ONLINE SUPPLEMENT

Complete search algorithm used in MEDLINE search.

Complete search algorithm used in SCOPUS search.

Supplementary Tables: S1, S2, S3, S4

Supplementary Figures: S1-S49

References used in the Supplement.

Complete search algorithm used in MEDLINE search.

("ischemic stroke"[All Fields] OR "stroke"[All Fields]) AND ("atrial fibrillation"[All Fields]) AND ("anticoagulation"[All Fields] OR "anticoagulant"[All Fields] OR "vitamin K antagonist"[All Fields] OR "warfarin"[All Fields] OR "NOAC"[All Fields]) OR "DOAC"[All Fields] OR "direct oral anticoagulant"[All Fields]) AND ("early"[All Fields]) AND ("initiation"[All Fields])

Complete search algorithm used in SCOPUS search.

(TITLE-ABS-KEY (({ischemic stroke} OR)) AND TITLE-ABS-KEY ({atrial fibrillation}) AND TITLE-ABS-KEY (({anticoagulation} OR { anticoagulant} OR { vitamin K antagonist} OR { warfarin} OR {NOAC} OR {DOAC} OR {direct oral anticoagulant})) AND TITLE-ABS-KEY ({early}) AND TITLE-ABS-KEY ({initiation}))

Supplementary Table-S1. Table of excluded studies with reasons for exclusion.

Study Name	Reason(s) for exclusion
Altavilla et al.[1]	No early initiation of anticoagulation - Bridging with low molecular weight heparin
Butcher et al.[2]	No history of atrial fibrillation
Cappellari et al.[3]	Overlapping data
De Marchis et al.[4]	Overlapping data
Paciaroni et al.[5]	Overlapping data
Seiffge et al.[6]	Overlapping data
Toyoda et al.[7]	Overlapping data
Tsivgoulis et al.[8]	Overlapping data
Wilson et al.[9]	Overlapping data
Yaghi et al.[10]	Retrospective design
Yaghi et al.[11]	Bridging with low molecular weight heparin

Supplementary Table-S2. Quality assessment of included cohort studies using the Risk Of Bias In Non-randomized Studies of Interventions (ROBINS-I) tool.[12]

Study name	Confounding	Selection	Classification of Interventions	Deviation from Interventions	Missing Data	Measurements of Outcomes	Reporting	Overall
Al Bakr et al. [13]	Serious	Low	Low	Low	Low	Low	Low	Serious
Alrohimi et al. [14]	Not Applicable	Low	Not Applicable	Not Applicable	Low	Low	Low	Low
Alrohimi et al. [15]	Not Applicable	Low	Not Applicable	Not Applicable	Low	Low	Low	Low
Gioia et al. [16]	Not Applicable	Low	Not Applicable	Not Applicable	Serious	Low	Low	Serious
SATES [17]	Not Applicable	Low	Not Applicable	Not Applicable	Serious	Low	Low	Serious
Seiffge et al. [18]	Serious	Low	Low	Low	Low	Low	Low	Serious

Supplementary Table-S3. Overview of the baseline characteristics of the patients included in the single-arm analysis according to the different time windows of initiating oral anticoagulants.

Variable	Time Windows	Prevalence			Test for Subgroup Differences
		N of studies	Pooled estimates (95%CI)	I^2, p for Cochran Q	
Women	Within 1 week	4	48.4% (36.8-60.2%)	91%, <0.001	p= 0.68
	Within 2 weeks	6	47.8% (37.3-59.0%)	92%, <0.001	
	Overall	8	48.3% (37.3-59.2%)	98%, <0.001	
Age (years)	Within 1 week	4	73 (68-77.9)	98%, <0.001	p= 1
	Within 2 weeks	6	73.2 (70.5-76)	90%, <0.001	
	Overall	8	73.3 (71.7-75)	96%, <0.001	
NIHSS	Within 1 week	4	5 (2-8)	99%, <0.001	p= 0.76
	Within 2 weeks	6	6 (2-9)	99%, <0.001	
	Overall	8	5 (3-7)	99%, <0.001	
CHA_2DS_2-VASc	Within 1 week	4	4 (3-5)	99%, <0.001	p= 0.65
	Within 2 weeks	4	4 (4-5)	98%, <0.001	
	Overall	6	4 (4-5)	99%, <0.001	
HAS-BLED	Within 1 week	3	2 (1-4)	99%, <0.001	p= 0.66
	Within 2 weeks	3	3 (2-4)	98%, <0.001	
	Overall	4	3 (2-3)	99%, <0.001	

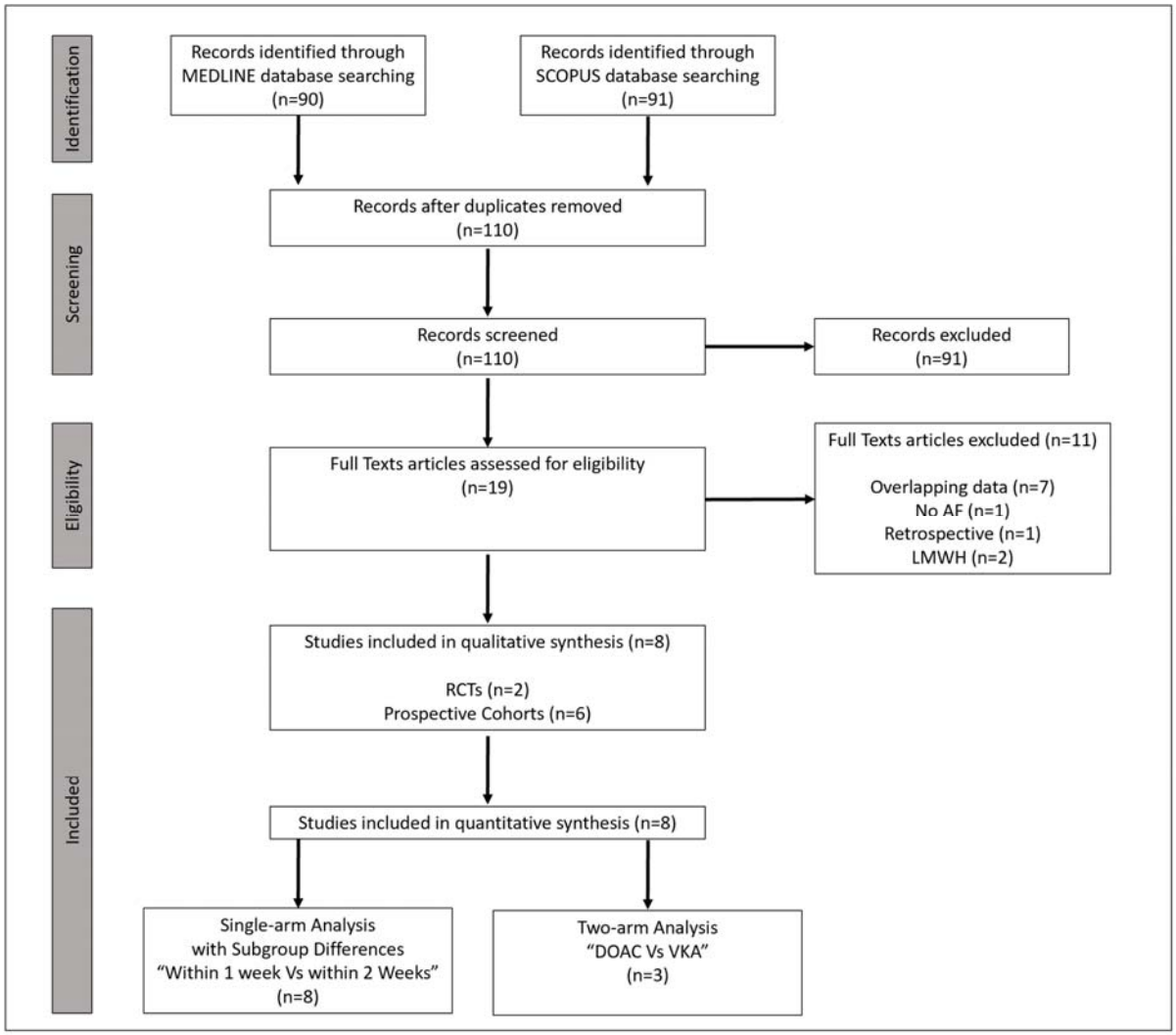
Lesion Volume (ml)	Within 1 week	1	5 (4-7)	NA	p= 0.83
	Within 2 weeks	3	5 (2-8)	89%, <0.001	
	Overall	4	5 (3-7)	87%, <0.001	
Prior Stroke	Within 1 week	3	14.5% (4.8-28.1%)	91%, <0.001	p= 0.74
	Within 2 weeks	3	16.1% (14.5-17.8%)	0%, 0.390	
	Overall	4	16.6% (11.9-21.9%)	91%, <0.001	
Hypertension	Within 1 week	4	73.1% (66-79.6%)	77%, 0.005	p= 0.31
	Within 2 weeks	3	82.3% (62.6-95.6%)	95%, <0.001	
	Overall	5	76.6% (71.7-81.2%)	89%, <0.001	
Dyslipidemia	Within 1 week	3	25.1% (14.9-36.9%)	92%, <0.001	p= 0.13
	Within 2 weeks	2	47.5% (15.2-81.0%)	98%, <0.001	
	Overall	4	32.8% (26.1-39.9%)	94%, <0.001	
Diabetes Mellitus	Within 1 week	4	23.3% (18.4-28.6%)	63%, 0.046	p= 0.14
	Within 2 weeks	3	36.7% (18.5-57%)	94%, <0.001	
	Overall	5	26.8% (22.1-31.7%)	87%, <0.001	
Chronic Kidney Failure	Within 1 week	2	19.9% (18.5-21.3%)	0%, 0.978	p= 0.82
	Within 2 weeks	2	22.9% (8.7-41.3%)	85%, 0.009	
	Overall	2	19.3% (15.6-23.3%)	83%, 0.001	

Supplementary Table-S4. Overview of the baseline characteristics of the patients included in the pairwise analysis comparing DOACs versus VKAs, stratified by the treatment initiation.

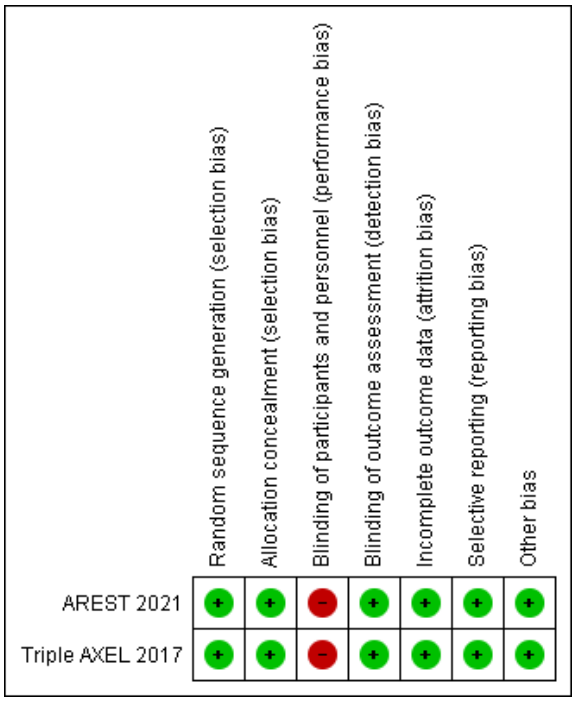
Variable	Time Windows	Effect			Test for Subgroup Differences
		N of studies	Estimates (95%CI)	I^2, p for Cochran Q	
Women	Within 1 week	2	RR 0.78 (0.49-1.26)	86%, 0.007	p= 0.008
	Within 2 weeks	2	RR 1.57 (1.29-1.92)	38%, 0.20	
	Overall	3	RR 1.08 (0.58-2.04)	99%, <0.001	
Age (years)	Within 1 week	2	MD -0.03 (-0.83 – 0.78)	0%, 0.80	p= 0.96
	Within 2 weeks	2	MD -0.06 (-1.12 – 0.99)	0%, 0.55	
	Overall	3	MD -0.04 (-0.68 – 0.60)	0%, 0.94	
NIHSS	Within 1 week	2	MD -0.34 (-3.67 – 2.99)	97%, <0.001	p= 0.35
	Within 2 weeks	2	MD -1.95 (-2.61- -1.29)	0%, 0.46	
	Overall	3	MD -0.92 (-2.41 – 0.56)	91%, <0.001	
CHA_2DS_2-VASc	Within 1 week	2	MD 0.14 (-0.23 – 0.52)	62%, 0.11	p= 0.32
	Within 2 weeks	2	MD -0.15 (-0.61 – 0.30)	50%, 0.16	
	Overall	3	MD 0.02 (-0.18 – 0.22)	43%, 0.15	
HAS-BLED	Within 1 week	2	MD 0.06 (-0.12 – 0.24)	60%, 0.11	p= 0.50
	Within 2 weeks	1	MD -1.00 (-1.04 - -0.96)	NA	
	Overall	2	MD -0.27 (-1.07 – 0.52)	100%, <0.001	

