A marginal model for relative survival

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Intenational Biometric Society 2020

Excess Mortality and Relative Survival

Excess Mortality

$$h(t|\boldsymbol{X}_i) = h^*(t|\boldsymbol{X}_i) + \lambda(t|\boldsymbol{X}_i)$$

- All cause mortality rate partitioned into two components
  - Expected mortality rate
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Relative Survival

$$R(t|\boldsymbol{X}_i) = \exp\left(-\int_0^t \lambda(u|\boldsymbol{X}_i)du\right)$$

- Interpreted as net survival under assumptions.

Marginal Relative Survival

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- Effect of age usually non-linear. Assumption of proportional excess hazards usually not appropriate.

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- A relative survival parametric model with no covariates is not similar to the non-parametric (Pohar Perme) estimate.

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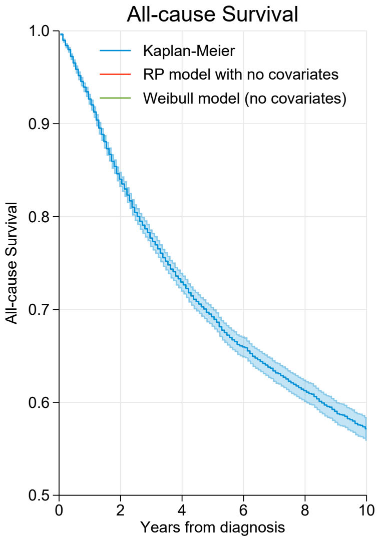

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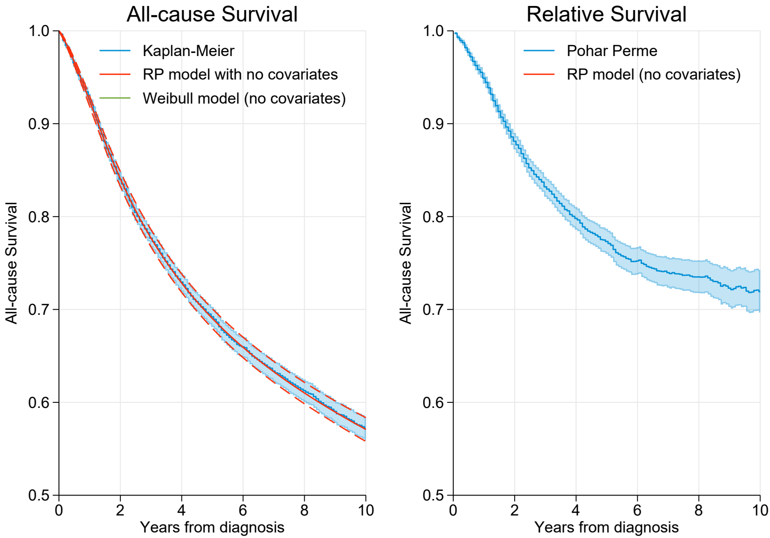

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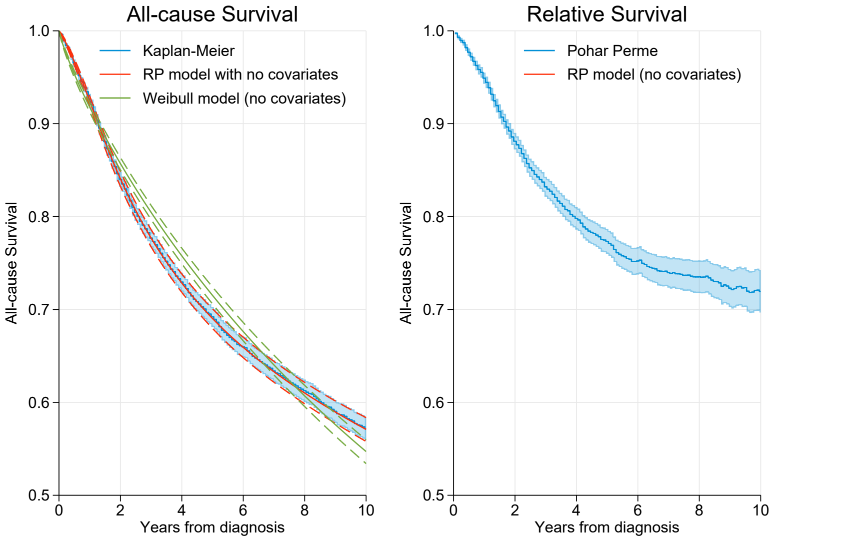

