FLEXIBLE DISTRIBUTIONAL MODELLING FOR PARAMETRIC SURVIVAL ANALYSIS

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Based on work done jointly with
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On the real line, we might model the continuous distribution of X with, say, a four-parameter family of distributions with

densities of the form $f((x-\mu)/\sigma; \alpha,\kappa)/\sigma$

where μ is location, σ is scale and α, κ are (density) shape parameters.

Typically, μ in particular, and maybe σ (maybe even the others) will depend on covariates.

The distributionologist's general approach to survival modelling

On the time line, we might model the continuous distribution of T with, say, a four-parameter family of distributions with

hazards of the form $\beta\, h(y/\sigma;\, \alpha,\kappa)/\sigma$

where β is vertical scale, σ is (horizontal) scale and α, κ are (hazard) shape parameters.

Typically, β and/or σ will depend on covariates (and maybe also the others) .

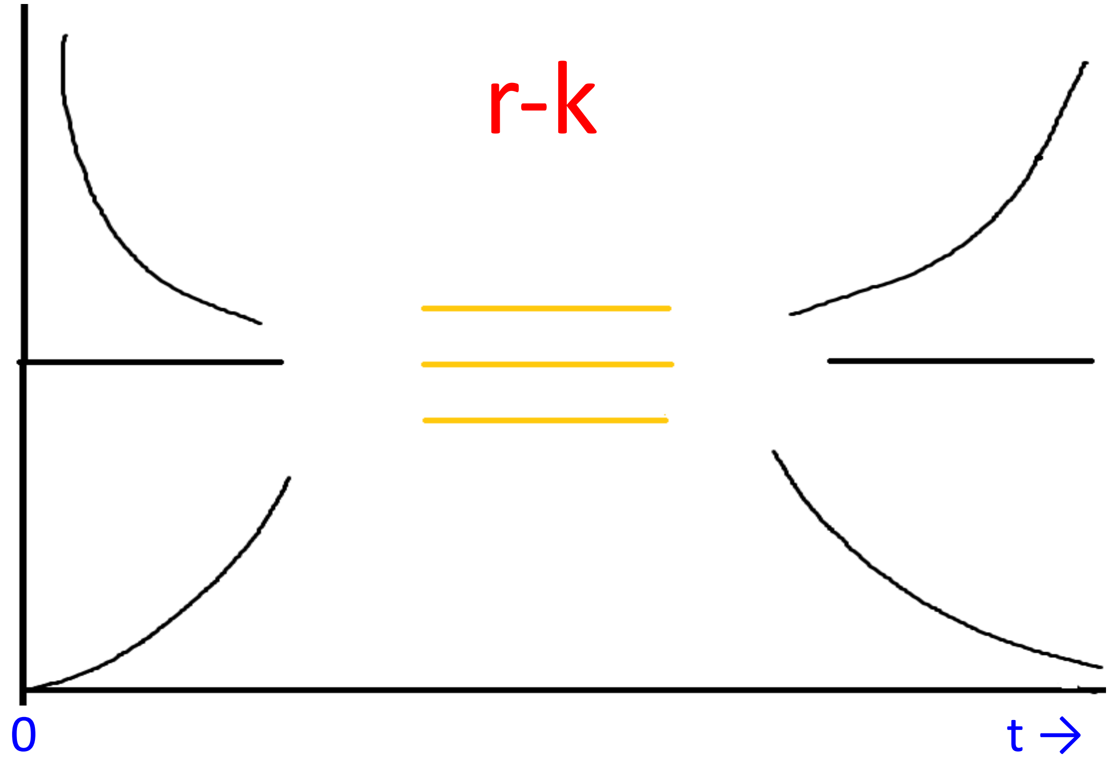
accelerated failure time

proportional hazards

EDEN HAZARD

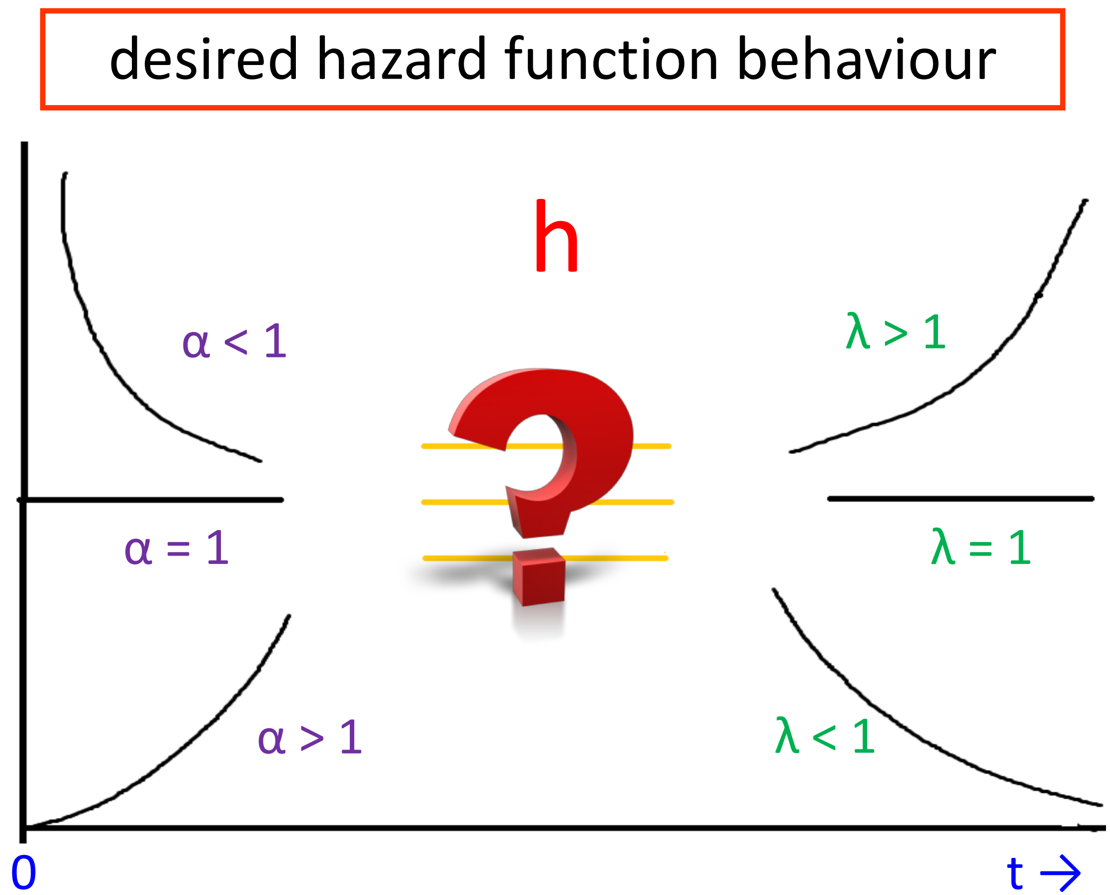
EDEN HAZARD scoring the second goal for BELGIUM as they beat ENGLAND 2-0 in the 3rd and 4th place play-off at the 2018 World Cup

HAL ROBSON-KANU scoring the second goal for WALES as they beat BELGIUM 3-1 in a quarter-final at the 2016 European Championships desired robson-kanu function behaviour



$h(y) \approx y^{\alpha-1}$ as $y \to 0$

$h(y) \approx y^{\lambda-1}$ as $y \to \infty$



Hoped-for shapes of h

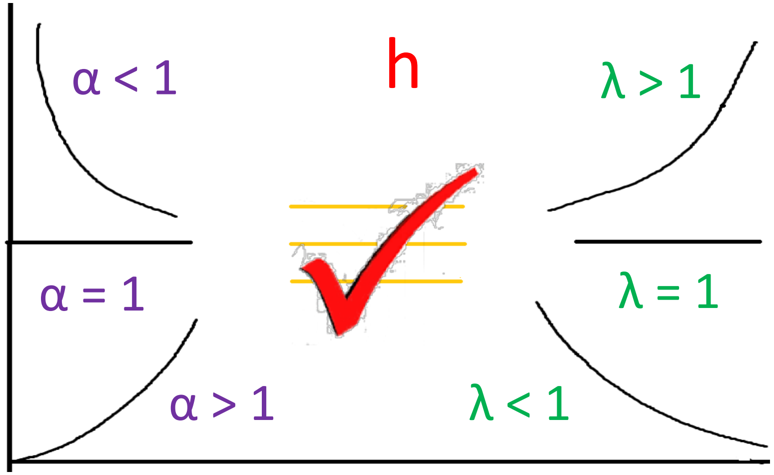
	α < 1	α = 1	α > 1
λ < 1	decreasing	decreasing	up-then-down
λ = 1	decreasing	constant	increasing
λ > 1	bathtub	increasing	increasing

