OHDSI APAC Community Call

20260618

Agenda

- OHDSI News
- **LEGEND-T2DM: Latest Updates**
  - Real-world Evidence for Comparative Safety of Second-Line Antihyperglycemic Agents in Older Adults with Type 2 Diabetes ***by Chungsoo Kim*** *(accepted by Nature Communication)*
  - Comparative Cardiovascular Effectiveness of Glucagon-Like Peptide 1 Receptor Agonists and Sodium-Glucose Cotransporter-2 Inhibitors in Diabetes Mellitus ***by Fan Bu*** *(accepted by JACC)*
- 2026 APAC Study: VALUE Study
  - Protocol

Building Community Generating Reliable Evidence Advancing Data Science

2026 OHDSI GLOBAL SYMPOSIUM

October 20-22

Hyatt Regency
2 Albany Street
New Brunswick, New Jersey
USA 08901

2026 OHDSI Global Symposium

- **Programme**
  - **Oct. 20:** Specialized tutorials to sharpen your skills and expand our collective expertise.
  - **Oct. 21:** High-impact plenaries and the celebrated Collaborator Showcase, featuring the latest breakthroughs from our community.
  - **Oct. 22:** Dynamic workgroup activities designed to solve real-world health challenges together.
- **Key dates**
  - Call for participation: Open now
  - Submission Deadline: Friday, June 5 by 8pm ET
  - **Scientific Review Period: June 5-July 6**
  - Email Notice of Submission Acceptance: Wednesday, July 15

Scan here for tutorial details!

2026 OHDSI APAC Symposium

Join us in Seoul for 2026 APAC Symposium!
Mark your calendars: Nov 13-15
@ Yonsei University, Seoul

https://biz.heraldcorp.com/article/3194576

2026 OHDSI APAC Symposium @ Seoul, Korea

- **Program:**
  - Nov. 13(Fri): Main Conference
  - Nov. 14(Sat): Tutorial + Datathon (Parallel sessions)
  - Nov. 15(Sun): Datathon
- **Main Conference:**
  - 5 sessions (‘Reproducible & Reliable’, ‘Robust’, ‘Regulatory’, ‘Rapid’, ‘Regional but global’)
- **Tutorial:**
  - Basic intro to OMOP CDM, Analyses/Application to diagnostics

2026 OHDSI APAC Symposium @ Seoul, Korea

- **Registration fee:**
  - Symposium: 250,000KRW (approx. $167) -> Early Bird 180,000KRW ($120)
  - Tutorial/Datathon: 150,000KRW ($100)

- **Registration page available soon!**

- Symposium info + Google Form will be uploaded first
  - **Abstract submission (~8/17)**

Community Survey

In the era of foundation models, does data standardization still matter?

LLMs and multimodal models now read unstructured text directly — so is OHDSI's decade-long investment in the OMOP CDM, vocabularies, and federated networks a trust mechanism, or a legacy cost?

Why now — the gap

Medical AI is moving fast from research artifact to clinical infrastructure. Large surveys have studied attitudes toward AI and its failure modes — but the technical community that builds and maintains the data infrastructure has never been studied. This survey fills that gap.

The survey at a glance

Design

Pre-registered, cross-sectional, global survey. Target N=300 (minimum analyzable N=200).

Recruitment

OHDSI Forums, regional chapters, and Working Group leads — that means you, in this room.

Let's gather APAC!!

Analysis

We map where the community diverges, not just aggregate agreement — pre-specified subgroups by AI-integration level, region, role, and tenure.

Scan here to participate!

Six sections (A–F)

- **A** OHDSI context & role
- **B** Current AI / ML engagement
- **C** Standardization in the AI era (primary)
- **D** Mitigating medical-AI failure modes
- **E** Future role for OHDSI
- **F** OMOP CDM strengths & limitations

Why your voice matters

Grounds real decisions

Results give Working Groups and the Steering Committee a data-grounded basis for prioritization.

Fully transparent

Full response distributions are reported, and de-identified data and analysis code are released openly at the Symposium.

Community-owned

Your responses don't just get counted — you help shape how we interpret the results.

Scan here to participate!

Pre-registered before any data was collected – protocol, instrument, and analysis plan all public

README

ohdsi-ai-survey

A pre-registered, cross-sectional survey of the OHDSI community examining (1) how the community positions itself on data standardization under foundation-model pressure, and (2) how it perceives OHDSI infrastructure's capacity to mitigate known medical-AI failure modes.

Joint the survey! →
[https://docs.google.com/forms/d/e/1FAIpQLSffujd8hZDtpTIoDb3RkFOn3_FsPzMtSdxYwZDFSGWqiigvZQ/viewform?usp=header]

> **Status:** Pre-data-collection. This repository contains the study protocol, instrument, and analysis plan. No data have been collected yet.

Overview

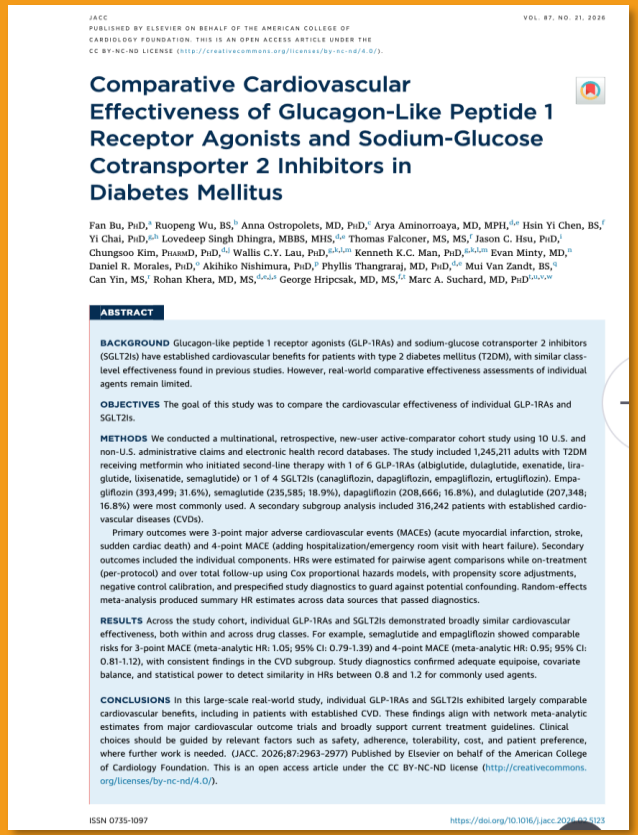
Study type	Cross-sectional online survey (pre-registered)
Primary question	Does data standardization still matter in the era of foundation models? How does the OHDSI community position itself — and where is it internally divided?
Secondary question	Across four medical-AI failure modes within OHDSI's structural scope, which does the community perceive its infrastructure as best positioned to mitigate?
Target sample	N = 300 (minimum analyzable N = 200)
Population	Active or recent OHDSI community members
Status	Protocol & instrument finalized; recruitment not yet started
Pre-	OSF — [link TBD]

↑ Scan here to participate!

↑ Scan here to see the protocol and instruments!

LEGEND-T2DM: Latest Updates

Congrats!!



