Within and beyond 12-month efficacy and safety of antithrombotic strategies in patients with established coronary artery disease: two companion network meta-analyses of the 2022 joint clinical consensus statement of the European Association of Percutaneous Cardiovascular Interventions (EAPCI), European Association for Acute CardioVascular Care (ACVC), and European Association of Preventive Cardiology (EAPC)

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Aims To appraise all available antithrombotic treatments within or after 12 months following coronary revascularization and/or acute coronary syndrome in two network meta-analyses.

Methods and results Forty-three (N = 189 261 patients) trials within 12 months and 19 (N = 139 086 patients) trials beyond 12 months were included for efficacy/safety endpoints appraisal. Within 12 months, ticagrelor 90 mg bis in die (b.i.d.) [hazard ratio (HR), 0.66; 95% confidence interval (CI), 0.49–0.88], aspirin and ticagrelor 90 mg (HR, 0.85; 95% CI, 0.76–0.95), or aspirin, clopidogrel and rivaroxaban 2.5 mg b.i.d. (HR, 0.66; 95% CI, 0.51–0.86) were the only treatments associated with lower cardiovascular mortality, compared with aspirin and clopidogrel, without or with greater bleeding risk for the first and the other treatment options, respectively. Beyond 12 months, no strategy lowered mortality; compared with aspirin; the greatest reductions of myocardial infarction (MI) were found with aspirin and clopidogrel (HR, 0.68; 95% CI, 0.55–0.85) or $P2Y_{12}$ inhibitor monotherapy (HR, 0.76; 95% CI: 0.61–0.95), especially ticagrelor 90 mg (HR, 0.54; 95% CI, 0.32–0.92), and of stroke with VKA (HR, 0.56; 95% CI, 0.44–0.76) or aspirin and rivaroxaban 2.5 mg (HR, 0.58; 95% CI, 0.44–0.76). All treatments increased bleeding except $P2Y_{12}$ monotherapy, compared with aspirin.

Conclusion Within 12 months, ticagrelor 90 mg monotherapy was the only treatment associated with lower mortality, without bleeding risk trade-off compared with aspirin and clopidogrel. Beyond 12 months, $P2Y_{12}$ monotherapy, especially ticagrelor 90 mg, was associated with lower MI without bleeding trade-off; aspirin and rivaroxaban 2.5 mg most effectively reduced stroke, with a more acceptable bleeding risk than VKA, compared with aspirin.

Registration URL: https://www.crd.york.ac.uk/PROSPERO/; Unique identifiers: CRD42021243985 and CRD42021252398.

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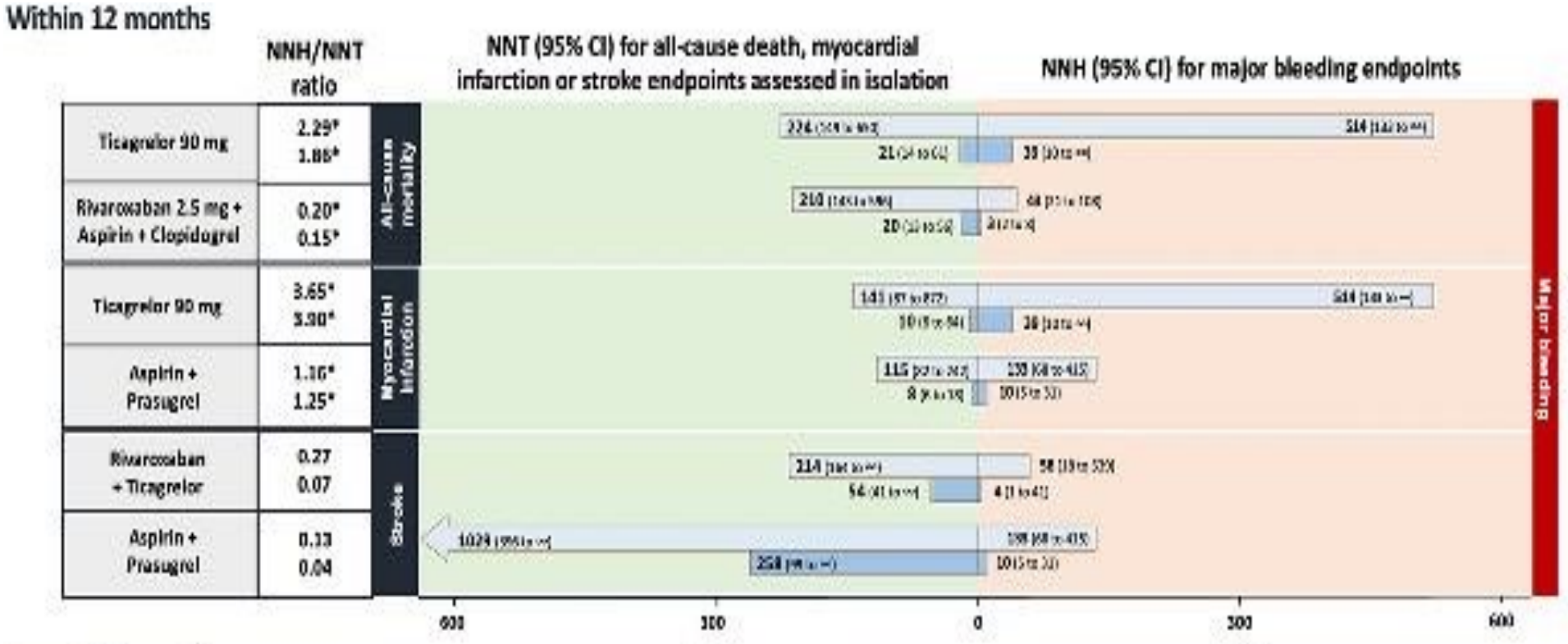

