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Safety of discontinuing oral anticoagulation after atrial fibrillation ablation: an updated systematic review and metaanalysis

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Supplemental Table 1. Search strategy

Database	Search No.	Search strategy
PubMed	#1	"Atrial Fibrillation"[MeSH] OR "atrial fibrillation"[Title/Abstract] OR "AF"[Title/Abstract] OR "A-fib"[Title/Abstract] OR "Afib"[Title/Abstract]
PubMed	#2	"Catheter Ablation"[MeSH] OR "Ablation"[Title/Abstract] OR "Catheter ablation"[Title/Abstract] OR "Ablation Catheter"[Title/Abstract] OR "Transvenous Catheter Ablation"[Title/Abstract] OR "Electrical Catheter Ablation"[Title/Abstract] OR "Electric Catheter Ablation"[Title/Abstract] OR "Transvenous Electric Ablation"[Title/Abstract] OR "Catheter Ablation Radiofrequency"[Title/Abstract] OR "Radiofrequency Catheter Ablation"[Title/Abstract] OR "Percutaneous Catheter Ablation"[Title/Abstract] OR "radiofrequency ablation"[Title/Abstract] OR "pulmonary vein isolation"[Title/Abstract] OR "PVI"[Title/Abstract] OR "pulmonary vein ablation"[Title/Abstract] OR "PVA"[Title/Abstract] OR "pulsed-field ablation"[Title/Abstract] OR "pulsed field ablation"[Title/Abstract] OR "PFA"[Title/Abstract] OR "cryoablation"[Title/Abstract]
PubMed	#3	"discontinuation"[Title/Abstract] OR "discontinued"[Title/Abstract] OR "discontinue"[Title/Abstract] OR "discontinuing"[Title/Abstract] OR "stop"[Title/Abstract] OR "stopping"[Title/Abstract] OR "cessation"[Title/Abstract]
PubMed	#4	#1 AND #2 AND #3

Database	Search No.	Search strategy
Cochrane Library	#1	MeSH descriptor: [Atrial Fibrillation] explode all trees OR ("atrial fibrillation" OR AF OR "A-fib" OR Afib):ti,ab,kw
Cochrane Library	#2	MeSH descriptor: [Catheter Ablation] explode all trees OR (Ablation OR "Catheter ablation" OR "Ablation Catheter" OR "Transvenous Catheter Ablation" OR "Electrical Catheter Ablation" OR "Electric Catheter Ablation" OR "Transvenous Electric Ablation" OR "Catheter Ablation Radiofrequency" OR "Radiofrequency Catheter Ablation" OR "Percutaneous Catheter Ablation" OR "radiofrequency ablation" OR "pulmonary vein isolation" OR PVI OR "pulmonary vein ablation" OR PVA OR "pulsed-field ablation" OR "pulsed field ablation" OR PFA OR cryoablation):ti,ab,kw
Cochrane Library	#3	(discontinuation OR discontinued OR discontinue OR discontinuing OR stop OR stopping OR cessation):ti,ab,kw
Cochrane Library	#4	#1 AND #2 AND #3

Abbreviations: AF = atrial fibrillation; MeSH = Medical Subject Headings; PFA = pulsed field ablation; PVA = pulmonary vein ablation; PVI = pulmonary vein isolation.

Supplemental Table 2. Standardized definitions of thromboembolic and bleeding endpoints

Study (Year)	Thromboembolic efficacy endpoint	Major bleeding safety endpoint
Oral (2006)	Thromboembolic events, including transient ischemic episodes, stroke, and peripheral emboli.	Not formally evaluated as a primary safety outcome.
Nademanee (2008)	Stroke, TIA, and systemic emboli.	Major and minor bleeding events.
Bunch (2009)	Ischemic stroke or TIA.	Fatal hemorrhage or severe bleeding requiring hospitalization.
Themistoclakis (2010)	Ischemic stroke (abrupt focal neurological deficit persisting > 24 hours).	Intracranial or retroperitoneal bleeding, or bleeding leading to death, hospitalization, or transfusion.
Guiot (2011)	Cerebrovascular events occurring during or after the procedure.	Not formally evaluated as a primary safety outcome.
Hunter (2011)	Stroke or TIA.	Procedural complications including tamponade or hematoma.
Hussein (2011)	Stroke.	Not explicitly defined as a primary independent endpoint.
Saad (2011)	Symptomatic ischemic cerebrovascular events.	Not explicitly defined as a primary independent endpoint.
Yagishita (2011)	Cerebrovascular events (TIA and ischemic stroke) presenting as an abrupt focal neurological deficit.	Hemorrhagic events.
Winkle (2013)	Thromboembolic cerebrovascular accidents or TIA.	Bleeding episodes requiring medical attention.

Study (Year)	Thromboembolic efficacy endpoint	Major bleeding safety endpoint
Karasoy (2014)	Hospitalization for ischemic stroke, TIA, or peripheral artery embolism.	Hospitalization for intracranial bleeding, or bleeding from the respiratory, gastrointestinal, or urinary tract.
Riley (2014)	Stroke (deficit > 24 hours) or TIA (deficit < 24 hours).	Bleeding severe enough to require hospitalization, transfusion, or resulting in permanent disability.
Uhm (2014)	Ischemic stroke with apparent brain lesion or TIA without lesion.	Hemorrhage requiring transfusion or intervention, and bleeding with a hemoglobin reduction ≥ 4.0 g/dL.
Gallo (2016)	Major adverse cardiac or cerebrovascular events, including focal neurological deficits.	ISTH standardized criteria.
Själander (2016)	Ischemic stroke.	Intracranial hemorrhage.
Kochhäuser (2017)	Stroke and TIA.	Not formally evaluated as a primary safety outcome.
Liang (2018)	Cerebrovascular events, defined as ischemic stroke or TIA.	Any bleeding episode severe enough to require hospitalization.
Arai (2019)	Ischemic stroke, hemorrhagic stroke, or transient ischemic attack (TIA).	Hemoglobin reduction of ≥ 2 g/dL, transfusion of ≥ 2 blood units, or symptomatic bleeding in a critical area or organ.
Okumura (2019)	Ischemic stroke, hemorrhagic stroke, or TIA.	Hemoglobin reduction of ≥ 2 g/dL, transfusion of ≥ 2 blood units, or symptomatic critical organ bleeding.

Study (Year)	Thromboembolic efficacy endpoint	Major bleeding safety endpoint
Hermida (2020)	Ischemic events comprising stroke, TIA, and systemic embolism.	Not explicitly defined as a primary independent endpoint.
Lauritzen (2020)	Major adverse cardiac and cerebrovascular events, defined as stroke, myocardial infarction, or percutaneous coronary intervention.	Not formally evaluated as a primary safety outcome.
Yang (2020)	Fatal or non-fatal ischemic stroke and systemic embolism.	Intracranial hemorrhage and other major bleeding per ISTH criteria.
Yu (2020)	Stroke and TIA.	Major bleeding.
Inoue (2021)	Composite of systemic embolism and ischemic stroke.	Evaluated using J-ROCKET AF major bleeding criteria.
Fei (2024)	Ischemic stroke, TIA, or systemic embolism.	Gastrointestinal or intracranial hemorrhage, hemothorax requiring hospitalization, hemoglobin drop > 2 g/dL, or blood transfusion.
Kanaoka (2024)	Ischemic stroke and systemic embolism, including acute myocardial infarction.	Composite of intracranial hemorrhage and gastrointestinal bleeding.
ODIn-AF (2024)	New silent micro-embolic or macro-embolic brain lesions on MRI and clinically relevant cardioembolic events after pulmonary vein isolation.	Bleeding events were assessed as part of the safety analysis; a harmonized major bleeding endpoint was not explicitly reported as an independent pooled endpoint.

Study (Year)	Thromboembolic efficacy endpoint	Major bleeding safety endpoint
ALONE-AF (2025)	First occurrence of a composite of stroke and systemic embolism.	Evaluated using standardized International Society on Thrombosis and Haemostasis (ISTH) criteria.
Iwawaki (2025)	Ischemic stroke, systemic embolism, and TIA confirmed by clinical and imaging evaluation.	ISTH standardized criteria.
Nakano (2025)	Fatal or non-fatal ischemic stroke and systemic embolism.	ISTH criteria (hemoglobin drop ≥ 2 g/dL, transfusion of ≥ 2 units, critical site bleeding, or death).
Oda (2025)	Ischemic stroke and systemic embolic events.	ISTH standardized criteria.
OCEAN-AF (2025)	Composite of stroke, systemic embolism, or new covert embolic stroke (infarct ≥ 15 mm on MRI).	ISTH standardized criteria.

Note. Definitions are presented as reported or summarized in the included studies. When isolated major bleeding was not reported as an independent endpoint, this is stated explicitly.
Abbreviations: AF = atrial fibrillation; ISTH = International Society on Thrombosis and Haemostasis; MRI = magnetic resonance imaging; TIA = transient ischemic attack.

Supplemental Table 3. Univariable meta-regression analyses for clinical outcomes

Outcome	Moderator	β coefficient	95% CI	P value	Residual I^2 (%)	R^2 (%)
Thromboembolic events	Design category	-0.3362	-0.9601 to 0.2878	0.291	54.41	10.64
Thromboembolic events	Total sample size	0.0000	-0.0000 to 0.0000	0.6026	49.38	0
Thromboembolic events	Male %	-0.0343	-0.0733 to 0.0047	0.0848	52.6	16.65
Thromboembolic events	Paroxysmal AF %	0.0014	-0.0155 to 0.0183	0.8695	11.44	0
Thromboembolic events	Follow-up duration, years	0.3186	0.0759 to 0.5612	0.0101	49.43	31.56
Major bleeding	Design category	-0.2223	-0.9656 to 0.5209	0.5577	61.31	4.83
Major bleeding	Total sample size	0.0000	-0.0000 to 0.0000	0.1579	46.77	5.51
Major bleeding	Male %	-0.0479	-0.1053 to 0.0095	0.1021	71.95	0
Major bleeding	Paroxysmal AF %	0.0030	-0.0351 to 0.0412	0.8754	54.66	0
Major bleeding	Follow-up duration, years	-0.1365	-0.5048 to 0.2318	0.4675	68.09	0

Note. β coefficients are from univariable random-effects meta-regression models and are reported on the log risk ratio scale. Positive values indicate higher study-level risk ratio estimates as the moderator increases. R^2 indicates the proportion of between-study variance explained by the moderator.
Abbreviations: AF = atrial fibrillation; CI = confidence interval; I^2 = inconsistency statistic; R^2 = proportion of between-study variance explained.

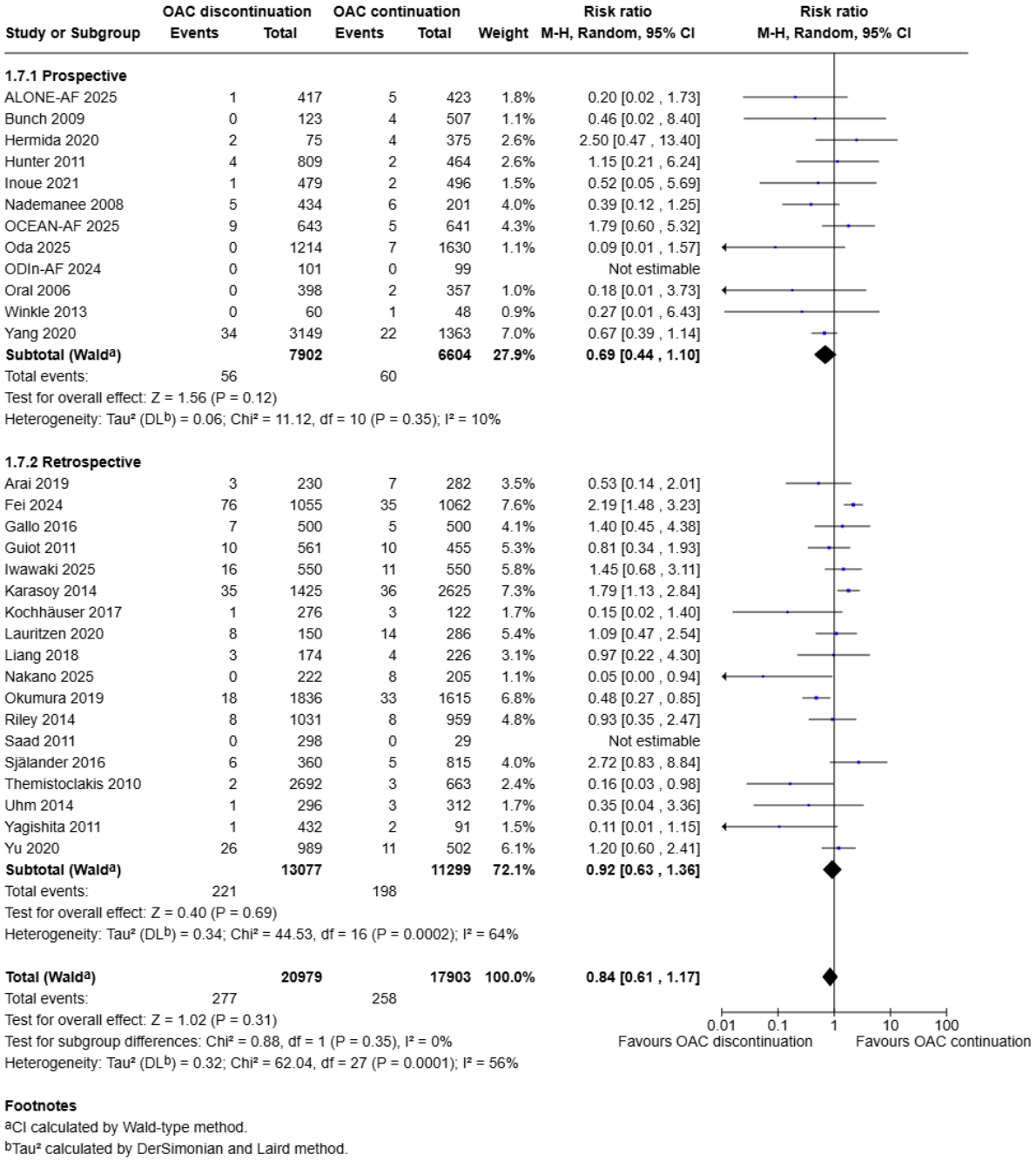
Supplemental Table 4. GRADE certainty of evidence assessment

