

International Journal of Population Data Science



Swansea University
Prifysgol Abertawe

Journal Website: www.ijpds.org

Estimating the effect of referral for nephrology care on the survival of adults with advanced chronic kidney disease in a real-world clinical setting

Liu, P¹, Karim, ME², Ronksley, PE¹, Hemmelgarn, BR¹, Quan, H¹, Quinn, RR¹, and Ravani, P¹

¹University of Calgary

²The University of British Columbia

Introduction

Longitudinal studies ascertain exposure, covariates, and outcomes over time. For estimating treatment effect on mortality, ignoring the time-varying nature of an exposure may lead to immortal time bias. Time-dependent confounding that affects future treatment may bias the estimated effects. Differences in baseline prognosis between treatment groups further complicate this issue.

Objectives and Approach

We applied sequential Cox modeling to estimate the causal effect of referral for nephrology care on the survival of adults with advanced chronic kidney disease, linking laboratory and administrative data from Alberta, Canada. We created pseudo-data by mimicking successive randomized controlled trials. To address immortal time bias, each “mini-trial” consisted of individuals starting treatment, and those not yet treated, in each 3-month time interval. We incorporated inverse-probability-of-treatment-weights (IPTW) to minimize treatment selection bias for each “mini-trial.” We fit a “mini-trial”-stratified, weighted Cox model to estimate the overall hazard ratio for death by averaging the effect estimates across “mini-trials.”

Results

We included 9,675 patients who entered the cohort between 2002 and 2013. The mean age was 82 years; 35% were male; and 33% were ultimately referred to a nephrologist after a median wait-period of 6 months. Compared to non-referred patients, those referred were younger and had fewer comorbidities at baseline. Referral was associated with a significant 45% lower hazard for death in an adjusted Cox model. The effect was attenuated in a multivariate Cox model with a time-varying exposure and in a sequential Cox model further controlling for potential time-dependent confounding by measures reflecting kidney-, cardiovascular-, and cerebrovascular-health. After incorporating IPTW for addressing treatment selection bias in the same sequential Cox model, the effect estimate was

toward the null and no longer significant.

Conclusion/Implications

We found that applying analytical strategies that addressed immortal time bias, time-dependent confounding, and treatment selection bias, the survival benefit associated with nephrology referral was attenuated. Inverse-probability-of-treatment weighted sequential Cox approach may be used to address these important biases and confounding that are common in real-world clinical settings.

