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PROPORTION OF WOMEN AND REPORTING OF OUTCOMES BY SEX IN CONTEMPORARY CLINICAL TRIALS OF ATRIAL FIBRILLATION

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Background: Underrepresentation of women in randomized clinical trials (RCTs) limits the generalizability and the quality of the evidence guiding the treatment of women.

Objective: To measure the sex disparities in participants’ recruitment and determine associated factors, and to describe the frequency of the reporting of outcomes by sex.

Methods: MEDLINE was searched to identify RCTs of AF published between January 1, 2011, and November 20, 2021 in 12 top tier journals. We measured the enrolment of women using the enrolment disparity difference (EDD) which is the difference between the proportion of women in the trial and the proportion of women with AF in the underlying general population (obtained from the Global Burden of Disease). Random-effects meta-analyses of the EDD were performed, and multivariable meta-regression was used to explore factors associated with disparity estimates. We also determined the proportion of trials that included sex-stratified results.

Results: Out of 1133 records screened, 142 trials were included, reporting on a total of 133,532 participants. The proportion of women in trials ranged from 10.0% to 72.8% (median 30.9%, interquartile range [IQR] 24.6%-38.1%), whereas the their proportion in the general population ranged from 34.7% to 55.9% (median 45.3%, IQR 40.6%-47.2%) (Figure 1). The random-effects summary EDD was −0.125 (95% CI, −0.143 to −0.108), indicating that women were underenrolled by 12.5 percentage points. Subgroup analyses are presented in Figure 2. Women enrolment was higher in trials published in 2020-2021 compared to those published in 2011-2013 (adjusted odds ratio [aOR] 1.058, 95% CI: 1.004-1.115), higher in trials with higher sample size (>250 vs 750), aOR 1.065, 95% CI: 1.008-1.125), higher mean participants’ age (per 1 year increase, aOR 1.006, 95% CI: 1.002-1.009), and lower in trials conducted in Northern America compared to Europe (aOR 0.945, 95% CI: 0.898-0.995). Only 36 (25.4%) reported outcomes by sex, and of these, 29 (80.6%) included sex-stratified results.

Conclusion: Women remain substantially less represented in RCTs of AF, and sex-stratified reporting of primary outcome is infrequent. These findings call for actions to improve sex equity in enrollment and sex-stratified outcomes’ reporting in RCTs of AF.

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NEW-ONSET BLEEDING AND SUBSEQUENT RISK OF CARDIOVASCULAR OUTCOMES IN ANTICOAGULATED PATIENTS WITH ATRIAL FIBRILLATION

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Background: The use of oral anticoagulation for stroke prevention in patients with atrial fibrillation (AF) increases their risk of bleeding. The prognosis of AF patients who experience a bleeding event is not well studied.

Objective: To assess the subsequent risk of cardiovascular outcomes and death in AF patients who experience bleedings.

Methods: AF patients taking oral anticoagulation were prospectively followed in a large multicenter cohort study. Information on bleedings was systematically collected during yearly follow-up visits; bleedings were adjudicated as major or clinically relevant non-major bleeding (CRNMB). Adverse outcomes were a composite of stroke, myocardial infarction and all-cause death, its individual components, and cardiovascular death. Bleeding was used as a time-updated covariate in multivariable Cox models to estimate the risk of cardiovascular outcomes in patients after a bleeding event compared to those without a bleeding.

Results: Of the 3,279 patients included (mean ± SD age 72 ± 9 years, 28.5% women), 297 patients (9.1%) developed a major bleed and 418 (12.7%) experienced a CRNMB during a median follow-up of 4.1 years. The incidence of the composite outcome was 26.71 and 4.07 per 100 person-years in patients with and without a major bleeding, respectively, while the incidence of stroke was 4.10 versus 0.82. The adjusted hazard ratios (aHRs) were 5.16 (95% confidence interval [CI], 4.24-6.26) for the composite outcome; 4.49 (95% CI, 2.80-7.18) for stroke; 2.57 (95% CI, 1.39-4.74) for myocardial infarction, and 6.42 (95% CI, 4.91-8.39) for cardiovascular death. In patients with and without CRNMB, the incidence of the composite outcome was 10.24 and 4.55, respectively and for stroke it was 1.41 and 0.92. The aHRs were 2.01 (95% CI, 1.63-2.47) for the composite outcome; 1.39 (95% CI, 0.82-2.36) for stroke; 1.67 (95% CI, 0.96-2.81) for...