

**Antithrombotic therapy for symptomatic peripheral arterial disease: a systematic review and network meta-analysis.**

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**Supplementary table 1:** estimated relative risk of the primary cardiovascular effectiveness outcome with 95%- confidence intervals

	A+CI	A+C	A+E	A+R1	A+T	A+VKA1	C	C+VKA1	A	P	R2	T	TP	VKA2
A+CI	NA	1.38 (0.62 - 3.09) <sup>4</sup>	0.45 (0.04 - 4.95) <sup>3</sup>	1.37 (0.62 - 3.03) <sup>3</sup>	1.47 (0.65 - 3.32) <sup>3</sup>	1.26 (0.56 - 2.85) <sup>3</sup>	1.48 (0.66 - 3.31) <sup>3</sup>	1.26 (0.35 - 4.58) <sup>3</sup>	1.16 (0.53 - 2.54) <sup>2</sup>	0.51 (0.17 - 1.52) <sup>4</sup>	1.26 (0.56 - 2.82) <sup>3</sup>	1.46 (0.65 - 3.27) <sup>3</sup>	0.57 (0.18 - 1.8) <sup>3</sup>	1.29 (0.58 - 2.86) <sup>3</sup>
A+C	0.73 (0.32 - 1.62) <sup>4</sup>	NA	0.33 (0.03 - 3.12) <sup>2</sup>	1 (0.81 - 1.22) <sup>2</sup>	1.07 (0.87 - 1.3) <sup>1</sup>	0.91 (0.69 - 1.22) <sup>2</sup>	1.08 (0.84 - 1.38) <sup>2</sup>	0.91 (0.33 - 2.52) <sup>2</sup>	0.84 (0.7 - 1.01) <sup>1</sup>	0.37 (0.17 - 0.8) <sup>3</sup>	0.91 (0.7 - 1.19) <sup>2</sup>	1.06 (0.81 - 1.38) <sup>2</sup>	0.41 (0.17 - 0.98) <sup>2</sup>	0.93 (0.74 - 1.18) <sup>2</sup>
A+E	2.2 (0.2 - 23.9) <sup>3</sup>	3.03 (0.32 - 28.64) <sup>2</sup>	NA	3.02 (0.32 - 28.81) <sup>3</sup>	3.23 (0.34 - 30.83) <sup>3</sup>	2.77 (0.29 - 26.68) <sup>3</sup>	3.26 (0.34 - 31.25) <sup>3</sup>	2.76 (0.23 - 32.55) <sup>3</sup>	2.54 (0.27 - 24.22) <sup>4</sup>	1.13 (0.11 - 12.14) <sup>4</sup>	2.76 (0.29 - 26.51) <sup>3</sup>	3.2 (0.33 - 30.74) <sup>3</sup>	1.25 (0.11 - 13.85) <sup>3</sup>	2.82 (0.3 - 27.04) <sup>3</sup>
A+R1	0.73 (0.33 - 1.61) <sup>3</sup>	1 (0.82 - 1.23) <sup>2</sup>	0.33 (0.03 - 3.16) <sup>3</sup>	NA	1.07 (0.85 - 1.35) <sup>2</sup>	0.92 (0.72 - 1.17) <sup>2</sup>	1.08 (0.89 - 1.31) <sup>2</sup>	0.92 (0.33 - 2.57) <sup>3</sup>	0.84 (0.76 - 0.93) <sup>1</sup>	0.37 (0.18 - 0.79) <sup>3</sup>	0.91 (0.75 - 1.12) <sup>1</sup>	1.06 (0.85 - 1.32) <sup>2</sup>	0.41 (0.18 - 0.97) <sup>2</sup>	0.94 (0.78 - 1.12) <sup>2</sup>
A+T	0.68 (0.3 - 1.53) <sup>3</sup>	0.94 (0.77 - 1.14) <sup>1</sup>	0.31 (0.03 - 2.95) <sup>3</sup>	0.93 (0.74 - 1.17) <sup>2</sup>	NA	0.86 (0.63 - 1.16) <sup>2</sup>	1.01 (0.77 - 1.32) <sup>2</sup>	0.86 (0.3 - 2.4) <sup>3</sup>	0.79 (0.64 - 0.97) <sup>1</sup>	0.35 (0.16 - 0.76) <sup>3</sup>	0.85 (0.64 - 1.14) <sup>2</sup>	0.99 (0.74 - 1.32) <sup>2</sup>	0.39 (0.16 - 0.92) <sup>2</sup>	0.87 (0.67 - 1.13) <sup>2</sup>
A+VKA1	0.79 (0.35 - 1.79) <sup>3</sup>	1.09 (0.82 - 1.45) <sup>2</sup>	0.36 (0.04 - 3.47) <sup>3</sup>	1.09 (0.86 - 1.39) <sup>2</sup>	1.17 (0.86 - 1.58) <sup>2</sup>	NA	1.18 (0.89 - 1.55) <sup>2</sup>	1 (0.35 - 2.85) <sup>3</sup>	0.92 (0.74 - 1.14) <sup>1</sup>	0.41 (0.19 - 0.89) <sup>3</sup>	1 (0.74 - 1.34) <sup>2</sup>	1.16 (0.86 - 1.55) <sup>2</sup>	0.45 (0.19 - 1.08) <sup>2</sup>	1.02 (0.78 - 1.33) <sup>3</sup>
C	0.67 (0.3 - 1.51) <sup>3</sup>	0.93 (0.72 - 1.19) <sup>2</sup>	0.31 (0.03 - 2.94) <sup>3</sup>	0.93 (0.76 - 1.13) <sup>2</sup>	0.99 (0.76 - 1.3) <sup>2</sup>	0.85 (0.64 - 1.12) <sup>2</sup>	NA	0.85 (0.3 - 2.39) <sup>4</sup>	0.78 (0.66 - 0.93) <sup>1</sup>	0.35 (0.16 - 0.74) <sup>3</sup>	0.85 (0.65 - 1.1) <sup>2</sup>	0.98 (0.89 - 1.08) <sup>1</sup>	0.38 (0.16 - 0.91) <sup>1</sup>	0.87 (0.69 - 1.09) <sup>2</sup>
