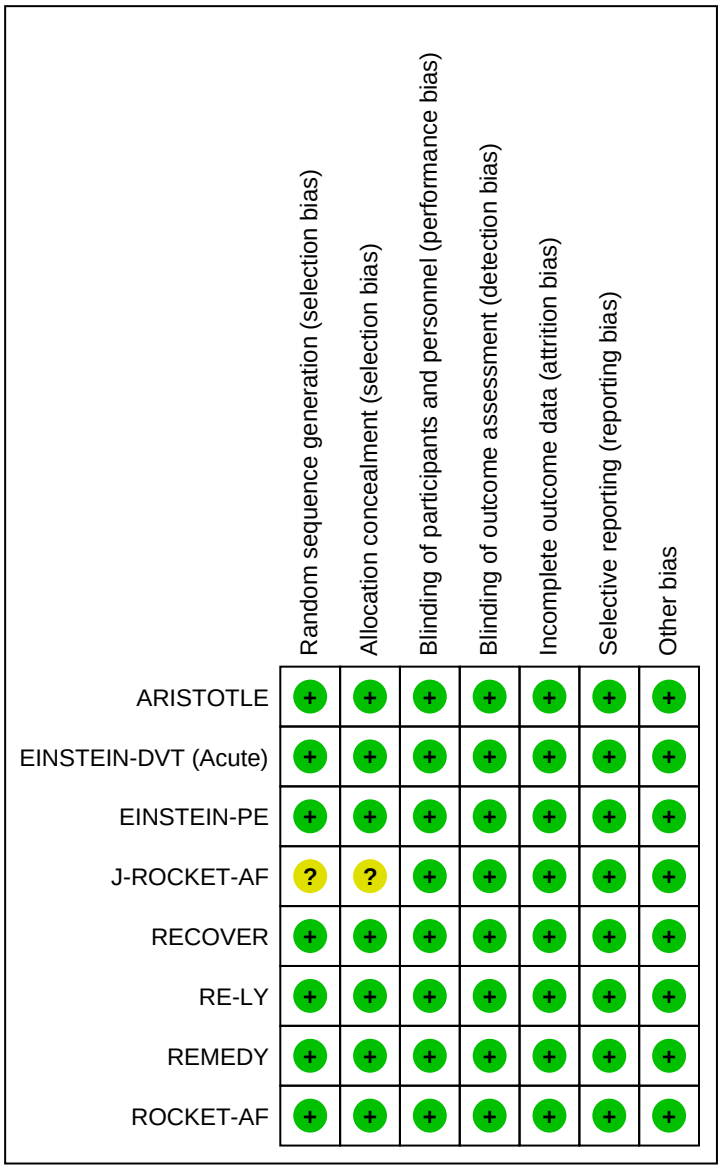
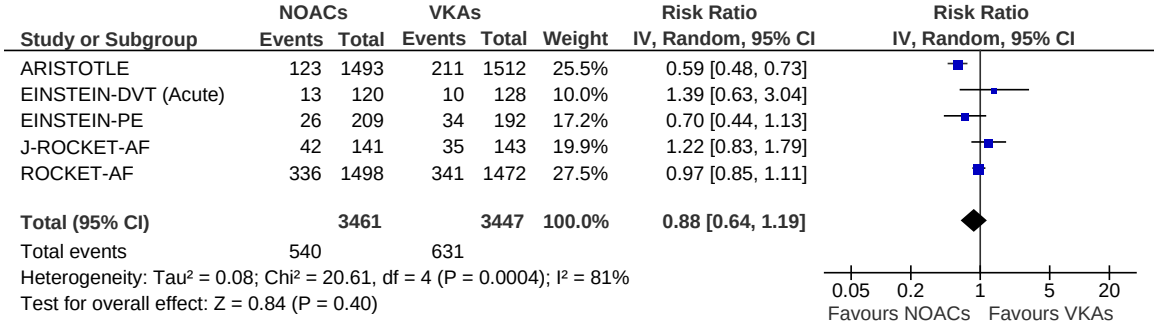


Supplementary Table 1: Risk of bias in included studies.