Outcome	Participants (studies)	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias / other considerations	Overall certainty	OAC discontinuation	OAC continuation	Relative effect (95% CI)	Absolute effect
Thromboembolic Events	152,421 (32 studies)	Very serious (a)	Serious (b)	Not serious	Serious (c)	Publication bias strongly suspected (f)	⨁◯◯◯ Very low (a,b,c,f)	789/77,782 (1.0%)	709/74,639 (0.9%)	RR 0.93 (0.72 to 1.20)	1 fewer per 1,000 (from 3 fewer to 2 more)
Major Bleeding	146,437 (22 studies)	Very serious (a)	Not serious	Serious (d)	Not serious	Strong association	⨁⨁◯◯ Low (a,d)	493/74,815 (0.7%)	871/71,622 (1.2%)	RR 0.37 (0.27 to 0.52)	8 fewer per 1,000 (from 9 fewer to 6 fewer)
All-Cause Mortality	17,453 (15 studies)	Very serious (a)	Not serious	Not serious	Serious (e)	Publication bias strongly suspected (g)	⨁◯◯◯ Very low (a,e,g)	130/8,349 (1.6%)	188/9,104 (2.1%)	RR 0.87 (0.70 to 1.08)	3 fewer per 1,000 (from 6 fewer to 2 more)

Explanations. a. Using ROBINS-I, most non-randomized studies had at least moderate concerns and many were judged serious or critical, mainly due to confounding and selection bias. This reduces certainty across outcomes. b. Statistical heterogeneity was present for thromboembolic events, and sensitivity analyses did not identify a clear source; several studies showed inconsistent directions of effect. c. The thromboembolic outcome had heterogeneity and wide confidence intervals crossing potentially important benefit and harm. d. The definition of major bleeding varied across studies. Although no major clinical discrepancies were observed, outcome-definition heterogeneity remained. e. For all-cause mortality, statistical heterogeneity was low, but the confidence interval crossed no effect and included clinically relevant benefit or harm. f. Small-study effects/publication bias were suspected for thromboembolic events by contour-enhanced funnel plot and Egger testing. g. Mortality reporting was not prespecified in several studies, raising concern for reporting or publication bias despite non-significant Egger testing.

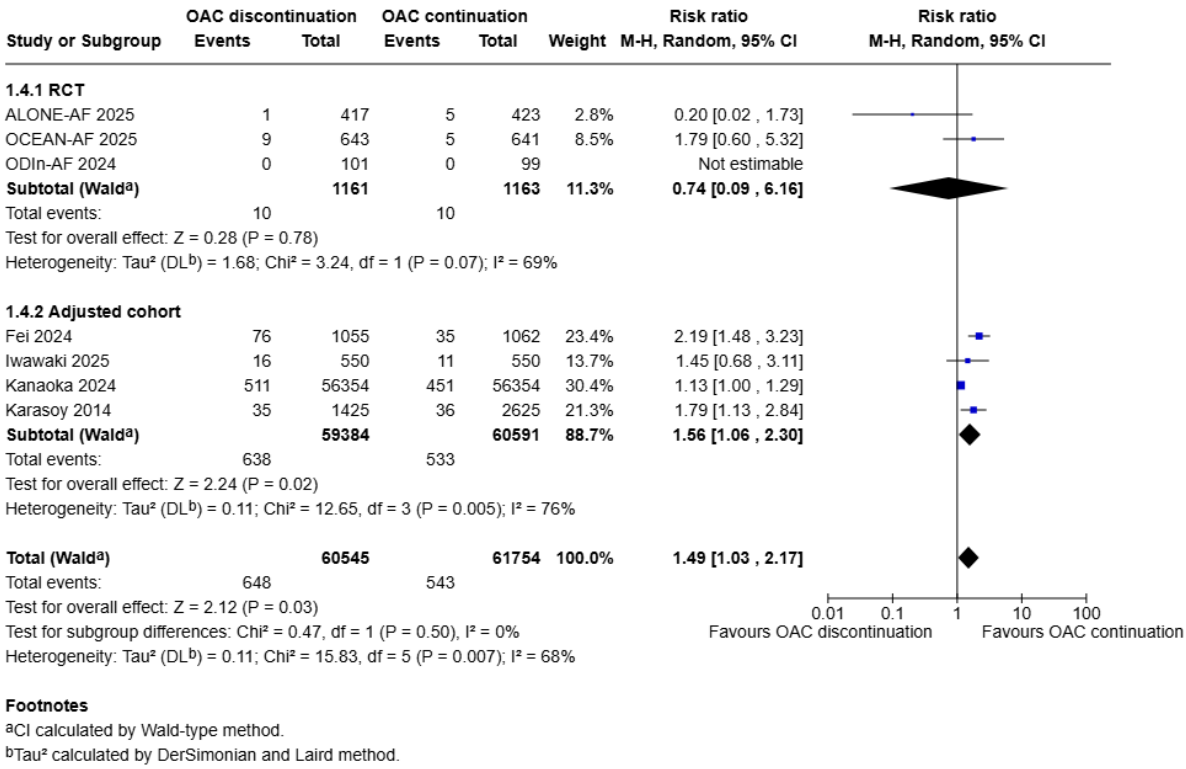
Abbreviations: CI = confidence interval; GRADE = Grading of Recommendations Assessment, Development, and Evaluation; OAC = oral anticoagulation; ROBINS-I = Risk Of Bias In Non-randomized Studies of Interventions; RR = risk ratio.

Supplemental Figure

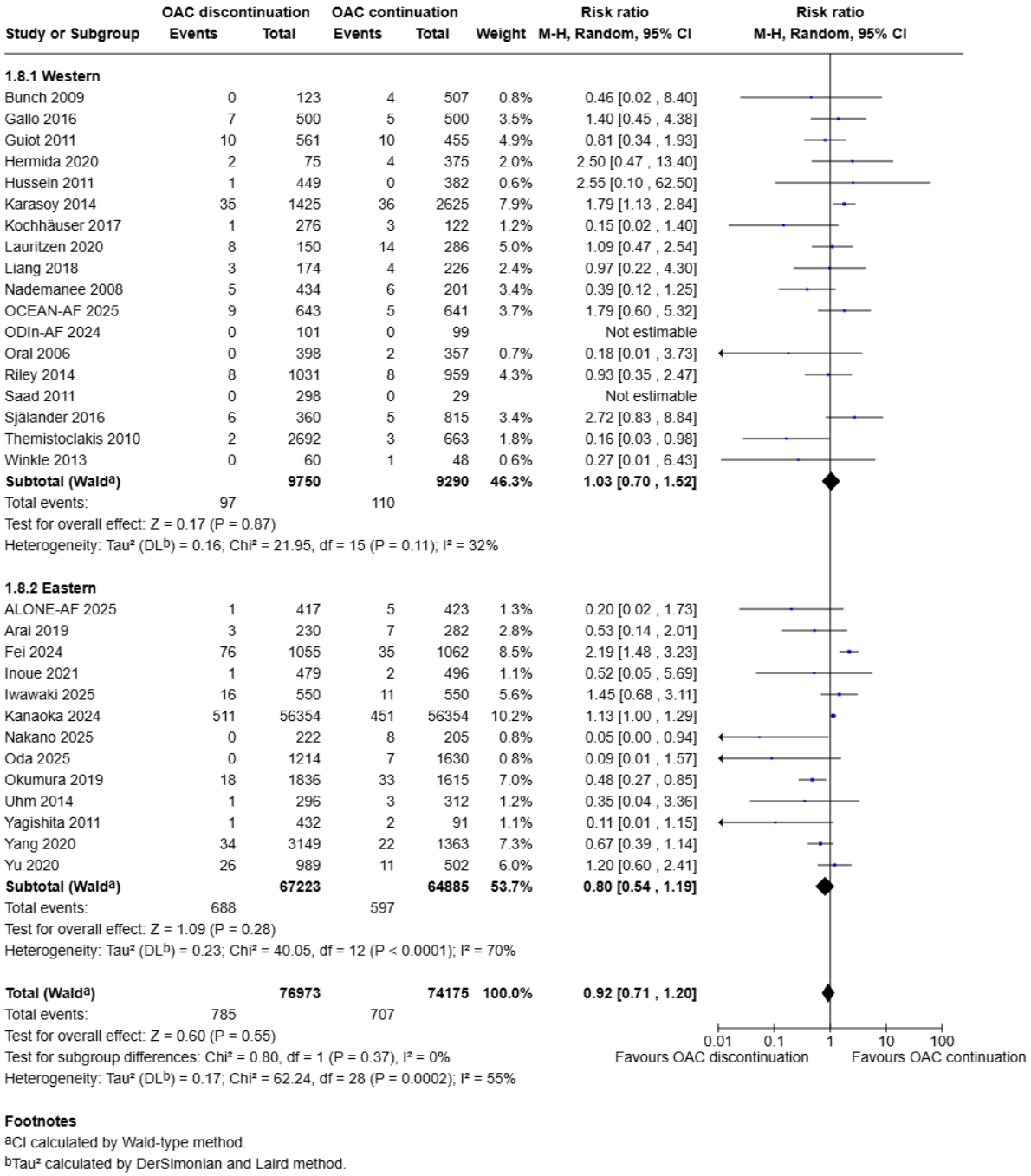


Supplemental Figure 1. Forest plots for subgroup analyses of thromboembolic events according to prospective versus retrospective study design in patients after atrial fibrillation ablation.

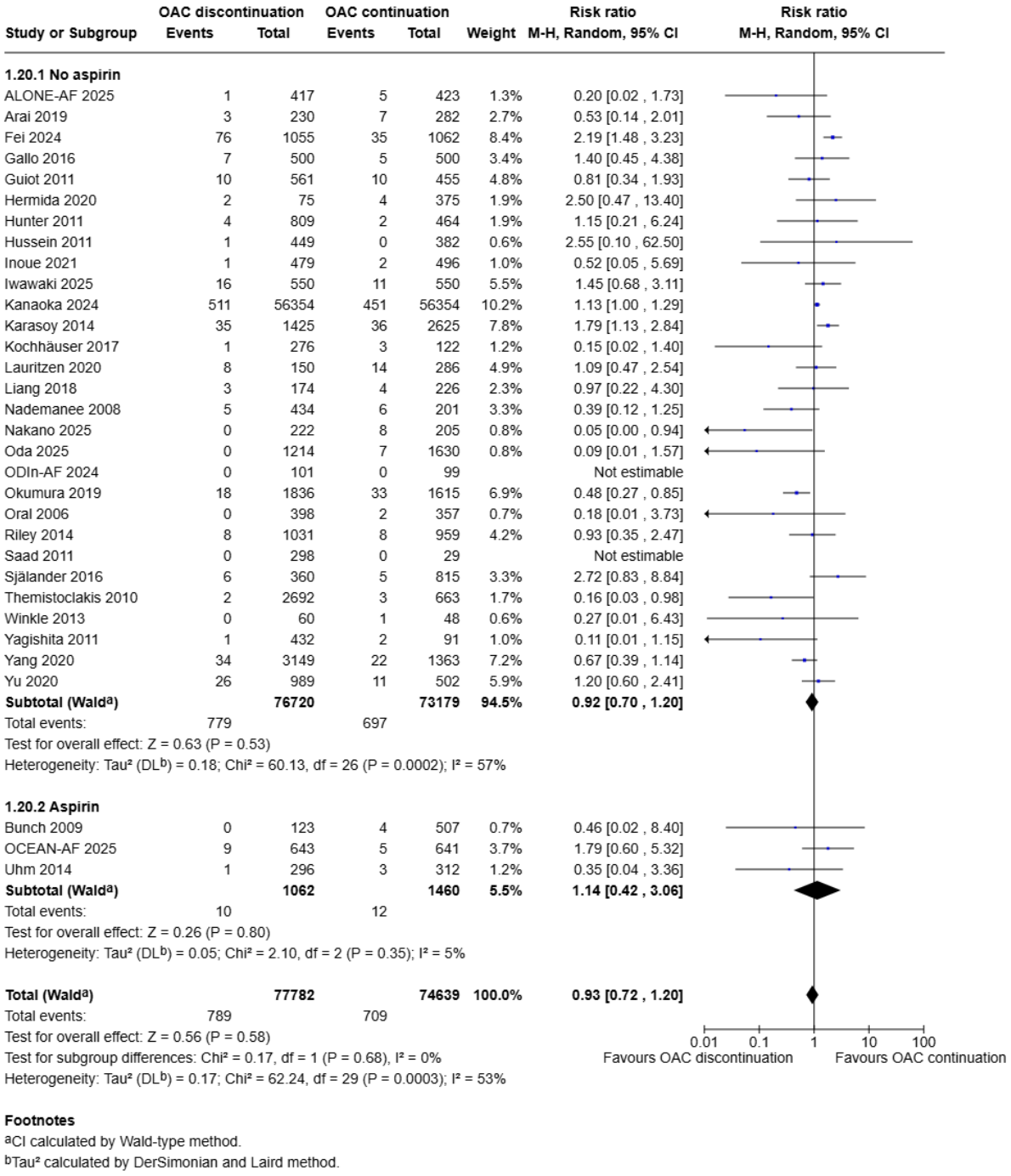
AF = atrial fibrillation; CI = confidence interval; OAC = oral anticoagulation; RR = risk ratio; I^2 = heterogeneity.



