

'survextrap': flexible and transparent Bayesian survival modelling using combinations of data and judgements

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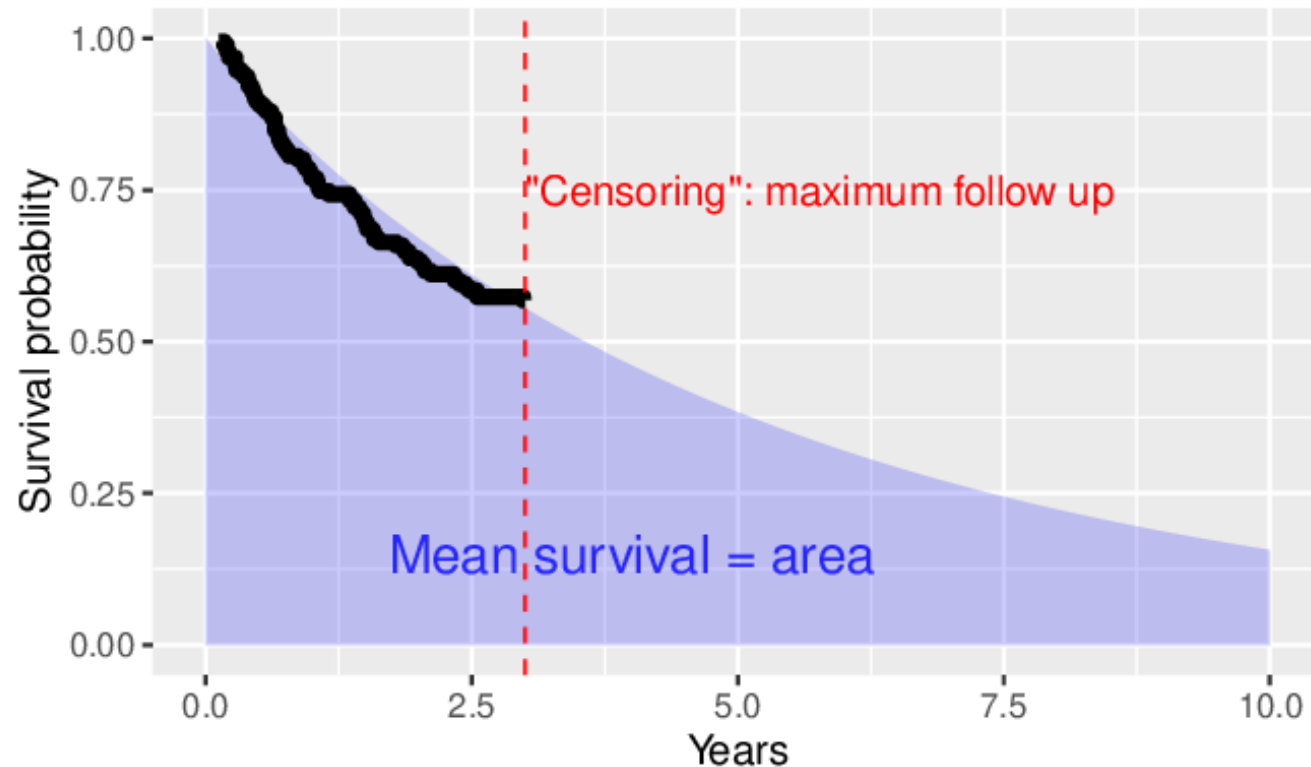


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Survival extrapolation: long-term decisions from short-term data



Limited trial follow up

Health economic decision making needs **expected survival** over the **longer term**

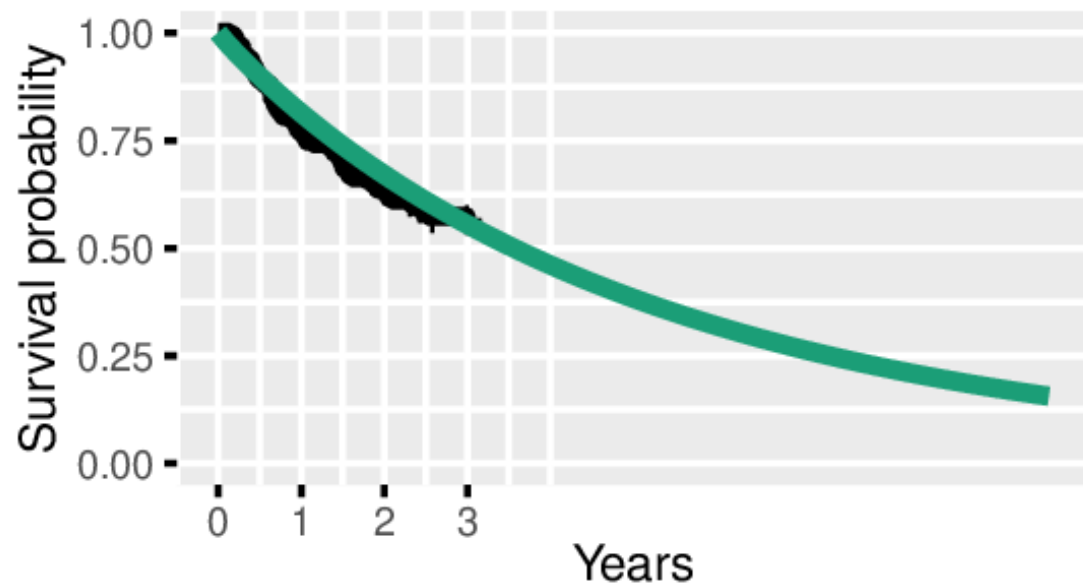
Area under the survival curve.
Estimated by **parametric models...**

