Multinational Patterns of Second-line Anti-hyperglycemic Drug Initiation Across Cardiovascular Risk Groups

A Federated Pharmacoepidemiologic Evaluation in LEGEND-T2DM

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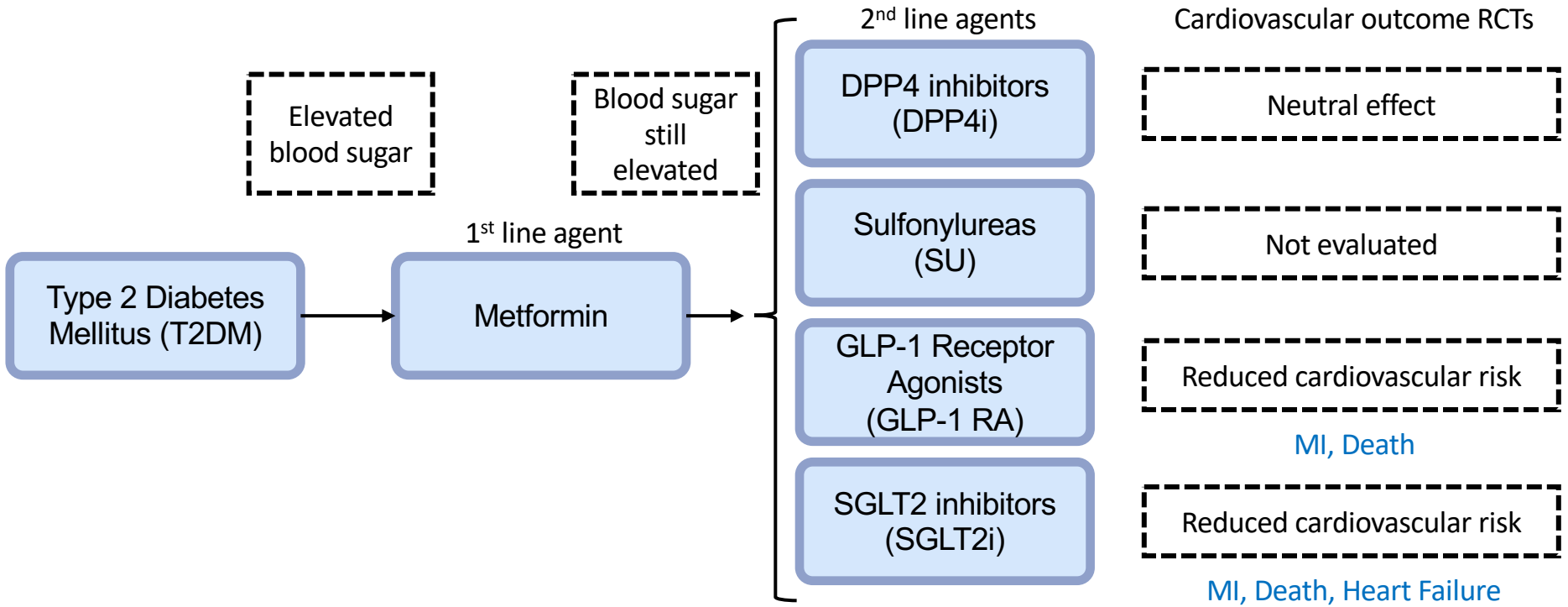
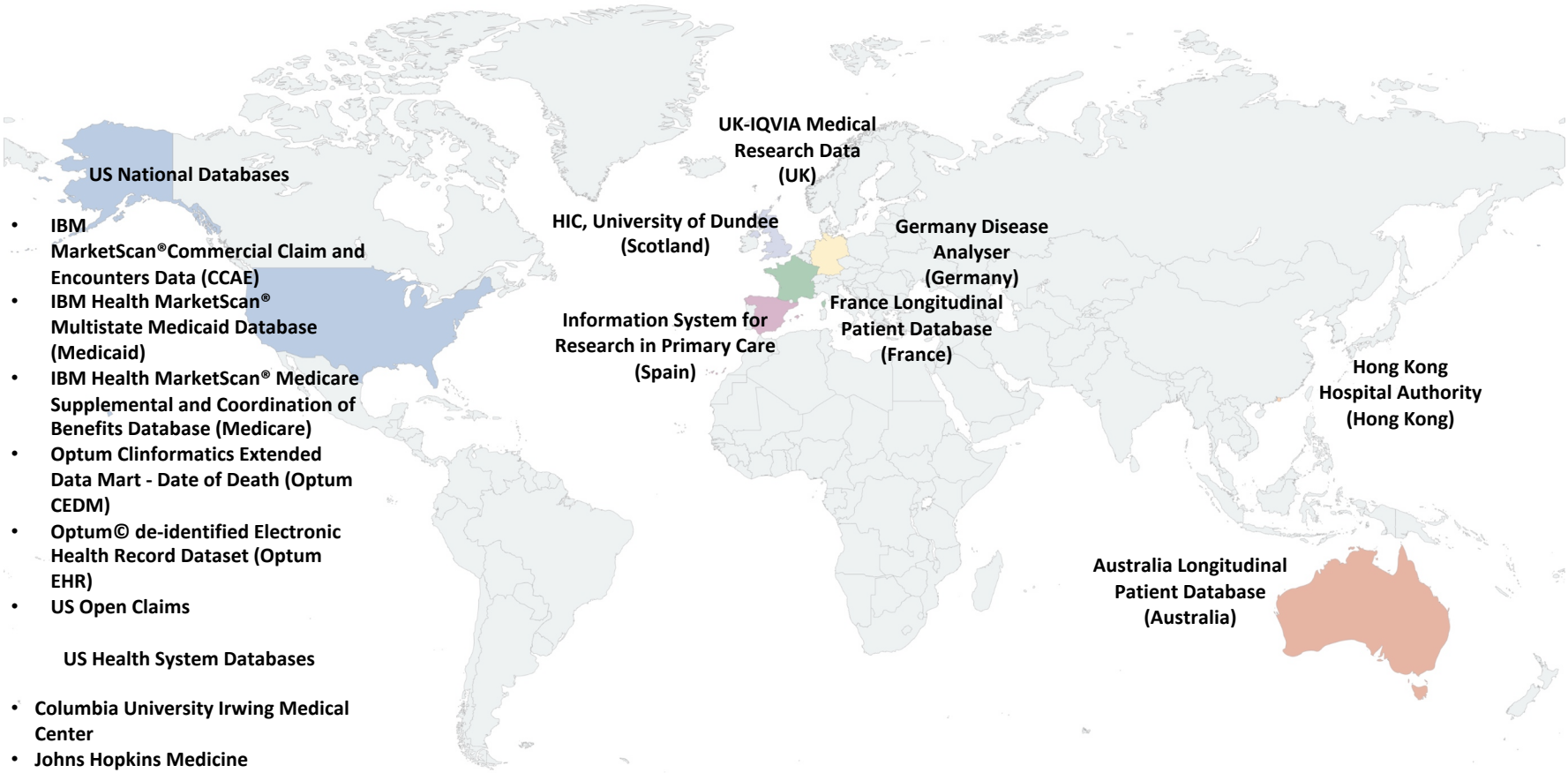
(for the LEGEND-T2DM investigators)