JACC
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VOL. 87, NO. 21, 2026

Comparative Cardiovascular Effectiveness of Glucagon-Like Peptide 1 Receptor Agonists and Sodium-Glucose Cotransporter 2 Inhibitors in Diabetes Mellitus

Fan Bu, PhD,[a] Ruopeng Wu, BS,[b] Anna Ostropolets, MD, PhD,[c] Arya Aminorroaya, MD, MPH,[d,e] Hsin Yi Chen, BS,[f] Yi Chai, PhD,[g,h] Lovedeep Singh Dhingra, MBBS, MHS,[d,e] Thomas Falconer, MS, MS,[f] Jason C. Hsu, PhD,[i] Chungsoo Kim, PharmD, PhD,[g,j] Wallis C.Y. Lau, PhD,[g,k,l,m] Kenneth K.C. Man, PhD,[g,n,l,m] Evan Minty, MD,[o] Daniel R. Morales, PhD,[p] Akihiko Nishimura, PhD,[q] Phyllis Thangraraj, MD, PhD,[d,e] Mui Van Zandt, BS,[q] Can Yin, MS,[r] Rohan Khera, MD, MS,[d,e,s,t] George Hripcsak, MD, MS,[f,t] Marc A. Suchard, MD, PhD[r,u,v,w]

ABSTRACT

BACKGROUND Glucagon-like peptide 1 receptor agonists (GLP-1RAs) and sodium-glucose cotransporter 2 inhibitors (SGLT2Is) have established cardiovascular benefits for patients with type 2 diabetes mellitus (T2DM), with similar class-level effectiveness found in previous studies. However, real-world comparative effectiveness assessments of individual agents remain limited.

OBJECTIVES The goal of this study was to compare the cardiovascular effectiveness of individual GLP-1RAs and SGLT2Is.

METHODS We conducted a multinational, retrospective, new-user active-comparator cohort study using 10 U.S. and non-U.S. administrative claims and electronic health record databases. The study included 1,245,211 adults with T2DM receiving metformin who initiated second-line therapy with 1 of 6 GLP-1RAs (albiglutide, dulaglutide, exenatide, lira-glutide, lixisenatide, semaglutide) or 1 of 4 SGLT2Is (canagliflozin, dapagliflozin, empagliflozin, ertugliflozin). Empa-gliflozin (393,499; 31.6%), semaglutide (235,585; 18.9%), dapagliflozin (208,666; 16.8%), and dulaglutide (207,348; 16.8%) were most commonly used. A secondary subgroup analysis included 316,242 patients with established cardio-vascular diseases (CVDs).

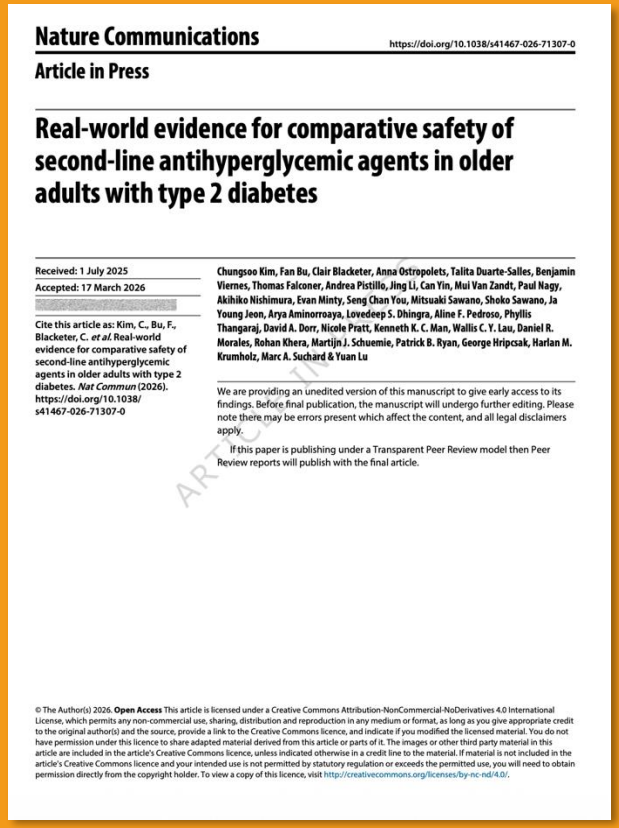
Primary outcomes were 3-point major adverse cardiovascular events (MACEs) (acute myocardial infarction, stroke, sudden cardiac death) and 4-point MACE (adding hospitalization/emergency room visit with heart failure). Secondary outcomes included the individual components. HRs were estimated for pairwise agent comparisons while on-treatment (per-protocol) and over total follow-up using Cox proportional hazards models, with propensity score adjustments, negative control calibration, and prespecified study diagnostics to guard against potential confounding. Random-effects meta-analysis produced summary HR estimates across data sources that passed diagnostics.

RESULTS Across the study cohort, individual GLP-1RAs and SGLT2Is demonstrated broadly similar cardiovascular effectiveness, both within and across drug classes. For example, semaglutide and empagliflozin showed comparable risks for 3-point MACE (meta-analytic HR: 1.05; 95% CI: 0.79-1.39) and 4-point MACE (meta-analytic HR: 0.95; 95% CI: 0.81-1.12), with consistent findings in the CVD subgroup. Study diagnostics confirmed adequate equipoise, covariate balance, and statistical power to detect similarity in HRs between 0.8 and 1.2 for commonly used agents.

CONCLUSIONS In this large-scale real-world study, individual GLP-1RAs and SGLT2Is exhibited largely comparable cardiovascular benefits, including in patients with established CVD. These findings align with network meta-analytic estimates from major cardiovascular outcome trials and broadly support current treatment guidelines. Clinical choices should be guided by relevant factors such as safety, adherence, tolerability, cost, and patient preference, where further work is needed. (JACC. 2026;87:2963-2977) Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

ISSN 0735-1097

https://doi.org/10.1016/j.jacc.2026.02.0123



Nature Communications

https://doi.org/10.1038/s41467-026-71307-0

Article in Press

Real-world evidence for comparative safety of second-line antihyperglycemic agents in older adults with type 2 diabetes

Received: 1 July 2025

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Chungsoo Kim, Fan Bu, Clair Blacketer, Anna Ostropolets, Talita Duarte-Salles, Benjamin Viernes, Thomas Falconer, Andrea Pistillo, Jing Li, Can Yin, Mui Van Zandt, Paul Nagy, Akihiko Nishimura, Evan Minty, Seng Chan You, Mitsuaki Sawano, Shoko Sawano, Ja Young Jeon, Arya Aminorroaya, Lovedeep S. Dhingra, Aline F. Pedroso, Phyllis Thangaraj, David A. Dorr, Nicole Pratt, Kenneth K. C. Man, Wallis C. Y. Lau, Daniel R. Morales, Rohan Khera, Martijn J. Schuemie, Patrick B. Ryan, George Hripcsak, Harlan M. Krumholz, Marc A. Suchard & Yuan Lu

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Cardiovascular Effectiveness of Individual GLP-1RA and SGLT2 Drugs in T2DM:

Findings from the LEGEND-T2DM Study

Fan Bu

University of Michigan, Dept. of Biostatistics

OHDSI APAC Meeting, June 18, 2026

With co-authors: Ruopeng Wu, Anna Ostropolets, Arya Aminorroaya, Hsin Yi Chen, Yi Chai, Lovedeep S Dhingra, Thomas Falconer, Jason C. Hsu, Chungsoo Kim, Wallis CY Lau, Kenneth KC Man, Evan Minty, Daniel R Morales, Akihiko Nishimura, Phyllis Thangraraj, Mui Van Zandt, Can Yin, Rohan Khera, George Hripcsak, and Marc A Suchard. And all LEGEND collaborators.

LEGEND-T2DM: comparative effectiveness & safety of 2nd-line T2DM treatments

- Drug classes: GLP-1RA, SGLT2I, DPP4I, SU
  - GLP-1RA: semaglutide, dulaglutide, etc.
  - SGLT2I: empagliflozin, dapagliflozin, etc.
- Outcomes: cardiovascular, renal, gastrointestinal, patient-centered, etc.
- ~4.7M T2DM patients (already on metformin)
- 17 multinational databases: US, UK, Spain, Germany, France, Japan, Korea, Australia, China mainland, Taiwan, etc.