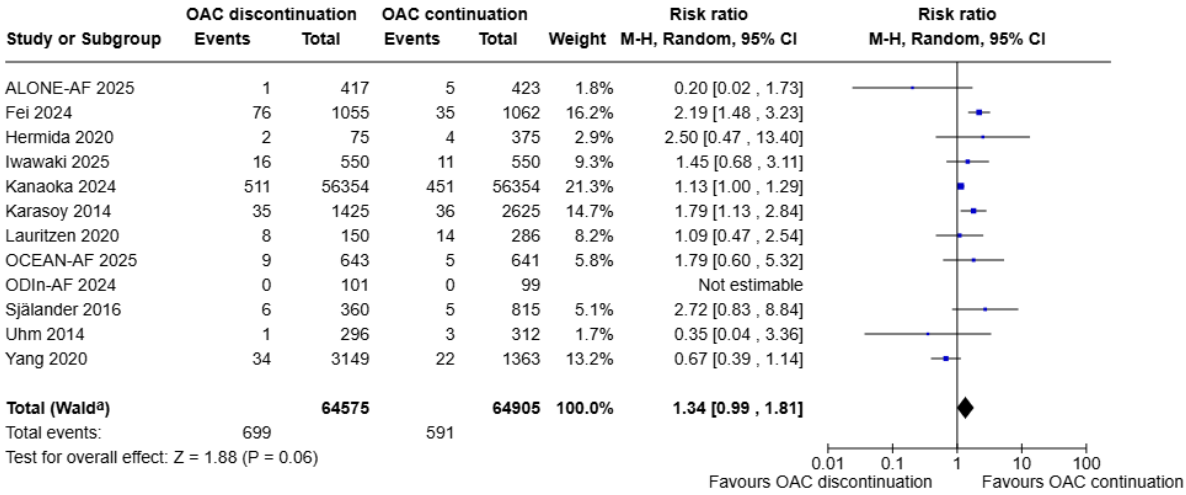
Supplemental Figure 2. Forest plots for subgroup analyses of thromboembolic events according to randomized trial versus adjusted observational cohort evidence in patients after atrial fibrillation ablation.
AF = atrial fibrillation; CI = confidence interval; OAC = oral anticoagulation; RR = risk ratio; I^2 = heterogeneity.



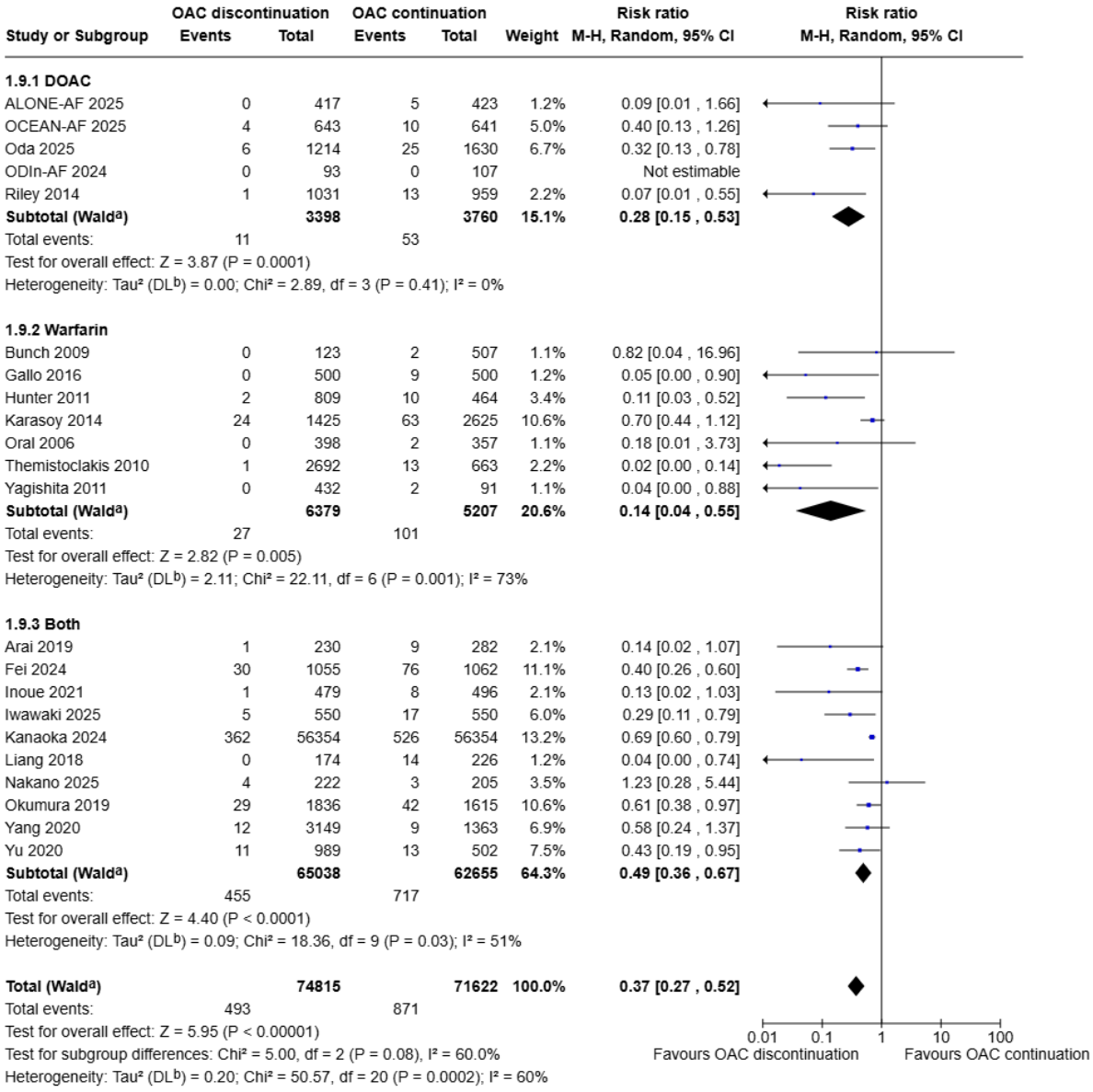
Supplemental Figure 3. Forest plots for subgroup analyses of thromboembolic events according to geographic region in patients after atrial fibrillation ablation.
AF = atrial fibrillation; CI = confidence interval; OAC = oral anticoagulation; RR = risk ratio; I^2 = heterogeneity.



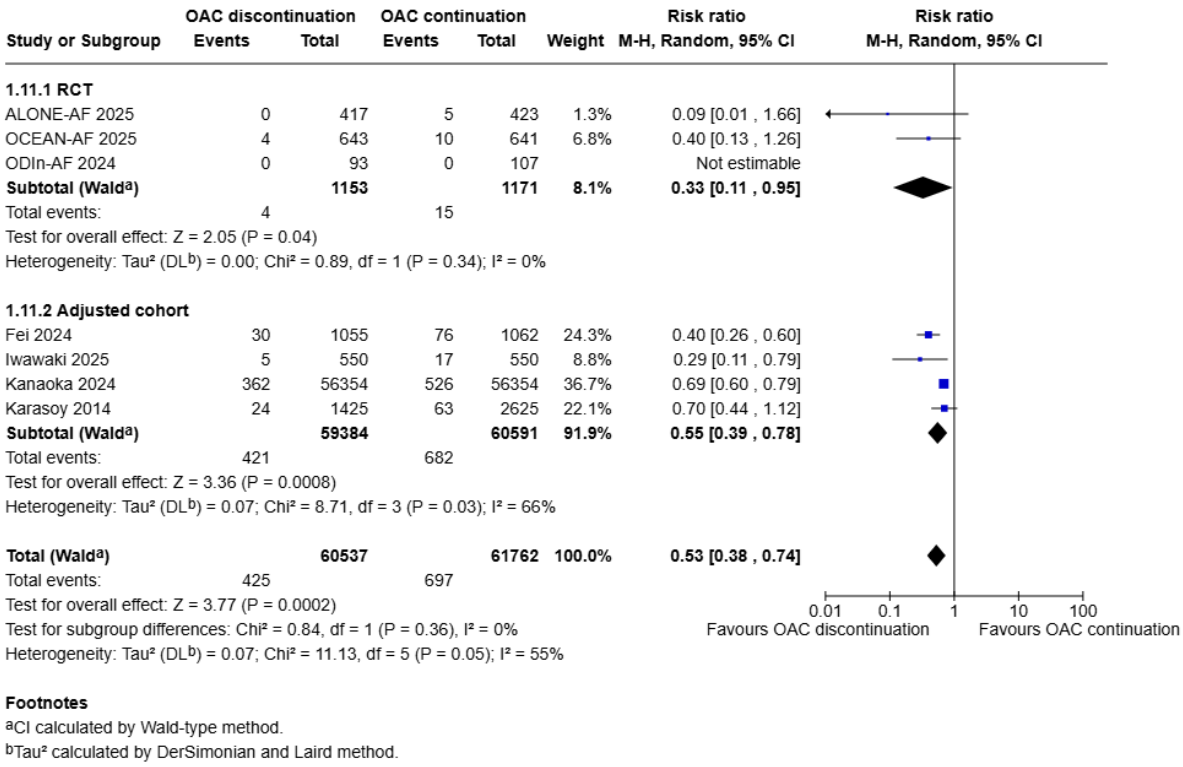
Supplemental Figure 4. Forest plots for subgroup analyses of thromboembolic events according to aspirin use in patients after atrial fibrillation ablation.
AF = atrial fibrillation; CI = confidence interval; OAC = oral anticoagulation; RR = risk ratio; I^2 = heterogeneity.



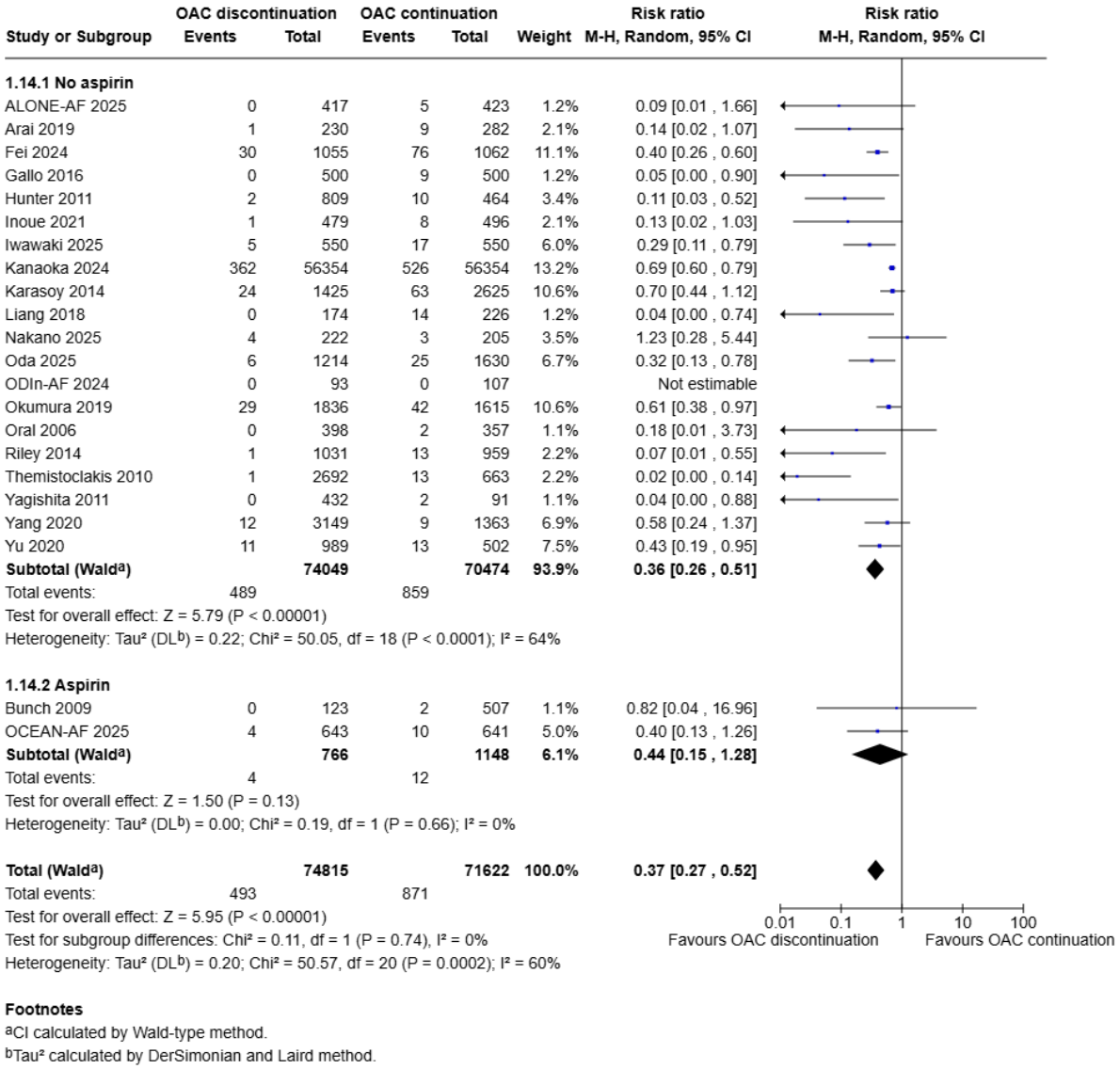
Supplemental Figure 5. Forest plot for the risk-of-bias restricted analysis of thromboembolic events in patients after atrial fibrillation ablation.
AF = atrial fibrillation; CI = confidence interval; OAC = oral anticoagulation; RR = risk ratio; I^2 = heterogeneity.



