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ASSOCIATION OF SODIUM-GLUCOSE COTRANSPORTER 2 INHIBITORS AND GLUCAGON-LIKE PEPTIDE-1 RECEPTOR AGONISTS WITH THE RISK OF DEVELOPING DEMENTIA IN PEOPLE WITH TYPE 2 DIABETES MELLITUS

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BACKGROUND

Dementia is the acquired, severe decline in cognitive ability from a previous level function (comprising learning and memory, complex attention, language, perceptual-motor, executive function, social cognition) (1). It is estimated that the number of individuals affected by dementia worldwide was about 57 million in 2019, which is expected to reach 153 million by 2050 (2). Type 2 Diabetes mellitus (T2DM) has been associated with an approximately 2-fold increase in the relative risk of cognitive decline and dementia later in life, while younger age at onset of T2DM, worse glycaemic control and history of severe hypoglycaemic episodes have been reported as contributing factors (3, 4, 5). The effect of antidiabetic pharmacotherapy on cognitive function also remains elusive, and considering the prevalence of DM and the fact that two classes of antidiabetic medications (sodium/glucose co-transporter-2 inhibitors [SGLT2i] and glucagon-like peptide receptor agonists [GLP-1-RA]) have been recently introduced and widely adopted in everyday use, their effects warrant further investigation.

OBJECTIVE

To compare the risk of all-cause dementia, Alzheimer's disease, and vascular dementia between (i) SGLT2i and (ii) GLP-1-RA against Dipeptidyl peptidase-4 inhibitors (DPP-4i) among people with T2DM.

METHODS

Using the medical anonymized real-world primary care-based database THIN®UK, two independent cohort studies employing a new user design were performed to compare the risk of all-cause dementia, Alzheimer's disease, and vascular dementia between (i) SGLT2i and (ii) GLP-1-RA against DPP-4i among people with T2DM (≥40 years). Following the propensity score fine stratification weighting, competing risk Cox proportional hazards regression models were applied to quantify the risk of developing all-cause dementia and its subtype between groups. Each model excluded those with the outcome at baseline. The SGLT2i cohort was from 12th Nov 2012 to 28th Feb 2021, while the GLP-1-RA cohort was from 21st Mar 2007 to 28th Feb 2021.

RESULTS

For the primary outcome of all-cause dementia, 11,679 SGLT2i users were compared with 21,329 DPP-4i users and 9,037 GLP-1-RA users were compared with 37,317 DPP-4i users, respectively (Figure 1).