	Within 1 week	1	RR 0.75 (0.63-0.89)	NA	p< 0.001
Prior Stroke	Within 2 weeks	2	RR 1.51 (1.18-1.92)	0%, 0.46	
	Overall	2	RR 1.06 (0.58-1.94)	91%, <0.001	
	Within 1 week	2	RR 1.03 (0.89-1.18)	49%, 0.16	p= 0.87
Hypertension	Within 2 weeks	2	RR 1.01 (0.90-1.14)	78%, 0.03	
	Overall	3	RR 1.01 (0.95-1.08)	65%, 0.04	
	Within 1 week	2	RR 0.81 (0.74-0.90)	0%, 0.96	p= 0.19
Dyslipidemia	Within 2 weeks	2	RR 0.69 (0.54-0.87)	51%, 0.15	
	Overall	3	RR 0.74 (0.62-0.88)	65%, 0.03	
	Within 1 week	2	RR 1.23 (0.43-5.52)	89%, 0.002	p= 0.44
Diabetes Mellitus	Within 2 weeks	2	RR 0.76 (0.42-1.38)	72%, 0.06	
	Overall	3	RR 0.90 (0.66-1.22)	81%, 0.001	

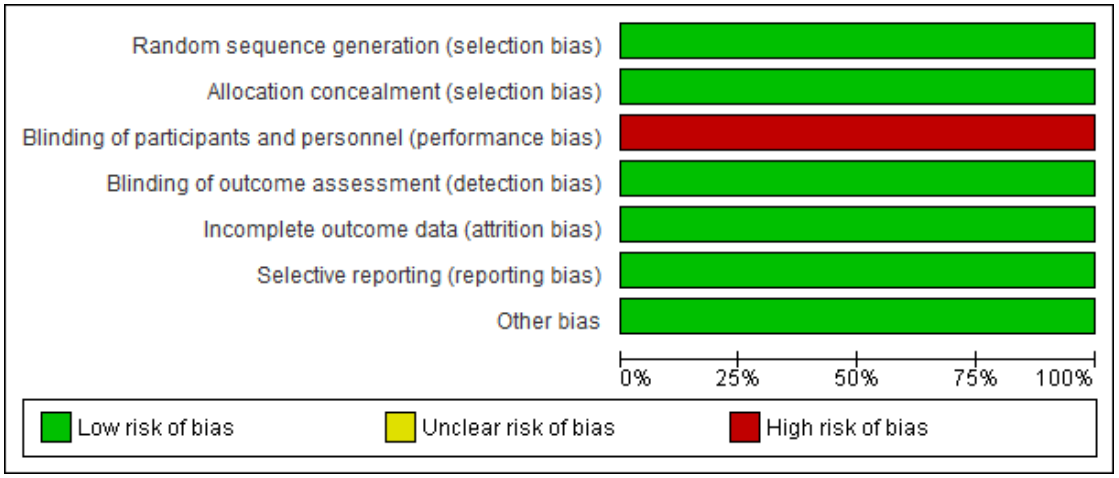
Supplementary Figure-S1. Flow chart presenting the selection of eligible studies.



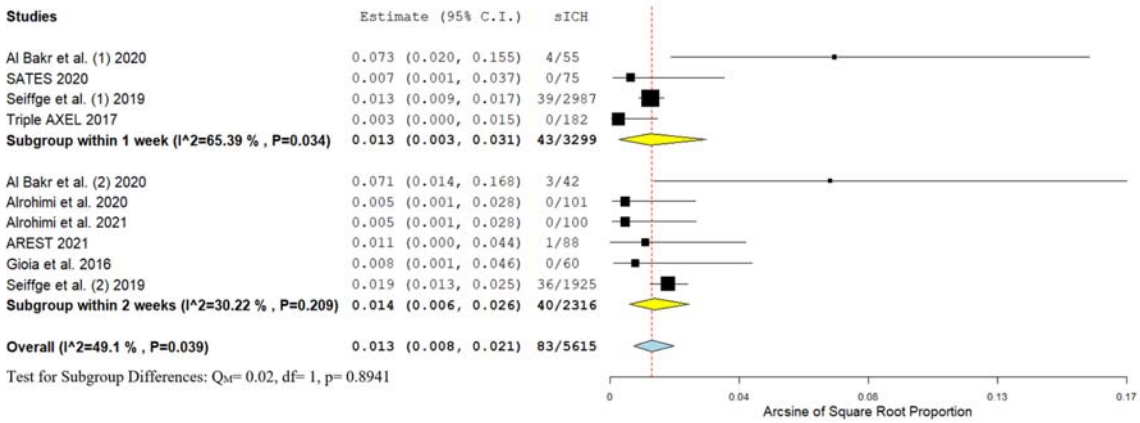
Supplementary Figure-S2. Risk of bias summary: review authors' judgments about each risk of bias item for each included study.



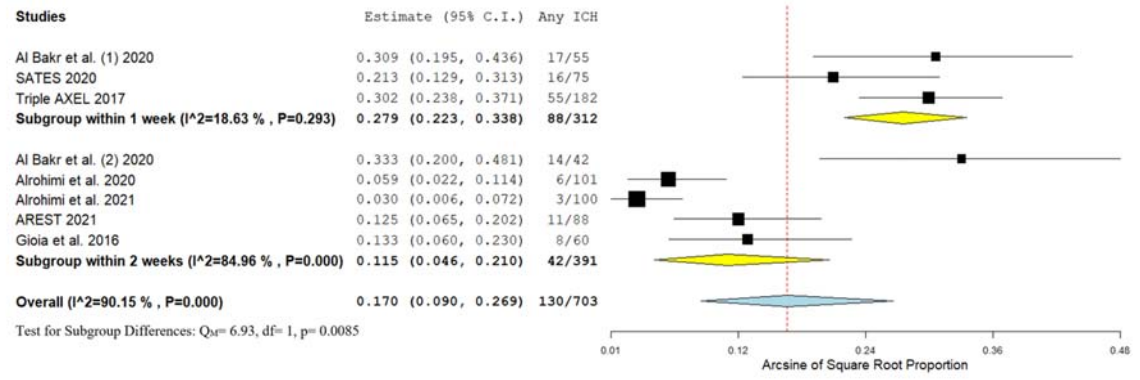
Supplementary Figure-S3. Risk of bias graph: review authors' judgments about each risk of bias item presented as percentages across all included studies.



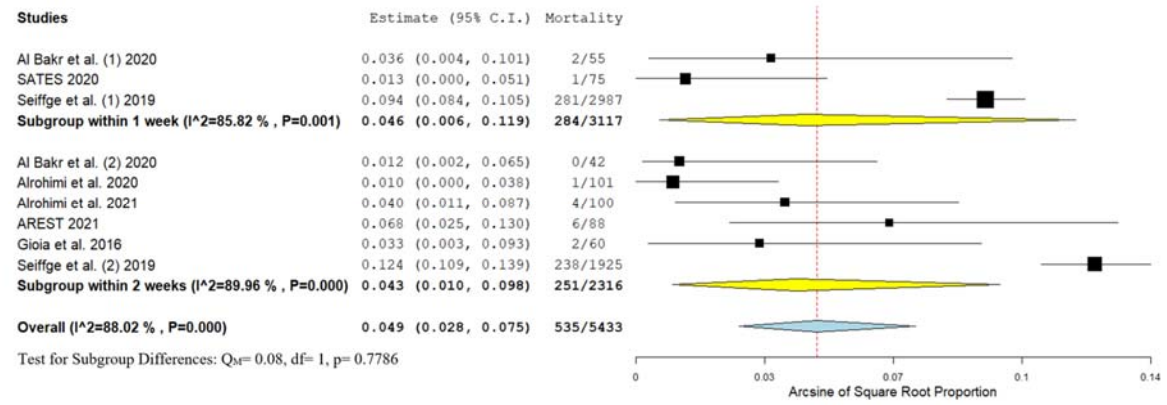
Supplementary Figure-S4. Forest plot presenting the pooled proportion of patients with symptomatic ICH following the initiation of oral anticoagulants.



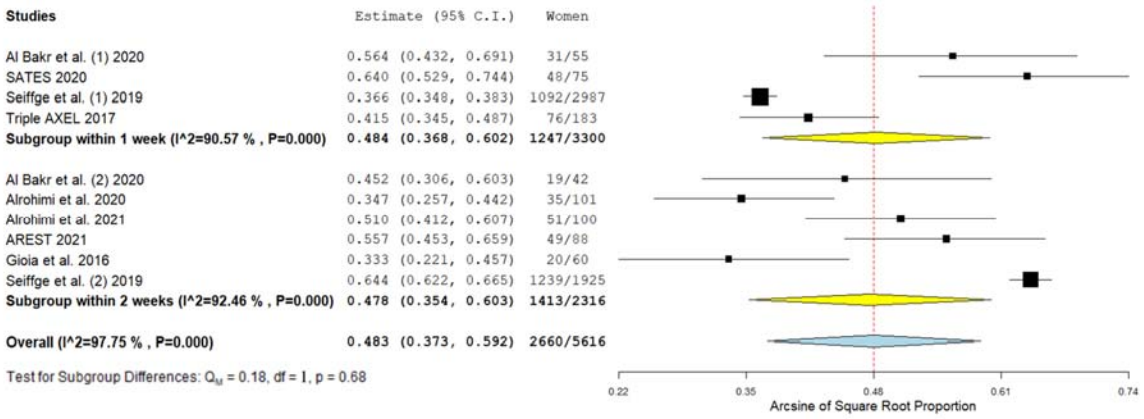
Supplementary Figure-S5. Forest plot presenting the pooled proportion of patients with any ICH following the initiation of oral anticoagulants.



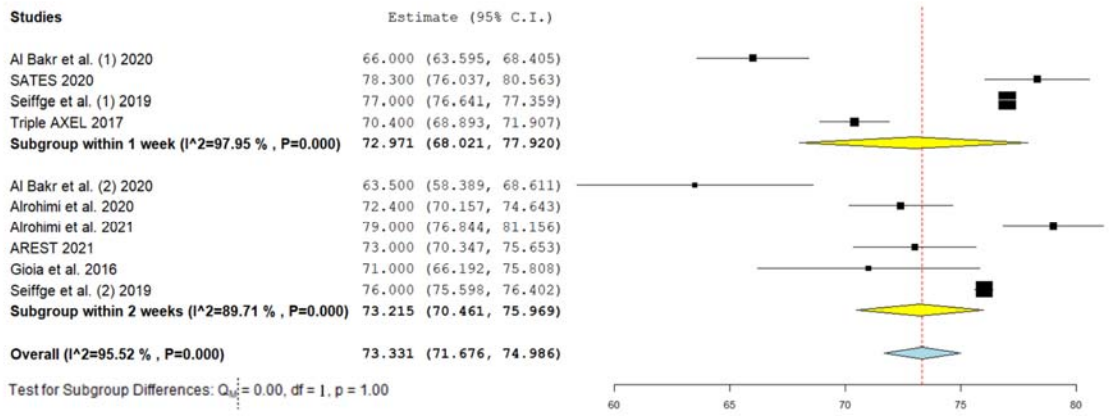
Supplementary Figure-S6. Forest plot presenting the pooled proportion of patients with all-cause mortality following the initiation of oral anticoagulants.



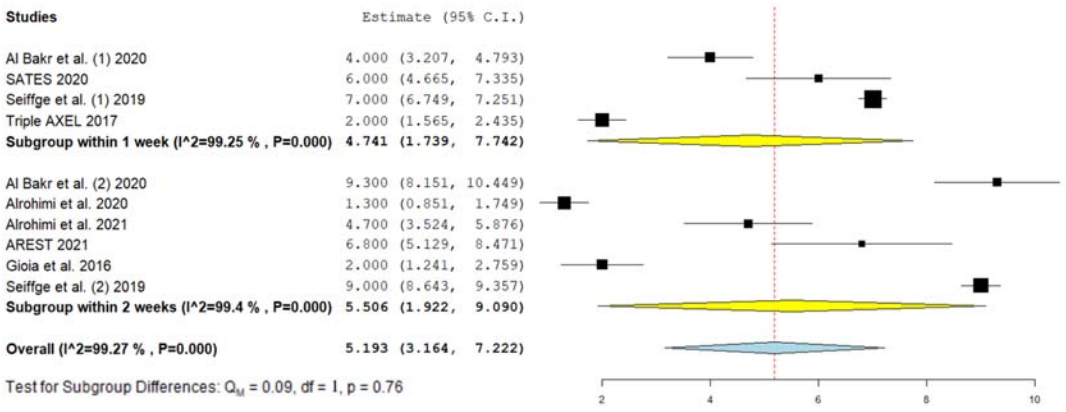
Supplementary Figure-S7. Forest plot presenting the pooled proportion of women initiating oral anticoagulants.



