Penalized logistic regression on time-to-event data using casebase sampling

Jesse Islam

2/27/2020

Popular methods in time-to-event analysis

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- They believe the stepwise nature is the reason, as it reduces interpretability. [2]
- A streamlined approach for reaching a **smooth absolute risk** curve. [2]

Dr. Cox's perspective

Reid: How do you feel about the cottage industry that's grown up around it [the Cox model]?
Cox: Don't know, really. In the light of some of the further results one knows since, I think I would normally want to tackle problems parametrically, so I would take the underlying hazard to be a Weibull or something. I'm not keen on nonparametric formulations usually.
Reid: So if you had a set of censored survival data today, you might rather fit a parametric model, even though there was a feeling among the medical statisticians that that wasn't quite right.
Cox: That's right, but since then various people have shown that the answers are very insensitive to the parametric formulation of the underlying distribution [see, e.g., Cox and Oakes, Analysis of Survival Data, Chapter 8.5]. And if you want to do things like predict the outcome for a particular patient, it's much more convenient to do that parametrically.

Itinerary

1. SUPPORT study

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2. Casebase sampling

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3. Penalized logistic regression on survival data

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- Design: Prospective cohort study.
- Setting: 5 academic care centers in the United States.
- Participants: 9105 hospitalized.
- Follow-up-time: 5.56 years.
- 68% incidence rate.

SUPPORT manual imputation [4]

- Notorious for missing data

Baseline Variable	Normal Fill-in Value
Bilirubin	1.01
BUN	6.51
Creatinine	1.01
PaO2/FiO2 ratio (pafi)	333.3
Serum albumin	3.5
Urine output	2502
White blood count	9 (thousands)

Table 1: Suggested imputation values. [3]

SUPPORT automated imputation

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3. polyreg(Bayesian polytomous regression) Factor Variables

Removed variables [4]

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- Previous model results. (6)

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- Tested on Phase II.
- Both on the scale of 180 days.

Original SUPPORT analysis [4]

SUPPORT physiology score (SPS) was developed.

$$\begin{aligned}\text{SPS} = {} & 259.9\{\text{ARF/MOSF}\} + 263.4\{\text{COPD/CHF}\} + 241.4\{\text{Cirrhosis/Coma}\} + 281.5\{\text{Lung/Colon Cancer}\} \\ & - 0.06174\ \min(Pa_{O_2}/Fi_{O_2}, 225) - 0.6316\ \min(\text{Mean BP}, 60) + 1.0205\ \text{WBC} \\ & - 0.3676(\text{WBC} - 8)_+ - 0.5631(\text{WBC} - 11)_+ + 0.2691\ \min(\text{Alb}, 4.6) + 0.2312\ \text{Aresp} \\ & - 2.362\ \text{Temp} + 1.326(\text{Temp} - 36.6)_+ + 2.473(\text{Temp} - 38.3)_+ \\ & - 1.579 \times 10^{-1}\ \text{HR} + 9.770 \times 10^{-5}\ (\text{HR-55})^3_+ - 2.189 \times 10^{-4}(\text{HR} - 80)^3_+ \\ & + 1.518 \times 10^{-4}(\text{HR} - 110)^3_+ - 3.062 \times 10^{-5}(\text{HR} - 149)^3_+ + 0.9763\ \text{Bil} \\ & - 0.7481(\text{Bil} - 7)_+ - 6.8761\ \text{Cr} + 11.6058(\text{Cr} - 0.600)^3_+ - 21.8413(\text{Cr} - 1.000)^3_+ \\ & + 10.3574(\text{Cr} - 1.500)^3_+ - 0.1219(\text{Cr} - 5.399)^3_+ - 0.6167096\ \text{Na} \\ & + 0.0021118(\text{Na} - 128)^3_+ - 0.0036730(\text{Na} - 135)^3_+ + 0.0006126(\text{Na} - 139)^3_+ \\ & + 0.0009486(\text{Na} - 148)^3_+ - 6.278\ \{\text{COPD/CHF}\} \times \min(\text{Alb}, 4.6) \\ & - 11.45\ \{\text{Lung/Colon Cancer}\} \times \min(\text{Alb}, 4.6) \\ & + \{\text{ARF/MOSF}\}[-2.3549\ \text{WBC} + 2.7494\ (\text{WBC} - 8)_+ - 0.4638\ (\text{WBC} - 11)_+]\end{aligned}$$

SUPPORT: my question

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- How does their SPS perform over 5.56 years?
- How does the Apache III physiology score (APS) perform over 5.56 years?
- How does a model with all the covariates, excluding SPS and APS, perform?

