
Absolutely everyone
Bruce’s BRB talk
“Is this about stable distributions again?”


Absolutely no one
Bruce’s BRB talk
“Is this the future of statistics?”

Background

- Big data needs scalable solutions
- Clustered survival times may need marginal models

Executive Summary aka tl;dr

- I made Bridged parametric survival models fast
- 4 perspective-parameterization estimands:
  - conditional hazard ratio
  - marginal hazard ratio
  - conditional acceleration factor
  - marginal acceleration factor

Q: Why Marginalize? A: Interpretation

x=1	Exp(xβ^{c}+b_i)	Exp(xβ^{m})
Diabetes	?	✅
Tobacco	?	✅
Male	?	✅

Q: Why Marginalize? A: b/c Reviewer

Q: Why Pos. Stable? A: Straight lines

id	time	status	x
1	10	0	0
1	11	1	9
1	20	1	7
1	21	1	8
2	30	1	9
2	31	1	9
2	40	1	8
2	41	1	6
2	50	0	2
2	51	0	1
2	60	0	2
2	61	1	8
2	70	0	1
2	71	0	2

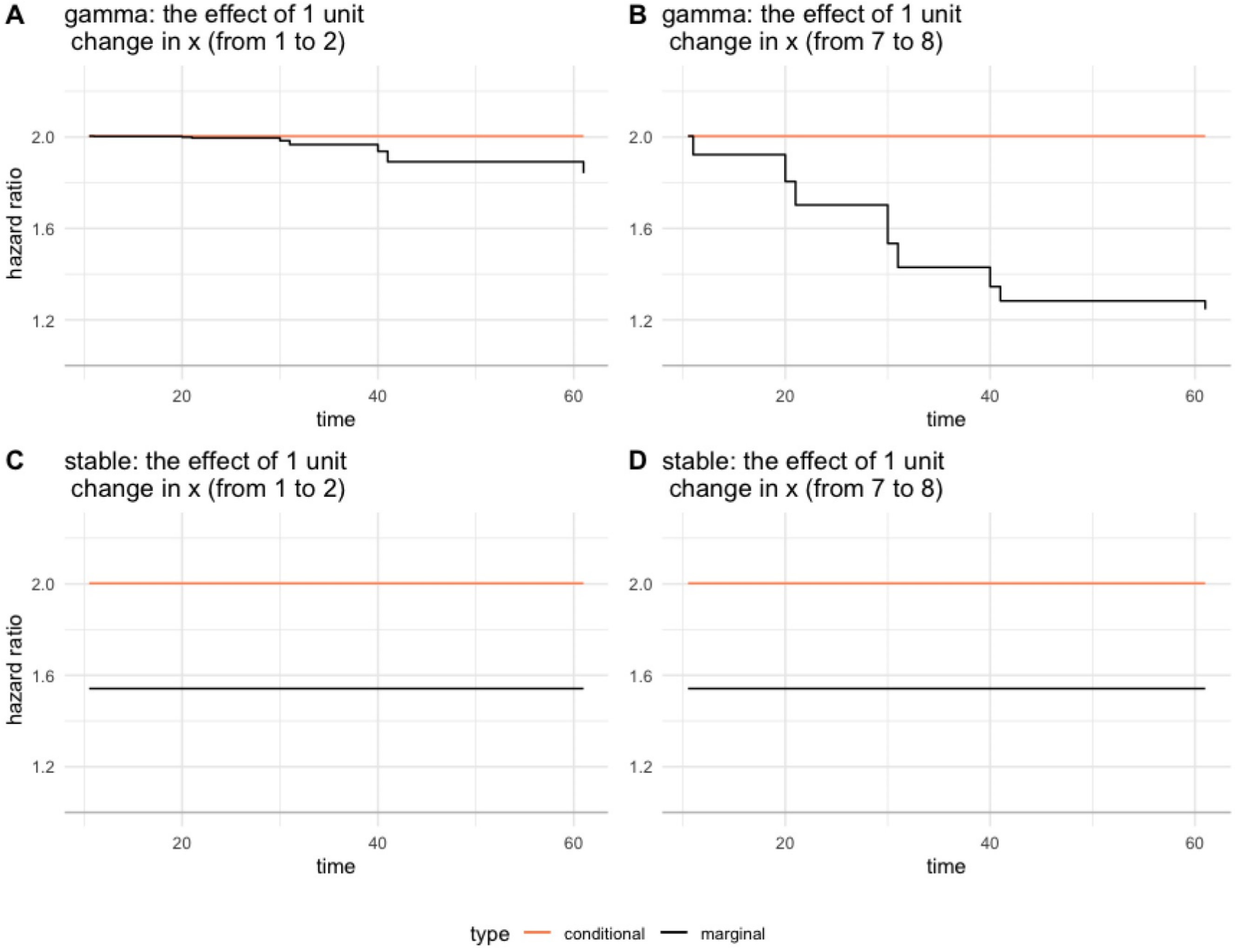
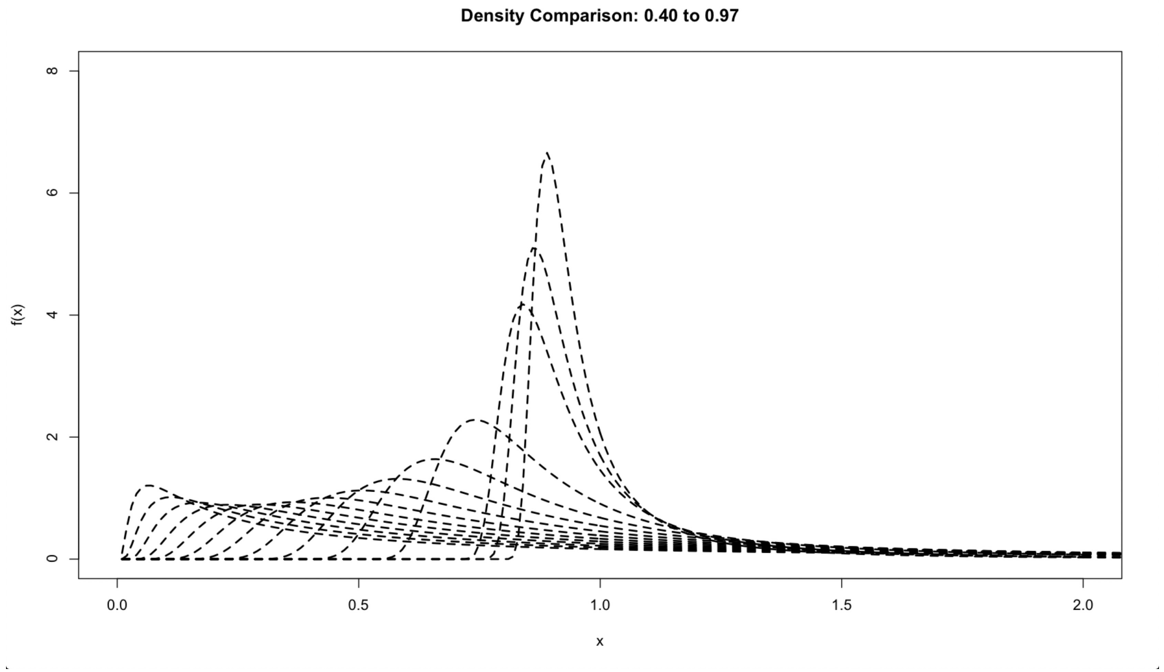
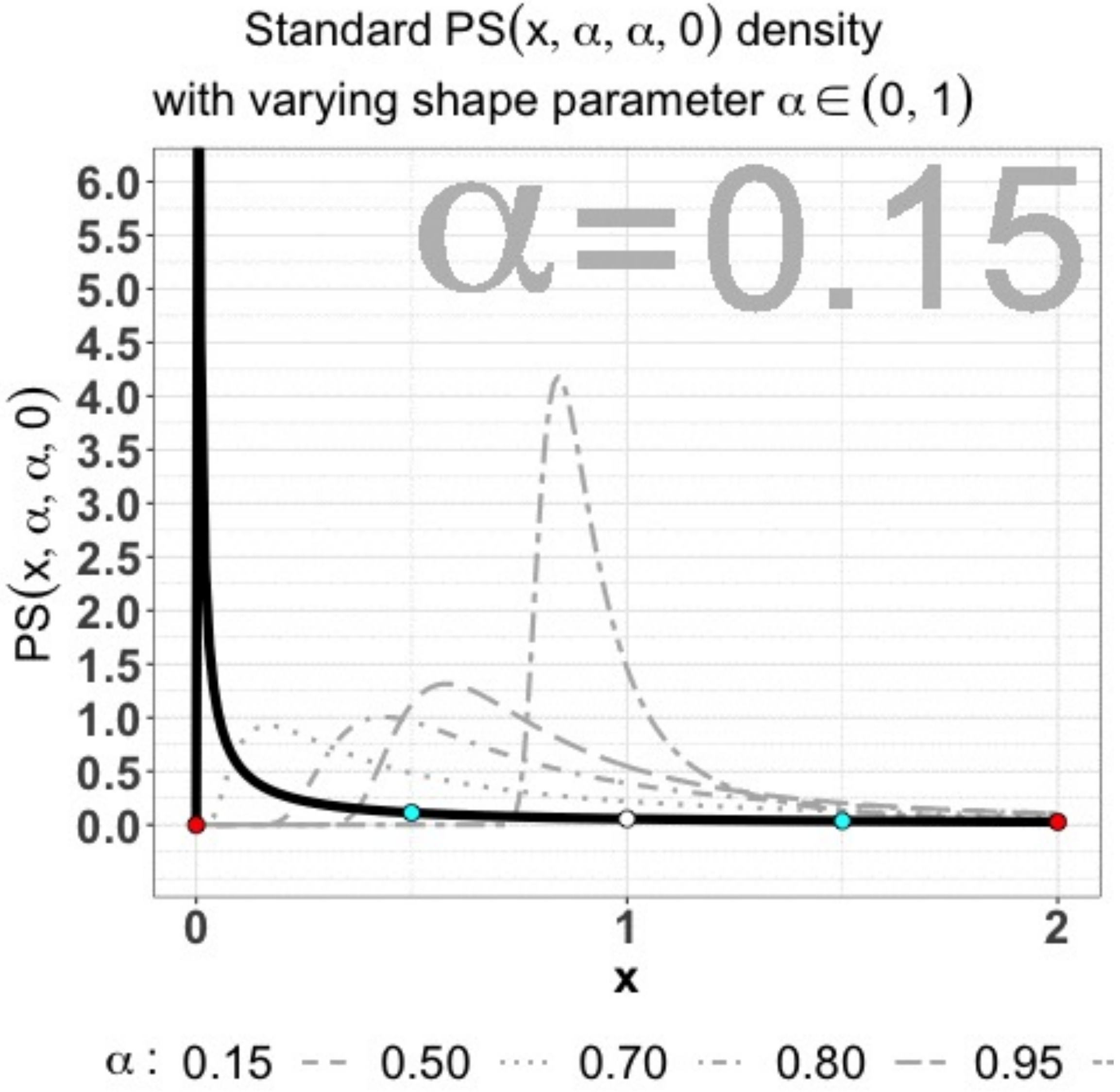