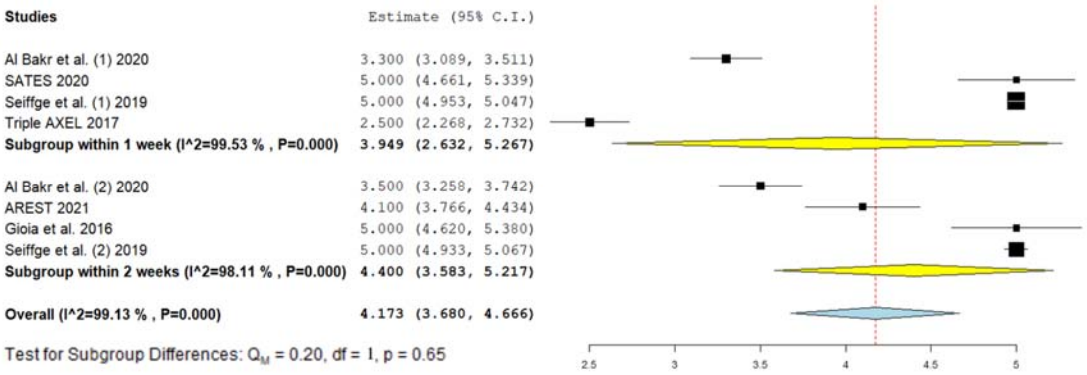
Supplementary Figure-S8. Forest plot presenting the mean age of patients initiating oral anticoagulants.



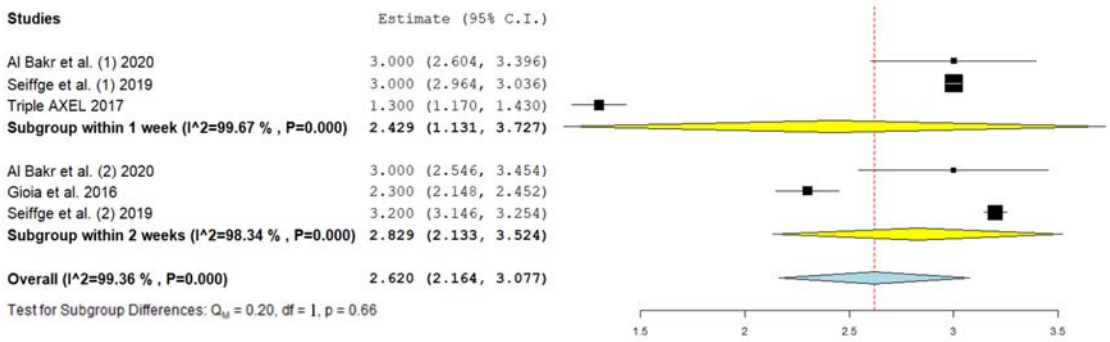
Supplementary Figure-S9. Forest plot presenting the mean baseline NIHSS score of patients initiating oral anticoagulants.



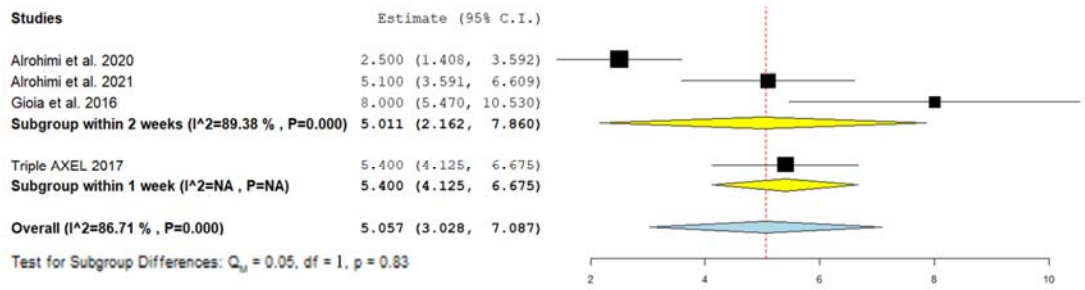
Supplementary Figure-S10. Forest plot presenting the mean baseline CHA_2DS_2-VASc score of patients initiating oral anticoagulants.



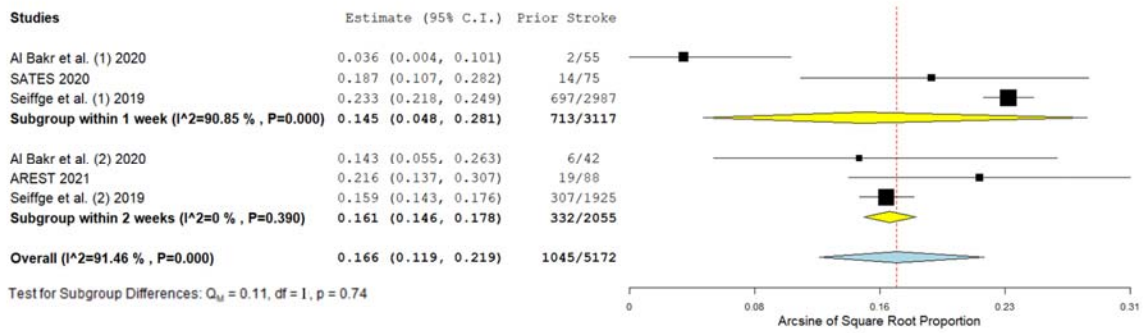
Supplementary Figure-S11. Forest plot presenting the mean baseline HAS-BLED score of patients initiating oral anticoagulants.



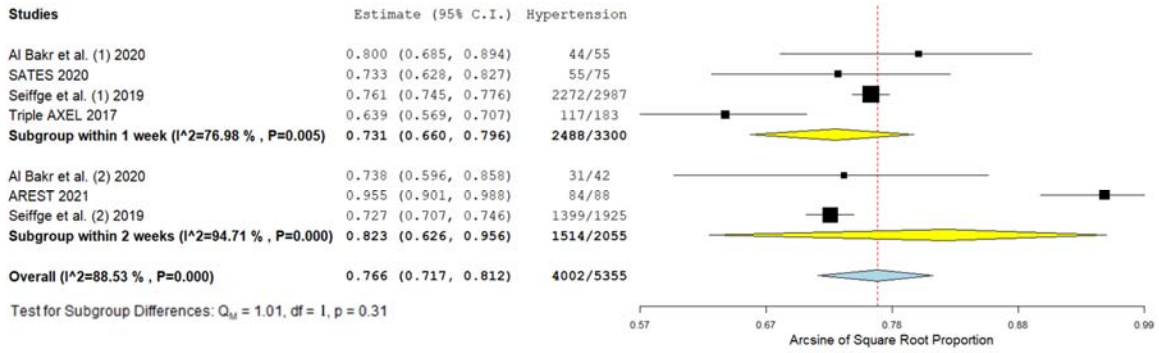
Supplementary Figure-S12. Forest plot presenting the mean baseline infarct volume (in ml) of patients initiating oral anticoagulants.



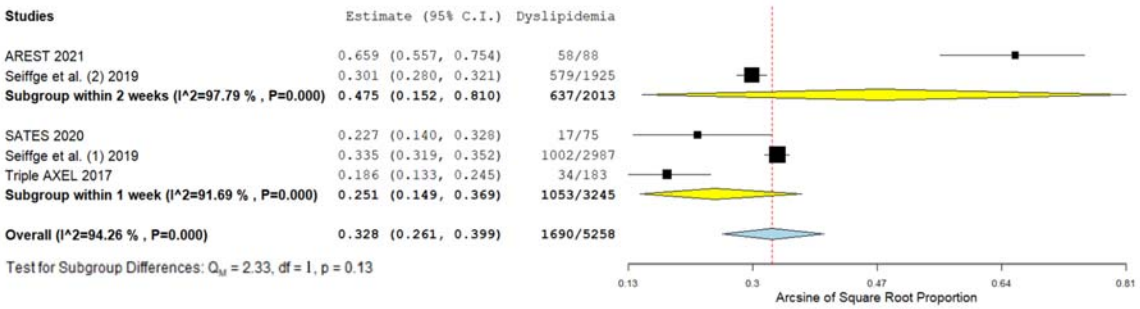
Supplementary Figure-S13. Forest plot presenting the pooled proportion of patients with a history of stroke prior the index event, initiating oral anticoagulants.



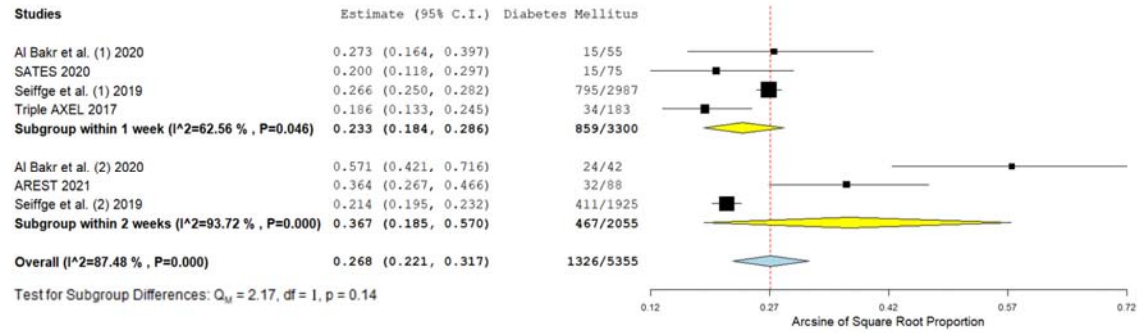
Supplementary Figure-S14. Forest plot presenting the pooled proportion of patients with hypertension, initiating oral anticoagulants.



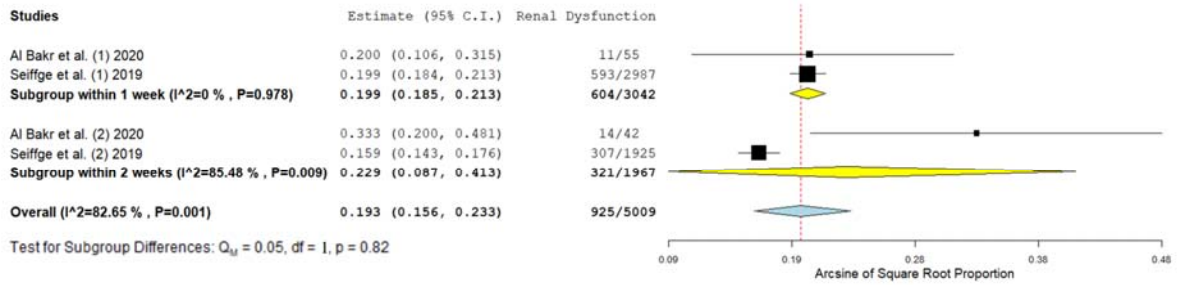
Supplementary Figure-S15. Forest plot presenting the pooled proportion of patients with dyslipidemia, initiating oral anticoagulants.



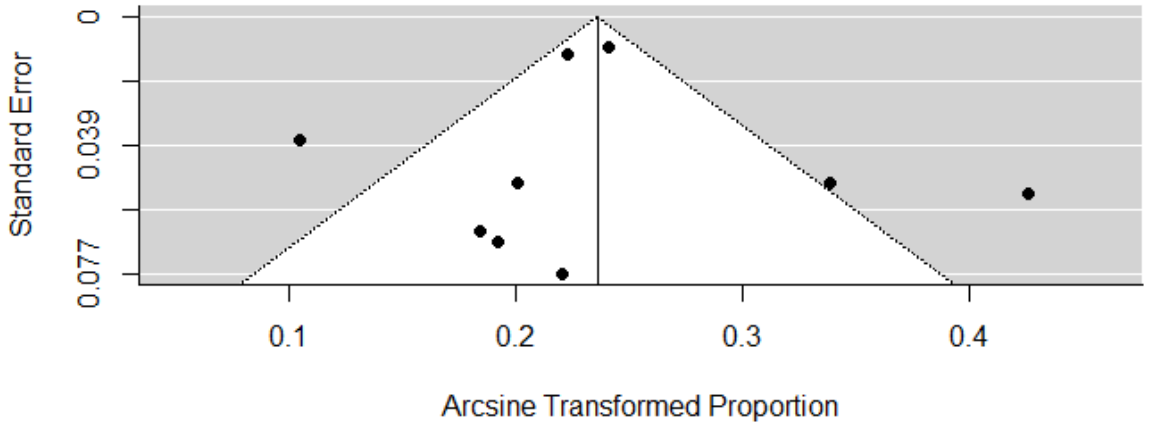
Supplementary Figure-S16. Forest plot presenting the pooled proportion of patients with diabetes mellitus, initiating oral anticoagulants.



