MSR159

A Novel Unanchored Simulated Treatment Comparison Approach for Time-to-event Data

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Background

The two well-known population-adjusted indirect treatment comparison methods for unanchored indirect treatment comparisons in the case of no common comparator are matching-adjusted indirect treatment comparison (MAIC) and simulated treatment comparison (STC). However, STC has been applied much less frequently than MAIC in health technology assessment (HTA) when evidence is from single-arm studies, due to the lack of guidance on the use of unanchored STC approach for time-to-event data.

Objectives

We propose a novel implementation of the unanchored STC approach for time-to-event data and demonstrate its performance using a simulation study.

Methods

We are interested in estimating the treatment effect of treatment B versus treatment A, where we have the individual patient-level data (IPD) available from a single-arm study for treatment B (the IPD population) and aggregate data (AgD) from another single-arm study for treatment A (the AgD population). STC, a form of outcome regression approach, utilises the regression technique to predict the survival outcomes when the AgD population receives the treatment B.

Procedures of unanchored STC approach for time-to-event data

Step 1: Fit outcome regression model.

Fit a cox regression model to the single-arm data B_IPD with prognostic factors and effect modifiers as covariates.

Step 2: Simulate covariates $X_{ij}(AgD)$.

Sample individual-level covariates for the aggregate population using Gaussian copula given the published summary statistics of the patient characteristics.

Step 3: Predict survival probabilities $S_t(B\_AgD)$.

The survival probabilities when the aggregate population receiving treatment B can be predicted with based on the outcome regression in step 1 and the simulated covariates $X_{ij}(AgD)$ in step 2.

Step 4: Reconstruct IPD for both arms in the aggregate population.

(1) The IPD of the aggregate population receiving treatment B can be reconstructed based on the predicted survival probabilities from step 3 by using Guyot's method.

(2) The IPD of the aggregate population receiving treatment A can be reconstructed based on the digitalized survival probabilities from the published Kaplan-Meier curves by using Guyot's method.

Step 5: Obtain the relative treatment effect.

Given the reconstructed IPD from step 4, standard survival extrapolation methods can be applied as usual.

Note: the bootstrap method is used to account for the uncertainty in the predictions and estimate the correct standard errors of such method.

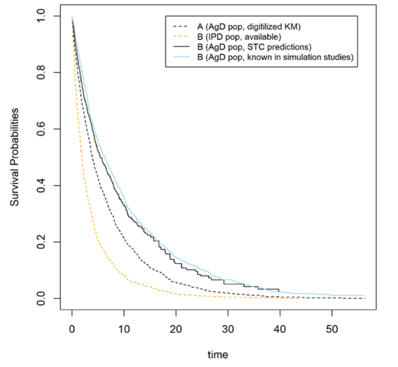


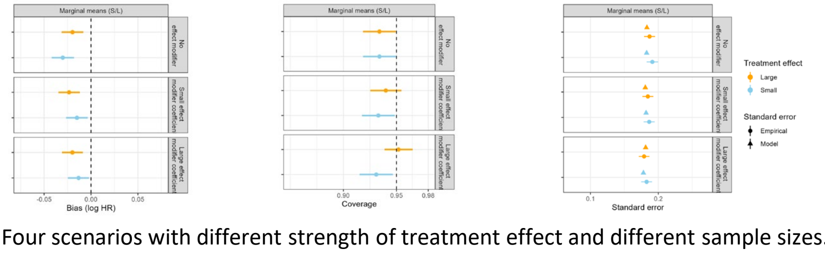
Figure 1: Kaplan-Meier curves of treatment A for the aggregate population, treatment B from the IPD population, treatment B from the STC predictions, and treatment B from the aggregate population.

Simulation study

We consider survival outcomes with two binary covariates representing prognostic factors and effect modifiers. The survival outcomes were generated from Weibull distributions with shape parameter 1 and scale parameter 0.15. The estimand of interest is the marginal log hazard ratio (HR) in the aggregate population. 1000 Monte Carlo replicates were generated for each scenario. The performance of the methods is evaluated using bias, coverage probability, empirical standard error and model standard error.

Results

(a) Six scenarios with different strength of treatment effect and different effect modifiers.



(b) Four scenarios with different strength of treatment effect and different sample sizes.

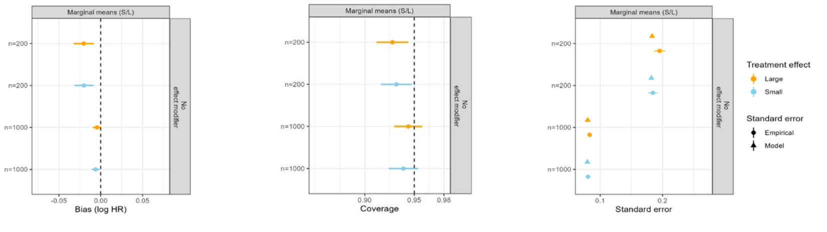


Figure 2: Bias, coverage probability, empirical standard error and model standard error along with 95% Monte Carlo confidence intervals for different scenarios. (S and L for marginal means indicate small and large marginal mean.)

Conclusions

Results from Figure 2 show that the unanchored STC performs well in all tested scenarios. The bias and standard error reduces with the increasing of the sample size.

Discussion

We provided a step-by-step guide on how to conduct an unanchored STC approach for time-to-event data. Our simulation study shows that the proposed approach performs well in the settings tested. We encourage analysts to consider using unanchored STC when conducting unanchored indirect comparisons with single-arm studies. At the same time, more simulation studies are still needed to evaluate the performance of the method in a variety of different scenarios.

Reference

Guyot, P., Ades, A., Ouwens, M.J. et al. Enhanced secondary analysis of survival data: reconstructing the data from published Kaplan-Meier survival curves. BMC Med Res Methodol 12, 9 (2012).

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