

Background

- Covariates usually enter a parametric hazard function, $\lambda(t)$, through the scale parameter only. This is the case for the popular proportional hazards (PH) model.
- $\lambda(t)$ is used to express the risk of a particular event occurring at time t .
- By adopting a multi-parameter regression (MPR) technique, where multiple distributional parameters depend on covariates, further flexibility can be achieved.

Power-Generalized Weibull (PGW)

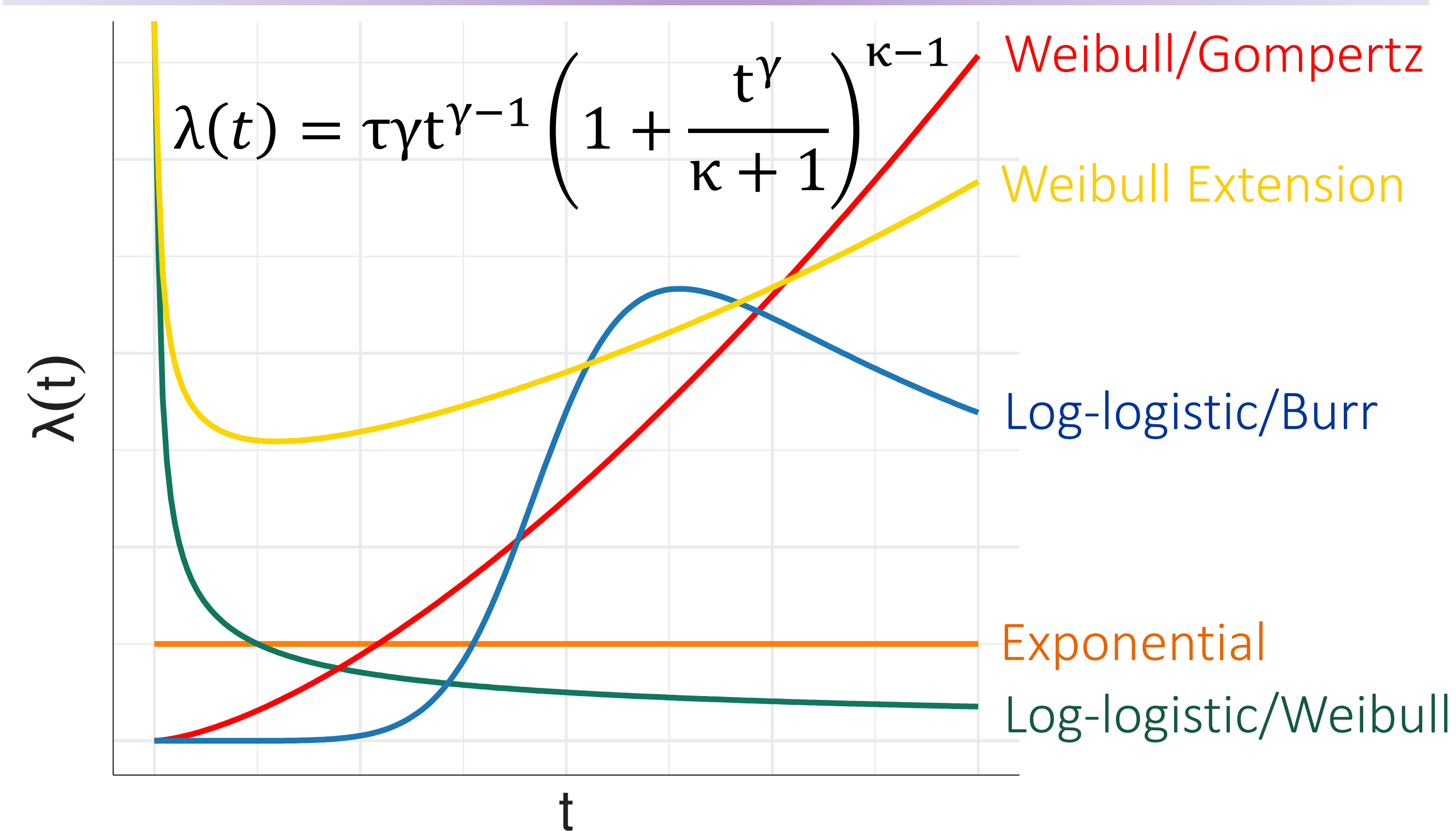


Figure 1. PGW hazard shapes.

Distributional Regression

The PGW MPR model used in this research allows covariates to enter the hazard through the scale (τ) and shape (γ) parameters where the additional shape (κ) parameter is independent of covariates:

$$\log(\tau) = x^T \beta \quad \log(\gamma) = x^T \alpha \quad \log(\kappa + 1) = \omega$$

where x is the covariate vector and β , α and ω are the regression coefficients associated with τ , γ and κ .