Supplementary Figure 1: Risk of combined bleeding endpoint (major bleeding and clinically relevant non-major bleeding) stratified by indication among participants with a creatinine clearance ≤ 50 mL/min given a novel oral anticoagulant (NOAC) versus a vitamin K antagonist (VKA). Values less than 1.0 indicate a decreased risk of outcome with NOAC use.

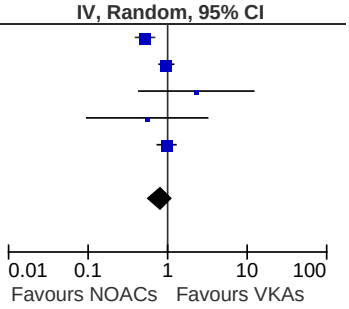


Supplementary Figure 2: Risk of major bleeding endpoint among participants with a creatinine clearance ≤ 50 mL/min given a novel oral anticoagulant (NOAC) versus a vitamin K antagonist (VKA). Values less than 1.0 indicate a decreased risk of outcome with NOAC use.

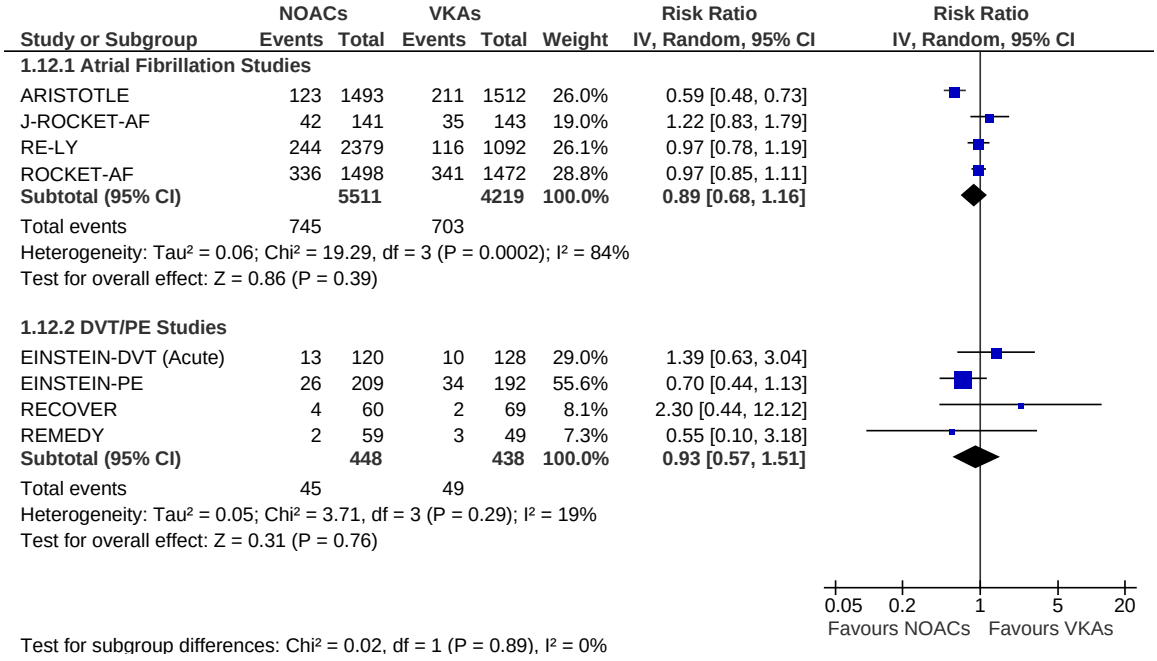
	NOACs		VKAs			Risk Ratio	Risk Ratio
Study or Subgroup	**Events**	**Total**	**Events**	**Total**	**Weight**	**IV, Random, 95% CI**	**IV, Random, 95% CI**
ARISTOTLE	73	1493	142	1512	29.8%	0.52 [0.40, 0.68]	
RE-LY	244	2379	116	1092	32.1%	0.97 [0.78, 1.19]	
RECOVER	4	60	2	69	4.2%	2.30 [0.44, 12.12]	
REMEDY	2	59	3	49	3.8%	0.55 [0.10, 3.18]	
ROCKET-AF	99	1498	100	1472	30.0%	0.97 [0.74, 1.27]	
Total (95% CI)		**5489**		**4194**	**100.0%**	**0.82 [0.57, 1.17]**	
Total events	422		363				

