

Incorporating Inverse Probability of Censoring Weighting (IPCW) into the OHDSI CohortMethod Workflow

Hsin Yi Chen, BS¹, Tara V. Anand, PhD¹, Linying Zhang, PhD², George Hripcsak, MD, MS¹

¹Department of Biomedical Informatics, Columbia University, New York, NY, USA

²Institute for Informatics, Data Science and Biostatistics, Washington University in St. Louis, St. Louis, MO, USA

Background

CohortMethod is an R package within the HADES¹ ecosystem for conducting new-user cohort studies in observational healthcare databases structured in the OMOP common data model². The package supports large-scale observational analyses, often involving high-dimensional covariates (often more than 10,000) and large populations. The package can be used to extract standardized covariates from the database (FeatureExtraction package³), implement large-scale propensity score^{4,5} stratification, matching, or weighting⁶, and modeling outcomes with logistic, Poisson, or Cox regression. This framework has been widely applied in previous OHDSI network studies, including LEGEND-T2DM^{7,8}, LEGEND-hypertension⁹, and the effect of semaglutide on nonarteritic anterior ischemic optic neuropathy and diabetic retinopathy^{10,11}.

While confounding adjustment is a central focus in observational research and the current CohortMethod package, informative censoring remains a potentially under-addressed source of bias in large-scale OHDSI studies. Censoring can induce bias when loss to follow-up or end of observation is associated with outcome risk. Standard survival analyses methods such as the Cox proportional hazards¹² and Kaplan-Meier¹³ models assume non-informative censoring^{14–16} and the violation of this assumption can lead to biased effect estimates due to systematic differences between censored and uncensored individuals. In practice, this assumption is difficult to verify, and this can be a particular concern to reviewers of observational studies when censoring is driven by factors related to disease severity, treatment response, or healthcare utilization.

One such solution to informative censoring is using inverse probability of censoring weighting (IPCW), where observed individuals to represent a pseudo-population in which censoring is independent of covariates and outcomes. Here, we extend the standard CohortMethod workflow to incorporate IPCW for adjustment of informative censoring. We evaluate its application as a sensitivity analysis in a large-scale hypertension study within the LEGEND framework and propose it as a sensitivity analysis for future OHDSI studies.

Methods

We propose an IPCW-augmented extension of the CohortMethod workflow for large-scale observational analyses in the OMOP Common Data Model, shown in the following algorithm:

Algorithm: IPCW-augmented CohortMethod workflow

1. Generate study cohorts and baseline covariates.

2. Fit a large-scale propensity score model and estimate IPTW.
3. Define censoring as end of observation or loss to follow-up.
4. Fit a penalized Cox model for censoring:

$$h_c(t | X) = h_0(t) \exp(X\beta)$$

5. Estimate subject-specific probabilities of remaining uncensored:

$$K_Z(t | X)$$

6. Compute IPCW:

$$IPCW(t) = \frac{1}{K_Z(t | X)}$$

7. Stabilize and truncate IPCW (optional)
8. Combine weights (if using IPTW):

$$W(t) = IPTW \times IPCW(t)$$

9. Fit weighted Cox outcome model.
10. Estimate uncertainty using m-out-of-n bootstrap.

Implementation builds on existing OHDSI tools: steps 1-2 are executed using CohortMethod and CohortGenerator. Steps 3-7 are implemented using Cyclops after feature extraction via the FeatureExtraction package. The final weighted survival models and bootstrap procedures are implemented using standard R survival modeling workflows. All code can be found in the Github: <https://github.com/ohdsi-studies/ExploringCensoringWeights/>

Results

We applied the IPCW-augmented CohortMethod workflow to one treatment comparison within the previously-published LEGEND-HTN study⁹ using the Columbia University Database. We evaluated ACE inhibitors (ACEi) versus thiazide diuretics in a comparative new-user cohort design with acute myocardial infarction (AMI) as the outcome.

A total of 46,891 new users were included, comprising 22,854 thiazide initiators and 24,037 ACEi initiators. Among ACE initiators, 71.82% were censored because of end of continuous drug exposure, 2.0% due to observation period end, and 26.18% due to treatment switching. The distribution of censoring reasons was similar for thiazide initiators: 69.05%, 1.96%, and 29.98%, respectively.

We estimated hazard ratios (Figure 1) under two analytic strategies: IPTW (confounding-adjustment only, as is standard for current OHDSI studies using the CohortMethod package), and IPTW-IPCW (confounding adjustment augmented with the proposed algorithm). IPCW had minimal impact when added to IPTW, with the HR estimate remaining similar to IPTW alone. This suggests that, in this comparison, censoring was unlikely to be a major source of bias in the treatment effect estimates, especially after adjusting for confounding.

One plausible explanation is that although censoring due to treatment discontinuation and switching was substantial, it was similarly distributed across treatment groups. Alternatively, the magnitude of confounding bias may have been substantially greater than the magnitude of censoring bias, such that the incremental benefit of IPCW was modest. As we demonstrated in our benchmarking study, the utility of IPCW likely depends on the underlying data-generating process, the relative magnitude of censoring bias, and the estimand of interest¹⁷.

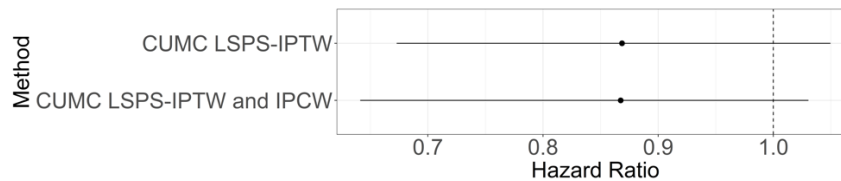


Figure 1. Hazard ratio estimates of our real world study, comparing thiazide diuretics to ACE inhibitors for the risk of AMI. A HR < 1 means that the outcome is more favorable for thiazide diuretics.

Conclusion

This work demonstrates the feasibility of incorporating IPCW into the standard OHDSI CohortMethod workflow using existing HADES infrastructure. The proposed extension can be implemented at scale and integrated with established propensity score-based analyses without substantial modification to the underlying pipeline. Although adding IPCW to IPTW did not materially change treatment effect estimates in our real-world example, its inclusion can serve as a structured sensitivity framework for assessing potential informative censoring. We therefore propose IPCW as a practical sensitivity analysis for future OHDSI studies, particularly in settings where censoring mechanisms may plausibly differ between exposure groups.

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