Figure 1: Plots of hazards ratios from fitting a proportional hazards model to the dataset in Table 1, with gamma (panel A and B) and positive stable (panel C and D) frailties. The conditional and marginal hazard ratios are presented in red and black, respectively.

$$f_{u_i}(u_i|\alpha) = -\frac{1}{\pi u_i}\sum_{k=1}^{\infty}\frac{\Gamma(k\alpha+1)}{k!}(-u_i^{-\alpha})^k \sin(\alpha k \pi)$$





$$
\begin{aligned}
f_{u_i}(u_i|\alpha) &= -\frac{1}{\pi u_i}\sum_{k=1}^{\infty}\frac{\Gamma(k\alpha+1)}{k!}(-u_i^{-\alpha})^k \sin(\alpha k \pi) \\
T|u_i &\sim Weibull(shape = p, scale = u_i\lambda) \\
f_{T|u_i}(t|p,\lambda,u_i) &= u_i\lambda p t^{p-1}\exp\{(-u_i\lambda t^p)\} \\
S_{T|u_i}(t|p,\lambda,u_i) &= \exp\{(-u_i\lambda t^p)\} \\
h_{T|u_i}(t|p,\lambda,u_i) &= u_i\lambda p t^{p-1} \\
T &\sim Weibull(shape = \alpha p, scale = \lambda^\alpha) \\
f_T(t|p,\lambda,\alpha) &= \lambda^\alpha \alpha p t^{\alpha p-1}\exp\{(-\lambda^\alpha t^{\alpha p})\} \\
S_T(t|p,\lambda,\alpha) &= \exp\{(-\lambda^\alpha t^{\alpha p})\} \\
h_T(t|p,\lambda,\alpha) &= \lambda^\alpha \alpha p t^{\alpha p-1}
\end{aligned}
$$

