

Metformin use in people with prediabetes delays diabetes diagnosis but does not protect against onset of microvascular complications

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Aims: Metformin is commonly recommended for diabetes prevention in people with prediabetes. The aim of this study was to determine whether metformin delays onset of the first microvascular complication of diabetes.

Methods: Single-centre retrospective cohort study of clinical data including 16,608 individuals with prediabetes at presentation (59.6% female; mean age at prediabetes diagnosis 44.4 ± 11.7 years; mean HbA1c $5.6 \pm 0.4\%$; mean fasting glucose 5.9 ± 0.7 mmol/L). 2940 individuals were treated with metformin for ≥ 1 year prior to onset of diabetes. The composite microvascular endpoint was first onset of any grade of diabetic retinopathy or first onset of microalbuminuria (defined as two separate urinary albumin-creatinine ratio ≥ 3.0 mg/mmol). Progression to diabetes was defined as first HbA1c $\geq 6.5\%$ or first addition of another hypoglycaemic agent for treatment of diabetes.

Results: Baseline HbA1c was 5.7 ± 0.4 in the metformin group and 5.6 ± 0.4 in the control group (baseline age: 45.7 ± 11.0 years metformin group, 44.1 ± 11.9 control group). 866 of 2940 individuals in the metformin group (29.5%) progressed to diabetes, compared with 3540 of 13668 in the control group (25.9%). The mean interval to the diabetes diagnosis endpoint was 6.2 ± 2.8 years in the metformin group and 4.6 ± 3.0 years in the control group. However, the mean interval to the first microvascular complication was 4.8 ± 3.3 years in the metformin group and 4.9 ± 3.2 years in the control group. Adjusted for sex, age, initial HbA1c, metabolic bariatric surgery status, and GLP-1RA use, metformin use in prediabetes was significantly associated with increased hazard of the composite microvascular endpoint (hazard ratio 1.13, 95%CI 1.01-1.25, $p < 0.05$).

Conclusions: Metformin use in prediabetes delays diagnosis, and does not protect against microvascular disease.