

Best available evidence regarding
the **DOAC** use in patients with
Renal impairment

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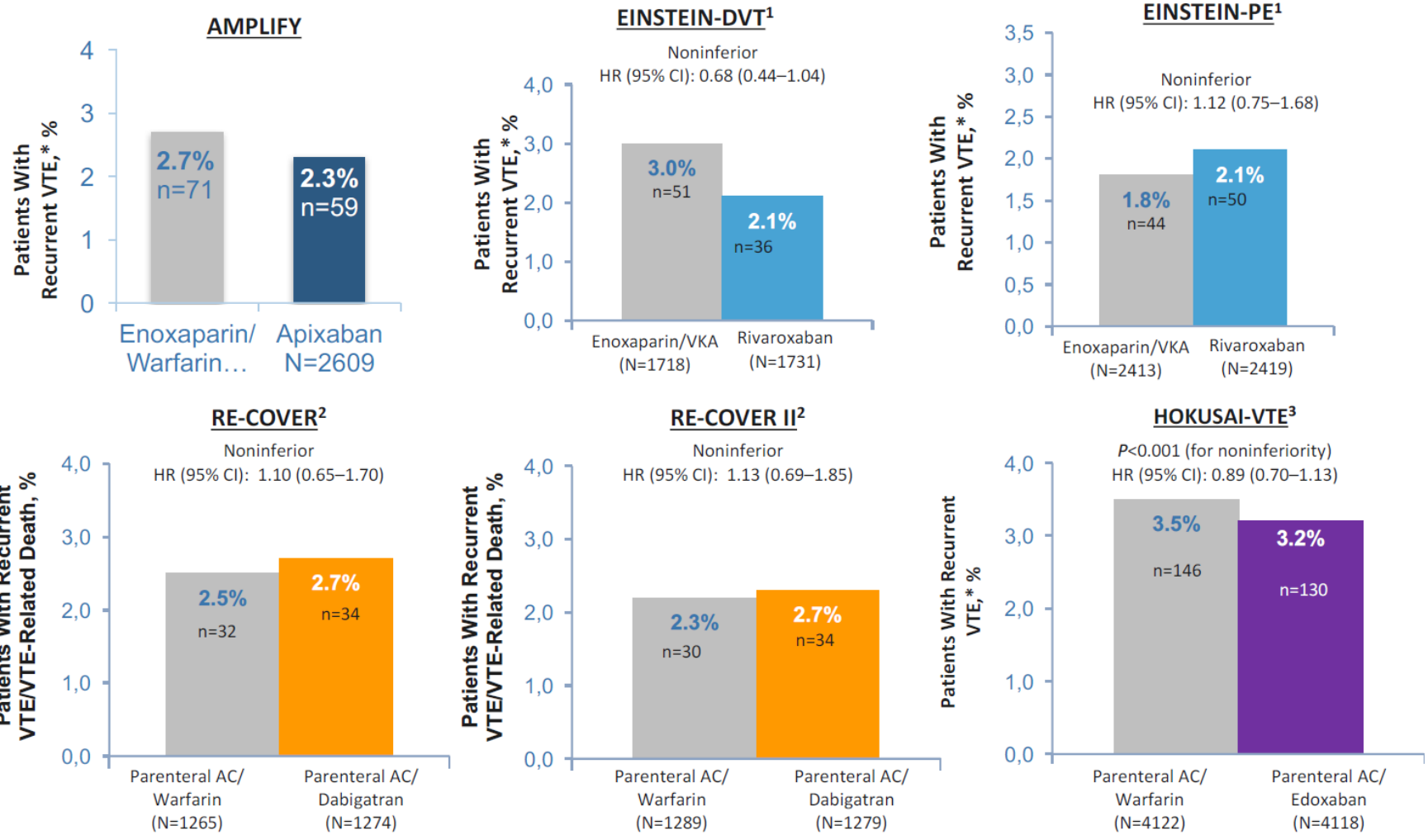
Disclosures

- Consultancy for Abidi, Actover, Arena, Bayer and Boehringer Ingelheim
- Research funding from Abidi, Actover, Arena, Bayer and Boehringer Ingelheim
- Advisory committee or board of ELAQUIT (Abidi), XARELTO (Bayer)