Analysis Process

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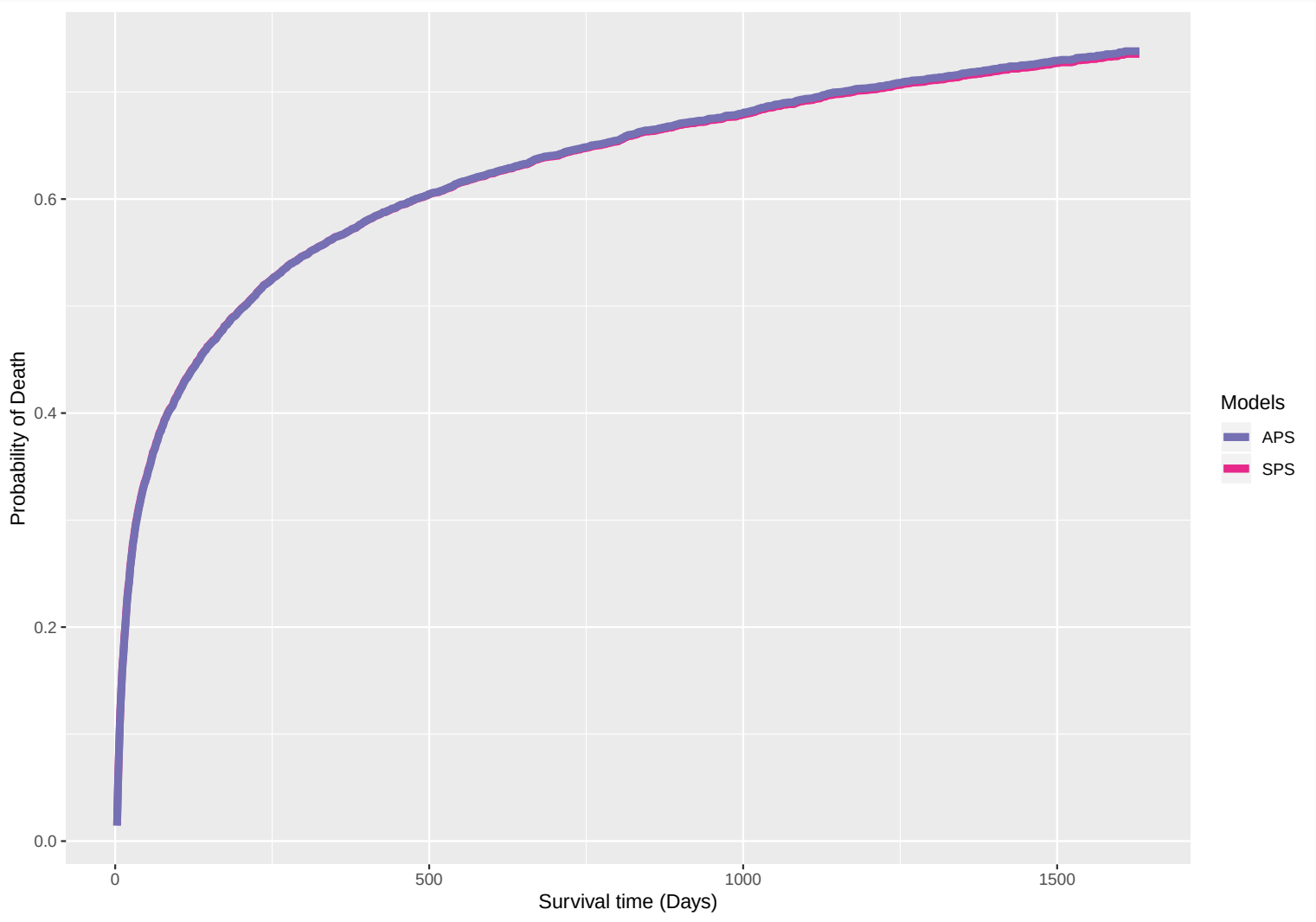
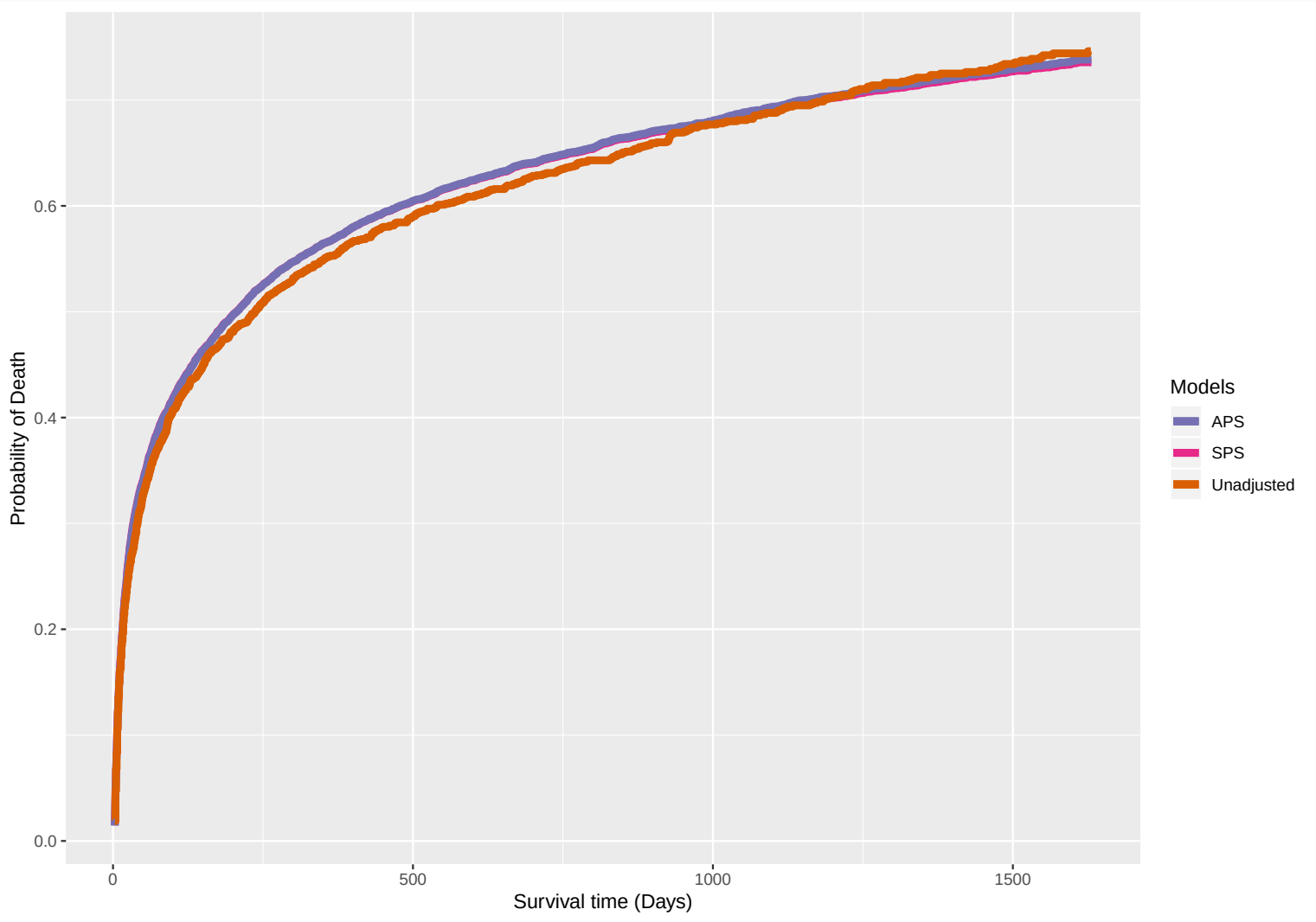
  - The absolute risk curve for each individual is averaged.
  - Averaged curve is expected to approach Kaplan-meier curve.