Consequences of policy decisions will last longer than the end of the data

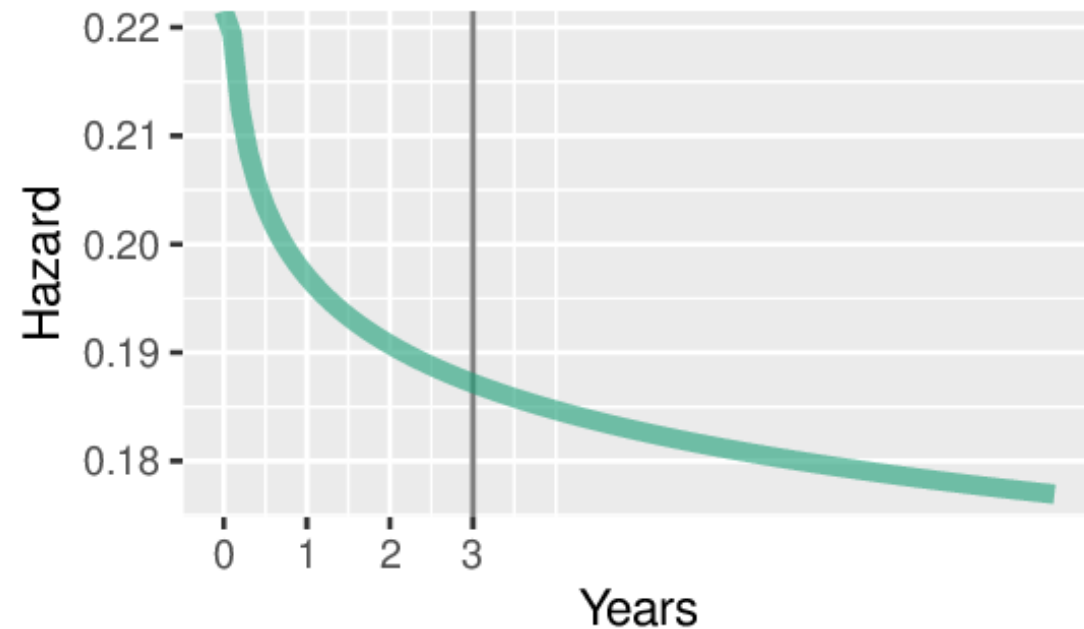
Parametric survival models: examples

Weibull distribution

Survivor function $S(t|\lambda, \alpha) = \exp(-\lambda t^\alpha)$



Hazard function $h(t|\lambda, \alpha) = \lambda \alpha t^{\alpha-1}$

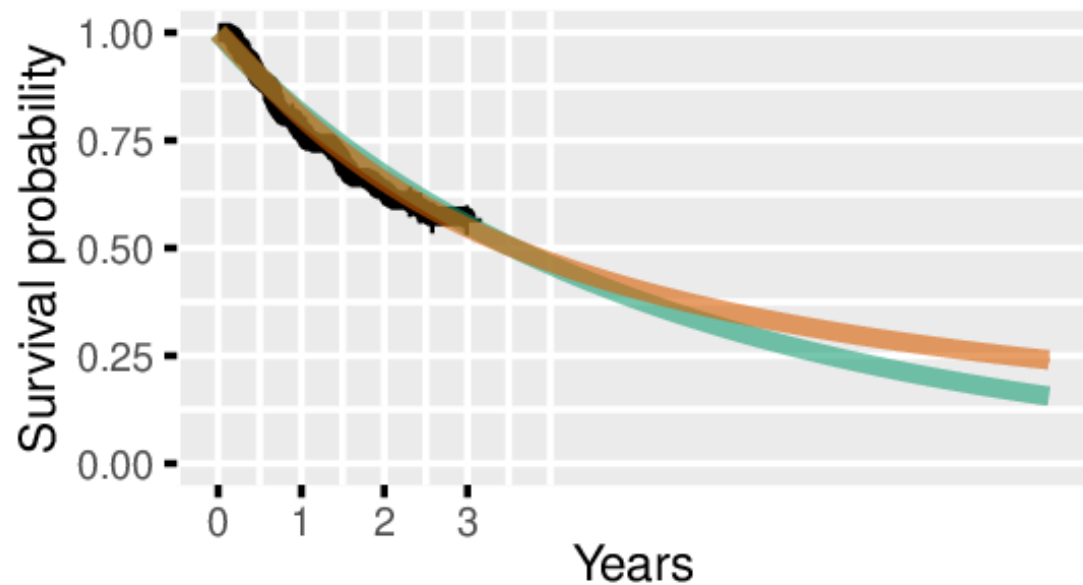


Parametric survival models: examples

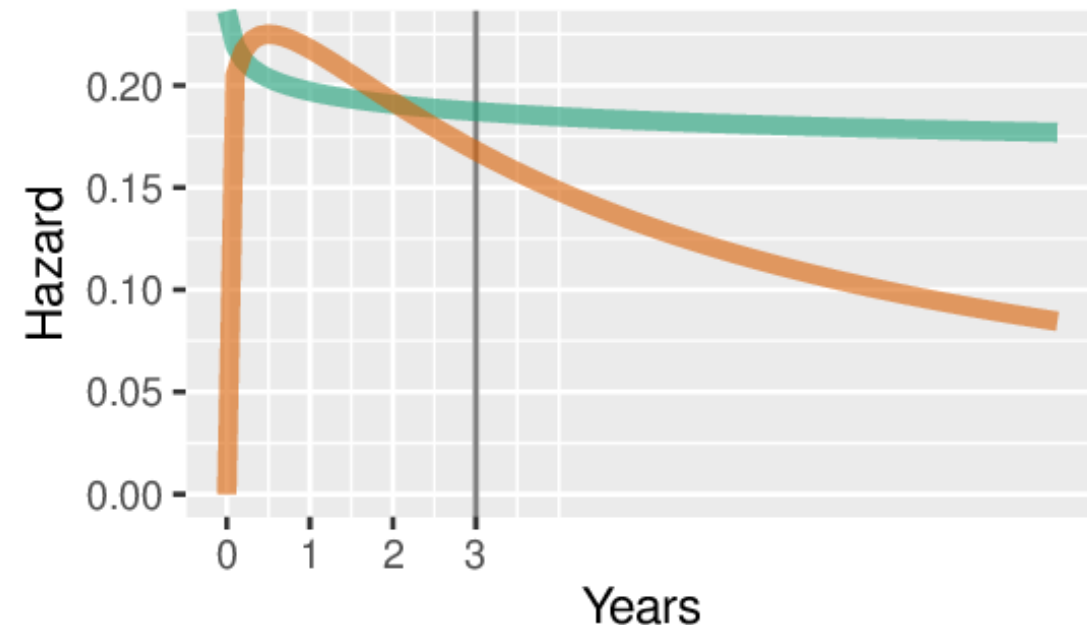
Log-logistic distribution

Survivor function

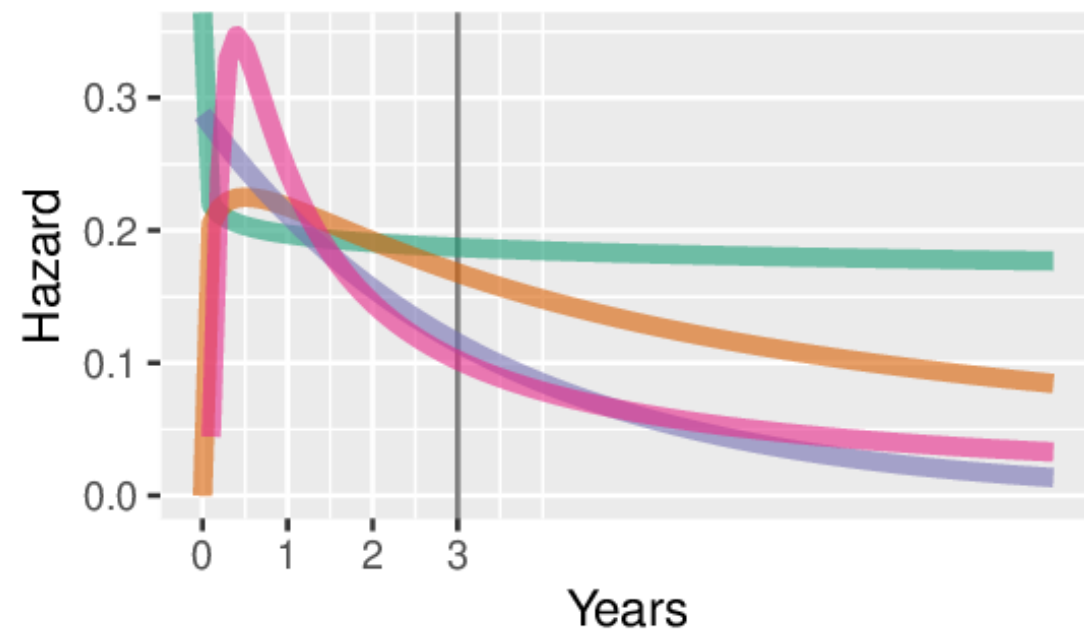
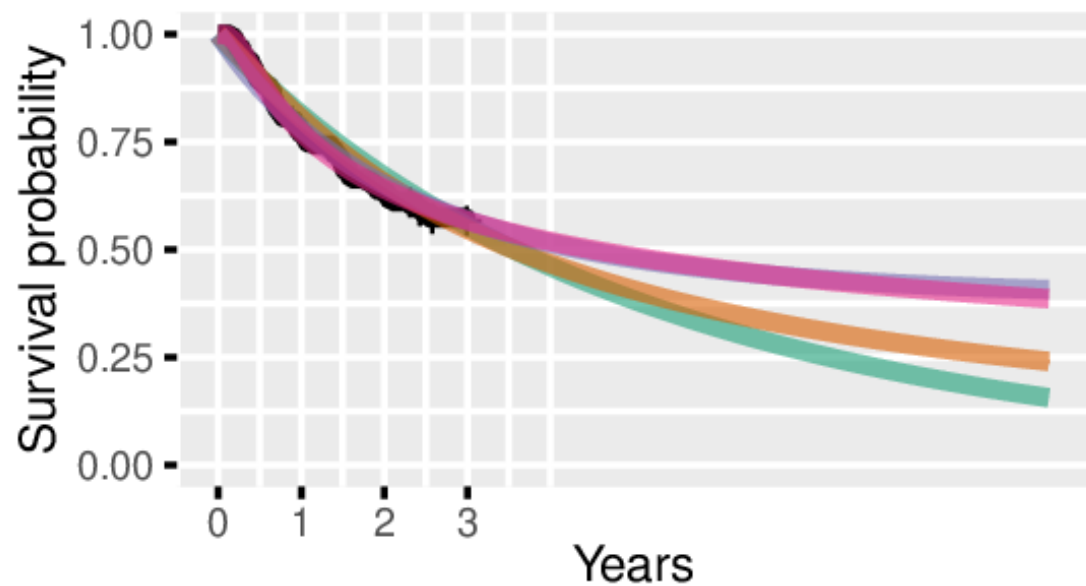
$$S(t|\lambda, \alpha) = 1/(1 + (t/b)^a)$$