C+VKA1	0.79 (0.22 - 2.9) <sup>3</sup>	1.1 (0.4 - 3.03) <sup>2</sup>	0.36 (0.03 - 4.26) <sup>3</sup>	1.09 (0.39 - 3.06) <sup>3</sup>	1.17 (0.42 - 3.29) <sup>3</sup>	1 (0.35 - 2.87) <sup>3</sup>	1.18 (0.42 - 3.32) <sup>4</sup>	NA	0.92 (0.33 - 2.57) <sup>3</sup>	0.41 (0.12 - 1.45) <sup>4</sup>	1 (0.35 - 2.84) <sup>3</sup>	1.16 (0.41 - 3.28) <sup>3</sup>	0.45 (0.12 - 1.71) <sup>3</sup>	1.02 (0.36 - 2.89) <sup>3</sup>
A	0.86 (0.39 - 1.9) <sup>2</sup>	1.19 (0.99 - 1.43) <sup>1</sup>	0.39 (0.04 - 3.74) <sup>4</sup>	1.19 (1.08 - 1.31) <sup>1</sup>	1.27 (1.03 - 1.57) <sup>1</sup>	1.09 (0.87 - 1.36) <sup>1</sup>	1.28 (1.08 - 1.52) <sup>1</sup>	1.09 (0.39 - 3.04) <sup>3</sup>	NA	0.44 (0.21 - 0.94) <sup>2</sup>	1.09 (0.89 - 1.32) <sup>1</sup>	1.26 (1.04 - 1.53) <sup>2</sup>	0.49 (0.21 - 1.15) <sup>2</sup>	1.11 (0.95 - 1.3) <sup>1</sup>
P	1.94 (0.66 - 5.73) <sup>4</sup>	2.68 (1.25 - 5.76) <sup>3</sup>	0.88 (0.08 - 9.48) <sup>4</sup>	2.67 (1.26 - 5.65) <sup>3</sup>	2.86 (1.32 - 6.18) <sup>3</sup>	2.45 (1.13 - 5.32) <sup>3</sup>	2.88 (1.35 - 6.17) <sup>3</sup>	2.44 (0.69 - 8.68) <sup>4</sup>	2.25 (1.07 - 4.73) <sup>2</sup>	NA	2.44 (1.13 - 5.26) <sup>3</sup>	2.83 (1.32 - 6.09) <sup>3</sup>	1.1 (0.71 - 1.71) <sup>4</sup>	2.5 (1.17 - 5.33) <sup>3</sup>
R2	0.8 (0.35 - 1.79) <sup>3</sup>	1.1 (0.84 - 1.43) <sup>2</sup>	0.36 (0.04 - 3.48) <sup>3</sup>	1.09 (0.9 - 1.33) <sup>1</sup>	1.17 (0.88 - 1.56) <sup>2</sup>	1 (0.75 - 1.35) <sup>2</sup>	1.18 (0.91 - 1.53) <sup>2</sup>	1 (0.35 - 2.85) <sup>3</sup>	0.92 (0.76 - 1.12) <sup>1</sup>	0.41 (0.19 - 0.88) <sup>3</sup>	NA	1.16 (0.88 - 1.53) <sup>2</sup>	0.45 (0.19 - 1.08) <sup>2</sup>	1.02 (0.8 - 1.31) <sup>2</sup>
T	0.69 (0.31 - 1.54) <sup>3</sup>	0.95 (0.73 - 1.23) <sup>2</sup>	0.31 (0.03 - 3) <sup>3</sup>	0.94 (0.76 - 1.17) <sup>2</sup>	1.01 (0.76 - 1.34) <sup>2</sup>	0.87 (0.64 - 1.16) <sup>2</sup>	1.02 (0.93 - 1.12) <sup>1</sup>	0.86 (0.31 - 2.44) <sup>3</sup>	0.79 (0.65 - 0.97) <sup>2</sup>	0.35 (0.16 - 0.76) <sup>3</sup>	0.86 (0.65 - 1.14) <sup>2</sup>	NA	0.39 (0.16 - 0.93) <sup>2</sup>	0.88 (0.69 - 1.13) <sup>2</sup>
TP	1.76 (0.55 - 5.62) <sup>3</sup>	2.43 (1.02 - 5.8) <sup>2</sup>	0.8 (0.07 - 8.93) <sup>3</sup>	2.42 (1.03 - 5.71) <sup>2</sup>	2.6 (1.08 - 6.23) <sup>2</sup>	2.23 (0.92 - 5.36) <sup>2</sup>	2.62 (1.1 - 6.22) <sup>1</sup>	2.22 (0.59 - 8.42) <sup>3</sup>	2.04 (0.87 - 4.78) <sup>2</sup>	0.91 (0.58 - 1.41) <sup>4</sup>	2.22 (0.93 - 5.3) <sup>2</sup>	2.57 (1.08 - 6.14) <sup>2</sup>	NA	2.27 (0.96 - 5.38) <sup>2</sup>
VKA2	0.78 (0.35 - 1.73) <sup>3</sup>	1.07 (0.85 - 1.36) <sup>2</sup>	0.35 (0.04 - 3.39) <sup>3</sup>	1.07 (0.89 - 1.28) <sup>2</sup>	1.14 (0.88 - 1.48) <sup>2</sup>	0.98 (0.75 - 1.28) <sup>3</sup>	1.15 (0.92 - 1.45) <sup>2</sup>	0.98 (0.35 - 2.77) <sup>3</sup>	0.9 (0.77 - 1.05) <sup>1</sup>	0.4 (0.19 - 0.86) <sup>3</sup>	0.98 (0.76 - 1.25) <sup>2</sup>	1.13 (0.88 - 1.45) <sup>2</sup>	0.44 (0.19 - 1.05) <sup>2</sup>	NA

