A combined **additive and relative** hazards model to supplement the existing toolbox in **cancer patient survival** research.

MSR142

Multi-State Modelling Incorporating a Combined Additive and Relative Hazards Model

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Objectives

Cancer is typically assumed to have an additive effect on mortality, hence relative survival is the standard method used in cancer patient survival. Such methods require accurate background mortality files, which are not always available. When moving from mortality to incidence and extending to the multi-state framework, tools for appropriate estimation of excess transition rates are lacking.

Our aim was to implement methods for combined estimation of the expected and excess hazards using a control population, and extend these to the multi-state setting.

Figure 1. The extended illness-death model for studying excess incidence of the diseases of the circulatory system (DCS) in Hodgkin lymphoma, illustrating different patient pathways.

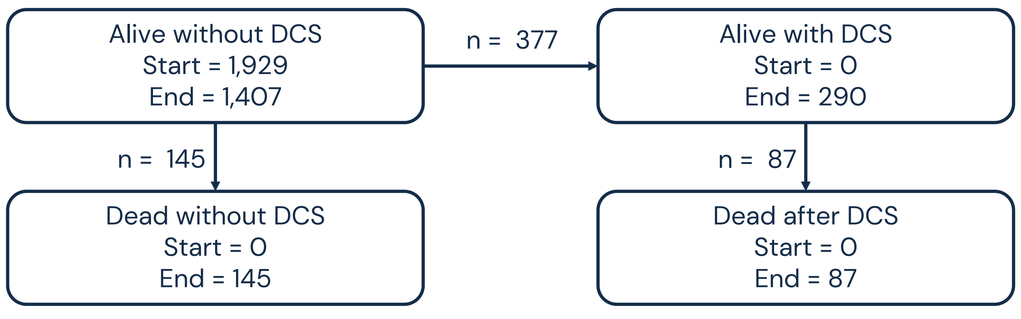
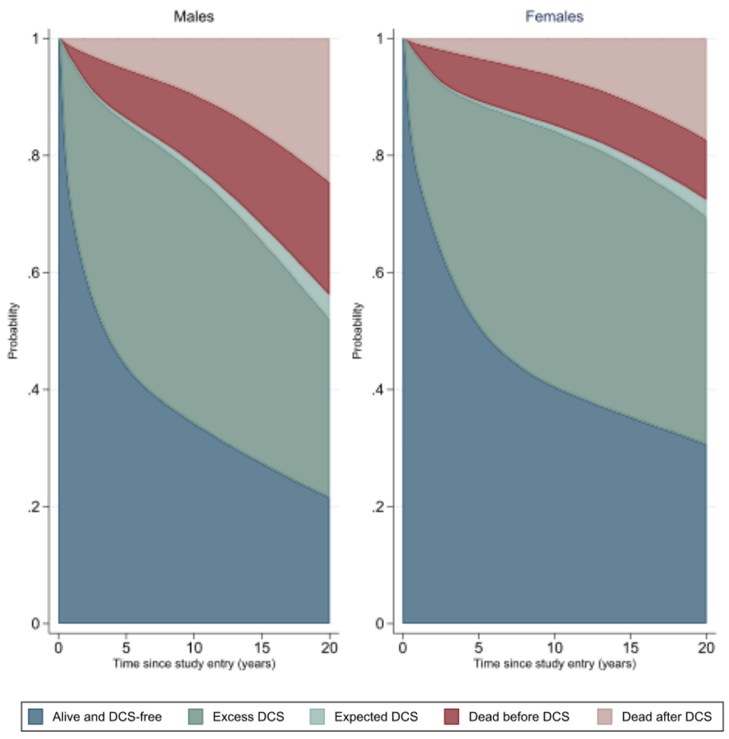


Figure 2. Predicted transition probabilities illustrating the proportion of patients in the different states across follow-up, by sex. The dark blue field are patients still alive and DCS-free, the green fields are patients with DCS (dark; excess, light; expected), and the red fields are deceased patients (dark; prior to DCS, light; after DCS).



Methods

By utilising a cohort of cancer patients together with (potentially matched) controls, we propose the use of a flexible parametric survival model that jointly models the expected, $h^*(t|\boldsymbol{x_1})$, and the excess, $\lambda(t|\boldsymbol{x_2})$, hazard functions.

$$h(t|\,\boldsymbol{x}) = h^*(t|\boldsymbol{x_1}) + v\,\cdot\lambda(t|\boldsymbol{x_2})$$
$$= h_0^*(t)\cdot\exp\{\boldsymbol{x_1\beta_1}\} + \,v\cdot\lambda_0^*(t)\cdot\exp\{\boldsymbol{x_2\beta_2}\},$$

$$\text{with } v = \begin{cases} 1 \text{ for cancer patients} \\ 0 \text{ else} \end{cases}$$

Covariate effects are assumed multiplicative within both hazard functions, while the presence of cancer has an additive effect. The model can be applied to one or more of the multi-state model transitions, and allows for time-varying effects and multiple timescales.

Results

The method is illustrated on excess incidence and mortality from diseases of the circulatory system (DCS) among 1,929 Swedish patients treated for Hodgkin lymphoma, using a multi-state model (Figure 1). Figure 2 shows the difference in transition probabilities between male and female patients over time since study entry. E.g., women had a higher probability to remain alive and DCS-free than men, and also experienced lower mortality after DCS.

Conclusion

The proposed method extends multi-state models by incorporating estimation of expected and excess hazards, the sharing of transition models, and multiple time scales. By modelling the expected rate, we can appropriately allow for uncertainty. This enables prediction of survivor trajectories in a real-world setting. We provide user-friendly Stata software.

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