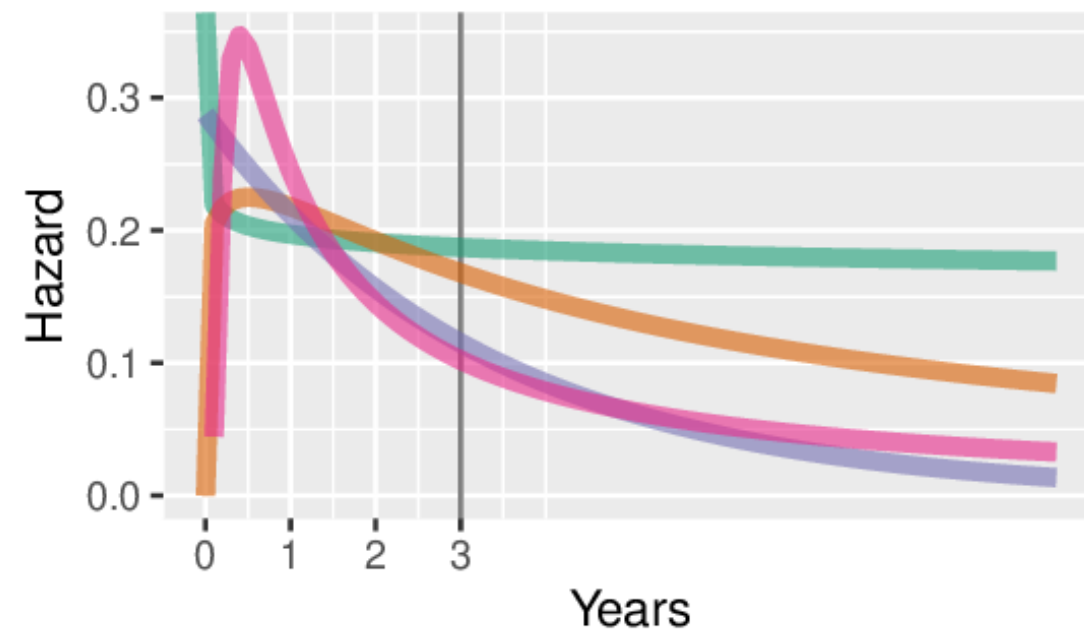
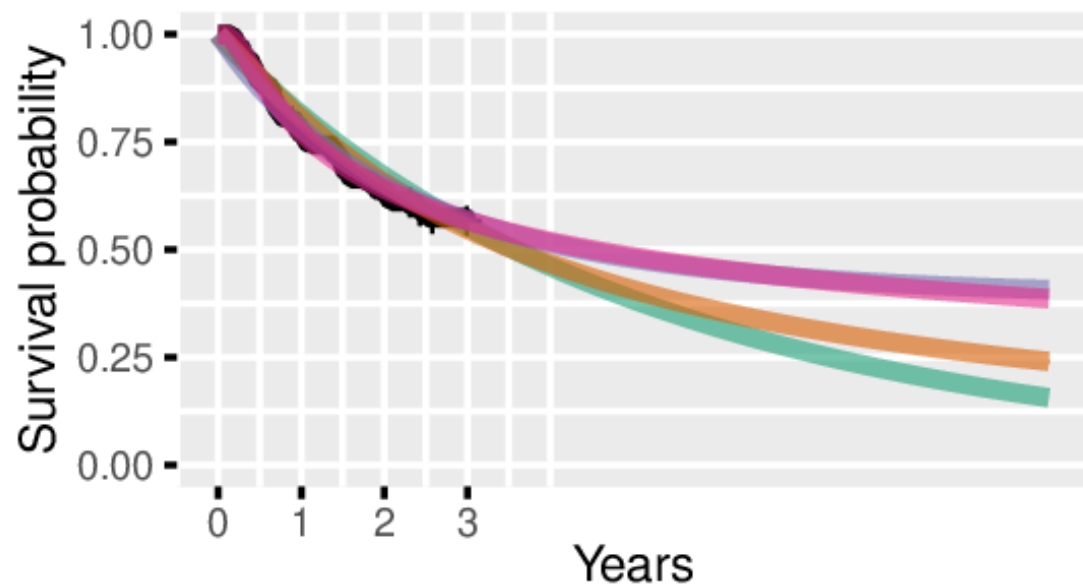
Hazard function $h(t|\lambda, \alpha) =$



Parametric survival models: examples



Parametric survival models: examples



Fit a set of models and judge which :

- ▶ fits the data best in the short term? (easy, e.g. AIC)
- ▶ gives more plausible risk changes in the long term? **harder**

External information about longer-term survival

Observed data

- ▶ survival on “standard of care” arm same as recent patients in a disease registry?
- ▶ survival of people with the disease cannot be better than comparable people in the general population?

Clinical judgements about the mechanism

- ▶ e.g. some people get cured of the disease, so disease-specific hazard of death reduces to zero

Formally-elicited judgements

e.g. probability of survival to 10 years, given survival to 5 years

Use such information in a transparent, statistically-principled way

<https://chjackson.github.io/survextrap>

Jackson, BMC Med Res Meth, 2023

Design goals:

1. Incorporate all available data: *Bayesian evidence synthesis*
2. Fit the data as well as possible: *Spline modelling*
3. Quantify uncertainty: *Bayesian*
4. Be easy to use: *R package wraps Stan, single commands to fit model / extract outputs*
5. Make key assumptions transparent: *user states these in their command, computer does the hard work*

Rapid tour...

survextrap R package

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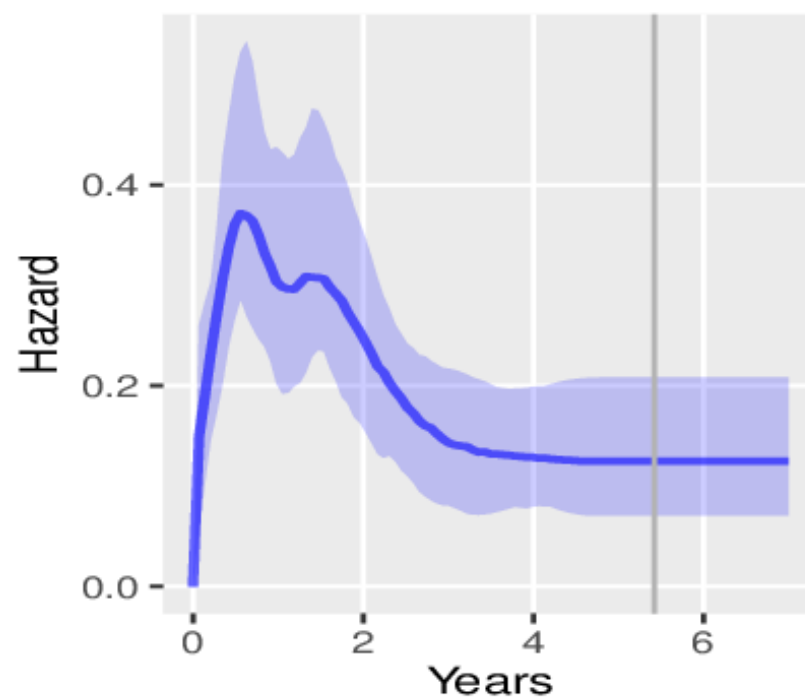
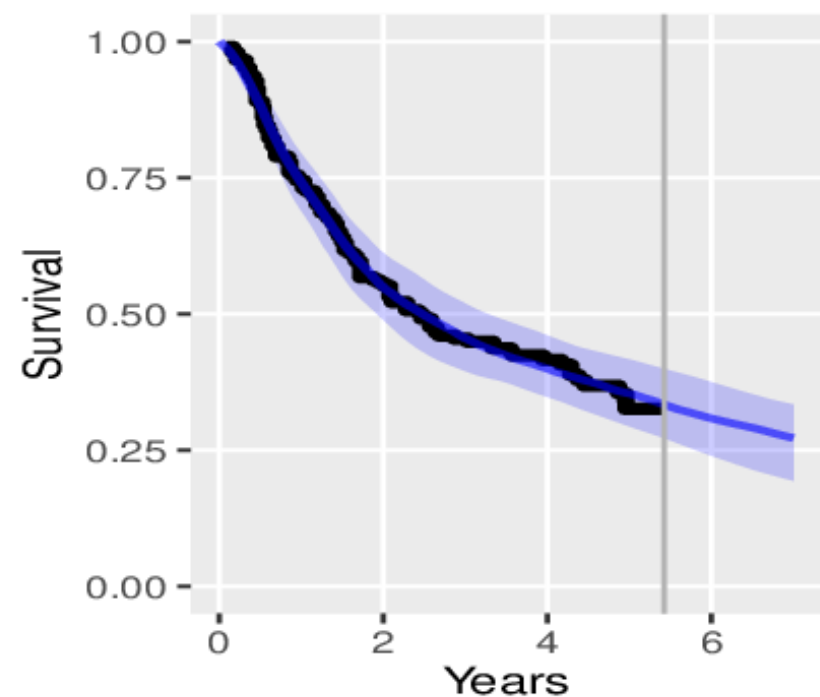
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Rapid tour...