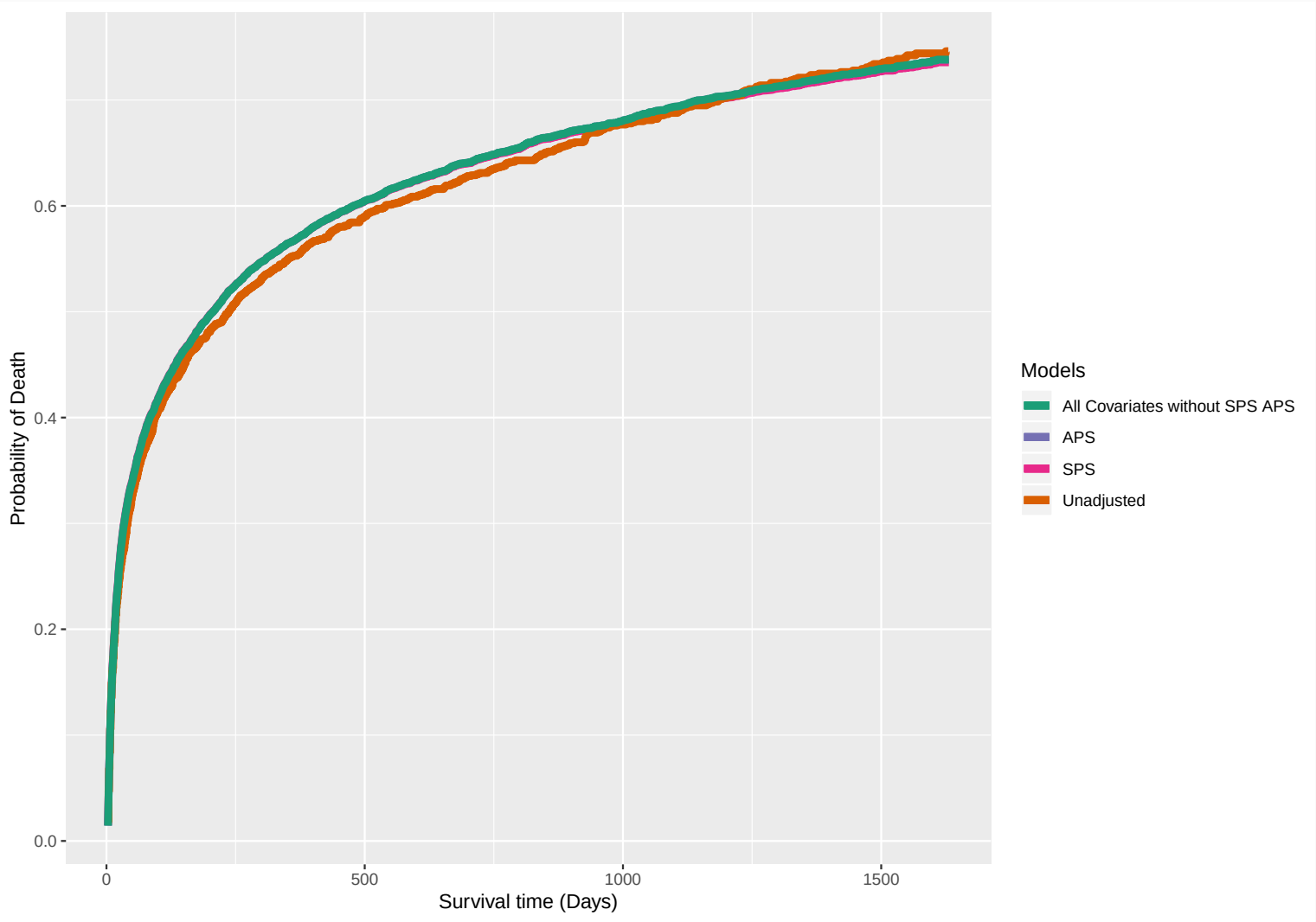
SPS vs APS


Probability of Death
0.0
0.2
0.4
0.6
0
500
1000
1500
Survival time (Days)
Models
APS
SPS