Background


Elevated blood sugar
Blood sugar still elevated
Type 2 Diabetes Mellitus (T2DM)
1st line agent
Metformin
2nd line agents
DPP4 inhibitors (DPP4i)
Sulfonylureas (SU)
GLP-1 Receptor Agonists (GLP-1 RA)
SGLT2 inhibitors (SGLT2i)
Cardiovascular outcome RCTs
Neutral effect
Not evaluated
Reduced cardiovascular risk
MI, Death
Reduced cardiovascular risk
MI, Death, Heart Failure

Multinational Serial Cross-sectional Study 2011-2021



US National Databases

- IBM MarketScan®Commercial Claim and Encounters Data (CCAE)
- IBM Health MarketScan® Multistate Medicaid Database (Medicaid)
- IBM Health MarketScan® Medicare Supplemental and Coordination of Benefits Database (Medicare)
- Optum Clinformatics Extended Data Mart - Date of Death (Optum CEDM)
- Optum© de-identified Electronic Health Record Dataset (Optum EHR)
- US Open Claims

US Health System Databases

- Columbia University Irwing Medical Center
- Johns Hopkins Medicine
- Stanford Medicine
- Department of Veterans Affairs Healthcare System

Multinational Serial Cross-sectional Study 2011-2021

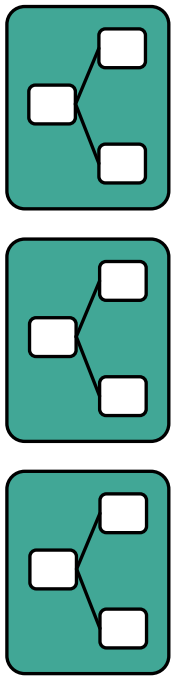
Inclusion Criteria

- Age ≥18 years
- Presence of T2DM
- Prior metformin use
- No prior second-line anti-hyperglycemic agent use

Exposures

- Presence of established cardiovascular disease
- Calendar Years

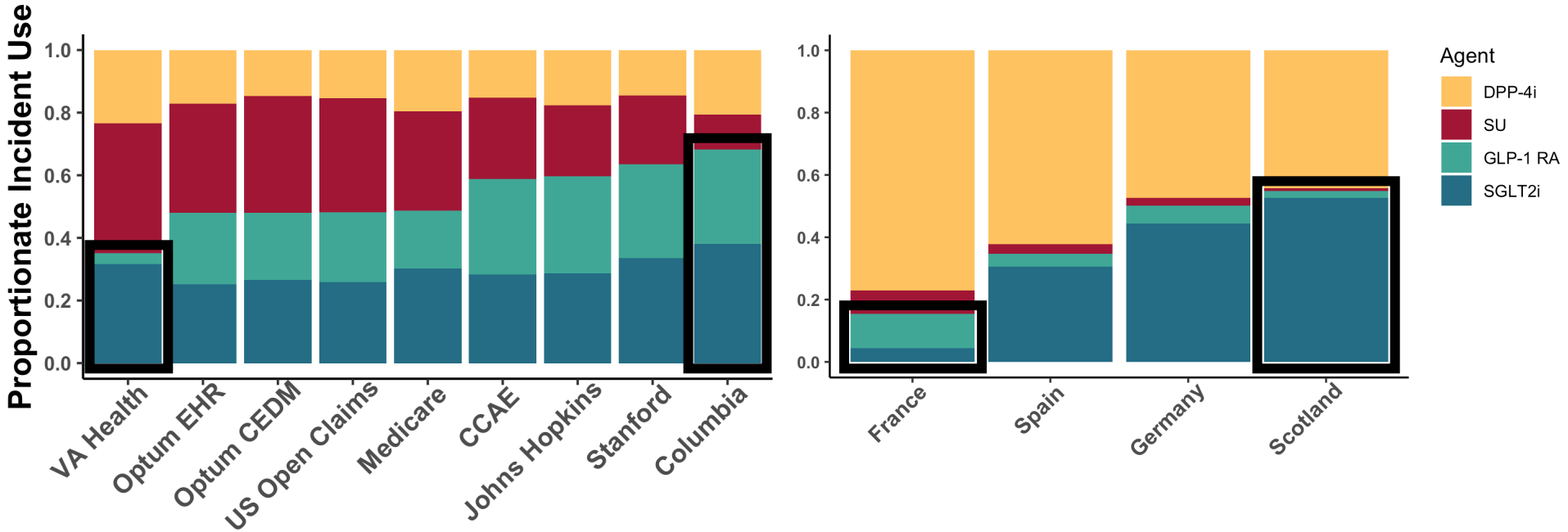
4.3 million patients across 17 data sources



