Figure A8. Major bleeding.

Study or Subgroup	NEW ANTICOAGULANT Events	Total	ENOXAPARIN Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
1.33.1 DABIGATRAN STUDIES						
01. RE-MODEL (TKR)	19	1402	9	699	6.7%	1.05 [0.48, 2.31]
02. RE-NOVATE (THR)	38	2331	18	1162	11.0%	1.05 [0.60, 1.84]
03. RE-MOBILIZE (TKR)	10	1739	12	876	6.1%	0.42 [0.18, 0.97]
04. RE-NOVATE II (THR)	14	1036	9	1019	6.1%	1.53 [0.67, 3.52]
Subtotal (95% CI)		**6508**		**3756**	**29.8%**	**0.94 [0.58, 1.52]**
Total events	81		48			
Heterogeneity: Tau² = 0.10; Chi² = 5.13, df = 3 (P = 0.16); I² = 41%						
Test for overall effect: Z = 0.27 (P = 0.79)						
1.33.2 RIVAROXABAN STUDIES						
05. RECORD 1 (THR)	40	2266	33	2275	13.9%	1.22 [0.77, 1.92]
06. RECORD 2 (THR)	23	1252	19	1257	9.9%	1.22 [0.67, 2.22]
07. RECORD 3 (TKR)	21	1254	17	1277	9.2%	1.26 [0.67, 2.37]
08. RECORD 4 (TKR)	27	1584	16	1564	9.6%	1.67 [0.90, 3.08]
09. PROOF CONCEPT (THR)	2	84	0	162	0.6%	9.59 [0.47, 197.46]
10. ODIXA KNEE (TKR)	0	102	2	105	0.6%	0.21 [0.01, 4.24]
11. ODIXA HIP BID (THR)	3	139	2	136	1.6%	1.47 [0.25, 8.65]
12. ODIXA HIP OD (THR)	1	147	3	160	1.0%	0.36 [0.04, 3.45]
Subtotal (95% CI)		**6828**		**6936**	**46.3%**	**1.29 [0.98, 1.69]**
Total events	117		92			
Heterogeneity: Tau² = 0.00; Chi² = 5.12, df = 7 (P = 0.65); I² = 0%						
Test for overall effect: Z = 1.82 (P = 0.07)						
1.33.3 APIXABAN STUDIES						
13. ADVANCE-1 (TKR)	11	1599	22	1596	7.7%	0.50 [0.24, 1.03]
14. ADVANCE-2 (TKR)	9	1528	14	1529	6.1%	0.64 [0.28, 1.48]
15. ADVANCE-3 (THR)	22	2708	18	2699	9.5%	1.22 [0.65, 2.27]
16. APROPOS (TKR)	4	310	0	152	0.6%	4.43 [0.24, 81.71]
Subtotal (95% CI)		**6145**		**5976**	**23.8%**	**0.81 [0.45, 1.43]**
Total events	46		54			
Heterogeneity: Tau² = 0.13; Chi² = 5.00, df = 3 (P = 0.17); I² = 40%						
Test for overall effect: Z = 0.74 (P = 0.46)						
Total (95% CI)		**19481**		**16668**	**100.0%**	**1.05 [0.83, 1.32]**
Total events	244		194			
Heterogeneity: Tau² = 0.05; Chi² = 19.24, df = 15 (P = 0.20); I² = 22%						
Test for overall effect: Z = 0.40 (P = 0.69)						
Test for subgroup differences: Chi² = 2.82, df = 2 (P = 0.24), I² = 29.0%						

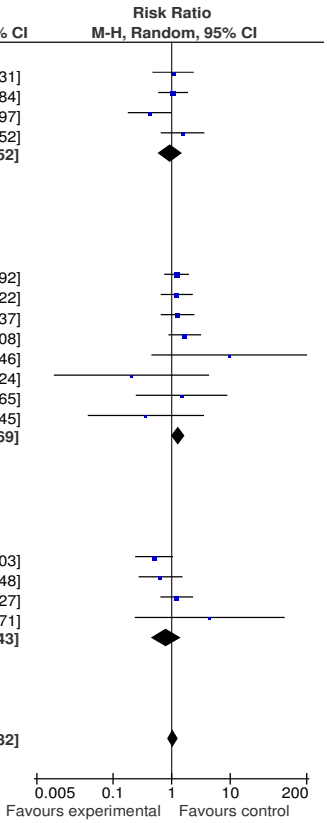


Figure A9. Clinically relevant minor bleeding.

