Survival Extrapolation Incorporating General Population Mortality using Excess Hazard and Cure Models

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BACKGROUND: Estimates of long-term survival are frequently required in cost-effectiveness analyses of new treatments.

Incorporation of background mortality rates into parametric models may help anchor long-term extrapolation.

METHODS

- Excess hazard (or relative survival) models estimate the excess mortality rate above background general population mortality (GPM) rates
- **Lifetables** are used for GPM rates
- An additional **cure assumption** forces the long-term excess hazard to approach zero
- Predictions of **marginal all-cause survival** from excess hazard models recombine excess and expected hazards
- We demonstrates these methods on a case-study in Breast Cancer

SOFTWARE IMPLEMENTATION

- Excess hazard models with and without cure are fitted in R package **flexsurv**
- Predictions of marginal all-cause survival, hazard, RMST, and contrasts are provided with post-estimation command **standsurv**

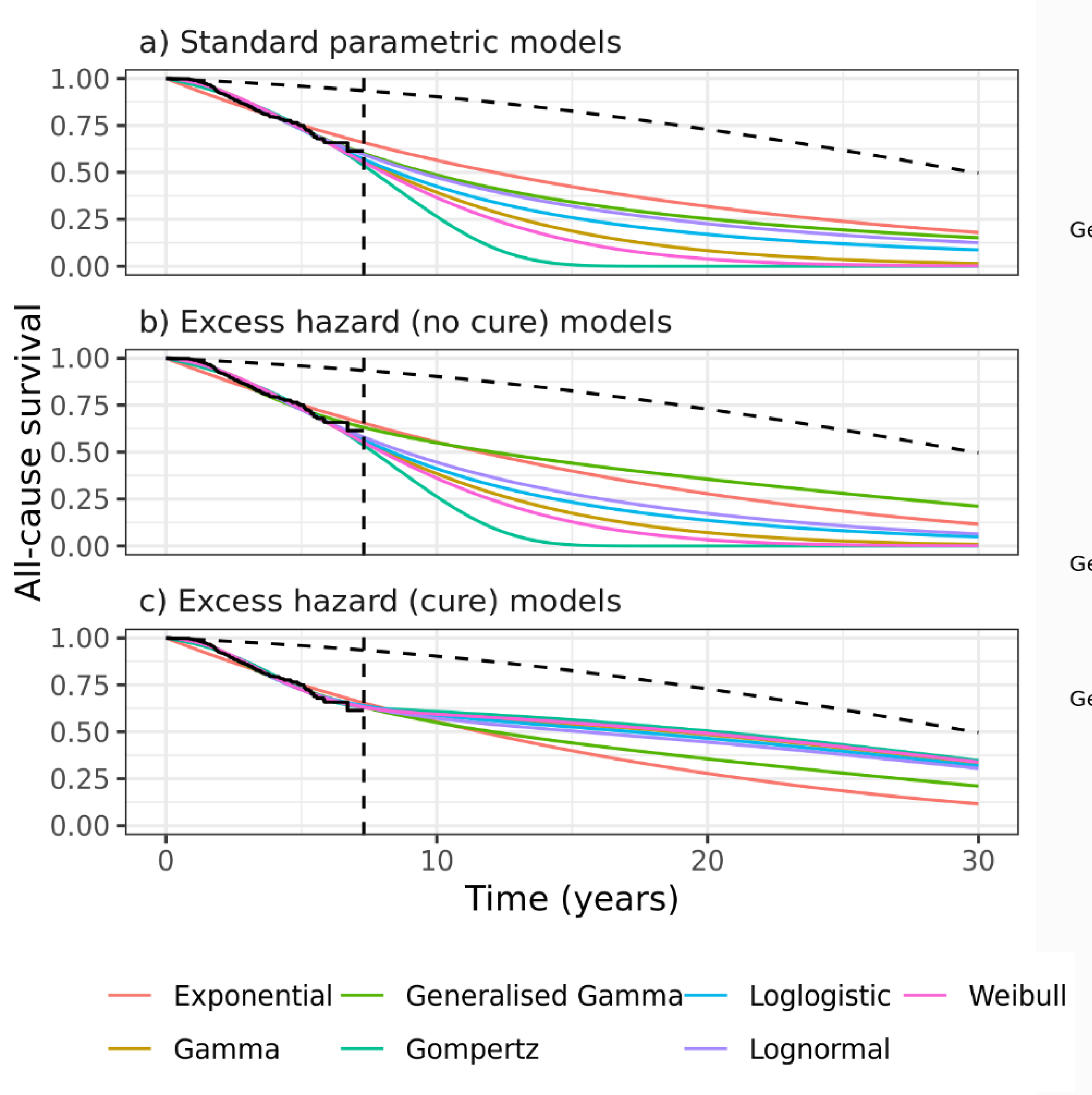
RESULTS OF CASE-STUDY

- Variability in survival extrapolation was extensive across standard parametric models without GPM rates incorporated
- **Excess hazard cure** models **substantially reduced** model uncertainty
- Excess hazard models were **generally robust to lifetable misspecification**

CONCLUSIONS

- Excess hazard models should be considered when extrapolating all-cause survival

Uncertainty in **survival extrapolation** can be reduced using **excess hazard and cure** models



Distribution	RMST	95% CI
Gompertz	7.5	(6.5, 8.7)
Weibull	8.9	(7.5, 10.5)
Gamma	9.7	(8.3, 11.3)
Loglogistic	11.2	(9.6, 13.1)
Lognormal	12.4	(10.6, 14.5)
Generalised Gamma	12.9	(10.0, 16.7)
Exponential	14.3	(12.8, 16.1)

Distribution	RMST	95% CI
Gompertz	7.5	(6.4, 8.7)
Weibull	8.8	(7.4, 10.4)
Gamma	9.4	(8.1, 11.0)
Loglogistic	10.6	(9.1, 12.2)
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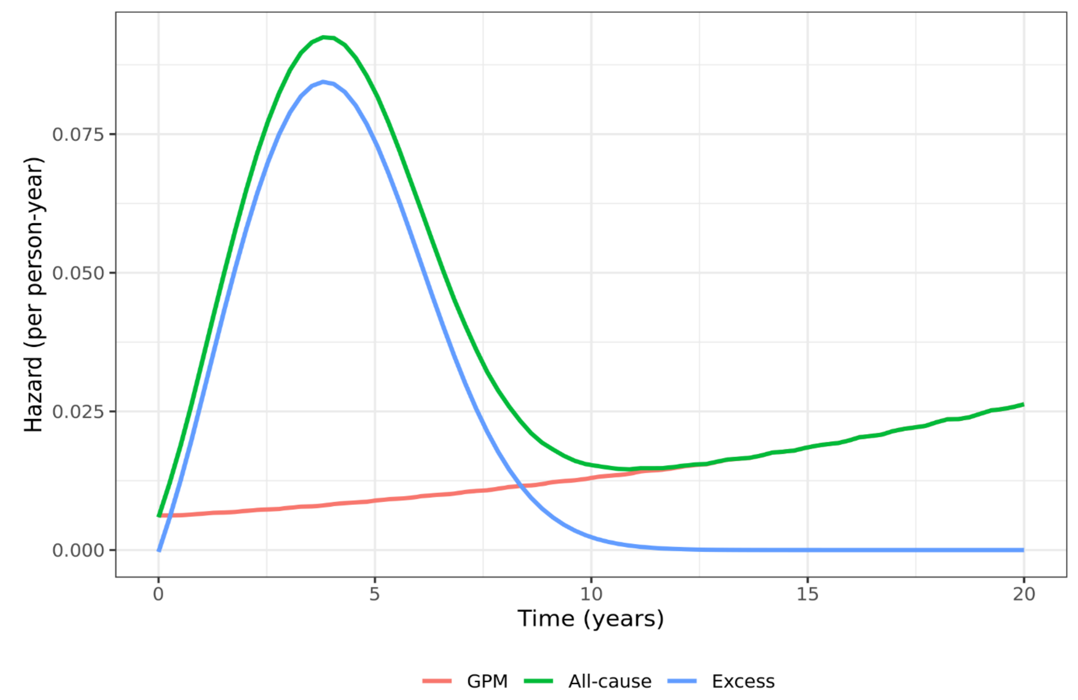
Take a picture to **download** the code **accompanying the tutorial**