- Multiple findings in class-level comparisons
- Cardiovascular benefits: GLP1≈SGLT2>DPP4,SU
- GLP1 thyroid tumor concern insignificant
- GLP1 increased risk of NAION (eye neural stroke)

Diabetes Care
American Diabetes Association

Risk of Thyroid Tumors With GLP-1 Receptor Agonists: A Retrospective Cohort Study

Daniel R. Morales, Fan Bu, Benjamin Viernes, Scott L. DuVall, Michael E. Matheny, Katherine R. Simon, Thomas Falconer, Lauren R. Richter, Anna Ostropolets, Wallis C. Y. Lau, Kenneth K. C. Man, Shounak Chattopadhyay, Nestoras Mathioudakis, Evan Minty, Akihiko Nishimura, Feng Sun, Can Yin, Sarah L. Seager, Yi Chai, Jin J. Zhou, Yuan Lu, Carlen Reyes, Andrea Pistillo, Talita Duarte-Salles, Clair Blacketer, Martijn J. Schuemie, Patrick B. Ryan, Harlan M. Krumholz, George Hripcsak, Rohan Khera, and Marc A. Suchard

Diabetes Care 2025;48(8):1–9 | https://doi.org/10.2337/dc25-0154

Comparative Effectiveness of Second-Line Antihyperglycemic Agents for Cardiovascular Outcomes

A Multinational, Federated Analysis of LEGEND-T2DM

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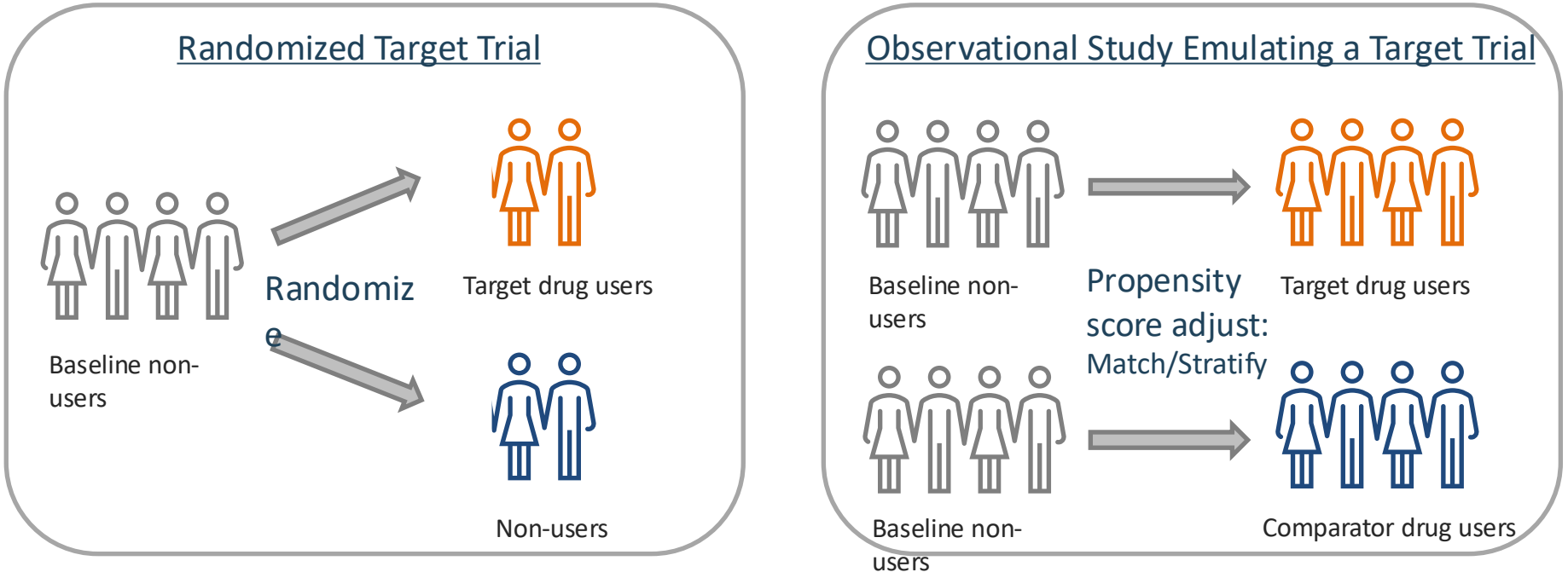
Protocol: Khera et al. *BMJ Open* 2022. doi:10.1136/bmjopen-2021-057977

Reliable evidence generation using observational data: "target trial emulation"



Design and analytic details in protocol: Khera et al. *BMJ Open* 2022. doi:10.1136/bmjopen-2021-057977

This study: individual drug-level cardiovascular effectiveness

- GLP-1RA vs SGLT2I (both cardio-protective)
  - GLP-1RA (6 agents): semaglutide (19%), dulaglutide (17%), albiglutide, exenatide, liraglutide, lixisenatide.
  - SGLT2I (4 agents) : empagliflozin (32%), dapagliflozin (17%), canagliflozin, ertugliflozin.
- Cardiovascular outcomes: 3-pt MACE (acute MI, stroke, cardiac death), 4-pt MACE (+ heart failure hospitalization); individual MACE components.
- 1.2M new-users of 2nd line drugs; 10 multinational databases.
- Hazard ratio (HR) via adjusted Cox PH model; then meta-analytic HR.

Main finding 1: increased proportional use of GLP-1RA & SGLT2I agents among all 2nd line drugs

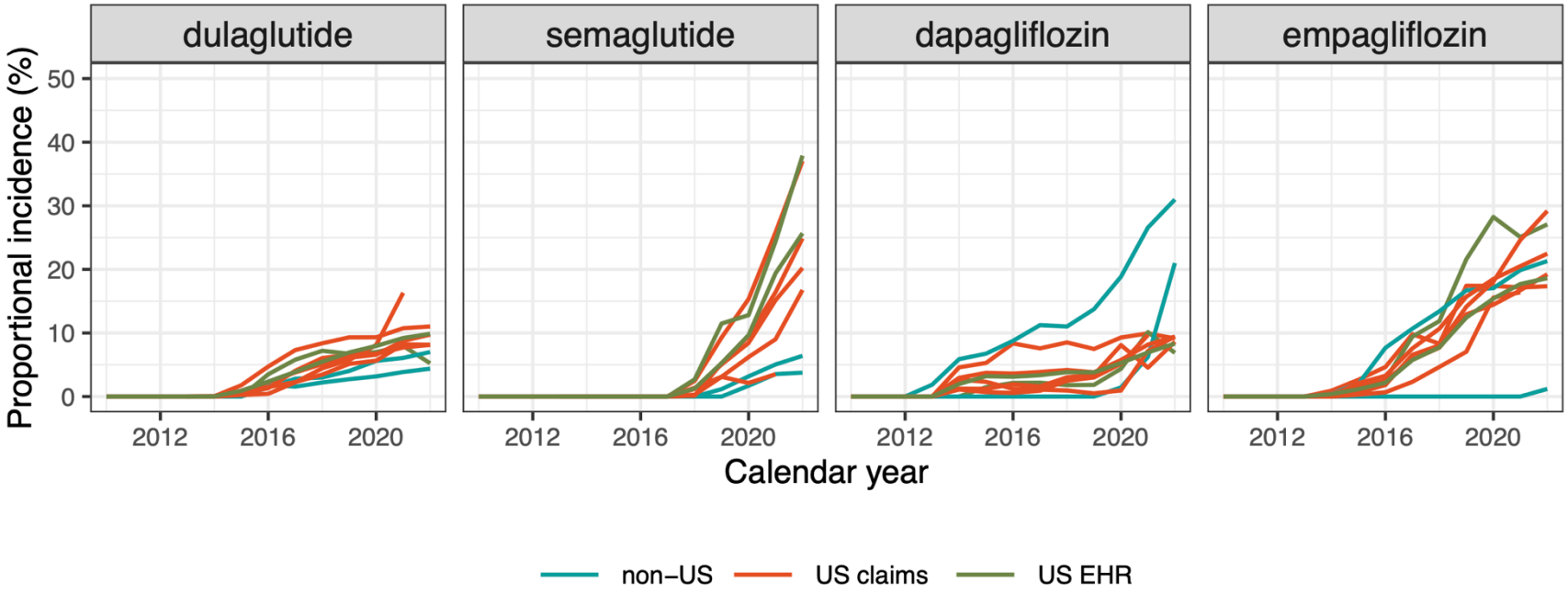


Figure. Yearly trends of proportional incidence of second-line drug initiation for a specific antihyperglycemic agent by year within each data source (one curve represents one data source for each drug).

