# Efficacy and safety of direct oral anticoagulants with diabetes and nonvalvular atrial fibrillation: a systematic review and meta-analysis

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**Funding Acknowledgement:** Type of funding sources: None.

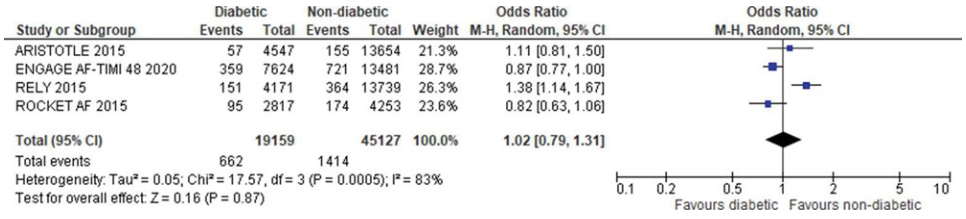
**Background:** Diabetes Mellitus (DM) is an independent risk factor for stroke and atrial fibrillation (AF). Therefore, the risk/benefit profile of the direct oral anticoagulants (DOAC) is of clinical interest.

**Purpose:** To compare efficacy and safety outcomes of DOAC for nonvalvular AF in patients with DM versus without DM.

**Methods:** We systematically searched PubMed, Embase and Cochrane databases, in January 2020, for interventional studies comparing DOAC efficacy and safety in patients with AF and diabetes versus without diabetes.

**Results:** Four randomized clinical trials were included, providing a total of 63987 patients, 18860 with DM and 45127 without DM. In terms of efficacy, our meta-analysis revealed a similar rate of stroke/systemic embolism (pooled OR 1.02 [0.79, 1.31], P=0.87, $I^2$=83%), stroke (pooled OR 1.98 [0.68, 1.40], P=0.90, $I^2$=90%) and all-cause mortality (pooled OR 1.18 [0.97, 1.43], P=0.10, $I^2$=87%), albeit with a significant heterogeneity. However, in direct factor Xa inhibitors sub analysis, diabetic patients had a lower trend of systemic embolism/stroke (pooled OR 0.90 [0.79, 1.02], P=0.09, $I^2$=18%), significantly lower stroke rate (pooled OR 0.82 [0.73, 0.93], P<0.01, $I^2$=0%), but a higher all-cause mortality (pooled OR 1.08 [1.00, 1.16], P<0.01, $I^2$=0%). In terms of safety, the diabetic patients receiving DOAC had higher rates of major bleeding events (pooled OR 1.28 [1.14, 1.45], P<0.01, $I^2$=50%), although with significant heterogeneity. Direct factor Xa inhibitors sub analysis also revealed a higher rate of major bleeding events (pooled OR 1.22 [1.08, 1.38], P<0.01, $I^2$=24%), but a similar intracranial bleeding events (pooled OR 1.03 [0.86, 1.24], P=0.72, $I^2$=0%).

**Conclusion:** Our pooled analysis suggests that diabetic patients on DOAC have an higher bleeding risk on DOAC, although with a superior embolic protection.




Systemic Embolism/Stroke in DM vs. NonDM