

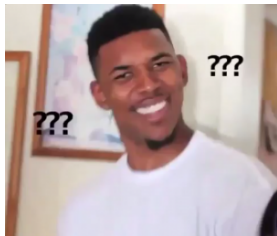
# Modelagem Estatística da incidência de cânceres via um GLMM Multinomial

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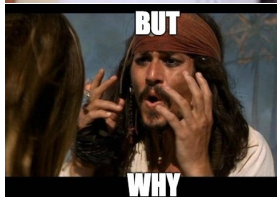
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O quê?



Por quê?



Como?



# Some continuous parametric failure time models

Random variable: failure time,  $T > 0$ .

Type: continuous.

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Common failure time distributions for homogeneous populations:

Now, let's better understand how this works.



# Generalized $F$

*Advantage: it can adapt to a wide variety of distributional shapes.*

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## Context

A location and scale model for  $Y = \log T$  in which the error distribution is assumed to be that of the logarithm of an  $F$  variate on  $2m_1$  and  $2m_2$  degrees of freedom.

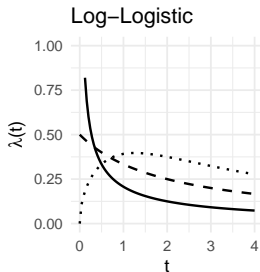
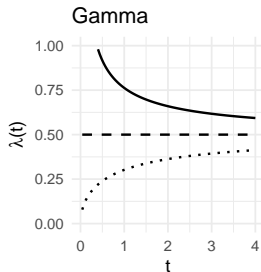
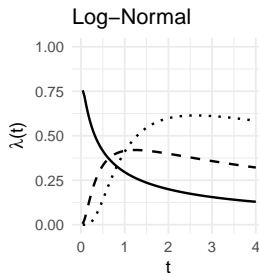
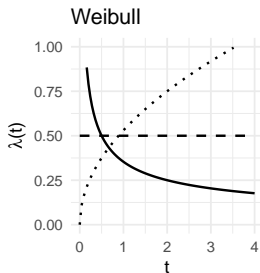
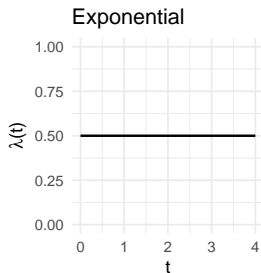
That is,  $Y = \mu + \sigma W$ , where

$$f_W(w) = \frac{(m_1/m_2)^{m_1} e^{wm_1} (1 + m_1 e^w / m_2)^{-(m_1+m_2)}}{B(m_1, m_2)}.$$

The resulting model for  $T$  is the generalized  $F$  distribution.



# Shapes of the hazard functions



# A door to another world

To be able to see these Generalized  $F$  special cases, the transformation  $Y = \mu + \sigma W$  is necessary.

However, this open a door for another world: **Extreme Value Theory**.

In the Generalized Gamma case and special cases,  $W$  is an extreme value (minimum) distribution.

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## Extreme Value Theory

- ↳ Generalized extreme value (GEV) distribution
  - ↳ Type I extreme value distribution: Gumbel family
  - ↳ Type II extreme value distribution: Fréchet family
  - ↳ Type III extreme value distribution: Weibull family



# Regression models

## ↳ Exponential and Weibull

Goal: obtain a regression model by allowing the failure rate to be a function of the derived covariates  $Z$ .

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The hazard at time  $t$  for an individual can be written as

$$\lambda(t; x) = \text{hazard} \times c(Z^T \beta),$$

three forms have been used for  $c$ :

- »  $c(s) = 1 + s$ , corresponding to the failure rate;
- »  $c(s) = (1 + s)^{-1}$ , corresponding to the mean survival time;
- »  $c(s) = \exp(s)$ .



## Exponential regression model

$$\lambda(t; x) = \lambda \exp(Z^\top \beta)$$

$$Y = -\log \lambda - Z^\top \beta + W$$

$W \sim \text{Extreme Value dist.}$

## Weibull regression model

$$\lambda(t; x) = \gamma(\lambda t)^{\gamma-1} \exp(Z^\top \beta)$$

$$Y = -\log \lambda - Z^\top \sigma \beta + \gamma^{-1} W$$

$W \sim \text{Extreme Value dist.}$

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## Accelerated failure time models

↳ general class of log-linear models

↳ covariates act additively on  $Y$ , or multiplication on  $T$

↳ log survival time,  $Y = \log T$

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More general model: Relative Risk or Cox Model.





# Relative risk model

Cox, 1972

$$\lambda(t; x) = \lambda_0(t) \exp(Z^\top \beta),$$

where  $\lambda_0(\cdot)$  is an arbitrary unspecified baseline hazard function for continuous  $T$ .

The conditional survivor function for  $T$  given  $Z$  is

$$F(t; x) = F_0^{\exp(Z^\top \beta)}(t), \quad \text{where} \quad F_0(t) = \exp \left[ - \int_0^t \lambda_0(u) du \right].$$

Thus the survivor function of  $t$  for a covariate value,  $x$ , is obtained by raising the baseline survivor function  $F_0(t)$  to a power.

Nice generalizations, \_\_\_\_\_

- » stratified Cox model;
- » time-dependent Cox model: *relative* risk model.



# Accelerated failure time model

Suppose  $Y = \log T$  and consider the linear model

$$Y = Z^T \beta + W.$$

Exponentiation gives  $T = \exp(Z^T \beta) S$ , where  $S = \exp(W) > 0$  has hazard function  $\lambda_0(s)$ , say, that is independent of  $\beta$ .

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The hazard function for  $T$  can be written as

$$\lambda(t; x) = \exp(-Z^T \beta) \lambda_0[t \exp(-Z^T \beta)].$$

The effect of the covariate is **multiplicative on  $t$**  rather than on the hazard function.

i.e.,

The role of  $Z$  is to **accelerate** (or decelerate) the time to failure.



# Comparison of regression models

## note

Exponential and Weibull regression models can be considered as special cases of both models.



# Discrete failure time models

## Discrete failure time?

- » Grouping of continuous data due to imprecise measurement;
  - » Time itself may be discrete
    - » e.g., when the response time represents the number of episodes that occur prior to a terminal event.
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## Discrete regression models?

- » Grouped relative risk model;
- » Discrete and continuous relative risk model;
- » Discrete logistic model.



# Discrete regression models

## » Grouped relative risk model:

Discrete baseline cumulative hazard function :  $\Lambda_0(t) = \sum_{a_i \leq t} \lambda_i$ ,

this model is the uniquely appropriate one for grouped data from the continuous relative risk model.

## » Discrete and continuous relative risk model:

$$d\Lambda(t; x) = \exp(Z^\top \beta) d\Lambda_0(t),$$

which retains the multiplicative hazard relationship.

## » Discrete logistic model:

$$\frac{d\Lambda(t; x)}{1 - d\Lambda(t; x)} = \frac{d\Lambda_0(t)}{1 - d\Lambda_0(t)} \exp(Z^\top \beta),$$

specifies a linear log odds model for the hazard probability at each potential failure time.