Study or Subgroup	NEW ANTICOAGULANT Events	Total	ENOXAPARIN Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
1.38.1 DABIGATRAN STUDIES						
01. RE-MODEL (TKR)	88	1402	37	699	10.1%	1.19 [0.82, 1.72]
02. RE-NOVATE (THR)	103	2331	40	1162	10.8%	1.28 [0.90, 1.84]
03. RE-MOBILIZE (TKR)	45	1739	21	876	5.8%	1.08 [0.65, 1.80]
04. RE-NOVATE II (THR)	23	1036	20	1019	4.4%	1.13 [0.63, 2.05]
Subtotal (95% CI)		**6508**		**3756**	**31.1%**	**1.19 [0.96, 1.48]**
Total events	259		118			
Heterogeneity: Tau² = 0.00; Chi² = 0.34, df = 3 (P = 0.95); I² = 0%						
Test for overall effect: Z = 1.61 (P = 0.11)						
1.38.2 RIVAROXABAN STUDIES						
05. RECORD 1 (THR)	65	2266	54	2275	10.9%	1.21 [0.85, 1.73]
06. RECORD 2 (THR)	40	1252	33	1257	7.2%	1.22 [0.77, 1.92]
07. RECORD 3 (TKR)	33	1254	28	1277	6.1%	1.20 [0.73, 1.97]
08. RECORD 4 (TKR)	39	1584	30	1564	6.7%	1.28 [0.80, 2.06]
09. PROOF CONCEPT (THR)	1	84	3	162	0.3%	0.64 [0.07, 6.09]
10. ODIXA KNEE (TKR)	3	102	3	105	0.7%	1.03 [0.21, 4.98]
11. ODIXA HIP BID (THR)	8	139	0	136	0.2%	16.64 [0.97, 285.42]
12. ODIXA HIP OD (THR)	3	147	5	160	0.8%	0.65 [0.16, 2.68]
Subtotal (95% CI)		**6828**		**6936**	**33.0%**	**1.21 [0.98, 1.50]**
Total events	192		156			
Heterogeneity: Tau² = 0.00; Chi² = 4.46, df = 7 (P = 0.73); I² = 0%						
Test for overall effect: Z = 1.80 (P = 0.07)						
1.38.3 APIXABAN STUDIES						
13. ADVANCE-1 (TKR)	35	1599	47	1596	7.9%	0.74 [0.48, 1.14]
14. ADVANCE-2 (TKR)	44	1528	58	1529	9.6%	0.76 [0.52, 1.12]
15. ADVANCE-3 (THR)	109	2708	120	2699	18.3%	0.91 [0.70, 1.17]
16. APROPOS (TKR)	0	310	2	152	0.2%	0.10 [0.00, 2.04]
Subtotal (95% CI)		**6145**		**5976**	**35.9%**	**0.83 [0.68, 1.00]**
Total events	188		227			
Heterogeneity: Tau² = 0.00; Chi² = 2.81, df = 3 (P = 0.42); I² = 0%						
Test for overall effect: Z = 1.95 (P = 0.05)						
Total (95% CI)		**19481**		**16668**	**100.0%**	**1.05 [0.92, 1.19]**
Total events	639		501			
Heterogeneity: Tau² = 0.01; Chi² = 16.75, df = 15 (P = 0.33); I² = 10%						
Test for overall effect: Z = 0.69 (P = 0.49)						
Test for subgroup differences: Chi² = 9.18, df = 2 (P = 0.01), I² = 78.2%						

