

## Reconstructing Individual Patient Level Survival Data from Aggregate Survival Data using a Simulation Approach

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### Rebecca Boucher

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Rebecca is a senior biostatistician at the Cancer Research Clinical Trials Unit at the University of Birmingham. Her research interests include statistical analysis of haematology trials, treatment switching methodology and the simulation of survival data.

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Sarwar Mozumder is a Statistician in AstraZeneca's Oncology Biometrics Statistical Innovation group. He mainly works on methods development and application in Oncology late-phase and payer studies. His general research and methodological interests are in estimands for time-to-event data, survival analysis, covariate adjustment for time-to-event endpoints, non-proportional hazards, competing risks, flexible parametric models and the reconstruction of individual-level survival data. He also holds an honorary research fellow position at the University of Leicester.

### Paul Lambert

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Paul Lambert is a biostatistician working at both the Cancer Registry of Norway, Oslo, Norway and as a visiting professor at Karolinska Institutet, Stockholm Sweden. Paul has developed statistical methods and software in the area of survival analysis with a particular interest in the methods used to analyse data obtained from cancer registries.

### Keith Abrams

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Keith Abrams is a Professor of Statistics & Data Science in the Department of Statistics and Adjunct Professor of Biostatistics in Warwick Medical School (WMS) at the University of Warwick, and a NIHR Senior Investigator Emeritus as well as being Honorary Professor in the Centre for Health Economics at the University of York. Prior to this he held academic positions at the University of Leicester, the London School of Hygiene & Tropical Medicine (LSHTM) and King's College London. His research interests centre around the development, evaluation, application and translation of (Bayesian) statistical methods in Health Technology Assessment (HTA) and Health Data Science.

### Single topic, multi-speaker session, Workshop or Single presentation submission

A single presentation/poster

### Single presentation or poster submission

The Guyot method is commonly used for reconstructing individual-level patient survival data (IPD) from digitised Kaplan-Meier curves. Although this performs well for reproducing survival curves, it may have limited performance for reproducing (or estimating if not reported) alternative summary measures to the hazard ratio (HR), especially when full information (risk table and total number of events) is unavailable. This limited performance is magnified when non-proportional hazards (NPH) are present. To estimate unreported summary measures with uncertainty, especially with crossing survival curves, a 'simulation approach' was developed for reconstructing IPD.

We simulate survival times from a log-cumulative hazards model with restricted cubic splines and censoring times using a piecewise exponential distribution. Uncertainty in the reconstruction process is obtained by producing multiple datasets from the data generating model. We average over the results to obtain a final point estimate for the target summary measure. This is compared with the Guyot method for estimating summary measures in the presence of NPH.

We demonstrate improved performance with respect to bias compared to the original IPD estimate for estimating alternative summary measures to survival probabilities such as the (average) HR and restricted mean survival time in the presence of NPH.

In the presence of NPH, reconstructing IPD using the Guyot method to obtain summary measures that are not reported may be inappropriate. Alternatively, a simulation approach is presented which demonstrates good performance for reproducing IPD and estimating summary measures with uncertainty. This can be extended for correlated endpoints such as PFS and OS.