Spline-based, flexible model for the hazard

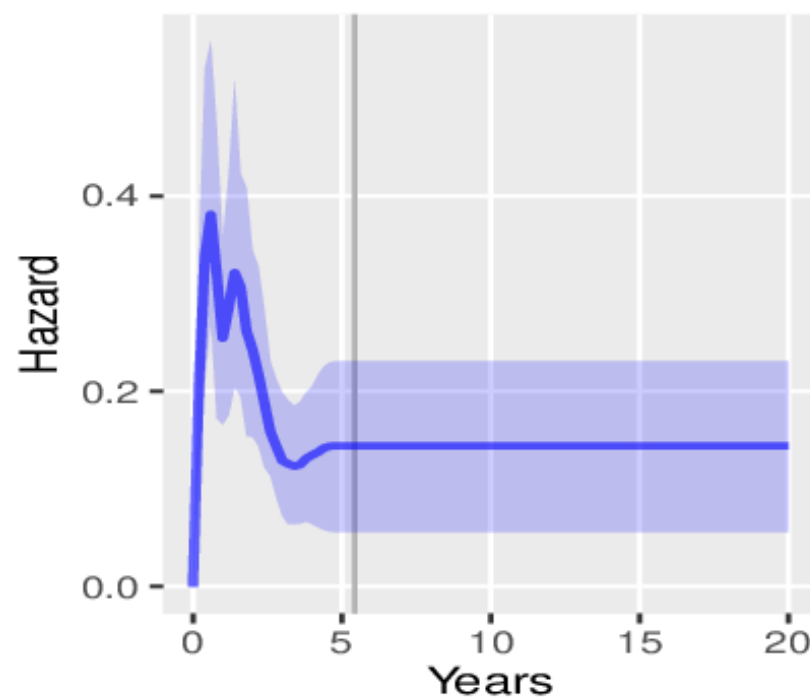
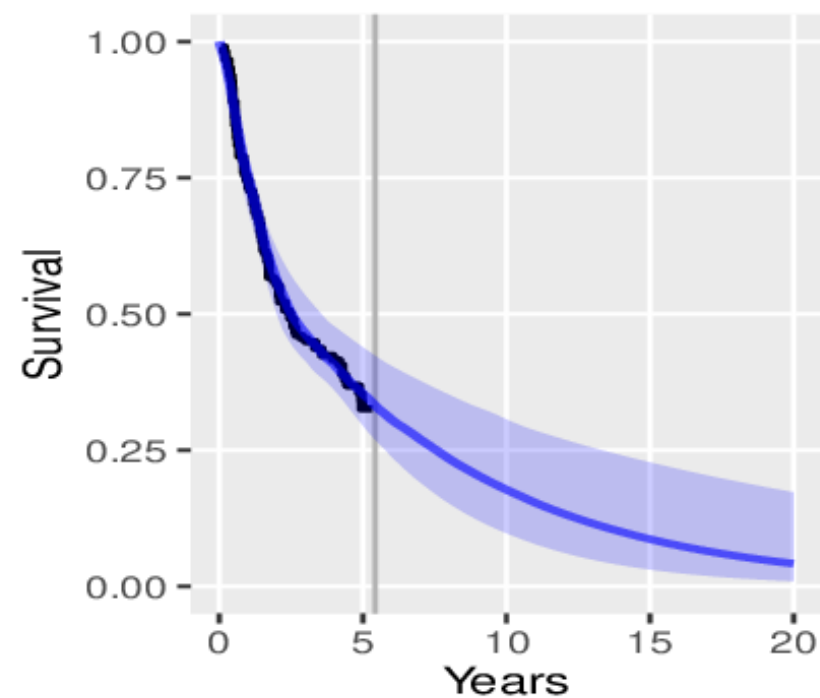


Running example:
head and neck cancer trial data from
Guyot et al. 2017

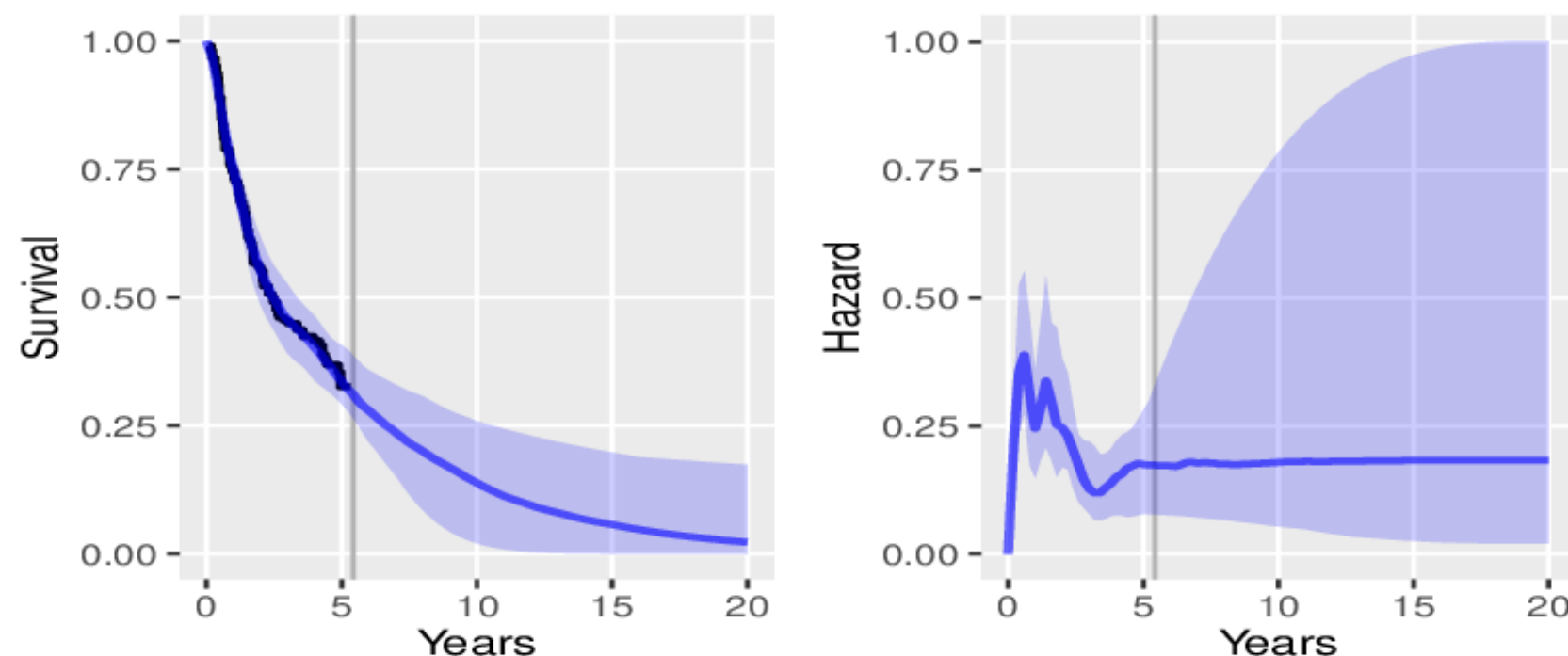
Default model: M-spline
10 parameters, penalized to control overfitting
Flexible hazard within data, constant beyond data

```
mod1 <- survextrap(Surv(years, d) ~ 1, data=dat)
```

Spline-based, flexible model for the hazard



Spline-based, flexible model for the hazard



Allow hazard to vary to 20 years, by adding a **spline “knot”**.

