Appendix

The shared-frailty Cox proportional hazards (PH) model

The conditional hazard function of the model, given the unobserved frailty variable \( w_i \) for the \( i \)th cluster and the covariate vector \( x_{ij} \) is defined by:

\[
h(y|w_i, x_{ij}) = h_0(y)w_i\exp(x_{ij}'\beta)
\]

where \( \beta \) is the vector of unknown model coefficients, \( h_0(\cdot) \) is the baseline hazard ratio common to all subjects, \( x_{ij} \) is the covariate vector for the \( j \)th subject in the \( i \)th cluster, and the frailty variables \( w_i \) are assumed to be independently Gamma distributed with a mean of 1 and unknown variance \( \Theta_i \). The interpretation of regression coefficients \( \beta \) remains the same as in the standard Cox PH model, but is conditionally made on the frailty variables \( w_i \) which explicitly account for the extra variance associated with unmeasured risk factors.

A likelihood ratio (LR) test for the variance of the frailty variable (LR test for \( \Theta_i = 0 \)) was used to compare the shared-frailty Cox PH specification versus the standard Cox PH specification.