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# Hypoglycemia Risk Is Similar With Dipeptidyl Peptidase 4 Inhibitors Monotherapy Versus Metformin Monotherapy

## INTRODUCTION

Tight management of diabetes without increasing hypoglycemia risk is a cornerstone of cardiovascular disease prevention. Prescribing dipeptyidyl peptidase 4 inhibitor (DPP4I) medications instead of metformin as a first-line treatment is common, although large-scale safety evidence favoring DPP4Is monotherapy is scarce.

## HYPOTHESIS

To compare the incidence of hypoglycemia in patients treated with a DPP4I monotherapy versus those receiving metformin monotherapy.

## METHODS

All U.S. patients in Komodo's Healthcare Map with a medical diagnosis of diabetes were studied. We abstracted 2,016,156 patients (59.3% female) on a single-gradient metformin monotherapy and 45,826 patients (52.6% female) on a DPP4I monotherapy between 2016 and 2020. The patients received no anti-diabetes treatment within a year before the first medication and were continuously enrolled one year before and six months after their first medication prescription. Propensity score matching (PSM) was performed using age categories, gender, U.S. regions, chronic kidney disease (CKD), obesity, emergency room visits, Charlson Comorbidity Index (CCI), and medication adherence measured by the Proportion of Days Covered (PDC). The PSM sample comprised 45,400 1:1-matched users of each group. The post-match incidence rate of hypoglycemia was calculated using Poisson regression. A  generalized estimating equation was employed to analyze the matched data.

## RESULTS

The participant baseline mean age (SD) was 64.3(14.0) in the DPP4I group and 50.5(15.8) years in the metformin group. CKD was recorded in 28.1% of the DPP4I users and 4.3% of metformin users. A CCI score of ≥5 was seen in 53.7% of DPP4I users and 15.9% of metformin users. PDC was ≥80% in 37.0% and 42.7% of DPP4I and metformin users. The estimated pre-matched incidence of hypoglycemia was 19.04 and 16.88 per 1,000 person-years in DPP4I and metformin users. The post-matching incidence rates were 19.17 for DPP4I and 16.82 for metformin users. The DPP4I-to-metformin incidence rate ratio was 1.14 (95% CI 0.99–1.31; p = 0.062).

## CONCLUSION

The incidence rate of hypoglycemia in a large cohort of patients treated with DPP4I was comparable to those treated with metformin. When managing CVD risk in diabetics, the sizable risk of hypoglycemia after DPP4Is should be considered in prescription decision-making.