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TO RECENSOR, OR NOT TO RECENSOR, THAT IS THE QUESTION: CRITICAL CONSIDERATIONS WHEN APPLYING STATISTICAL METHODS TO ADJUST FOR TREATMENT SWITCHING IN CLINICAL TRIALS
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OBJECTIVES: To determine when re-censoring should be incorporated in statistical analyses undertaken to adjust for treatment switching in randomised controlled trials, and to demonstrate the utility of inverse probability weighting (IPW) as an alternative to re-censoring. Treatment switching often has a crucial impact on estimates of the effectiveness and cost-effectiveness of new oncology treatments. Switching adjustment methods such as rank preserving structural failure time models (RPSFTM) and two-stage estimation estimate 'counterfactual' (i.e. in the absence of switching) survival times and incorporate re-censoring to guard against informative censoring in the counterfactual dataset. However, re-censoring often involves a loss of longer term survival information which is problematic when estimates of long-term survival effects are required. METHODS: A simulation study was conducted, testing RPSFTM and two-stage adjustment methods with and without re-censoring, and with IPW in place of re-censoring, across scenarios with various switch proportions and sizes and time dependencies of the treatment effect. Methods were assessed according to their estimation of true restricted mean survival (in the absence of switching) at the end of trial follow-up. RESULTS: RPSFTM analyses that incorporated re-censoring were prone to bias when the treatment effect decreased over time – overestimating the treatment effect by approximately 311% in these scenarios, compared to bias of approximately 02% for RPSFTM and two-stage analyses that did not incorporate re-censoring. Two-stage analyses usually overestimated the treatment effect when re-censoring was incorporated and consistently underestimated the treatment effect when re-censoring was not incorporated. Using IPW in place of re-censoring resulted in low levels of bias when the censoring proportion and switching proportion were relatively low (both approximately 25%). CONCLUSIONS: Re-censoring should not always be incorporated in adjustment analyses when the objective is to estimate the long-term treatment effect. Conducting analyses with and without re-censoring may provide useful information on the size of the true treatment effect.