Type 2 diabetes drug shown to reduce major cardiovascular events in men more than women

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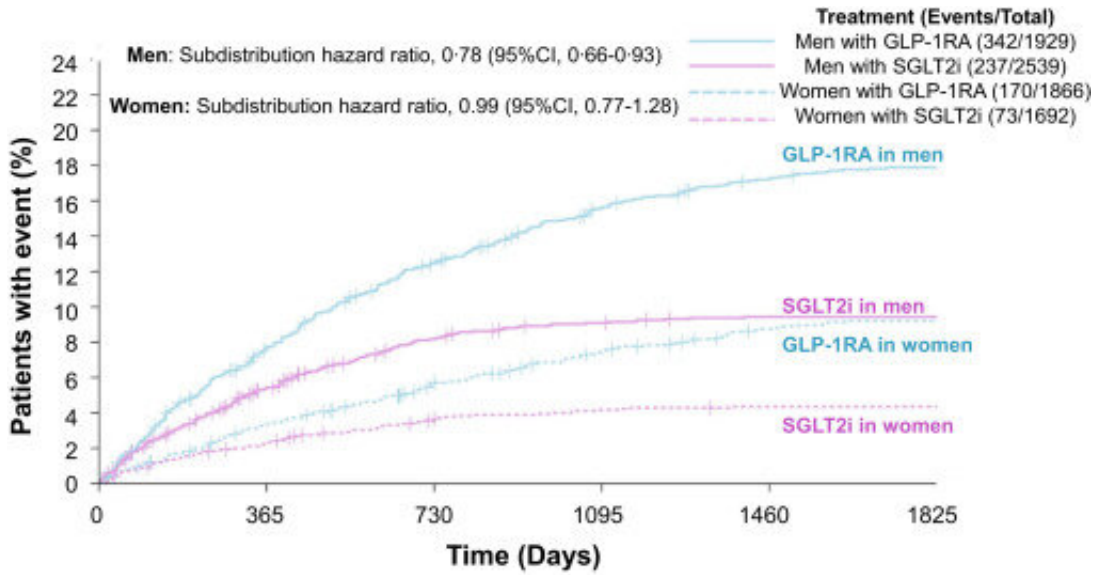

No. at Risk (No. Cumulative Events)

Men with GLP-1RA	1929 (0)	1766 (147)	1666 (240)	1596 (299)	1561 (329)	1547 (342)
Men with SGLT2i	2539 (0)	2377 (137)	2295 (206)	2267 (299)	2256 (237)	2256 (237)
Women with GLP-1RA	1866 (0)	1795 (63)	1737 (106)	1699 (138)	1668 (162)	1660 (170)
Women with SGLT2i	1692 (0)	1646 (40)	1619 (62)	1608 (70)	1604 (73)	1604 (73)

Incidence of major adverse cardiovascular events (MACE) in men and women dispensed either a sodium glucose co-transporter 2 inhibitor (SGLT2i) or glucagon-like peptide receptor 1 agonist (GLP-1RA) 60-days after their index discharge date. Follow up of people is until 30th June 2018. Symbols on curves indicate competing risk events (i.e. non-MACE related death). Credit: *The Lancet Regional Health - Western Pacific* (2023). DOI: 10.1016/j.lanwpc.2023.100692

A new Australian population-based cohort study by Monash University has directly compared two classes of drugs used to treat type 2 diabetes (T2D) and found that one of the two classes is associated with a greater reduction of major adverse cardiovascular events in men than in women.

The two classes of drugs are SGLT2 inhibitors (SGLT2i) and GLP-1 receptor agonists (GLP-1RA). Both classes of medication reduce major adverse cardiovascular events in people with T2D.

Despite women with T2D having a higher risk of developing cardiovascular disease and heart failure than men with T2D, treatment approaches for diabetes-induced cardiovascular disease remain the same across the sexes.

As such, the team of Monash Institute of Pharmaceutical Sciences (MIPS) researchers set out to directly compare and report the sex-specific effects of SGLT2i with GLP-1RAs on major adverse cardiovascular events in men and women, with further subgroup analyses based on age and heart failure history.

The study, published in the journal *The Lancet Regional Health—Western Pacific*, included 8,026 Australian men and women with T2D (≥30 years), discharged from a Victorian hospital between July 1, 2013 and July 1, 2017, and dispensed an SGLT2i or GLP-1RA within 60 days of discharge.

In a median follow-up period of 756 days, exposure to SGLT2i reduced the risk of major adverse cardiovascular events, such as heart failure and stroke, to a greater extent in men of all ages with T2D than women in the same age cohort.

Overall, men dispensed SGLT2i had a 22 percent reduction rate in major adverse cardiovascular events compared to men supplied a GLP-1RA, while in women there was no significant difference between SGLT2i and GLP-1RAs for their effects on major adverse cardiovascular events.

The team also demonstrated for the first time that SGLT2i, in a head-to-head comparison GLP-1RAs, reduces major cardiovascular rates in both older men and women (≥65 years) with T2D, in men with a history of heart failure, and in women with baseline atherosclerotic cardiovascular disease.

The study's first author and MIPS Ph.D. candidate, Abhipree Sharma, said the apparent disparity between the relative benefits of SGLT2i versus GLP-1RAs in T2D men and women warrants further investigation.

"Treatment recommendations for T2D-associated cardiovascular disease and heart failure remain the same in men and women despite known sex differences in the development and presentation of these diseases. Our analyses suggest that these newer classes of glucose-lowering therapies can in fact exert more favorable effects depending on age and sex, which is something we believe needs to be explored further," said Ms Sharma.

Leader of Heart Failure Pharmacology at MIPS and corresponding senior author, Professor Rebecca Ritchie, said there may be a number of reasons women with T2D are more at risk of developing cardiovascular disease and heart failure than men with T2D.

"Typically women with T2D present with greater insulin resistance, endothelial dysfunction, inflammation, abdominal adiposity, body mass index, and blood glucose and cholesterol levels than men with T2D. Additionally, increases in cardiovascular disease and heart failure risk in

postmenopausal women suggests an integral role for estrogen in cardioprotection in women," said Professor Ritchie.

"Our hope is that the findings from this large population-based study will lead to a deeper dive into the most effective pharmacological treatment recommendations based on factors including sex, age and heart failure history," Professor Ritchie concluded.

More information: Abhipree Sharma et al, Sex differences in risk of cardiovascular events and mortality with sodium glucose co-transporter-2 inhibitors versus glucagon-like peptide 1 receptor agonists in Australians with type 2 diabetes: a population-based cohort study, *The Lancet Regional Health—Western Pacific* (2023). DOI: 10.1016/j.lanwpc.2023.100692

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