



Universiteit
Leiden
The Netherlands

Modelling long term survival with non-proportional hazards

Perperoglou, A.

Citation

Perperoglou, A. (2006, October 18). *Modelling long term survival with non-proportional hazards*. Retrieved from <https://hdl.handle.net/1887/4918>

Version: Corrected Publisher's Version

License: [Licence agreement concerning inclusion of doctoral thesis in the Institutional Repository of the University of Leiden](#)

Downloaded from: <https://hdl.handle.net/1887/4918>

Note: To cite this publication please use the final published version (if applicable).

Contents

1	Introduction	1
1.1	The Cox proportional hazards model	2
1.2	Time varying effects models	4
1.3	Reduced-Rank hazard regression	5
1.4	Frailty models	6
1.5	Relaxed Burr model	8
1.6	Cure rate mixture models	9
1.7	Overdispersion modelling with individual deviance effects and penalized likelihood	9
1.8	Software	10
1.9	Submission and publication	11
2	Reduced-rank hazard regression	13
2.1	Introduction	13
2.2	Time varying effects and frailty models	15
2.2.1	Cox model with time varying effects of the covariates	15
2.2.2	Frailty models	16
2.2.3	Reduced-rank regression	17
2.2.4	Estimation	18
2.2.5	Choice of rank and time functions	19
2.3	Application to ovarian cancer patients	20
2.3.1	Comparison between the different models	26
2.4	Discussion	27
3	A fast routine for fitting Cox models with time varying effects	33
3.1	Introduction	33
3.2	Cox model with time varying effects of the covariates	36
3.3	Reduced-Rank Hazard Regression	37
3.4	Description of the software	39
3.5	Applications	41
3.5.1	Survival of breast cancer patients	41
3.5.2	Survival of ovarian cancer patients	44

3.5.3	Simulated data	47
3.6	Discussion	49
4	A relaxation of the Gamma frailty (Burr) model.	51
4.1	Introduction	51
4.2	Burr model and autocorrelated frailties	53
4.2.1	Extension from the simple frailty model	54
4.3	A relaxation of the Burr model	55
4.3.1	Estimation	55
4.3.2	Properties	56
4.4	Simulations	57
4.5	Applications	59
4.6	Discussion	65
4.7	Appendix	68
5	Approaches in modelling long term survival	69
5.1	Introduction	69
5.2	IASO breast cancer data and proportional hazards analysis	71
5.3	Cox models with time varying effects of the covariates	73
5.4	Frailty models	79
5.5	Cure models	83
5.6	Assessment of model fitting and evaluation of uncertainty	85
5.6.1	Use of pseudo-observations	85
5.6.2	Brier Scores	86
5.7	Comparison	87
5.7.1	Survival plots	87
5.7.2	Assessment of predictive value	89
5.8	Discussion	93
6	Overdispersion Modelling with Individual Deviance Effects and Penalized Likelihood	97
6.1	Introduction	97
6.2	Penalized Regression with Individual Deviance Effects	100
6.2.1	Smoothing with P-splines and PRIDE	102
6.2.2	Binomial data	102
6.2.3	Smoothing of life tables	102
6.3	Inference	103
6.3.1	Optimal penalty weights	103
6.4	Efficient computation	104

CONTENTS

6.5	Applications	105
6.5.1	Number of faults in fabric rolls	105
6.5.2	Comparison of gynaecological practices	107
6.5.3	Digit preference in demographic data	108
6.5.4	Simulation studies	111
6.5.5	Survival of Mediterranean flies	111
6.6	Discussion	114
7	Discussion	119
A	The coxvc_1-1-1 package	123
A.1	Introduction	123
A.2	Statistical background	123
A.3	Examples	124
	Bibliography	135
	Summary	143
	Sammenvatting	145
	Curriculum Vitae	149