Scale: $\tau > 0 \Rightarrow$ Magnitude of the hazard

Shape: $\gamma > 0 \Rightarrow$ Time evolution of the hazard

Shape: $\kappa > -1 \Rightarrow$ Specifies the baseline distribution

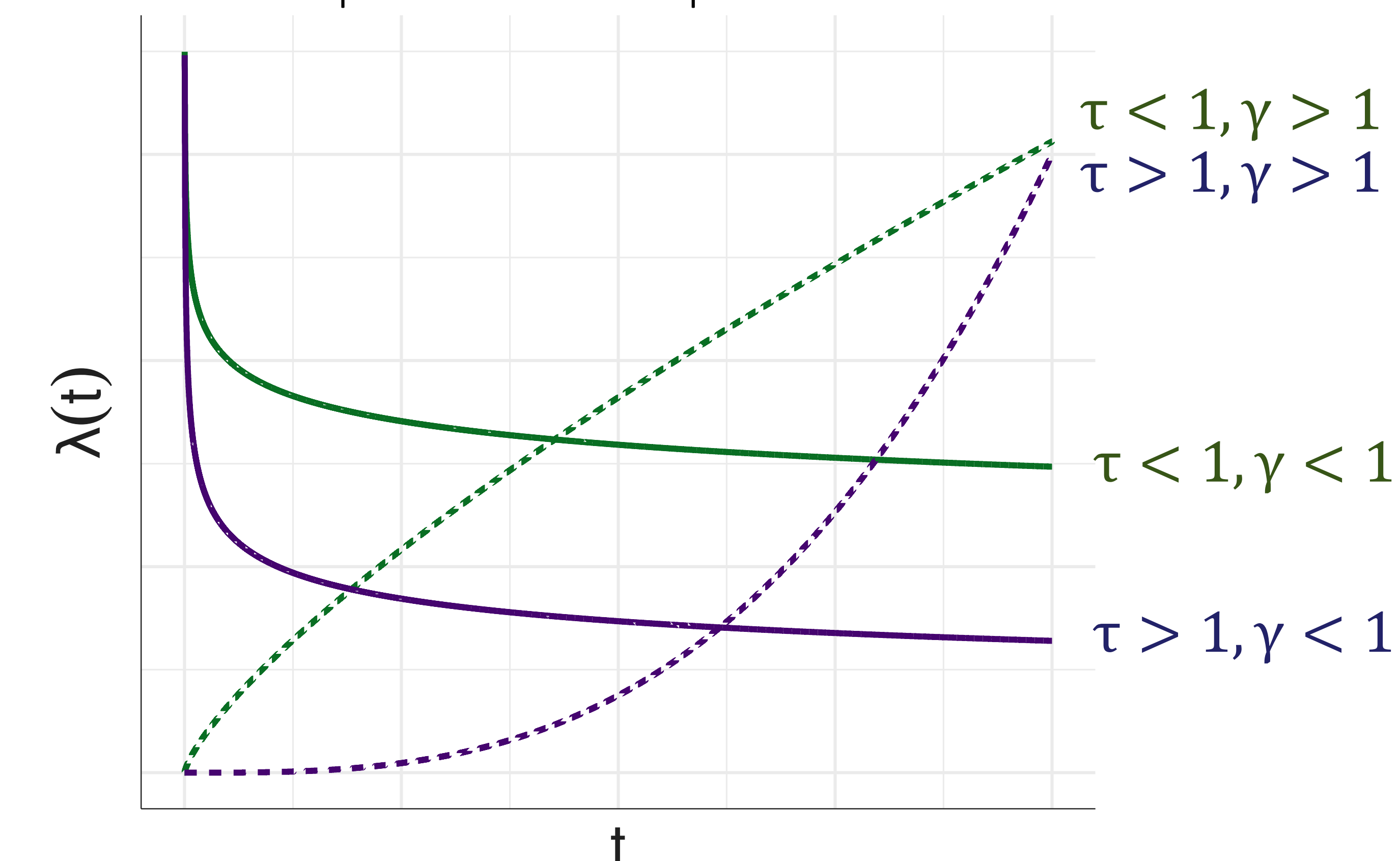


Figure 2. Impact of the shape (γ) and scale (τ) on the hazard.

- Variable selection and parameter estimation are carried out using penalized regression (adaptive lasso penalty).

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Simulation Study

n	Scale (β)			Shape (α)		
	C(7)	MSE	PT	C(7)	MSE	PT
500	6.86	0.02	0.87	6.78	0.00	0.81
2000	6.95	0.00	0.96	6.96	0.00	0.96

Table 1. C, average correct zeros; MSE, average mean squared error; PT, probability of choosing the true model.

- The model performs well from a variable selection perspective where the average correct zeros is tending towards the oracle values as the sample size increases.
- Inference was also carried out which showed good performance.

Data Application

- Veteran dataset – Survival package in R
- Randomized trial of two treatment groups for lung cancer
- 137 observations

	PH	MPR
cell type: squamous	β	α
cell type: large	β	β
karno	β	α, β
Tuning Parameter	0.01706318	0.02833773
BIC	1466.42	1463.72

Table 2. β = “selected in scale”, α = “selected in shape”, and those which are non-significant (at the 5% level) are shown in gray.

