Appendix figure 1. Subgroup analyses

A. Occurrence of arterial thrombosis during treatment with DOACs and VKA

	DOA	AC	Vitamin K an	tagonist		Peto Odds Ratio				Peto Odds Ra	atio	
Study or Subgroup	Events	Total	Events	Total	Weight	Peto, Fixed, 95% CI	Year		P	eto, Fixed, 95	5% CI	
Woller et al. (ASTRO-APS) 2022	6	23	0	25	21.4%	10.33 [1.90, 56.25]	2022			_	•	
Ordi-Ros et al. 2019	11	95	3	95	52.1%	3.41 [1.15, 10.10]	2019					
Pengo et al. (TRAPS) 2018	7	59	0	61	26.5%	8.52 [1.86, 38.96]	2018			-		
Goldhaber et al. 2016	0	71	0	80		Not estimable	2016					
Cohen et al. (RAPS) 2016	0	57	0	58		Not estimable	2016					
Total (95% CI)		305		319	100.0%	5.51 [2.52, 12.07]						
Total events	24		3									
Heterogeneity: $Chi^2 = 1.59$, $df =$	2 (P = 0.	.45); I ²	= 0%					0.01	0 1		10	100
Test for overall effect: $Z = 4.27$ (P < 0.000	01)						0.01 Fa	0.1 vours [exper	imental] Favo	10 ours [control]	100

B. Occurrence of venous thrombosis during treatment with DOACs and VKA

	DOA	'C	Vitamin K anta	gonist		Peto Odds Ratio		Peto Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	Peto, Fixed, 95% CI	Year	Peto, Fixed, 95% CI
Woller et al. (ASTRO-APS) 2022	0	23	0	25		Not estimable	2022	
Ordi-Ros et al. 2019	2	95	3	95	38.9%	0.66 [0.11, 3.91]	2019	
Pengo et al. (TRAPS) 2018	1	59	0	61	7.9%	7.64 [0.15, 385.43]	2018	
Cohen et al. (RAPS) 2016	0	57	0	58		Not estimable	2016	
Goldhaber et al. 2016	3	71	4	80	53.2%	0.84 [0.18, 3.82]	2016	
Total (95% CI)		305		319	100.0%	0.91 [0.30, 2.76]		
Total events	6		7					
Heterogeneity: $Chi^2 = 1.26$, $df =$	2 (P = 0.	53); I ²	= 0%				H	0.01 0.1 1 10 100
Test for overall effect: $Z = 0.16$ (P = 0.87						(Favours [experimental] Favours [control]

C. Occurrence of thrombosis during treatment with DOACs and VKA in patients with previous arterial thrombosis

	DOA	C	Vitamin K anta	agonist		Peto Odds Ratio			Peto	Odds Ratio		
Study or Subgroup	Events	Total	Events	Total	Weight	Peto, Fixed, 95% CI	Year		Peto, I	Fixed, 95% CI		
Woller et al. (ASTRO-APS) 2022	4	6	0	11	18.3%	32.69 [3.36, 318.04]	2022					
Ordi-Ros et al. 2019	7	37	3	34	53.7%	2.28 [0.60, 8.60]	2019					
Pengo et al. (TRAPS) 2018	5	21	0	22	27.9%	9.61 [1.52, 60.74]	2018					
Cohen et al. (RAPS) 2016	0	0	0	0		Not estimable	2016					
Goldhaber et al. 2016	0	0	0	0		Not estimable	2016					
Total (95% CI)		64		67	100.0%	5.55 [2.09, 14.70]						
Total events	16		3									
Heterogeneity: $Chi^2 = 4.40$, $df =$	2 (P = 0.	11); I ²	= 55%				F	.01	0 1	1	10	100
Test for overall effect: $Z = 3.45$ (P = 0.000	06)					U		o.1 ours [experimen ^e	tal] Favours [10 control]	100

D. Occurrence of thrombosis during treatment with DOACs and VKA in patients with previous venous thrombosis

	DOAC	Vitamin K anta	gonist		Peto Odds Ratio		Peto Odds	s Ratio	
Study or Subgroup	Events Tot	al Events	Total	Weight	Peto, Fixed, 95% CI	Year	Peto, Fixed,	, 95% CI	
Woller et al. (ASTRO-APS) 2022	5 2	20 0	18	18.3%	8.42 [1.31, 54.01] 2	2022		•	
Ordi-Ros et al. 2019	6 6	59 3	70	34.8%	2.06 [0.54, 7.92] 2	2019	- 		
Pengo et al. (TRAPS) 2018	5 3	38 0	39	19.4%	8.49 [1.40, 51.42] 2	2018			<u> </u>
Cohen et al. (RAPS) 2016	0 5	57 0	58		Not estimable 2	2016			
Goldhaber et al. 2016	3 7	71 4	80	27.5%	0.84 [0.18, 3.82] 2	2016	-		
Total (95% CI)	25	55	265	100.0%	2.74 [1.24, 6.07]		-		
Total events	19	7							
Heterogeneity: $Chi^2 = 5.43$, $df =$	3 (P = 0.14);	$1^2 = 45\%$				0.01	01 1	10	100
Test for overall effect: $Z = 2.49$ ((P = 0.01)						0.1 1 ours [experimental] F	avours [control]	100

E. Occurrence of thrombosis during treatment with DOACs and VKA in patients with triple positivity

	DOA	C	Vitamin	K antag	onist		Peto Odds Ratio		Peto Odds Ratio
Study or Subgroup	Events	Total	Ever	its	Total	Weight	Peto, Fixed, 95% CI	Year	Peto, Fixed, 95% CI
Woller et al. (ASTRO-APS) 2022	2	7		0	7	8.2%	8.73 [0.49, 156.28]	2022	-
Ordi-Ros et al. 2019	10	58		5	57	58.4%	2.10 [0.71, 6.18]	2019	
Pengo et al. (TRAPS) 2018	8	59		0	61	33.4%	8.68 [2.08, 36.23]	2018	· · · · · · · · · · · · · · · · · · ·
Cohen et al. (RAPS) 2016	0	7		0	12		Not estimable	2016	
Goldhaber et al. 2016	0	0		0	0		Not estimable	2016	
Total (95% CI)		131			137	100.0%	3.79 [1.66, 8.65]		
Total events	20			5					
Heterogeneity: $Chi^2 = 2.77$, $df =$	2 (P = 0.	25); I ²	= 28%						
Test for overall effect: $Z = 3.16$ (P = 0.002	2)							0.01 0.1 1 10 100 Favours [experimental] Favours [control]