$$
\begin{aligned}
f_{u_i}(u_i|\alpha) &= -\frac{1}{\pi u_i}\sum_{k=1}^{\infty}\frac{\Gamma(k\alpha+1)}{k!}(-u_i^{-\alpha})^k \sin(\alpha k\pi) \\
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f_{T|u_i}(t|p,\lambda,u_i) &= u_i\lambda p t^{p-1}\exp\{(-u_i\lambda t^p)\} \\
S_{T|u_i}(t|p,\lambda,u_i) &= \exp\{(-u_i\lambda t^p)\} \\
h_{T|u_i}(t|p,\lambda,u_i) &= u_i\lambda p t^{p-1}
\end{aligned}
$$

Parameterization	Perspective	Shape	Scale
PH	Cond.	p_c	$u_i \exp\left(\gamma_h^c + x\beta_h^c\right)$
PH	Marg.	$\frac{p_m}{\alpha}$	$u_i \exp\left(\frac{1}{\alpha}\left(\gamma_h^m + x\beta_h^m\right)\right)$
AFT	Cond.	p_c	$u_i \exp\left(-p\left(\gamma_f^c + x\beta_f^c\right)\right)$
AFT	Marg.	$\frac{p_m}{\alpha}$	$u_i \exp\left(\frac{-p}{\alpha}\left(\gamma_f^m + x\beta_f^m\right)\right)$

$$f_{u_i}(u_i|\alpha) \;=\; -\frac{1}{\pi u_i}\sum_{k=1}^{\infty}\frac{\Gamma(k\alpha+1)}{k!}(-u_i^{-\alpha})^k \sin(\alpha k\pi)$$

$$\text{Hazard Ratio} = \frac{\lambda_h(x=1)}{\lambda_h(x=0)} = \frac{\exp(\gamma_h+\beta_h)}{\exp(\gamma_h)} = \exp(\beta_h)$$

$$\text{Acceleration Factor} = \frac{\substack{\text{time−quantile}\\ \text{for x=1}}}{\substack{\text{time−quantile}\\ \text{for x=0}}} = \frac{(-\log q)^{\frac{1}{p}}\exp(\gamma_f+\beta_f)}{(-\log q)^{\frac{1}{p}}\exp(\gamma_f)} = \exp(\beta_f)$$

Parameterization	Perspective	Shape	Scale
PH	Cond.	p_c	$u_i \exp(\gamma_h^c + x\beta_h^c)$
PH	Marg.	$\frac{p_m}{\alpha}$	$u_i \exp\left(\frac{1}{\alpha}(\gamma_h^m + x\beta_h^m)\right)$
AFT	Cond.	p_c	$u_i \exp\left(-p(\gamma_f^c + x\beta_f^c)\right)$
AFT	Marg.	$\frac{p_m}{\alpha}$	$u_i \exp\left(\frac{-p}{\alpha}(\gamma_f^m + x\beta_f^m)\right)$

$$
\begin{aligned}
f_{u_i}(u_i|\alpha) &= -\frac{1}{\pi u_i}\sum_{k=1}^{\infty}\frac{\Gamma(k\alpha+1)}{k!}(-u_i^{-\alpha})^k \sin(\alpha k\pi) \\
L_i^I &= L_i(p,\lambda,\alpha|t_{ij},\delta_{ij}) \\
&= \int \prod_{j=1}^{J_i}\left[h_{T|u_i}(t|p,\lambda,u_i)\right]^{\delta_{ij}} S_{T|u_i}(t|p,\lambda,u_i) f_{u_i}(u_i|\alpha)du_i
\end{aligned}
$$

$$
L_i^I = (\lambda_{i1}^{\delta_{i1}}\ldots\lambda_{iJ_i}^{\delta_{iJ_i}})(t_{i1}^{\delta_{i1}}\cdots t_{iJ_i}^{\delta_{iJ_i}})^{p-1}\int u_i^{n_i}\exp\left(-u_i\sum_{j=1}^{J_i}\lambda_{ij}t_{ij}^{p}\right)f_{u_i}(u_i|\alpha)du_i
$$

