Phenotype Development and Evaluation of Heart Failure: A Case Study in using Patient Level Prediction to Improve Phenotype Validity

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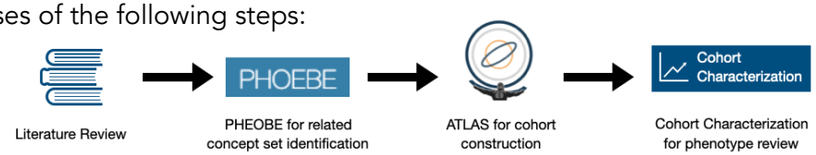
INTRODUCTION

- Establishing robust, high fidelity phenotypes to isolate incident cases (i.e., new onset) of a chronic condition is challenging. A common reason is **index date misspecification**, when a condition's actual onset date differs from the onset date of record.
- The proposed OHDSI pipeline for rigorous phenotype development and evaluation comprises of the following steps:



- This study demonstrates how Patient Level Prediction (PLP), a tool intended for use after phenotype evaluation, **can be used as a second round evaluation to test, validate and further refine phenotype definitions.**

CASE STUDY: HEART FAILURE & TZD USE

- Thiazolidines (TZDs) are a potent class of anti-diabetic drugs that can increase the risk of heart failure (HF) exacerbations, even among patients without a known HF diagnosis.
- **Case Study Aim:** Predict the risk of HF-related hospitalization among TZD mono-therapy patients with and without a prior history of HF using both Columbia University Irving Medical Center (CUIMC) and Commercial Claims and Encounters (CCAE) data.
- Following literature review, we defined HF as: (1) a condition occurrence of HF diagnostic codes, (2) observation of HF related condition codes, (3) condition occurrence of HF-related codes, or (4) ECG ejection fraction measurement under 50%.
- A total of 30,361 TZD mono-therapy patients hospitalized for HF were identified (CUMC N=1,330; CCAE N=29,031). 96.3% of all patients (N=29, 230) appeared to have no prior HF.

FINDINGS

- Initial ATLAS cohort characterization suggested face validity and appeared to clearly distinguish between TZD patients with and without prior HF.
  - **TZD Patients with HF:** Top drug occurrence showed aspirin, hydrochlorothiazide, and furosemide (drugs indicative of HF). Top condition occurrences showed diabetes, hypertension and congenital HF.
  - **TZD Patients without HF:** Top drug showed aspirin but no HF specific drugs. Top condition occurrences showed diabetes and hypertension.
- PLP models appeared able to predict HF hospitalization for patients with HF (CUMC AUC=0.55 ; CCAE AUC= 0.756) and without HF (CUMC AUC=0.527; CCAE AUC=0.804).
- However, a review of top PLP features showed drug and condition features specific to HF were predictive of future hospitalization, even among patients without a history of HF.
  - **Drug Predictors**: Furosemide (β =0.68, CCAE); Beta-Blockers (β =0.43, CCAE; β =0.34, CUMC)
  - **Condition Predictors:** Heart Disease (β =0.41, CUMC)
- This indicates flaws in our HF definition despite face validity, likely due to index date misspecification.

LESSONS FOR THE OHDSI COMMUNITY

1. Incorporate and test multiple time windows when establishing a look-back period for phenotype definitions if calculating incidence rates.
2. Leverage existing OHDSI tools (e.g. Cohort Diagnostics) to understand potential inconsistencies, particularly ones that are temporal in nature.
3. Utilize the PLP package as a second evaluation of outcome and target phenotype definitions by reviewing inconsistencies features that appear most predictive in the models produced.