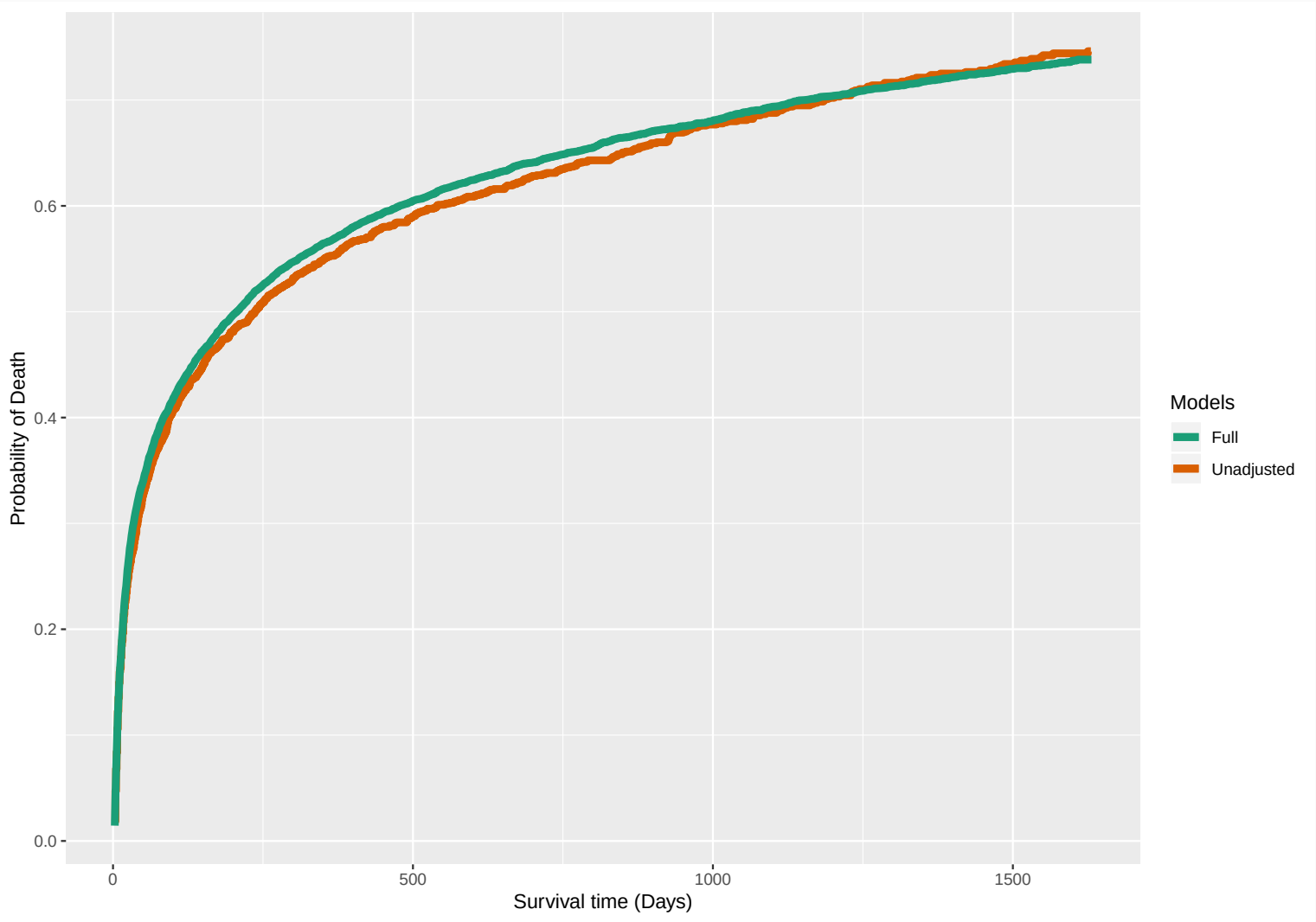
SPS vs. Kaplan-Meier



All covariates vs. physiology scores vs unadjusted



Chosen absolute risk comparisons



Chosen absolute risk comparisons: conclusion

- Linear associations without physiology scores perform similarly to SPS and APS alone.

Chosen absolute risk comparisons: conclusion

- Linear associations without physiology scores perform similarly to SPS and APS alone.
- We choose the linear associations without physiology scores as the model of choice (Full model).

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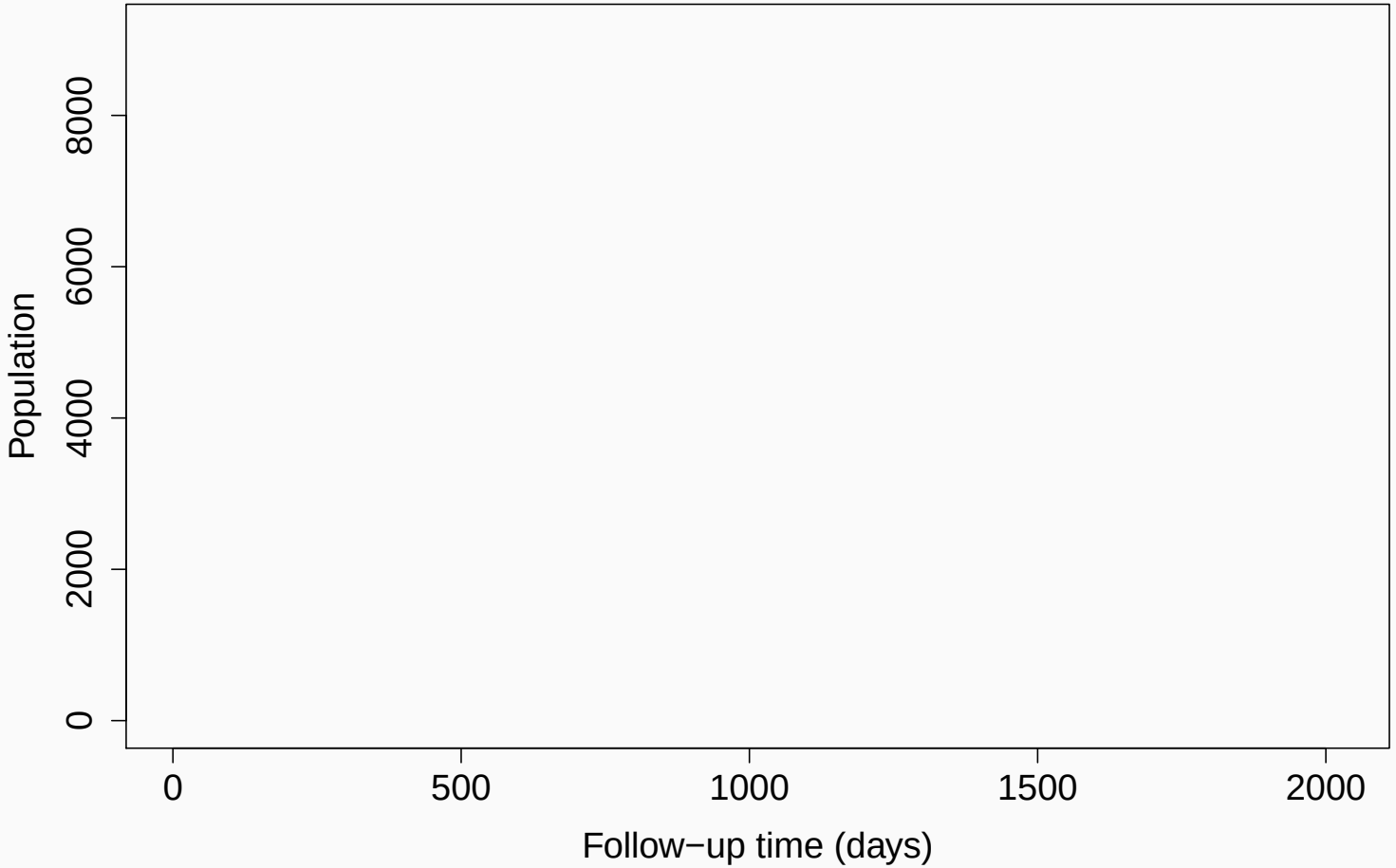
- Casebase is parametric, and allows different parametric fits by incorporation of the time component.
- Package contains an implementation for generating *population-time* plots.