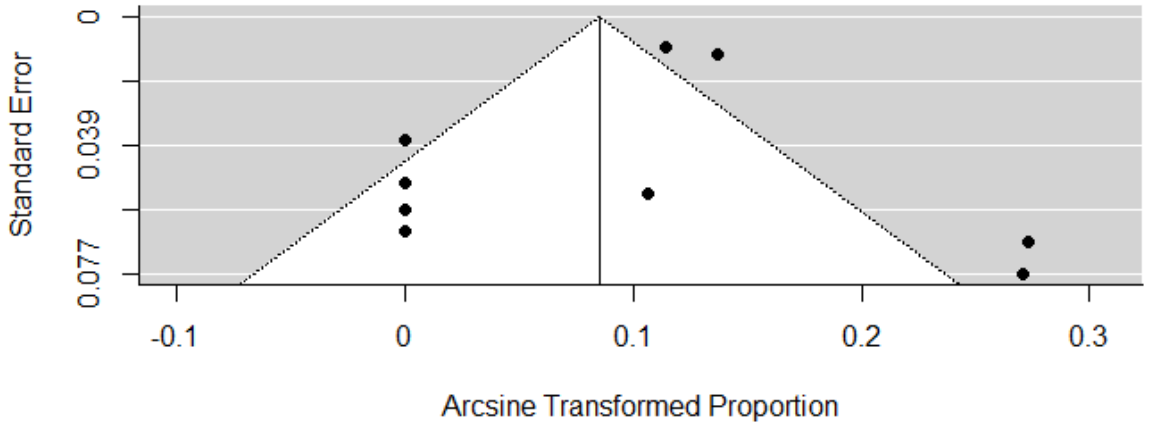
Supplementary Figure-S17. Forest plot presenting the pooled proportion of patients with chronic kidney failure, initiating oral anticoagulants.



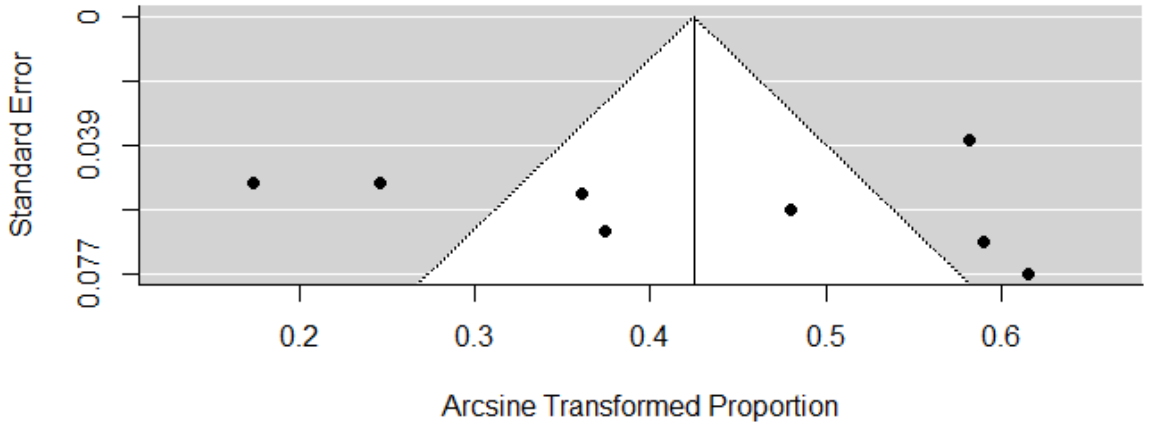
Supplementary Figure-S18. Funnel plot on the reported rates of ischemic stroke recurrence in patients with early initiation of oral anticoagulants (p for Egger's test= 0.8507).



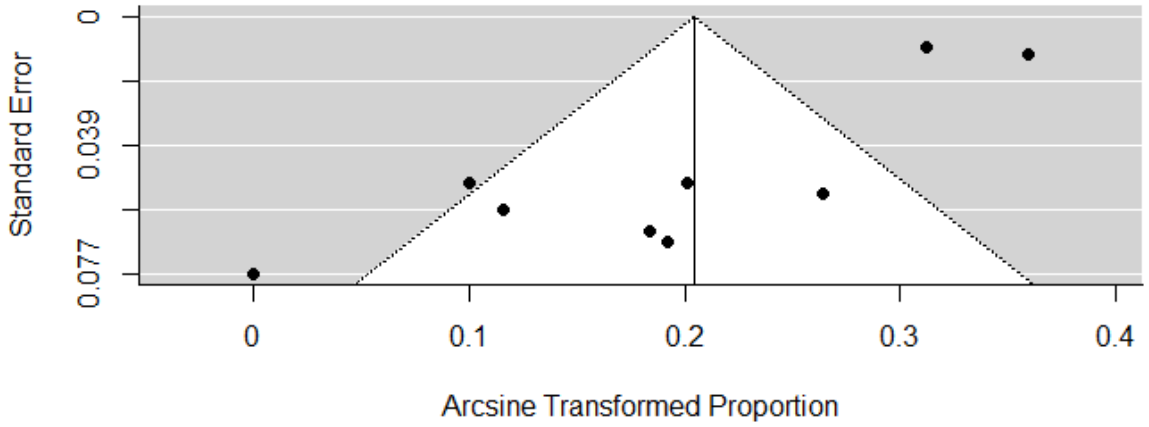
Supplementary Figure-S19. Funnel plot on the reported rates of symptomatic ICH in patients with early initiation of oral anticoagulants (p for Egger's test= 0.7688).



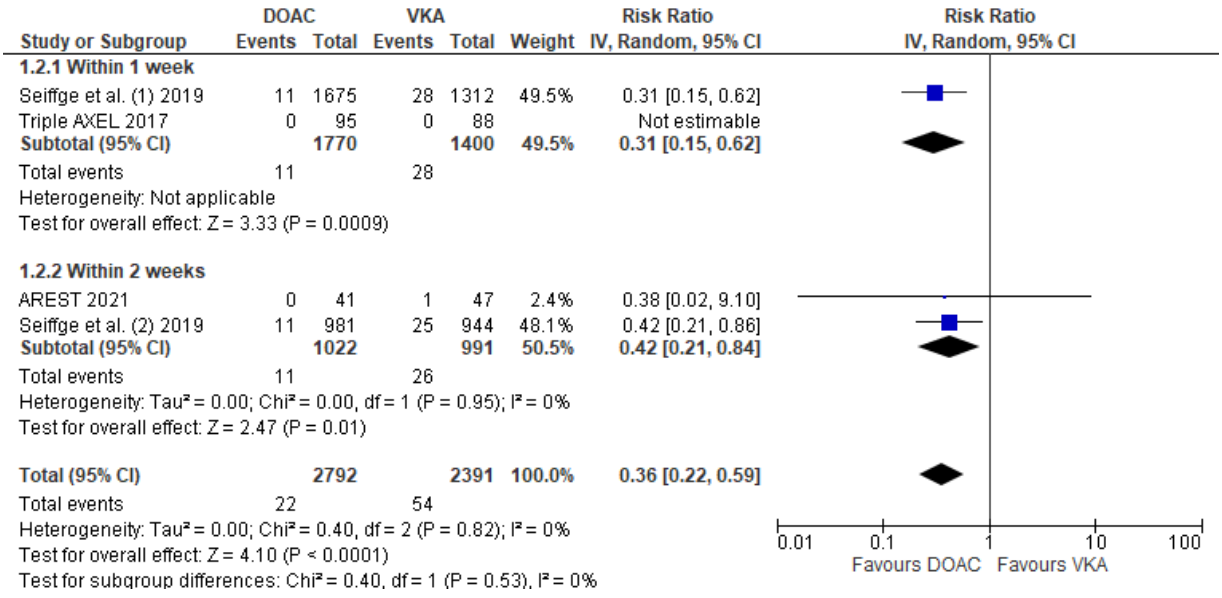
Supplementary Figure-S20. Funnel plot on the reported rates of any ICH in patients with early initiation of oral anticoagulants (p for Egger's test= 0.3874).



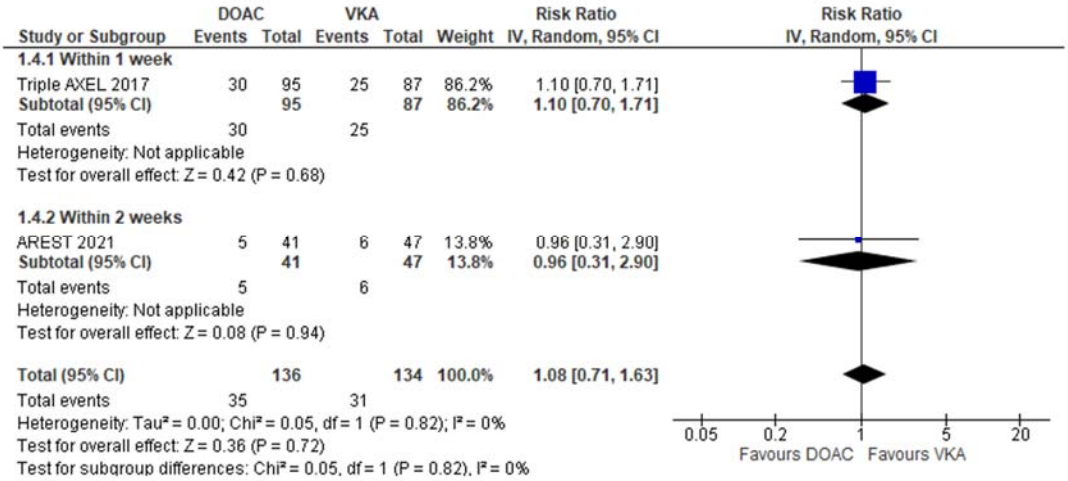
Supplementary Figure-S21. Funnel plot on the reported rates of all-cause mortality in patients with early initiation of oral anticoagulants (p for Egger's test< 0.001).



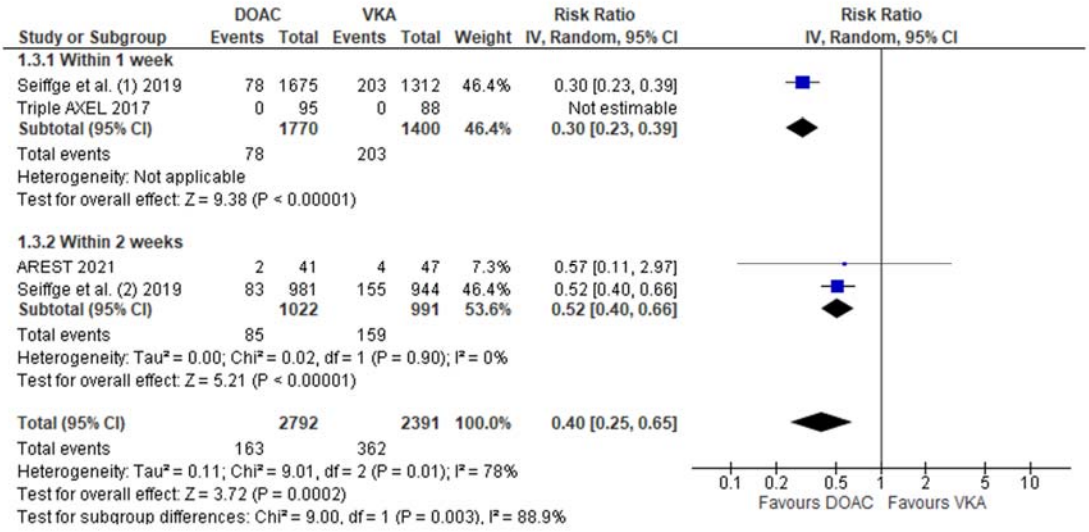
Supplementary Figure-S22. Forest plot presenting the risk ratio of symptomatic ICH among patients treated with DOACs versus VKAs, stratified by the timing of treatment initiation.