Weak assumption: hazard is **smooth** — short-term extrapolation influenced weakly by **latest** data.

Posterior represents **“structural” uncertainty due to lack of data**

```
mod2 <- survextrap(Surv(years, d) ~ 1, add_knots=20)
```

Including data external to the trial

Supplied as **aggregate conditional survival counts** over any number of different time intervals. Example:

Follow-up period		Number		Covariates
From t	To u	Alive at t	Still alive at u	
5	10	358	325	...
10	15	308	285	...
etc.				

- ▶ Registry data, population data, and elicited judgements... can often be expressed in this form
- ▶ Each count of survivors is a binomial outcome, with probability defined by the spline model and covariates
- ▶ Bayesian evidence synthesis: posterior for parameters determined given individual and external data together

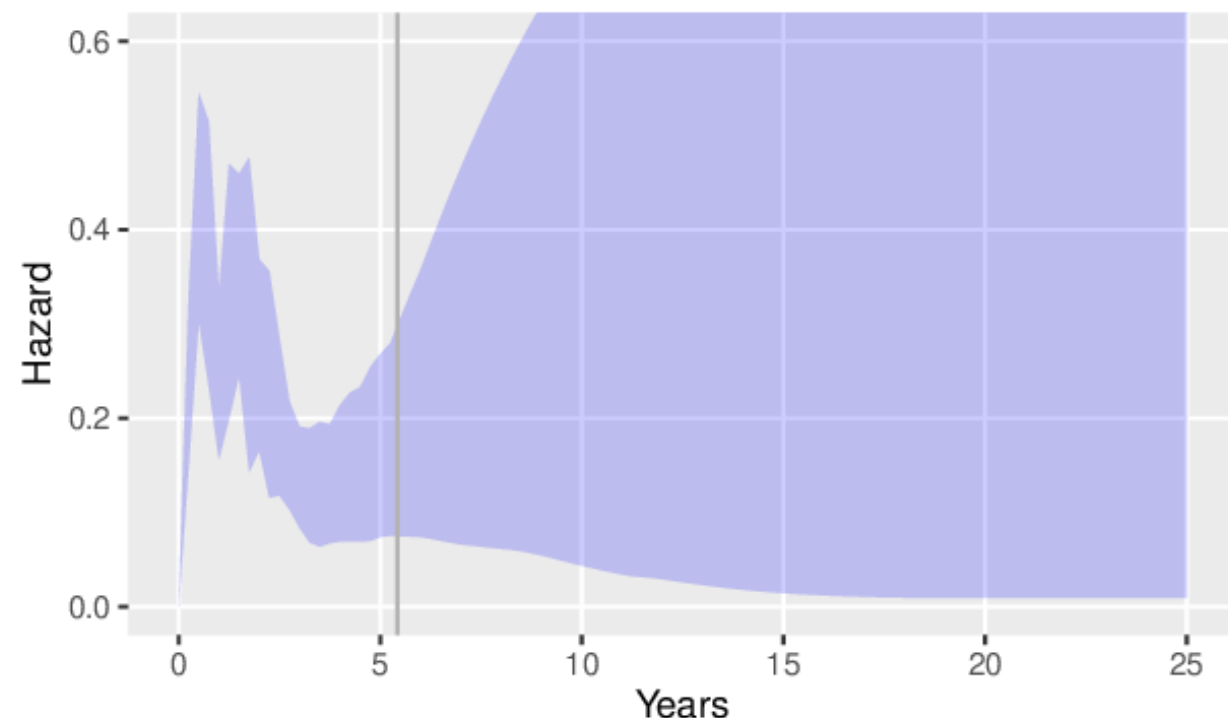
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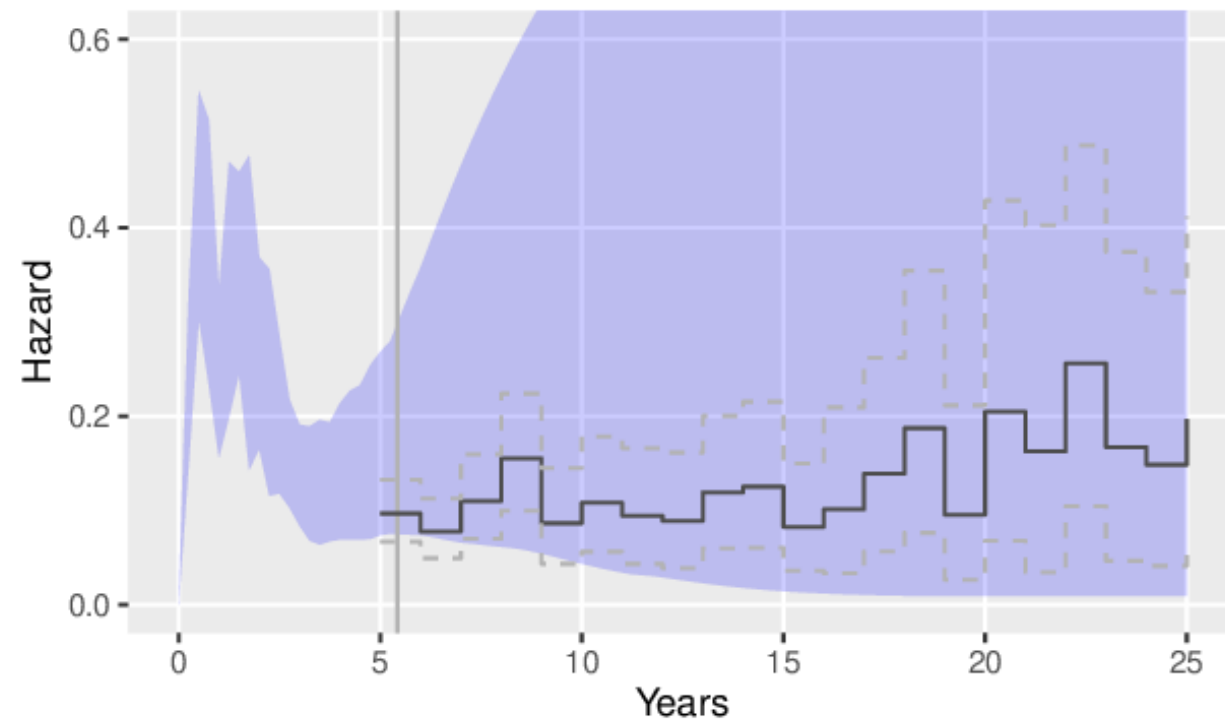
Survival modelling with external data: example



With no external data, and just a smoothness assumption, estimated long-term hazard is extremely uncertain