Main finding 2: GLP1 ≈ SGLT2 at ingredient-level in cardiovascular effectiveness, among general & CVD populations

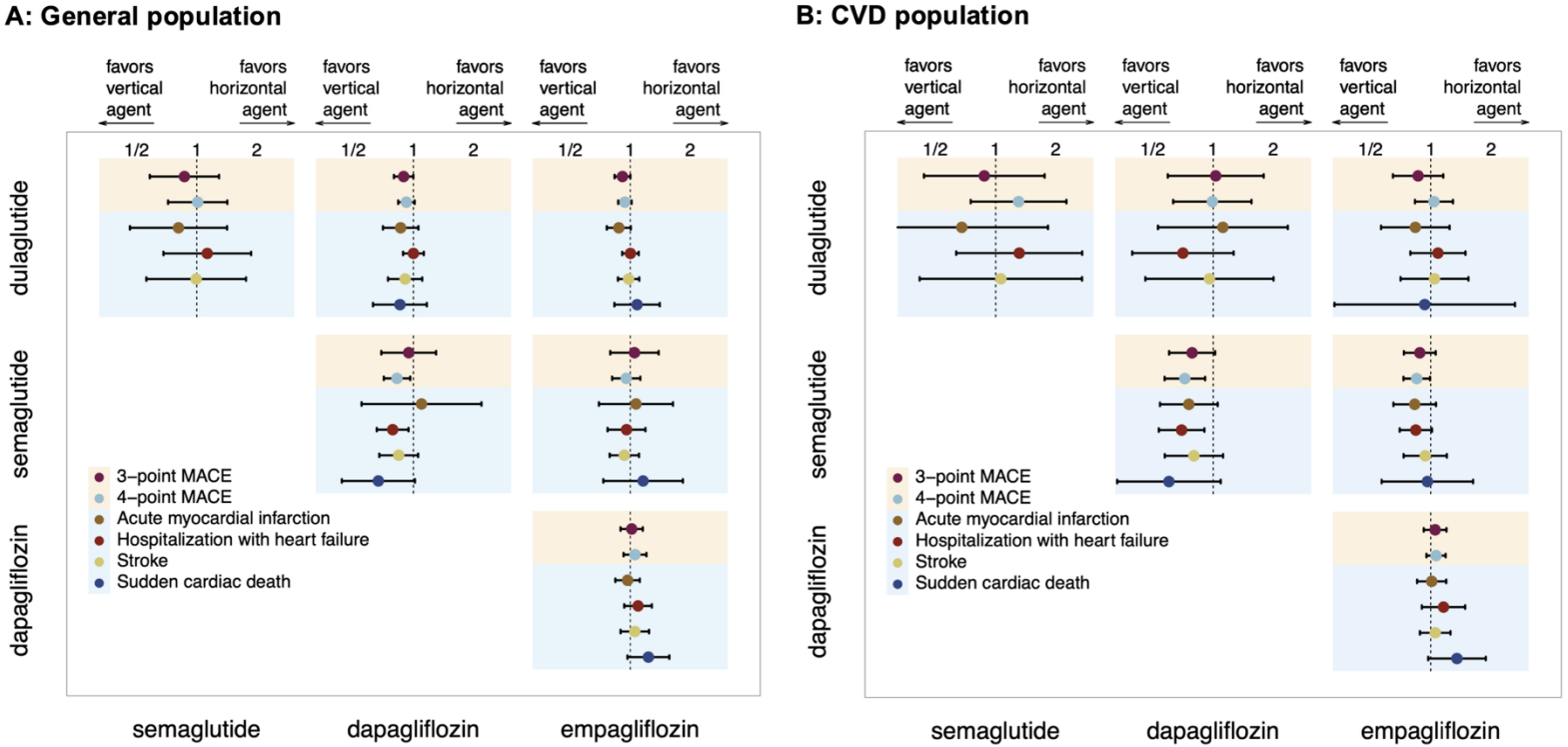


Figure. Meta-analytic HR estimates for cardiovascular effectiveness between GLP-1RA and SGLT2I drug new-users, among general population (**A**) & CVD subpopulation (**B**).

All results in paper: Bu et al. *JACC* 2026. doi:10.1016/j.jacc.2026.02.5123.

Discussion

- Findings support guideline flexibility between GLP-1RA and SGLT2I for cardiovascular benefits at ingredient level
- Future work:
  - Safety outcomes: gastrointestinal outcomes, DKA risks, etc.
  - Expanding treatments: newer agents (tirzepatide), combo therapy, etc.
  - More data partners (esp. from APAC!) for more generalizability
    - On-going conversations with partners from Thailand, Hong Kong, …

• 1 community

Full manuscript: Bu et al. *JACC* 2026. doi:10.1016/j.jacc.2026.02.5123.

Comparative Safety of Second-Line Antihyperglycemic Agents in Older Adults with Type 2 Diabetes : Insight from the LEGEND-T2DM study

Chungsoo Kim

on behalf of the OHDSI Legend T2DM initiative

Background

Why older adults?

- The prevalence of diabetes in the elderly (approximately 30%) is 1.5 times that of the middle-aged.
- Multiple comorbidities, polypharmacy, and frailty can impede diabetes management and diminish the quality of life (ADA guidelines)
- Older adults are underrepresented in the randomized controlled trial.

American Diabetes Association Professional Practice Committee; 13. Older Adults: Standards of Care in Diabetes—2024. Diabetes Care 1 January 2024; 47 (Supplement_1): S244–S257. https://doi.org/10.2337/dc24-S013

Tyler Drake, Adrienne Landsteiner, Lisa Langsetmo, et al. Newer Pharmacologic Treatments in Adults With Type 2 Diabetes: A Systematic Review and Network Meta-analysis for the American College of Physicians. Ann Intern Med. [Epub 19 April 2024]. doi:10.7326/M23-1490

Background

Why safety outcomes?

- Older adults are more vulnerable to safety issues, which can lead to worse diabetes outcomes.
- However, safety issues are hard to investigate because of the event rate or often overlooked compared to efficacy/effectiveness.
- The systematic safety profiles on second-line antihyperglycemic agents are fragmented and limited.
  - Recently published systematic reviews and new ACP guidelines also present only limited data such as hypoglycemia.

American Diabetes Association Professional Practice Committee; 13. Older Adults: Standards of Care in Diabetes—2024. Diabetes Care 1 January 2024; 47 (Supplement_1): S244–S257. https://doi.org/10.2337/dc24-S013

Tyler Drake, Adrienne Landsteiner, Lisa Langsetmo, et al. Newer Pharmacologic Treatments in Adults With Type 2 Diabetes: A Systematic Review and Network Meta-analysis for the American College of Physicians. *Ann Intern Med. [Epub 19 April 2024]. doi:*10.7326/M23-1490

Objectives

We aim to determine the comparative safety of second-line antihyperglycemic agents among older adults with type 2 diabetes.

