Designing a Strategus Study

Research question

GLP-1 receptor agonists are primarily used to treat type 2 diabetes, and have recently seen more widespread use because they can also help reduce weight. Although all antidiabetic drugs help reduce the risk of cardiovascular outcomes, it is yet unclear what the effect of GLP-1s is on acute mycordial infarction compared to other antidiabetic drugs.

Design the study that answers this question, using Strategus

Hint: we may wat to compare GLP-1s to DPP-4 inhibitors.

Fill in the template!

Does exposure to **<insert your favorite drug>** have a different risk of experiencing **<insert any outcome (safety or benefit) >** within **<time horizon following exposure start>,** relative to **<insert your comparator treatment>**?

Filled-in template

Does exposure to **GLP-1s** have a different risk of experiencing **AMI** while **exposed to drug**, relative to **DPP-4s**?

Cohort definition for GLP-1s

- What is the index event? (Cohort start)
- What inclusion / exclusion criteria?
- What are the cohort exit criteria? (Cohort end)

Cohort definition for DPP-4s

- What is the index event? (Cohort start)
- What inclusion / exclusion criteria?
- What are the cohort exit criteria? (Cohort end)

What should we do with people who have used both GLP-1s and DPP-4s?

a. Create exclusion criteria that remove them from both exposure cohorts
b. Create exclusion criteria that remove people from GLP-1s who have used DPP-4s before, and the other way around
c. Trust the OHDSI analytics to solve this

What is the advantage of this?

What is the indication cohort definition?

If you create an indication cohort, people in the exposure groups are automatically required to also be in the indication cohort. This increases the likelihood that they are taking the drugs for the same indication.

(Advanced: the self-controlled case series design uses the indication cohort to restrict patient time included in the model)

- What is the index event? (Cohort start)
- What inclusion / exclusion criteria?
- What are the cohort exit criteria? (Cohort end)

Acute Myocardial Infarction

- What is the index event? (Cohort start)
- What inclusion / exclusion criteria?
- What are the cohort exit criteria? (Cohort end)

According to your definition, what is the minimum gap that can exist between subsequent AMIs? (Clean window)

Should we restrict the outcome cohort to people in the exposure cohorts?

a. Yes
b. No, trust the OHDSI analytics to do this

What is the advantage of this?

What is the time-at-risk?

What time period, relative to exposure start and end, do we want to estimate the causal effect?

What covariates should go in the propensity model?

a. Age and sex
b. The following 10 covariates: …
c. Large-scale propensity scores: all covariates (all conditions, exposures, demographics, etc.) except those for GLP-1s and DPP-4s

Negative control outcomes

Which of the following are not good negative control outcomes when comparing GLP-1s to DPP-4s?

- Contusion of knee
- Hammer toe
- Heart failure
- Foreign body in ear
- Opioid abuse
- Poisoning by tranquilizer
- Weight loss

Why not?

Strategus inputs

- Target cohort
- Comparator cohort
- (Indication cohort)
- Outcome cohort
- Time at risk
- Covariates to exclude from propensity model
- Negative controls

Standard Strategus outputs

- Characterization
  - Incidence rates of AMI in people using GLP-1s and DPP-4s, and in people with the indication (T2DM)
  - Dechallenge / rechallenge statistics for GLP-1s and DPP-4s
  - Patient characteristics (demographics, co-morbidities, other medications, etc.) of patients starting GLP-1s or DPP-4s, either restricted to those who go on to have AMI.
- Prediction
  - Model for predicting probability of AMI in people starting GLP-1s

  With full model diagnostics and performance measurements
- Estimation
  - Cohort method results for GLP-1s vs DPP-4s for AMI
  - SCCS results for GLP-1s vs unexposed time for AMI

  With full diagnostics to evaluate key assumptions, including negative controls

Design your exposure and outcome cohorts in ATLAS

- Go to https://atlas-demo.ohdsi.org/
- Make sure to give your cohorts unique names