Heterogeneity: Tau² = 0.10; Chi² = 16.20, df = 4 (P = 0.003); I² = 75%

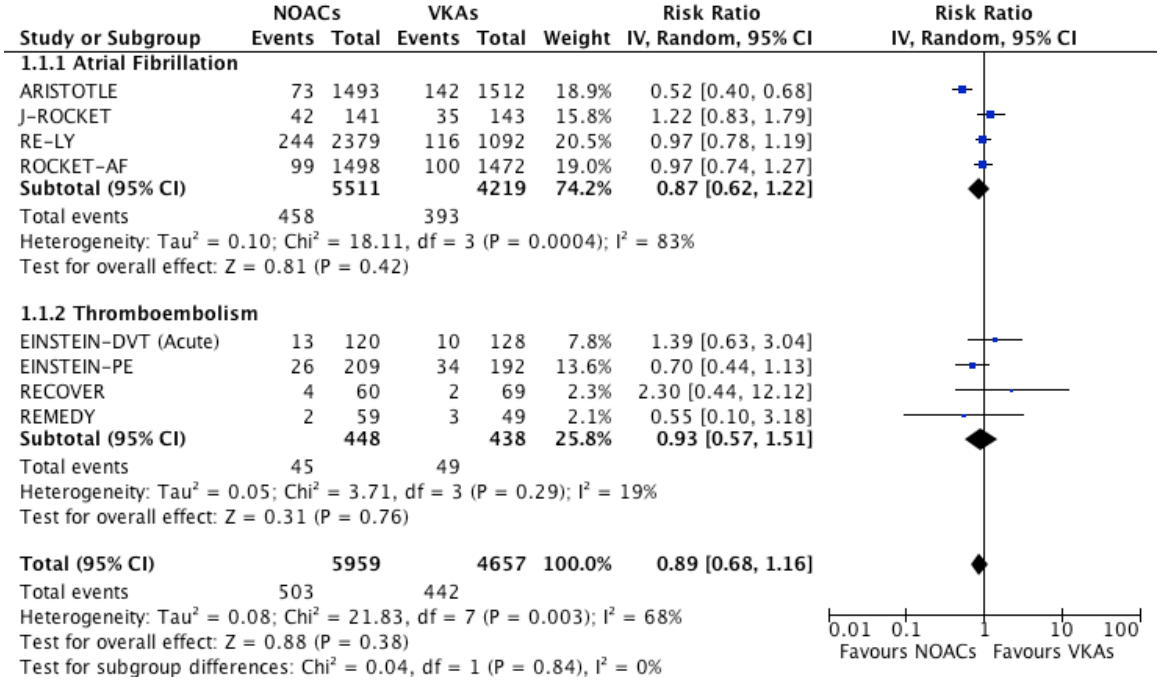
Test for overall effect: Z = 1.09 (P = 0.28)



