An online translational tool for time to event data

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Abstract

Translational Statistics (Newell et al. 2014; McCabe 2014) aims to develop tools that facilitate the communication of complicated statistical findings to a non-technical audience. For example, in the analysis of survival data, meaningful and easily interpretable summaries, like the mean residual life function (MRL), can be used to determine the length of the patient's survival experience, avoiding hazard ratios or probability scales that are very often not easily understood. In this presentation, a clinical example is presented to demonstrate how the MRL function can be used in this context, using a novel hybrid MRL estimator that combines existing non-parametric methods with an extreme value tail model. An online translational tool that incorporates, along with the estimated MRL other useful survival plots, will also be presented.

The Mean Residual Life Function

The MRL function is defined as the expected remaining lifetime given survival up to time t:

$$m(t) = E(T - t|T > t) = \frac{\int_t^\infty S(u)du}{S(t)}$$

where T are the random survival times. The numerator and denominator can be estimated using the Kaplan-Meier (KM) estimate of the survival function, except in the presence of type I censoring, in which case the right tail of the distribution is missing (Figure 1)

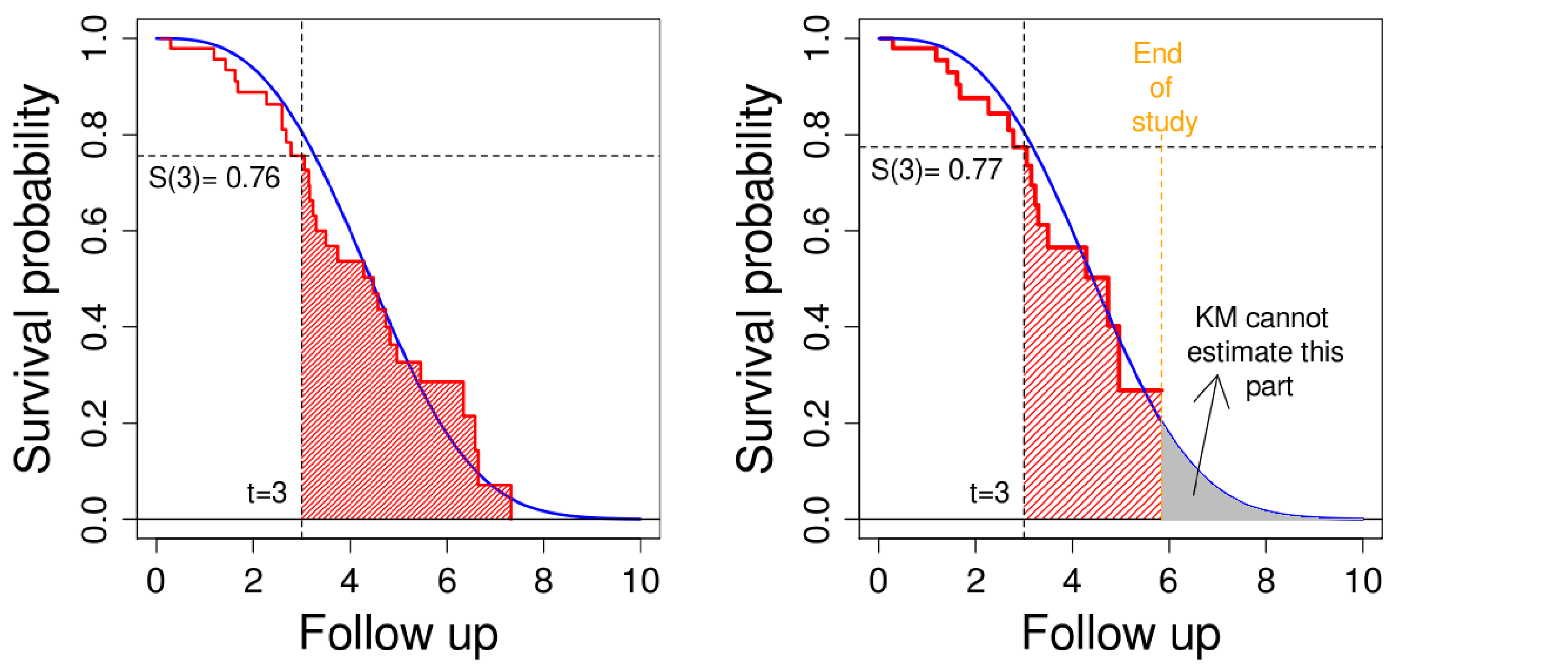
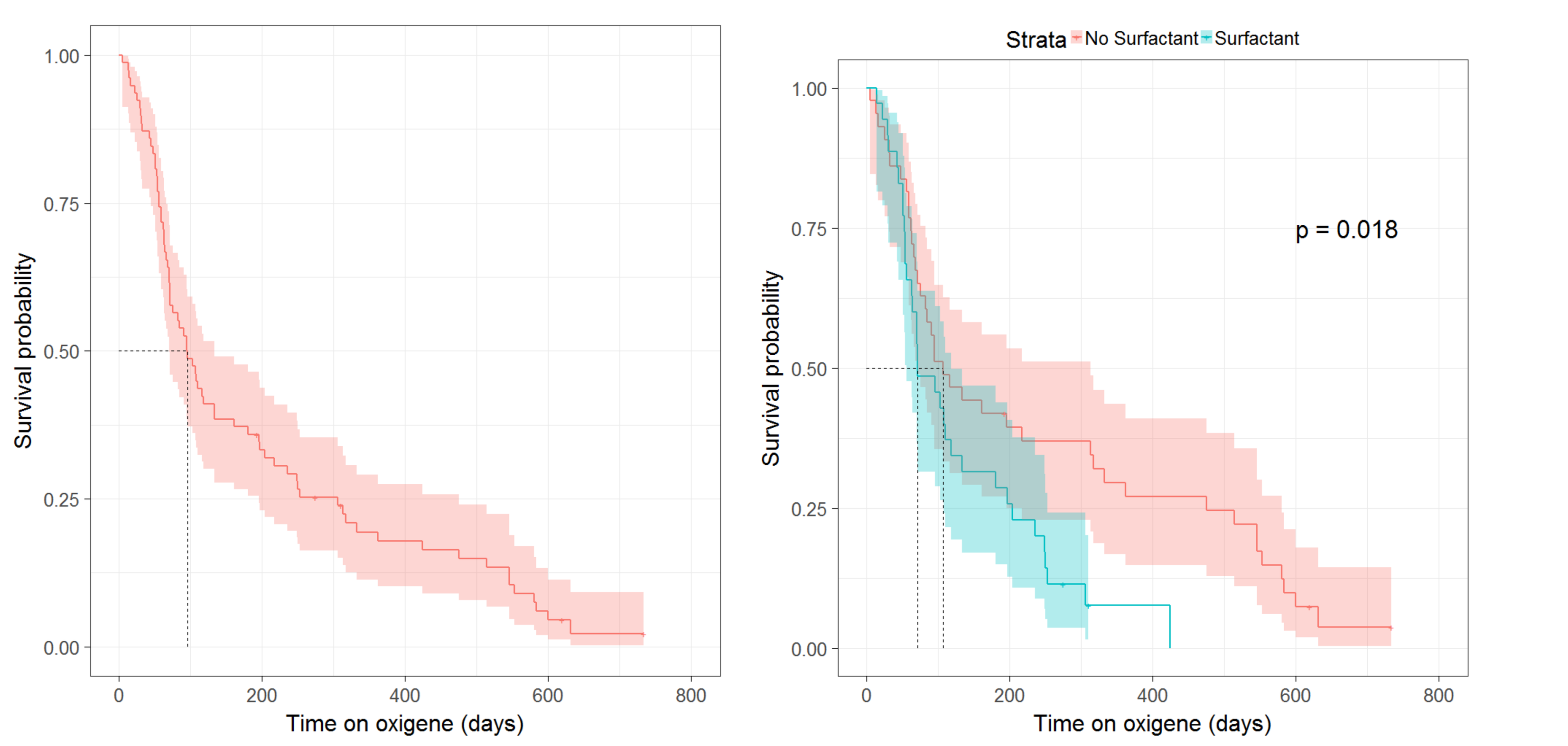


Figure 1: An example of the Kaplan-Meier estimate of the S(t) (left) No patients were censored due to the termination of the study (right) Some patients finished the study without experiencing the event (type I censoring).

To overcome this problem, Alvarez-Iglesias et al (2015) proposed a hybrid estimator of the MRL function which combines the KM estimate of the survival function with a parametric tail model based on the generalised Pareto distribution.

Clinical Example

In the analysis of the number of days low birth weight infants with bronchopulmonary dysplasia BPD (a chronic lung disorder) were treated with oxygen, 78 babies displayed survival probabilities depicted in Figure 2 a) (Hosmer and Lemeshow 1999, note that low values are associated with a good outcome) (approximate median oxygen time 95 days).



a) b)

Figure 2: Kaplan-Meier estimates of the survival probabilities for the BPD dataset (low values represent a good outcome) a) All 78 infants combined. b) Survival probabilities by therapy.