Casebase: Sampling



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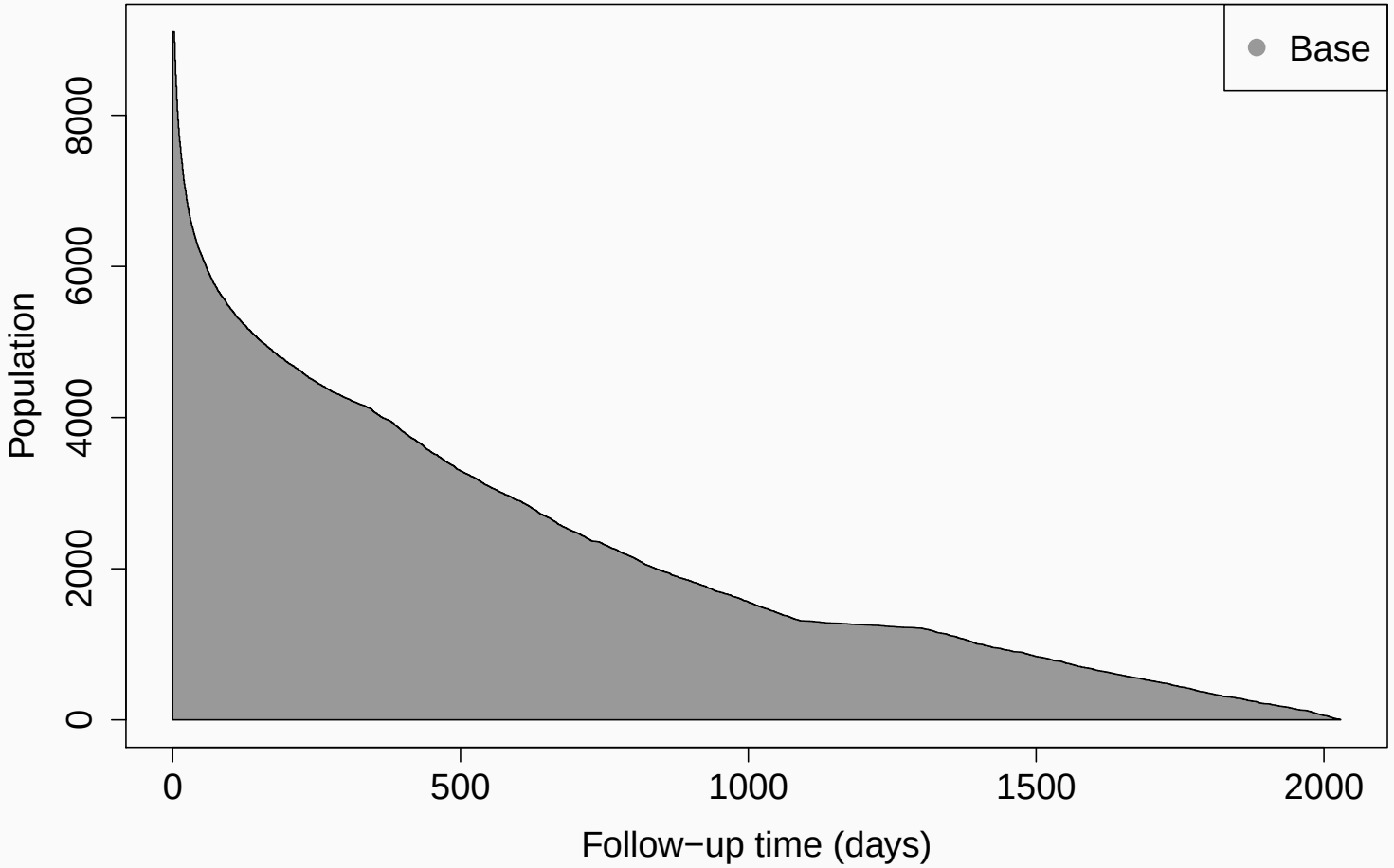

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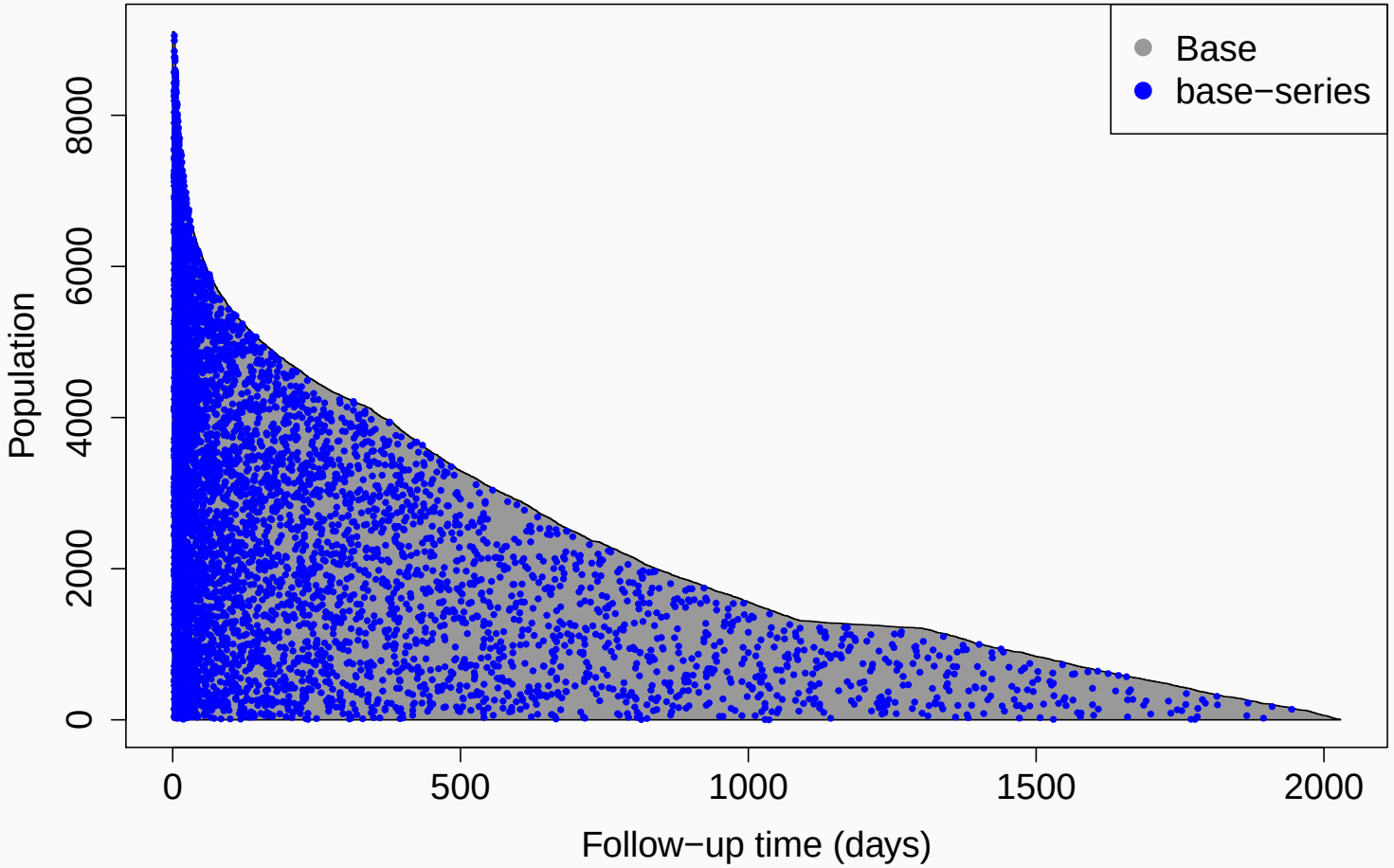