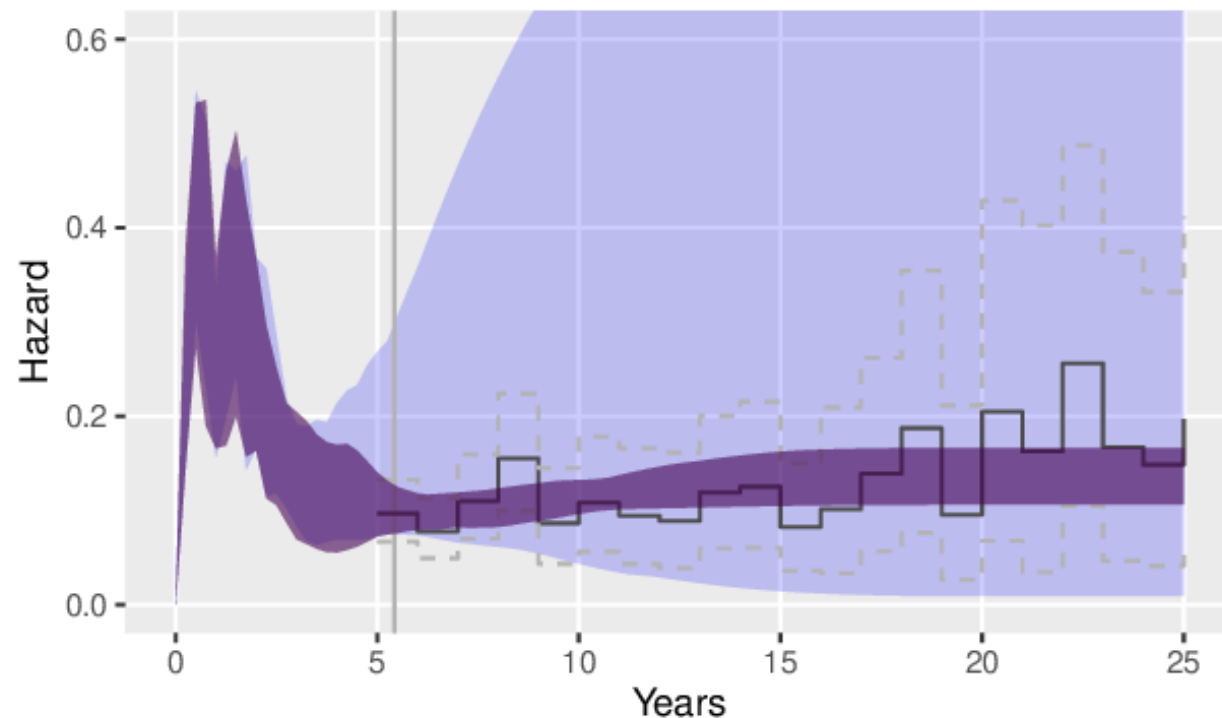
```
mod_seer <- survextrap(Surv(years, d) ~ 1, data=dat,  
                        add_knots=20)
```


Survival modelling with external data: example



Registry data give annual survival rates from 5 to 25 years.

Survival modelling with external data: example

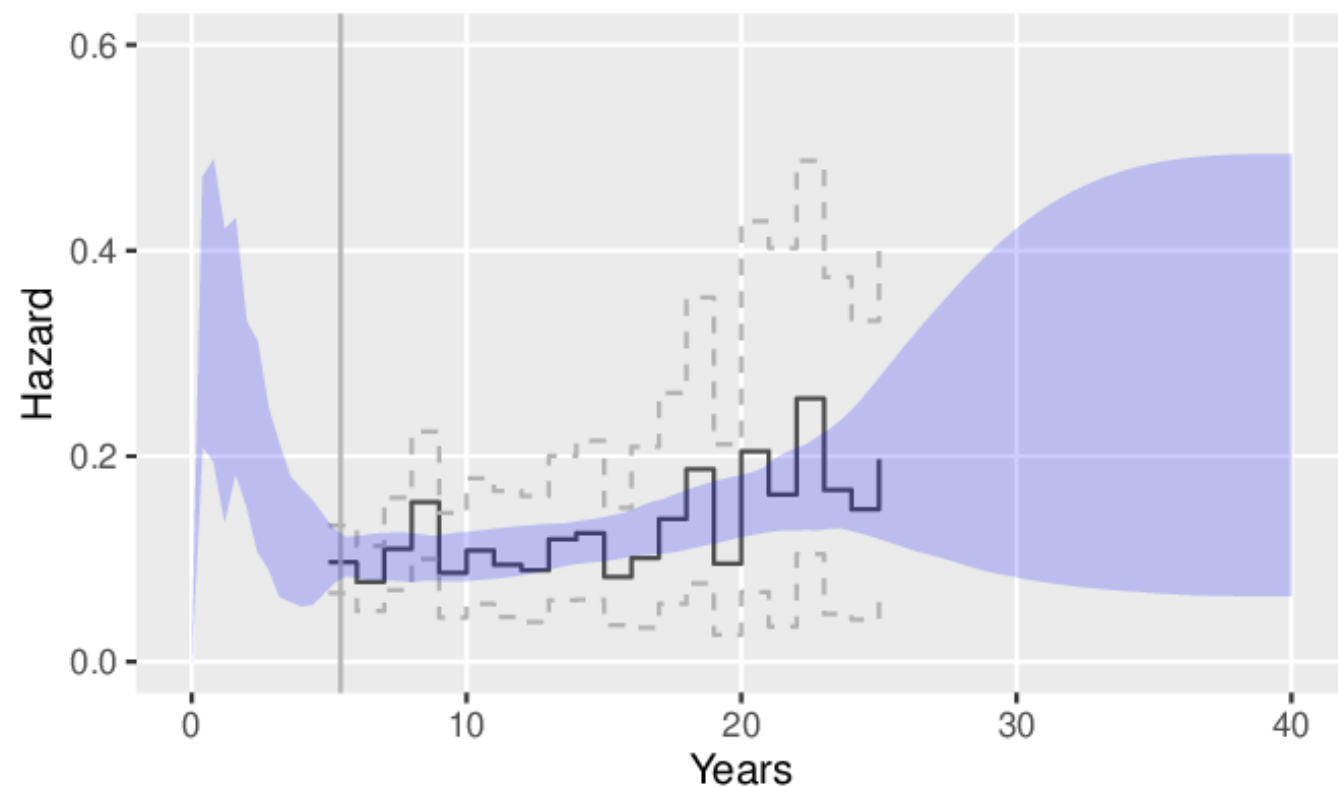


Registry data give annual survival rates from 5 to 25 years.

- Enables a confident “extrapolation” of the hazard for control group survival

```
mod_seer <- survextrap(Surv(years, d) ~ 1, data=dat,  
                       external=ext_dat, add_knots=20)
```

Survival modelling with external data: example



Extrapolating up to 40 years now...

```
mod_seer <- survextrap(Surv(years, d) ~ 1, data=dat,  
                        external=ext_dat,  
                        add_knots=c(20,30,40))
```

Additive hazards model

Can supply a **known background hazard** $h_b(t)$

- ▶ e.g. national mortality statistics for people of comparable age/sex

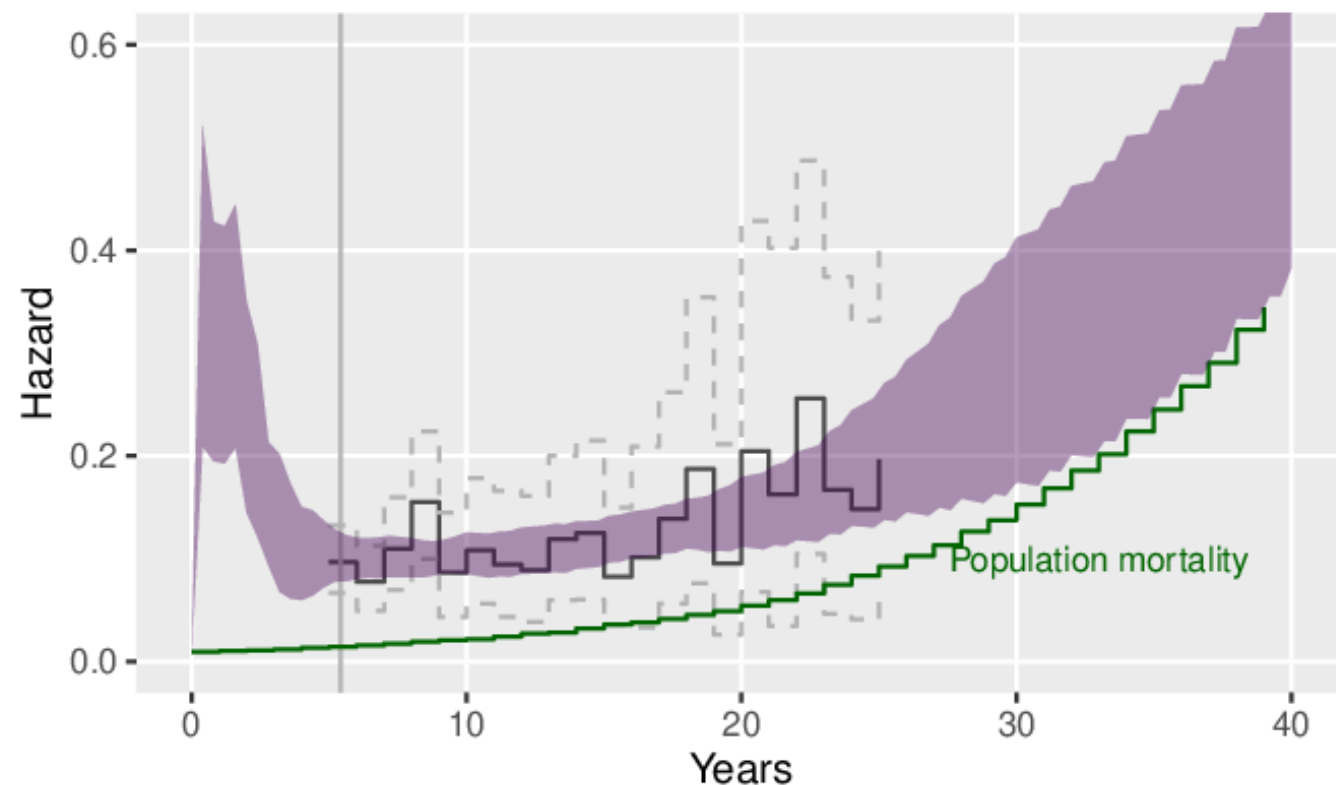
Hazard for trial patients modelled as **additive**