Methods

Study design

Study population

- **Older adult (≥65) patients** with type 2 diabetes
    1) Previous observation ≥ 365 days
    2) Previous T2DM diagnosis but no T1DM or secondary DM
    3) ≥ 90 days metformin
    4) Exclude patients who used insulin as a long-term (> 30 days)

Target-comparator pairs

Target	Comparator
SGLT2I	GLP1RA
SGLT2I	DPP4I
SGLT2I	SU
GLP1RA	DPP4I
GLP1RA	SU
DPP4I	SU

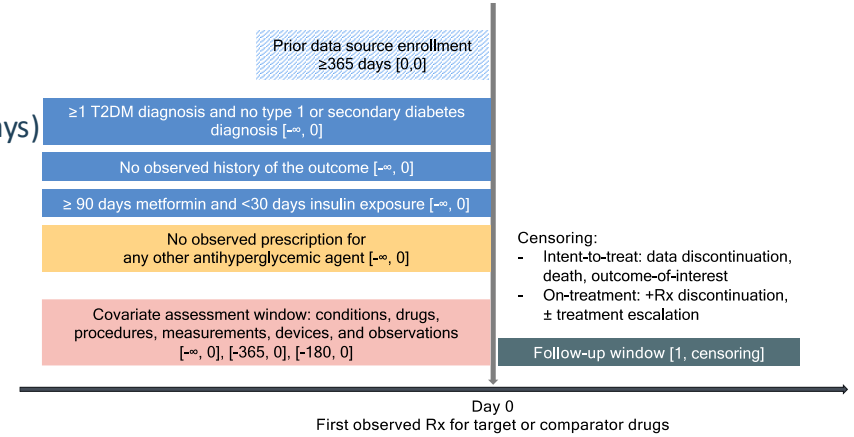


Figure 1. Study design scheme

Methods

Outcomes

Patient centric safety outcomes (22)		
Metabolic and endocrine complications (6)	**Organ system complications** Gastrointestinal, musculoskeletal, circulatory, skin and infection **(10)**	**Cancer and systemic complications (6)**
Abnormal weight gain	Acute pancreatitis	Bladder cancer
Abnormal weight loss	Nausea	Breast cancer
Diabetic ketoacidosis	Vomiting	Renal cancer
Hyperkalemia	Diarrhea	Thyroid tumor
Hypoglycemia	Bone fracture	All-cause mortality
Hypotension	Joint pain	Venous thromboembolism
	Lower extremity amputation	
	Peripheral edema	
	Genitourinary infection	
	Photosensitivity	

Reporting separately

Total 18 safety outcomes were included for this study

Methods

Data sources

Twenty databases were included the LEGEND T2DM projects.

Excluded

- Databases having no data for older adult population
- Databases having incomplete results for older adult population
  (Excluded Australia_LPD, CUIMC, China_WD, France_LPD, HIC Dundee, JHM, SG_KTPH, STARR, UK-IMRD)
- Databases with quality issue
  (Excluded HK-HA-DM
  due to median (IQR) f/u was 1 (1-1) in their results)

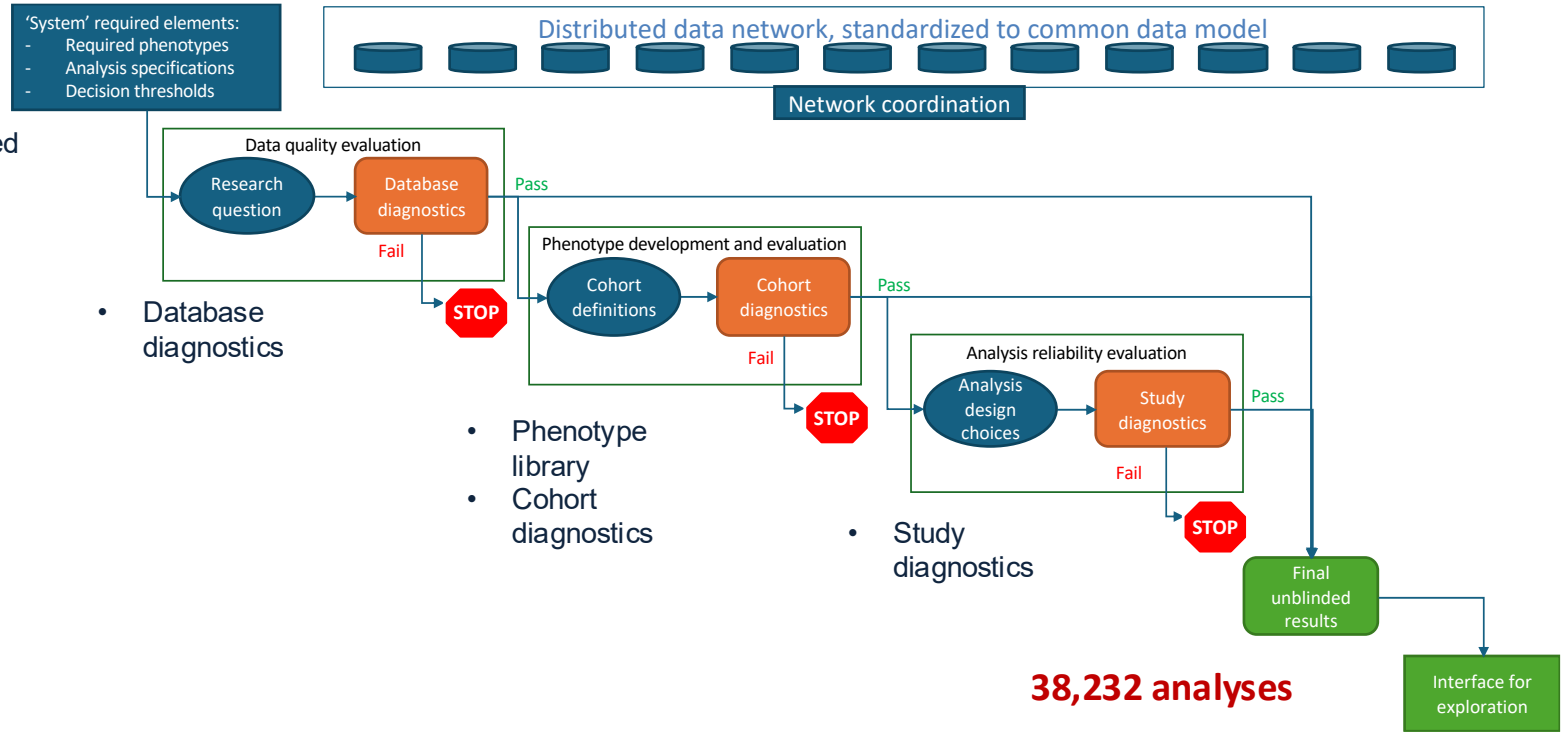
→ **Finally, 9 databases included**

→ We only used results when each arm meet the min number of patients (≥1000 patients)

Database	SGLT2I older-age	GLP1RA older-age	DPP4I older-age	SU older-age
Australia_LPD	326	10	732	40
CCAE	749	435	2089	3916
CUIMC	404	171	944	887
China_WD	145	8	222	244
France_LPD	41	165	4860	676
Germany_DA	2727	217	12158	4149
HIC Dundee	513	16	1620	465
HK-HA-DM	237	11	2087	3591
JHM	330	160	352	494
MDCD	178	101	1210	2488
MDCR	3511	2135	17961	43297
OptumDod	11619	5627	27244	66309
OptumEHR	7828	3573	23345	58387
SG_KTPH	<5	<5	9	50
SIDIAP	3746	289	26465	8667
STARR	195	118	316	742
UK-IMRD	921	184	8631	3014
US_Open_Claims	135495	62268	358700	741462
VA-OMOP	8539	848	15844	147244

Methods

- Prespecified Protocol



- Database diagnostics
- Phenotype library
- Cohort diagnostics
- Study diagnostics

38,232 analyses

= 9 database * 6 comparison pairs
* 118 outcomes (safety + NCO)
* 2 PS methods * 3 follow-up

https://ohdsi.org/sos-challenge/

Methods

Statistical analysis (main)

- Follow-up: On-treatment
- Confounder adjustment: Propensity score stratification
- Calibrated HRs from Cox hazard models and empirical calibration using negative controls
- Study diagnostics criteria
  - Empirical equipoise (proportion of PS overlap >0.25)
  - Max SDM (<0.15)
  - MDRR (<4.0)
- Pooled estimates by random-effect meta-analysis
- Multiple comparison problem: Bonferroni correction

Sensitivity analyses

- Different PS adjustment methods – variable ratio matching
- Different follow-up strategies – on-treatment with censoring at treatment escalation, intent-to-treat

Results

Table 1. Number of new users and followed days according to on-treatment or total follow-up within each database.