DOAC trough RCT

	Dabigatran (RE-LY ¹⁻³)		Apixaban (ARISTOTLE ^{4,5})	Rivaroxaban (ROCKET AF ⁶)	Edoxaban (ENGAGE AF-TIMI 48 ⁷)
	150 mg BID	110 mg BID	5/2.5 mg BID	20/15 mg OD	60/30 mg OD
Stroke/SE	↓ 35%	Similar	↓ 21%	Similar	Similar
Ischemic stroke	↓ 24%	Similar	Similar	Similar	Similar
CV mortality	↓ 15%	Similar	Similar	Similar	↓ 14%
Major bleeding	Similar	↓ 20%	↓ 31%	Similar	↓ 20%
ICH	↓ 70%	↓ 59%	↓ 58%	↓ 33%	↓ 53%

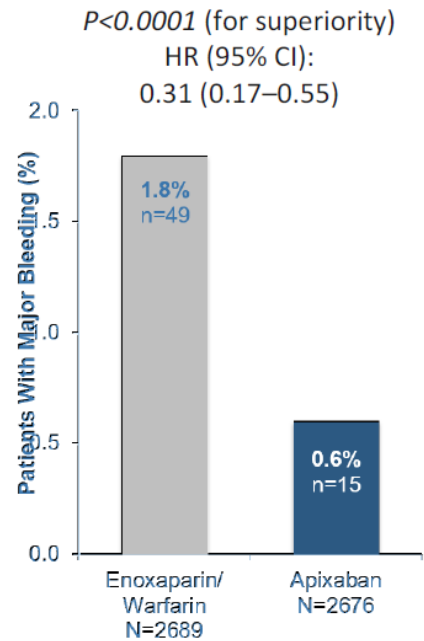
DOAC trough RCT



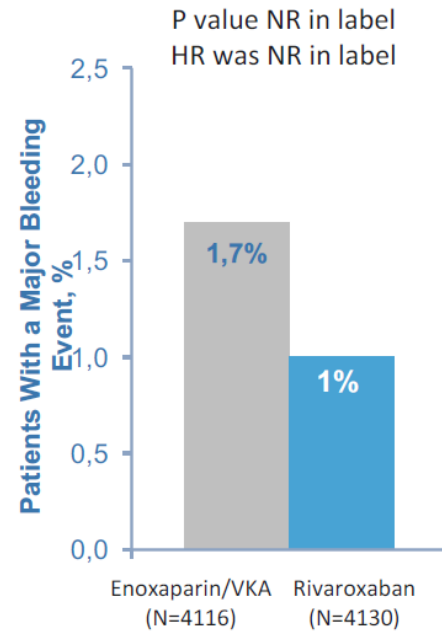
Ruff CT et al. Comparison of the efficacy and safety of new oral anticoagulants with warfarin in patients with atrial fibrillation: a meta-analysis of randomised trials. Lancet. 2014 Mar 15;383(9921):955-62.