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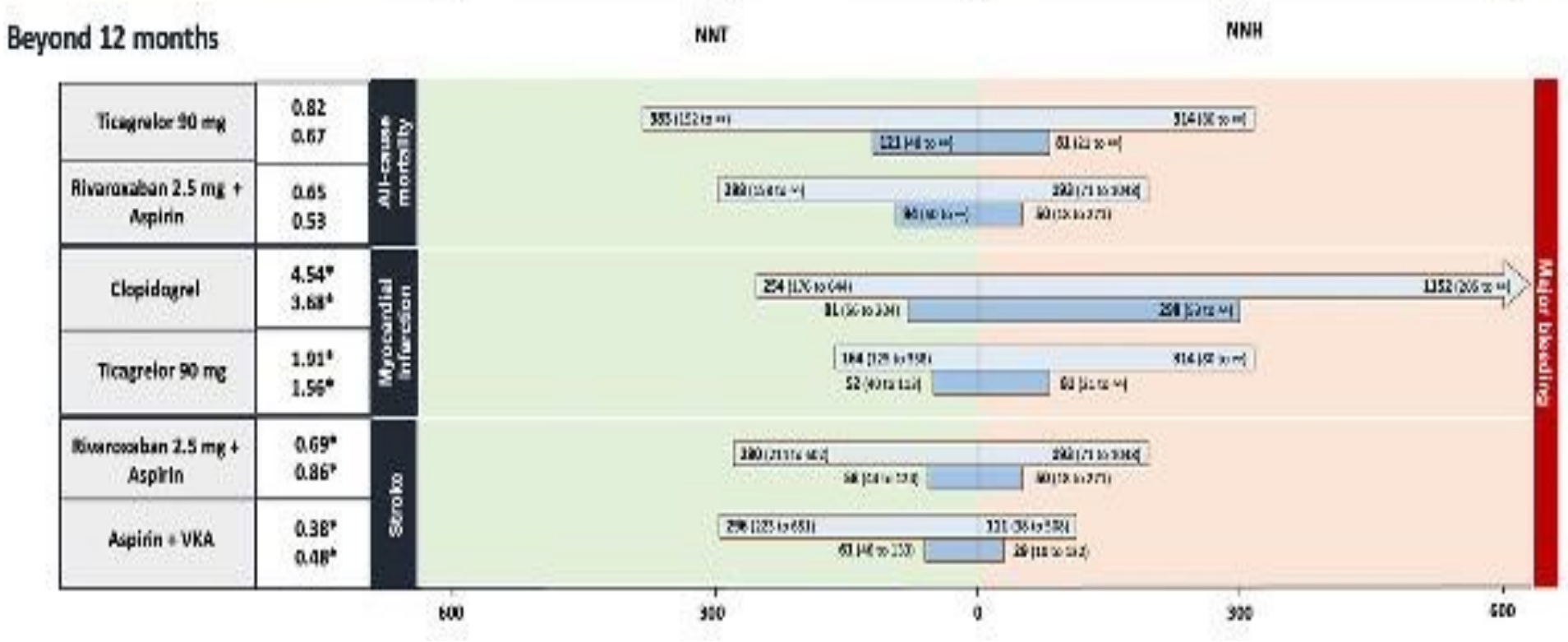