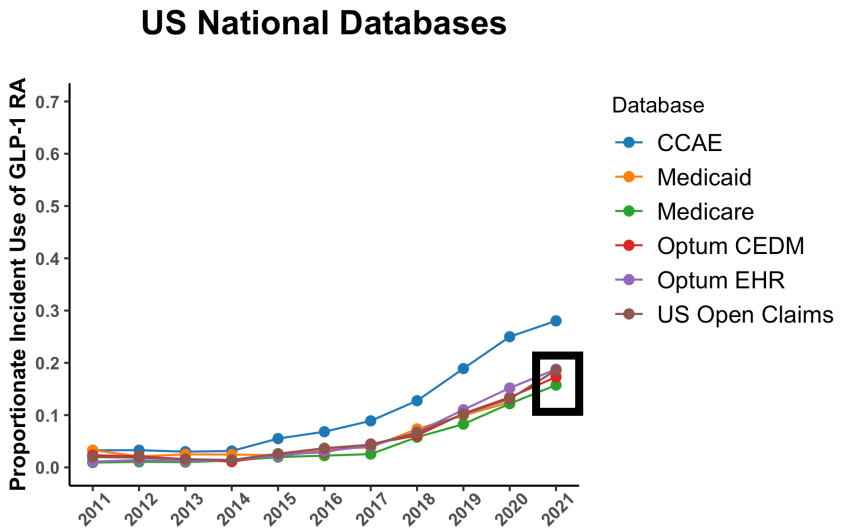
Outcomes

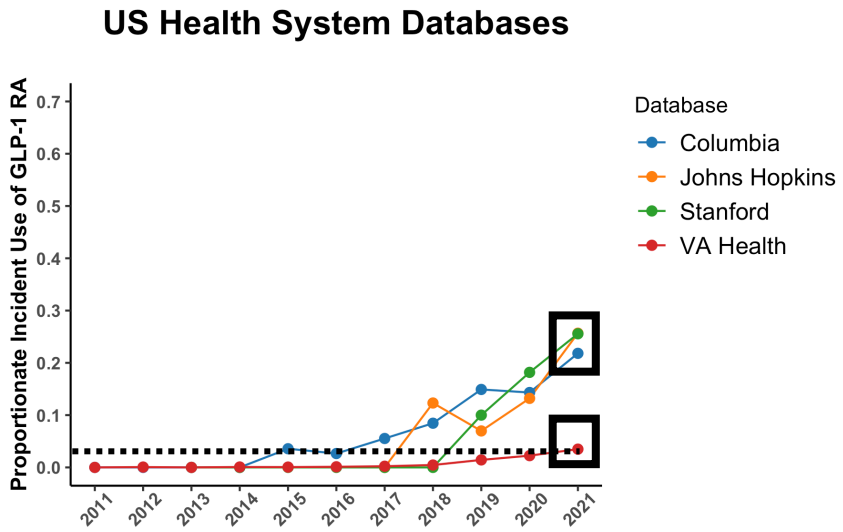
- Calendar-year trends for proportionate initiation 2nd line agents
- Comparison of annualized change in initiation of GLP-1 RA and SGLT2i in patients with and without CVD

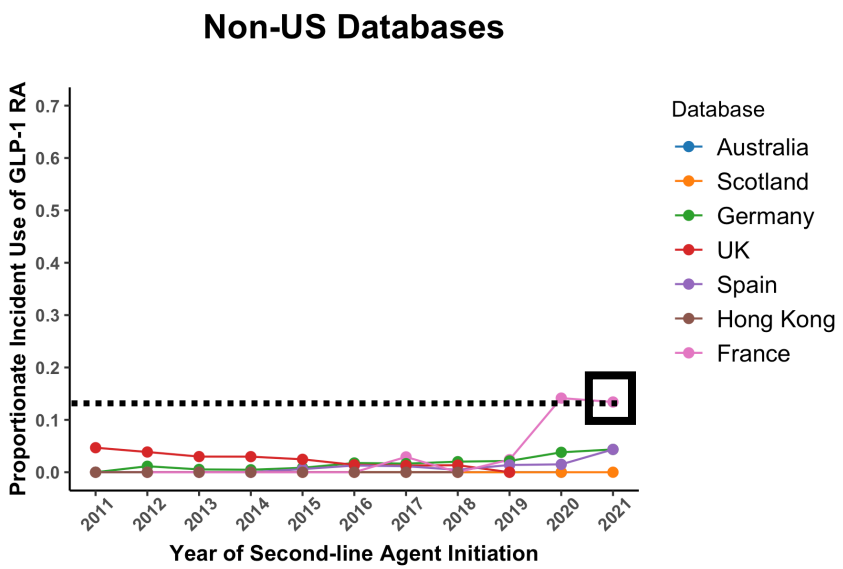
Proportionate Incident Use of Second-line Anti-hyperglycemic Agents in 2021