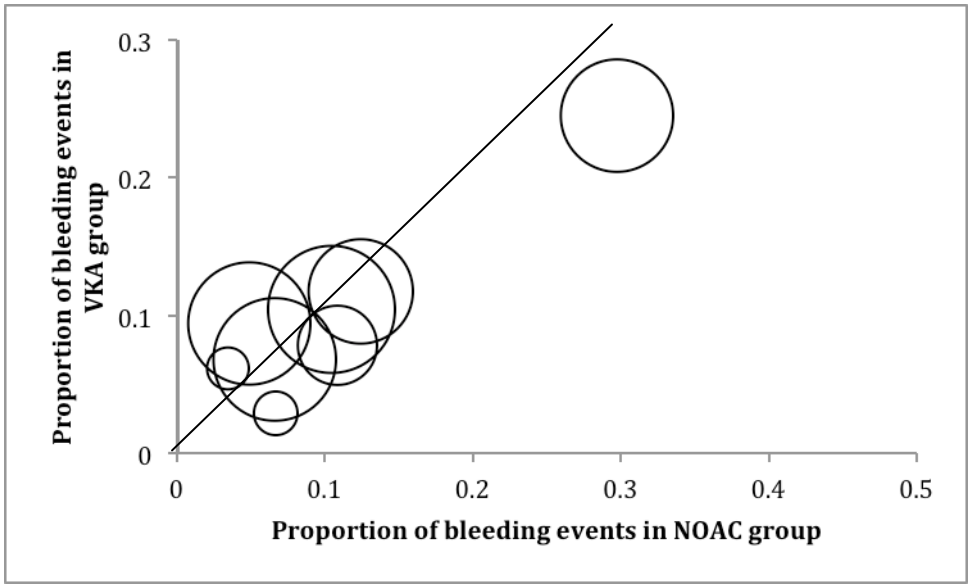
Supplementary Figure 3: a) Stroke and systemic thromboembolism, and b) recurrent thromboembolism or thromboembolism related death; among participants with a creatinine clearance ≥ 80 mL/min given a novel oral anticoagulant (NOAC) versus a vitamin K antagonist (VKA) Values less than 1.0 indicate a decreased risk of outcome with NOAC use.



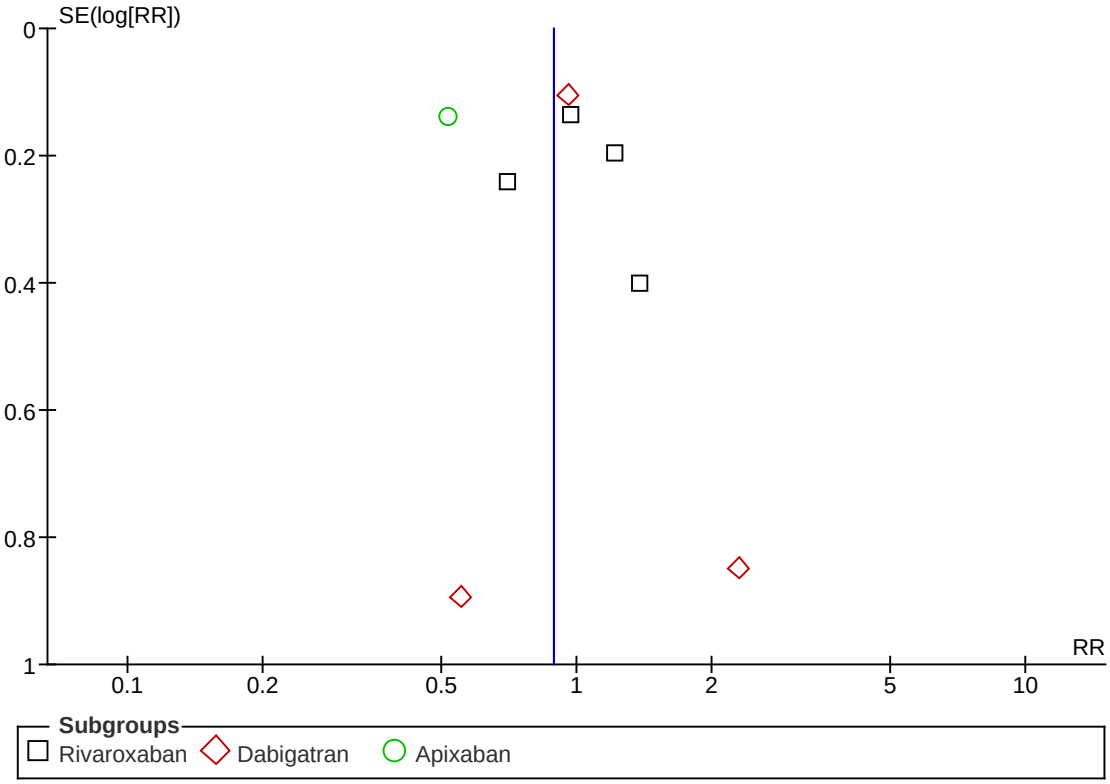
Supplementary Figure 4: Risk of major bleeding or combined bleeding endpoint (major bleeding and clinically relevant non-major bleeding) among participants with creatinine clearance ≤ 50 mL/min given a novel oral anticoagulant (NOAC) versus a vitamin K antagonist (VKA) stratified by indication for NOAC.