Clinical Example (cont)

Among these patients, those who received a novel surfactant replacement therapy had a better outcome (approximate median oxygen time 71 days) compared to those who did not received the therapy, Figure 2 b) (approximate median oxygen time 107 days).
Alternatively, the estimated MRL function (Alvarez-Iglesias et al 2015) offers a novel interpretation, with babies in the no surfactant therapy having an acute phase of approximately 150 days, where the average number of days on oxygen increases over time, up to a point of more than 300 days for babies who still needed oxygen after 150 days (Figure 3).

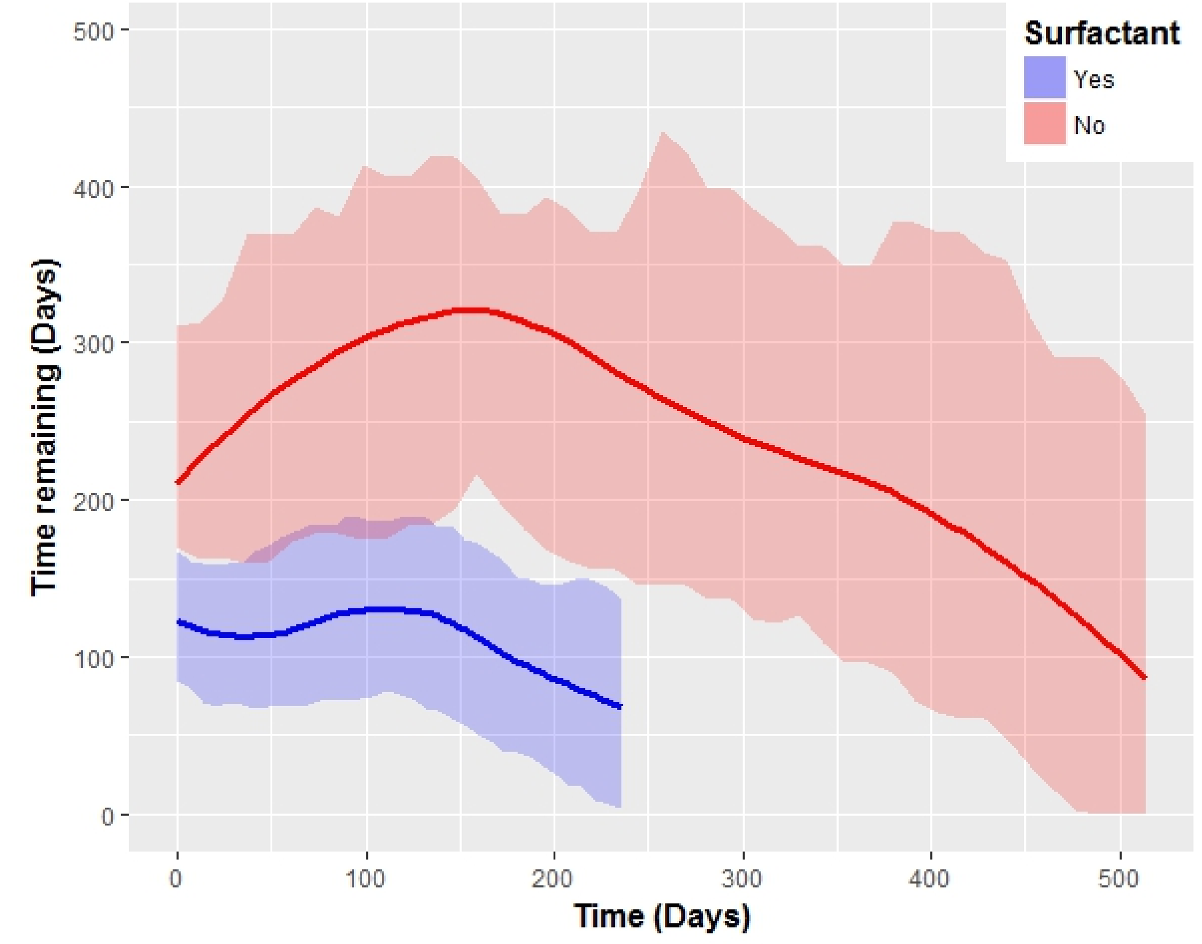


Figure 3: Estimated MRL function for the BPD dataset with bootstrap point-wise confidence bands.