Total N of older adults = 1,808,003

Drug class and database	n	Median (IQR) in On-treatment time, day	Median (IQR) in total follow-up time, day
SGLT2I			
ODOD	11,619	114 (55-273)	390 (146-799)
MDCR	3,511	121 (38-344)	419 (156-880)
USOC	135,495	125 (59-309)	681 (293-1,342)
OEHR	7,828	59 (29-99)	596 (295-1,081)
DAG	2,727	157 (97-372)	598 (293-1,155)
SIDIAP	3,746	246 (84-617)	498 (155-875)
VA	8,539	144 (71-306)	283 (124-592)
Total	**173,465**		
GLP1RA			
ODOD	5,627	95 (40-219)	345 (124-728)
MDCR	2,135	108 (36-300)	513 (159-1,129)
USOC	62,268	105 (50-258)	585 (241-1,130)
OEHR	3,573	55 (29-102)	527 (273-983)
Total	**73,603**		
DPP4I			
CCAE	2,089	86 (29-144)	110 (56-180)
ODOD	27,244	157 (63-375)	832 (342-1,581)
MDCR	17,961	191 (87-491)	815 (333-1,533)
MDCD	1,210	130 (56-330)	834 (357-1,539)
USOC	358,700	158 (59-416)	1,575 (806-2,430)
OEHR	23,345	90 (89-194)	1,076 (537-1,827)
DAG	12,158	219 (97-509)	1,174 (564-2,065)
SIDIAP	26,465	719 (200-1464)	1,207 (567-2,137)
VA	15,844	235 (90-523)	756 (348-1,337)
Total	**485,016**		
SU			
CCAE	3,916	84 (29-146)	113 (57-189)
ODOD	66,309	193 (89-504)	882 (352-1,709)
MDCR	43,297	186 (72-496)	890 (354-1,780)
MDCD	2,488	126 (48-311)	1,020 (464-1,874)
USOC	741,462	203 (89-547)	1,498 (717-2,419)
OEHR	58,387	102 (89-231)	1,219 (587-2,042)
DAG	4,149	211 (119-467)	2,043 (1003-3,325)
SIDIAP	8,667	741 (188-1615)	2,879 (1674-3,808)
VA	147,244	224 (90-544)	2,071 (1043-3,330)
Total	**1,075,919**		

IQR: interquartile range; DPP4I: dipeptidyl peptidase inhibitor 4; GLP1RA: glucagon-like peptide-1 receptor agonist; SGLT2I: sodium glucose cotransporter 2 inhibitor; SU: sulfonylurea; MDCR: IBM MarketScan Medicare Supplemental and Coordination of Benefits Database; Optum DOD: Optum© Clinformatics Extended Data Mart - Date of Death Database; Optum EHR: Optum© de-identified Electronic Health Records Database.

Results

Table 2. Baseline patient characteristics for SGLT2I and GLP1RA new users in the US Open Claims Database.

Characteristics	Before adjustment			After stratification		
	SGLT2I (%)	GLP1RA (%)	StdDiff	SGLT2I (%)	GLP1RA (%)	StdDiff
Age group						
65-69	43.1	49.1	0.12	44.9	44.9	0.00
70-74	29.2	29.8	0.01	29.5	29.4	0.00
75-79	17.5	14.2	-0.09	16.4	16.6	0.00
80-84	9.5	6.4	-0.12	8.5	8.6	0.00
85-89	0.8	0.5	-0.03	0.7	0.6	-0.01
Gender: female	44.7	57.3	0.25	48.8	48.3	-0.01
Medical history: General						
Acute respiratory disease	11.5	11.8	0.01	11.7	11.7	0.00
Attention deficit hyperactivity disorder	0.2	0.4	0.03	0.3	0.3	0.00
Chronic liver disease	0.9	0.9	-0.01	0.9	0.9	0.00
Chronic obstructive lung disease	7.2	7.1	0.00	7.3	7.1	0.00
Crohn's disease	0.2	0.1	0.00	0.2	0.1	-0.01
Dementia	1.0	0.8	-0.02	1.0	1.0	0.00
Depressive disorder	6.0	8.8	0.10	6.9	7.0	0.00
Gastroesophageal reflux disease	8.9	10.0	0.04	9.3	9.4	0.00
Gastrointestinal hemorrhage	1.4	1.3	-0.01	1.4	1.4	0.00
Human immunodeficiency virus infection	0.2	0.2	0.00	0.2	0.2	0.00
Hyperlipidemia	48.5	46.1	-0.05	47.8	47.8	0.00
Hypertensive disorder	54.8	53.5	-0.03	54.5	54.6	0.00
Lesion of liver	0.8	0.8	0.00	0.8	0.8	0.00
Obesity	9.6	16.2	0.20	11.6	11.9	0.01
Osteoarthritis	18.0	22.1	0.10	19.3	19.4	0.00
Pneumonia	2.8	2.5	-0.01	2.7	2.6	0.00
Psoriasis	1.0	1.2	0.03	1.1	1.1	0.01
Renal impairment	10.4	9.4	-0.03	10.2	10.0	-0.01
Rheumatoid arthritis	1.2	1.5	0.03	1.3	1.3	0.00
Schizophrenia	0.1	0.1	0.00	0.2	0.1	0.00
Urinary tract infectious disease	5.0	6.3	0.06	5.9	5.8	-0.01
Viral hepatitis C	0.3	0.2	-0.01	0.3	0.2	0.00
Visual system disorder	25.0	25.2	0.00	25.1	25.0	0.00