Supplementary Figure 5: L'Abbe plot of bleeding risk of included studies. Each circle represents a study, with the size of the circle inversely proportional to the standard error (reflecting size of study). The continuous line represents an equal risk of bleeding between the NOACs and VKAs.



Supplementary Figure 6: Funnel plot of included studies.



Supplementary Appendix: Search strategy.
MEDLINE:

The search strategy for OvidSP MEDLINE (1946 to **March, 2013**). We used a combination of MeSH and free text terms for

Set	History
1	(dabigatran or "bibr 953" or "bibr953" or pradax or Pradaxa or prazaxa).mp.
2	warfarin/ or (coumadin* or aldocumar or tedicumar).mp. warfarin/ or
3	(controlled clinical trial or randomized controlled trial).pt. or controlled clinical trials as topic/ or randomized controlled trials as topic/ or (random* or (doubl* adj2 dummy) or ((Singl* or doubl* or trebl* or tripl*) adj5 (blind* or mask*)) or RCT or RCTs or (control* adj5 trial*) or multicent* or placebo* or metaanalys* or (meta adj5 analys*) or sham or effectiveness or efficacy or compar*).ti,ab. or cohort studies/ or longitudinal studies/ or follow-up studies/ or prospective studies/ or ((observation* adj2 study) or (observation* adj2 studies)).mp.
4	1 and 2 and 3
5	(rivaroxaban or "bay 59 7939" or "bay 59-7939" or "bay 597939" or "bay59 7939" or "bay59-7939" or bay597939 or xarelto).mp.
6	2 and 3 and 5
7	(apixaban or "bms 562247" or bms562247 or eliques or eliquis).mp.
8	2 and 3 and 7

EMBASE
The search strategy for OvidSP EMBASE (1980 to 2013 March). I used a combination of EMBASE and free text terms for

Set	History
1	(dabigatran or "bibr 953" or "bibr953" or pradax or Pradaxa or prazaxa).mp.
2	warfarin/ or coumarin anticoagulant/ or coumarin derivative/
3	randomized controlled trial/ or controlled clinical trial/ or "randomized controlled trial (topic)"/ or

	"controlled clinical trial (topic)"/ or (random* or (doubl* adj2 dummy) or ((Singl* or doubl* or trebl* or tripl*) adj5 (blind* or mask*)) or RCT or RCTs or (control* adj5 trial*) or multicent* or placebo* or metaanalys* or (meta adj5 analys*) or sham or effectiveness or efficacy or compar*).ti,ab. or randomization/ or ct.fs. or cohort analysis/ or longitudinal study/ or prospective study/ or case control study/ or hospital based case control study/ or population based case control study/ or retrospective study/ or ((observation* adj2 study) or (observation* adj2 studies)).mp.
4	1 and 2 and 3
5	rivaroxaban/ or (rivaroxaban or "bay 59 7939" or "bay 59-7939" or "bay 597939" or "bay59 7939" or "bay59-7939" or bay597939 or xarelto).mp.
6	2 and 3 and 5
7	apixaban/ or (apixaban or "bms 562247" or bms562247 or eliques or eliquis).mp.
8	2 and 3 and 7

EBM Reviews - Cochrane Central Register of Controlled Trials

The search strategy for OvidSP EBM Reviews - CCTR (March 2013). This database consists exclusively of RCTs, no study design terms were used. I used a combination of primarily MeSH and free text terms for

Set	History
1	dabigatran/ or (dabigatran or "bibr 953" or "bibr953" or pradax or Pradaxa or prazaxa).mp. or rivaroxaban/ or (rivaroxaban or "bay 59 7939" or "bay 59-7939" or "bay 597939" or "bay59 7939" or "bay59-7939" or bay597939 or xarelto).mp. or apixaban/ or (apixaban or "bms 562247" or bms562247 or eliques or eliquis).mp.
2	warfarin/ or coumarin anticoagulant/ or coumarin derivative/ or (coumadin* or aldocumar or tedicumar).mp.
3	1 and 2