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## Combination treatment with glucagon-like peptide-1 receptor agonists and sodium-glucose co-transporter-2 inhibitors on the incidence of cardiovascular and serious renal events: population-based cohort study

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Glucagon-like peptide-1 receptor agonists (GLP-1 RAs), which include Ozempic<sup>®</sup>, Rybelsus<sup>®</sup> and other widely-used drugs, and sodium-glucose cotransporter (SGLT)-2 inhibitors, such as Brenzavvy<sup>™</sup>, Invokana<sup>®</sup>, Farxiga<sup>®</sup>, Jardiance<sup>®</sup> and Steglatro<sup>®</sup>, have been shown to be effective treatments in type 2 diabetes, with large randomized controlled trials demonstrating cardiovascular and renal benefits.

In this study, our objective was to determine whether the combined use of GLP-1 RAs and SGLT-2 inhibitors is associated with a decreased risk of major adverse cardiovascular events (MACE) and serious renal events compared with either drug class alone among patients with type 2 diabetes. A secondary objective was to assess the effect of the combination on the individual components of major adverse cardiovascular events (MACE), heart failure, and all-cause mortality. Previous observational studies did not use either drug class alone as the comparator.

Using the United Kingdom Clinical Practice Research Datalink, which was linked to hospital and vital statistics databases, and a prevalent new-user design, the study matched patients initiating a GLP-1 RA–SGLT-2 inhibitor combination with patients continuing their GLP-1 RA or SGLT2 inhibitor treatment alone.

Overall, the findings indicate the GLP-1 RA–SGLT-2 inhibitor combination is associated with a 30% reduction in the risk of cardiovascular and renal events compared with either medication class alone. As this combination is increasingly used among patients with type 2 diabetes, the results highlight a potentially beneficial treatment strategy for managing type 2 diabetes and mitigating cardiovascular and renal risks.

The results of our study have the potential to inform treatment guidelines for type 2 diabetes and guide the treatment of those at an increased risk of cardiovascular and adverse renal events. In particular, this information can help physicians decide if their patients on a GLP-1 RA or SGLT-2 inhibitor would benefit from combination treatment.