sweden. The course provided foundational concepts of causal inference such as the difference between association and causation, the counterfactual framework, exchangeability, directed acyclic graphs, methods for estimating a causal effect, etc. Additionally, it provided an introduction to more advanced methods such as instrumental variables and Mendelian randomisation.

- *Using simulation studies to evaluate statistical methods*, on May 22<sup>nd</sup> 2017, organised by University College London. The course was delivered by Dr. Tim Morris, Prof. Ian White and Dr. Michael Crowther, and it covered the rationale for using simulation studies, important concepts to keep in mind when planning a simulation study, computational tools, estimates of uncertainty, and tools for improving reporting and dissemination.
- Workshop on *Joint modelling of longitudinal and time-to-event data with R*, on July 5<sup>th</sup>, 2017, organised by the Department of Biostatistics of the University of Liverpool. The course was delivered by Dr. Graeme Hickey, and provided an introduction to joint models of longitudinal and survival data, including extensions to incorporate competing risks and multiple longitudinal processes and a practical session using R.

I have attended a few courses within the University and not offered on PROSE; specifically, I attended a course on *Time series analysis with R* (November 10<sup>th</sup>, 2016), a course on *Data visualisation* (November 15<sup>th</sup>, 2016), and a course on *High performance computing at Leicester* (February 8<sup>th</sup>, 2017). The latter was particularly important, as it allowed me to make better use of the high-performance computing facilities offered by the University. I also attended the *Preparing to teach in higher education* workshop, strand A (July 24<sup>th</sup> and 27<sup>th</sup> 2017).

Additionally, I have attended the following PROSE training sessions to develop personal and communication skills in research settings. These are listed below:

- *Planning your literature search*, October 21<sup>st</sup> 2016;
- *Conducting your literature search*, October 25<sup>th</sup> 2016 ;
- *Assertiveness*, November 14<sup>th</sup> 2016;
- *Introduction to critical thinking*, December 15<sup>th</sup> 2016;
- *Presentations A: Fundamentals of an effective presentation*, January 30<sup>th</sup> 2017;
- *Communication in research and other work settings*, January 31<sup>st</sup> 2017;
- *Enhancing your digital profile*, February 2<sup>nd</sup> 2017;
- *Saying it with your abstract*, February 10<sup>th</sup> 2017;
- *Designing a poster*, February 27<sup>th</sup> 2017;
- *Leadership in research and other work environments*, February 28<sup>th</sup> 2017;
- *Preparing for the probation review (Physical natural and medical sciences)*, May 30<sup>th</sup> 2017.

### 10.3 Conferences

I have attended a number of conferences during this year, in which I delivered the following oral presentations:

- Survival Analysis for Junior Researchers conference, held in Leicester, UK, on April 5<sup>th</sup> and 6<sup>th</sup> 2017. I delivered a talk titled *Direct likelihood maximisation using numerical quadrature to approximate intractable terms*;

- Statistical Analysis of Multi-Outcome Data (SAM) conference, held in Liverpool, UK, on July 3<sup>rd</sup> and 4<sup>th</sup> 2017. I delivered a talk titled *Impact of model misspecification in survival models with frailties*;
- Annual Conference of the International Society for Clinical Biostatistics conference, held in Vigo, Spain, on July 9<sup>th</sup> to July 13<sup>th</sup> 2017. I delivered two talks: a titled *Impact of model misspecification in survival models with frailties* during the main conference, and a talk titled *Exploring results from simulation studies interactively* during the Students' Day organised on July 13<sup>th</sup>.

Additionally, I delivered an oral presentation on previous work external to my PhD project during the 54<sup>th</sup> ERA-EDTA Congress held in Madrid, Spain, between June 3<sup>rd</sup> and June 6<sup>th</sup>. The ERA-EDTA Congress is the main conference in the field of Nephrology in Europe, with approximately 10,000 participants in 2017. I delivered my presentation, titled *Inappropriate prescription of nephrotoxic drugs to individuals with chronic kidney disease*, to an audience of clinicians, epidemiologists, clinical researchers, and other stakeholders.



# Appendix A

## Slides



**Appendix B**

**Manuscript**





# Bibliography