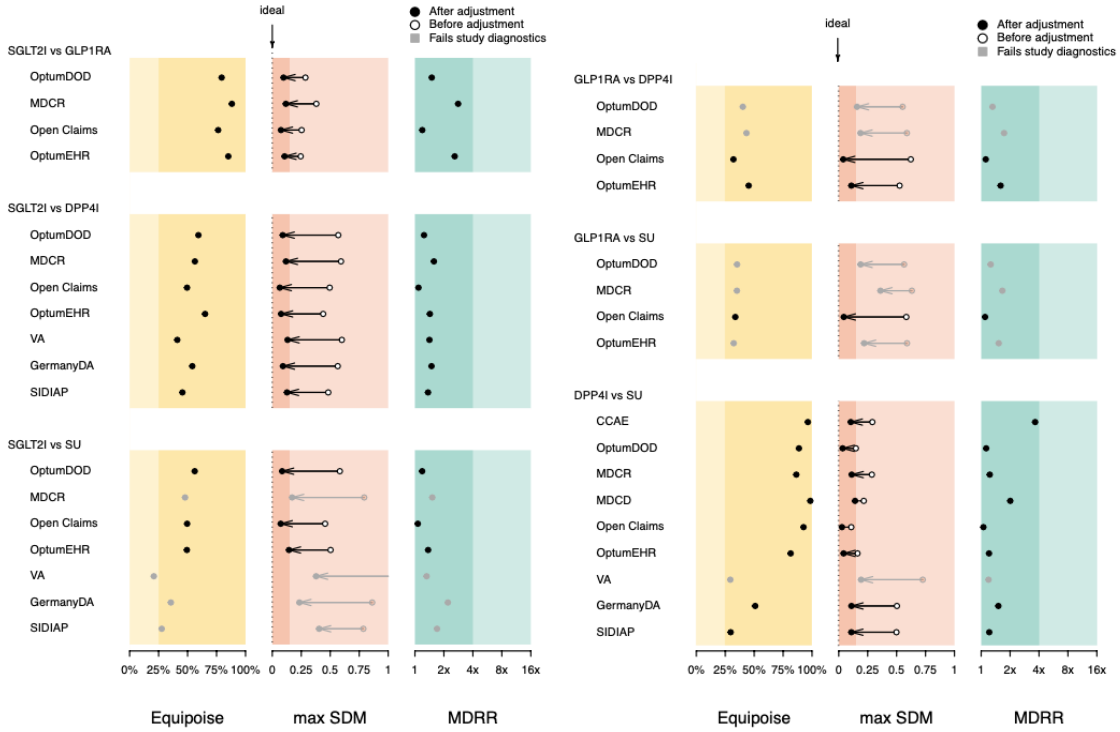
SGLT2I: sodium glucose transporter-2 inhibitor; GLP1RA: glucagon-like peptide-1 receptor agonist; StdDiff: standardized difference of mean.

Results

Study diagnostics

T-C pairs	N of databases 'PASSED' diagnostics across outcomes, Median (IQR)
SGLT2I vs GLP1RA	3.5 (1.75-4.0)
SGLT2I vs DPP4I	6.0 (5.0-7.0)
SGLT2I vs SU	3.0 (3.0-3.0)
GLP1RA vs DPP4I	2.0 (1.0-2.0)
GLP1RA vs SU	1.0 (1.0-1.0)
DPP4I vs SU	6.5 (5.0-8.0)

- Only US Open Claims was used for most of GLP1RA vs SU..
- Mostly databases are dropped due to the *covariate balance*



Results

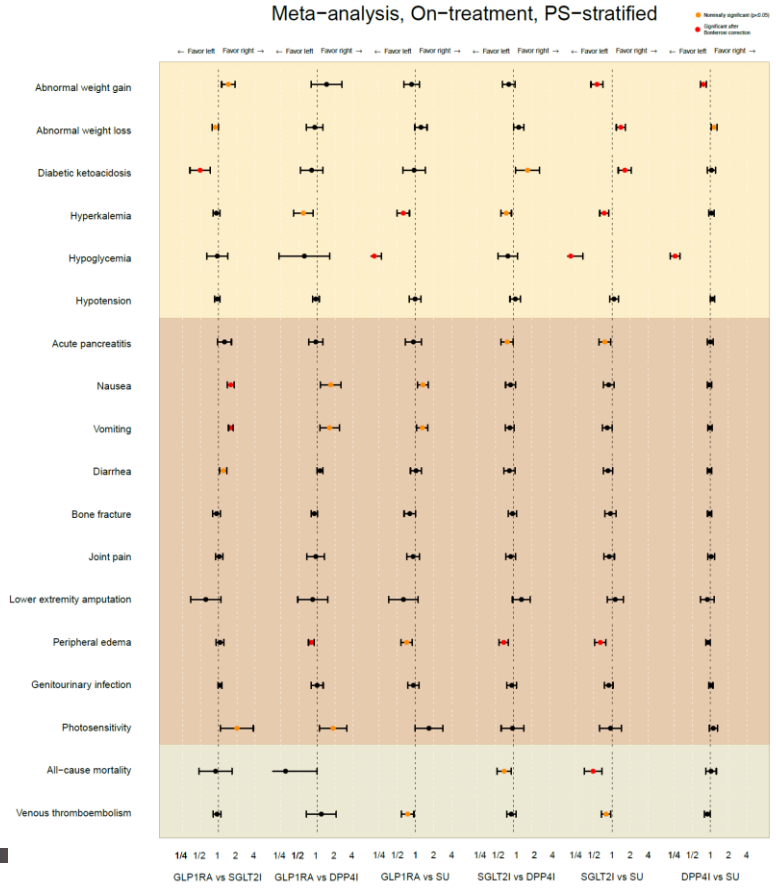


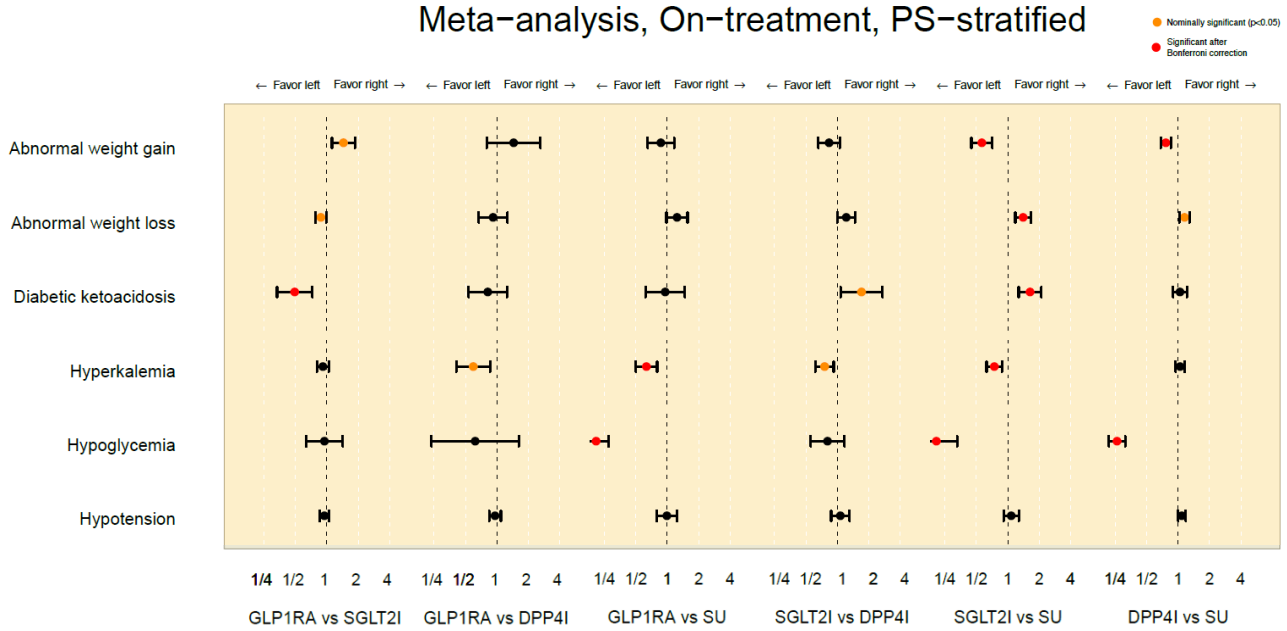
Figure 2. Meta-analytic safety profiles comparing new users of SGLT2I to GLP1RA, DPP4I, and SU across 22 outcomes. Points and lines identify HR estimates with their 95% CIs, respectively.

Outcomes in orange mean that $p<0.05$ and outcomes in red mean statistically significant after Bonferroni correction ($p<0.00227$) for the multiple testing.

Result for all-cause mortality in the GLP1RA vs SU comparison was not presented because there was no valid result after the study diagnostic process.

