A novel approach to competing risks analysis using case-base sampling

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Acknowledgements

This project is joint work with:

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- Olli Saarela (U. Toronto)
- Jim Hanley

Introduction

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  - A **smooth** absolute risk curve.

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  - E.g. Fine-Gray model.

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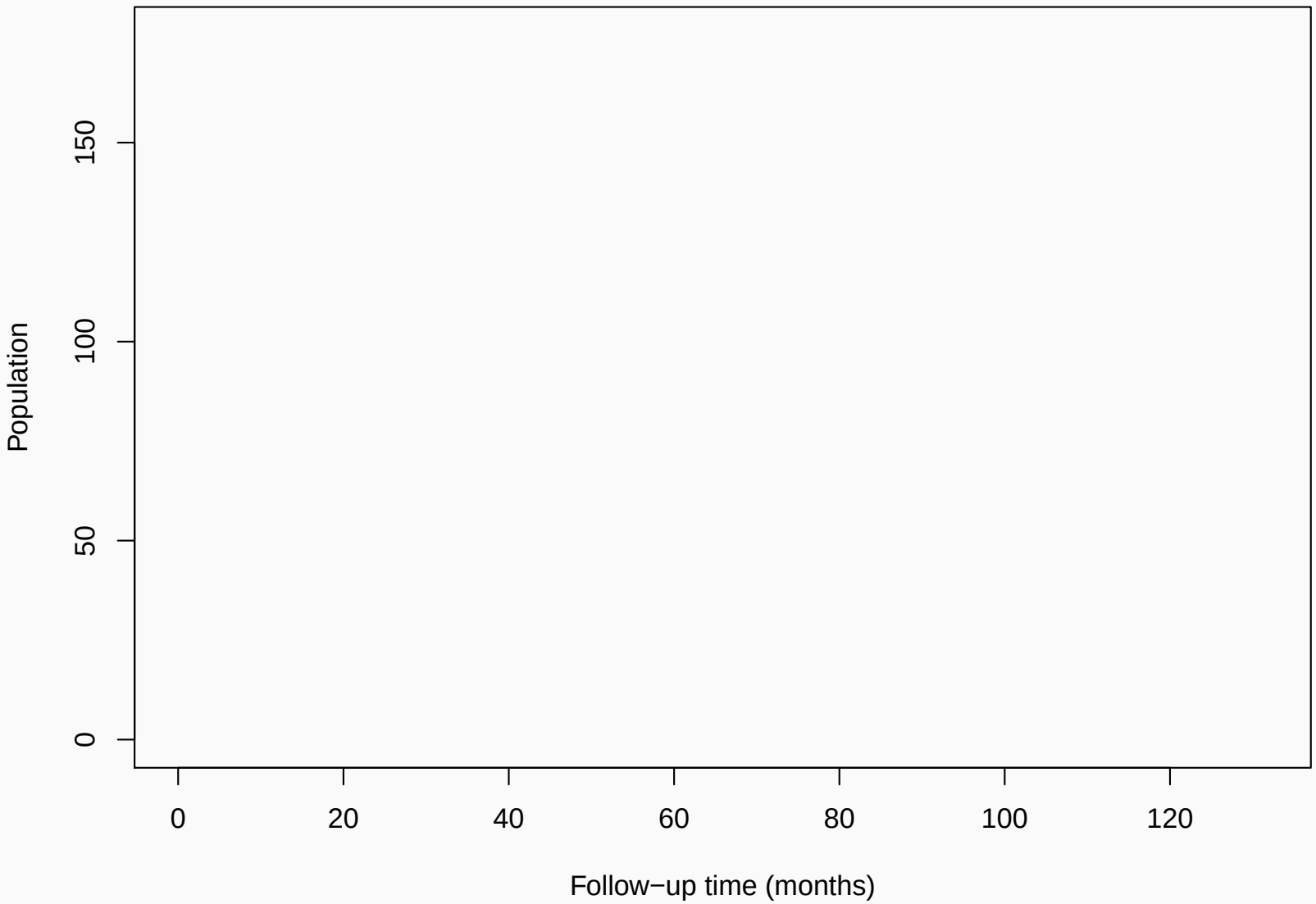
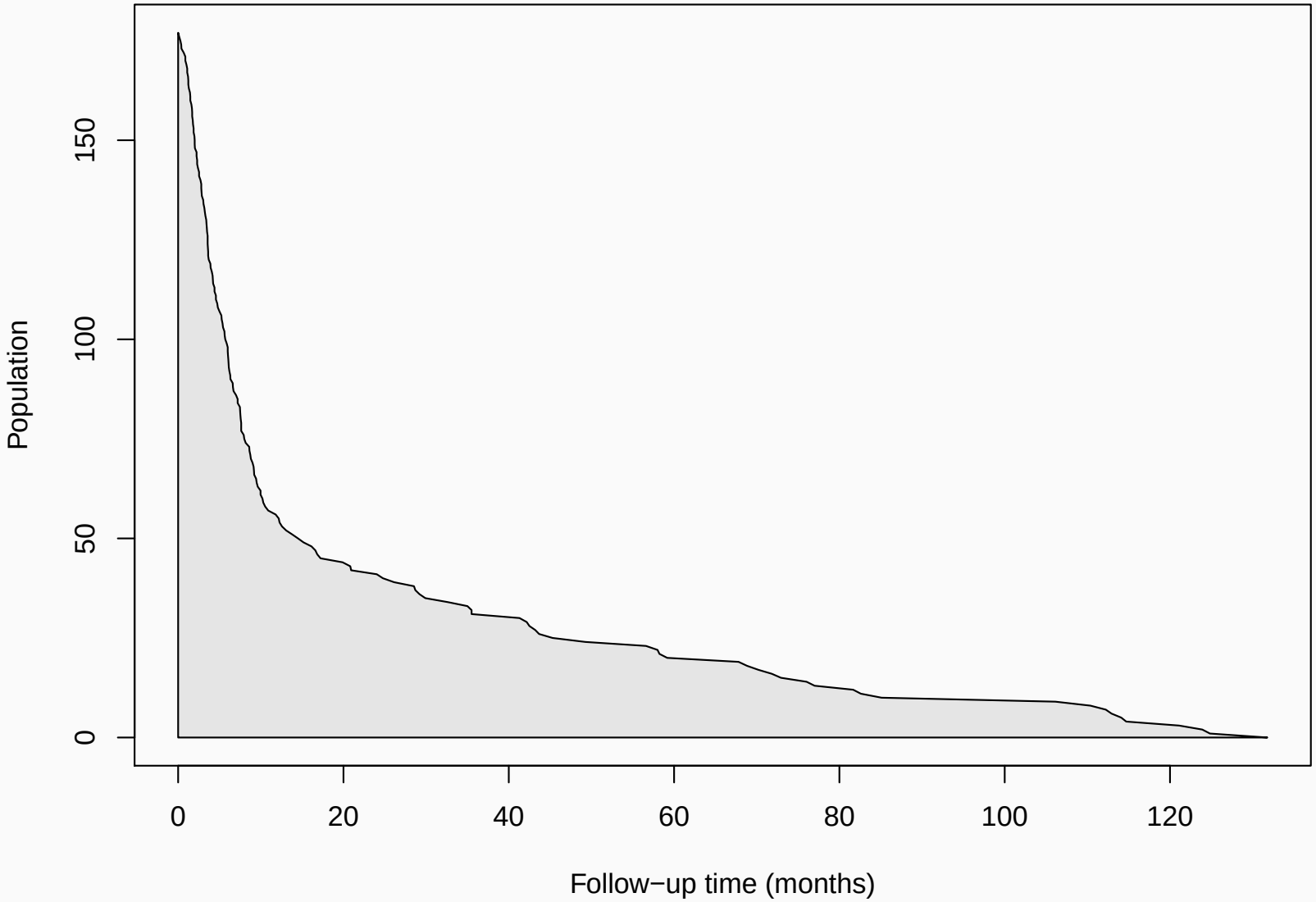
This method is currently available in the R package `casebase` on CRAN.

