

Marginalized frailty-based illness-death model with application to biobank data

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Abstract: The UK Biobank is a large-scale health resource comprising genetic, environmental and medical information on approximately 500,000 volunteer participants in the UK, recruited at ages 40--69 during the years 2006--2010. The project monitors the health and well-being of its participants. This work demonstrates how these data can be used to estimate in a semi-parametric fashion the effects of genetic and environmental risk factors on the hazard functions of various diseases, such as colorectal cancer. An illness-death model is adopted, which inherently is a semi-competing risks model, since death can censor the disease, but not vice versa. Using a shared-frailty approach to account for the dependence between time to disease diagnosis and time to death, we provide a new illness-death model that assumes Cox models for the marginal hazard functions. The recruitment procedure used in this study introduces delayed entry to the data. An additional challenge arising from the recruitment procedure is that information coming from both prevalent and incident cases must be aggregated. Lastly, we do not observe any deaths prior to the minimal recruitment age, 40. In this work we provide an estimation procedure for our new illness-death model that overcomes all the above challenges.