GLP-1 RA Uptake in Patients with Established CVD

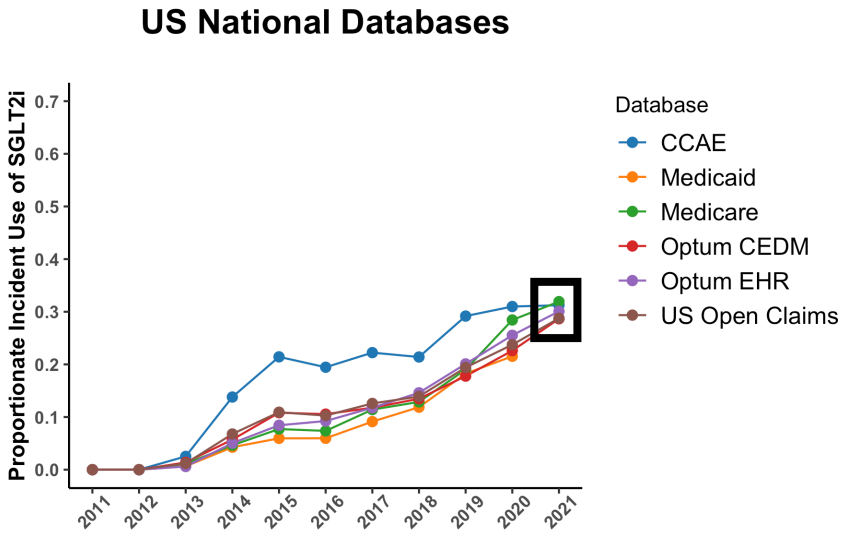


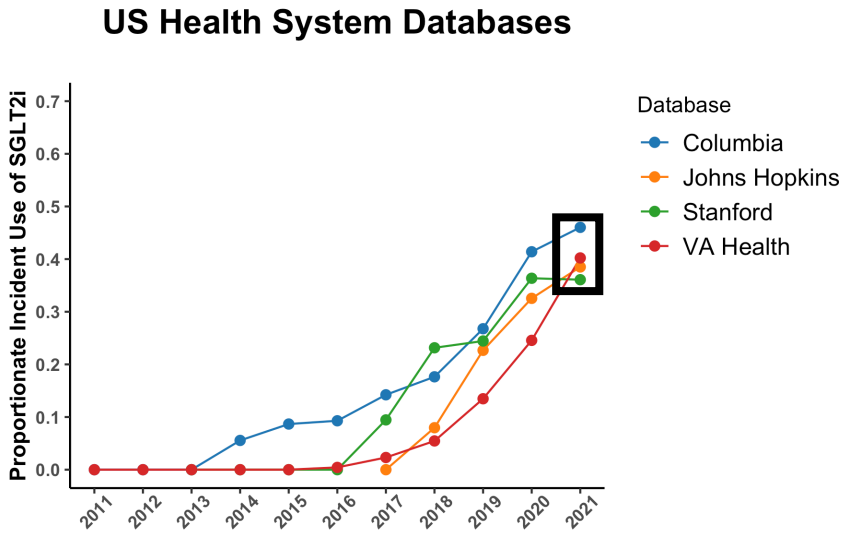


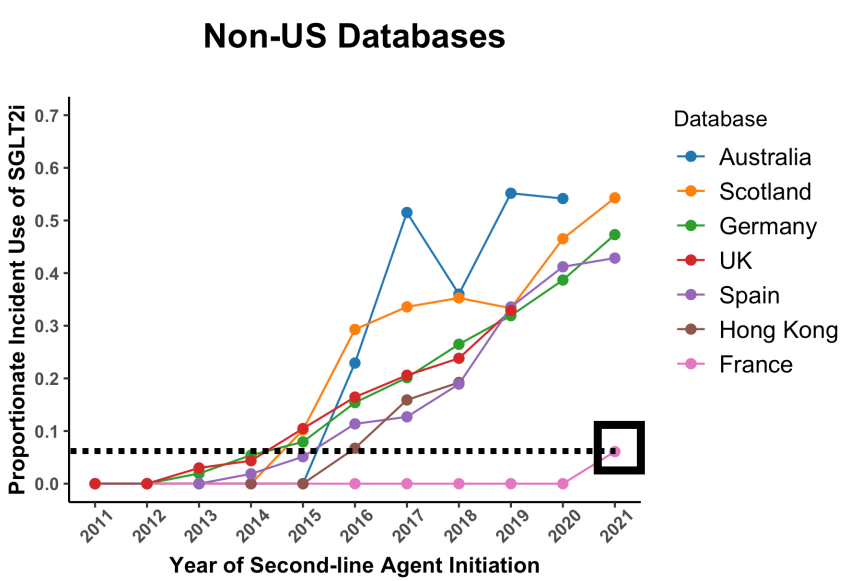


- Initiation of GLP-1 RAs increased to 20-25% across most US populations
- Initiation was <5% in the VA
- Initiation was low across non-US databases, reaching a maximum of 14% in France in 2021

SGLT2i Uptake in Patients with Established CVD







- Initiation of SGLT2is increased to ~35% across US populations
- In the non-US databases, the initiation of SGLT2is was higher in most databases, reaching up to 54% in Scotland in 2021
- In France, the initiation was lower, reaching only to 6% in 2021

Slope Interaction for Annualized Change in Cardioprotective Agent Initiation in Patients with and without CVD (2016-2021)

Representative Examples for GLP-1 RA Initiation

Data Source	With-CVD Slope	Without-CVD Slope	P-Value
CCAE	0.019 (0.011 to 0.026)	0.068 (0.037 to 0.099)	0.003
Columbia	0.017 (0.011 to 0.023)	0.031 (0.016 to 0.047)	0.040
Medicare	0.051 (0.009 to 0.092)	0.051 (0 to 0.102)	0.986
France	0.003 (0.001 to 0.006)	0.014 (0.004 to 0.023)	0.024
Spain	0.003 (-0.001 to 0.006)	0.010 (0.001 to 0.019)	0.062

Representative Examples for SGLT2i Initiation

Data Source	With-CVD Slope	Without-CVD Slope	P-Value
CCAE	0.014 (0.006 to 0.023)	0.035 (0.011 to 0.059)	0.053
Columbia	0.037 (0.022 to 0.052)	0.024 (0.013 to 0.034)	0.074
Medicare	0.092 (0.011 to 0.172)	0.056 (0.008 to 0.104)	0.325
France	0.001 (-0.001 to 0.003)	0.005 (-0.001 to 0.011)	0.132
Spain	0.033 (0.016 to 0.049)	0.065 (0.017 to 0.112)	0.115

Conclusion

- LEGEND-T2DM is the largest multinational pharmacoepidemiology study of anti-hyperglycemic therapy.
- Despite increased uptake, there is vast variation in use of cardioprotective therapies uses across populations with CVD.
- The uptake of these has been lower in the US, relative to other countries, particularly in patients with established CVD.
- Lack of selective use in CVD patients despite specific benefit in the population.

Thank you for your attention!

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cards-lab.org/legend-t2dm-disclosures