See also our website: http://sahirbhatnagar.com/casebase/

Case-base sampling


Population
0
50
100
150
0
20
40
60
80
100
120
Follow−up time (months)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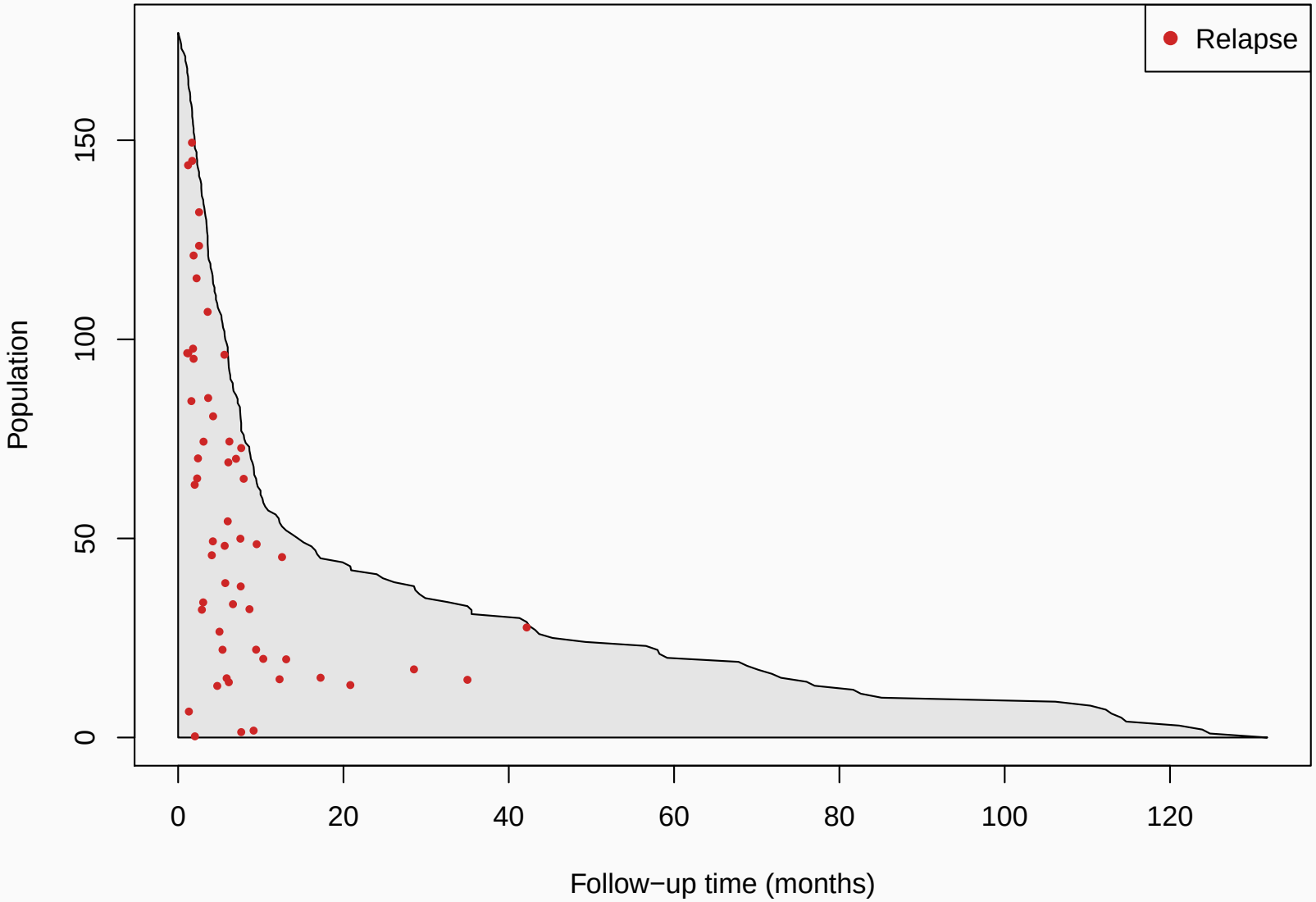
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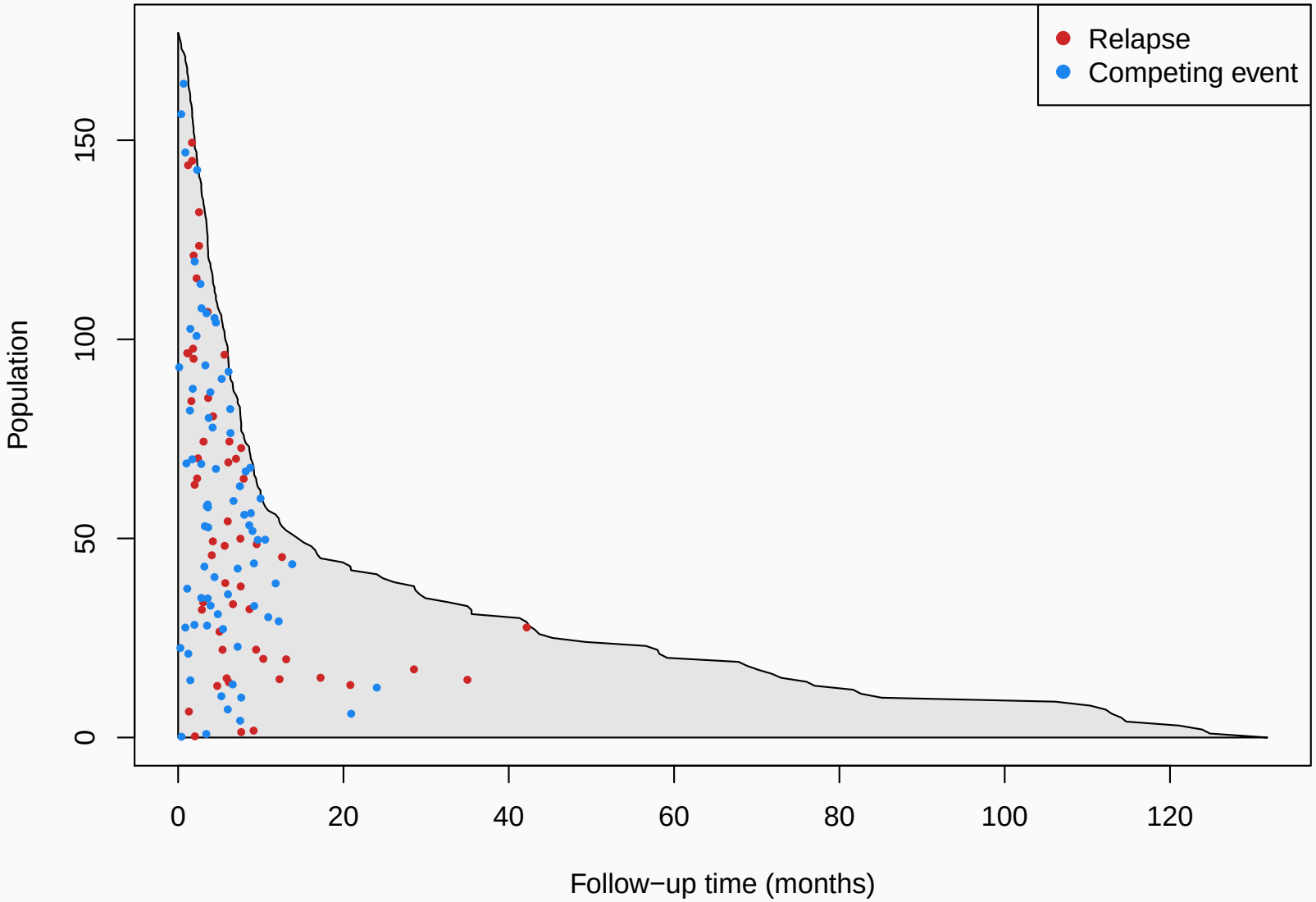