DOAC trough RCT

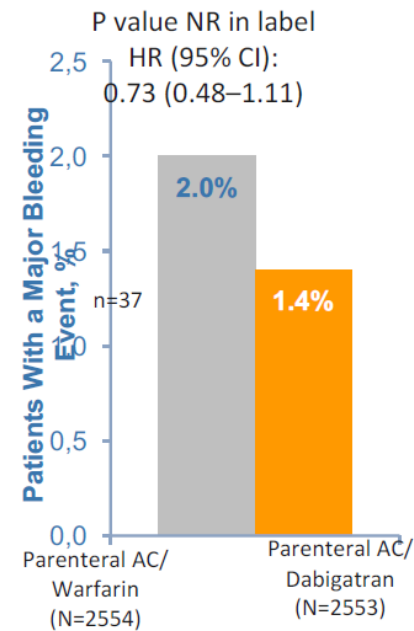
AMPLIFY¹



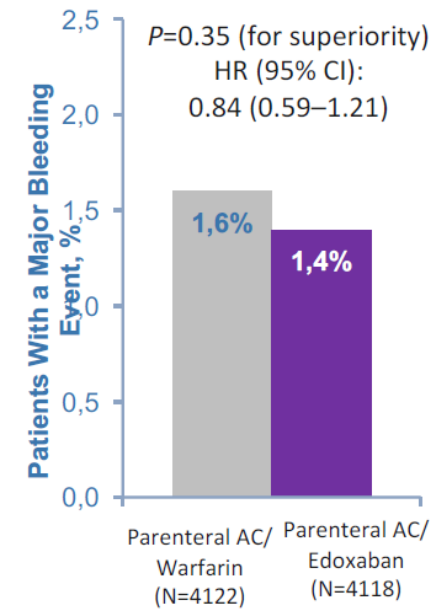
**EINSTEIN-DVT/PE
Pooled Analysis¹**



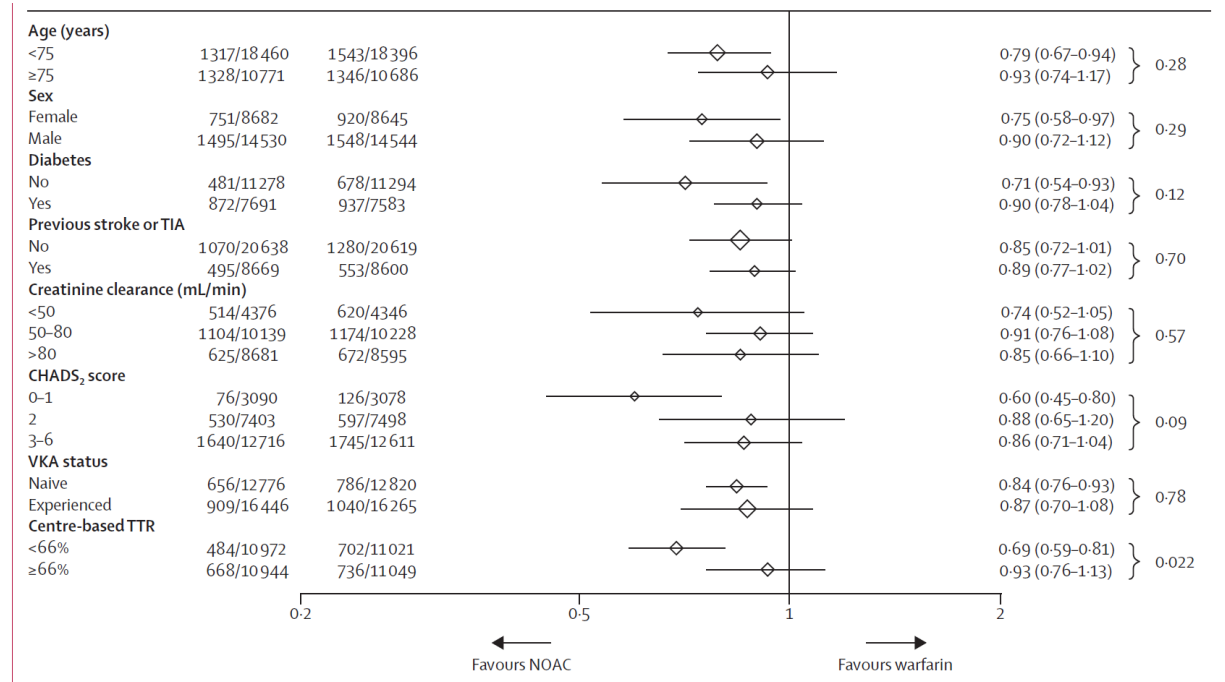
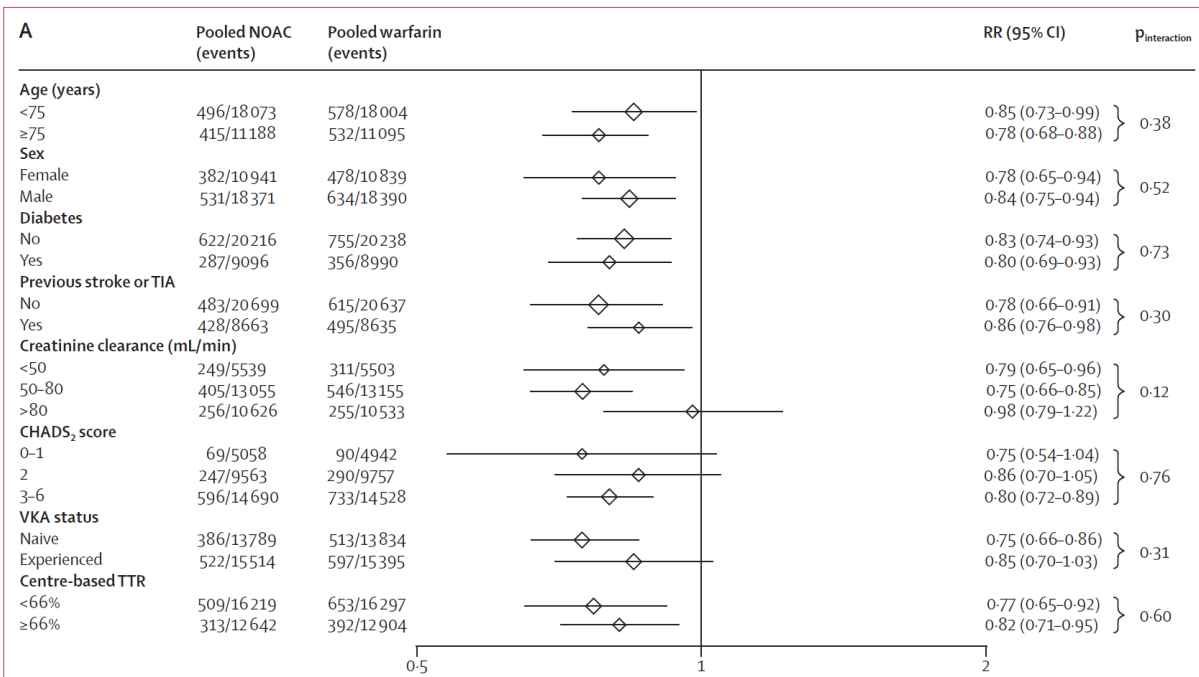
**RE-COVER/RE-COVER II
Pooled Analysis*²**