A = Acetylsalicylic acid 75-325 mg daily; CI = cilostazol 200 mg once daily; C = Clopidogrel 75 mg once daily; E = Edoxaban 60 mg once daily; R1 = Rivaroxaban 2.5 mg twice daily; T = Ticagrelor 60-90 mg twice daily; VKA1 = Vitamin K antagonist with target INR between 1.4 and 3; P = Placebo only; R2 = Rivaroxaban 5 mg twice daily; TP = Ticlopidine 200-250 mg twice daily; VKA2 = Vitamin K antagonist with target INR between 3 and 4.5. The certainty of the evidence (according to GRADE) was incorporated in this figure. <sup>1</sup>High quality of evidence, <sup>2</sup>Moderate quality of evidence, <sup>3</sup>Low quality of evidence, <sup>4</sup>Very low quality of evidence

**Supplementary table 2:** estimated relative risk of the primary safety outcome with 95%- confidence intervals

MB	A+CI	A+C	A+E	A+R1	A+T	A+VKA1	C	C+VKA1	A	R2	T	VKA2
A+CI	NA	2.53 (0.1 - 60.94) <sup>3</sup>	12.51 (0.16 - 1009.02) <sup>3</sup>	1.98 (0.08 - 46.58) <sup>3</sup>	3.04 (0.12 - 74.38) <sup>3</sup>	1.04 (0.04 - 24.84) <sup>3</sup>	6.31 (0.07 - 590.84) <sup>4</sup>	2.25 (0.09 - 58.84) <sup>3</sup>	2.88 (0.12 - 67.41) <sup>2</sup>	1.95 (0.08 - 46.49) <sup>3</sup>	6.06 (0.06 - 572.15) <sup>4</sup>	1.5 (0.06 - 35.56) <sup>3</sup>
A+C	0.4 (0.02 - 9.55) <sup>3</sup>	NA	4.95 (0.24 - 101.83) <sup>2</sup>	0.78 (0.48 - 1.28) <sup>2</sup>	1.2 (0.84 - 1.72) <sup>1</sup>	0.41 (0.23 - 0.73) <sup>2</sup>	2.5 (0.1 - 63.56) <sup>4</sup>	0.89 (0.44 - 1.82) <sup>2</sup>	1.14 (0.73 - 1.78) <sup>1</sup>	0.77 (0.45 - 1.34) <sup>2</sup>	2.4 (0.09 - 61.74) <sup>3</sup>	0.59 (0.34 - 1.02) <sup>2</sup>
A+E	0.08 (0 - 6.45) <sup>3</sup>	0.2 (0.01 - 4.15) <sup>2</sup>	NA	0.16 (0.01 - 3.38) <sup>3</sup>	0.24 (0.01 - 5.1) <sup>3</sup>	0.08 (0 - 1.81) <sup>3</sup>	0.5 (0.01 - 42.31) <sup>4</sup>	0.18 (0.01 - 4.03) <sup>3</sup>	0.23 (0.01 - 4.9) <sup>3</sup>	0.16 (0.01 - 3.38) <sup>3</sup>	0.48 (0.01 - 40.98) <sup>4</sup>	0.12 (0.01 - 2.58) <sup>3</sup>
A+R1	0.51 (0.02 - 11.91) <sup>3</sup>	1.28 (0.78 - 2.08) <sup>2</sup>	6.32 (0.3 - 135.3) <sup>3</sup>	NA	1.54 (0.87 - 2.73) <sup>2</sup>	0.53 (0.35 - 0.8) <sup>2</sup>	3.19 (0.12 - 84.23) <sup>4</sup>	1.14 (0.48 - 2.7) <sup>3</sup>	1.46 (1.18 - 1.8) <sup>1</sup>	0.99 (0.72 - 1.35) <sup>2</sup>	3.06 (0.11 - 81.8) <sup>4</sup>	0.76 (0.52 - 1.1) <sup>2</sup>
A+T	0.33 (0.01 - 8.05) <sup>3</sup>	0.83 (0.58 - 1.18) <sup>1</sup>	4.11 (0.2 - 86.39) <sup>3</sup>	0.65 (0.37 - 1.15) <sup>2</sup>	NA	0.34 (0.18 - 0.65) <sup>2</sup>	2.07 (0.08 - 53.85) <sup>4</sup>	0.74 (0.33 - 1.64) <sup>3</sup>	0.95 (0.56 - 1.62) <sup>3</sup>	0.64 (0.34 - 1.2) <sup>2</sup>	1.99 (0.08 - 52.3) <sup>4</sup>	0.49 (0.26 - 0.92) <sup>2</sup>
A+VKA1	0.96 (0.04 - 22.94) <sup>3</sup>	2.43 (1.37 - 4.29) <sup>2</sup>	12.02 (0.55 - 260.74) <sup>3</sup>	1.9 (1.25 - 2.88) <sup>2</sup>	2.92 (1.53 - 5.57) <sup>2</sup>	NA	6.06 (0.23 - 162.18) <sup>4</sup>	2.17 (0.87 - 5.39) <sup>2</sup>	2.77 (1.93 - 3.97) <sup>1</sup>	1.88 (1.16 - 3.05) <sup>2</sup>	5.82 (0.22 - 157.5) <sup>4</sup>	1.44 (0.89 - 2.32) <sup>2</sup>