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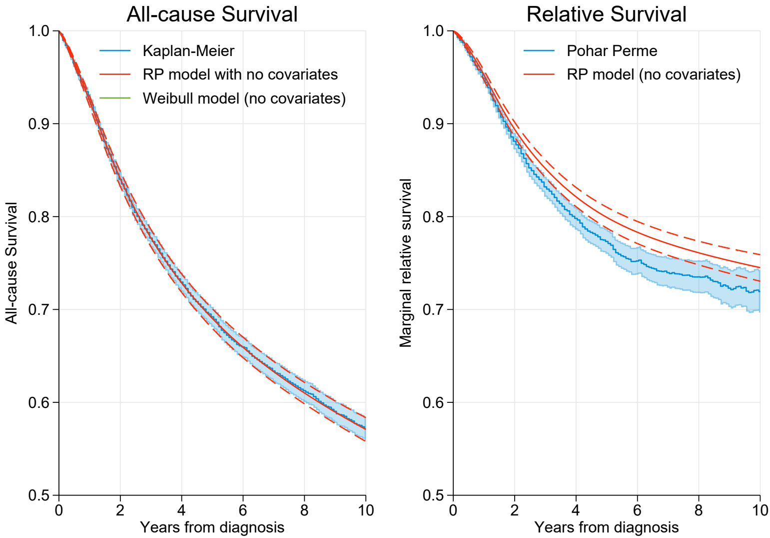

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- Consider a model with no covariates for the excess mortality,

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- The model assumes excess mortality rate is constant between individuals
- Which is not what we want to estimate.....

Marginal hazard function

$$\lambda_m(t) = \frac{E_{\boldsymbol{X}}[R(t|\boldsymbol{X})\lambda(t|\boldsymbol{X})]}{E_{\boldsymbol{X}}[R(t|\boldsymbol{X})]}$$

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- $\lambda_m(t)$ is the hazard in the hypothetical situation where it is not possible to die from other causes.

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- How to define $h_m^*(t)$?
- $\lambda_m(t)$ is the hazard in the hypothetical situation where it is not possible to die from other causes.
- As time increases those more likely to die from other causes increasingly underrepresented.
- Estimation needs to account for this through incorporation of weights.

Weights

- Weights the same as in non-parametric Pohar Perme estimator.

Expected survival at time t

$$S^*(t|\boldsymbol{X}_i) = \exp\left(-\int_0^t h^*(u|\boldsymbol{X}_i)du\right)$$

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$$w_i^*(t) = \frac{1}{S^*(t|\boldsymbol{X}_i)}$$

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- Weights are....
    - Incorporated into likelihood
    - Used to calculate weighted marginal expected mortality rate.

Likelihood

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$$\ln L_i = d_i \; w_i^*(t_i) \; \ln\left[h_m^*(t_i) + \lambda_m(t_i|\gamma)\right] - \int_0^{t_i} w_i^*(u) \; \lambda_m(u|\gamma) du$$

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Marginal expected hazard

$$h_m^*(t_i) = \frac{\sum\limits_{j \in \mathcal{R}(t_i)} w_j^*(t_i) \; h^*(t_i|\boldsymbol{X}_j)}{\sum\limits_{j \in \mathcal{R}(t_i)} w_j^*(t_i)}$$

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- We approximate the integral in the likelihood by splitting the time-scale into a number of intervals and assume that the weight is constant within each interval.

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- This means that standard software to fit relative survival models can be used.
- The software needs to be able to,
  - incorporate weights
  - incorporate delayed entry
- When choosing number of split points there is a balance between accuracy versus computational efficiency.
- Stata software `mrsprep` calculates weights and restructures the data.

Simulation

	Time		
	1	5	10
Pohar Perme	**-0.0012**	**0.0006**	**0.0033**
	95.1	*96.1*	*95.2*
	215.703	323.095	505.115
Conditional Model	**0.0292**	**0.0590**	**0.0584**
	45.9	*10.3*	*15.0*
	1058.174	3806.964	3802.487
Regression standardization*	**0.0007**	**0.0014**	**0.0030**
	94.6	*97.6*	*96.9*
	194.753	309.939	449.500
Marginal model	**0.0007**	**0.0009**	**0.0035**
	95.7	*96.9*	*95.2*
	194.764	307.189	498.378

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External (Age) standardization and contrasts

- When comparing different populations there is a need to standardize to the same covariate distribution.
- Common to standardize to external age distribution.
  - E.g. The International Cancer Survival Standard (ICSS)
- Let p_i^a be the proportion in the age group to which the i^{th} individual belongs
- Let p_i^R be the corresponding proportion in the reference population.