The power generalised Weibull (PGW) distribution

$$h(y) = \lambda y^{\alpha-1}(1+y^{\alpha})^{\frac{\lambda}{\alpha}-1}$$

$h(y) \approx y^{\alpha-1}$ as $y \rightarrow 0$

$h(y) \approx y^{\lambda-1}$ as $y \rightarrow \infty$



Shapes of h for PGW distribution

	α < 1	α = 1	α > 1
λ < 1	decreasing	decreasing	up-then-down
λ = 1	decreasing	constant	increasing
λ > 1	bathtub	increasing	increasing

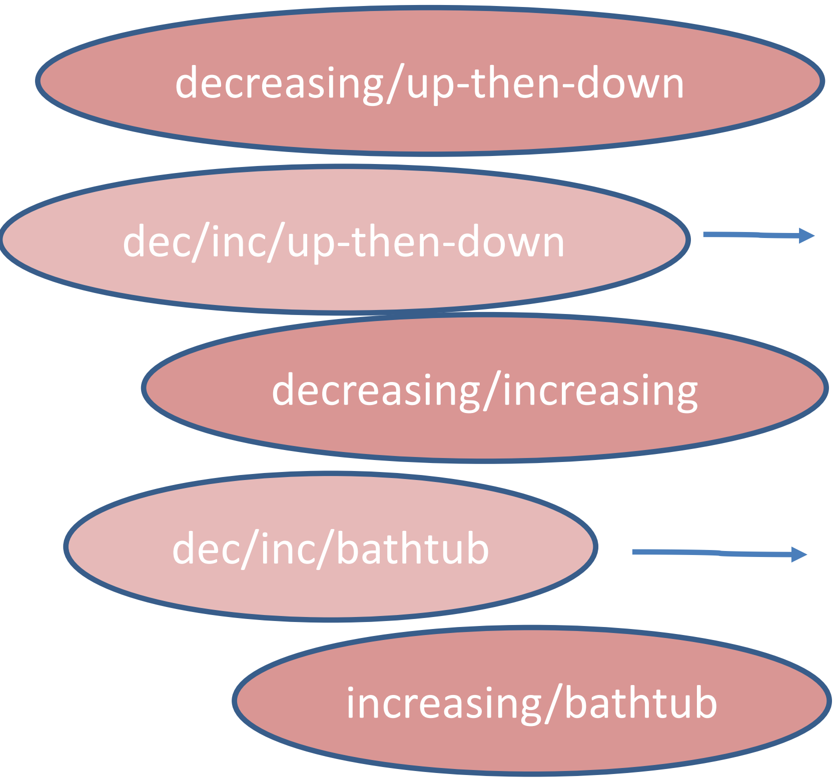
The APGW distribution (A for Adapted)

Reparametrise: $\kappa = \lambda / \alpha$

PGW cumulative hazard: $H(y) = (1 + y^{\alpha})^{\kappa} - 1$

Horizontally and vertically rescale to: $H(y) = \frac{\kappa + 1}{\kappa} \left\{ \left(1 + \frac{y^{\alpha}}{\kappa + 1} \right)^{\kappa} - 1 \right\}$

κ	distribution	more distributions
0	log-logistic	(with vscale parameter) Burr Type XII
1	Weibull	α = 1: exponential
2	"powered linear hazard"	α = 1: linear hazard
∞	Weibull extension	α = 1: Gompertz



κ	distribution	more distributions
0	log-logistic	(with vscale parameter) Burr Type XII
⋮	PGWs	⋮ ⋮ ⋮ ⋮
1	Weibull	$\alpha = 1$: exponential
⋮	PGWs	⋮ ⋮ ⋮ ⋮
∞	Weibull extension	$\alpha = 1$: Gompertz

In the lung cancer data application in our five-times-rejected-without-refereeing paper Burke, Jones & Noufaily (2018), our best models comprise:

- *one* scale parameter (PH β or AFT σ) and *one* shape parameter (α) depending on the covariate;

- APGW conditionals with κ averaging around 0.4, indicating hazard/tail behaviour between Weibull and log-logistic [decreasing/increasing/up-then-down hazards].

The (A)PGW distributions can also be "stepped through" by so-called frailty mixing.

- let PGW(β, α, κ) be the distribution with survival function $\exp[\, \beta \{ 1-(1+y^{\alpha})^{\kappa} \} \,]$,
- and TS(ω, ζ) be Tweedie/Hougaard's tempered stable or power variance distribution which has Laplace transform $\exp[\, \zeta \{1-(1+s)^{\omega}\} / \omega]$, $0 < \omega < 1$.