Parameterization	Perspective	Shape	Scale
PH	Cond.	p_c	$u_i \exp\big(\gamma_h^c + x\beta_h^c\big)$
PH	Marg.	$\frac{p_m}{\alpha}$	$u_i \exp\big(\frac{1}{\alpha}\big(\gamma_h^m + x\beta_h^m\big)\big)$
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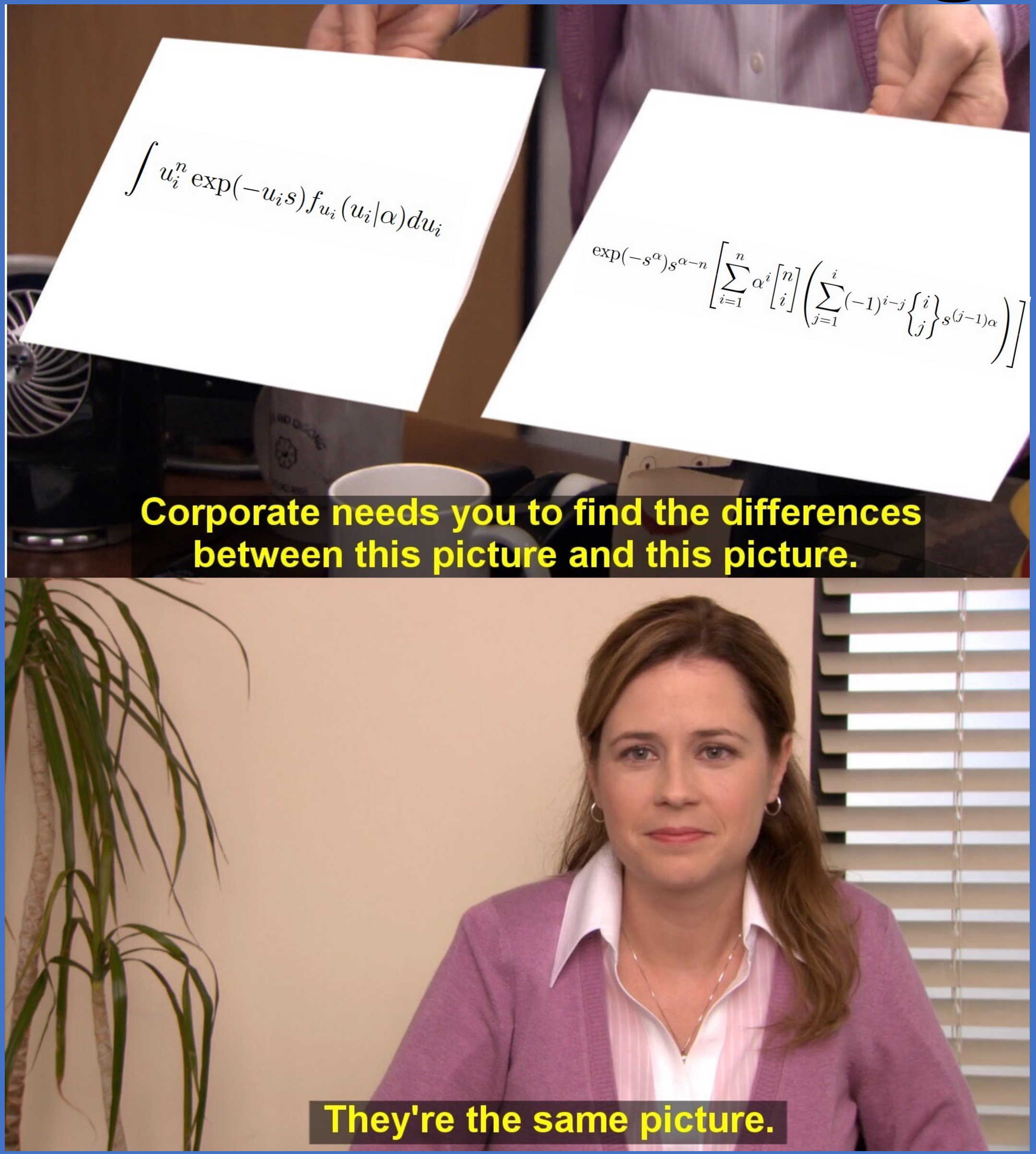
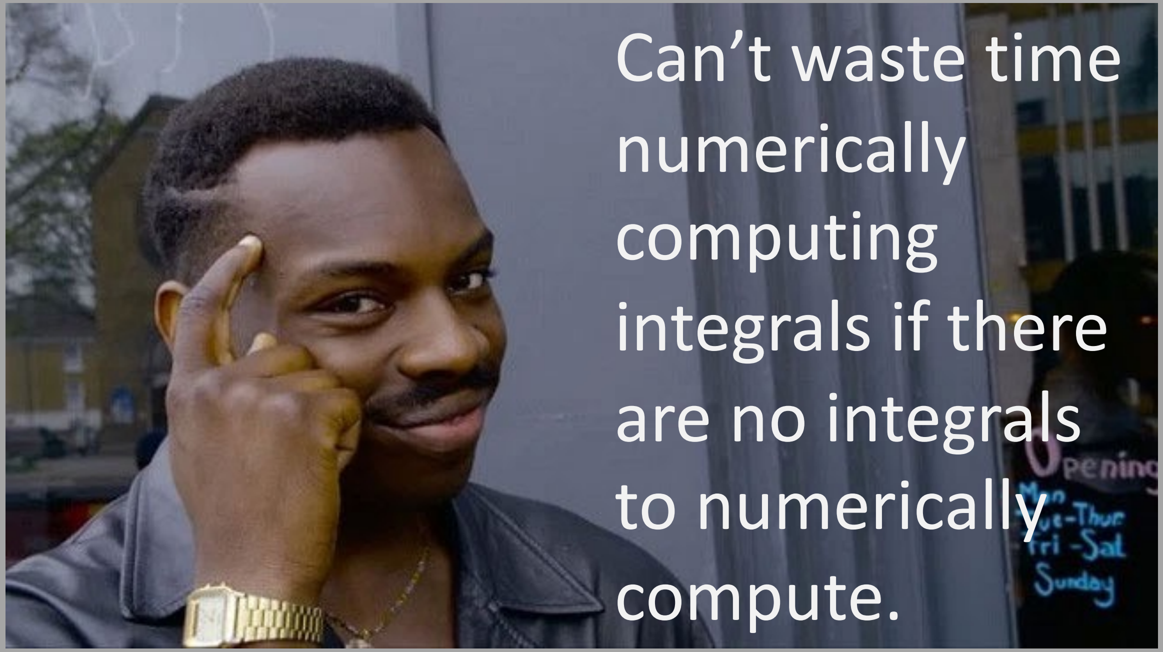
AFT	Marg.	$\frac{p_m}{\alpha}$	$u_i \exp\big(\frac{-p}{\alpha}\big(\gamma_f^m + x\beta_f^m\big)\big)$

