R exercises – part II

Recurrent events: `rr.csv`

Intensity models. Use `survival` package.

1. Plot Nelson-Aalen estimates for the recurrent event rate by treatment group.
2. Fit an Andersen-Gill model with treatment as covariate.
3. Add a binary time-dependent variable defined as 'had a previous event' (yes/no). What happened to the treatment effect?
4. Investigate treatment effect on death using Nelson-Aalen estimator and Cox model.
5. Investigate in a similar way 'time to first event' and the composite endpoint 'time to first event or death'.

Marginal models. Use `mets` and `survival` packages.

6. Estimate (and plot) expected no of events (EE) by treatment group using the Cook-Lawless estimator. Add **wrong** curves by censoring for death.
7. Fit a Ghosh-Lin model for EE with treatment as covariate.
8. Fit a LWYY model for EE with treatment as covariate (i.e., censor for death).
9. Fit a Mao-Lin model for composite endpoint of 'recurrent event or death'.
10. Look at time to first event and demonstrate the bias when using 1−Kaplan-Meier instead of Aalen-Johansen estimator to estimate the cumulative incidence. Any similarity to exercise 6?

Fine-Gray: PBC3

Use `survival` package.

Competing risks: 1=transplantation and 2=death without transplantation

1. Plot the Aalen-Johansen (AJ) estimator by treatment for each transition.
2. Fit a Fine-Gray model for each transition with `tment` as the only covariate.
3. Fit a Fine-Gray model for each transition with `tment, alb, log2bili` as covariates.
4. Predict cumulative incidences for females and males based on Fine-Gray models for each transition. Compare to non-parametric AJs.

PBC3 – repetition

Use `survival` package.

Two-state model: transplantation or death (failure of medical treatment)

1. Plot the Kaplan-Meier estimator by treatment.
2. Estimate the treatment risk difference with 95% CI at year 3. Use function `riskdiff()` (see homepage for course).
3. Estimate the treatment RMST difference with 95% CI at year 3. Use function `rmstdiff()`.
4. Fit a Cox model with `tment` as the only covariate.
5. Fit a Cox model with `tment, alb, log2bili` as covariates.

Competing risks: 1=transplantation and 2=death without transplantation

6. Plot the Aalen-Johansen estimator by treatment for each transition.
7. Estimate the treatment risk differences with 95% confidence interval at year 3 for each transitions. Use function `cidiff()`.
8. Estimate the treatment years lost (YL) difference before year 3 with 95% confidence intervals for each transitions. Use function `yldiff()`.
9. Recall Fine-Gray model for each transition with `tment` as the only covariate.
10. Recall Fine-Gray model for each transition with `tment, alb, log2bili` as covariates.

Pseudo values – two-state model: PBC3

Use `survival`, `pseudo`, and `geepack` packages.

Two-state model: transplantation or death (failure of medical treatment)

1. Calculate the pseudo observations (POs) based on Kaplan-Meier at year 3 and add to the PBC3 data.
2. Estimate the treatment risk difference at year 3 using POs and the `identity` link function. Compare to repetition 2. Adjust for `alb` and `log2bili`. Try also, `log` link function (targeting the risk ratio).
3. Estimate for treatment RMST difference using POs at year 3 and the 'identity' link function. Compare to repetition 3. Adjust for `alb` and `log2bili`.
4. Calculate the POs at year 1, 2, 3, 4 in 'one go' and create a data set of long format and estimate a joint model using the 'cloglog' link function and 'tment' as the only covariate. Compare to Cox model from repetition 4.
5. Repeat 6, but now adjusted for 'alb' and 'log2bili'. Compare to Cox model from repetition 5.

Pseudo values – competing risks: PBC3

Use `survival`, `pseudo` and `geepack` packages.

Competing risks: 1=transplantation and 2=death without transplantation

6. Calculate the POs based on Aalen-Johansen for each transition type at year 3 and add to the PBC3 data.
7. Estimate the treatment risk difference for each transition using POs for each transition using `identity` link function. Compare to repetition 7. Adjust for `alb` and `log2bili`.
8. Estimate the treament difference in YL before year 3 for each transition using POs and the `identity` link function. Compare to repetition 8. Adjust for `alb` and `log2bili`.
9. For the transition *death without transplantation*, calculate the POs at year 1, 2, 3, 4 and create a data set with long format and estimate a joint model using the 'cloglog' link function and `tment` as the only covariate. Compare to Fine-Gray model from repetition 9.
10. Repeat 7, but now adjusted for `alb` and `log2bili`. Compare to Fine-Gray model from repetition 10.