	Intercept	Large	Squamous	Karno
β	-2.38	-0.42	-	-0.06
α	0.59	-	-0.13	0.01
ω	0.35	-	-	-

Table 4. Coefficient estimation from MPR output where those which are non-significant (at the 5% level) are shown in gray.

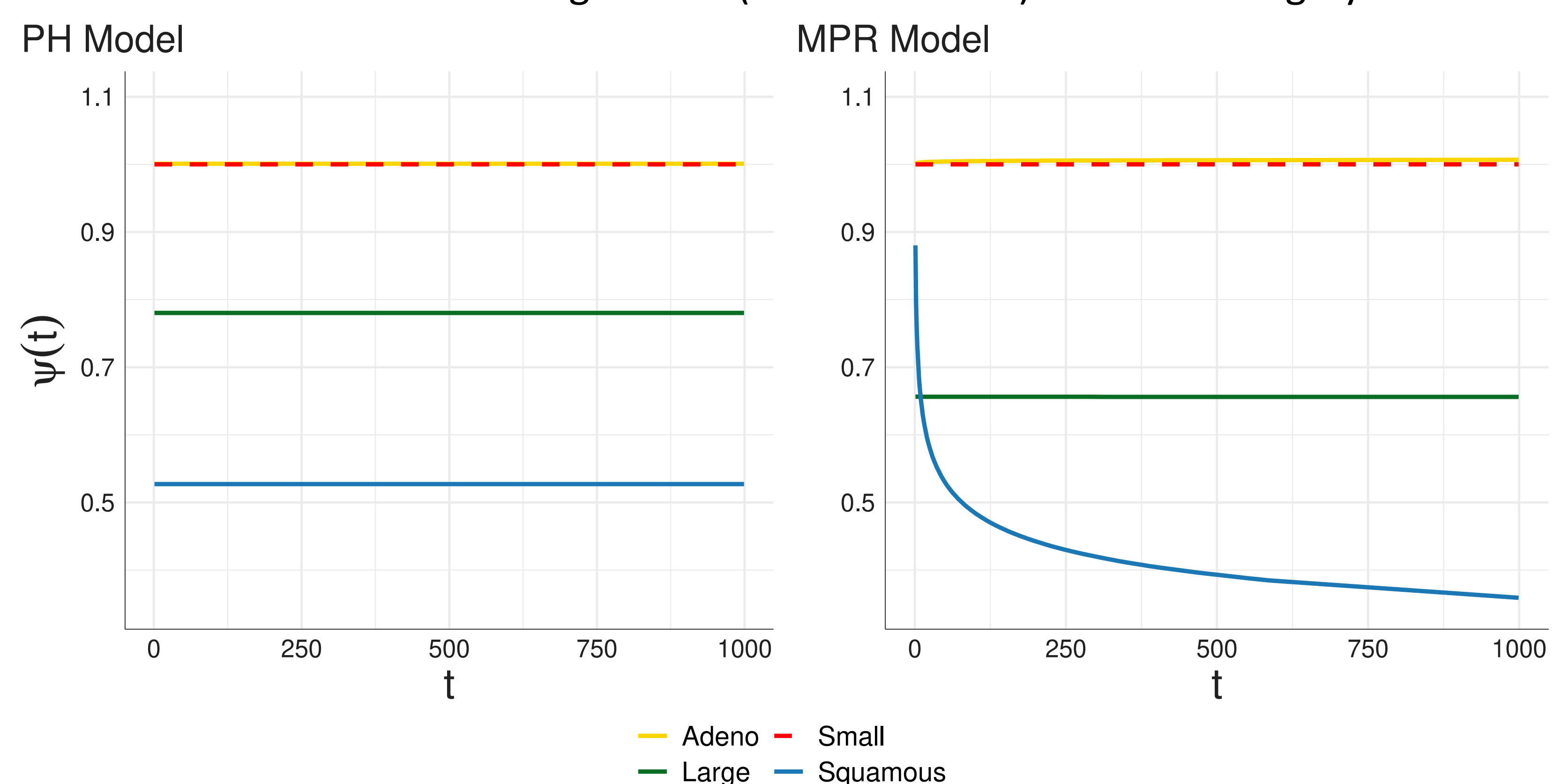


Figure 4. Cell type hazard ratios.

- Unlike PH models, MPR models allow for time-varying hazard ratios.
- This is the case for the squamous cell which has a smaller hazard relative to the reference category and this hazard is also decreasing over time

Conclusions

- Greater flexibility can be achieved by using an MPR model.
- Time-varying hazard ratios occur naturally by allowing the shape parameter to depend on covariates.
- Increased understanding of real-world data.

References

- Burke et al. (2017). Multi-parameter regression survival modeling. Biometrics.
- Jaouimaa et al. (2019). Penalized Variable Selection in Multi-Parameter Regression Survival Modelling. arXiv:1907.01511.
- Burke et al. (2020). A flexible parametric modelling framework for survival analysis. IRSS-C