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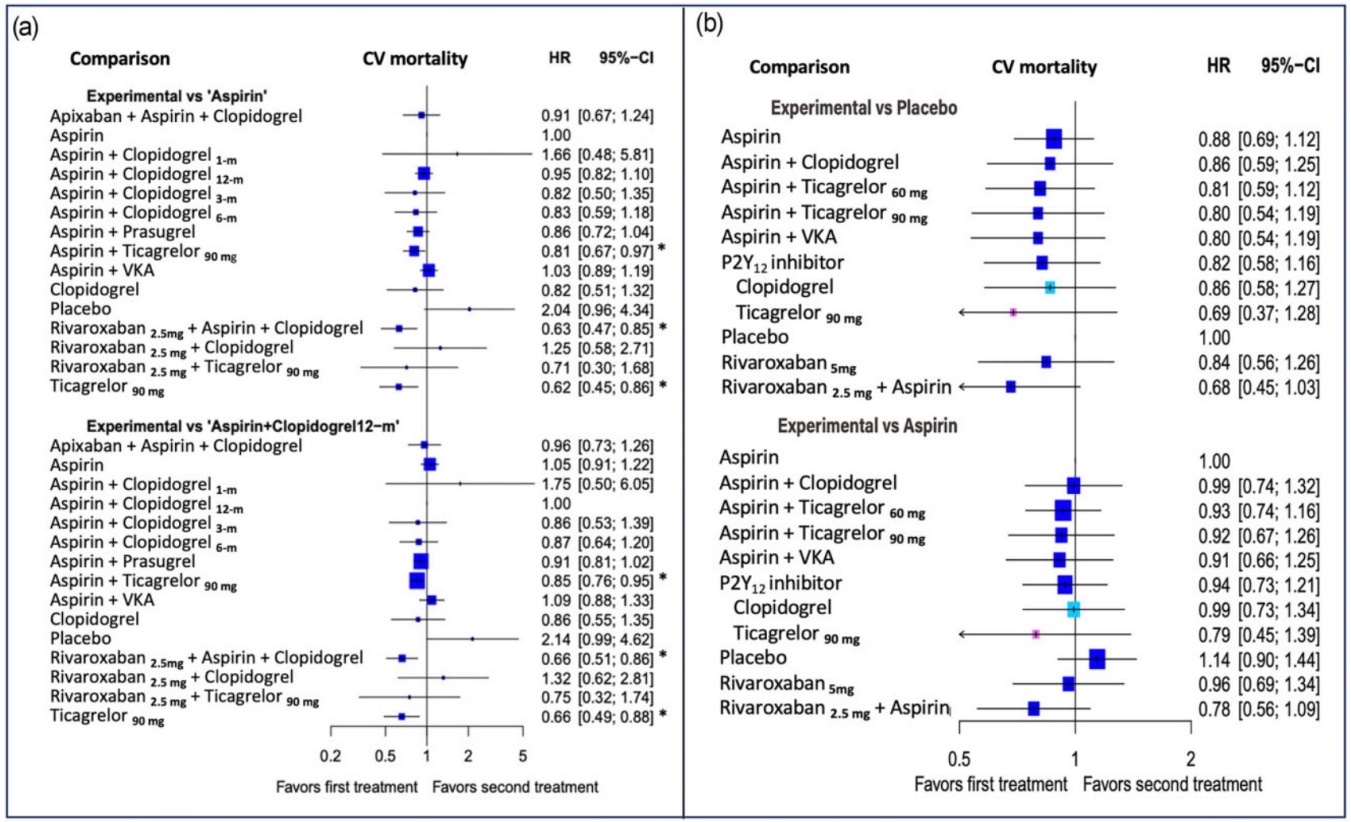

Figure 1 Within (*a*) and beyond (*b*) 12 months treatment effects for cardiovascular mortality. Pooled hazard ratios (HRs) and 95% confidence intervals (CIs) are determined by network meta-analysis. *denotes statistically significant differences.