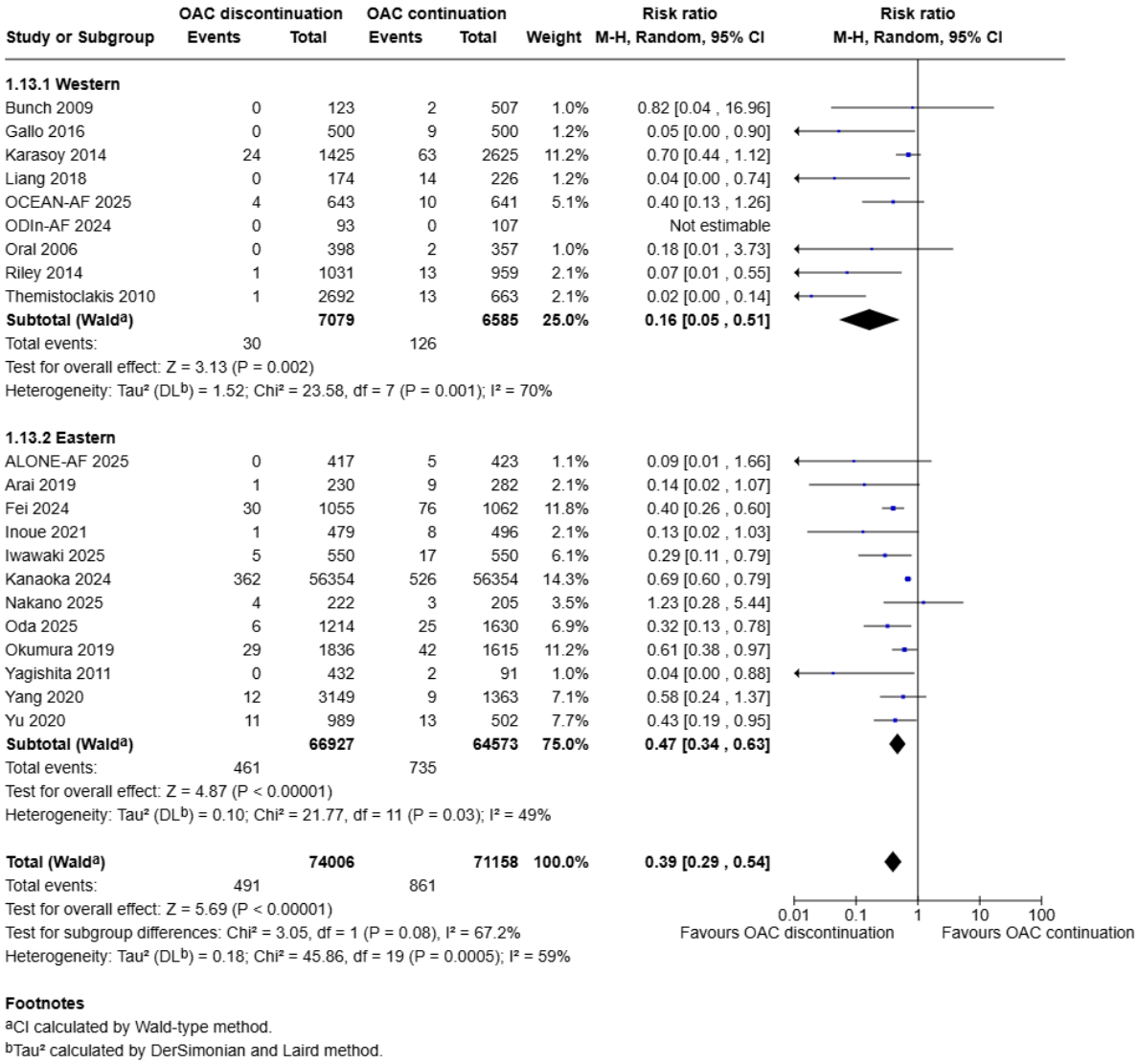
Supplemental Figure 6. Forest plots for subgroup analyses of major bleeding according to oral anticoagulant type in patients after atrial fibrillation ablation.
AF = atrial fibrillation; CI = confidence interval; OAC = oral anticoagulation; RR = risk ratio; I^2 = heterogeneity.



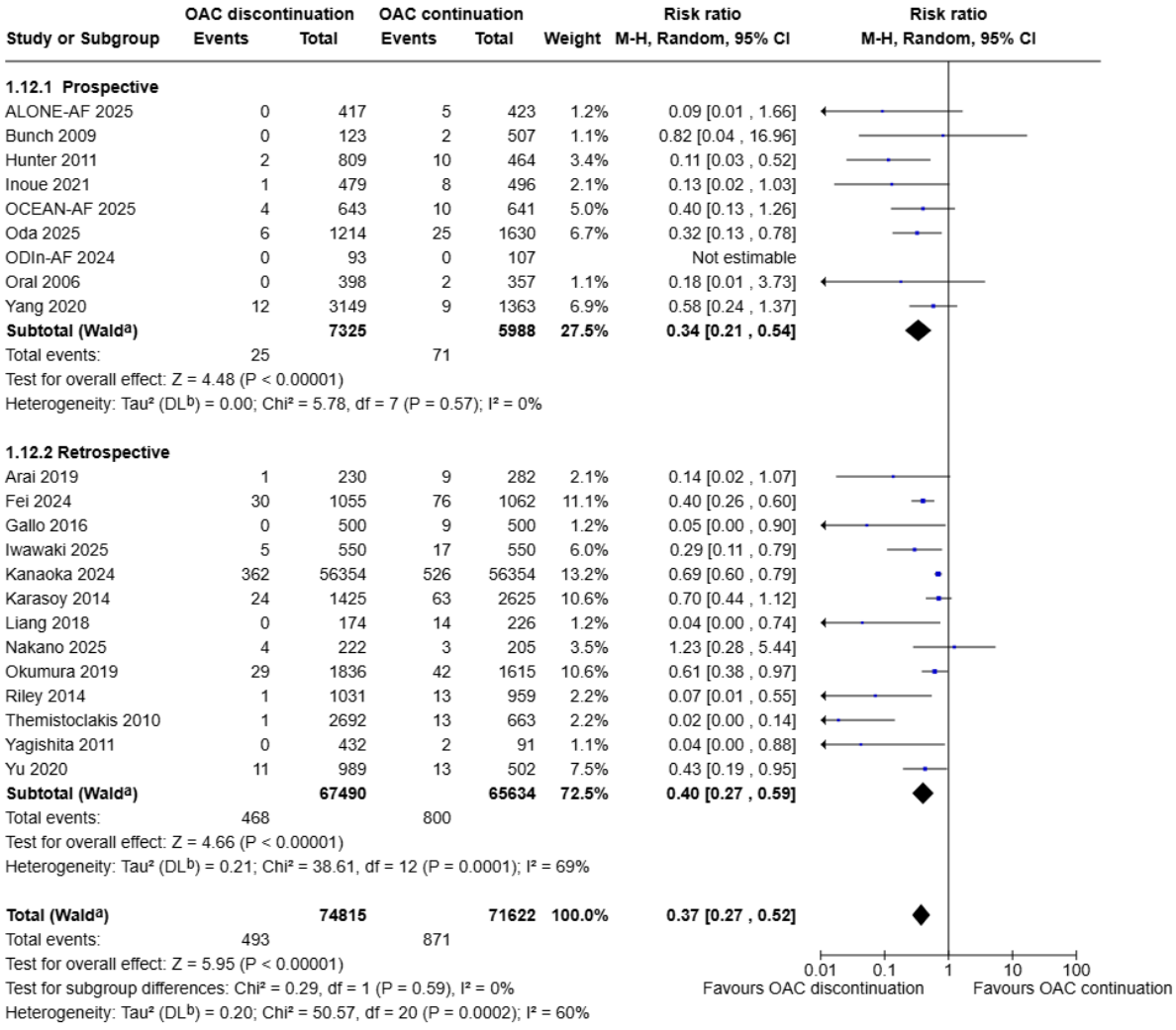
Supplemental Figure 7. Forest plots for subgroup analyses of major bleeding according to randomized trial versus adjusted observational cohort evidence in patients after atrial fibrillation ablation.
AF = atrial fibrillation; CI = confidence interval; OAC = oral anticoagulation; RR = risk ratio; I^2 = heterogeneity.



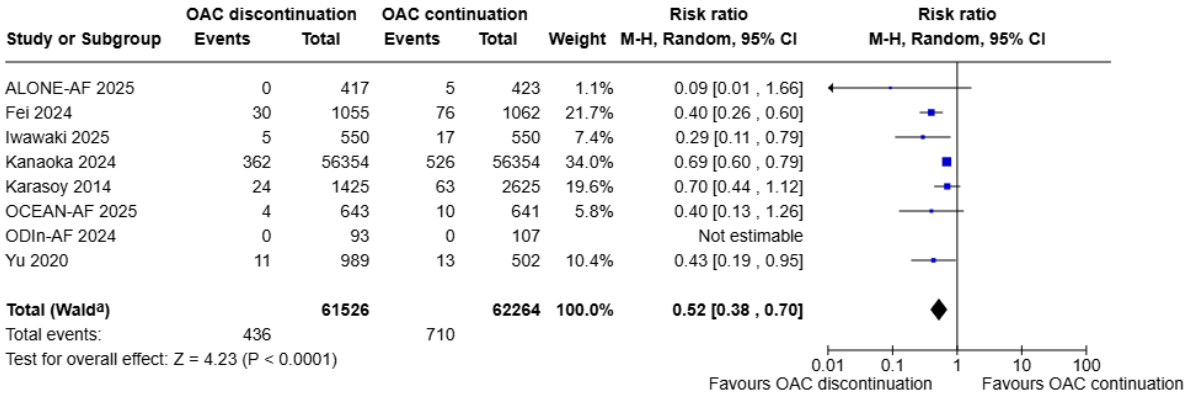
Supplemental Figure 8. Forest plots for subgroup analyses of major bleeding according to aspirin use in patients after atrial fibrillation ablation.
AF = atrial fibrillation; CI = confidence interval; OAC = oral anticoagulation; RR = risk ratio.



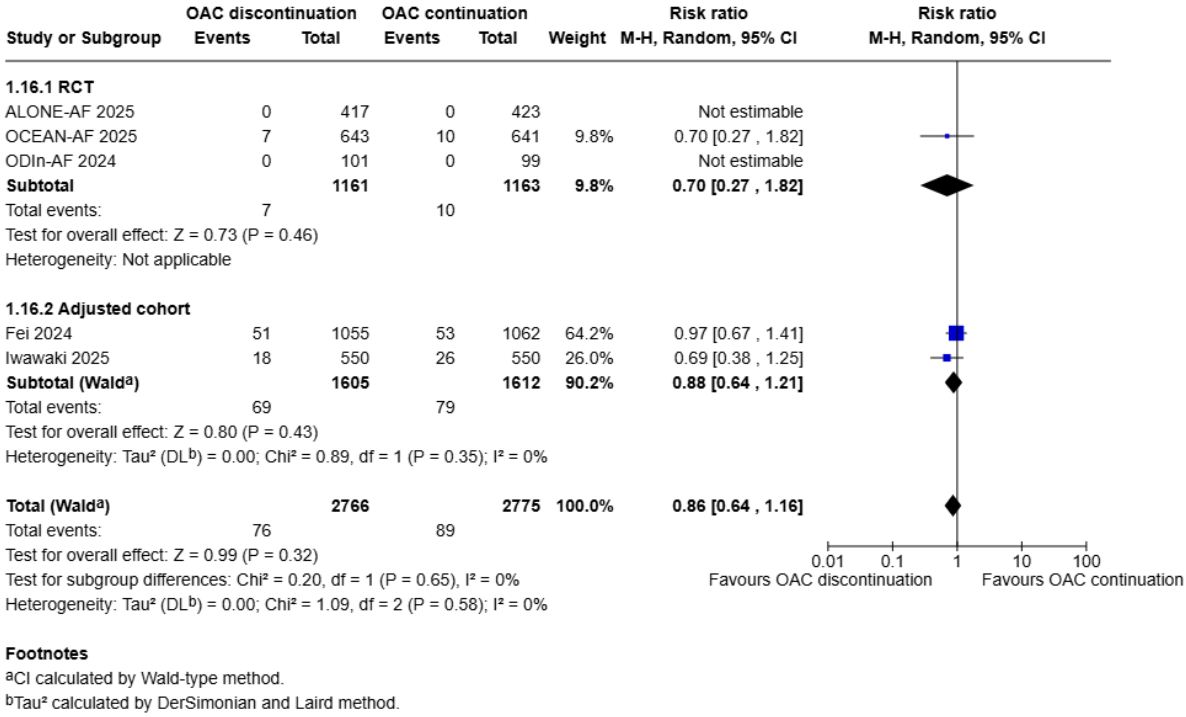
Supplemental Figure 9. Forest plots for subgroup analyses of major bleeding according to geographic region in patients after atrial fibrillation ablation.
AF = atrial fibrillation; CI = confidence interval; OAC = oral anticoagulation; RR = risk ratio; I^2 = heterogeneity.