Closed form integrals save time





Q: Which one?

A: All of them!

Covariate	R		SAS
	Recursive-Ω	Static-Stirling	Gaussian Quadrature
α	0.561 (0.010)	0.561 (0.010)	0.561 (0.010)
p	1.111 (0.015)	1.111 (0.015)	1.111 (0.015)
Diabetes			
β_h^c	0.384 (0.133)	0.384 (0.134)	0.384 (0.134)
β_h^m		0.215 (0.075)	0.215 (0.075)
β_f^c		-0.346 (0.121)	-0.346 (0.121)
β_f^m		-0.193 (0.068)	-0.194 (0.068)
Tobacco Use			
β_h^c	1.412 (0.097)	1.411 (0.102)	1.411 (0.102)
β_h^m		0.792 (0.056)	0.792 (0.056)
β_f^c		-1.271 (0.092)	-1.271 (0.092)
β_f^m		-0.713 (0.051)	-0.713 (0.051)
Sex (Male)			
β_h^c	0.220 (0.081)	0.220 (0.088)	0.220 (0.088)
β_h^m		0.123 (0.049)	0.124 (0.049)
β_f^c		-0.198 (0.079)	-0.198 (0.079)
β_f^m		-0.111 (0.044)	-0.111 (0.044)
Loglikelihood	-13982.045	-13982.045	-13982.035
Run time$_h^c$	36.1 minutes	2.7 minutes	4.6 days
Run time$_h^m$		2.4 minutes	1.3 days
Run time$_f^c$		2.1 minutes	1.4 days
Run time$_f^m$		2.8 minutes	1.4 days