Let $T|B=b \sim \mathrm{PGW}(b, \alpha, \kappa)$ and $B \sim \mathrm{TS}(\omega, \omega\lambda)$.

Then $T \sim \mathrm{PGW}(\lambda, \alpha, \omega\kappa)$.

For example (case $\omega = ½$): let $T|B=b \sim \mathrm{PGW}(b, \alpha, \kappa)$ and $B \sim \mathrm{IG}(½, ½)$; then $T \sim \mathrm{PGW}(\lambda, \alpha, ½\kappa)$.

Dear M. C. Jones,

Greetings and good day.

I represent Editorial Office of Whioce Publishing Pte. Ltd. from Singapore. We have come across your recent article, "A bivariate" published in *Statistical Methods and Applications*. We feel that the topic of this article is very interesting. Therefore, we are delighted to invite you to join the Editorial Board of our journal, entitled International Journal of Mathematical Physics We also hope that you can submit your future work in our journal. Please reply to this email if you are interested in joining the Editorial Board.

I look forward to hearing your positive response. Thank you for your kind consideration.

Best regards,

MF Sim

Editorial Office

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The frailty property can be taken advantage of to produce a “natural” bi-(multi-)variate model with PGW marginals via the shared frailty approach:

Univariate (from a previous slide): $T|B=b \sim PGW(b, \alpha, \kappa)$ and $B \sim TS(\omega, \omega\lambda)$

Bivariate: $T_1|B=b \sim PGW(b, \alpha_1, \kappa_1)$, $T_2|B=b \sim PGW(b, \alpha_2, \kappa_2)$, and $B \sim TS(\omega, \omega\lambda)$

Then,

$$P(T_1 \geq t_1, T_2 \geq t_2) = \exp\left(\lambda\left[1 - \{(1 + t_1^{\alpha_1})^{\kappa_1} + (1 + t_2^{\alpha_2})^{\kappa_2} - 1\}^{\omega}\right]\right)$$

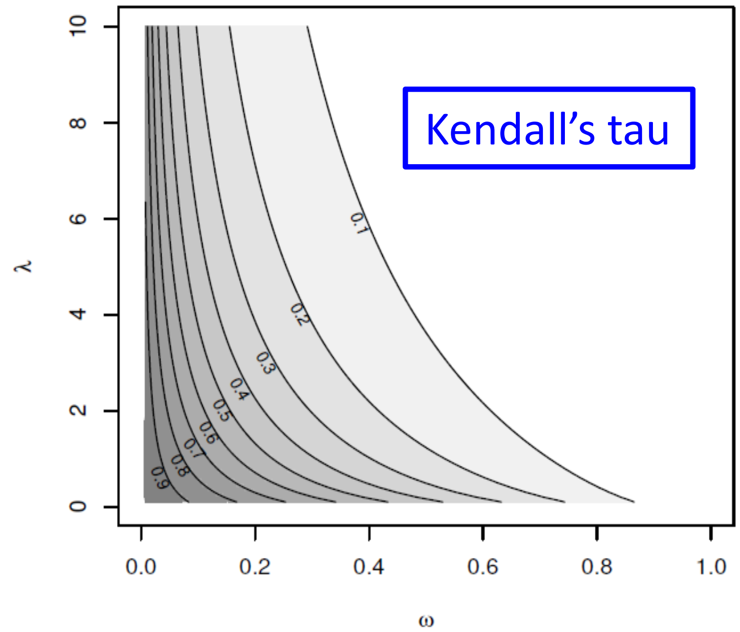
Writing $\tau_i = \omega\kappa_i$, $i = 1,2$, marginally we have

$T_1 \sim PGW(\lambda, \alpha_1, \tau_1)$, $T_2 \sim PGW(\lambda, \alpha_2, \tau_2)$

joined by the BB9 or power variance function (PVF) copula

$$C(u, v) = \exp\left[\lambda - \left\{(\lambda - \log u)^{1/\omega} + (\lambda - \log v)^{1/\omega} - \lambda^{1/\omega}\right\}^{\omega}\right]$$

- $\omega = 1$: independence
- $\omega \to 0$: marginals equal
- $\lambda \to \infty$: independence
- $\lambda \to 0$: Gumbel copula



And he’s right! The above gives us PGW marginals when we’d prefer to have APGW marginals.