C	0.16 (0 - 14.86) <sup>4</sup>	0.4 (0.02 - 10.2) <sup>4</sup>	1.98 (0.02 - 166.47) <sup>4</sup>	0.31 (0.01 - 8.29) <sup>4</sup>	0.48 (0.02 - 12.52) <sup>4</sup>	0.17 (0.01 - 4.42) <sup>4</sup>	NA	0.36 (0.02 - 8.41) <sup>4</sup>	0.46 (0.02 - 12) <sup>4</sup>	0.31 (0.01 - 8.27) <sup>4</sup>	0.96 (0.74 - 1.25) <sup>1</sup>	0.24 (0.01 - 6.33) <sup>4</sup>
C+VKA1	0.44 (0.02 - 11.58) <sup>3</sup>	1.12 (0.55 - 2.28) <sup>2</sup>	5.55 (0.25 - 123.93) <sup>3</sup>	0.88 (0.37 - 2.08) <sup>3</sup>	1.35 (0.61 - 2.99) <sup>3</sup>	0.46 (0.19 - 1.15) <sup>2</sup>	2.8 (0.12 - 65.8) <sup>4</sup>	NA	1.28 (0.55 - 2.96) <sup>3</sup>	0.87 (0.35 - 2.13) <sup>3</sup>	2.69 (0.11 - 63.92) <sup>4</sup>	0.66 (0.27 - 1.63) <sup>3</sup>
A	0.35 (0.01 - 8.11) <sup>2</sup>	0.88 (0.56 - 1.37) <sup>1</sup>	4.34 (0.2 - 92.18) <sup>3</sup>	0.69 (0.56 - 0.85) <sup>1</sup>	1.05 (0.62 - 1.8) <sup>3</sup>	0.36 (0.25 - 0.52) <sup>1</sup>	2.19 (0.08 - 57.42) <sup>4</sup>	0.78 (0.34 - 1.81) <sup>3</sup>	NA	0.68 (0.49 - 0.94) <sup>1</sup>	2.1 (0.08 - 55.76) <sup>4</sup>	0.52 (0.38 - 0.71) <sup>1</sup>
R2	0.51 (0.02 - 12.17) <sup>3</sup>	1.29 (0.75 - 2.24) <sup>2</sup>	6.4 (0.3 - 138.34) <sup>3</sup>	1.01 (0.74 - 1.38) <sup>2</sup>	1.56 (0.83 - 2.91) <sup>2</sup>	0.53 (0.33 - 0.87) <sup>2</sup>	3.23 (0.12 - 86.07) <sup>4</sup>	1.15 (0.47 - 2.84) <sup>3</sup>	1.47 (1.06 - 2.05) <sup>1</sup>	NA	3.1 (0.12 - 83.58) <sup>4</sup>	0.77 (0.49 - 1.21) <sup>2</sup>
T	0.17 (0 - 15.58) <sup>4</sup>	0.42 (0.02 - 10.73) <sup>3</sup>	2.06 (0.02 - 174.53) <sup>4</sup>	0.33 (0.01 - 8.71) <sup>4</sup>	0.5 (0.02 - 13.16) <sup>4</sup>	0.17 (0.01 - 4.64) <sup>4</sup>	1.04 (0.8 - 1.35) <sup>1</sup>	0.37 (0.02 - 8.85) <sup>4</sup>	0.48 (0.02 - 12.61) <sup>4</sup>	0.32 (0.01 - 8.69) <sup>4</sup>	NA	0.25 (0.01 - 6.65) <sup>4</sup>
VKA2	0.67 (0.03 - 15.87) <sup>3</sup>	1.69 (0.98 - 2.9) <sup>2</sup>	8.36 (0.39 - 180.38) <sup>3</sup>	1.32 (0.91 - 1.93) <sup>2</sup>	2.03 (1.09 - 3.78) <sup>2</sup>	0.7 (0.43 - 1.12) <sup>2</sup>	4.21 (0.16 - 112.24) <sup>4</sup>	1.51 (0.62 - 3.69) <sup>3</sup>	1.93 (1.41 - 2.64) <sup>1</sup>	1.31 (0.83 - 2.05) <sup>2</sup>	4.05 (0.15 - 109) <sup>4</sup>	NA

A = Acetylsalicylic acid 75-325 mg daily; CI = cilostazol 200 mg once daily; C = Clopidogrel 75 mg once daily; E = Edoxaban 60 mg once daily; R1 = Rivaroxaban 2.5 mg twice

daily; T = Ticagrelor 60-90 mg twice daily; VKA1 = Vitamin K antagonist with target INR between 1.4 and 3; R2 = Rivaroxaban 5 mg twice daily; VKA2 = Vitamin K antagonist

with target INR between 3 and 4.5. The certainty of the evidence (according to GRADE) was incorporated in this figure. <sup>1</sup>High quality of evidence, <sup>2</sup>Moderate quality of

evidence, <sup>3</sup>Low quality of evidence, <sup>4</sup>Very low quality of evidence

**Supplementary table 3:** estimated relative risk of the secondary outcome major adverse limb events with 95%- confidence intervals