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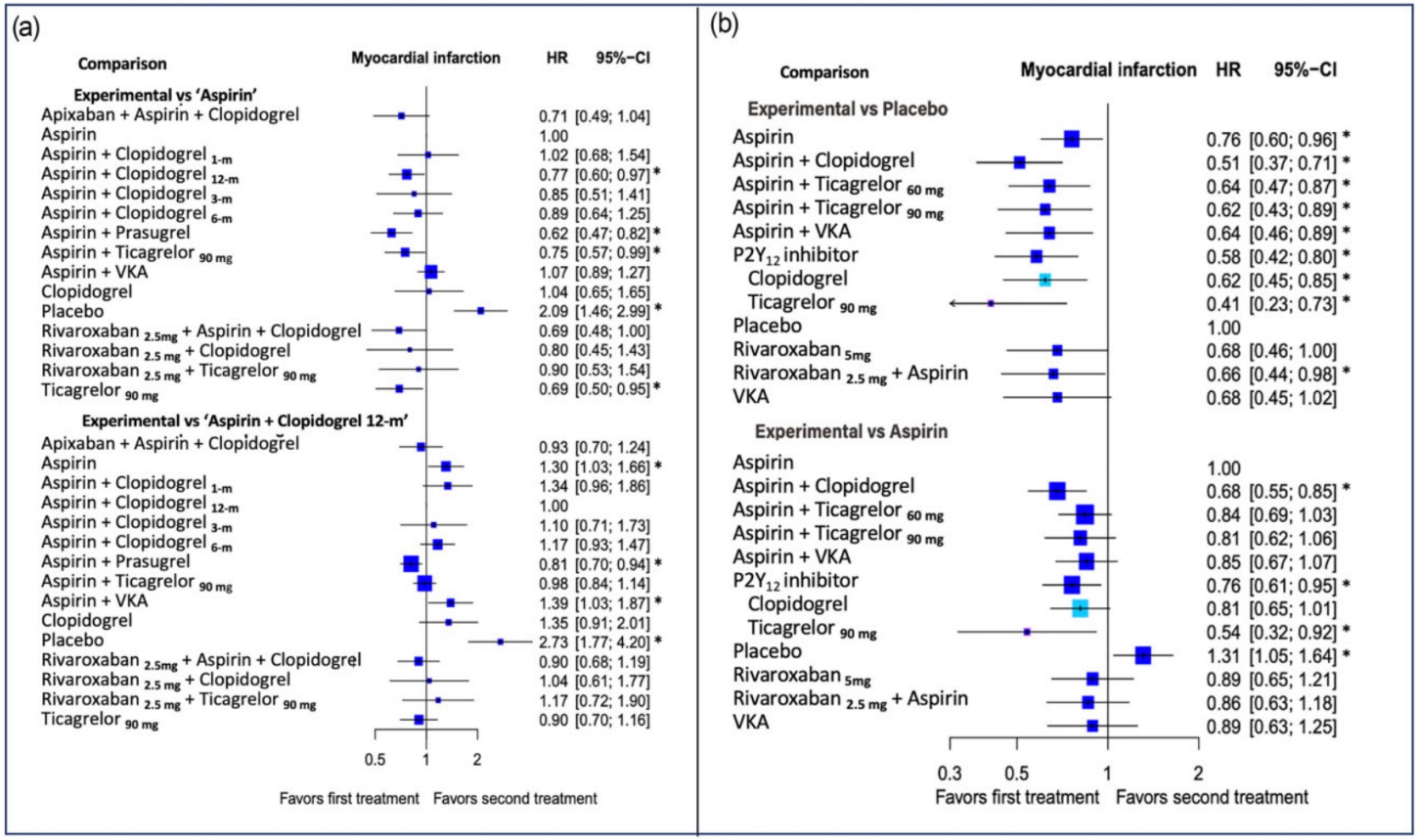

Figure 2 Within (*a*) and beyond (*b*) 12 months treatment effects for myocardial infarction. Pooled hazard ratios (HRs) and 95% confidence intervals (CIs) are determined by network meta-analysis. * denotes statistically significant differences.