The problem is that in the APGW case we need the frailty distribution to depend on κ … which is not the same in both margins in general.

So we ***define*** the marginals to be

$T_1 \sim \mathrm{APGW}(\lambda, \alpha_1, \tau_1),\ T_2 \sim \mathrm{APGW}(\lambda, \alpha_2, \tau_2)$

and join them by the BB9/PVF copula

$$C(u, v) = \exp\left[\lambda - \left\{(\lambda - \log u)^{1/\omega} + (\lambda - \log v)^{1/\omega} - \lambda^{1/\omega}\right\}^{\omega}\right]$$

in the usual way by marginal transformation

The result is slightly messier but still tractable with essentially the same properties (exactly the same properties where they depend solely on the copula)

In the retinopathy application in our once-rejected-without-refereeing paper Jones, Noufaily & Burke (2018), our best models comprise:

- *separate* scale parameters (AFT $\sigma_i(x)$) depending on the covariates (including treatment) and *common* shape parameters (both $\alpha(x)$ and τ);
- τ estimated to be 0.15, CI (-0.26, 0.78): log-logistic, perhaps, but not Weibull;
- dependence parameters are such that Kendall's tau is about 0.2 (down from 0.3 when inappropriate Weibull marginals are used)

Reminder: the PGW distribution has cumulative hazard function [c.h.f.] $(1+y^{\alpha})^{\kappa} - 1$.

This is of the form $H\{\kappa H^{-1}(y^{\alpha})\} = H_{\kappa}(y^{\alpha})$, say, where H and H^{-1} are themselves c.h.f.s. In fact,

$H(y) = e^{y} - 1$ (Gompertz)

$H^{-1}(y) = \log(1+y)$ (log-logistic)

I'm currently exploring this general set-up with Karim Anaya-Izquierdo & Alice Davis (Bath, UK)

Swap the choice of H and H^{-1}: consider $H_\kappa(y) = H\{\kappa H^{-1}(y)\}$ with

$H(y) = \log(1+y)$ $\quad$ $H^{-1}(y) = e^y - 1$

(log-logistic) $\quad$ (Gompertz)

This gives the distribution with c.h.f. $\log(1 - \kappa + \kappa e^y)$ …

… which is nothing other than the proportional odds (PO) model, which has

$$\frac{S_\kappa(y)}{1 - S_\kappa(y)} = \frac{1}{\kappa} \frac{e^{-y}}{1 - e^{-y}}$$

(This distribution is also known as a Marshall-Olkin (MO) distribution)

The (A)PO/MO distribution can also be "stepped through" by frailty mixing:

- let PO(β, α, κ) be the distribution with survival function $(1-\kappa+\kappa e^{y^{\alpha}})^{-\beta}$,
- and NB(ω, ζ) be the distribution of ζ/ω + NegativeBinomial (ζ/ω, 1/ω) which has Laplace transform $(1-\omega+\omega e^{t})^{-\zeta/\omega}$, ω > 1.

Let T|B=b ~ PO(b, α, κ) and B ~ NB(ω, ωλ).

Then T ~ PO(λ, α, ωκ).

Bivariate: $T_1|B=b \sim PO(b, \alpha_1, \kappa_1)$, $T_2|B=b \sim PO(b, \alpha_2, \kappa_2)$, and $B \sim NB(\omega, \omega\lambda)$

Writing $\tau_i = \omega\kappa_i$, $i = 1,2$, marginally we have

$T_1 \sim PO(\lambda, \alpha_1, \tau_1)$, $T_2 \sim PO(\lambda, \alpha_2, \tau_2)$

joined by the BB10 copula

$$C(u,v) = \frac{uv}{\left\{1-\left(1-\frac{1}{\omega}\right)(1-u^{1/\lambda})(1-v^{1/\lambda})\right\}^{\lambda}}$$

In summary:

- I have looked at a general parametric framework for the modelling of survival distributions with cumulative hazard functions of the form $\beta\, H(y/\sigma;\ \alpha,\kappa)$, which have two scale-type parameters and two shape parameters;
- I have recommended a particular choice of H, that of the PGW distribution with $H(y;\ \alpha,\kappa) = \ (1+y^{\alpha})^{\kappa} - 1$;
- I have noted that one often needs one scale-type parameter and one shape parameter to depend on covariates;
- I have looked at attractive bivariate extension through shared frailty;
- and briefly suggested a parallel development for proportional odds models.

A natural extension would be to allow non-parametric dependence of parameter(s) on covariates.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