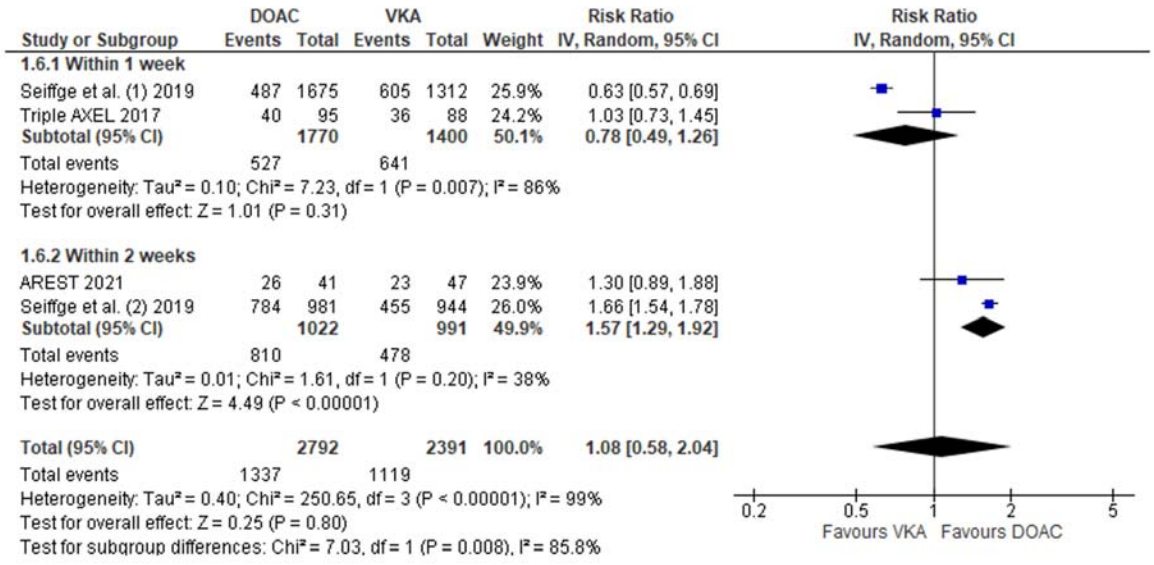
Supplementary Figure-S23. Forest plot presenting the risk ratio of any ICH among patients treated with DOACs versus VKAs, stratified by the timing of treatment initiation.



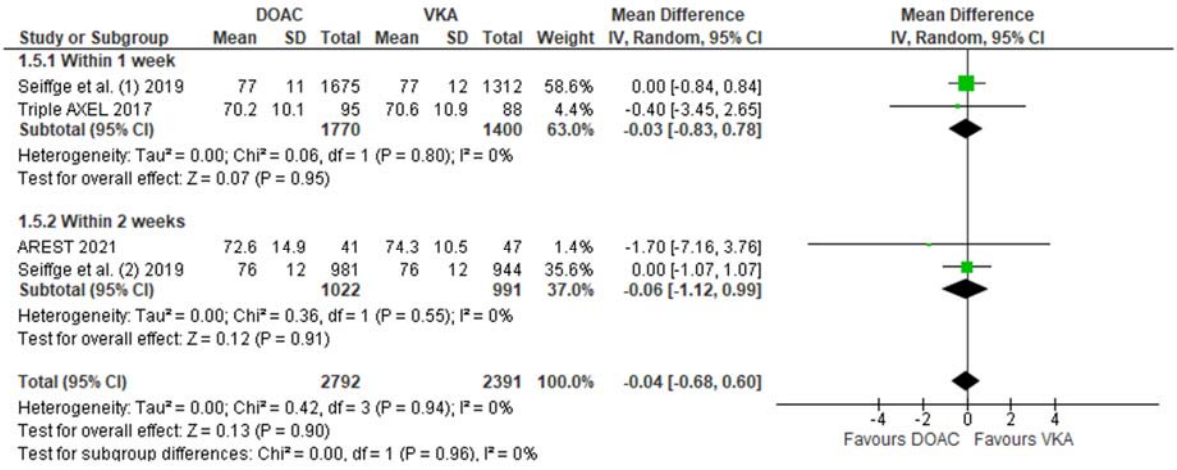
Supplementary Figure-S24. Forest plot presenting the risk ratio of all-cause mortality among patients treated with DOACs versus VKAs, stratified by the timing of treatment initiation.



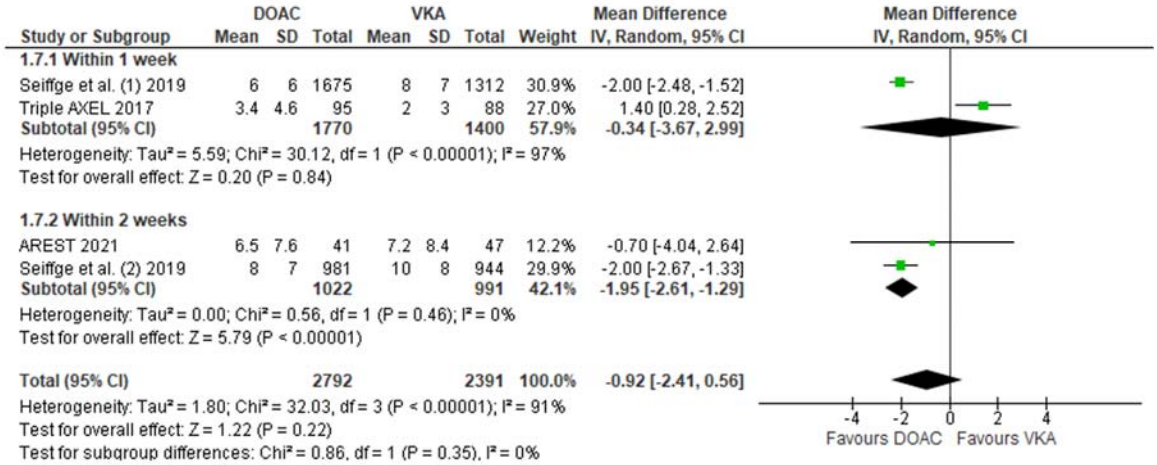
Supplementary Figure-S25. Forest plot presenting the risk ratio of women among patients treated with DOACs versus VKAs, stratified by the timing of treatment initiation.



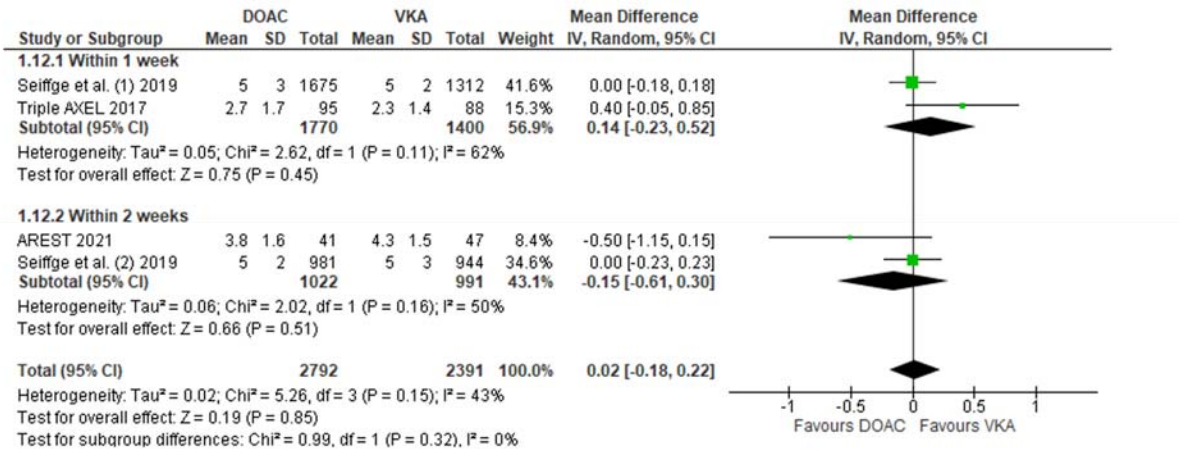
Supplementary Figure-S26. Forest plot presenting the mean difference of age (in years) among patients treated with DOACs versus VKAs, stratified by the timing of treatment initiation.



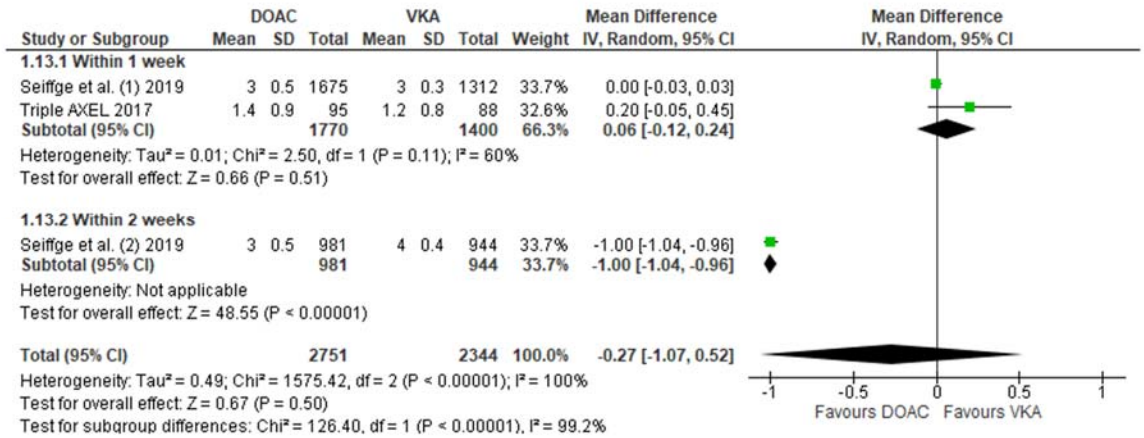
Supplementary Figure-S27. Forest plot presenting the mean difference of baseline NIHSS score among patients treated with DOACs versus VKAs, stratified by the timing of treatment initiation.



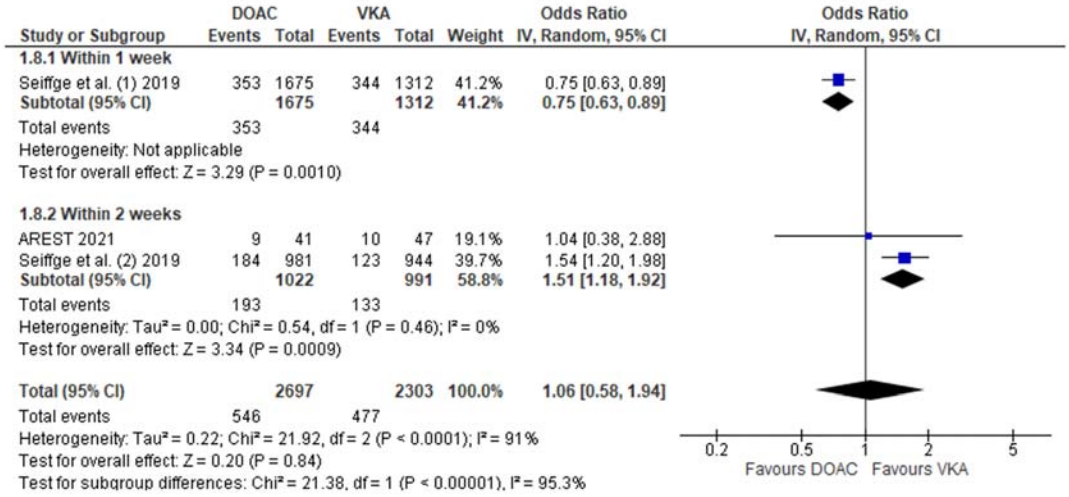
Supplementary Figure-S28. Forest plot presenting the mean difference of baseline CHA_2DS_2-VASc score among patients treated with DOACs versus VKAs, stratified by the timing of treatment initiation.