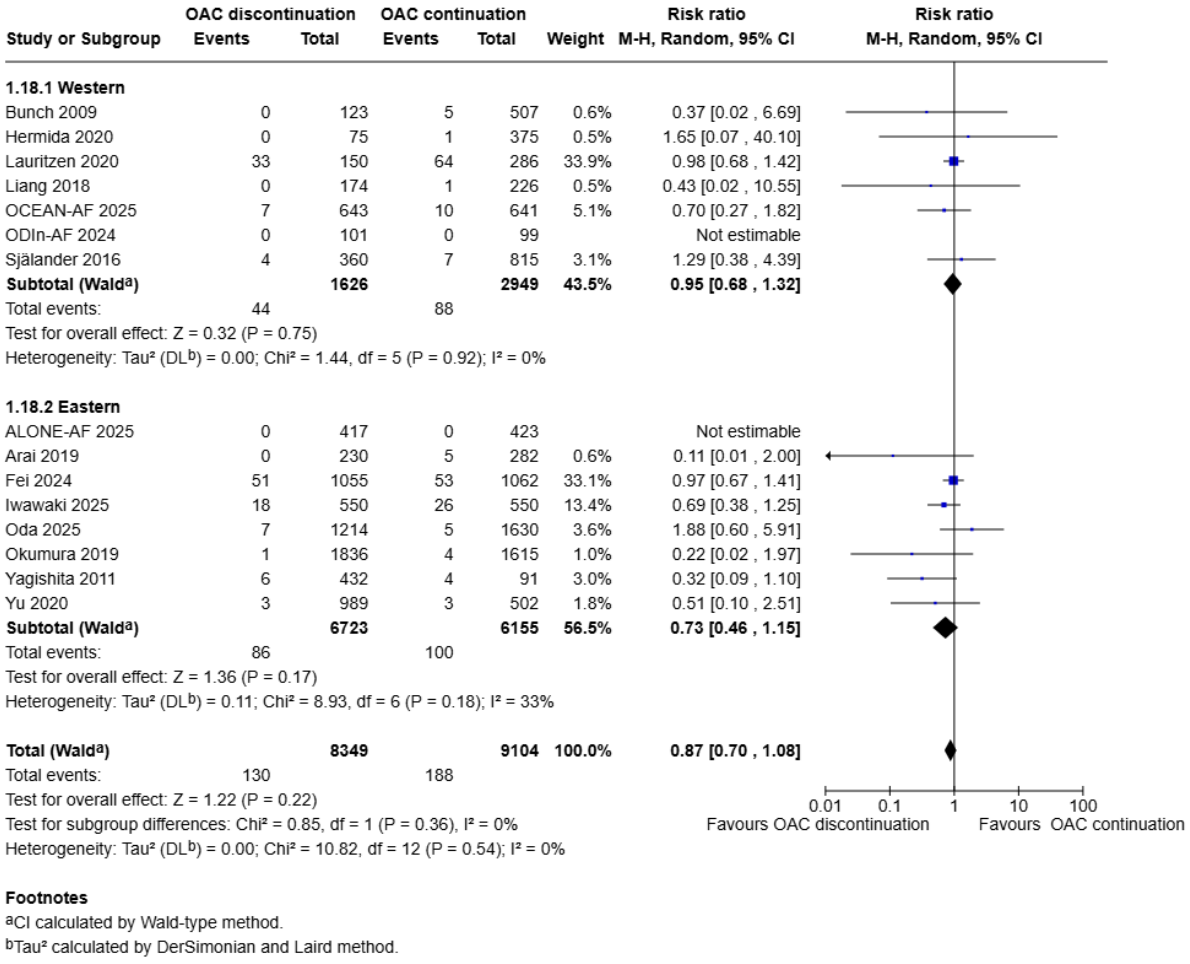
Supplemental Figure 10. Forest plots for subgroup analyses of major bleeding according to prospective versus retrospective study design in patients after atrial fibrillation ablation. AF = atrial fibrillation; CI = confidence interval; OAC = oral anticoagulation; RR = risk ratio; I^2 = heterogeneity.



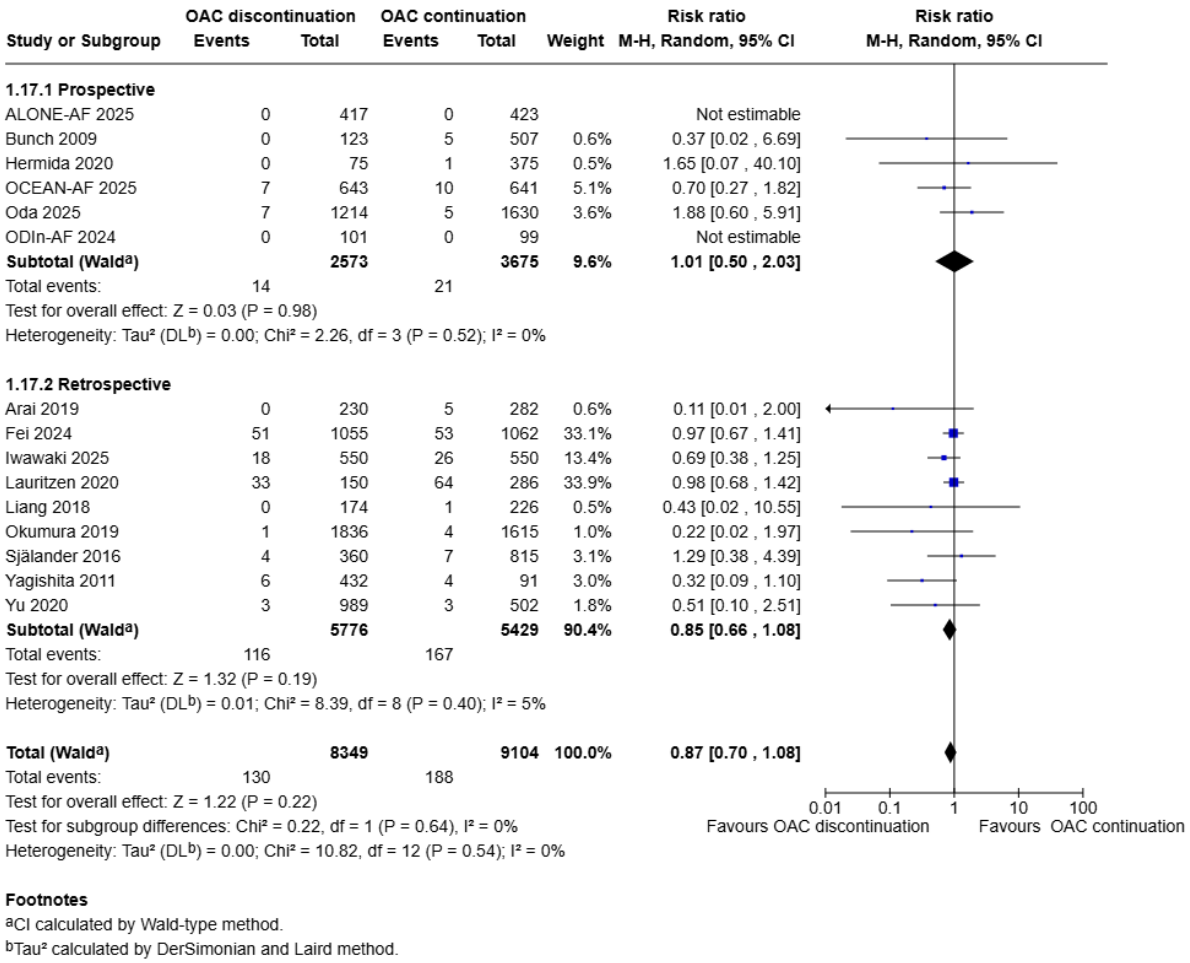
Supplemental Figure 11. Forest plot for the risk-of-bias restricted analysis of major bleeding in patients after atrial fibrillation ablation.
AF = atrial fibrillation; CI = confidence interval; OAC = oral anticoagulation; RR = risk ratio; I^2 = heterogeneity.



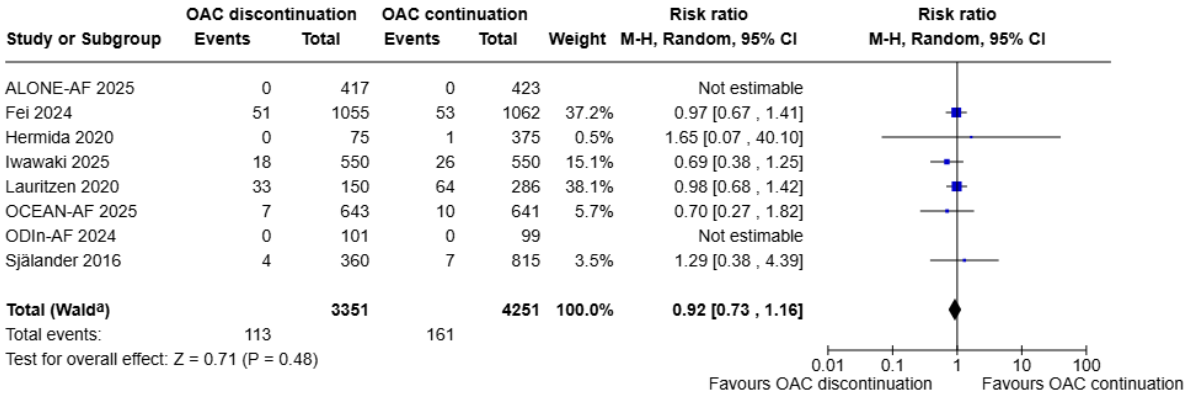
Supplemental Figure 12. Forest plots for subgroup analyses of all-cause mortality according to randomized trial versus adjusted observational cohort evidence in patients after atrial fibrillation ablation.
AF = atrial fibrillation; CI = confidence interval; OAC = oral anticoagulation; RR = risk ratio; I^2 = heterogeneity.



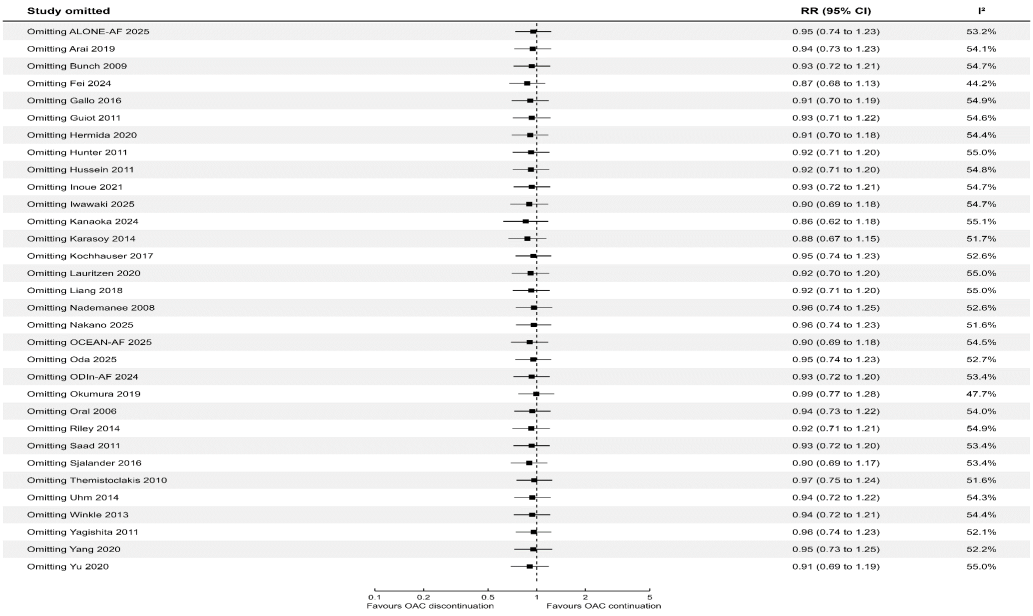
Supplemental Figure 13. Forest plots for subgroup analyses of all-cause mortality according to geographic region in patients after atrial fibrillation ablation.
AF = atrial fibrillation; CI = confidence interval; OAC = oral anticoagulation; RR = risk ratio; I^2 = heterogeneity.



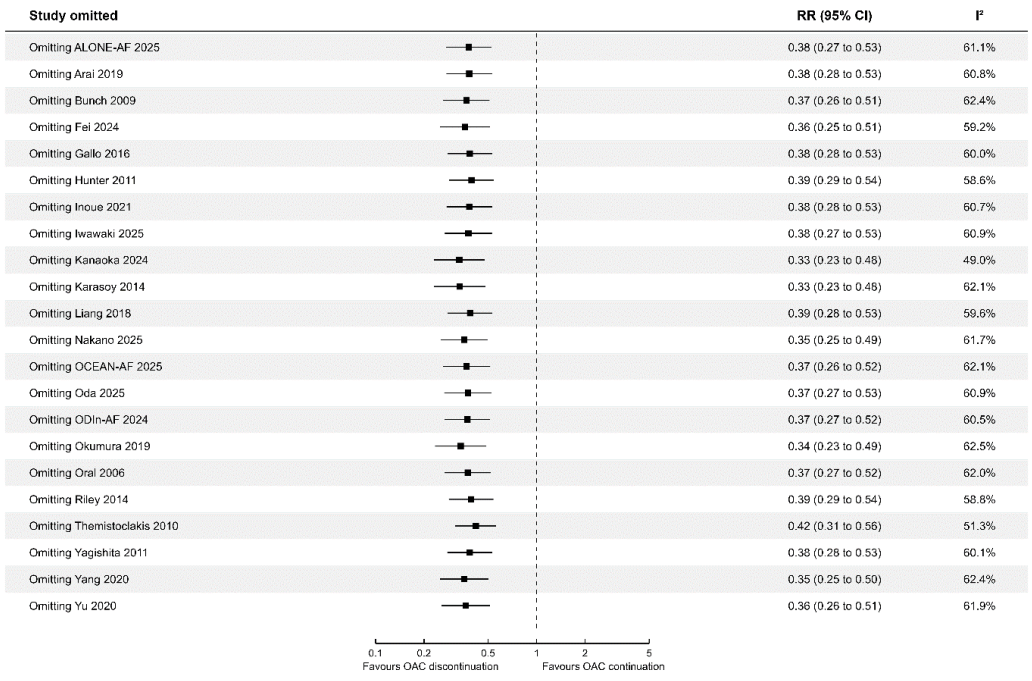
Supplemental Figure 14. Forest plots for subgroup analyses of all-cause mortality according to prospective versus retrospective study design in patients after atrial fibrillation ablation. AF = atrial fibrillation; CI = confidence interval; OAC = oral anticoagulation; RR = risk ratio; I^2 = heterogeneity.



