



## The Effect of SGLT-2i and GLP-1RA on Major Cardiovascular Conditions: A Meta-Analysis

Arjun V. Jogimahanti<sup>\*</sup>, Kevin A. Honan<sup>1</sup>, Talha Ahmed<sup>2</sup>, Luis Leon-Novelo<sup>3</sup>, Tarif Khair, M.D.<sup>2</sup>

### Abstract

**Purpose:** Sodium-glucose co-transporter 2 inhibitors (SGLT-2i) and Glucagon-like Peptide-1 Receptor Agonists (GLP-1RA) are two common anti-hyperglycemic agents prescribed by clinicians. The effects on cardiovascular conditions such as heart failure (HF) hospitalization, stroke, myocardial infarctions (MI), and other cardiovascular conditions are not well studied. The purpose of this study is to analyze existing data on the effect of SGLT-2i and GLP-1RA on preventing these cardiovascular conditions.

**Methods:** A retrospective meta-analysis of all existing literature of the effect of SGLT-2i and GLP-1RA on the rates of the following categories was researched: primary cardiovascular outcomes, HF hospitalizations, atrial fibrillation (AF), stroke, MI and HF symptoms. Hazard ratios for each category were obtained, and overall Hazard Ratio (HR)'s to determine overall statistical significance were computed.

**Result:** Both medication classes provided statistically significant reduction in preventing major cardiovascular events. Only SGLT-2i provided statistically significant reduction in heart failure hospitalizations. Only GLP-1RA provided statistically significant reduction in preventing stroke. Neither medication class provided a statistically significant benefit in preventing myocardial infarctions. More studies are needed on effects of either SGLT-2i or GLP-1RA agonists on preventing HF symptoms or AF.

**Conclusion:** This study demonstrates that SGLT-2i and GLP-1RA are important for improving both diabetic and cardiovascular health. In patients at risk for a major cardiovascular event, SGLT-2i or GLP-1RA may be prescribed by clinicians. More studies must be performed to draw more conclusions.

### List of Abbreviations

1. SGLT-2 Inhibitors: Sodium-glucose co-transporter 2 inhibitors
2. GLP-1RA Agonists: Glucagon-like Peptide-1 agonists
3. FDA: Food and Drug Administration
4. T2DM: Type 2 Diabetes Mellitus
5. AF: Atrial Fibrillation
6. MI: Myocardial Infarction
7. HF: Heart Failure

### Affiliation:

<sup>1</sup>University of Texas Medical School at Houston, Department of Internal Medicine, Houston, TX, United States of America

<sup>2</sup>University of Texas Medical School at Houston, Department of Cardiology, Houston, TX, United States of America

<sup>3</sup>University of Texas School of Public Health, Department of Biostatistics, Houston, TX, United States of America

### \*Corresponding authors:

Arjun V. Jogimahanti, University of Texas Medical School at Houston, Department of Internal Medicine, Houston, TX, United States of America

**Citation:** Arjun V. Jogimahanti, Kevin A. Honan, Talha Ahmed, Luis Leon-Novelo, Tarif Khair. The Effect of SGLT-2i and GLP-1RA on Major Cardiovascular Conditions: A Meta-Analysis. *Cardiology and Cardiovascular Medicine*. 8 (2024): 36-50.

**Received:** January 14, 2024

**Accepted:** January 19, 2024

**Published:** January 29, 2024





























23. McMurray JJV, Solomon SD, Inzucchi SE, Køber L, Kosiborod MN, et al. Dapagliflozin in Patients with Heart Failure and Reduced Ejection Fraction. *N Engl J Med* 381 (2019): 1995-2008.
24. Anker SD, Butler J, Filippatos G, Ferreira JP, Bocchi E, et al. Empagliflozin in Heart Failure with a Preserved Ejection Fraction. *N Engl J Med* 385 (2019): 1451-1461.
25. Packer M, Anker SD, Butler J, Filippatos G, Pocock SJ, et al. Cardiovascular and Renal Outcomes with Empagliflozin in Heart Failure. *N Engl J Med* 383 (2020): 1413-1424.
26. Zelniker TA, Bonaca MP, Furtado RHM, Mosenson O, Kuder JF, et al. Effect of Dapagliflozin on Atrial Fibrillation in Patients With Type 2 Diabetes Mellitus: Insights From the DECLARE-TIMI 58 Trial. *Circulation* 141 (2020): 1227-1234.
27. Usman MS, Siddiqi TJ, Memon MM, Khan MS, Rawasia WF, Talha Ayub M, Sreenivasan J, Golzar, Y. Sodium-glucose co-transporter 2 inhibitors and cardiovascular outcomes: a systematic review and meta-analysis. *Eur J Prev Cardiol* 25 (2018): 495-502.
28. Patoulias D, Toumpourleka M, Papadopoulos C, Doumas M. Meta-analysis evaluating the risk of atrial fibrillation with newer antidiabetics across the cardiovascular and renal outcome trials. *Am J Cardiol* 139 (2021): 139-141.
29. Ingelheim B (2020) This Study Tests Emagliflozin in Patients with Chronic Heart Failure with Preserved Ejection Fraction (HFpEF). The Study Looks at How Far Patients Can Walk in 6 Minutes and at Their Heart Failure Symptoms. Retrieved from: <https://clinicaltrials.gov/ct2/show/NCT03448406>. Date Accessed: 01 April 2023
30. Abraham WT, Lindenfeld J, Ponikowski P, Agostoni P, Butler J, Desai AS, et al. Effect of empagliflozin on exercise ability and symptoms in heart failure patients with reduced and preserved ejection fraction, with and without type 2 diabetes. *Eur Heart J* 42 (2021): 700-710.
31. Núñez J, Palau P, Domínguez E, Mollar A, Núñez E, Ramón JM, Miñana G, Santas E, Fácila L, Górriz JL, Sanchis J, Bayés-Genís A. Early effects of empagliflozin on exercise tolerance in patients with heart failure: A pilot study. *Clin Cardiol* 41 (2018): 476-480.
32. Giugliano D, Scappaticcio L, Longo M, Bellastella G, Esposito K. GLP-1RA receptor agonists vs. SGLT-2 inhibitors: the gap seems to be leveling off. *Cardiovasc. diabetol* 20 (2021): 205.
33. Paterno E, Htoo PT, Glynn RJ, Schneeweiss S, Wexler DJ, et al. Sodium-Glucose Cotransporter-2 Inhibitors Versus Glucagon-like Peptide-1 Receptor Agonists and the Risk for Cardiovascular Outcomes in Routine Care Patients With Diabetes Across Categories of Cardiovascular Disease. *Ann Intern Med* 174 (2021): 1528-1541.
34. Paterno E, Goldfine AB, Schneeweiss S, Everett BM, Glynn RJ, Liu J, Kim SC. Cardiovascular outcomes associated with canagliflozin versus other non-gliflozin antidiabetic drugs: population based cohort study. *BMJ* 360 (2018): 119.
35. Lopaschuk GD, Verma S. Mechanisms of Cardiovascular Benefits of Sodium Glucose Co-Transporter 2 (SGLT2) Inhibitors: A State-of-the-Art Review. *J Am Coll Cardiol. Basic to translational science* 5 (2020): 632-644.
36. Cox E, Alicic R, Neumiller J, Tuttle K. Clinical Evidence and Proposed Mechanisms for Cardiovascular and Kidney Benefits from Glucagon-like Peptide-1 Receptor Agonists. *US Endocrinol* 16 (2020): 80-87.