Flexible spline model placed on the **excess** hazard $h_e(t)$ instead of $h(t)$

$$h(t) = h_b(t) + h_e(t)$$

i.e. **no lower than population hazard**

Additive hazards model

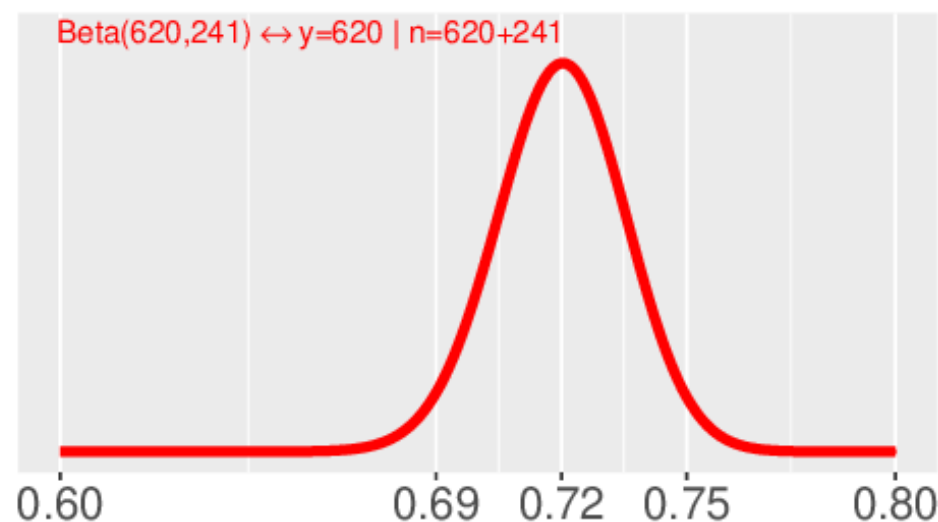


```
mod_seer <- survextrap(Surv(years, d) ~ 1, data=dat,  
                        external=ext_dat, bh=back_dat,  
                        add_knots=c(20,30,40))
```

Including expert judgements on long-term survival

Elicited survival probabilities with credible intervals can be interpreted as aggregate survival counts

- ▶ Example: suppose we judge that over some interval, the survival probability is 0.72 (0.69, 0.75)
- ▶ Find $Beta(a, b)$ distribution that best fits this belief



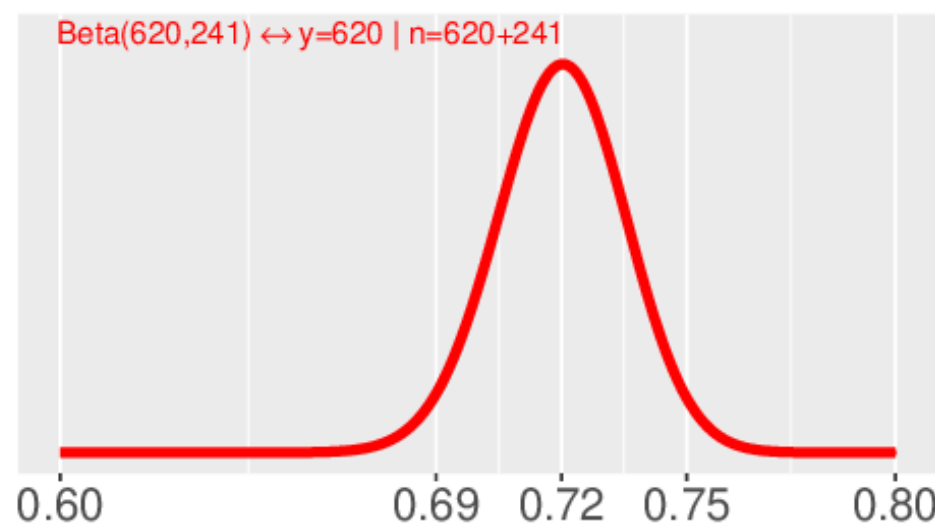
- ▶ Find Binomial data ($y|n$) that would give the (conjugate) posterior $Beta(a, b)$ when combined with a vague prior