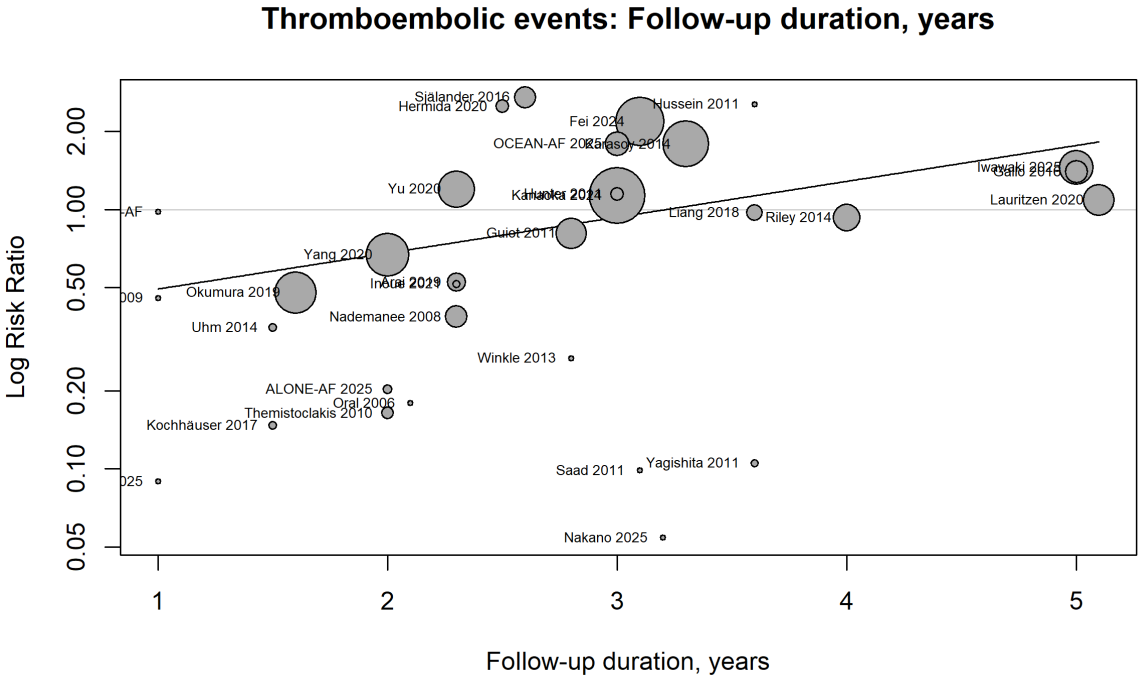
Supplemental Figure 15. Forest plot for the risk-of-bias restricted analysis of all-cause mortality in patients after atrial fibrillation ablation.
AF = atrial fibrillation; CI = confidence interval; OAC = oral anticoagulation; RR = risk ratio; I^2 = heterogeneity.



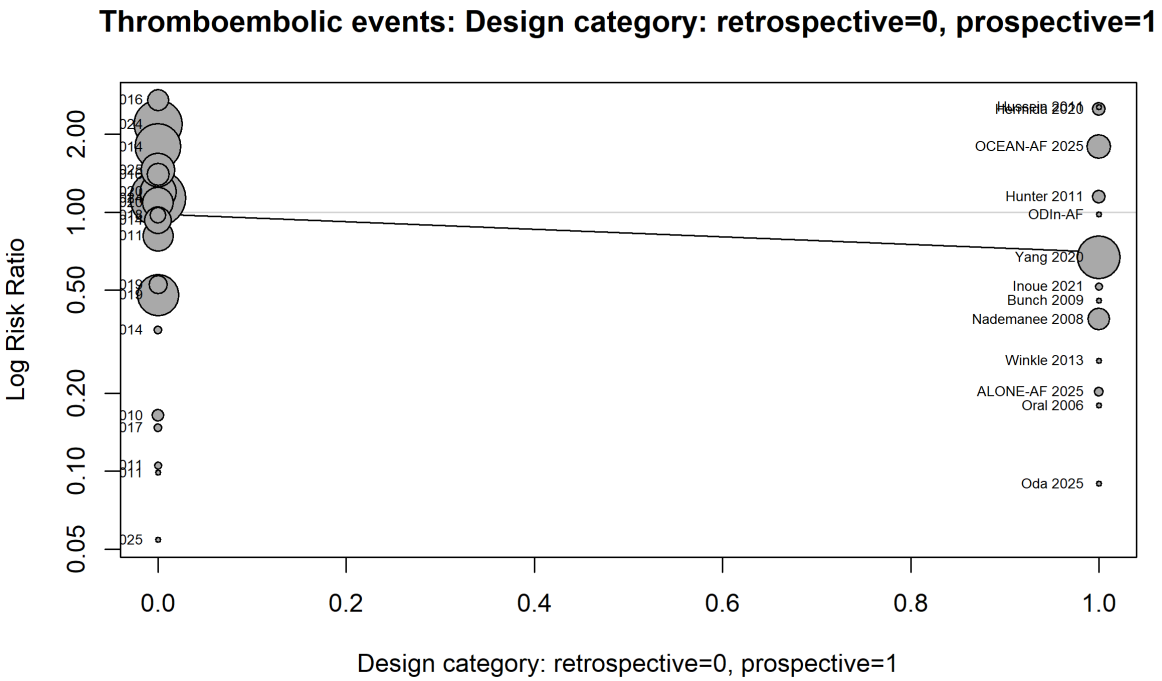
Supplemental Figure 16. Leave-one-out sensitivity analysis of thromboembolic events in patients after atrial fibrillation ablation.
AF = atrial fibrillation; CI = confidence interval; OAC = oral anticoagulation; RR = risk ratio; I^2 = heterogeneity.



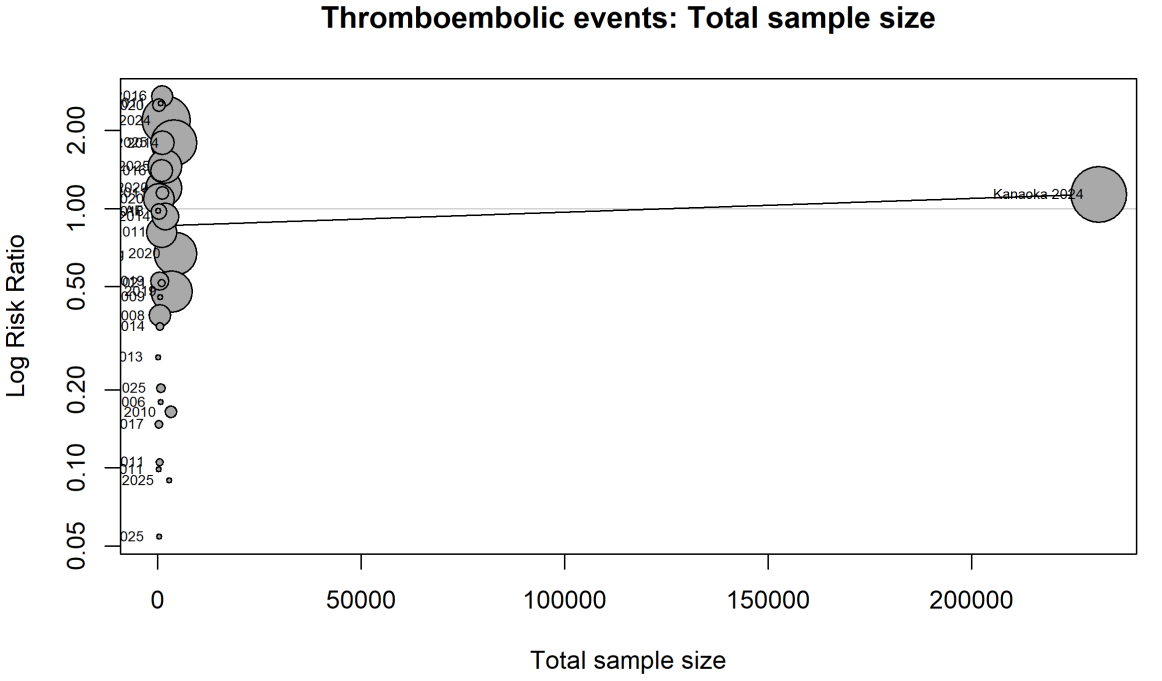
Supplemental Figure 17. Leave-one-out sensitivity analysis of major bleeding in patients after atrial fibrillation ablation.
AF = atrial fibrillation; CI = confidence interval; OAC = oral anticoagulation; RR = risk ratio; I^2 = heterogeneity.



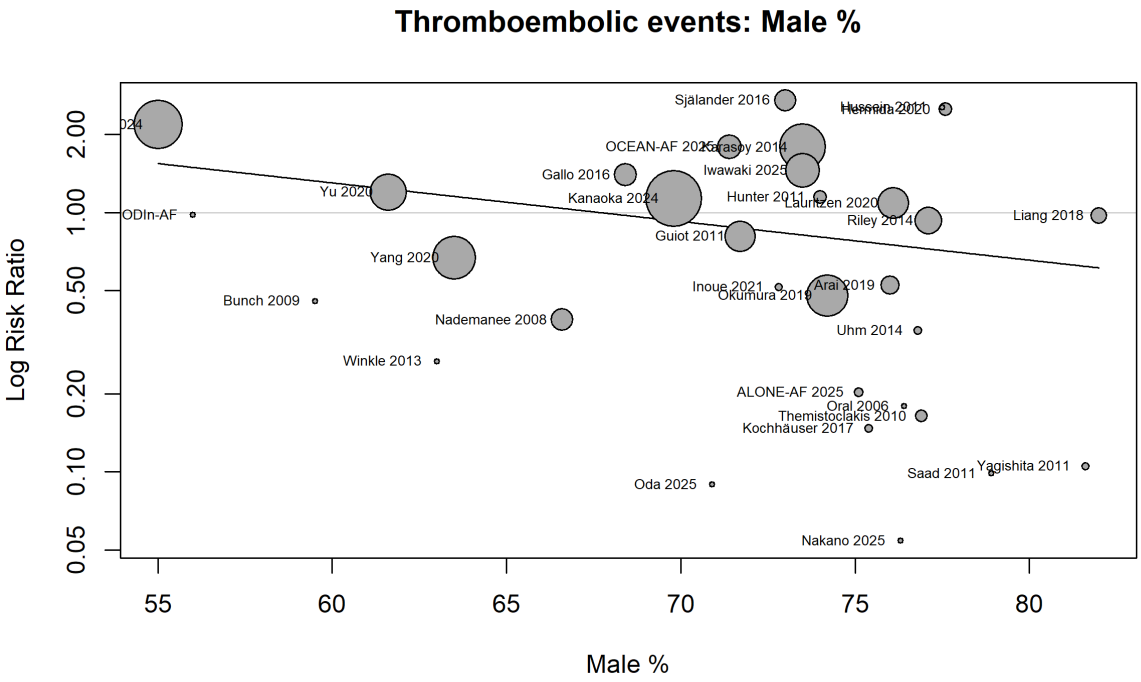
Supplemental Figure 18. Bubble plot for univariable meta-regression of thromboembolic events according to follow-up duration.



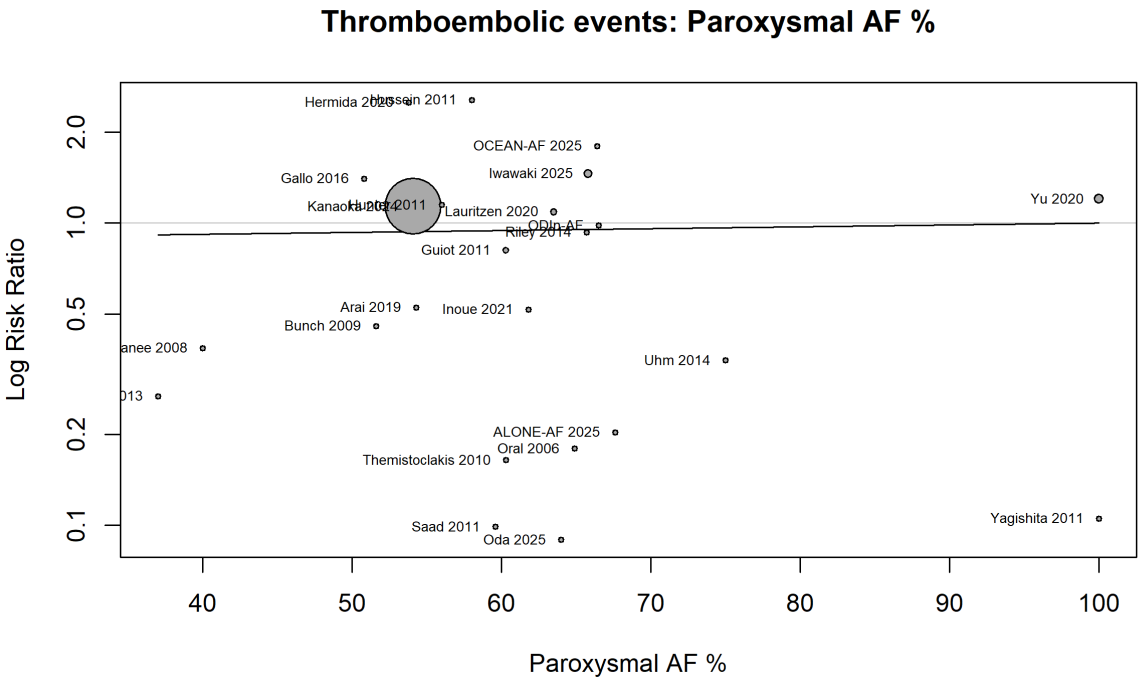
Supplemental Figure 19. Bubble plot for univariable meta-regression of thromboembolic events according to design category.