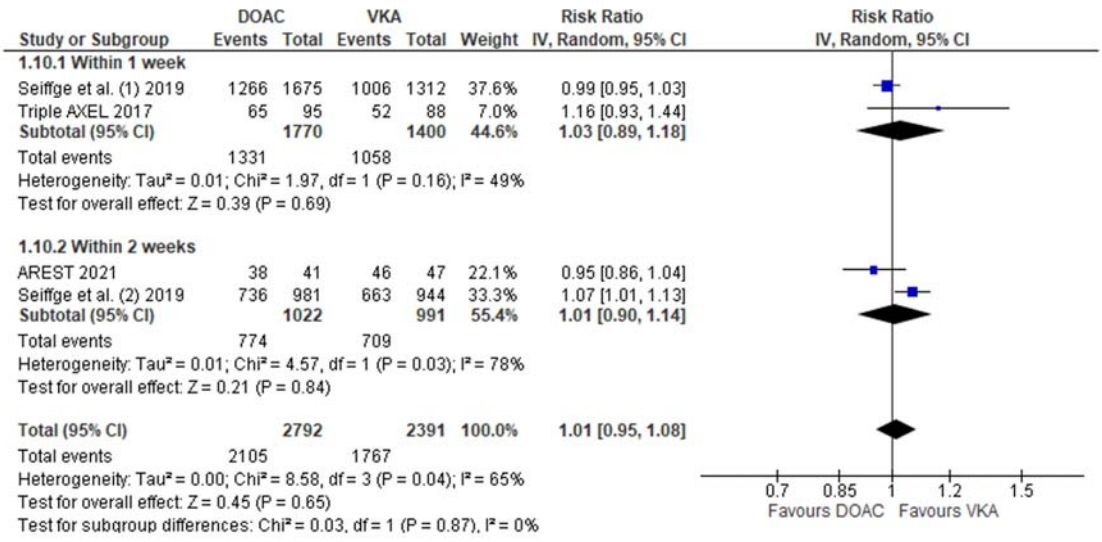
Supplementary Figure-S29. Forest plot presenting the mean difference of baseline HAS-BLED score among patients treated with DOACs versus VKAs, stratified by the timing of treatment initiation.



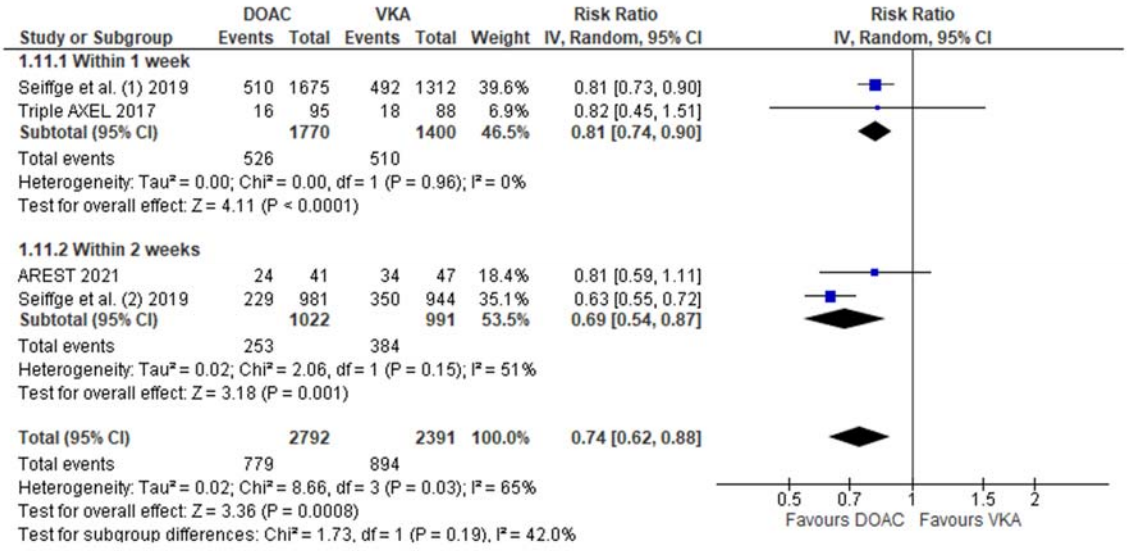
Supplementary Figure-S30. Forest plot presenting the risk ratio of prior stroke among patients treated with DOACs versus VKAs, stratified by the timing of treatment initiation.



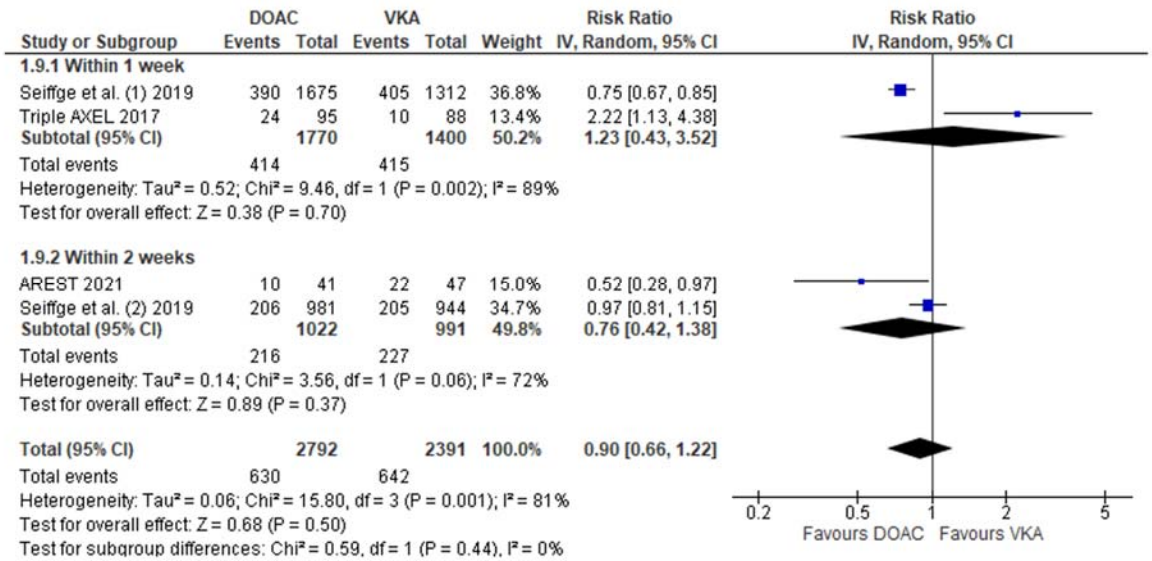
Supplementary Figure-S31. Forest plot presenting the risk ratio of hypertension among patients treated with DOACs versus VKAs, stratified by the timing of treatment initiation.



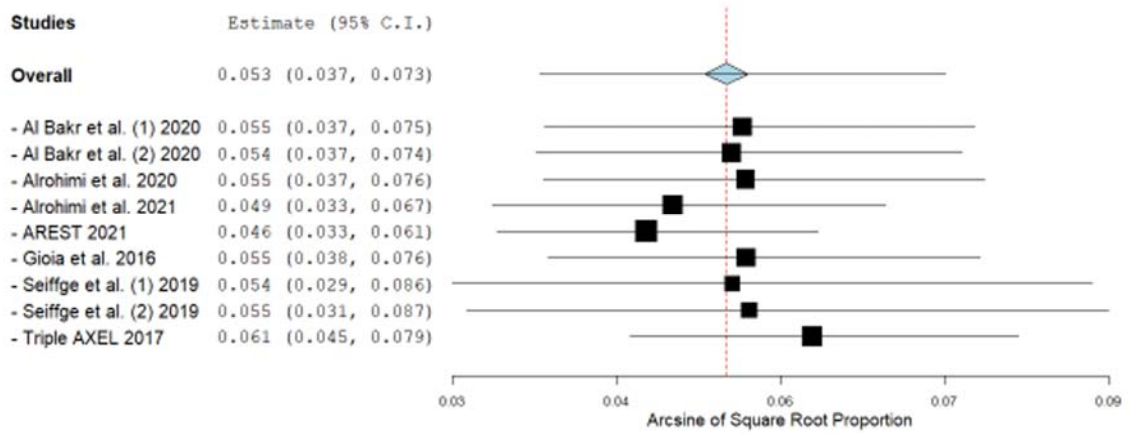
Supplementary Figure-S32. Forest plot presenting the risk ratio of dyslipidemia among patients treated with DOACs versus VKAs, stratified by the timing of treatment initiation.



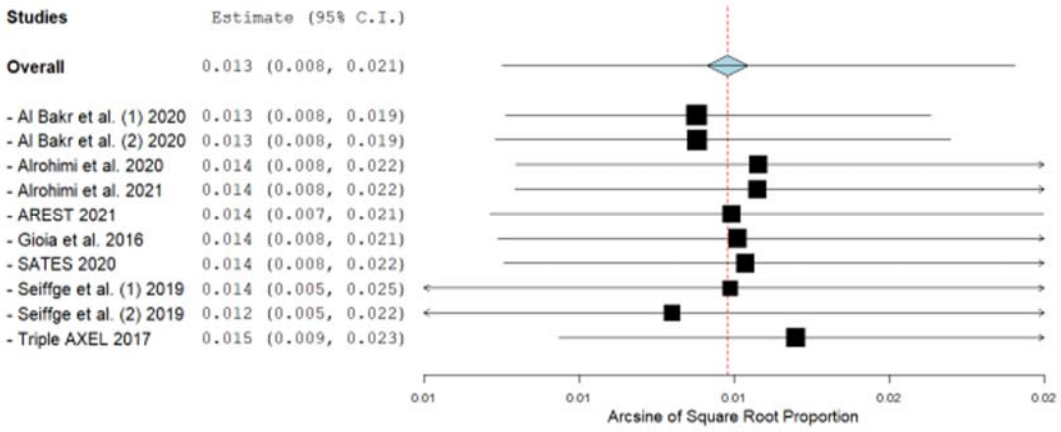
Supplementary Figure-S33. Forest plot presenting the risk ratio of diabetes mellitus among patients treated with DOACs versus VKAs, stratified by the timing of treatment initiation.



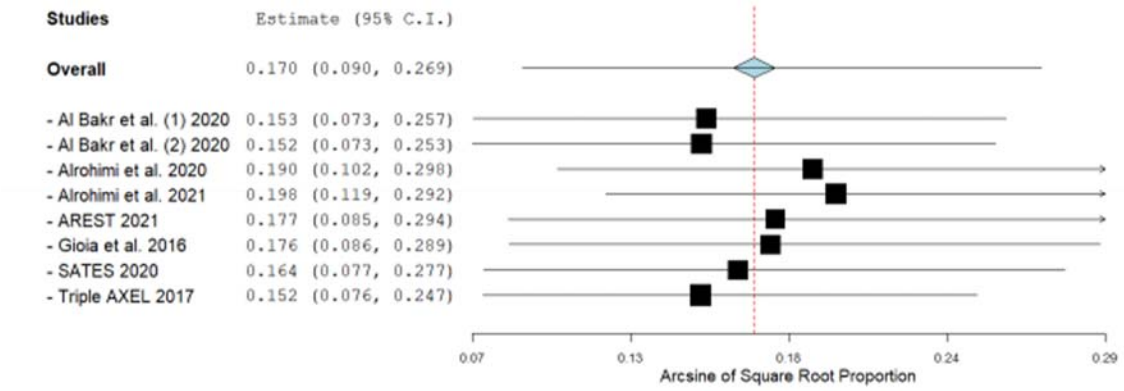
Supplementary Figure-S34. Forest plot of leave-one-out analysis for the pooled proportion of patients with IS recurrence following the initiation of oral anticoagulants.



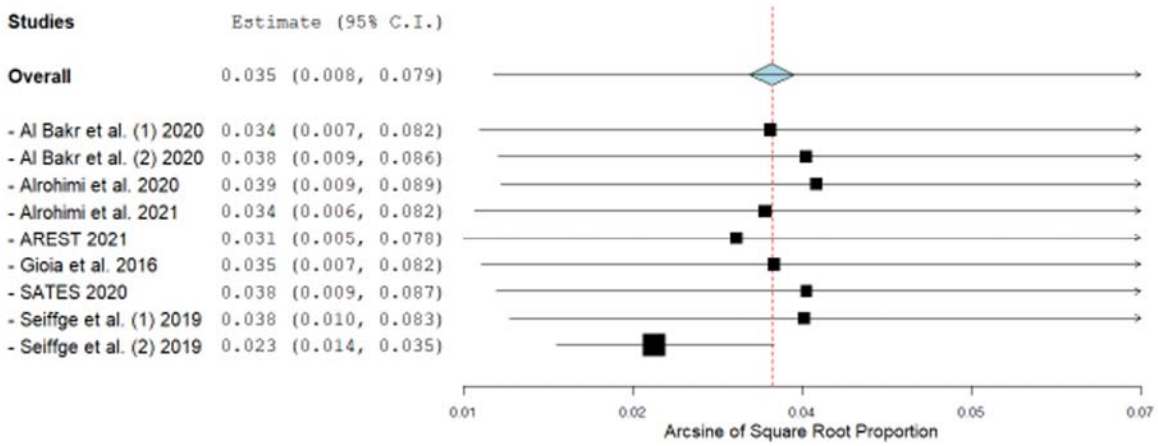
Supplementary Figure-S35. Forest plot of leave-one-out analysis for the pooled proportion of patients with symptomatic ICH following the initiation of oral anticoagulants.