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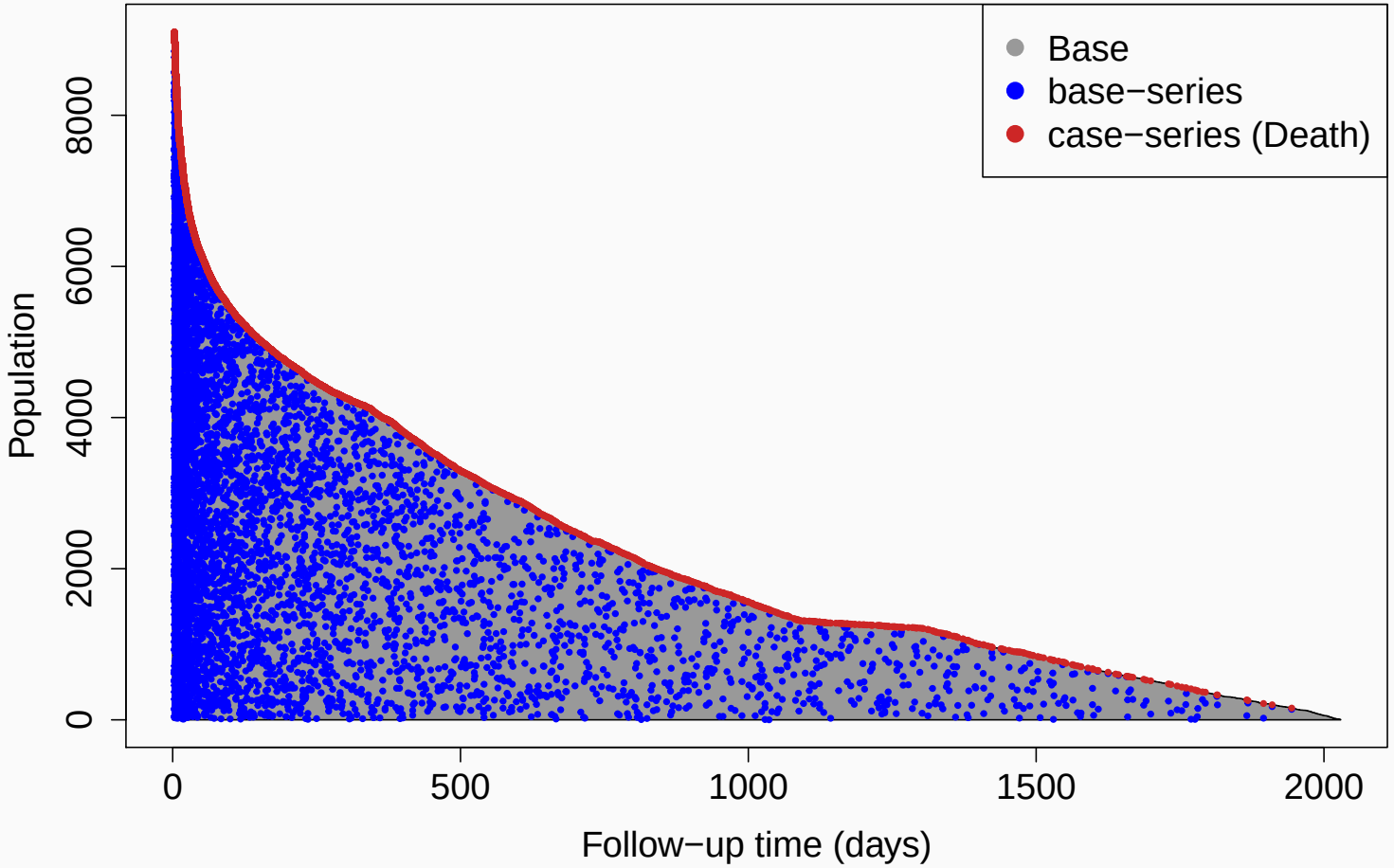