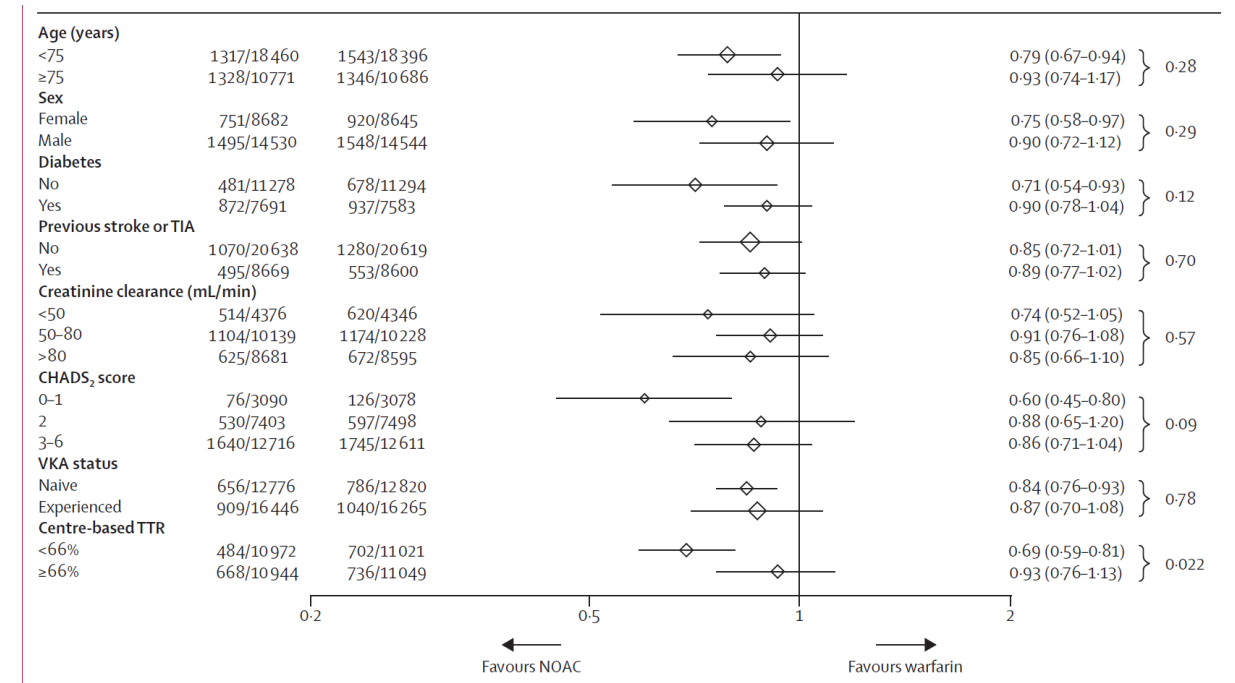
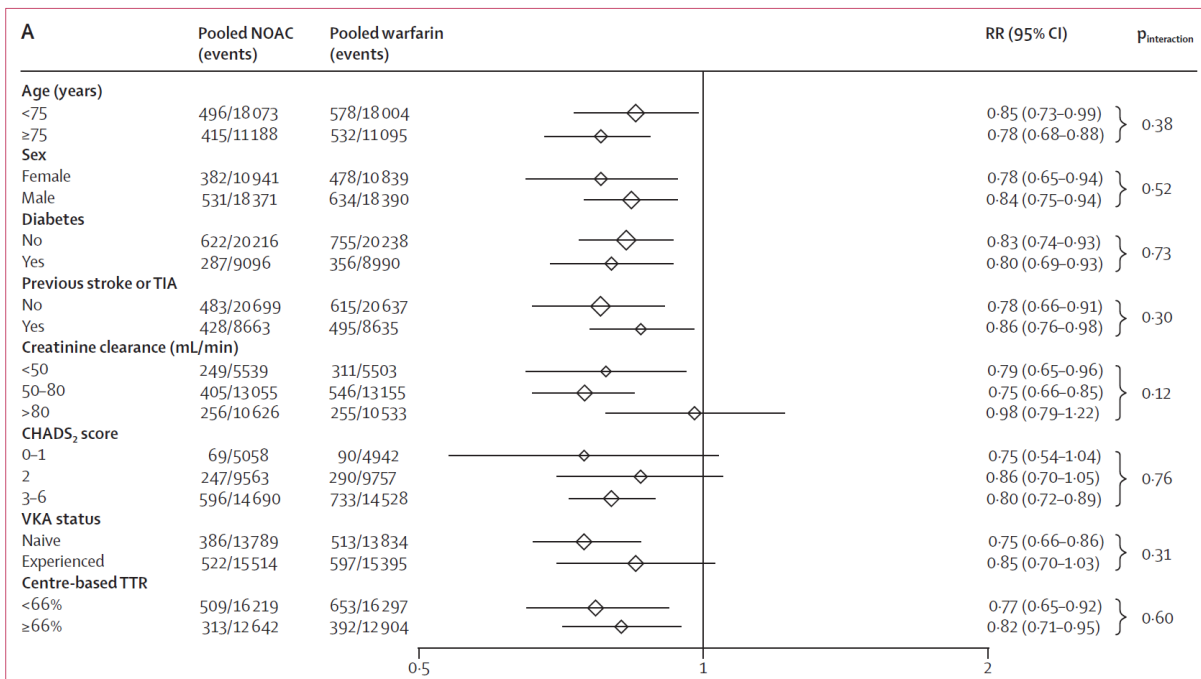
HOKUSAI-VTE³