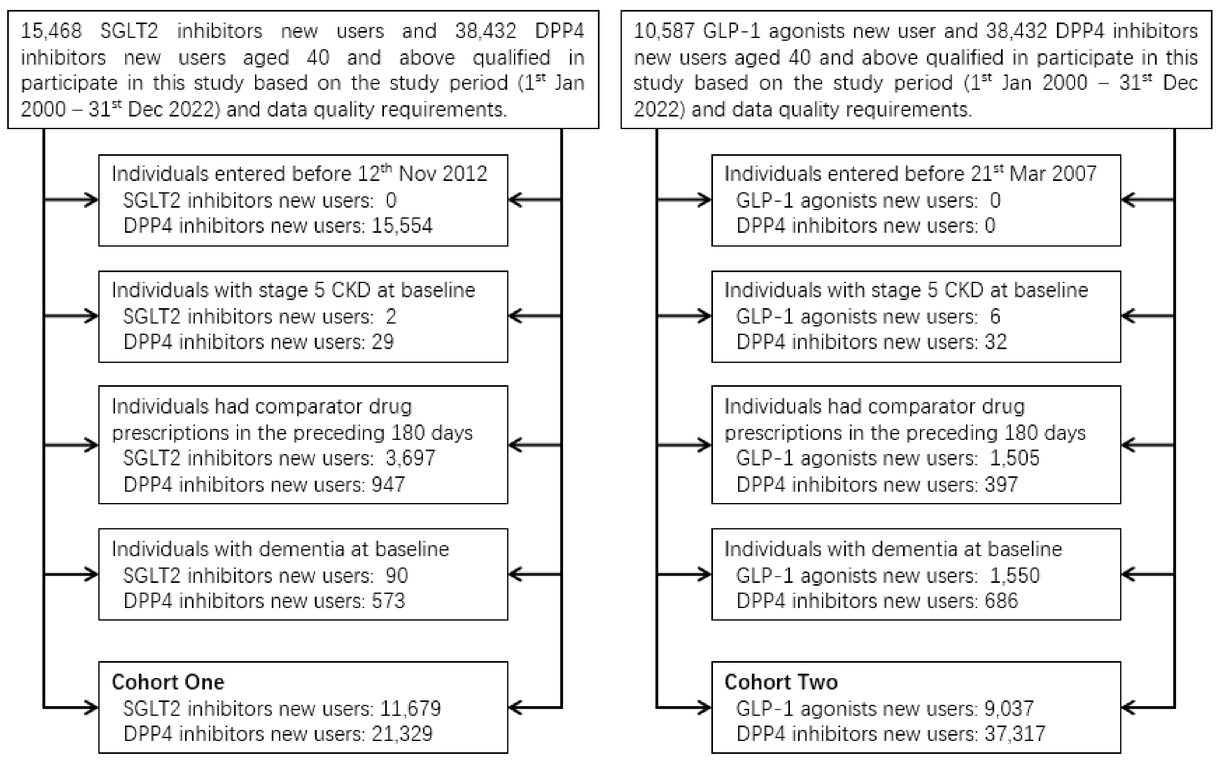

Figure 1. Flow Chart

Following propensity score fine stratification weighting, baseline characteristics between groups were well balanced. With a median follow-up period of 1.3 (interquartile range: 0.5 – 2.4) years, the initiation of SGLT2i vs DPP-4i was potentially associated with a reduction in the risk of all-cause dementia (adjusted HR, 0.77; 95% CI, 0.57-1.05) and vascular dementia (adjusted HR, 0.87; 95% CI, 0.50-1.51), and unchanged risk of Alzheimer's disease (adjusted HR, 0.97; 95% CI, 0.54-1.73). Over a median follow-up of 1.8 (interquartile range: 0.8 – 3.8) years, compared to DPP-4i users, GLP-1-RA users may have a lower risk of Alzheimer's disease (adjusted HR, 0.87; 95% CI, 0.52-1.45), but not all-cause dementia (adjusted HR, 0.92; 95% CI, 0.74-1.14) and vascular dementia (adjusted HR, 1.00; 95% CI, 0.68-1.46) (Figure 2)

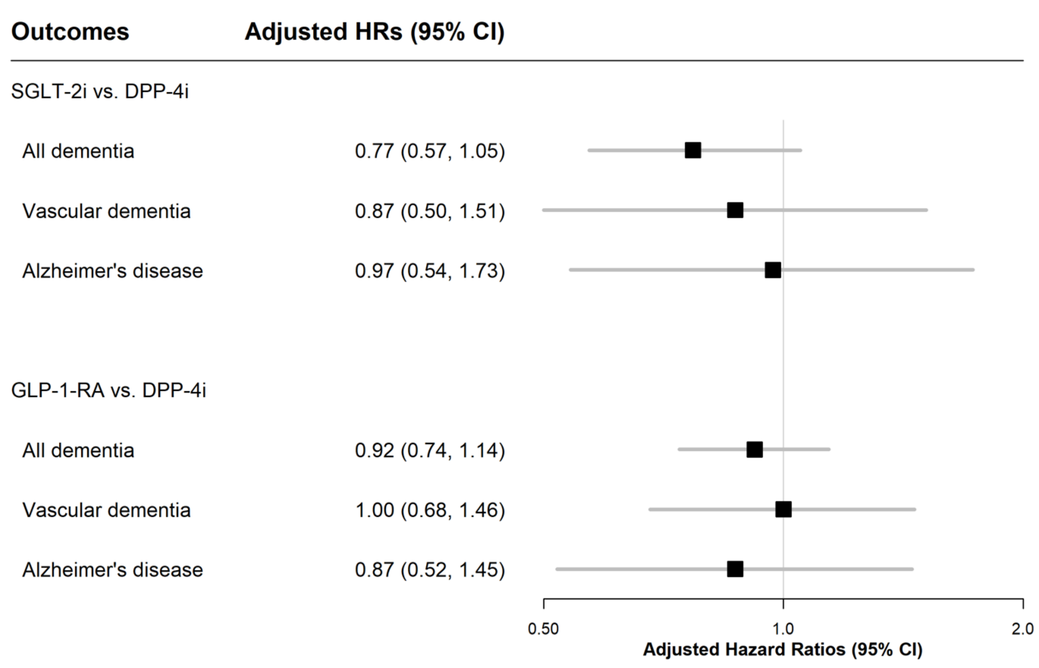

Figure 2. Dementia Hazard ratios

CONCLUSION

This study shows that the initiation of SGLT2i might be associated with reduced risks of all-cause dementia and vascular dementia, while the initiation of GLP-1-RA might be associated with a lower risk of Alzheimer's disease, compared to DPP-4i.

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