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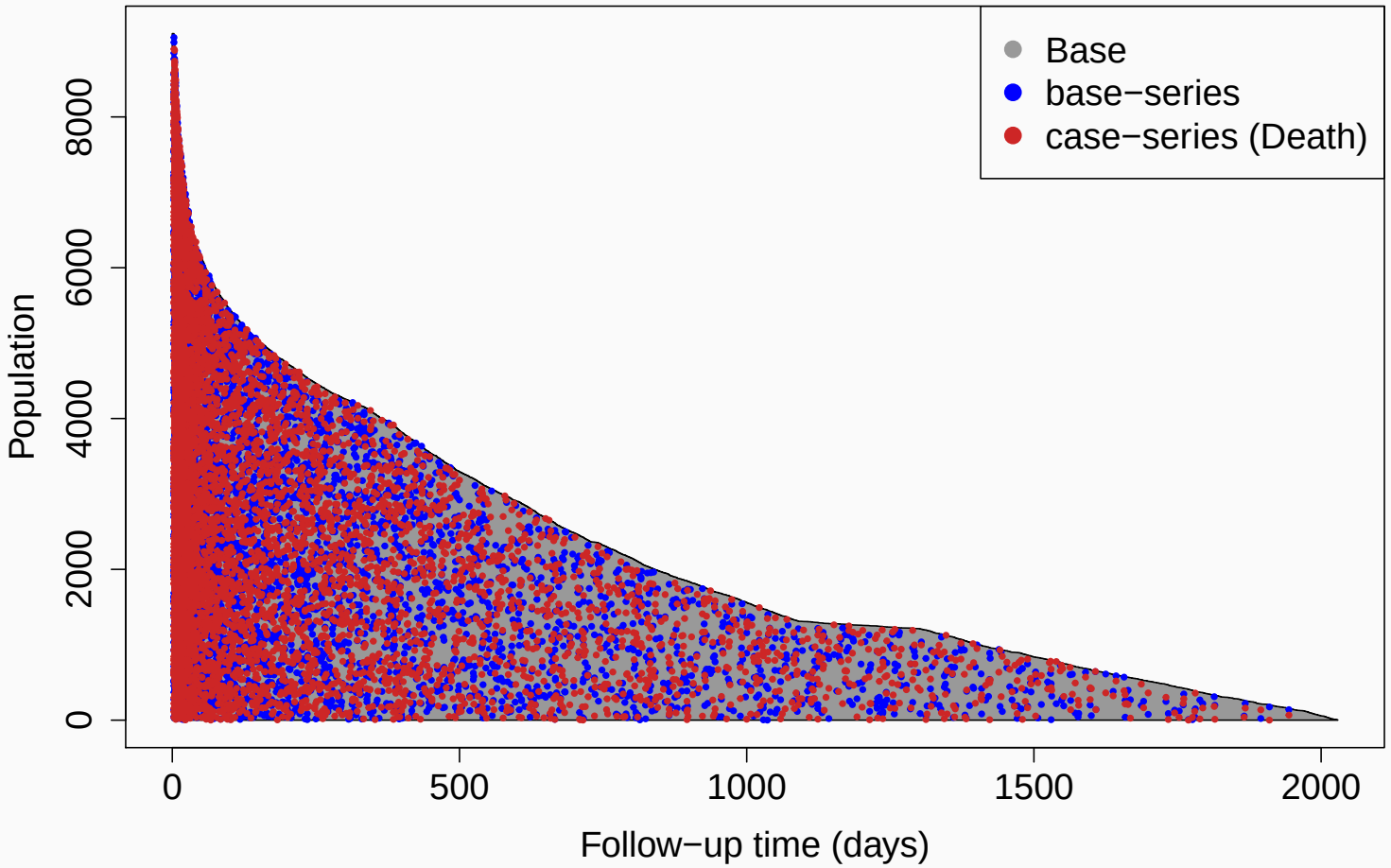

Casebase: Sampling

$$e^L = \frac{Pr(Y=1|x,t)}{Pr(Y=0|x,t)} = \frac{h(x,t) * B(x,t)}{b[B(x,t)/B]} = \frac{h(x,t) * B}{b}$$

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- $B =$ Base.
- $B(x,t) =$ Risk-set for survival time t.

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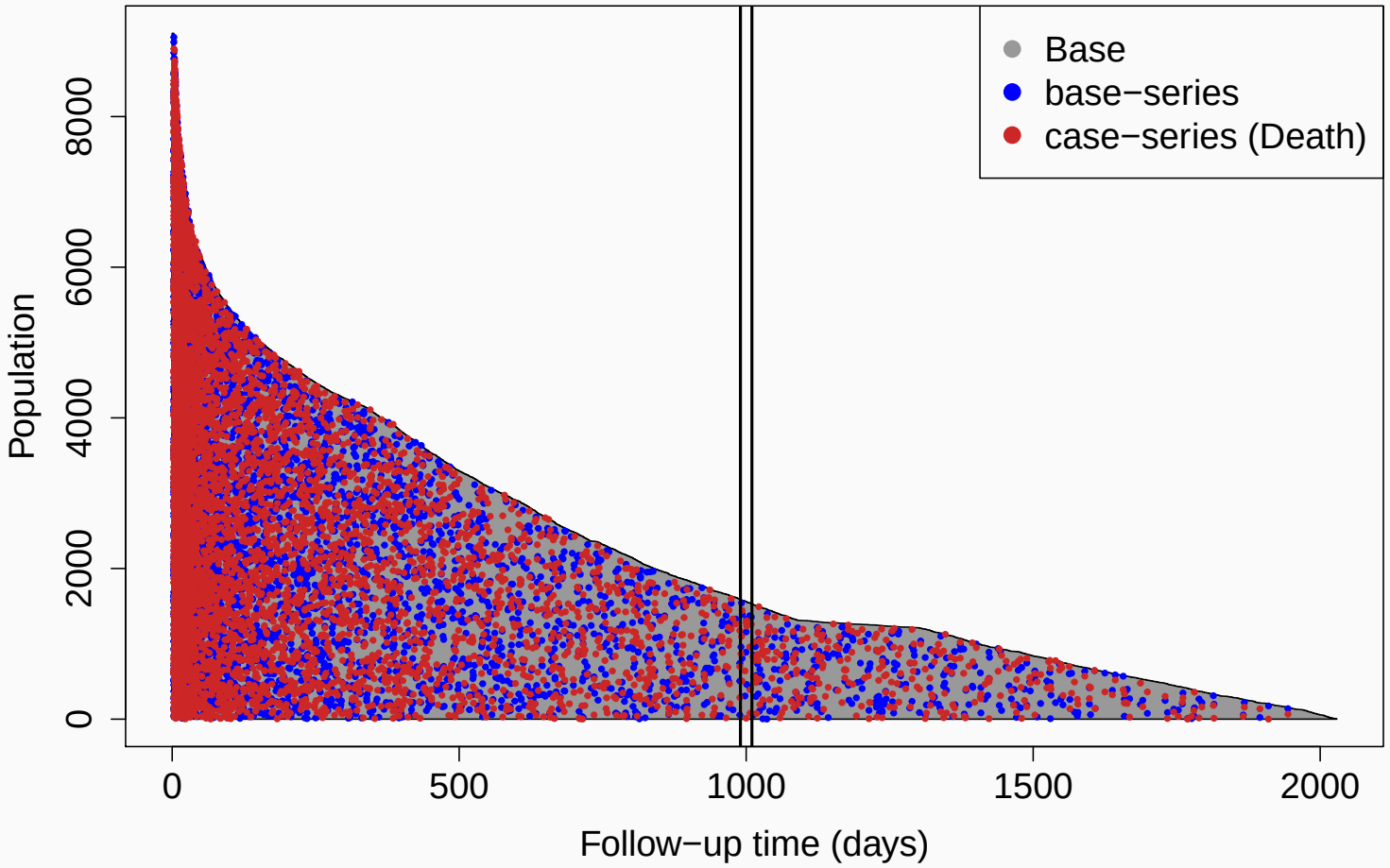

log-odds = log hazard

$$e^L = \frac{\hat{h}(x,t) * B}{b}$$

$$\hat{h}(x,t) = \frac{b * e^L}{B}$$

$$log(\hat{h}(x,t)) = L + log(\frac{b}{B})$$

Maximum log-likelihood [1]

$$log(l(\beta_0, \beta)) = \frac{1}{N} \sum_{i=1}^{N} \{y_i(\beta_0 + {x_i}^T \beta) - log(1 + e^{\beta_0 + {x_i}^T \beta})\}$$