Hypothesised hazard functions in a cancer clinical trial where cure is possible.

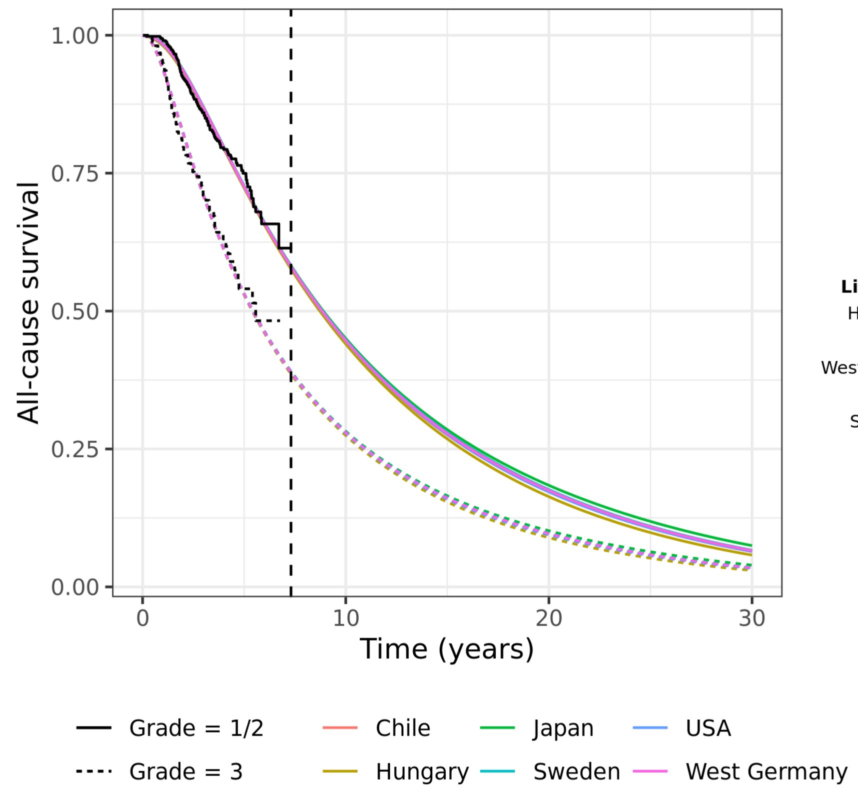
KEY FEATURES OF EXCESS HAZARD MODELS

- Excess Hazards (EHs) are likely to have simpler shape and so easier to model and extrapolate (see Figure above)
- GPM rates from lifetables are matched to cohort by age, sex, calendar year and country

LIFETABLE MISSPECIFICATION

- We investigated using incorrect lifetables (from various countries) for both estimation of excess hazards and prediction of all-cause hazards
- Estimation of excess hazards generally robust to use of different lifetables
- Changing lifetable for prediction results in targeting a different population

Excess hazard model without cure
(same lifetable for estimation and prediction)



Lifetable	Difference in RMST	95% CI
Hungary	3.2	(0.6, 5.7)
Chile	3.2	(0.6, 5.9)
West Germany	3.2	(0.6, 5.9)
USA	3.2	(0.6, 5.9)
Sweden	3.3	(0.6, 5.9)
Japan	3.3	(0.6, 6.1)

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