After this acute phase, the average number of days on oxygen seems to gradually decrease, suggesting a progressive improvement in the babies condition. On the other hand, infants on the surfactant therapy display much better outcome with a fairly constant average number of days on oxygen of approximately 120 days for a period of a 150 days, after which a gradual improvement is observed (decreasing MRL function).

Visualisation Tool

A web-based interactive shiny app is available to generate the graphical time-to-event summaries (https://amir.shinyapps.io/survapp) highlighted in this poster. This visualisation tool could provide a useful intuitive overview of the results of survival studies. A screen-shot of this application applied to the BPD data is given in Figure 4.

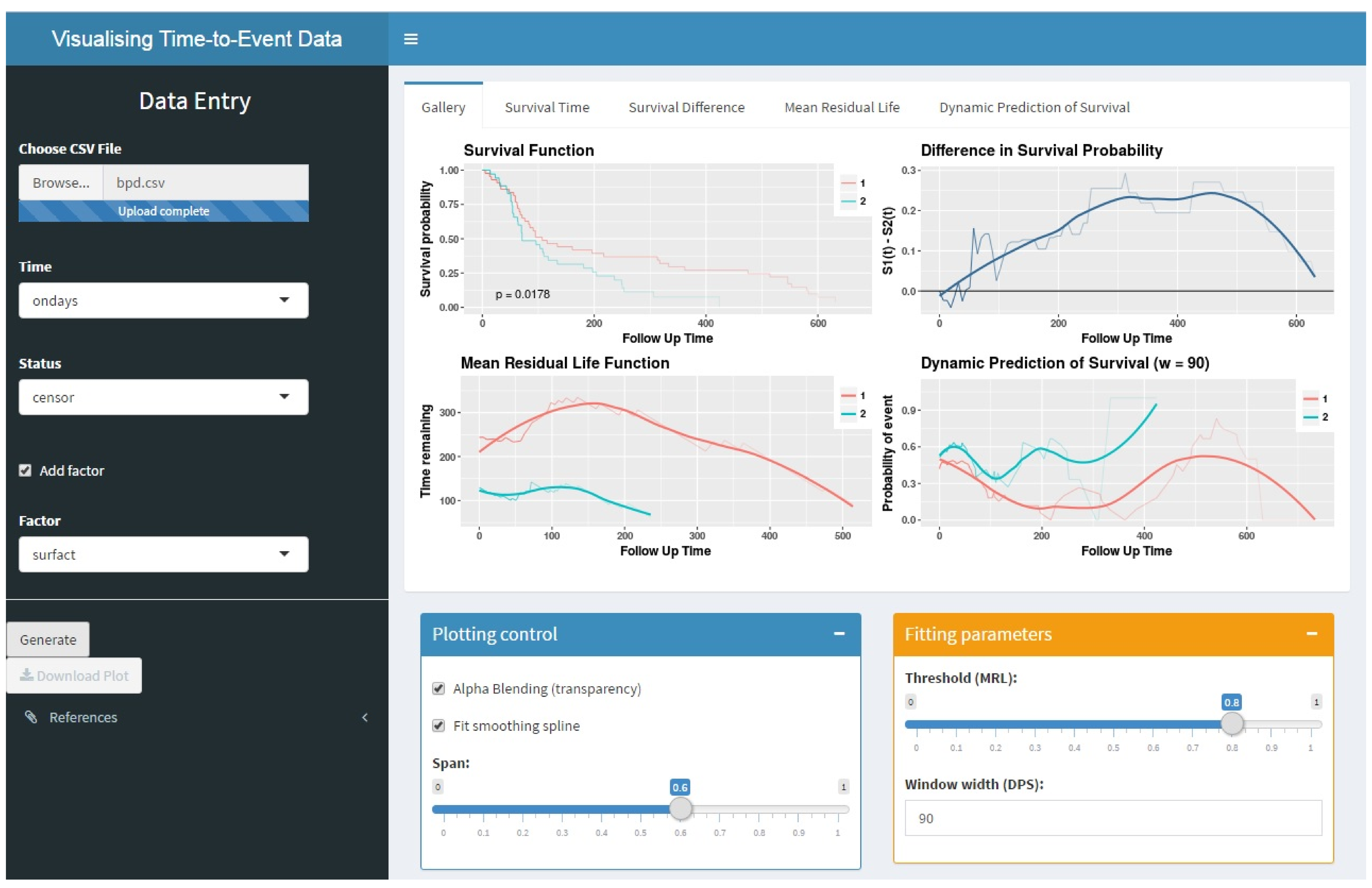


Figure 4: Visualisation tool to generate a suite of graphical summaries for time to event data.

References

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