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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- In some settings, the analysis is complicated by the presence of competing events (e.g. complications due to bone-marrow transplant in a study of acute leukemia recurrence).
- A proper estimation of absolute risks needs to take these competing events into account.

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- A common alternative is the Cox proportional hazards model.
    - However, this model leads to a two-step procedure for estimating the hazard function.

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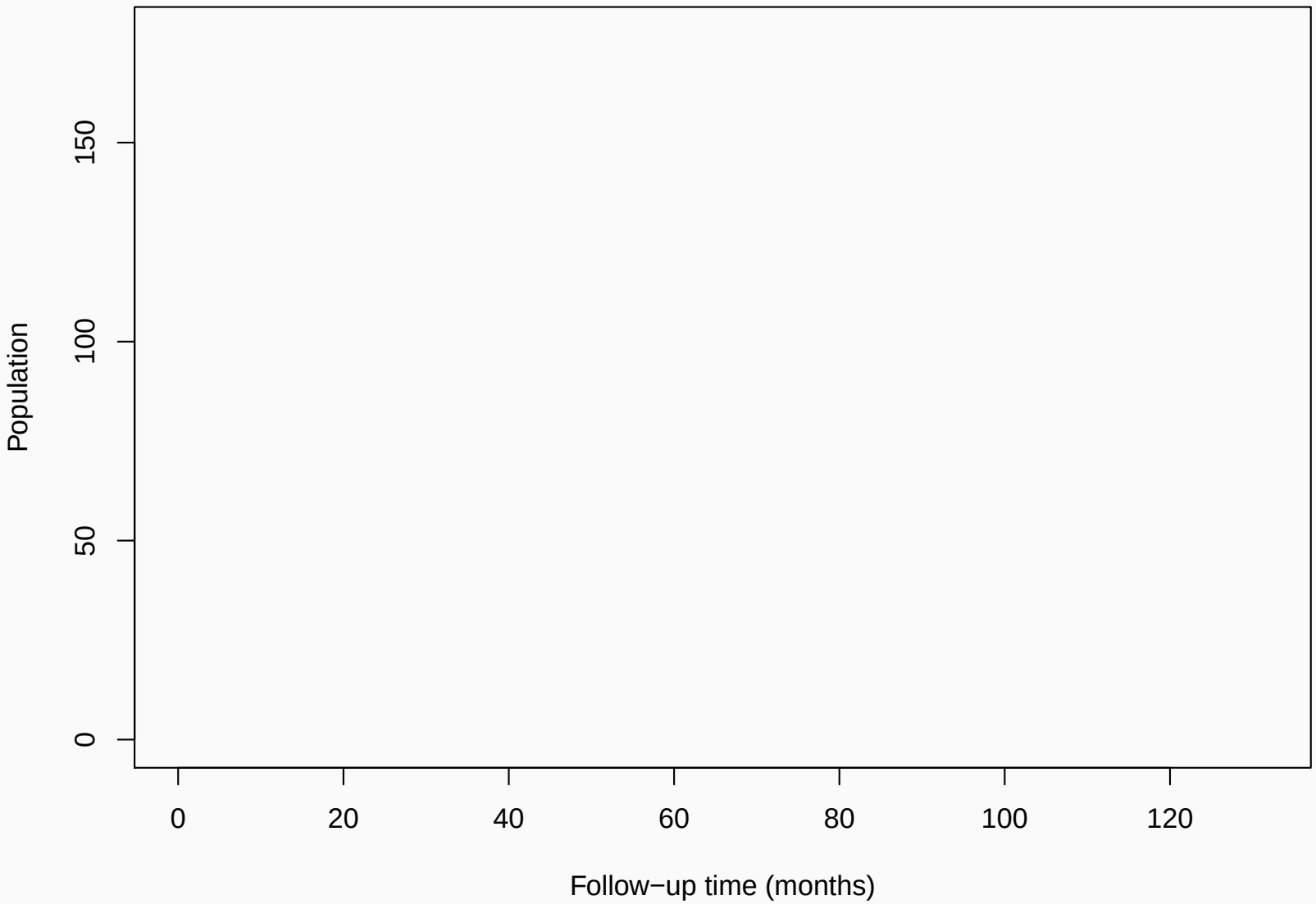
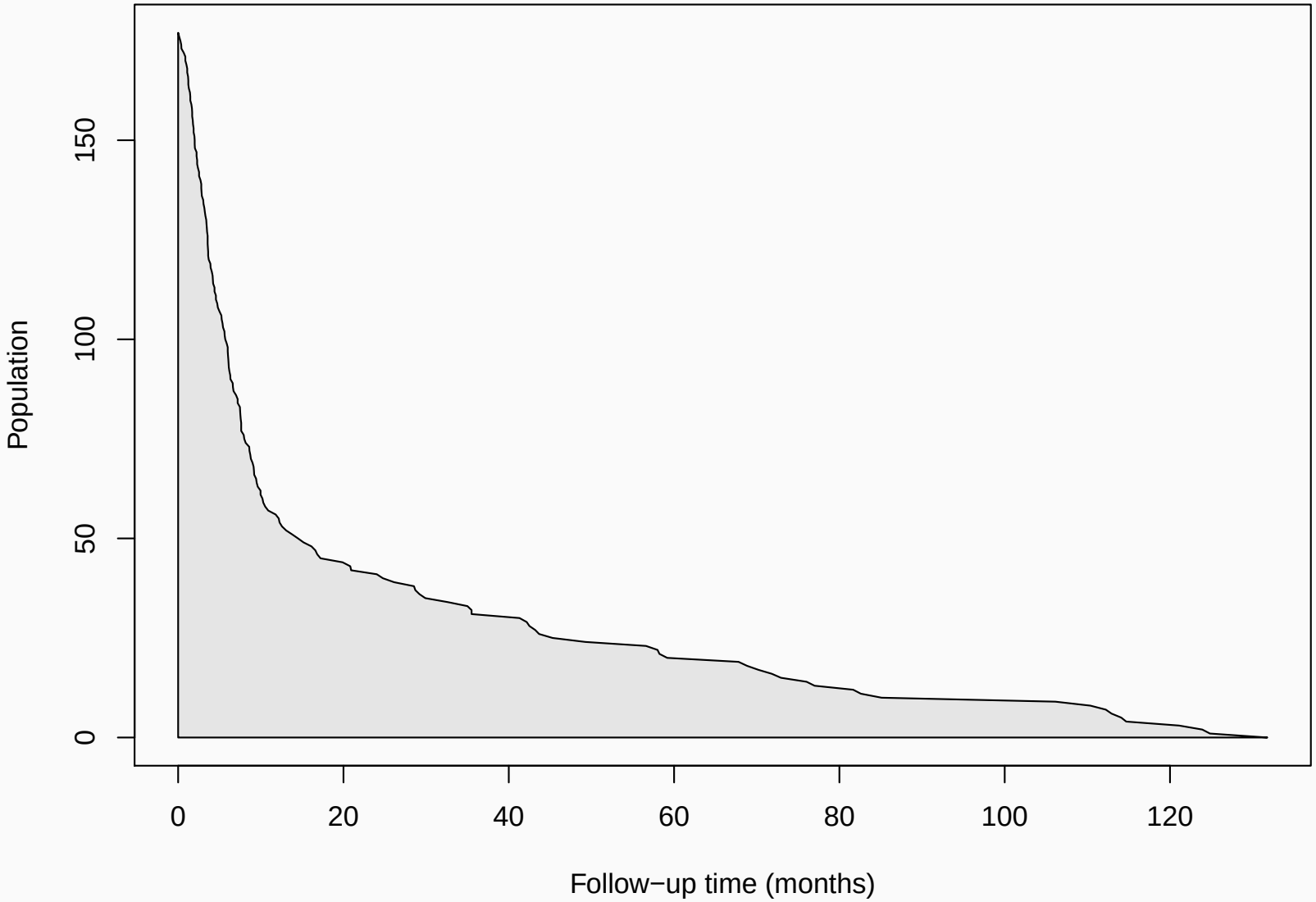
This method is currently available as an R package:
http://sahirbhatnagar.com/casebase/

