

# ANTIDIABETIC MEDICATION USE AND THE RISK OF FRACTURE IN TYPE 2 DIABETIC PATIENTS: A NESTED CASE-CONTROL STUDY

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**Background:** Patients with type 2 diabetes mellitus (T2DM) have an increased risk of fragility fractures due to several factors, such as a greater risk of falling due to hypoglycaemia and/or impaired bone quality. Anti-diabetic oral agents and insulin may also impact on fracture risk. There is however scarce data available on the effect of such therapies combined as usually prescribed in real-life practice conditions.

**Objectives:** The objective of this study was to compare the risk of fracture among T2DM patients who are users of different antidiabetic treatments.

**Methods:** A nested case-control study was conducted using incident T2DM patients registered in computerised primary care records in the Sistema d'Informació per al Desenvolupament de la Investigació en Atenció Primària (SIDIAP) between 2006- 2012, with follow-up available until end/2013. Each case (incident fractures of the hip, spine, wrist, or proximal humerus in 2006-2013) was risk-set matched with five controls of the same gender, calendar year of T2DM diagnosis and age at index date ( $\pm 10$  years). Study exposure included metformin mono-therapy (reference category), insulin monotherapy, and other antidiabetic medications (alone or in combination as prescribed in actual practice) in the 180 days before the index date. Conditional logistic regression analysis was used to estimate odds ratios and 95% confidence interval adjusting for the following confounders: age, gender, HbA1c level, body mass index, history of fracture, co-morbidities, and concomitant medication use.

**Results:** Data on 12,277 T2DM patients (2,049 cases and 10,228 controls) was analysed. Insulin use was associated with increased fracture risk (adjusted OR 1.63 [95%CI 1.30- 2.04]), as was the combination of metformin + sulphonylureas (adjusted OR 1.29 [1.07-1.56]). No significant association was found with other antidiabetic medications and/or combinations.

Discussion: Insulin and sulphonylureas use appear to be associated with an increased fracture risk when compared to metformin amongst recently diagnosed T2DM patients. Residual confounding cannot be ruled out, and more studies are needed to confirm these findings. Given their impact, risk of fracture should be taken into account in the management of T2DM patients.