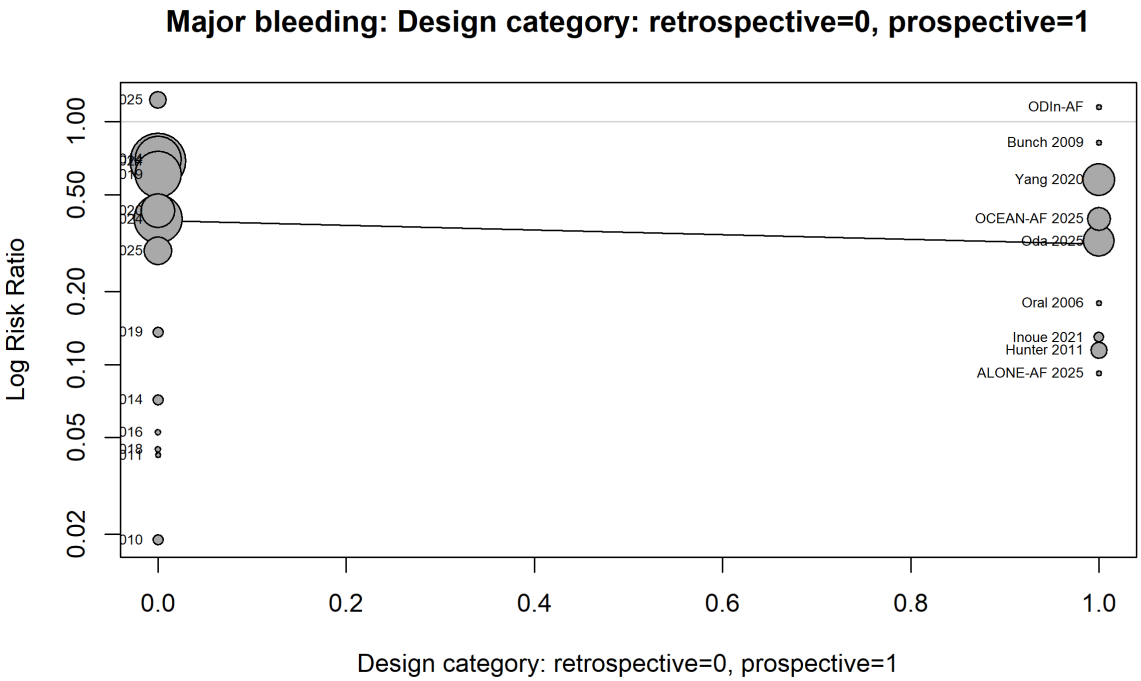
Supplemental Figure 20. Bubble plot for univariable meta-regression of thromboembolic events according to total sample size.



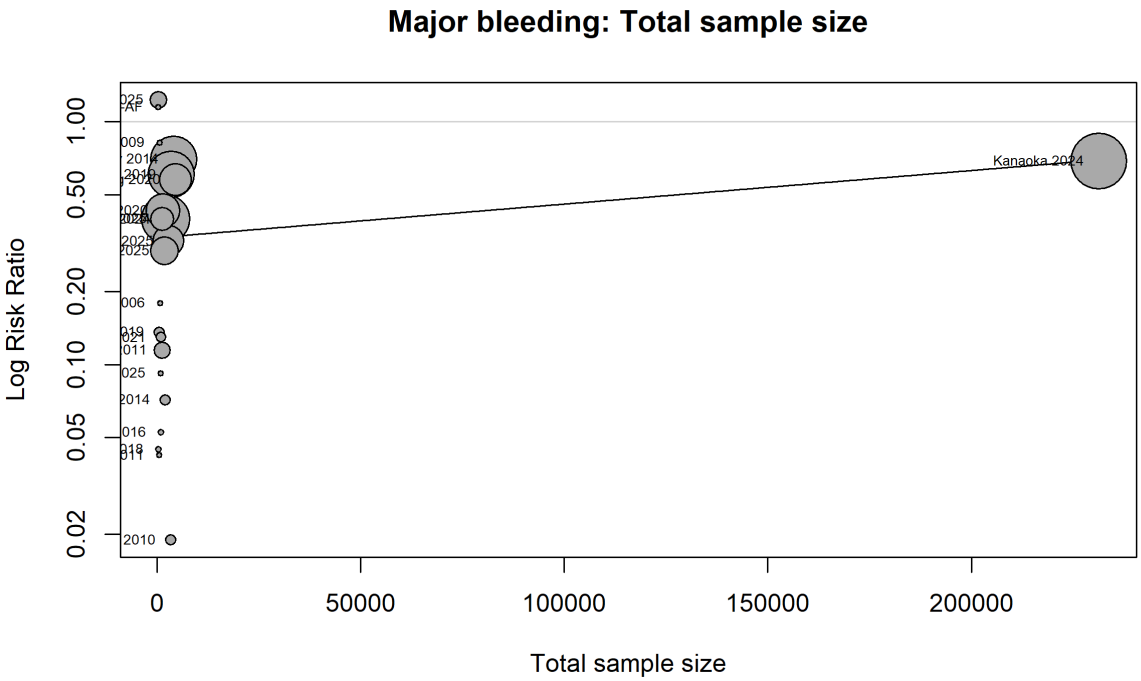
Supplemental Figure 21. Bubble plot for univariable meta-regression of thromboembolic events according to male proportion.



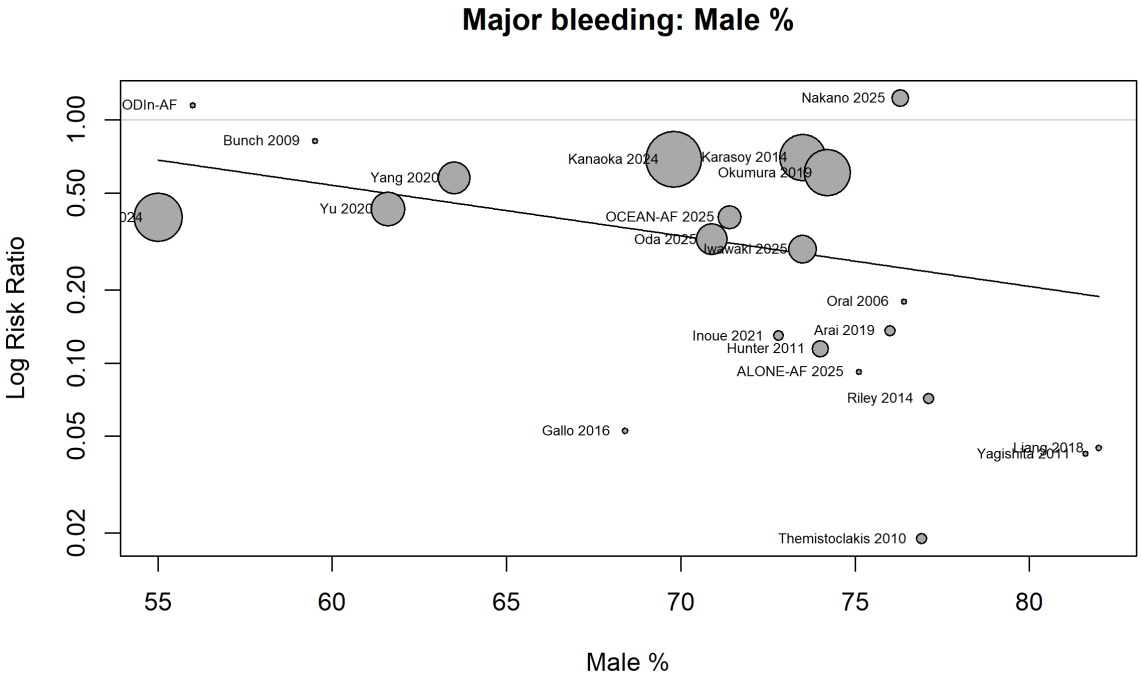
Supplemental Figure 22. Bubble plot for univariable meta-regression of thromboembolic events according to paroxysmal atrial fibrillation proportion.
AF = atrial fibrillation.



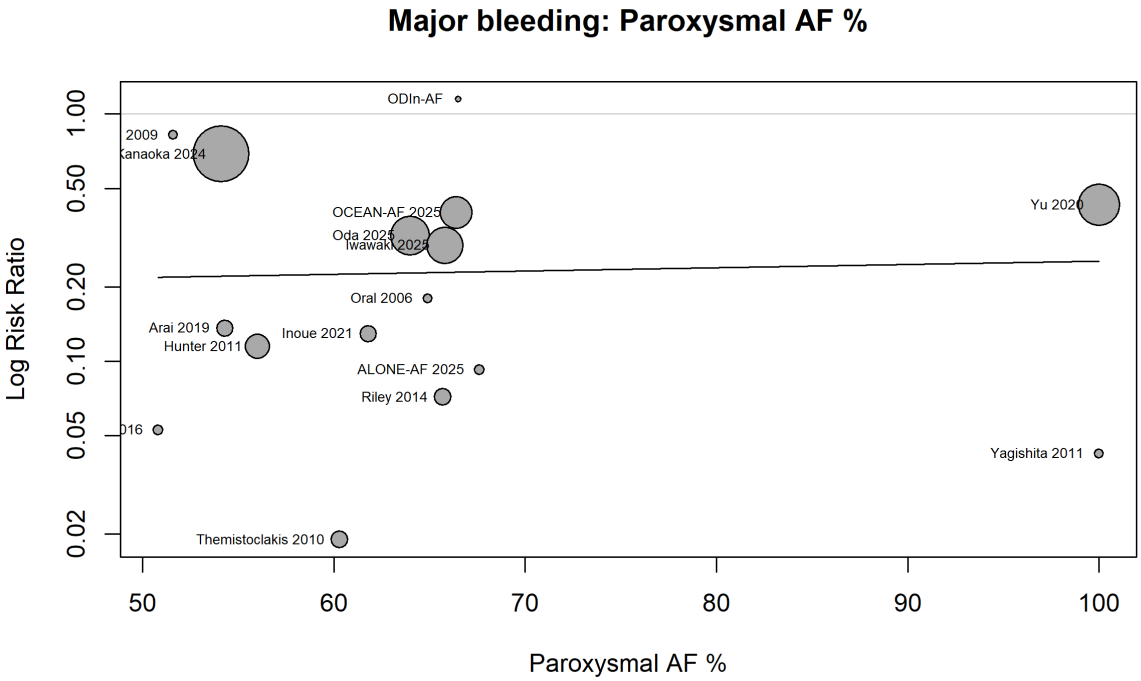
Supplemental Figure 23. Bubble plot for univariable meta-regression of major bleeding according to design category.



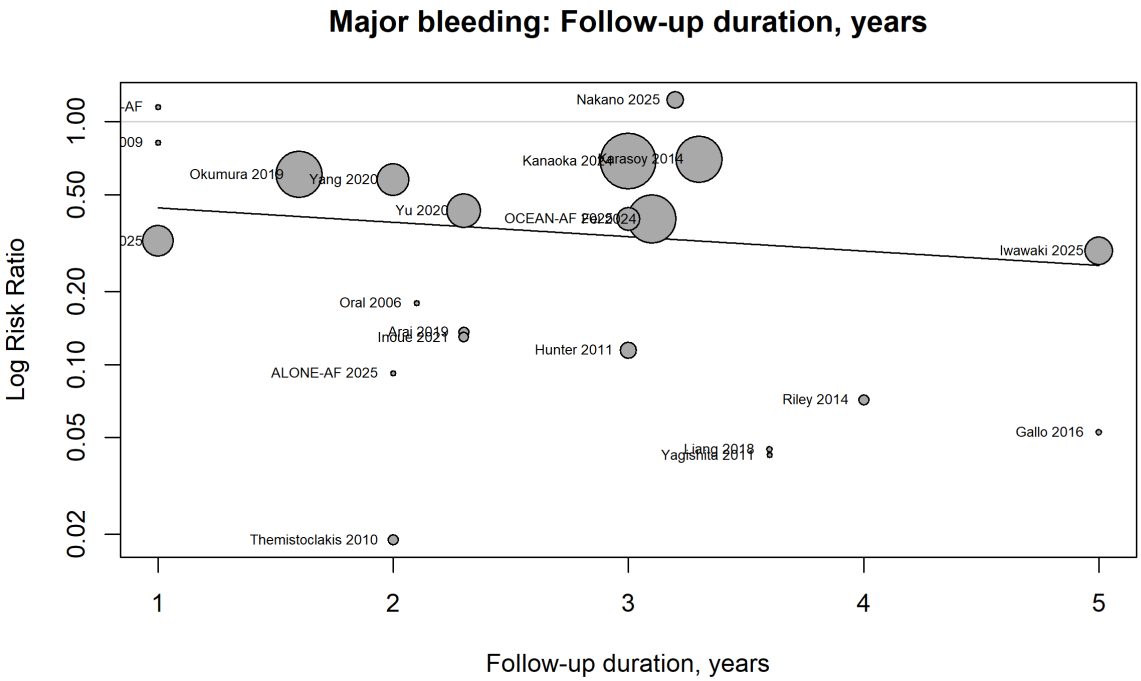
Supplemental Figure 24. Bubble plot for univariable meta-regression of major bleeding according to total sample size.



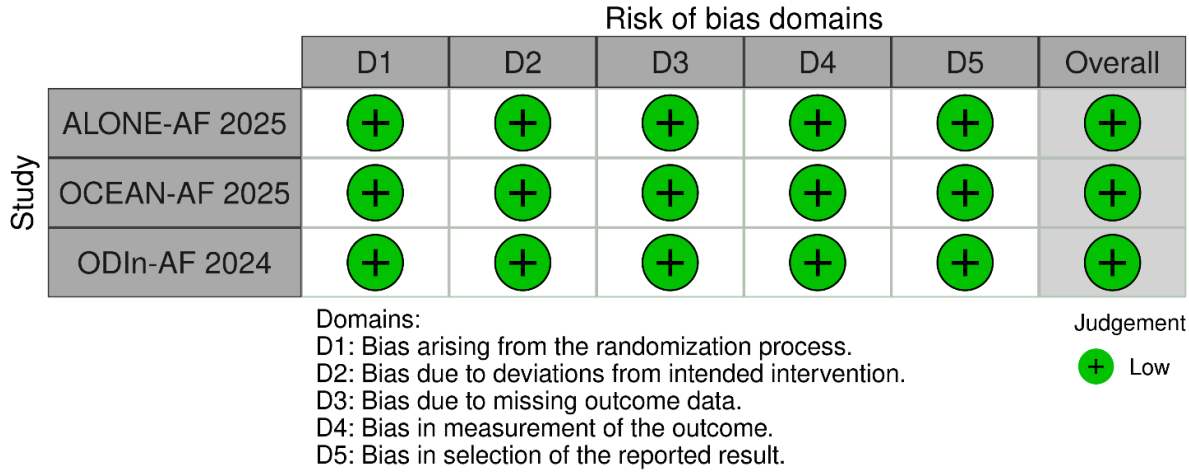
Supplemental Figure 25. Bubble plot for univariable meta-regression of major bleeding according to male proportion.



