Explained variation in excess hazard models

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Background

- Frequent multivariable modelling of excess hazard of death
- P-values not so useful for population-based analyses
- No measure of explained variation available

RE – ranks explained – Stare et al.

► Measures the variation in the ranks of failure explained by a given model

- Applicable to multiple end-point survival
- Model-free interpretation
- Easy to incorporate time-varying or dynamic covariates or time-dependent effects
- Applicable to parametric and semi-parametric models
- Consistency under general independent censoring mechanisms

RE – technicalities

► Comparison of ranks of failure

i.e. predicted position at which the record under observation will fail, among observations in the risk set

Some definitions: at time t,

✓Null model: all records i in risk set are given the same mean rank

>> $r_{i,null}$

✓Perfect model: the record i that fails next is always given rank 1

>> $r_{i,perfect} = 1$

RE – technicalities

► Contrast what variation in ranks is explained by our model vs. the total variation there is to explain

$$RE = \frac{\sum_i (r_{i,null} - r_{i,model})}{\sum_i (r_{i,null} - r_{i,perfect})}$$

✓Weighting available to account for informative censoring

✓There is an estimate of the variance of RE

✓Time-varying RE

RE – for excess hazard models

► Contrast what variation in ranks is explained by our model vs. the total variation there is to explain

$$RE = \frac{\sum_i (r_{i,null} - r_{i,model})}{\sum_i (r_{i,null} - r_{i,perfect})}$$

□ Predicted ranks $r_{i,model}$ relate to cancer mortality ***only***

□ Observed ranks $r_{i,perfect}$ based on overall mortality

i.e. we may say that the next patient who fails as $r_{i,perfect} = 1$, but in truth he may not have failed due to the cause under observation