DOAC trough RCT



DOAC trough RCT



DOAC trough RCT

	Dabigatran (RE-LY)	Rivaroxaban (ROCKET-AF)	Apixaban (ARISTOTLE)	Edoxaban (ENGAGE AF-TIMI 48)
Number of patients	18,113	14,264	18,201	21,105
Dose	150 mg or 110 mg twice daily	20 mg once daily	5 mg twice daily	60 mg or 30 mg once daily
Moderate CKD Definition (CrCl)	31–49 mL/min	25–50 mL/min	30–49 mL/min	30–50 mL/min
Dose adjustment for moderate CKD	75 mg twice daily	15 mg once daily	2.5 mg twice daily	30 mg once daily
Number of patients with moderate CKD	3554 (20%)	2950 (21%)	3017 (17%)	2740 (19.5%)
Exclusion criteria based on CrCl	< 30 mL/min	< 30 mL/min	Serum Cr > 2.5 mg/dL or CrCl < 25 mL/min	< 30 mL/min
Primary efficacy outcome: stroke and SE vs. warfarin (HR, 95% CI)	150 mg: 0.56 (0.37–0.85) 110 mg: 0.85 (0.59–1.24)	0.84 (0.57–1.23)	0.79 (0.55–1.14)	0.87 (0.64–1.19)
Primary safety outcome: major bleeding (HR, 95% CI)	150 mg: 1.02 (0.79–1.30) 110 mg: 0.99 (0.77–1.28)	0.95 (0.72–1.26)	0.5 (0.38–0.66)	0.76 (0.58–0.98)

