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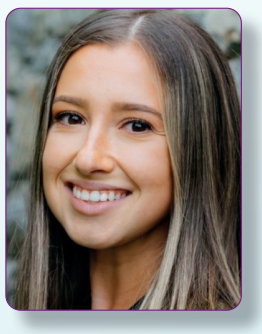

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Glucagon-like peptide-1 receptor agonists and risk of suicidality among patients with type 2 diabetes: active comparator, new user cohort study

Samantha B. Shapiro, Hui Yin, Oriana Hoi Yun Yu, Soham Rej, Samy Suissa, and Laurent Azoulay.

The glucagon-like peptide-1 (GLP-1) receptor agonist drug class, which includes Ozempic® and Rybelsus® for example, is widely prescribed to manage type 2 diabetes. In large trials of cardiovascular outcomes, GLP-1 receptor agonists were highly effective in achieving glycaemic control, showing beneficial cardiorenal effects and reducing all cause mortality. Despite these benefits, recent reports linking GLP-1 receptor agonists to suicidal ideation and self-harm have raised significant concerns.

We did a large, observational study, utilizing data from the UK Clinical Practice Research Datalink (CPRD) to determine the effect of GLP-1 receptor agonist use compared with dipeptidyl peptidase-4 (DPP-4) inhibitor or sodium-glucose cotransporter-2 (SGLT-2) inhibitor use on suicidal ideation, self-harm, and suicide among patients with type 2 diabetes.

The main outcome of interest to us was suicidality, defined as a composite of suicidal ideation, self-harm, and suicide. We also analysed each of these events separately. After accounting for a wide range of potentially confounding factors, the use of GLP-1 receptor agonists was not associated with an increased risk of suicidality compared with DPP-4 inhibitors (3.9 v 3.7 per 1000 person years, respectively) or when compared with SGLT-2 inhibitors (4.3 v 4.6 per 1000 person years, respectively). Similar findings were found when suicidal ideation, self-harm, and suicide were analysed separately in both groups.

In summary, the results of our large active comparator, new user cohort study indicate that GLP-1 receptor agonists are not associated with an increased risk of suicidal ideation, self-harm, and suicide when compared with DPP-4 inhibitors or SGLT-2 inhibitors among patients with type 2 diabetes. These findings should provide some reassurance with respect to the psychiatric safety of these drugs.

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