External (Age) standardization and contrasts 2

- Weights can be defined to upweight or downweight individual relative to the reference population.

Incorporating weights

$$w_i^a = \frac{p_i^R}{p_i^a}$$

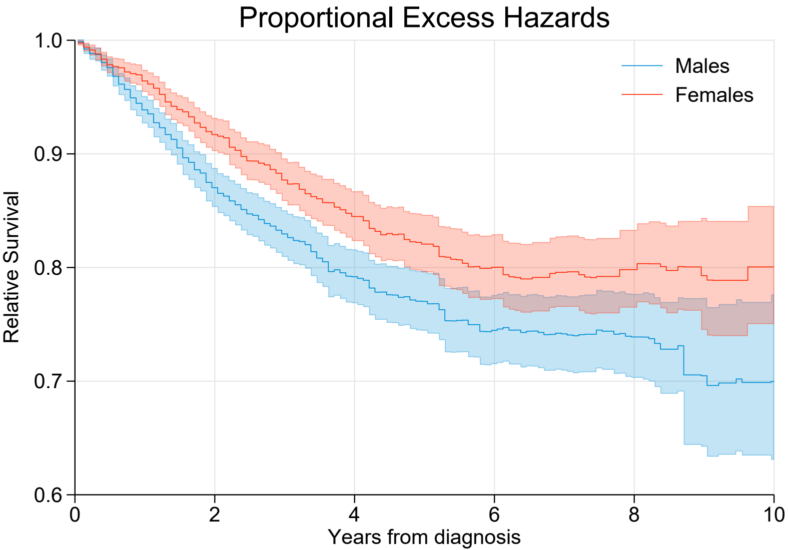
$$w_i(t) = w_i^a w_i^*(t)$$

- Enables externally age-standardized estimates to be obtained without the need to model, or stratify by, age.
- When modelling covariates (e.g. different regions/countries, socio-economic groups, time-periods or sexes) weights should be calculated separately within subgroups.

Melanoma Example

- 4,744 patients diagnosed with Melanoma between 1985–1994.
- Data distributed with `strs` Stata package.
- I will compare relative survival of males and females.
- Need to age standardize to same age distribution (ICSS).
- Use Flexible Parametric (Royston-Parmar) models.

Melanoma Example



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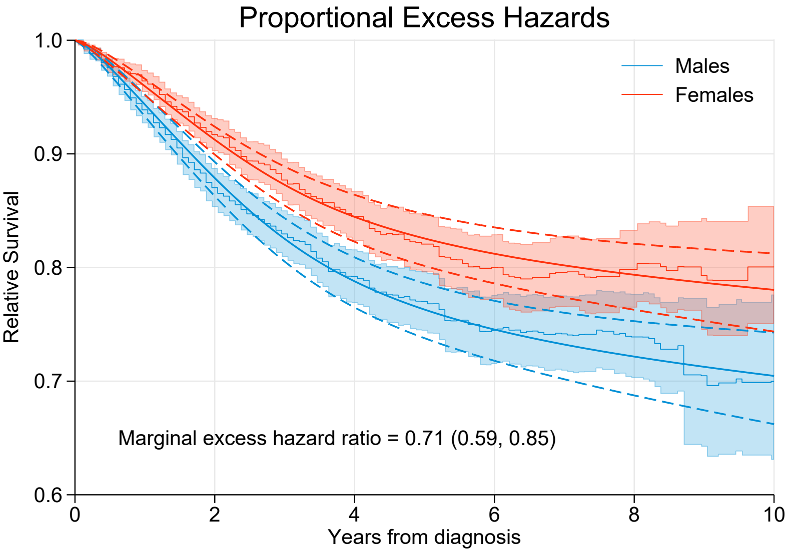

