MSR 150

# Incorporating Real-World Data to inform **survival extrapolations** can improve performance compared to using **trial data alone**.

## Assessing the Improved Precision of Extrapolated Survival Estimates When Incorporating Real-World Data in Bayesian M-spline Models

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## Introduction

Survival extrapolations are needed to estimate the long-term costs and benefits of new treatments for HTA decision making.

Bayesian methods offer an approach to incorporate external data (e.g., RWE, clinical expert opinions) to help inform survival extrapolations.

We use a simulation study design to understand the performance of a newly proposed Bayesian survival model, implemented in `survextrap` R package (Jackson, 2023). This is a Bayesian evidence synthesis model that can flexibly model trial and external data using M-splines.

## Methods

Data was generated from a flexible model based on the fit of OS data for head and neck cancer patients treated with radiotherapy (Bonner et al, 2006). We extrapolated from this model fit of trial data to provide our true hazard and survival model for timepoints up to 40 years (Figure 1).

We simulated survival times for 1,000 trial datasets of $N$ = 200 patients, with 5-years follow-up. We also generated real-world datasets with $N$ = 600 patients with annual aggregated event counts between 6 and 25 years (starting after the trial ends at 5 years).

For the real-world datasets, we generated data based on the same hazard function for the trial data but with varying levels of relative bias in the hazard rates (i.e., shifting the hazard in Figure 1 up/down proportionately by up to +/-20%).

We fitted `survextrap` models jointly to the trial and real-world data. The `survextrap` models assumed a constant hazard extrapolation from the point at which the trial or external data ends. Our primary estimand was the restricted mean survival at 40 years.

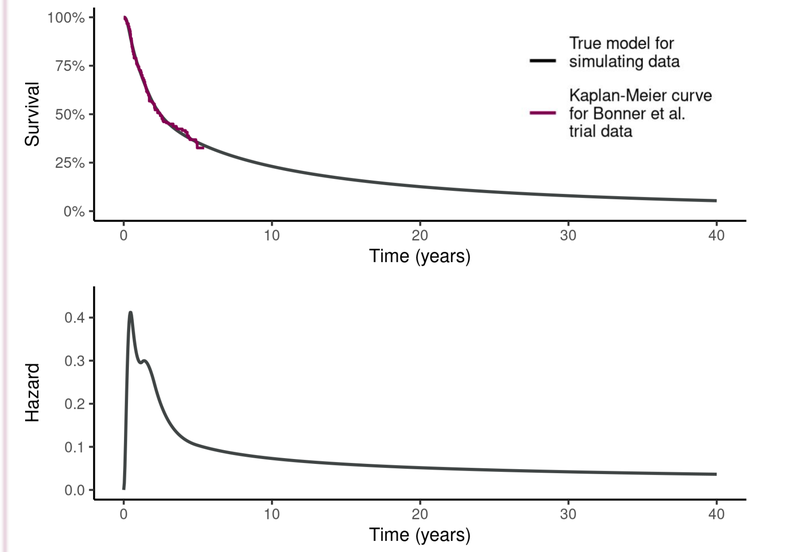


**Figure 1:** Survival and hazard functions for the data generating model, which was based on a survival model fitted and extrapolated from the radiotherapy arm of the Bonner et al. (2006) trial data (Kaplan-Meier curve shown).