MALE	A+CI	A+C	A+R1	A+T	A	R2
A+CI	NA	0.7 (0.29 - 1.71) <sup>3</sup>	0.92 (0.41 - 2.08) <sup>3</sup>	0.84 (0.31 - 2.29) <sup>3</sup>	0.69 (0.34 - 1.39) <sup>2</sup>	0.86 (0.34 - 2.18) <sup>3</sup>
A+C	1.43 (0.59 - 3.49) <sup>3</sup>	NA	1.32 (0.66 - 2.65) <sup>3</sup>	1.21 (0.49 - 2.98) <sup>3</sup>	0.99 (0.57 - 1.73) <sup>2</sup>	1.23 (0.53 - 2.82) <sup>3</sup>
A+R1	1.08 (0.48 - 2.44) <sup>3</sup>	0.76 (0.38 - 1.52) <sup>3</sup>	NA	0.91 (0.4 - 2.09) <sup>1</sup>	0.75 (0.49 - 1.14) <sup>1</sup>	0.93 (0.49 - 1.75) <sup>2</sup>
A+T	1.18 (0.44 - 3.21) <sup>3</sup>	0.83 (0.34 - 2.05) <sup>3</sup>	1.09 (0.48 - 2.5) <sup>1</sup>	NA	0.82 (0.4 - 1.67) <sup>3</sup>	1.02 (0.4 - 2.61) <sup>3</sup>
A	1.44 (0.72 - 2.9) <sup>2</sup>	1.01 (0.58 - 1.76) <sup>2</sup>	1.33 (0.88 - 2.03) <sup>1</sup>	1.22 (0.6 - 2.49) <sup>3</sup>	NA	1.24 (0.67 - 2.3) <sup>2</sup>
R2	1.16 (0.46 - 2.95) <sup>3</sup>	0.82 (0.35 - 1.87) <sup>3</sup>	1.08 (0.57 - 2.03) <sup>2</sup>	0.98 (0.38 - 2.53) <sup>3</sup>	0.81 (0.43 - 1.5) <sup>2</sup>	NA

A = Acetylsalicylic acid 75-325 mg daily; C = Clopidogrel 75 mg once daily; R1 = Rivaroxaban 2.5 mg twice daily; T = Ticagrelor 60-90 mg twice daily; R2 = Rivaroxaban 5 mg twice daily. The certainty of the evidence (according to GRADE) was incorporated in this figure. <sup>1</sup>High quality of evidence, <sup>2</sup>Moderate quality of evidence, <sup>3</sup>Low quality of evidence

**Supplementary table 4:** estimated relative risk of the secondary outcome acute limb ischaemia with 95%- confidence intervals

ALI	A+R1	A+T	A+VKA1	A	R2
A+R1	NA	0.98 (0.26 - 3.66) <sup>3</sup>	0.7 (0.44 - 1.1) <sup>2</sup>	0.67 (0.55 - 0.8) <sup>1</sup>	1.11 (0.65 - 1.89) <sup>2</sup>
A+T	1.03 (0.27 - 3.85) <sup>3</sup>	NA	0.72 (0.18 - 2.82) <sup>2</sup>	0.68 (0.18 - 2.53) <sup>2</sup>	1.14 (0.28 - 4.66) <sup>3</sup>
A+VKA1	1.43 (0.91 - 2.26) <sup>2</sup>	1.4 (0.35 - 5.52) <sup>2</sup>	NA	0.96 (0.63 - 1.45) <sup>2</sup>	1.59 (0.81 - 3.1) <sup>2</sup>
A	1.5 (1.24 - 1.81) <sup>1</sup>	1.46 (0.4 - 5.42) <sup>2</sup>	1.05 (0.69 - 1.58) <sup>2</sup>	NA	1.66 (0.98 - 2.81) <sup>1</sup>
R2	0.9 (0.53 - 1.54) <sup>2</sup>	0.88 (0.21 - 3.61) <sup>3</sup>	0.63 (0.32 - 1.23) <sup>2</sup>	0.6 (0.36 - 1.02) <sup>1</sup>	NA

A = Acetylsalicylic acid 75-325 mg daily; R1 = Rivaroxaban 2.5 mg twice daily; T = Ticagrelor 60-90 mg twice daily; VKA1 = Vitamin K antagonist with target INR between 1.4 and 3; R2 = Rivaroxaban 5 mg twice daily. The certainty of the evidence (according to GRADE) was incorporated in this figure. <sup>1</sup>High quality of evidence, <sup>2</sup>Moderate quality of evidence, <sup>3</sup>Low quality of evidence