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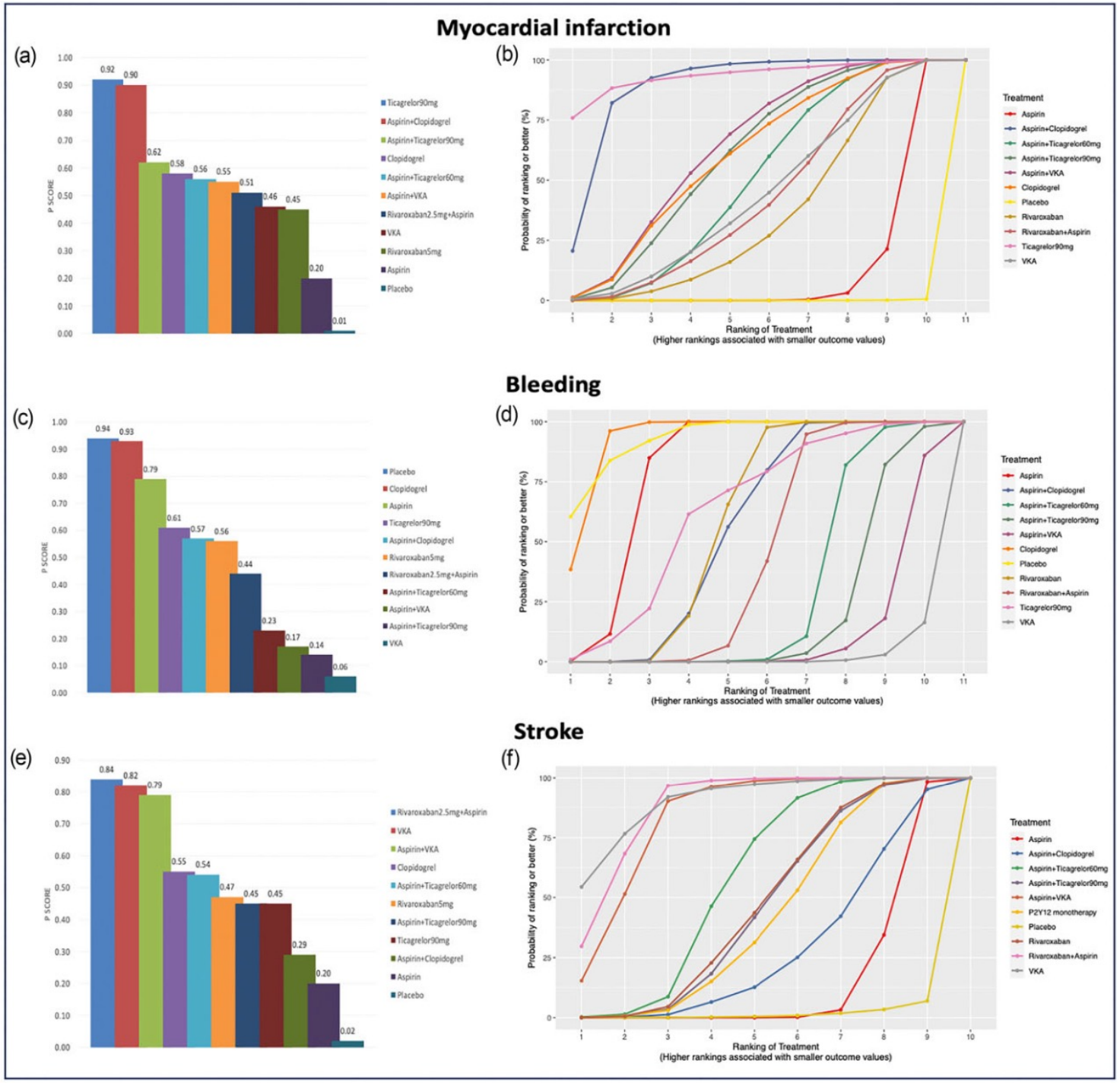

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Figure 3 Standard and Bayesian ranking for myocardial infarction (MI), bleeding, and stroke. In the beyond 12-month network meta-analysis, *P* score values for each intervention for MI (*a*), bleeding (*c*), and stroke (*e*). Corresponding Bayesian probability inferences to be the most effective treatment for MI (*b*), the safest agent for bleeding (*d*), and the most effective agent for stroke (*f*). The value of *P* score varies from 0 to 1, i.e. higher the value, higher the likelihood that a therapy is highly effective or safe, and lower value demonstrates that a therapy is ineffective.