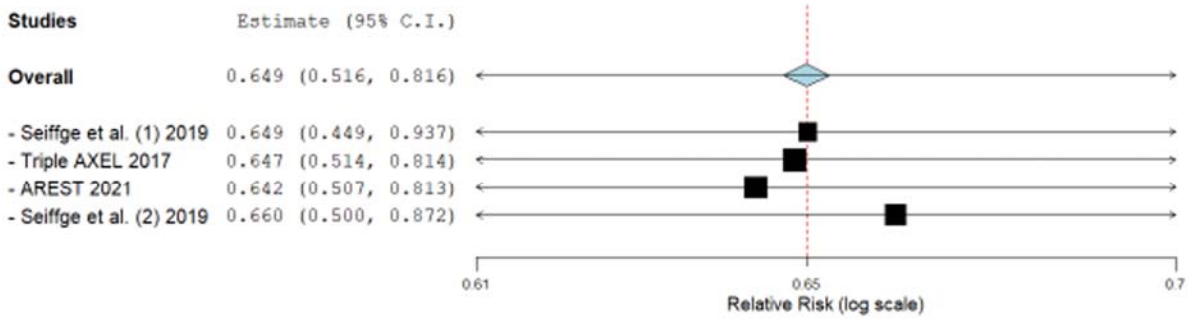
Supplementary Figure-S36. Forest plot of leave-one-out analysis for the pooled proportion of patients with any ICH following the initiation of oral anticoagulants.



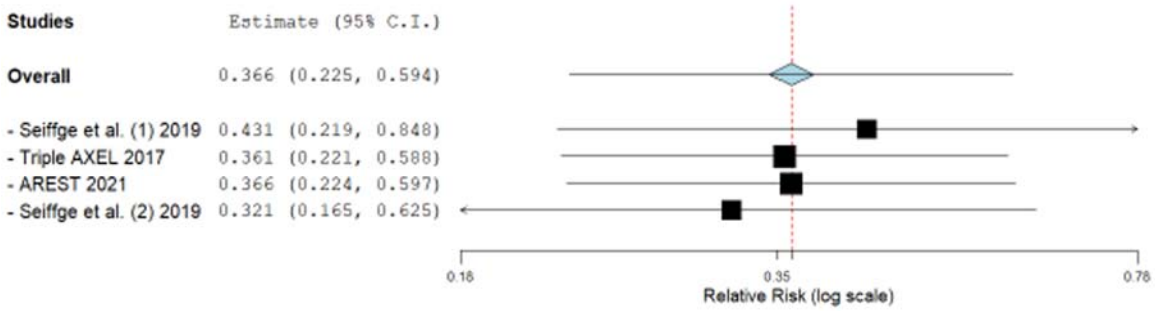
Supplementary Figure-S37. Forest plot of leave-one-out analysis for the pooled proportion of patients with all-cause mortality following the initiation of oral anticoagulants.



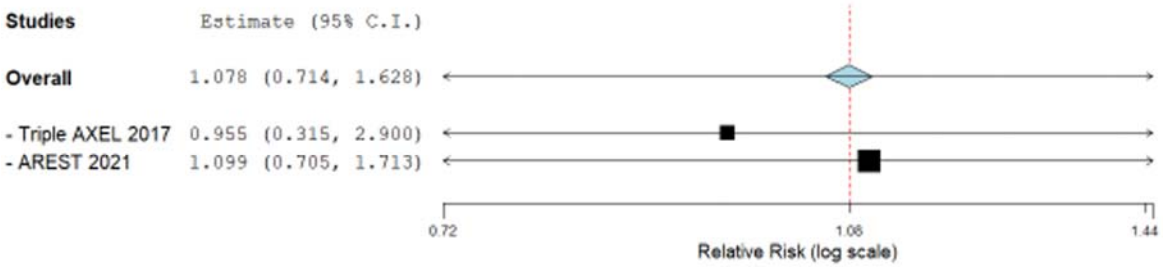
Supplementary Figure-S38. Forest plot of leave-one-out analysis for the risk ratio of IS recurrence among patients treated with DOACs versus VKAs.



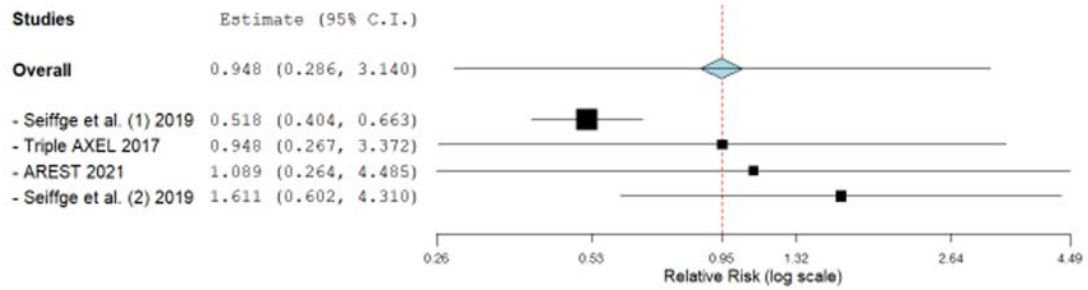
Supplementary Figure-S39. Forest plot of leave-one-out analysis for the risk ratio of symptomatic ICH among patients treated with DOACs versus VKAs.



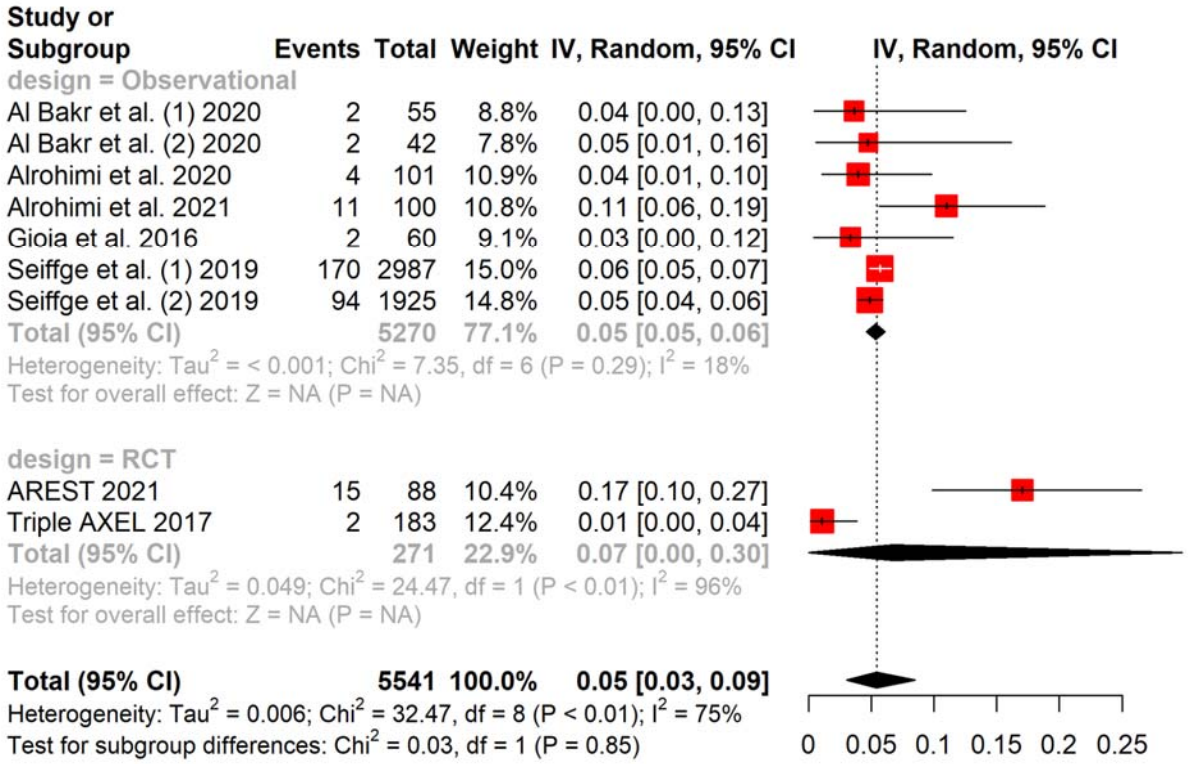
Supplementary Figure-S40. Forest plot of leave-one-out analysis for the risk ratio of any ICH among patients treated with DOACs versus VKAs.



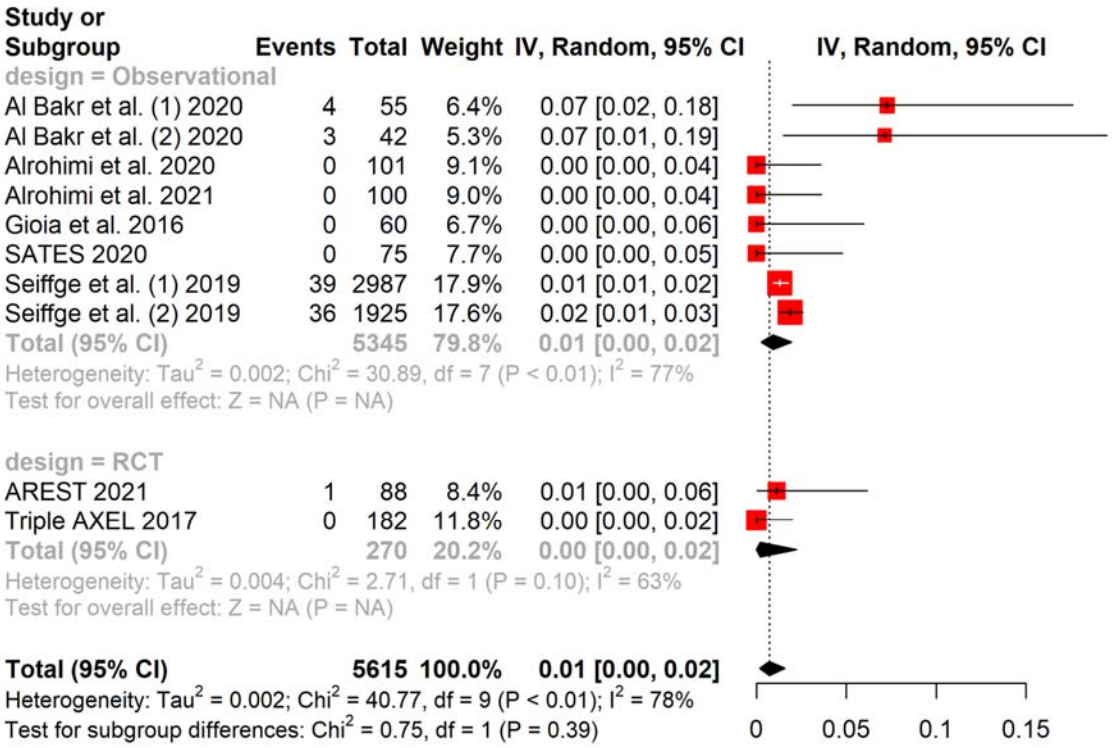
Supplementary Figure-S41. Forest plot of leave-one-out analysis for the risk ratio of all-cause mortality among patients treated with DOACs versus VKAs.



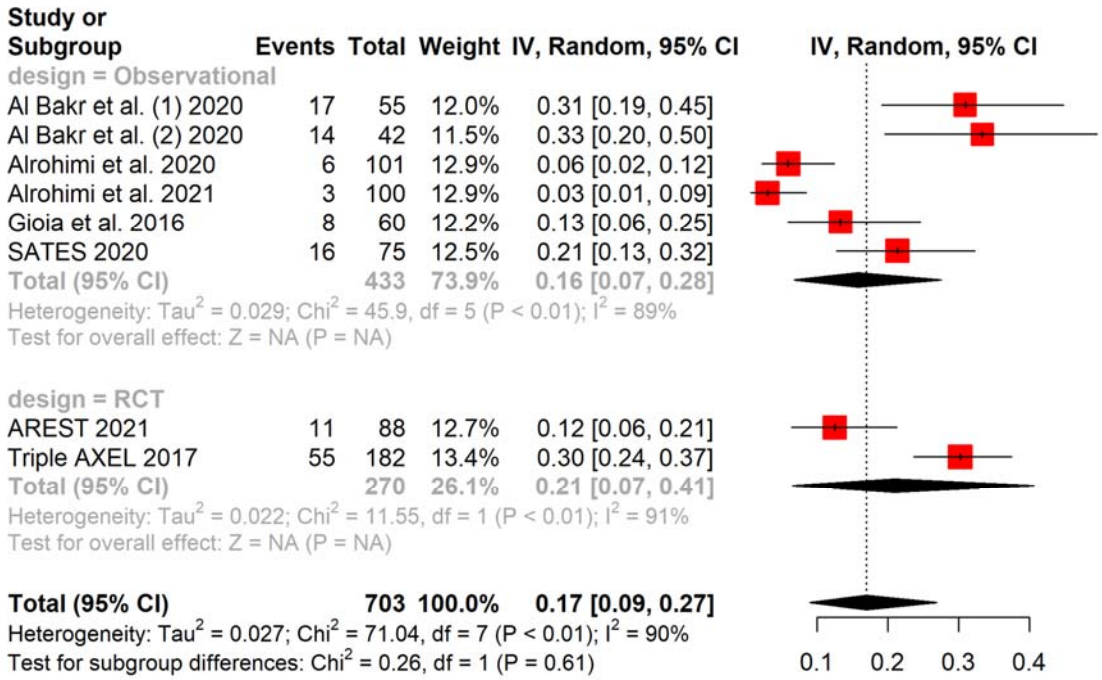
Supplementary Figure-S42. Forest plot presenting the pooled proportion of patients with IS recurrence following the initiation of oral anticoagulants, stratified by study design (observational studies versus RCTs).