## Appendix A: Search Strategy

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### **Pubmed:**

("Peripheral Arterial Disease"[Mesh] OR "Peripheral Vascular Diseases"[MeSH] OR "Peripheral Arterial Disease"[Tiab] OR "Peripheral Arterial Diseases"[Tiab] OR "Peripheral Artery Disease"[Tiab] OR "Peripheral Artery Diseases"[Tiab] OR "Peripheral Arterial Occlusive Disease"[Tiab] OR "Peripheral Arterial Occlusive Diseases"[Tiab] OR "Peripheral Vascular Disease"[Tiab] OR "Peripheral Vascular Diseases"[Tiab] OR "Intermittent Claudication"[Tiab] OR "Critical Limb Ischemia"[Tiab] OR "Aortic Occlusive Disease"[Tiab] OR "Aortic Occlusive Diseases"[Tiab] OR "Aortic Artery Disease"[Tiab] OR "Aortic Artery Diseases"[Tiab] OR "Aortic Arterial Disease"[Tiab] OR "Aortic Arterial Diseases"[Tiab] OR "Iliac Occlusive Disease"[Tiab] OR "Iliac Occlusive Diseases"[Tiab] OR "Iliac Artery Disease"[Tiab] OR "Iliac Artery Diseases"[Tiab] OR "Iliac Arterial Disease"[Tiab] OR "Iliac Arterial Diseases"[Tiab] OR "Femoral Occlusive Disease"[Tiab] OR "Femoral Occlusive Diseases"[Tiab] OR "Femoral Artery Disease"[Tiab] OR "Femoral Artery Diseases"[Tiab] OR "Femoral Arterial Disease"[Tiab] OR "Femoral Arterial Diseases"[Tiab] OR "Popliteal Occlusive Disease"[Tiab] OR "Popliteal Occlusive Diseases"[Tiab] OR "Popliteal Artery Disease"[Tiab] OR "Popliteal Artery Diseases"[Tiab] OR "Popliteal Arterial Disease"[Tiab] OR "Popliteal Arterial Diseases"[Tiab] OR "Femoropopliteal Occlusive Disease"[Tiab] OR "Femoropopliteal Occlusive Diseases"[Tiab] OR "Femoropopliteal Artery Disease"[Tiab] OR "Femoropopliteal Artery Diseases"[Tiab] OR "Femoropopliteal Arterial Disease"[Tiab] OR "Femoropopliteal Arterial Diseases"[Tiab]) AND ("Anticoagulants"[Pharmacological Action] OR anticoagula\*[tiab] OR anti-coagula\*[tiab] OR antithrombot\*[tiab] OR anti-thrombo\*[tiab] OR "platelet aggregation inhibitors"[tiab] OR "platelet aggregation inhibitor"[tiab] OR "platelet inhibitor"[tiab] OR "platelet inhibitors"[tiab] OR "antiplatelet"[tiab] OR "antiplatelets"[tiab] OR "anti-platelet"[tiab] OR "anti-platelets"[tiab] OR P2Y12[tiab] OR thienopyridine[tiab] OR thienopyridines[tiab] OR Aspirin[tiab] OR "Acetylsalicylic acid"[tiab] OR Nitroaspirin[tiab] OR ASA[tiab] OR Clopidogrel[tiab] OR Prasugrel[tiab] OR Satigrel[tiab] OR Pyragrel[tiab] OR Elinogrel[tiab] OR Ticagrelor[tiab] OR Cangrelor[tiab] OR "Carbasalate calcium"[tiab] OR Dipyridamole[tiab] OR Ticlopidine[tiab] OR Picotamide[tiab] OR Triflusal[tiab] OR Cilostazol[tiab] OR Vorapaxar[tiab] OR Indobufen[tiab] OR "factor Xa"[tiab] OR Rivaroxaban[tiab] OR Apixaban[tiab] OR Edoxaban[tiab] OR Otamixaban[tiab] OR Betrixaban[tiab] OR Darexaban[tiab] OR Argatroban[tiab] OR Melagatran[tiab] OR Inogatran[tiab] OR Terutroban[tiab] OR Dabigatran[tiab] OR Ximelagatran[tiab] OR Lepirudin[tiab] OR Desirudin[tiab] OR Bivalirudin[tiab] OR Idraparinux[tiab] OR Idrabiotaparinux[tiab] OR Fondaparinux[tiab] OR "vitamin K"[tiab] OR coumarin[tiab] OR Warfarin[tiab] OR Acenocoumarol[tiab] OR Phenprocoumon[tiab] OR Phenindione[tiab] OR Fluindione[tiab] OR Difenacoum[tiab] OR Dicumarol[tiab] OR Heparin[tiab] OR LMWH[tiab] OR LMH[tiab] OR heparinoids[tiab] OR Tinzaparin[tiab] OR Reviparin[tiab] OR Parnaparin[tiab] OR Nadroparin[tiab] OR Enoxaparin[tiab] OR Danaparoid[tiab] OR Dalteparin[tiab] OR Certoparin[tiab] OR Bemiparin[tiab] OR Ardeparin[tiab]) AND (((("Randomized Controlled Trial"[Publication Type]) OR ("Controlled Clinical Trial"[Publication Type]) OR (randomized[Title/Abstract]) OR (placebo[Title/Abstract]) OR ("drug therapy"[MeSH Subheading]) OR ("drug therapy"[MeSH Terms]) OR (randomly[Title/Abstract]) OR (trial[Title/Abstract]) OR (groups[Title/Abstract])) NOT ((animal[MeSH Terms]) NOT (human[MeSH Terms])))