>> values of RE are unrelated to the adequacy of the model

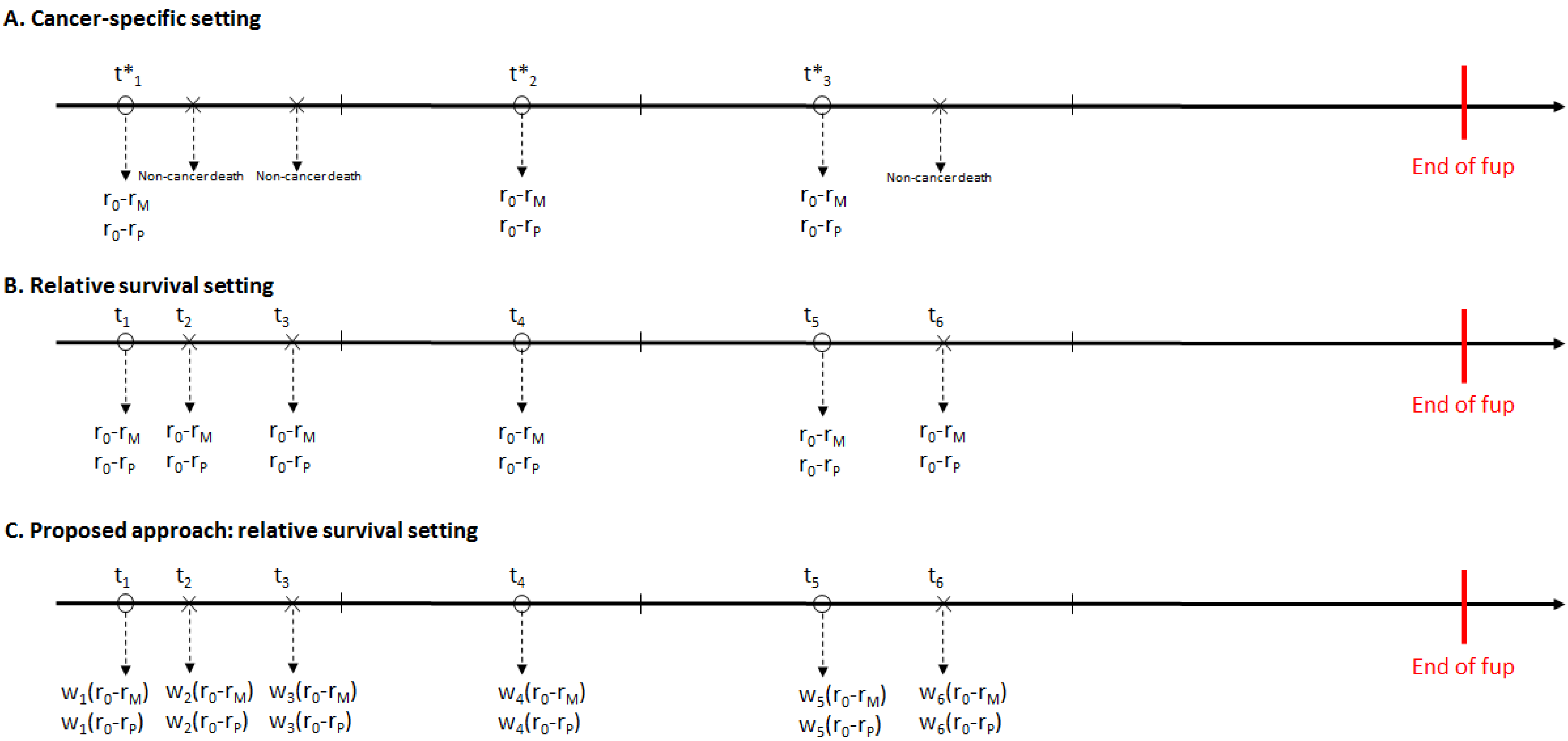
RE – for excess hazard models

► Trick: weight each failure by the probability that the failure is a failure of interest (i.e. cancer death)

$$w_i = p(dN_{E_i}(t) = 1 | dN_i(t) = 1)$$

Given that we observe a failure at time t, that is $dN_i(t) = 1$, what is the probability that it is an event of interest?

RE – for excess hazard models



○ Time of cancer death
× Time of non-cancer death
| Time of censoring

r_M: rank as estimated from the model-derived hazard of death
r_0: average rank of the records in the risk set
r_P: 1

RE – for excess hazard models

- Trick: weight each failure by the probability that the failure is a failure of interest (i.e. cancer death)

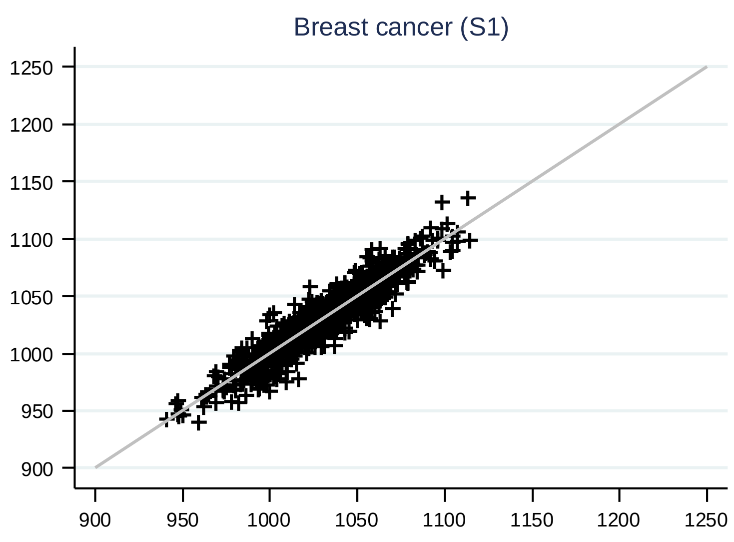
$p\left(dN_{E_i}(t)=1\right)$ is the unconditional probability to observe a failure of interest,

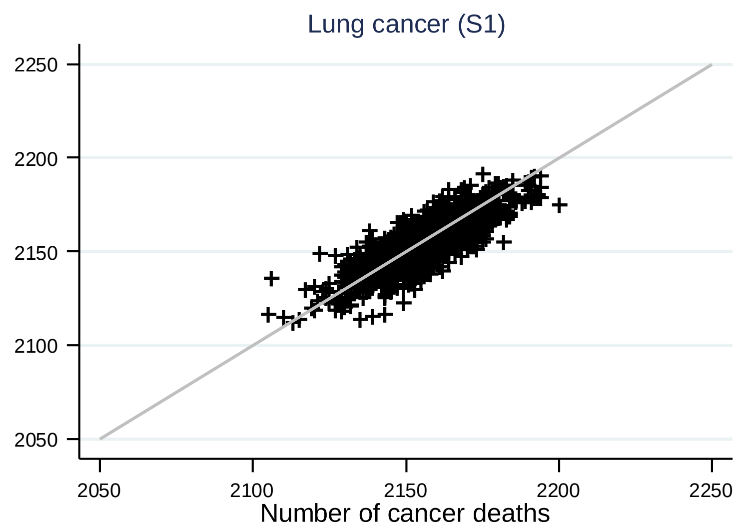
$$p\left(dN_{E_i}(t)=1\right)=p\left(dN_{E_i}(t)=1|dN_i(t)=1\right)*p(dN_i(t)=1)$$
$$+p\left(dN_{E_i}(t)=1|dN_i(t)=0\right)*p(dN_i(t)=0)$$

Therefore our weights can be written as:

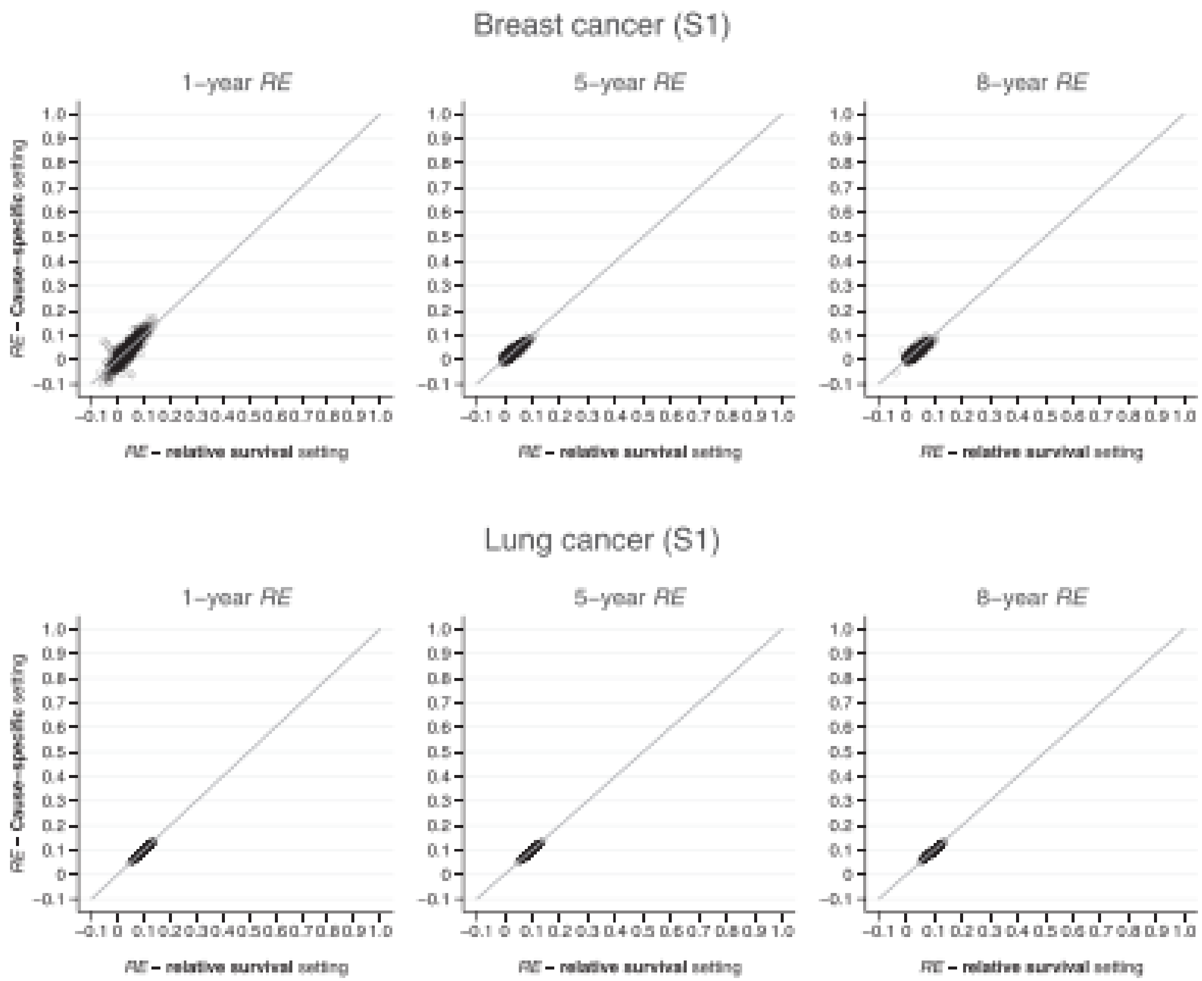
$$w_i=p\left(dN_{E_i}(t)=1|dN_i(t)=1\right)$$
$$=\frac{p\left(dN_{E_i}(t)=1\right)}{p(dN_i(t)=1)}$$
$$=\frac{\lambda_{E_i}(t_i)}{\lambda_{E_i}(t_i)+\lambda_{P_i}(t_i)}$$

Properties of the weights





Cause-specific vs. relative survival setting



Application

			Change* in REw			
			Inclusion[3]		Exclusion[3]	
		REw at 12 months (95% CI)	Diff. in REw	Prop. of Initial Model (%)	Diff. in REw	Prop. of Full Model (%)
Non-small cell lung cancer (Men)						
Initial Model:	Age, deprivation	0.141 (0.112 ; 0.171)				
	Age, deprivation, **stage**	0.422 (0.403 ; 0.441)	0.280	198.5	0.058	10.5
	Age, deprivation, **treatment[1]**	0.257 (0.235 ; 0.280)	0.116	81.9	0.003	0.6
	Age, deprivation, **Charlson Comorbidty index (CCI)**	0.141 (0.111 ; 0.170)	-0.001	-0.5	0.000	0.1
	Age, deprivation, **performance status (PS)**	0.434 (0.409 ; 0.459)	0.293	207.3	0.069	12.4
	Age, deprivation, **presentation (EP vs. non-EP)**	0.325 (0.295 ; 0.354)	0.183	129.8	0.013	2.4
Full Model:	Age, deprivation, stage, treatment, CCI, PS, presentation	0.558 (0.539 ; 0.576)				

Application

Lung cancer

A

B