→ treat ($y|n$) as "external data" to be analysed jointly with the main data

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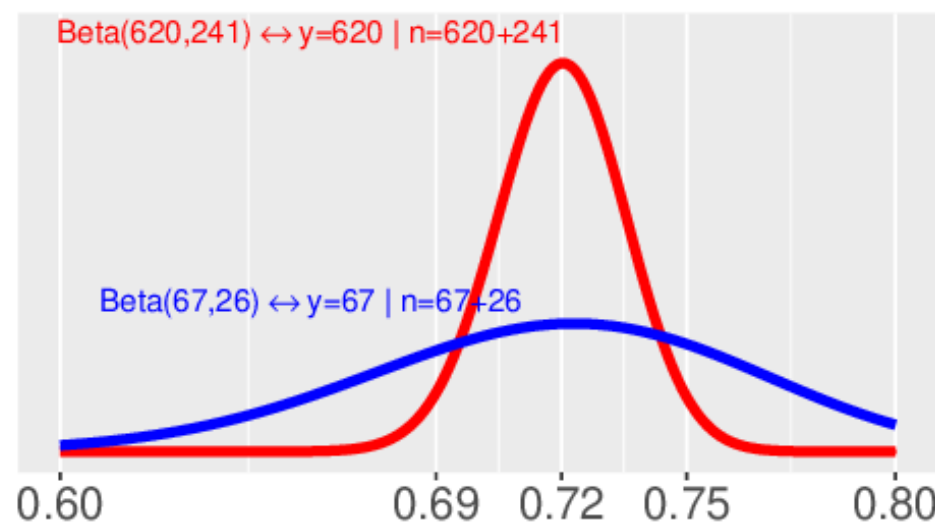
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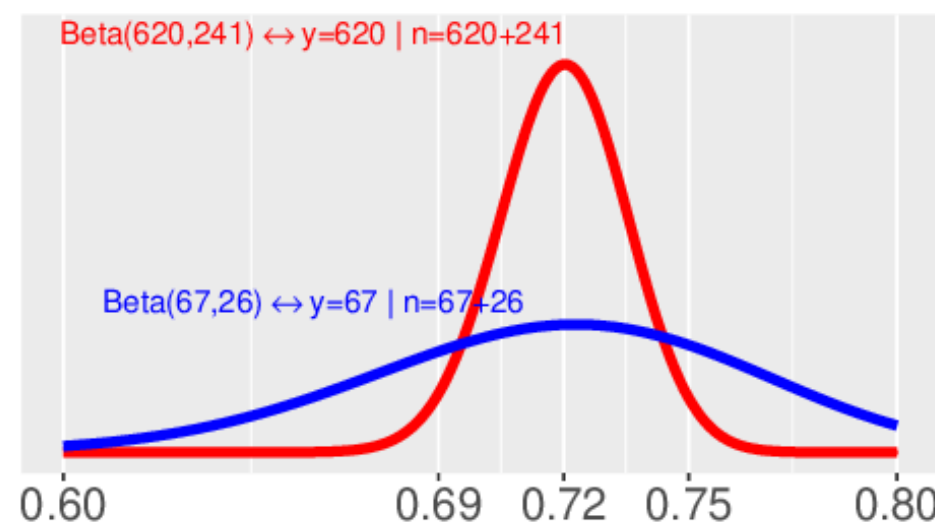
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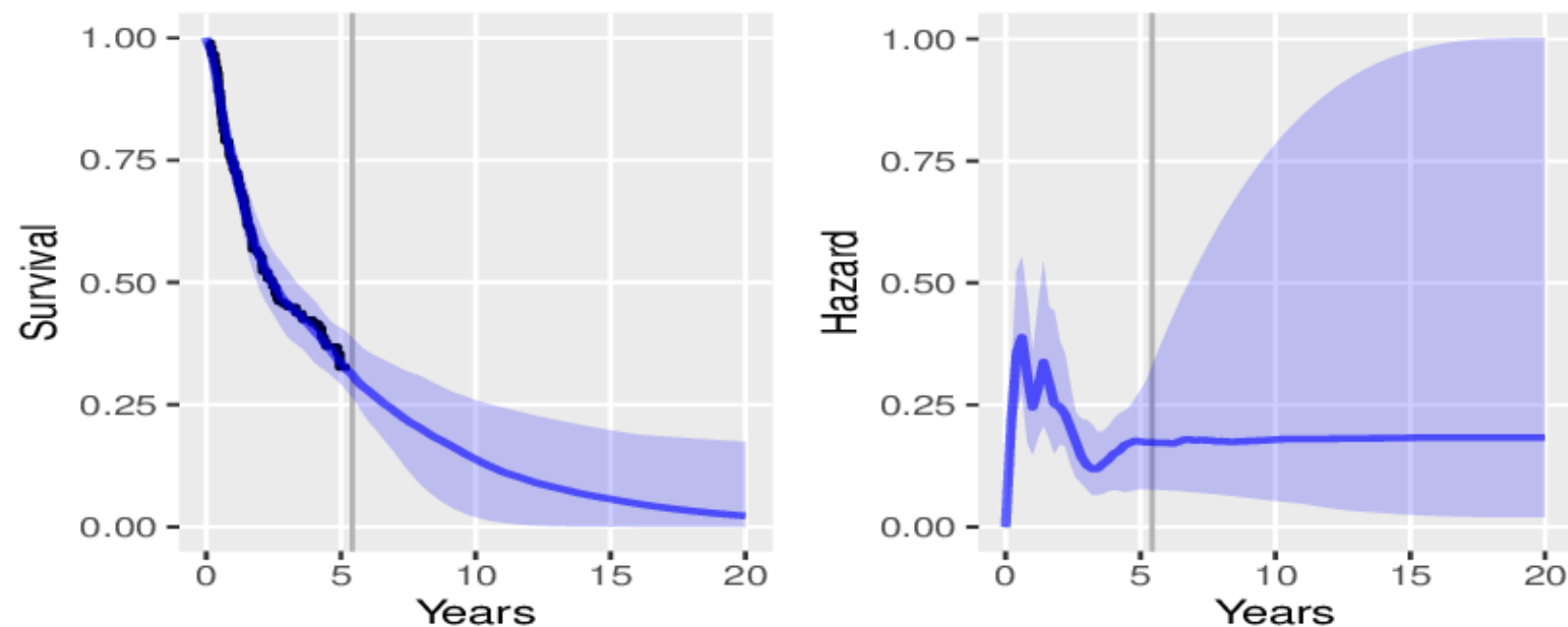
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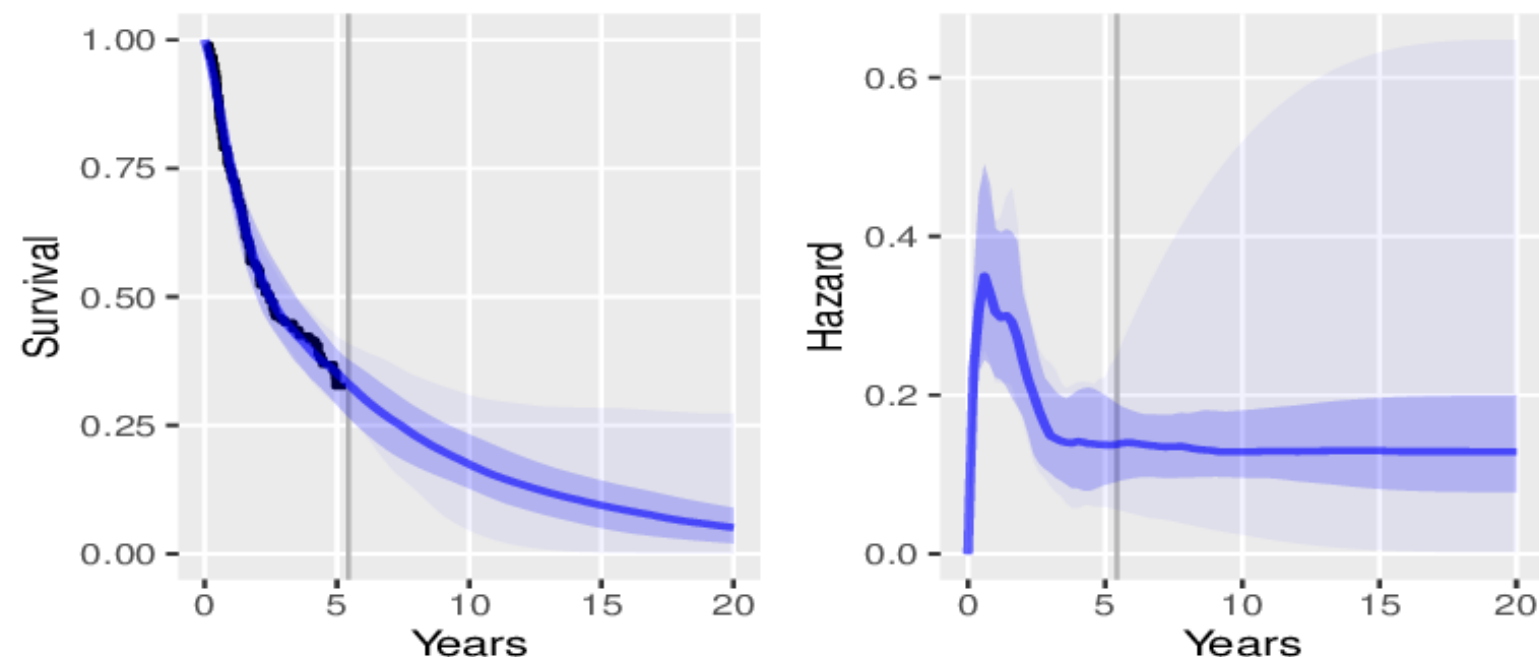
Model combining trial data and expert judgement



Trial data only

```
mod_seer <- survextrap(Surv(years, d) ~ 1, data=dat,  
                        add_knots=c(20))
```

Model combining trial data and expert judgement



Trial data + elicited probability that patients who survive the trial (5 years) are still alive at 20 years: 12% (95% CI 4% to 25%).

```
mod_seer <- survextrap(Surv(years, d) ~ 1, data=dat,  
  external = data.frame(r=5, n=35, start=5, stop=20),  
  add_knots=c(20))
```

Treatment or covariate effects

Proportional hazards model

```
mod_seer <- survextrap(Surv(years, d) ~ treat + age,  
                        data=dat, external=ext_dat)
```

Flexible non-proportional hazards model

```
mod_seer <- survextrap(Surv(years, d) ~ treat + age,  
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```

Additionally can impose a **waning effect** when predicting

- ▶ log hazard ratio for a treatment decreases from modelled value to zero over some time period
- ▶ for sensitivity analysis to what happens after trial data

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Technical details, nuisance choices

- ▶ Prior distributions, detailed specification of spline (knots, smoothness penalty...), can all be customised
- ▶ Sensible package defaults demonstrated by simulation

Detailed documentation and worked examples

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Simulation studies

Timmins I., Torabi F., Jackson C., Lambert P., Sweeting M. (2025) *Simulation-based assessment of a Bayesian survival model with flexible baseline hazard and time-dependent effects*. 10.48550/arXiv.2503.21388 and ongoing work

Further information

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