Relapse
Competing event
Population
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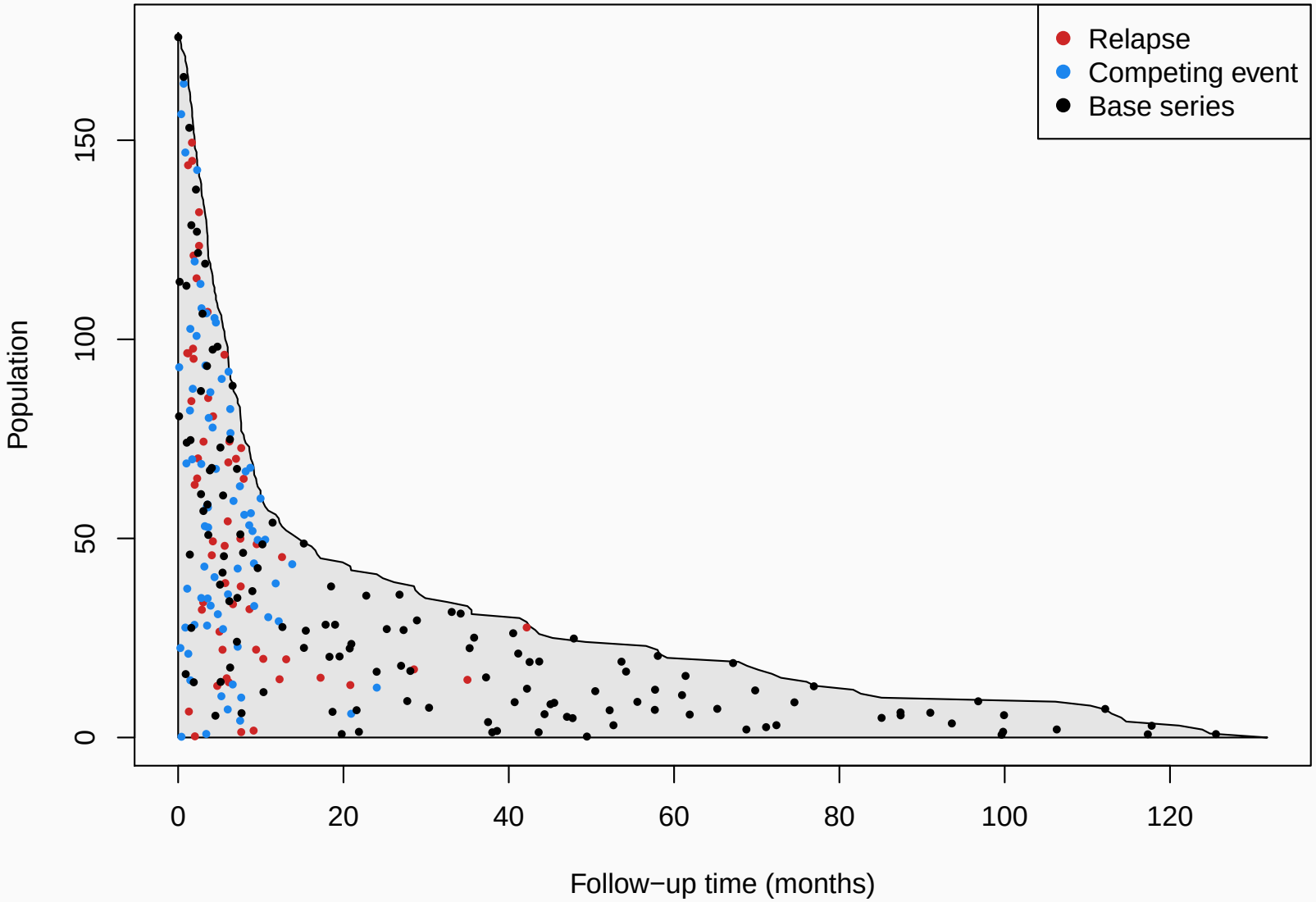
Follow−up time (months)