Results

Metabolic and endocrine complications



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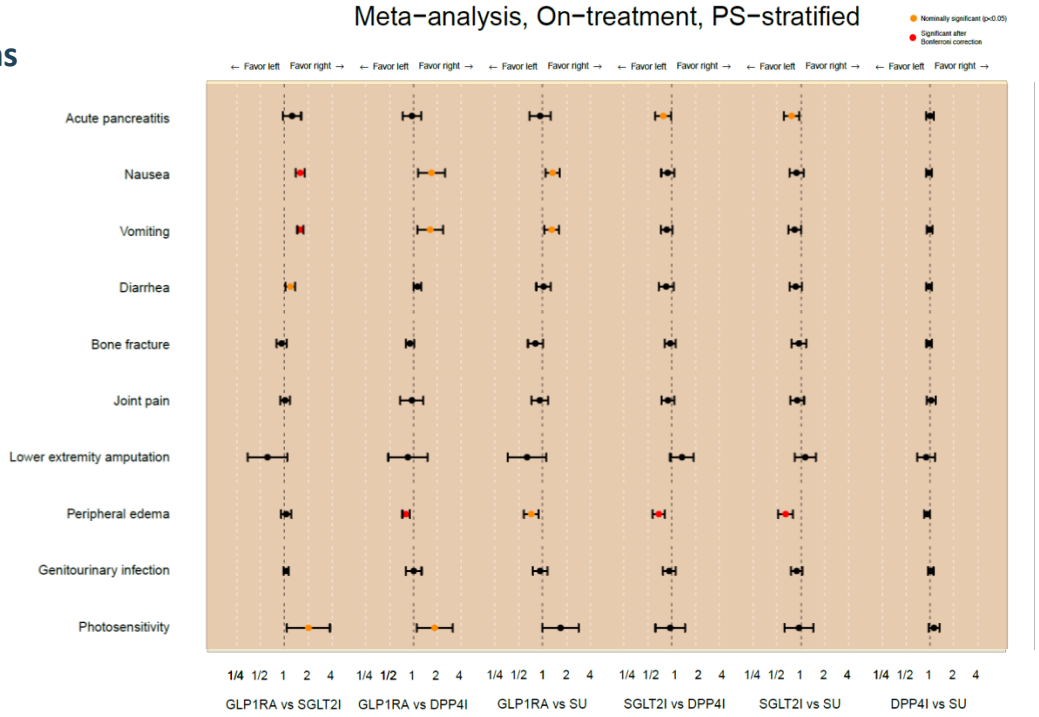
Results

Organ system complications



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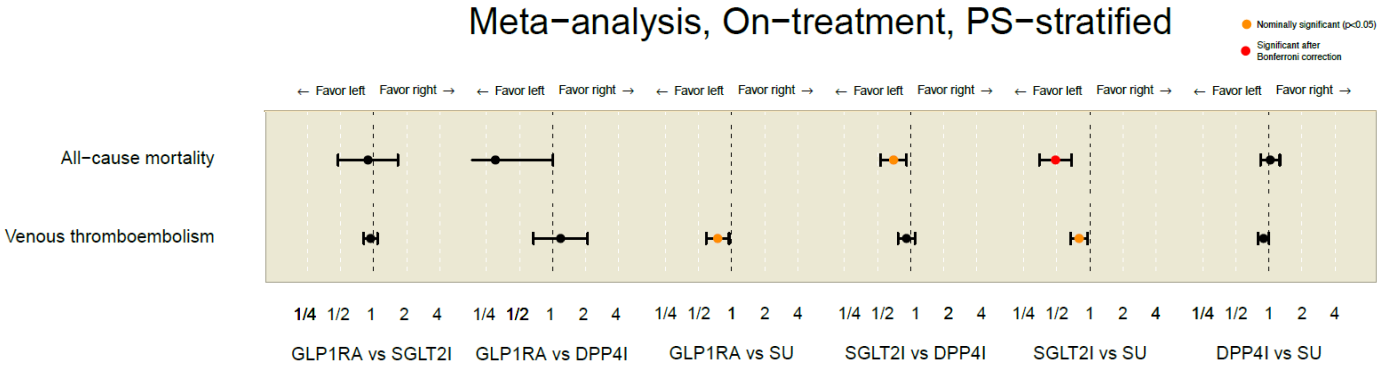
Results

Systemic outcomes



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Discussion

Highlights

- In older adults with type 2 diabetes, the safety profile of each second line antihyperglycemic agent was diverse.
- The GLP-1 RA and SGLT2 inhibitor showed not only better effectiveness *(Khera et al., JACC, 2024)* but also better safety outcomes, esp., hypoglycemia, hyperkalemia, and peripheral edema, than DPP4i and SU in older adults.
- However, there were unique challenges for those agents, SGLT2 inhibitors showed elevated diabetic ketoacidosis and GLP-1RAs showed a higher risk of GI adverse events, which may affect drug compliance and continuity of care in older adults.

Discussion

Novelty

- Even though most of the results are reassuring, however, a direct head-to-head safety study between drug classes with large sample size is still novel.
- This fill the gap in evidence regarding the older adult population, which generally underrepresented in randomized controlled trials.
- We applied sophisticated analysis pipelines (e.g., study diagnostics) to enhance the quality of observational studies.

Limitation

- Inherit fundamental problems (misclassification/unmeasured/residual bias) of the observational study
- Short follow-up period, no labs.
- Not included neuropsychiatric outcomes (e.g., impaired cognition, suicide, dementia), even though those are crucial for older adults

Discussion

Challenges in the APAC databases

How can APAC data contribute to global studies?

- Accessibility/Visibility
- Data Readiness
- Data quality
- Methodologies: Covariate balance for small datasets *(Hripcsak et al, Statistical Medicine, 2025)*
- Other approach?

Paper

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Article | Open access | Published: 04 April 2026

Real-world evidence for comparative safety of second-line antihyperglycemic agents in older adults with type 2 diabetes

Chungsoo Kim, Fan Bu, Clair Blacketer, Anna Ostropolets, Talita Duarte-Salles, Benjamin Viernes, Thomas Falconer, Andrea Pistillo, Jing Li, Can Yin, Mui Van Zandt, Paul Nagy, Akihiko Nishimura, Evan Minty, Seng Chan You, Mitsuaki Sawano, Shoko Sawano, Ja Young Jeon, Arya Aminorroaya, Lovedeep S. Dhingra, Aline F. Pedroso, Phyllis Thangaraj, David A. Dorr, Nicole Pratt, ... Yuan Lu + Show authors

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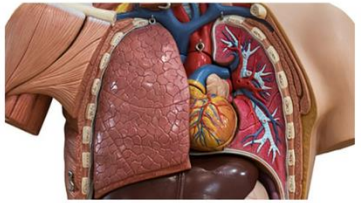
Focus | 26 January 2021

Translational and clinical research

Translational research describes the process of converting basic scientific findings into novel treatments and diagnostics aimed to address unmet clinical needs. Here, we showcase a plethora of diverse studies, ranging from the investigation of the molecular mechanisms underlying the onset and course of a disease using preclinical models, to the development of innovative interventions in human subjects with the goal to guide health care policy and clinical practice.



Article
Open Access
4 Apr 2026
Nature Communications

Real-world evidence for comparative safety of second-line antihyperglycemic agents in older adults with type 2 diabetes

Here the authors report real-world evidence through a retrospective analysis of a multinational cohort of 1.8 M older adults showing that GLP1RAs and SGLT2 inhibitors carry lower risk for hyperkalemia than sulfonylureas. However, SGLT2 inhibitors increased risk of ketoacidosis. Findings support safety-conscious prescribing for older adults, who are often underrepresented in clinical trials.

Chungsoo Kim, Fan Bu ... Yuan Lu

Featured in the journal's "Translational and clinical research" focus section!!

Thank you