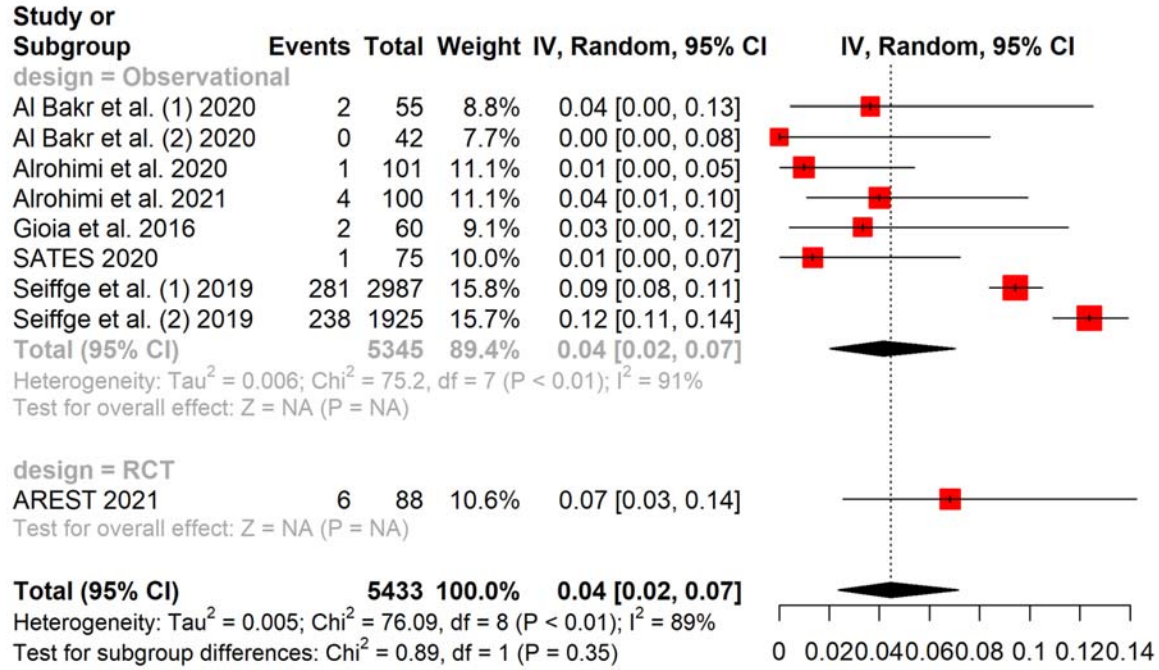
Supplementary Figure-S43. Forest plot presenting the pooled proportion of patients with symptomatic ICH following the initiation of oral anticoagulants, stratified by study design (observational studies versus RCTs).



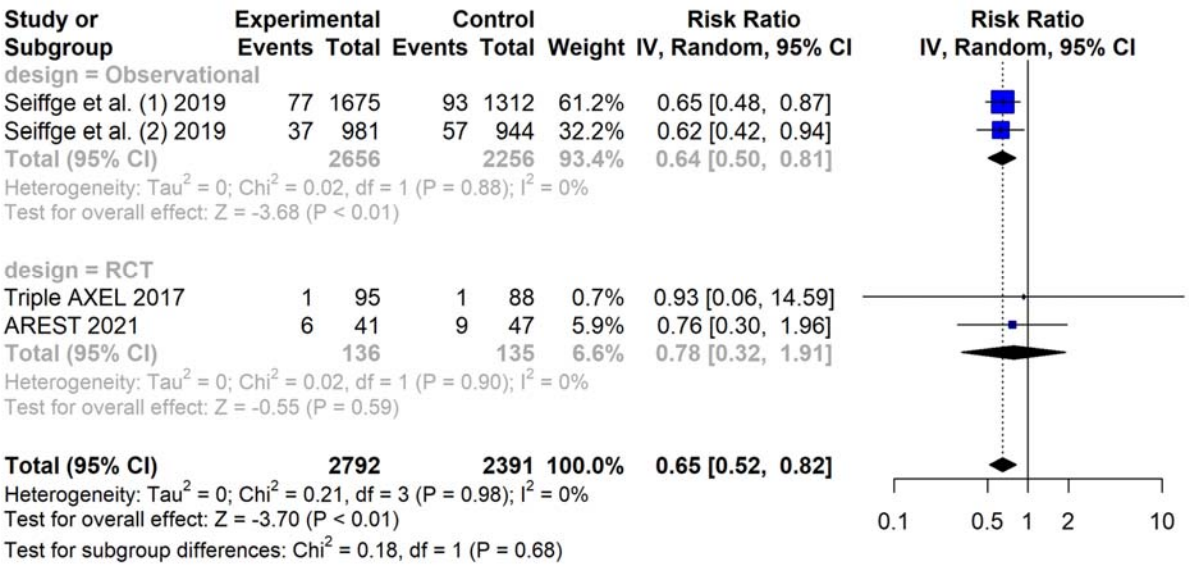
Supplementary Figure-S44. Forest plot presenting the pooled proportion of patients with any ICH following the initiation of oral anticoagulants, stratified by study design (observational studies versus RCTs).



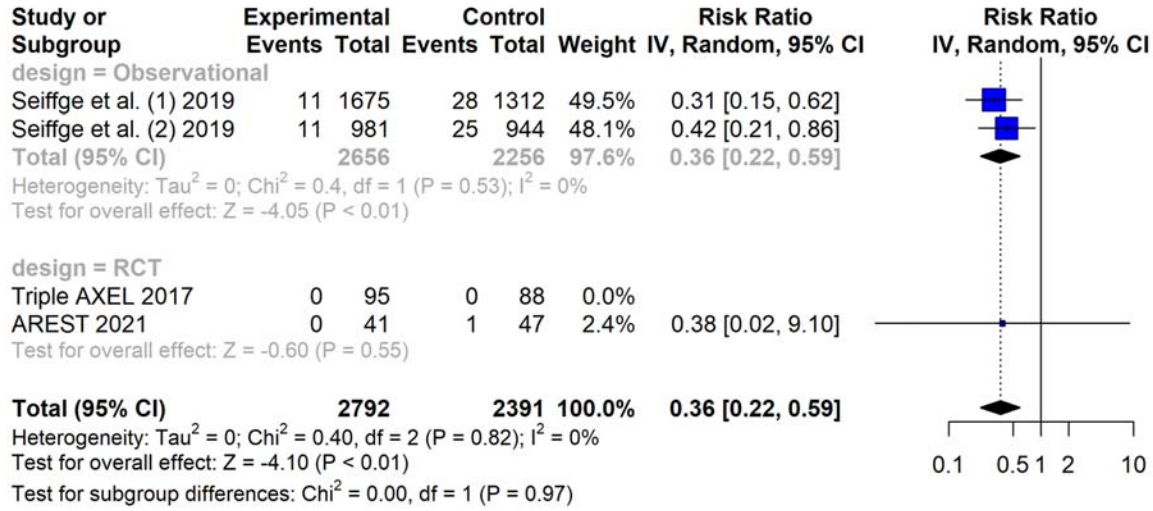
Supplementary Figure-S45. Forest plot presenting the pooled proportion of patients with all-cause mortality ICH following the initiation of oral anticoagulants, stratified by study design (observational studies versus RCTs).



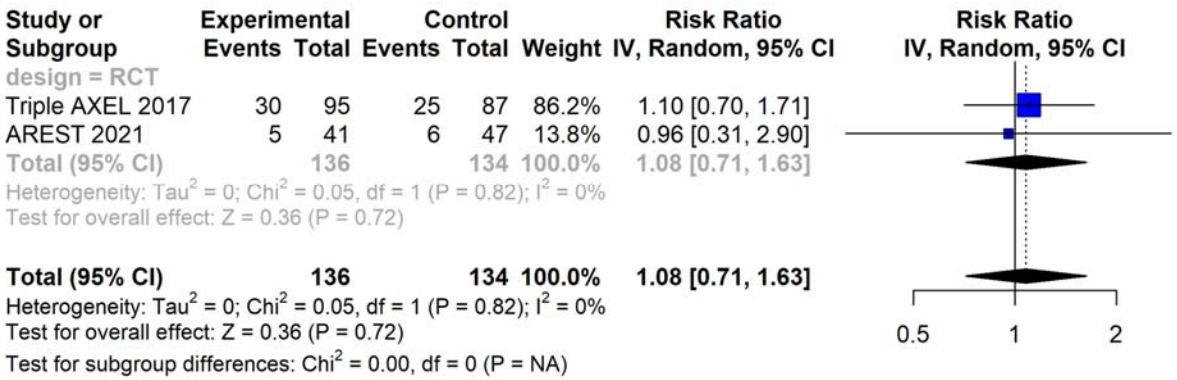
Supplementary Figure-S46. Forest plot presenting the risk ratio of IS recurrence among patients treated with DOACs versus VKAs, stratified by study design (observational studies versus RCTs).



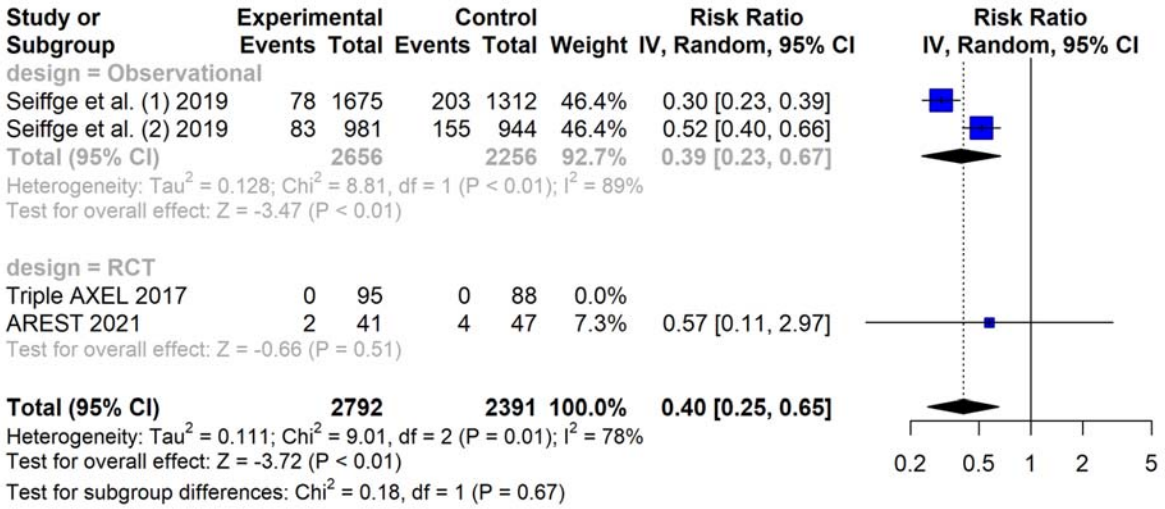
Supplementary Figure-S47. Forest plot presenting the risk ratio of symptomatic ICH among patients treated with DOACs versus VKAs, stratified by study design (observational studies versus RCTs).



Supplementary Figure-S48. Forest plot presenting the risk ratio of any ICH among patients treated with DOACs versus VKAs, stratified by study design (observational studies versus RCTs). In the present analysis, only RCTs were included.



Supplementary Figure-S49. Forest plot presenting the risk ratio of all-cause mortality among patients treated with DOACs versus VKAs, stratified by study design (observational studies versus RCTs).



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