Maximum log-likelihood, with offset

$$log(l(log(\frac{b}{B}), \beta)) = \frac{1}{N}\sum_{i=1}^{N}\{y_i(log(\frac{b}{B}) + x_i^T\beta) - log(1 + e^{log(\frac{b}{B}) + x_i^T\beta})\}$$

Maximum log-likelihood, with offset and lasso

$$log(l(log(\frac{b}{B}), \beta)) =$$
$$\frac{1}{N}\sum_{i=1}^{N}\{y_i(log(\frac{b}{B}) + x_i^T\beta) - log(1 + e^{log(\frac{b}{B})+x_i^T\beta})\} - \lambda||\beta||$$

Casebase: Parametric families

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- By changing the function $g(t; \alpha)$, we can model different parametric families easily:

Casebase: Parametric models

Exponential: $g(t; \alpha)$ is equal to a constant

```
casebase::fitSmoothHazard(status ~ X1 + X2)
```

Gompertz: $g(t; \alpha) = \alpha t$

```
casebase::fitSmoothHazard(status ~ time + X1 + X2)
```

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

```
casebase::fitSmoothHazard(status ~ log(time) + X1 + X2)
```

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- Lets use the weibull hazard.

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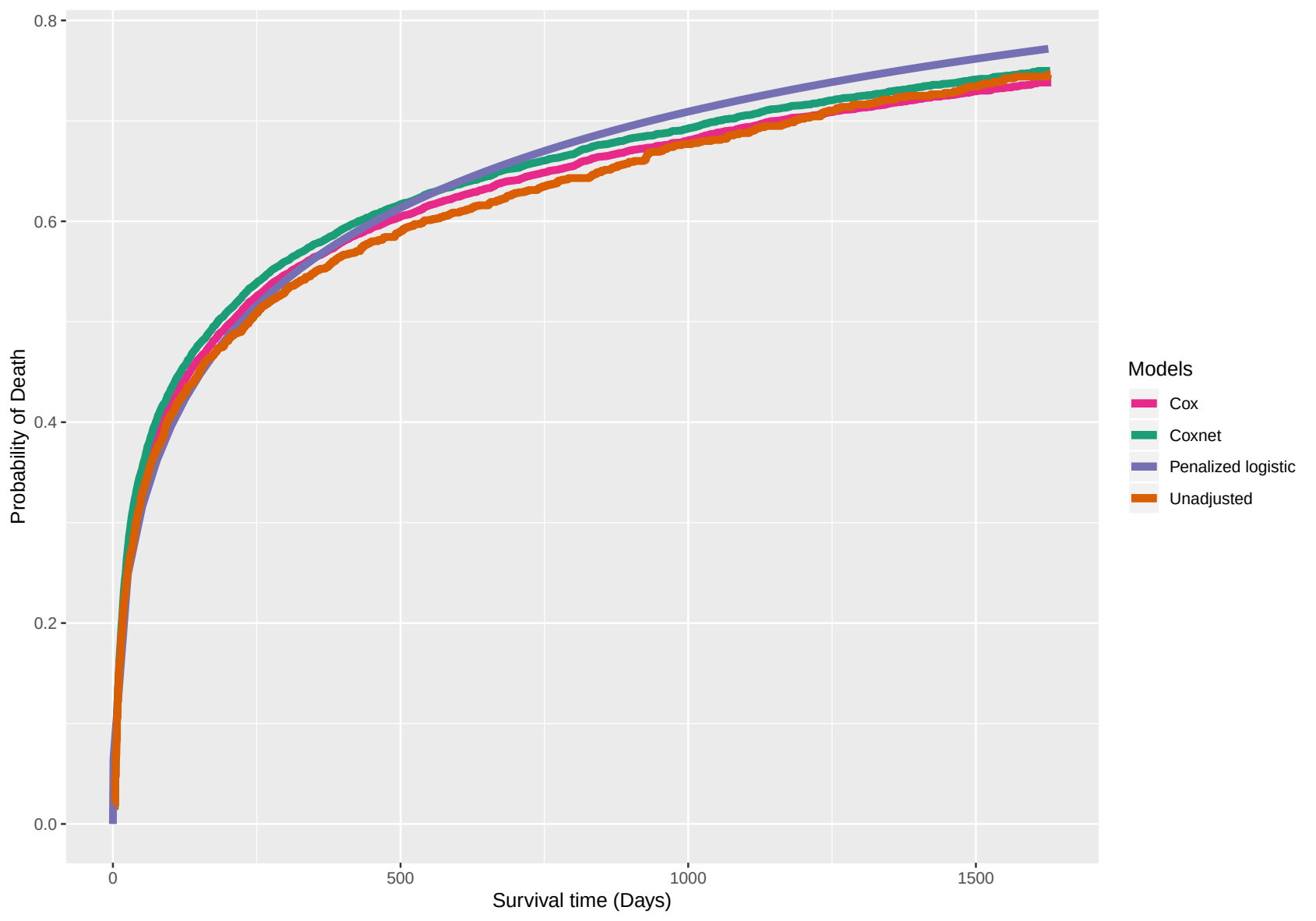
- Recall: Case study to demonstrate regularization using our method.
- **unadjusted**: (death, time) ~ 1
- **Cox**: (death, time) $\sim \beta X$
- **Coxnet**: (death, time) $\sim \beta X$ <–Lasso
- **Penalized logistic**: death $\sim \log(\text{time}) + \beta X$ <–Lasso

Survival comparison



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Conclusions / take homes

- Classical survival analysis requires methods to encorporate censorship in our data.
- Case-base sampling is a techinique that implicitly encorporates censorship implicitly.
- Logistic regression on SUPPORT dataset had slightly different results near the end of follow-up time.

Future work

- Comparative measure.

Future work

- Comparative measure.
- Survival GWAS.

References 1

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Tutorial and slides

Tutorial:

http://sahirbhatnagar.com/casebase/

Slides:

https://github.com/Jesse-Islam/ATGC_survival_presentation_Feb.27.2020

Questions?