USE OF NEGATIVE CONTROL OUTCOMES TO ASSESS THE COMPARABILITY OF TREATMENTS FOR HYPERCHOLESTEROLEMIA

Abstract Category: Session 2108 – Prevention & Health Promotion: Population Science 1

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Abstract

Background: The real-world effectiveness of proprotein convertase subtilisin/kexin type 9 inhibitors (PCSK9i) in lowering risk of cardiovascular events has not been well studied. Selection of hypercholesterolemia treatment may be related to a patient's prognosis, possibly leading to confounding bias when comparing treatments in non-interventional studies. We used negative control outcomes to assess residual bias and identify the optimal study design for comparative effectiveness studies of PCSK9i.

Methods: Using commercial claims, we identified patients who initiated high intensity statin (HIS), ezetimibe, or PCSK9i between 2015 and 2018. Initiation was the index date. Eligible patients had at least one of the following: use of a different lipid lowering treatment (LLT) one year prior to index (LLT cohort) or a diagnosis for atherosclerotic cardiovascular disease (ASCVD) 90 days prior to index (ASCVD cohort). We compared PCSK9i to HIS and ezetimibe using 12 negative control outcomes identified by experts. For each outcome, we estimated the 12-month cumulative risk difference (RD) between treatment groups using inverse probability of treatment and censoring weights.

Results: The LLT cohort included 3,233 PCSK9i, 28,389 ezetimibe and 157,363 HIS initiators. For most outcomes, there were no clear differences in risk by treatment group. However, compared to HIS, PCSK9i users had lower risks of decubitus ulcer (RD = -2.0%, 95% CI: -3.1%, -0.8%) and fractures (RD = -1.2%, 95% CI: -1.9%, -0.4%). Risks of these outcomes were also lower compared to ezetimibe. The ASCVD cohort included 3,418 PCSK9i, 15,539 ezetimibe and 148,110 HIS initiators. Compared to HIS, PCSK9i users had lower risks of ulcer (RD = -3.6%, 95% CI: -4.7%, -2.5%), accidents (RD = -5.4%, 95% CI: -8.9%, -1.9%) and visual tests (RD = -1.6%, 95% CI: -3.1%, -0.1%), but higher risk of obesity (RD = 4.4%, 95% CI: 0.0%, 8.8%), with similar findings for PCSK9i versus ezetimibe.

Conclusion: Caution is warranted when comparing PCSK9i to other treatments. Observed associations with negative control outcomes suggest the potential for residual confounding and bias between PCSK9i patients and those taking HIS or ezetimibe.