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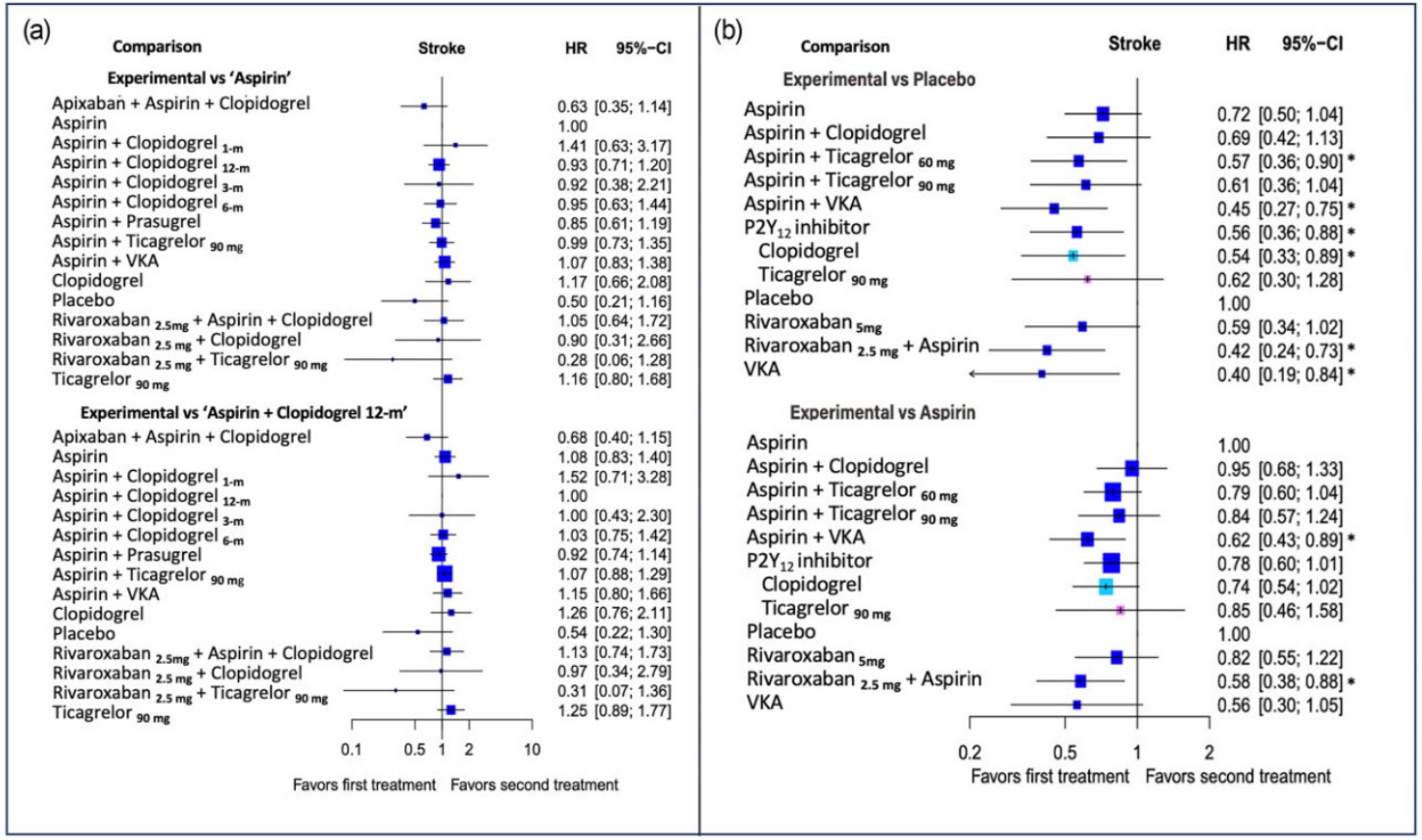

Figure 4 Within (*a*) and beyond (*b*) 12 months treatment effects for stroke. Pooled hazard ratios (HRs) and 95% confidence intervals (CIs) are determined by network meta-analysis. * denotes statistically significant differences.

