Background: Analyses of legacy effects are mainly based on post-trial follow-up study after initial randomized controlled trials (RCT). However, the differential event rates between arms may cause a violation of randomization balance and induce selection bias in the post-trial analysis. We conducted a simulation to illustrate the bias and explore if marginal structural model (MSM) can address it.
Methods: Our simulation combined an RCT and an extended follow-up study. The scenarios investigated include different settings of direct treatment effect, legacy effect and underlying event rate. To fit the MSM, we used the inverse probability weighting method. The performance of MSM was compared to the standard model with and without adjustment of baseline covariate.
Results: Post-trial analysis without making adjustment resulted in biased estimates, and the bias increased with the underlying event rate and treatment effect. Both MSM and standard baseline covariate adjustment equally corrected for the bias if no patients took treatment after the trial. We are currently undertaking analysis for scenarios where some people continue treatment post-trial, and there is treatment confounder feedback; these results will be presented at the Congress.
Conclusions: Estimation of legacy effects using post-trial data without adjusting for differential survival between randomised treatment arms results in biased estimates. Although both standard covariate adjustment and MSM correct the bias if no patients take treatment in the post-trial period, MSM is expected to be the best method in the more realistic scenario where some patients continue to take treatment, and there is treatment confounder feedback.
Key messages: Post-trial analysis without making adjustment results in biased estimation of legacy effect. Marginal structural models may be used to address the selection bias.

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Using marginal structural models to account for selection bias in the analysis of legacy effect

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