Case-base sampling


Population
0
50
100
150
0
20
40
60
80
100
120
Follow−up time (months)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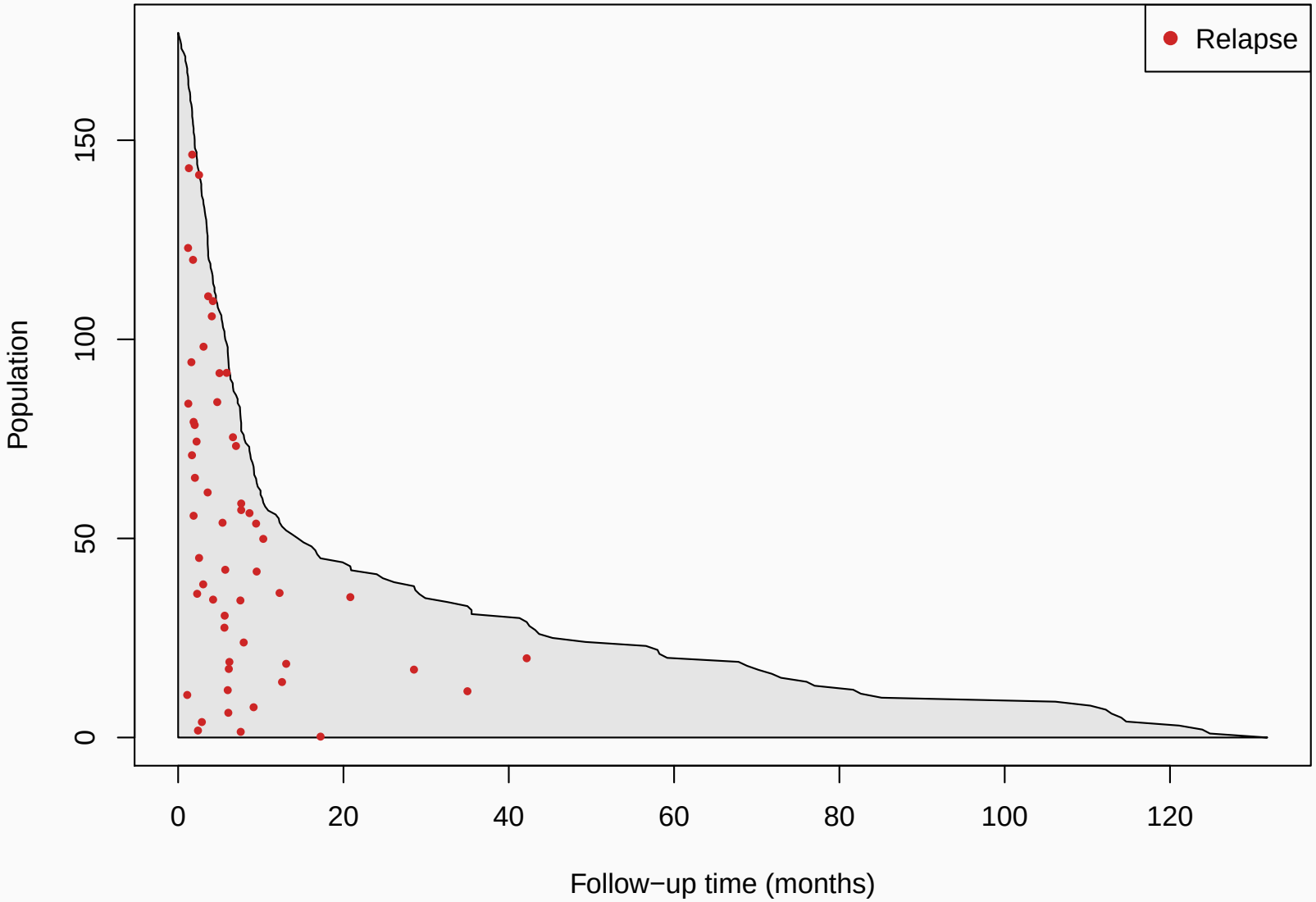
Relapse
Population
0
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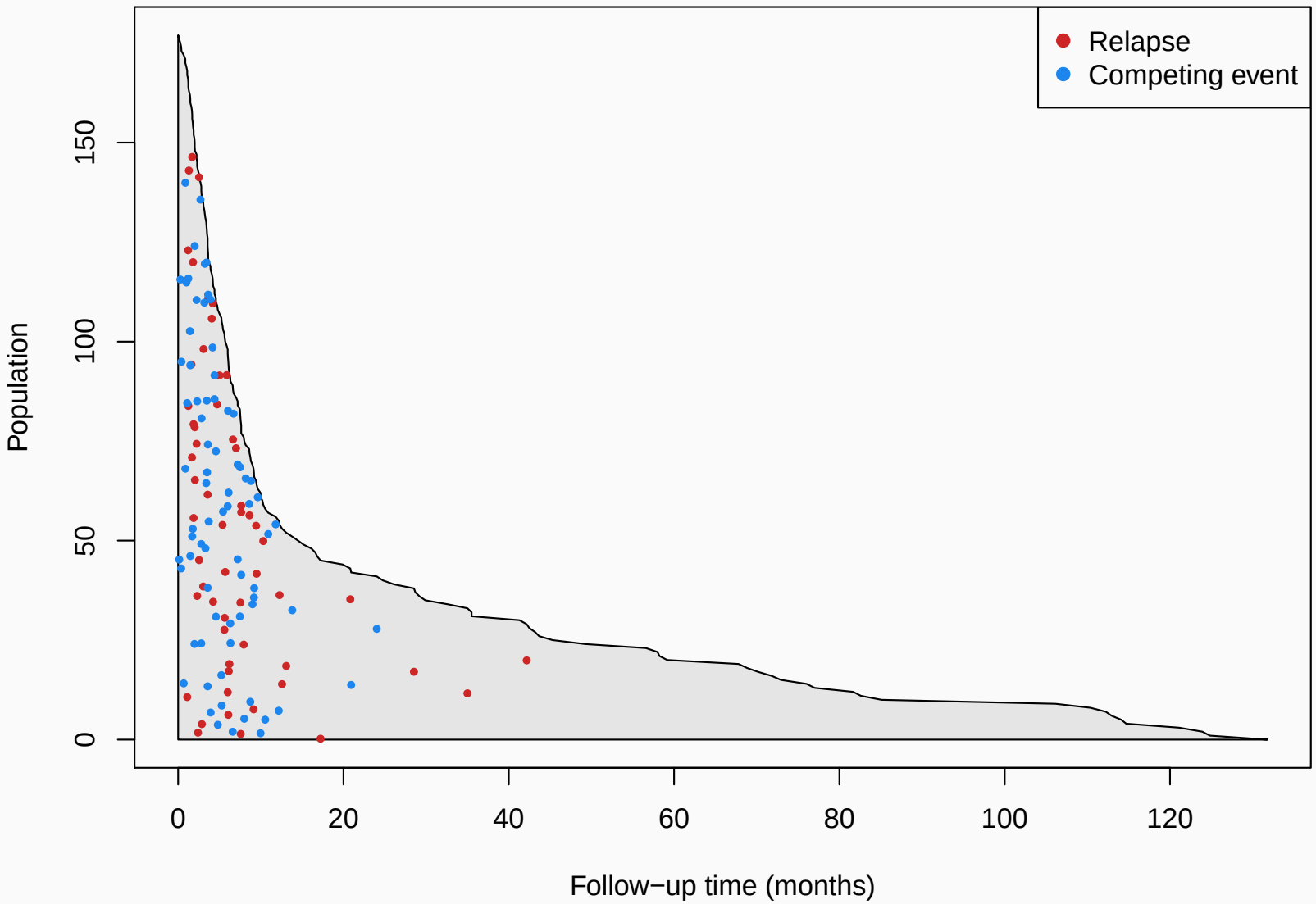