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## **EMBASE**

("Peripheral Arterial Disease" OR "Peripheral Arterial Diseases" OR "Peripheral Artery Disease" OR "Peripheral Artery Diseases" OR "Peripheral Arterial Occlusive Disease" OR "Peripheral Arterial Occlusive Diseases" OR "Peripheral Vascular Disease" OR "Peripheral Vascular Diseases" OR "Intermittent Claudication" OR "Critical Limb Ischemia" OR "Aortic Occlusive Disease" OR "Aortic Occlusive Diseases" OR "Aortic Artery Disease" OR "Aortic Artery Diseases" OR "Aortic Arterial Disease" OR "Aortic Arterial Diseases" OR "Iliac Occlusive Disease" OR "Iliac Occlusive Diseases" OR "Iliac Artery Disease" OR "Iliac Artery Diseases" OR "Iliac Arterial Disease" OR "Iliac Arterial Diseases" OR "Femoral Occlusive Disease" OR "Femoral Occlusive Diseases" OR "Femoral Artery Disease" OR "Femoral Artery Diseases" OR "Femoral Arterial Disease" OR "Femoral Arterial Diseases" OR "Popliteal Occlusive Disease" OR "Popliteal Occlusive Diseases" OR "Popliteal Artery Disease" OR "Popliteal Artery Diseases" OR "Popliteal Arterial Disease" OR "Popliteal Arterial Diseases" OR "Femoropopliteal Occlusive Disease" OR "Femoropopliteal Occlusive Diseases" OR "Femoropopliteal Artery Disease" OR "Femoropopliteal Artery Diseases" OR "Femoropopliteal Arterial Disease" OR "Femoropopliteal Arterial Diseases").mp.) AND ((exp Anticoagulants/) OR (anticoagula\* OR anti-coagula\* OR antithrombot\* OR anti-thrombo\* OR "platelet aggregation inhibitors" OR "platelet aggregation inhibitor" OR "platelet inhibitor" OR "platelet inhibitors" OR "antiplatelet" OR "antiplatelets" OR "anti-platelet" OR "anti-platelets" OR P2Y12 OR thienopyridine OR thienopyridines OR Aspirin OR "Acetylsalicylic acid" OR Nitroaspirin OR ASA OR Clopidogrel OR Prasugrel OR Satigrel OR Pyragrel OR Elinogrel OR Ticagrelor OR Cangrelor OR "Carbasalate calcium" OR Dipyridamole OR Ticlopidine OR Picotamide OR Triflusal OR Cilostazol OR Vorapaxar OR Indobufen OR ("Factor Xa" adj1 (antagon\* OR inhibit\*)) OR Rivaroxaban OR Apixaban OR Edoxaban OR Otamixaban OR Betrixaban OR Darexaban OR Argatroban OR Melagatran OR Inogatran OR Terutroban OR Dabigatran OR Ximelagatran OR Lepirudin OR Desirudin OR Bivalirudin OR Idraparinux OR Idrabioparin OR Fondaparinux OR ("vitamin k" adj1 (antagoni\* OR inhibit\*)) OR coumarin OR Warfarin OR Acenocoumarol OR Phenprocoumon OR Phenindione OR Fluindione OR Difenacoum OR Dicumarol OR Heparin OR LMWH OR LMH OR heparinoids OR Tinzaparin OR Reviparin OR Parnaparin OR Nadroparin OR Enoxaparin OR Danaparoid OR Dalteparin OR Certoparin OR Bemiparin OR Ardeparin).mp.) AND ((randomized controlled trial.pt. OR controlled clinical trial.pt. OR randomized.ab. OR placebo.ab. OR drug therapy.fs. OR randomly.ab. OR trial.ab. OR groups.ab.) NOT (exp animals/ not humans.sh.))

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## **MEDLINE**

("Peripheral Arterial Disease" OR "Peripheral Arterial Diseases" OR "Peripheral Artery Disease" OR "Peripheral Artery Diseases" OR "Peripheral Arterial Occlusive Disease" OR "Peripheral Arterial Occlusive Diseases" OR "Peripheral Vascular Disease" OR "Peripheral Vascular Diseases" OR "Intermittent Claudication" OR "Critical Limb Ischemia" OR "Aortic Occlusive Disease" OR "Aortic Occlusive Diseases" OR "Aortic Artery Disease" OR "Aortic Artery Diseases" OR "Aortic Arterial Disease" OR "Aortic Arterial Diseases" OR "Iliac Occlusive Disease" OR "Iliac Occlusive Diseases" OR "Iliac Artery Disease" OR "Iliac Artery Diseases" OR "Iliac Arterial Disease" OR "Iliac Arterial Diseases" OR "Femoral Occlusive Disease" OR "Femoral Occlusive Diseases" OR "Femoral Artery Disease" OR "Femoral Artery Diseases" OR "Femoral Arterial Disease" OR "Femoral Arterial Diseases" OR "Popliteal Occlusive Disease" OR "Popliteal Occlusive Diseases" OR "Popliteal Artery Disease" OR "Popliteal Artery Diseases" OR "Popliteal Arterial Disease" OR "Popliteal Arterial Diseases" OR

"Femoropopliteal Occlusive Disease" OR "Femoropopliteal Occlusive Diseases" OR "Femoropopliteal Artery Disease" OR "Femoropopliteal Artery Diseases" OR "Femoropopliteal Arterial Disease" OR "Femoropopliteal Arterial Diseases").mp.) AND ((exp Anticoagulants/) OR (anticoagula\* OR anti-coagula\* OR antithrombot\* OR anti-thrombo\* OR "platelet aggregation inhibitors" OR "platelet aggregation inhibitor" OR "platelet inhibitor" OR "platelet inhibitors" OR "antiplatelet" OR "antiplatelets" OR "anti-platelet" OR "anti-platelets" OR P2Y12 OR thienopyridine OR thienopyridines OR Aspirin OR "Acetylsalicylic acid" OR Nitroaspirin OR ASA OR Clopidogrel OR Prasugrel OR Satigrel OR Pyragrel OR Elinogrel OR Ticagrelor OR Cangrelor OR "Carbasalate calcium" OR Dipyridamole OR Ticlopidine OR Picotamide OR Triflusal OR Cilostazol OR Vorapaxar OR Indobufen OR ("Factor Xa" adj1 (antagon\* OR inhibit\*)) OR Rivaroxaban OR Apixaban OR Edoxaban OR Otamixaban OR Betrixaban OR Darexaban OR Argatroban OR Melagatran OR Inogatran OR Terutroban OR Dabigatran OR Ximelagatran OR Lepirudin OR Desirudin OR Bivalirudin OR Idraparinux OR Idrabioparinux OR Fondaparinux OR ("vitamin k" adj1 (antagoni\* OR inhibit\*)) OR coumarin OR Warfarin OR Acenocoumarol OR Phenprocoumon OR Phenindione OR Fluindione OR Difenacoum OR Dicumarol OR Heparin OR LMWH OR LMH OR heparinoids OR Tinzaparin OR Reviparin OR Parnaparin OR Nadroparin OR Enoxaparin OR Danaparoid OR Dalteparin OR Certoparin OR Bemiparin OR Ardeparin).mp.) AND ((randomized controlled trial.pt. OR controlled clinical trial.pt. OR randomized.ab. OR placebo.ab. OR drug therapy.fs. OR randomly.ab. OR trial.ab. OR groups.ab.) NOT (exp animals/ not humans.sh.))