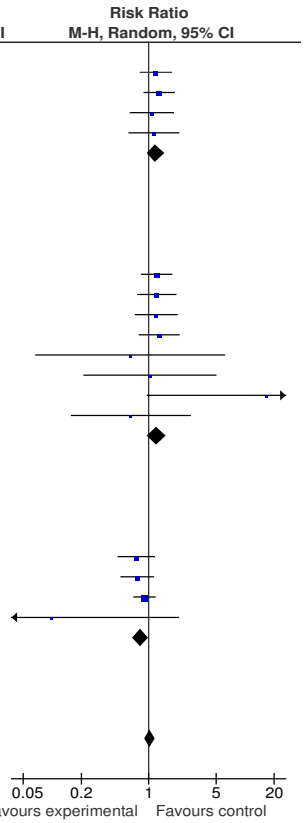
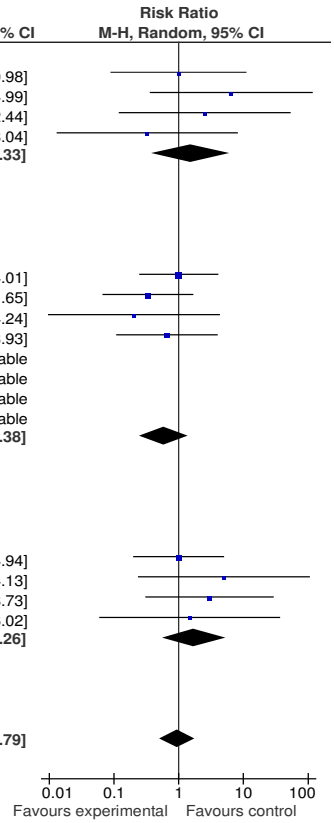


Figure A10. Mortality.

Study or Subgroup	NEW ANTICOAGULANT Events	Total	ENOXAPARIN Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
1.47.1 DABIGATRAN STUDIES						
01. RE-MODEL (TKR)	2	1402	1	699	6.6%	1.00 [0.09, 10.98]
02. RE-NOVATE (THR)	6	2331	0	1162	4.6%	6.48 [0.37, 114.99]
03. RE-MOBILIZE (TKR)	2	1739	0	876	4.1%	2.52 [0.12, 52.44]
04. RE-NOVATE II (THR)	0	1036	1	1019	3.7%	0.33 [0.01, 8.04]
Subtotal (95% CI)		**6508**		**3756**	**19.1%**	**1.54 [0.38, 6.33]**
Total events	10		2			
Heterogeneity: Tau² = 0.00; Chi² = 2.16, df = 3 (P = 0.54); I² = 0%						
Test for overall effect: Z = 0.60 (P = 0.55)						
1.47.2 RIVAROXABAN STUDIES						
05. RECORD 1 (THR)	4	2266	4	2275	19.8%	1.00 [0.25, 4.01]
06. RECORD 2 (THR)	2	1252	6	1257	14.9%	0.33 [0.07, 1.65]
07. RECORD 3 (TKR)	0	1254	2	1277	4.1%	0.20 [0.01, 4.24]
08. RECORD 4 (TKR)	2	1584	3	1564	11.9%	0.66 [0.11, 3.93]
09. PROOF CONCEPT (THR)	0	84	0	162		Not estimable
10. ODIXA KNEE (TKR)	0	102	0	105		Not estimable
11. ODIXA HIP BID (THR)	0	139	0	136		Not estimable
12. ODIXA HIP OD (THR)	0	147	0	160		Not estimable
Subtotal (95% CI)		**6828**		**6936**	**50.8%**	**0.58 [0.24, 1.38]**
Total events	8		15			
Heterogeneity: Tau² = 0.00; Chi² = 1.55, df = 3 (P = 0.67); I² = 0%						
Test for overall effect: Z = 1.24 (P = 0.22)						
1.47.3 APIXABAN STUDIES						
13. ADVANCE-1 (TKR)	3	1599	3	1596	14.9%	1.00 [0.20, 4.94]
14. ADVANCE-2 (TKR)	2	1528	0	1529	4.1%	5.00 [0.24, 104.13]
15. ADVANCE-3 (THR)	3	2708	1	2699	7.4%	2.99 [0.31, 28.73]
16. APROPOS (TKR)	1	310	0	152	3.7%	1.48 [0.06, 36.02]
Subtotal (95% CI)		**6145**		**5976**	**30.2%**	**1.71 [0.56, 5.26]**
Total events	9		4			
Heterogeneity: Tau² = 0.00; Chi² = 1.17, df = 3 (P = 0.76); I² = 0%						
Test for overall effect: Z = 0.94 (P = 0.35)						
Total (95% CI)		**19481**		**16668**	**100.0%**	**0.97 [0.52, 1.79]**
Total events	27		21			
Heterogeneity: Tau² = 0.00; Chi² = 7.59, df = 11 (P = 0.75); I² = 0%						
Test for overall effect: Z = 0.11 (P = 0.92)						
Test for subgroup differences: Chi² = 2.76, df = 2 (P = 0.25), I² = 27.6%