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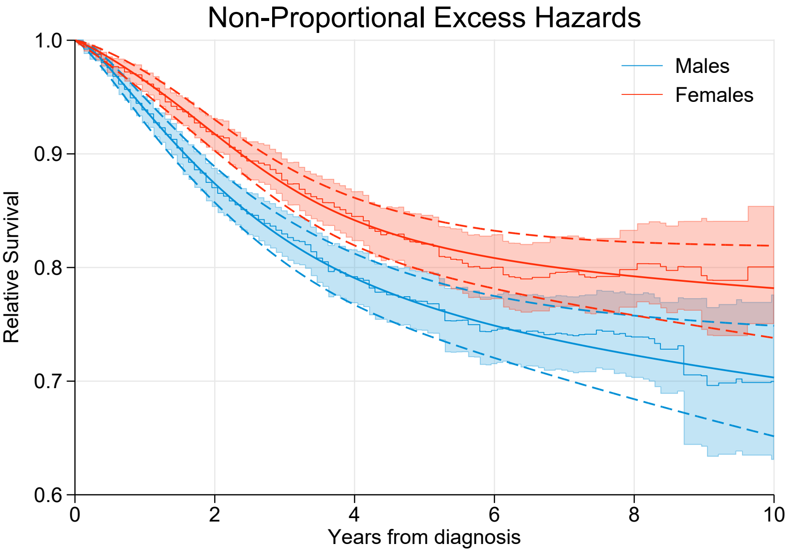
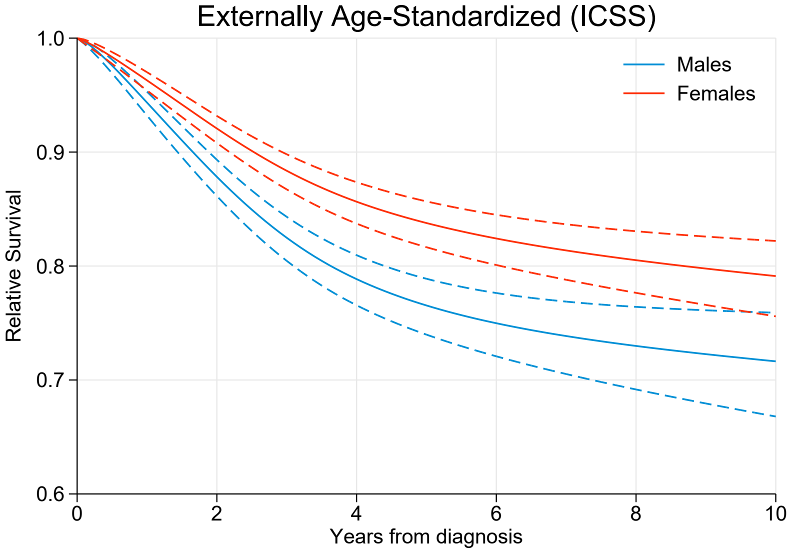


External Age Standardization



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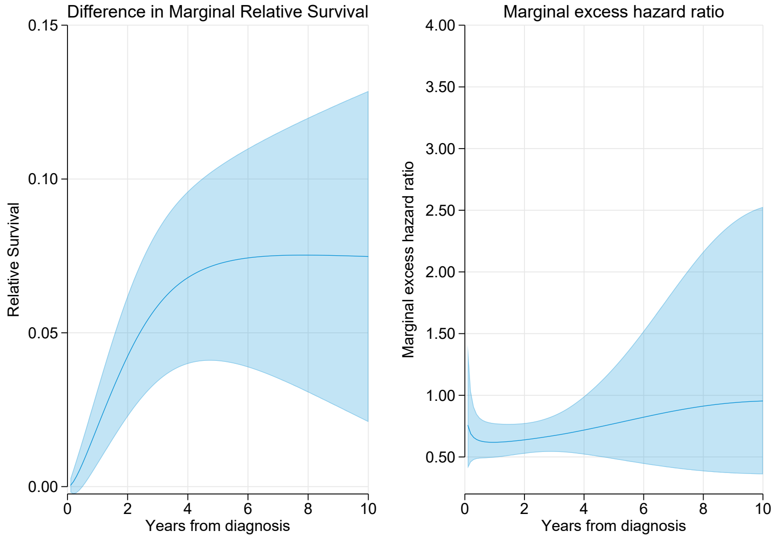

Conclusion

- Enables estimation of (externally) standardized marginal relative survival without the need to model or stratify by age (or other covariates affecting expected mortality rates).
- Approach enables further adjustment of relative survival models using IPW (See Betty Syrioupoulou's talk)
- Useful way to obtain summary measure, but conditional model is useful for more detailed comparisons of population groups.