Relapse
Competing event
Base series
Population
0
50
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Follow−up time (months)

Case-base sampling

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    - The sampling process is taken into account using an offset term.
- By sampling a large base series, the information loss eventually becomes negligible.
- This framework can easily be used with time-varying covariates (e.g. time-varying exposure).

Theoretical details

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  - At most one event type can occur.
- Non-informative censoring.
- Case-base sampling occurs following a non-homogenous Poisson process with hazard $\rho(t)$.

Likelihood

Each person-moment's contribution to the likelihood is of the form:

$$\prod_{j=1}^{m} \frac{\lambda_j(t)^{dN_j(t)}}{\rho(t) + \sum_{j=1}^{m} \lambda_j(t)}.$$

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This is reminiscent of a multinomial likelihood, with offset $\log(1/\rho(t))$**.**

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Implication: All the GLM machinery (e.g. deviance tests, information criteria, regularization) is available to us.

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- Weibull: $g(t; \alpha) = \alpha \log t$.

Simulation study

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- We simulate 1000 datasets from an exponential and a Gompertz family.
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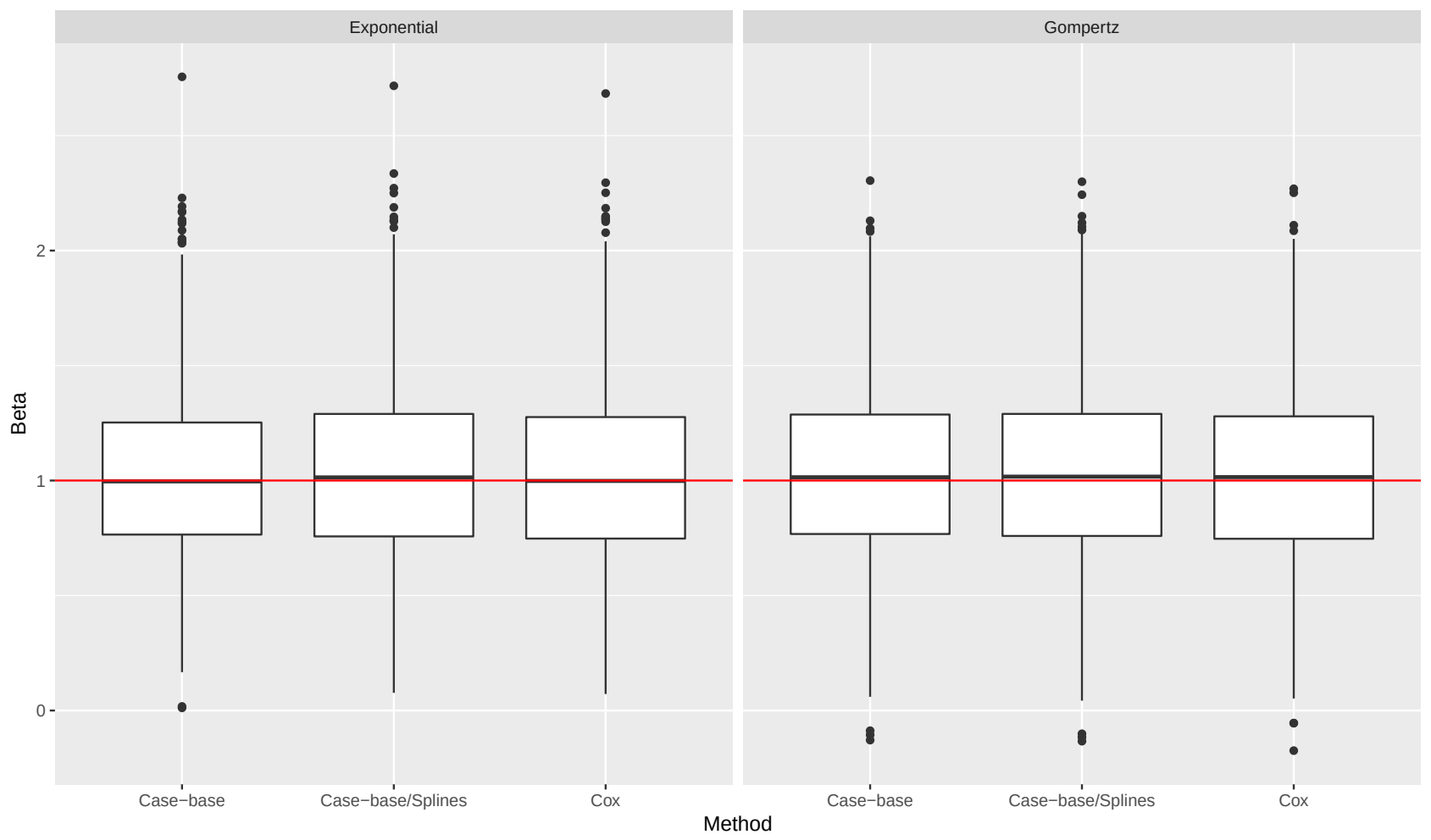
- Random censoring
- We compare case-base with a correctly specified family, case-base with splines, and Cox regression.