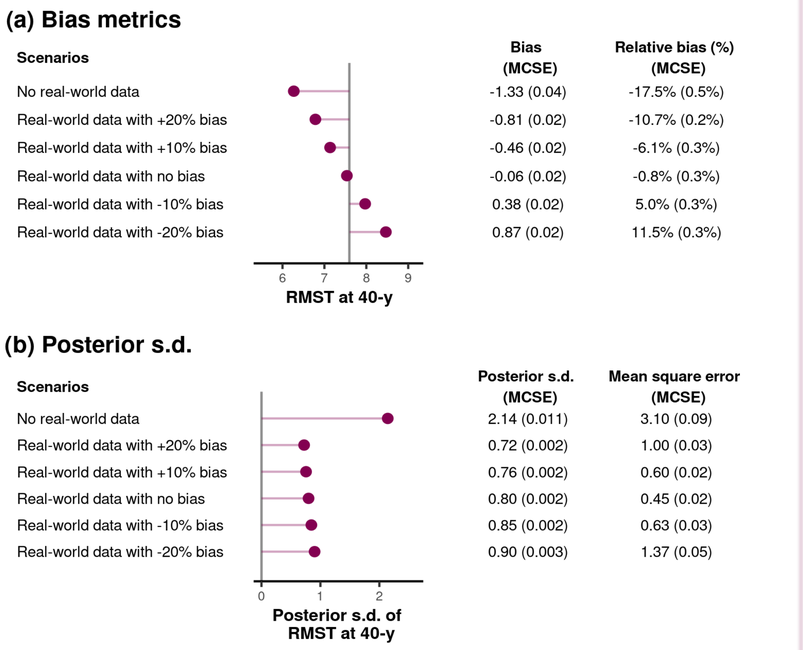


**Figure 2: (a)** Bias and **(b)** posterior standard deviation and mean square error metrics for estimating 40-year RMST. MCSE (Monte Carlo standard error)

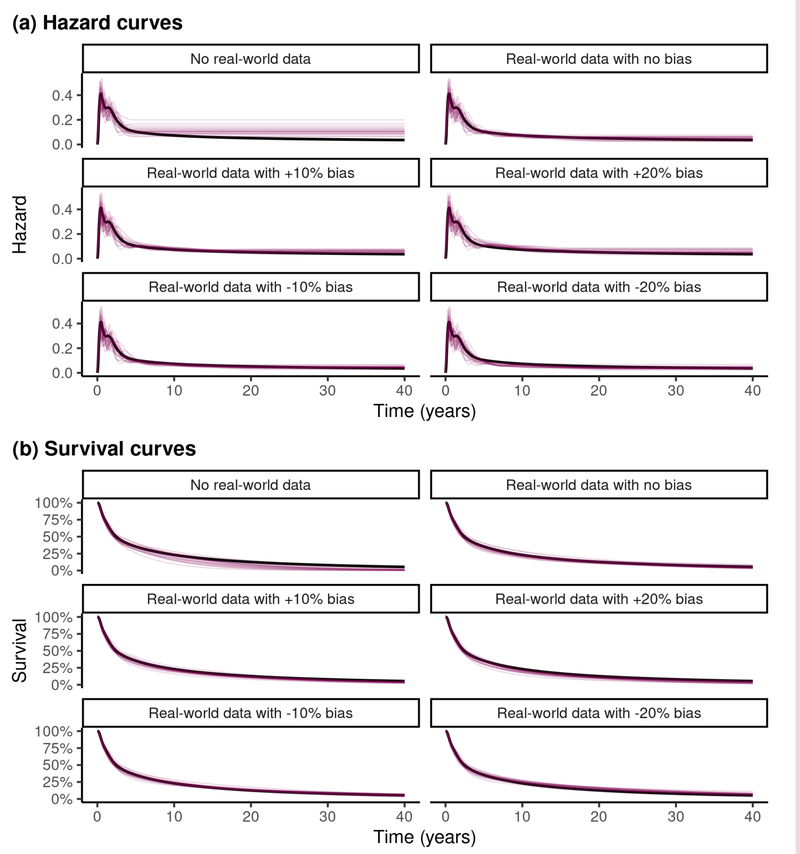


**Figure 3: (a)** Survival and **(b)** hazard curves for 20 simulation iterates, with and without incorporation of biased and unbiased real-world datasets.

## Results

In Figure 2 we show the performance of models with and without the inclusion of real-world data, when estimating the restricted mean survival time at 40-years, where the true value was 7.60 years. The hazard and survival curves for each modelling scenario for a sample of simulations are shown in Figure 3.

Models with no real-world data had the highest bias at -17.5% and highest uncertainty (posterior standard deviation) as well as highest mean square error. When incorporating imperfect real-world data (with up to +/-20% bias in hazard rates) the relative bias was at most 11.5%.

## Conclusions

- Incorporating real-world data using `survextrap` allows us to identify longer-term changes in the hazard, which leads to more accurate and precise survival extrapolations.

## References

Jackson CH. survextrap: a package for flexible and transparent survival extrapolation. *BMC Med Res Methodol* 2023; **23**(1): 282.

Bonner JA, Harari PM, Giralt J, et al. Radiotherapy plus cetuximab for squamous-cell carcinoma of the head and neck. *N Engl J Med* 2006; **354**(6): 567-78.

## Disclosures

Iain R Timmins, Michael J. Sweeting, Robert Hettle and Jack Williams are employees and/or shareholders of AstraZeneca PLC

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