OHDSI Reproducibility Challenge

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Thank you, Yasser Albogami

OBJECTIVE
Emerging data from animal and human pilot studies suggest potential benefits of glucagon-like peptide 1 receptor agonists (GLP-1RA) on lung function. We aimed to assess the association of GLP-1RA and chronic lower respiratory disease (CLRD) exacerbation in a population with concomitant type 2 diabetes (T2D) and CLRD.

RESEARCH DESIGN AND METHODS
A new-order active-comparator analysis was conducted with use of a national claims database of beneficiaries with employer-sponsored health insurance spanning 2005–2017. We included adults with T2D and CLRD who initiated GLP-1RA or comparator peptide 4 inhibitors (EPI-4) as an add-on therapy to their antipseudo-

RESULTS
The study sample consisted of 4,316 GLP-1RA and 12,540 DPP-4i new users with con-

CONCLUSIONS
GLP-1RA users had fewer CLRD exacerbations in comparison with DPP-4i users. Con-

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OHDSI Reproducibility Experiment

OHDSI 2021 Symposium

9 teams of highly qualified experts + Pre-made concept sets + ATLAS instance + Full day

Reproduce cohort logic for Target, Comparator and Outcome cohorts
Focus: Target cohort – GLP1-RA users

Study Sample
The study sample comprised patients aged >17 years who have had at least one inpatient or two outpatient encounters with T2D and CLRD, defined based on the presence of diagnoses or medication dispensing (Supplementary Tables 1 and 2) during the year before index date. Exposure assignment and start of follow-up (index date) were defined based on the first observed prescription for GLP-1RA and dipeptidyl peptidase 4 inhibitors (DPP-4I) (whichever came first) in the database. Patients whose first prescription fill did not follow at least 365 days’ continuous health plan enrollment were excluded to achieve a new-user design. We included patients who used either study drug class as an add-on to other antidiabetes agents, e.g., metformin. Patients using insulin prior to the index date or with a diagnosis of type 1 diabetes were excluded. Patients with a history of cystic fibrosis, lung cancer, pulmonary embolism, and pulmonary hypertension, which may independently worsen lung function, were excluded, as were women with pregnancy at index date. Patients with thyroid carcinoma who would likely be channeled to DPP-4I agents because of the related GLP-1RA contraindication were also excluded. Finally, patients with clinical conditions (except chronic obstructive pulmonary disease [COPD] and asthma) that frequently require chronic systemic corticosteroid treatment, which is protective against lung exacerbations, were excluded.
Master implementation

Concept sets were discussed with the author and provided to the teams

1. Cohort entry

Cohort Entry Events

Events having any of the following criteria:

- a drug exposure of GLP-1RA without insulin
  - occurrence start is: between 2006-01-01 and 2017-12-31

with continuous observation of at least 365 days before and 0 days after event index date

Limit initial events to: earliest event per person.

3. Cohort exit

Cohort Exit

Event Persistence:
Event will persist until end of a continuous drug exposure

Continuous Exposure Persistence:
Specify a concept set that contains one or more drugs. A drug era will be derived from all drug exposures within a window to the final exposure event. If no exposure event end date is provided, then an exposure event era greater than the drug era end date.

Concept set containing the drug(s) of interest:
GLP-1RA without insulin

- Surveillance window: allow for a maximum of 63 days between exposure records when initiated
- Use days supply and exposure end date for exposure duration

Censoring Events:
Exit Cohort based on the following criteria:

- a drug exposure of DPP-4i

Cohort Bias:
-Specify era collapse gap size: 0 days
- Left censor cohort start date to: 2005-01-01
- Right censor cohort end date to: 2017-12-31

2. Exclusion and inclusion criteria (10)

- no GLP1 exposure in 365d prior to index
- age > 17
- has type 1 diabetes in 365d prior to index
- has type 2 diabetes mellitus in 365d prior to index
- has CLRD in prior 365d prior to or on index based 1 IP dx OR 2 OP dx days OR (1 OP dx AND 1 rx)
- no conditions of exclusion in 365d prior to index
- no pregnancy observations in 180d prior to or after index
- no prior DPP4 exposure in 365d prior to or on index
- no prior insulin exposure in 365d prior to or on index
- must have other T2DM drug that starts before index and ends on or after index
Teams’ implementations

9 different GLP1-RA user cohorts
All teams were confident they were able to translate the logic of the paper into a cohort definition
On average, the teams did not reproduce 60% of the criteria
Only the simplest criteria are easy to reproduce

Easy to reproduce

Complex criteria with multiple sub-elements (conditions, drugs, visits)

Not a simple criteria but a complex phenotype

Variable temporal logic
Influence on patient selection
Average agreement between the master cohort and teams’ implementations (patient overlap) was low and varied from 0% to 35.4%.

* Agreement was calculated as number of patients in both cohorts divided by the number of patients in either cohort.
Compared to the master, teams’ cohorts are different in baseline prevalence of CLRD and antidiabetic drug exposure.

* Blank spaces correspond to standardized difference of means < 0.1
Conclusions

Researchers tend to underestimate the amount of information needed to reproduce a study.

Design choices cannot be reproduced using free-text alone. Supplements and figures may introduce additional ambiguity.

Sharing analytical code supported by a common data model allows reproducing a study in an unambiguous way.