		Hazard Ratio		Acceleration Factor	
Parameterization	Perspective	Cond.	Marg.	Cond.	Marg.
PH	Cond.	$\exp(\beta_h^c)$	$\exp(\alpha\beta_h^c)$	$\exp(\frac{1}{-p}\beta_h^c)$	$\exp(\frac{\alpha}{-p}\beta_h^c)$
PH	Marg.	$\exp(\frac{1}{\alpha}\beta_h^m)$	$\exp(\beta_h^m)$	$\exp(\frac{1}{-p\alpha}\beta_h^m)$	$\exp(\frac{1}{-p}\beta_h^m)$
AFT	Cond.	$\exp(-p\beta_f^c)$	$\exp(-p\alpha\beta_f^c)$	$\exp(\beta_f^c)$	$\exp(\alpha\beta_f^c)$
AFT	Marg.	$\exp(\frac{-p}{\alpha}\beta_f^m)$	$\exp(-p\beta_f^m)$	$\exp(\frac{1}{\alpha}\beta_f^m)$	$\exp(\beta_f^m)$

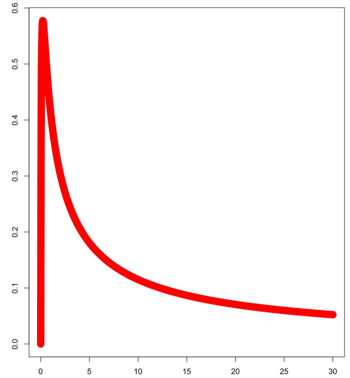
4.1 Diabetes and tooth failure

The coefficients from a conditional perspective would have a subject-specific interpretation, that is, a subject who is not diabetic would be $\exp(\beta_h^c) = 1.47$ times as likely to experience tooth failure, if they became diabetic, however, diabetics as a group (marginal interpretation) would have a $\exp(\beta_h^m) = 1.24$ times higher risk of tooth failure than non-diabetics. For acceleration factors, $\exp(\beta_f^c) = 0.71$ indicates that if a non-diabetic subject were to acquire diabetes, the corresponding time to tooth failure would be reduced by 29%, however, diabetics as a population tend to have a tooth failure 18% sooner, with a population-average acceleration factor of $\exp(\beta_f^m) = 0.82$.

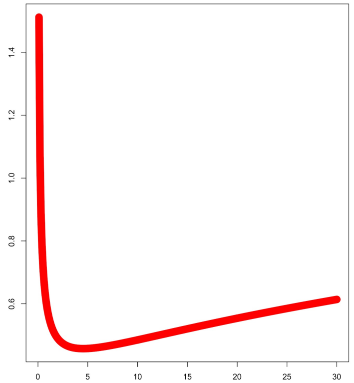
4.2 Tobacco use and tooth failure

The coefficients from a conditional perspective would have a subject-specific interpretation, that is, a non-tobacco user subject would be $\exp(\beta_h^c) = 4.10$ times as likely to experience tooth failure if they started using, however, tobacco-users (as a group) marginally would have a $\exp(\beta_h^m) = 2.21$ times higher risk of tooth failure than non-users. Similarly, for acceleration factors, $\exp(\beta_f^c) = 0.28$ indicates that if a never-user of tobacco were to become a user, the corresponding time to tooth failure would be reduced by 72%, however, tobacco users as a population tend to have a tooth failure 51% sooner, with a population-average acceleration factor of $\exp(\beta_f^m) = 0.49$.

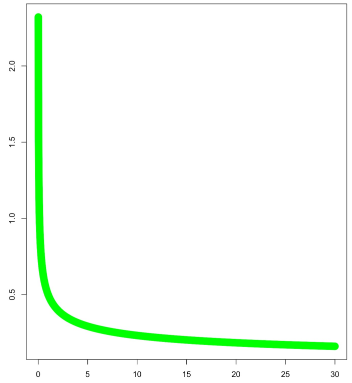
Weibull Hazard Capabilities



Unimodal



Bathtub



Monotonic

Software Options

proc nlmixed

parfm

Static-Stirling