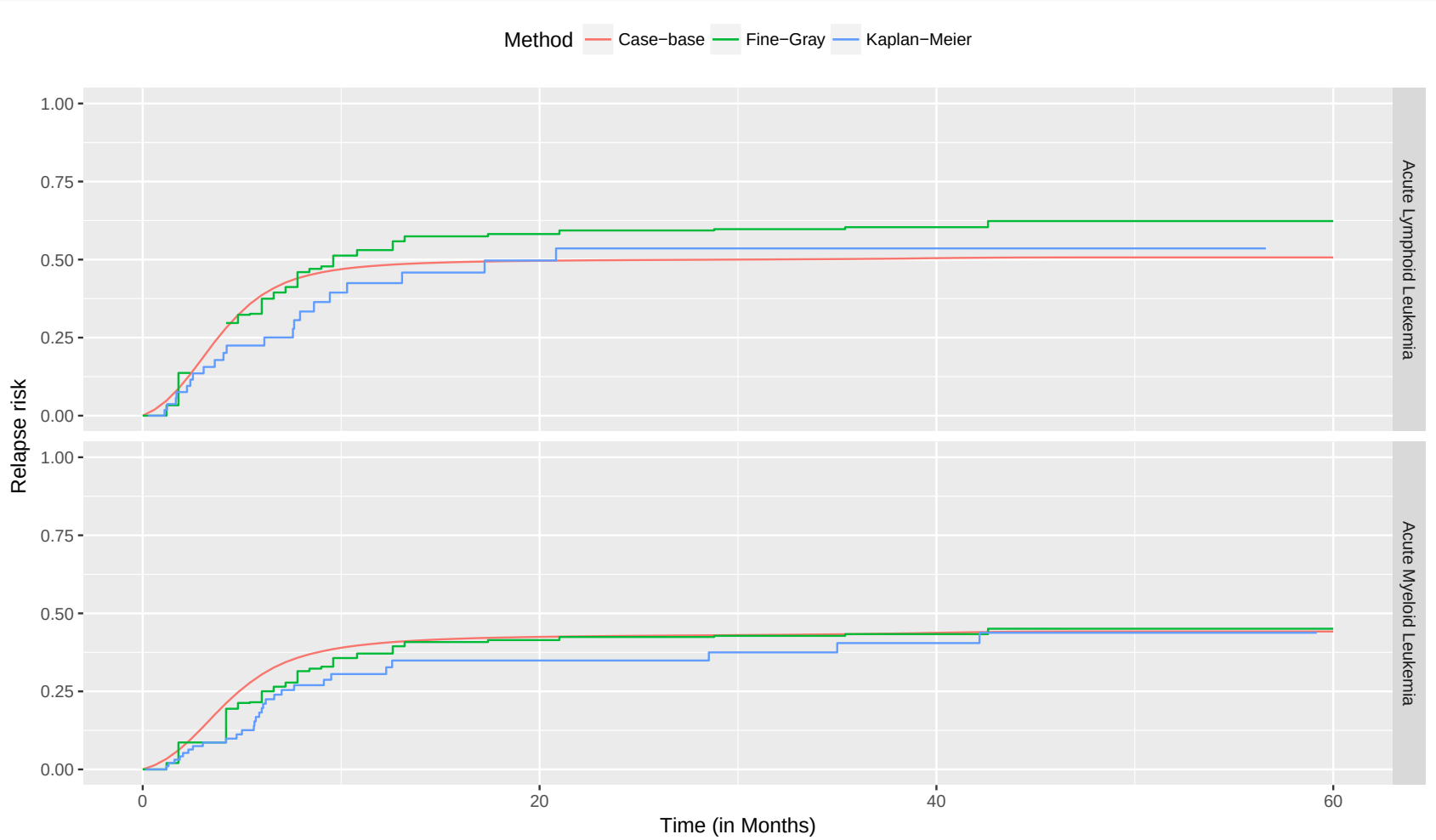
Simulation results



Data analysis

Data

Variable description	Statistical summary
Sex	M=Male (87)
	F=Female (72)
Disease	ALL (59)
	AML (100)
Phase	CR1 (43)
	CR2 (40)
	CR3 (10)
	Relapse (65)
Type of transplant	BM+PB (15)
	PB (144)
Age of patient (years)	16–62
	33 (IQR 19.5)
Failure time (months)	0.13–131.77
	20.28 (30.78)
Status indicator	0=censored (40)
	1=relapse (49)
	2=competing event (70)



Absolute risk for female patient, median age, in relapse at transplant (stem cells from peripheral blood).

Model fit

	Case-base		Cox regression	
Variable	Hazard ratio	95% CI	Hazard ratio	95% CI
Sex	0.64	(0.35, 1.20)	0.75	(0.42, 1.35)
Disease	0.54	(0.27, 1.07)	0.63	(0.34, 1.19)
Phase CR2	1.00	(0.37, 2.70)	0.95	(0.36, 2.51)
Phase CR3	1.25	(0.24, 6.53)	1.38	(0.28, 6.76)
Phase Relapse	4.71	(2.11, 10.54)	4.06	(1.85, 8.92)
Source	1.89	(0.40, 8.99)	1.49	(0.32, 6.85)
Age	0.99	(0.97, 1.02)	0.99	(0.97, 1.02)

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- We are explicitely modeling time.
- We can test the significance of covariates.

References I

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Fitting smooth-in-time prognostic risk functions via logistic regression.
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Questions or comments?

For more details, visit
http://sahirbhatnagar.com/casebase/