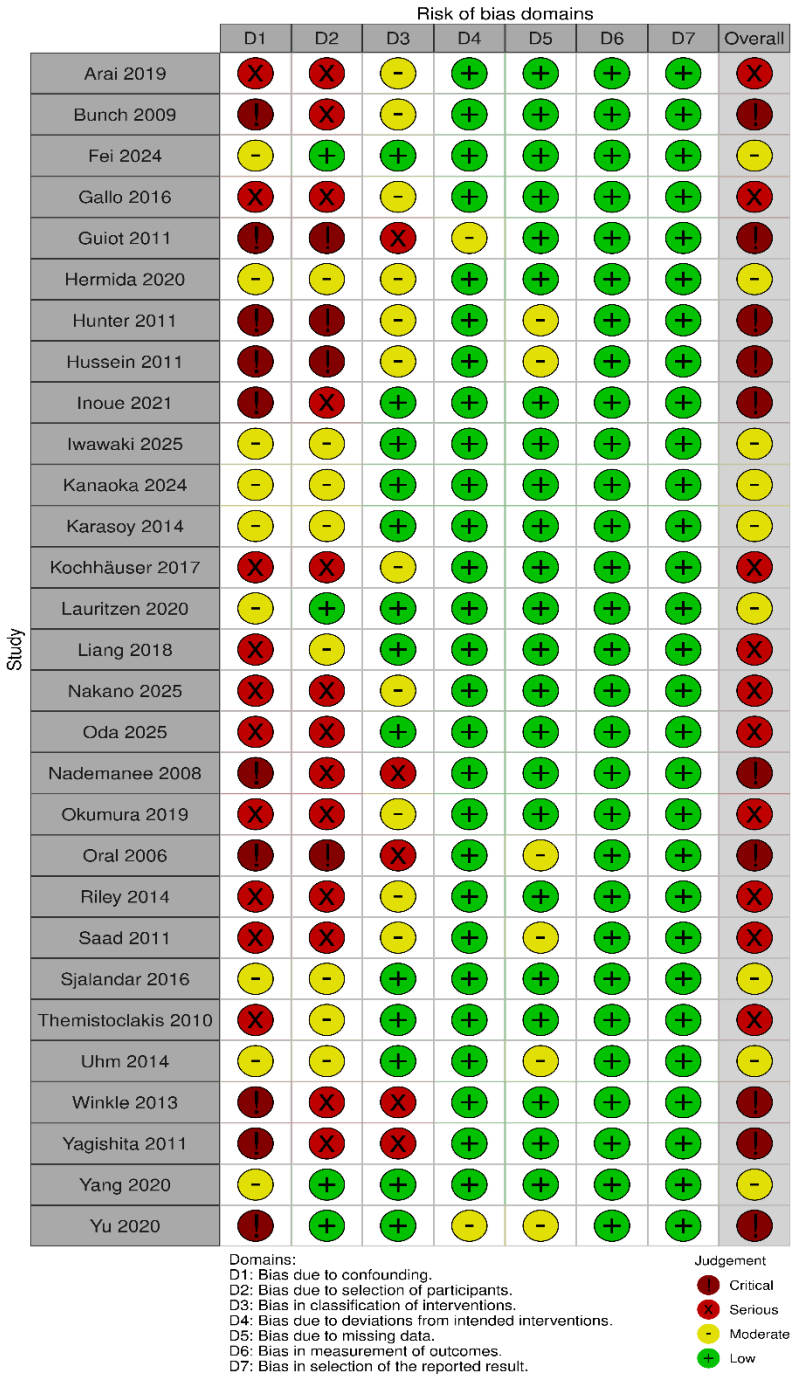
Supplemental Figure 26. Bubble plot for univariable meta-regression of major bleeding according to paroxysmal atrial fibrillation proportion.
AF = atrial fibrillation.



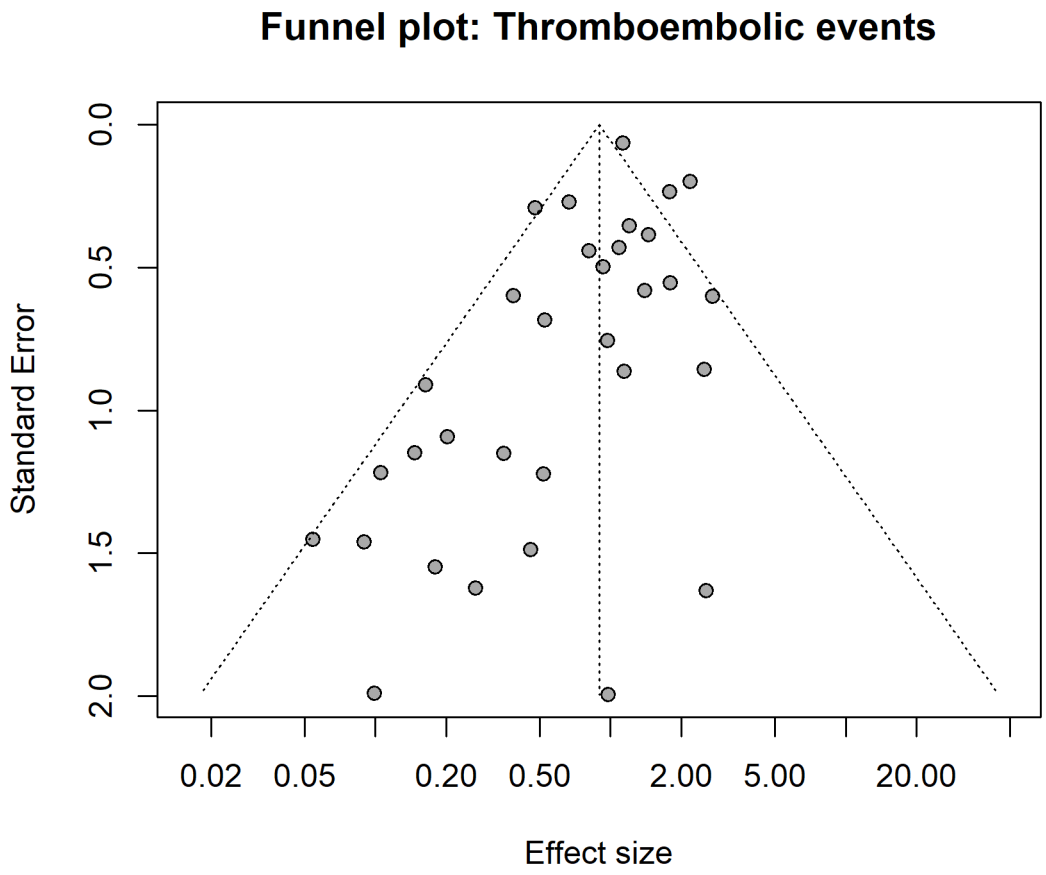
Supplemental Figure 27. Bubble plot for univariable meta-regression of major bleeding according to follow-up duration.



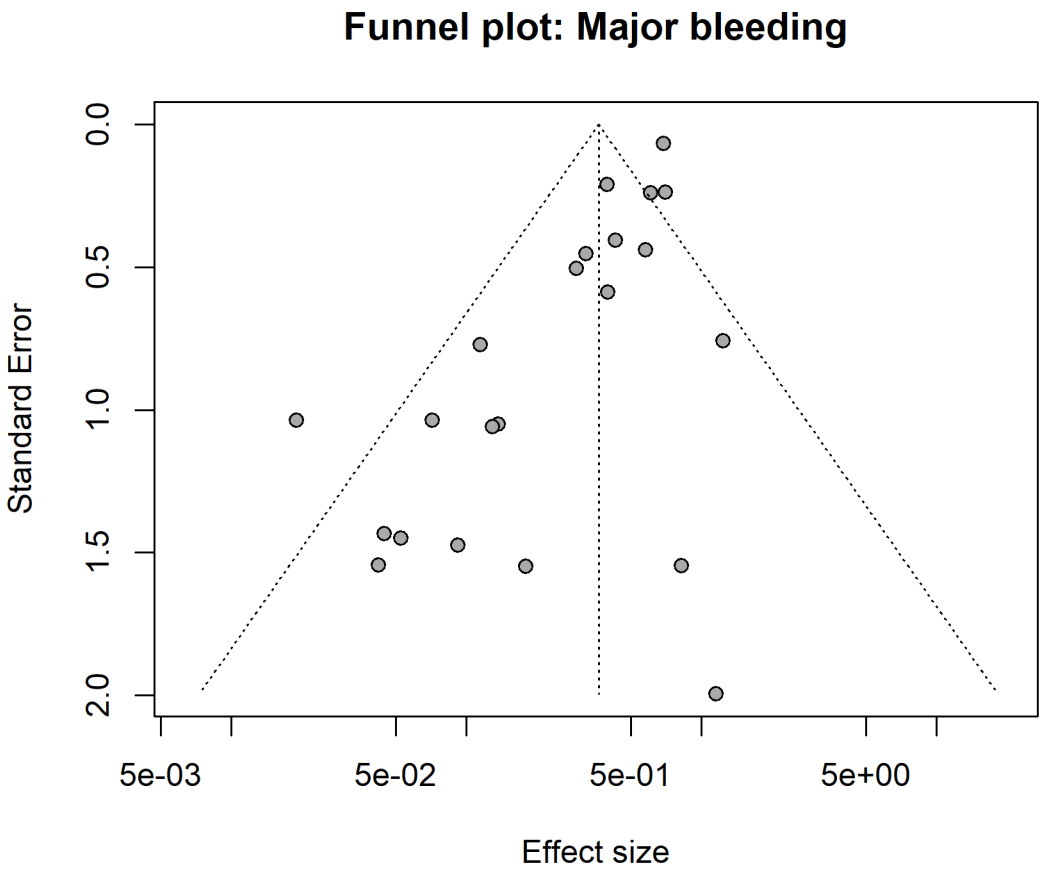
Supplemental Figure 28. Risk of bias assessment of the included randomized controlled trials using the revised Cochrane Risk of Bias 2 tool.
D1 = randomization process; D2 = deviations from intended interventions; D3 = missing outcome data; D4 = outcome measurement; D5 = selection of the reported result; RoB 2 = revised Cochrane Risk of Bias tool for randomized trials.



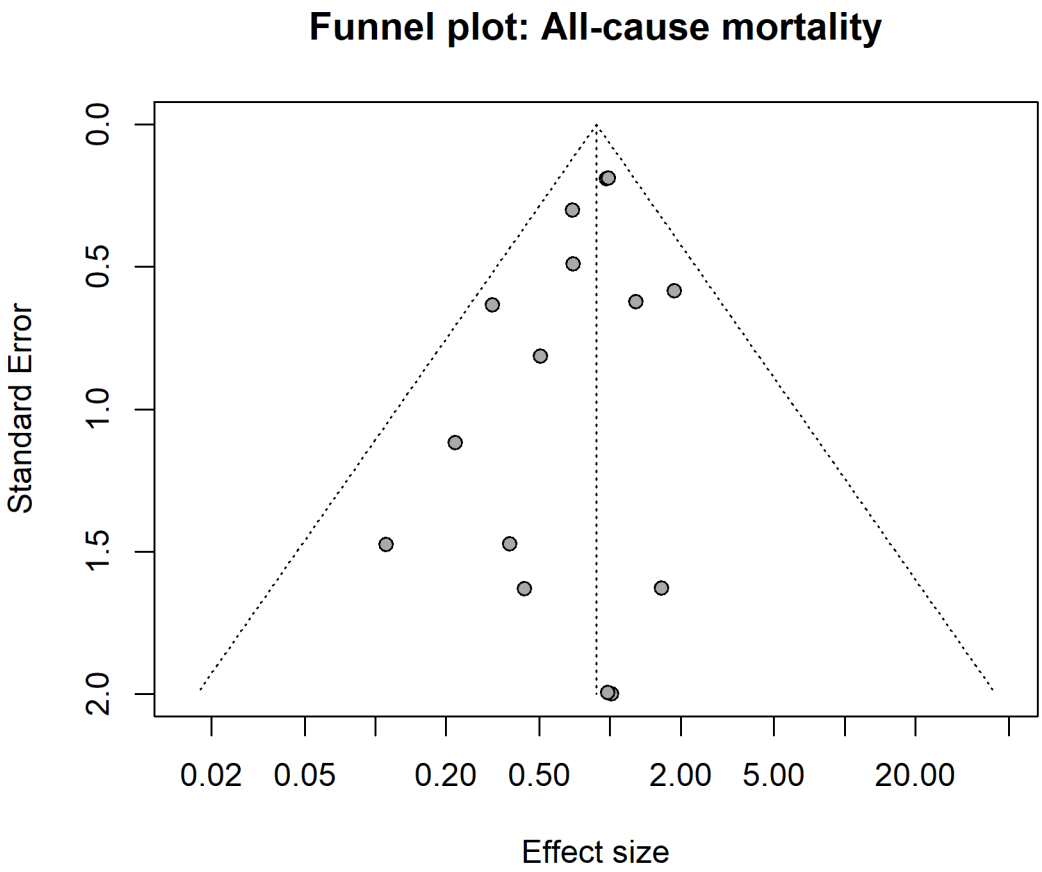
Supplemental Figure 29. Risk of bias assessment of the included observational studies using the Risk Of Bias In Non-randomized Studies of Interventions tool.
ROBINS-I = Risk Of Bias In Non-randomized Studies of Interventions.



Supplemental Figure 30. Funnel plot for thromboembolic events in patients after atrial fibrillation ablation.



Supplemental Figure 31. Funnel plot for major bleeding in patients after atrial fibrillation ablation.



Supplemental Figure 32. Funnel plot for all-cause mortality in patients after atrial fibrillation ablation.