Relapse
Competing event
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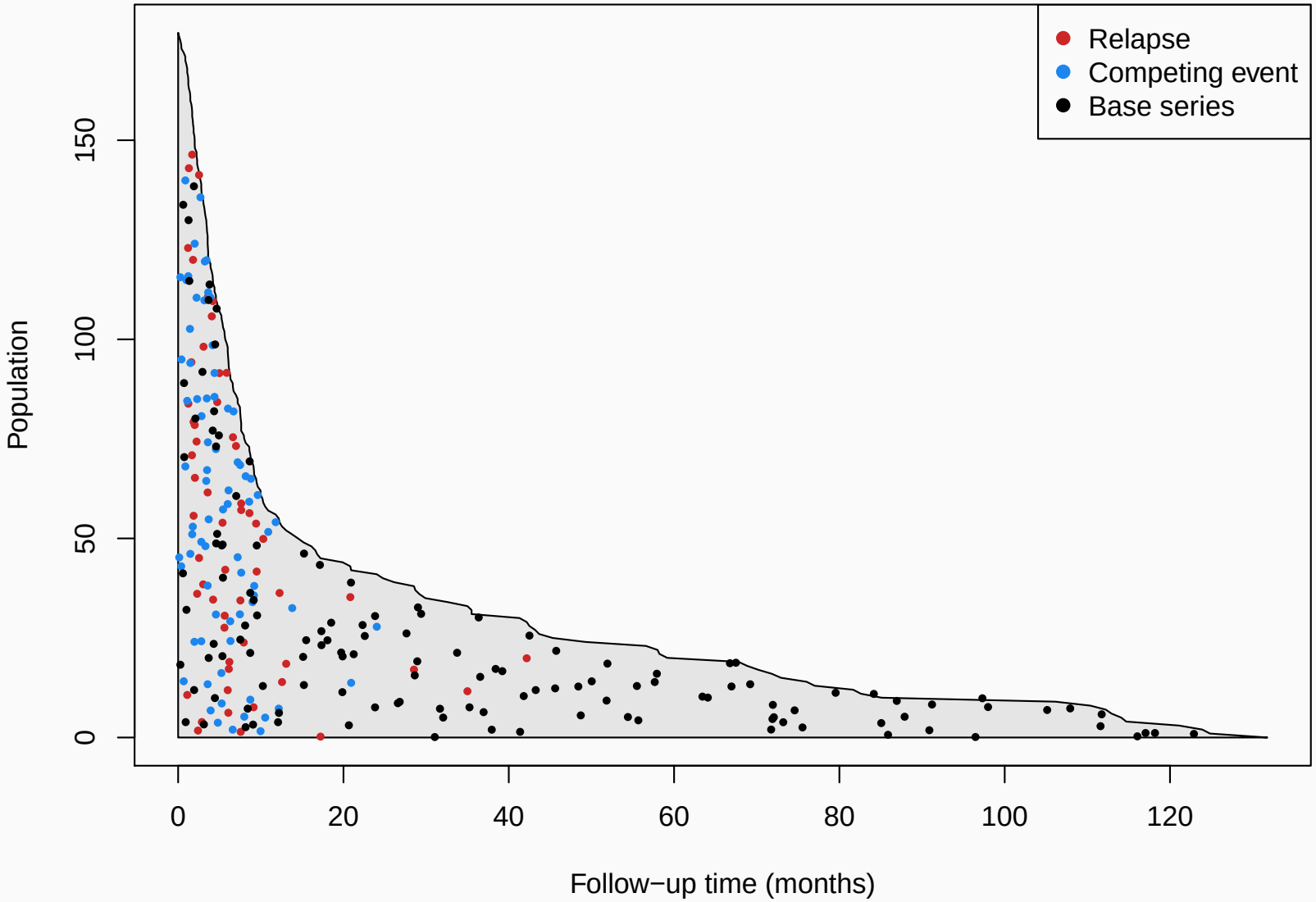
Relapse
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- Case-base sampling reduces the model fitting to a familiar multinomial regression.
    - The sampling process is taken into account using an offset term.
- By sampling a large base series, the information loss eventually becomes negligible.
- This framework can easily be used with time-varying covariates (e.g. time-varying exposure).