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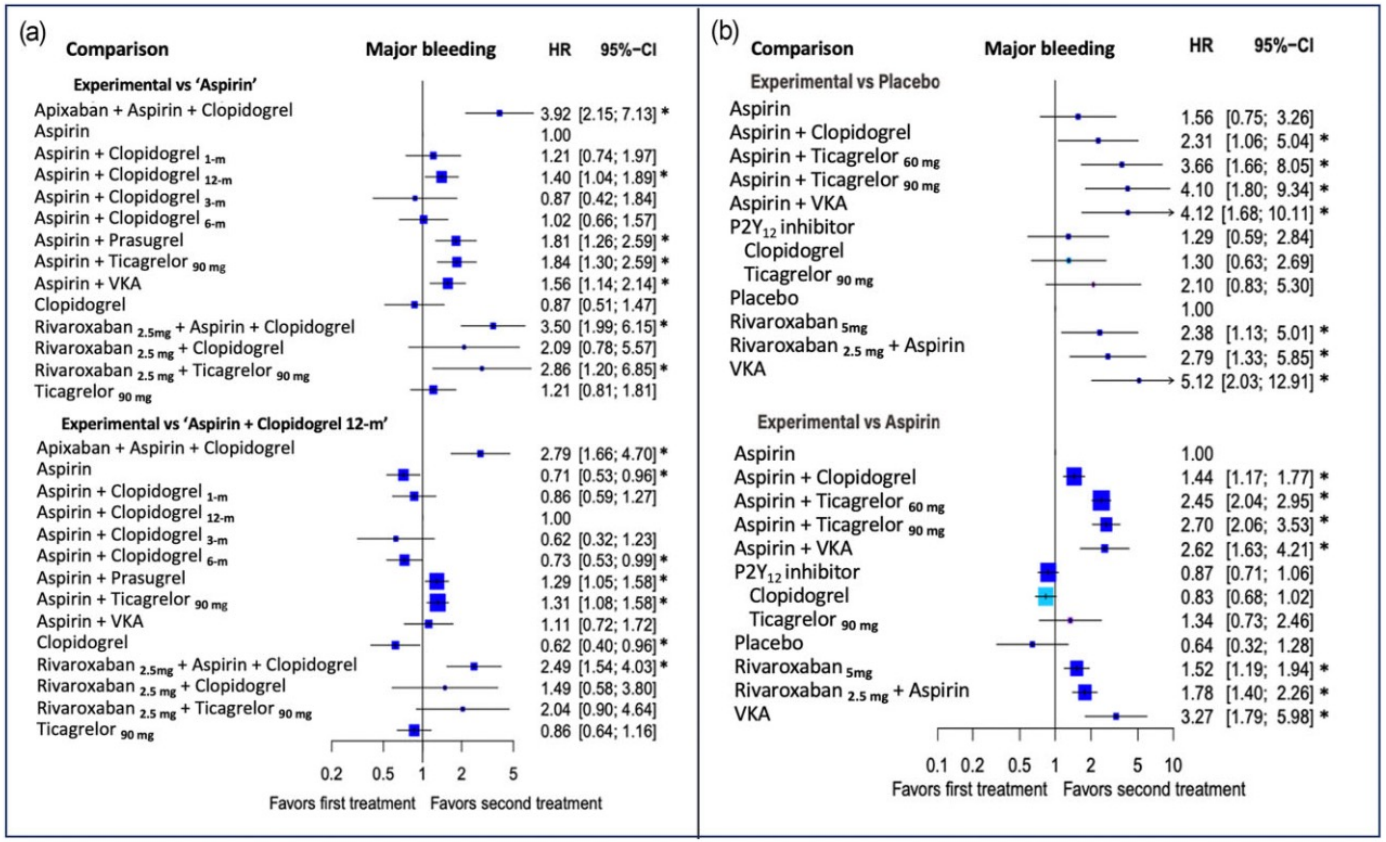

Figure 5 Within (*a*) and beyond (*b*) 12 months treatment effects for major bleeding. Pooled hazard ratios (HRs) and 95% confidence intervals (CIs) are determined by network meta-analysis. * denotes statistically significant differences.

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