

## Antiplatelets in patients with atrial fibrillation: a systematic review and meta-analysis of randomized clinical trials

Benz A.<sup>1</sup>; Johansson I.<sup>1</sup>; Dewilde W.<sup>2</sup>; Lopes RD.<sup>3</sup>; Mehran R.<sup>4</sup>; Sartori S.<sup>4</sup>; Sarafoff N.<sup>5</sup>; Yasuda S.<sup>6</sup>; McIntyre WF.<sup>1</sup>; Healey JS.<sup>1</sup>; Shoamanesh A.<sup>1</sup>; Eikelboom JW.<sup>1</sup>; Connolly SJ.<sup>1</sup>

<sup>1</sup>Population Health Research Institute, Hamilton, Canada

<sup>2</sup>Imeldaziekenhuis, Department of Cardiology, Bonheiden, Belgium

<sup>3</sup>Duke Clinical Research Institute, Durham, United States of America

<sup>4</sup>The Zena and Michael A. Wiener Cardiovascular Institute, New York, United States of America

<sup>5</sup>Deutsches Herzzentrum Muenchen Technical University of Munich, Munich, Germany

<sup>6</sup>Tohoku University Graduate School of Medicine, Department of Cardiovascular Medicine, Tohoku, Japan

**Funding Acknowledgements:** Type of funding sources: Private grant(s) and/or Sponsorship. Main funding source(s): Dr. Benz reports a personal research grant from the German Heart Foundation (Deutsche Herzstiftung e.V.). Dr. Johansson reports personal unrestricted research grants from Swedish Heart-Lung Foundation (Hjärt-Lungfonden) and from Stockholm County Council (Region Stockholm). Dr. McIntyre holds a fellowship award from the Canadian Institutes for Health Research (CIHR). Dr. Shoamanesh reports funding support from the Marta and Owen Boris Foundation and the Heart and Stroke Foundation of Canada.

**Background/Introduction:** There is an ongoing controversy surrounding the efficacy and safety of antiplatelet agents in patients with atrial fibrillation (AF).

**Purpose:** We aimed to systematically assess the effects of antiplatelets on stroke and other outcomes in patients with AF, both receiving oral anticoagulation or not.

**Methods:** We searched MEDLINE, Embase and CENTRAL up until September 2020 to identify randomized trials allocating patients with AF to aspirin or a P2Y12 inhibitor, versus control. Where applicable, we obtained unpublished data from study authors. Random-effects models were applied for meta-analysis.

**Results:** Based on 21,518 patients from 18 randomized trials, there was no reduction in stroke with antiplatelet therapy (risk ratio [RR] 0.89, 95% confidence interval [CI] 0.76-1.04). There was a significant qualitative interaction according to whether patients were receiving concomitant oral anticoagulation or not ( $p < 0.001$ ). Without concomitant anticoagulation, antiplatelets reduced stroke (RR 0.77, 95% CI 0.69-0.86), while they appeared to increase stroke with it (RR 1.33, 95% CI 0.98-1.79). A similar pattern emerged for ischaemic stroke. Antiplatelets increased major bleeding (RR 1.54, 95% CI 1.35-1.77) and intracranial haemorrhage (RR 1.64, 95% CI 1.20-2.24), and reduced myocardial infarction (RR 0.79, 95% CI 0.65-0.94), consistently and irrespective of concomitant anticoagulation. Antiplatelets had a neutral effect on mortality (RR 1.02, 95% CI 0.89-1.17).

**Conclusions:** Antiplatelet therapy did not reduce stroke and increased major bleeding in patients with AF. Antiplatelets did not affect mortality. Subgroup analysis suggests a reduction in stroke with antiplatelets in patients without concomitant oral anticoagulation, and a corresponding signal for harm in those with it.

Abstract Figure.