Parametric families

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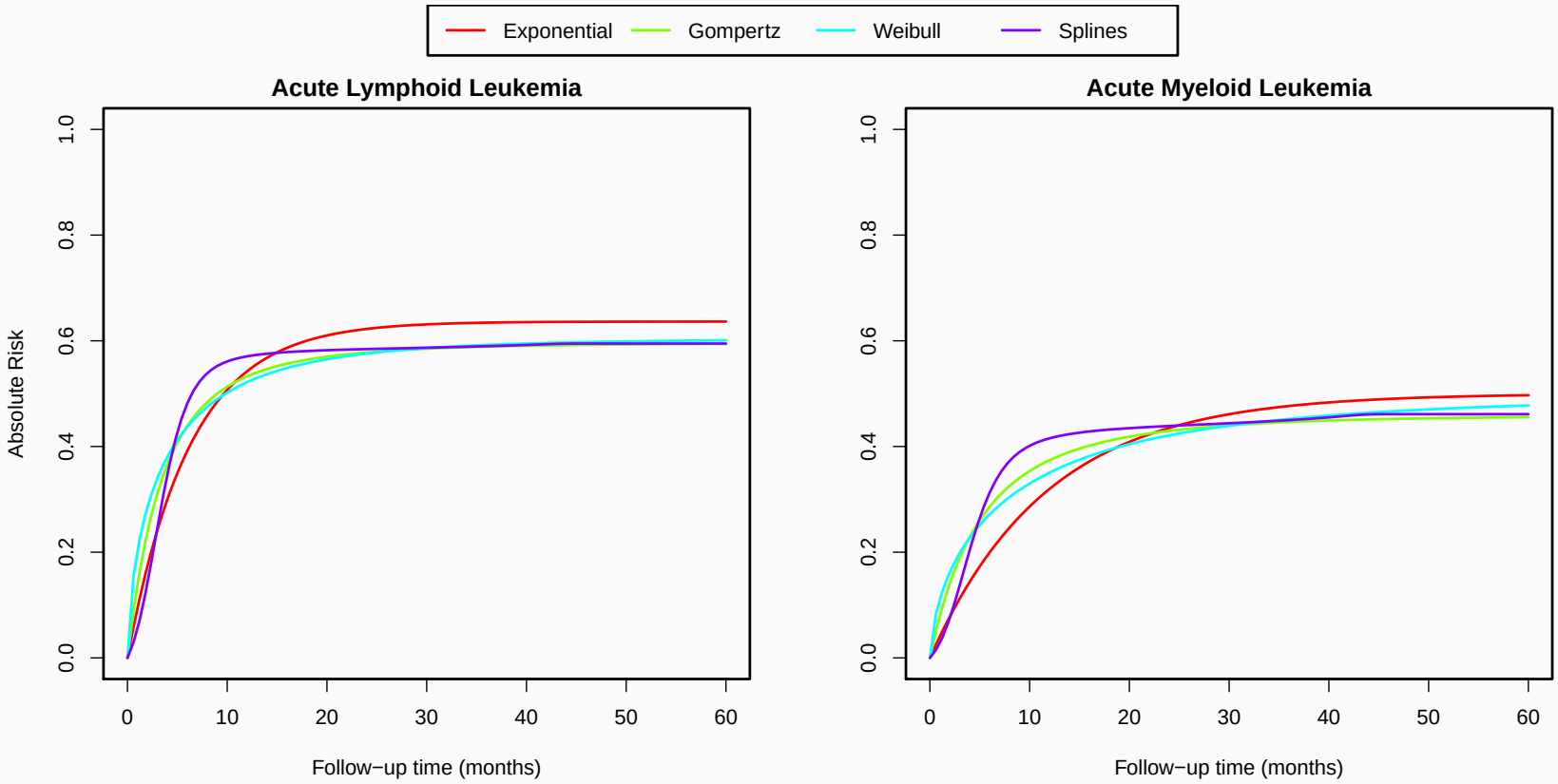
- Gompertz: $g(t; \alpha) = \alpha t$.
- Weibull: $g(t; \alpha) = \alpha \log t$.

Data analysis

Data

Variable description	Statistical summary
Sex	M=Male (100)
	F=Female (77)
Disease	ALL (73)
	AML (104)
Phase	CR1 (47)
	CR2 (45)
	CR3 (12)
	Relapse (73)
Type of transplant	BM+PB (21)
	PB (156)
Age of patient (years)	4–62
	30.47 (13.04)
Failure time (months)	0.13–131.77
	20.28 (30.78)
Status indicator	0=censored (46)
	1=relapse (56)
	2=competing event (75)



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

Model fit

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Variable	Hazard ratio	95% CI
Sex	0.68	(0.39, 1.20)
Disease	0.51	(0.28, 0.92)
Phase CR2	1.18	(0.47, 2.96)
Phase CR3	1.51	(0.39, 5.86)
Phase Relapse	4.38	(2.01, 9.54)
Source	1.37	(0.45, 4.23)
Age	0.99	(0.97, 1.02)

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    - This leads to smooth estimates of the absolute risks.
- We are explicitely modeling time, and we cant therefore how to model the effect of time on the hazard function.
- We can test the significance of covariates, in a similar way to traditional competing risks approaches.

References I

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Questions or comments?

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