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#### **ClinicalTrials.gov**

**Conditions:** Peripheral Arterial Disease, Peripheral Artery Disease, Peripheral Vascular Disease, Peripheral Artery Occlusive Disease, Critical Limb Ischemia, Intermittent Claudication

**Treatment:** Anticoagulants, Antithrombotic Drugs, Platelet Aggregation Inhibitors, Antiplatelet, anti-platelet, Thienopyridine, Aspirin, Acetylsalicylic acid, ASA, Nitroaspirin, Clopidogrel, Prasugrel, Elinogrel, Ticagrelor, Cangrelor, Carbasalate calcium, Dipyridamole, Ticlopidine, Triflusal, Cilostazol, Vorapaxar, Indobufen, Factor Xa, Rivaroxaban, Apixaban, Edoxaban, Otamixaban, Betrixaban, Darexaban, Argatroban, Melagatran, Dabigatran, Ximelagatran, Lepirudin, Desirudin, Bivalirudin, Idraparinux, idrabioparinux, Fondaparinux, Vitamin K antagonist, Coumarin, Warfarin, Acenocoumarol, Phenprocoumon, Phenindione, Fluindione, Difenacoum, Heparin, Low molecular weight heparin, Imwh, Tinzaparin, Reviparin, Parnaparin, Nadroparin, Enoxaparin, Danaparoid, Dalteparin, Certoparin, Bemiparin

*All conditions were combined with all treatment search terms.*

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#### **Cochrane Central Register of Controlled Trials:**

("Peripheral Arterial Disease" OR "Peripheral Arterial Diseases" OR "Peripheral Artery Disease" OR "Peripheral Artery Diseases" OR "Peripheral Arterial Occlusive Disease" OR "Peripheral Arterial Occlusive Diseases" OR "Peripheral Vascular Disease" OR "Peripheral Vascular Diseases" OR "Intermittent Claudication" OR "Critical Limb Ischemia" OR "Aortic Occlusive Disease" OR "Aortic Occlusive Diseases" OR "Aortic Artery Disease" OR "Aortic Artery Diseases" OR "Aortic Arterial Disease" OR "Aortic Arterial Diseases" OR "Iliac Occlusive Disease" OR "Iliac Occlusive Diseases" OR "Iliac Artery Disease" OR "Iliac Artery Diseases" OR "Iliac Arterial Disease" OR "Iliac Arterial Diseases" OR "Femoral Occlusive Disease" OR "Femoral Occlusive Diseases" OR "Femoral Artery Disease" OR "Femoral Artery Diseases" OR "Femoral Arterial Disease" OR "Femoral Arterial Diseases" OR "Popliteal Occlusive Disease" OR "Popliteal Occlusive Diseases" OR "Popliteal Artery Disease" OR "Popliteal Artery Diseases" OR "Popliteal Arterial Disease" OR "Popliteal Arterial Diseases" OR "Femoropopliteal

Occlusive Disease" OR "Femoropopliteal Occlusive Diseases" OR "Femoropopliteal Artery Disease" OR "Femoropopliteal Artery Diseases" OR "Femoropopliteal Arterial Disease" OR "Femoropopliteal Arterial Diseases") in Title Abstract Keyword AND (anticoagulant OR antithrombotic OR "platelet aggregation inhibitors" OR "platelet aggregation inhibitor" OR "platelet inhibitor" OR "platelet inhibitors" OR "antiplatelet" OR "antiplatelets" OR "anti-platelet" OR "anti-platelets" OR P2Y12 OR thienopyridine OR thienopyridines OR Aspirin OR "Acetylsalicylic acid" OR Nitroaspirin OR ASA OR Clopidogrel OR Prasugrel OR Satigrel OR Pyragrel OR Elinogrel OR Ticagrelor OR Cangrelor OR "Carbasalate calcium" OR Dipyridamole OR Ticlopidine OR Picotamide OR Triflusal OR Cilostazol OR Vorapaxar OR Indobufen OR "factor Xa" OR Rivaroxaban OR Apixaban OR Edoxaban OR Otamixaban OR Betrixaban OR Darexaban OR Argatroban OR Melagatran OR Inogatran OR Terutroban OR Dabigatran OR Ximelagatran OR Lepirudin OR Desirudin OR Bivalirudin OR Idraparinux OR Idrabiotaparinux OR Fondaparinux OR "vitamin K" OR coumarin OR Warfarin OR Acenocoumarol OR Phenprocoumon OR Phenindione OR Fluindione OR Difenacoum OR Dicumarol OR Heparin OR LMWH OR LMH OR heparinoids OR Tinzaparin OR Reviparin OR Parnaparin OR Nadroparin OR Enoxaparin OR Danaparoid OR Dalteparin OR Certoparin OR Bemiparin OR Ardeparin) in Title Abstract Keyword - (Word variations have been searched)