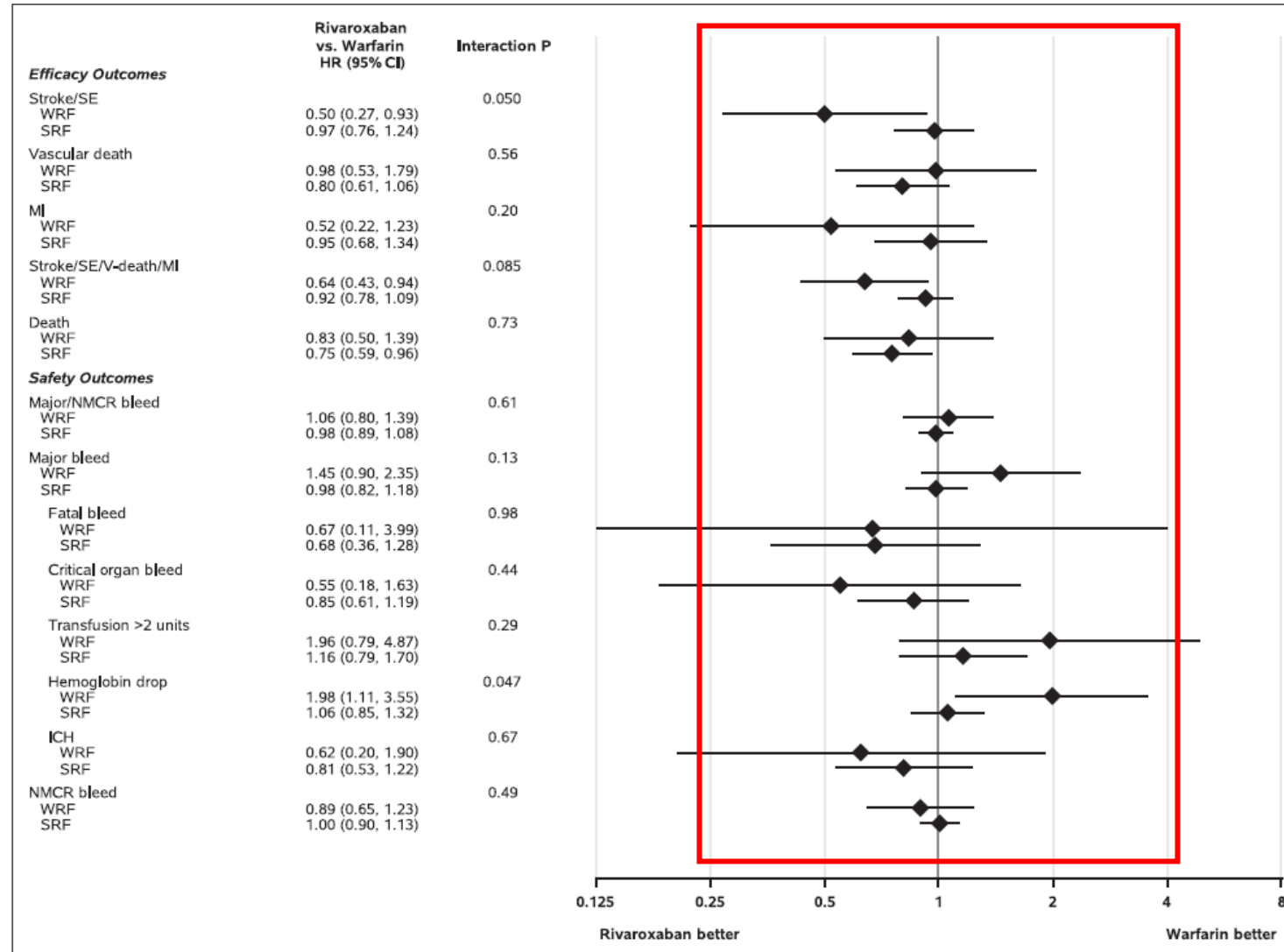
Efficacy and Safety of Dabigatran Compared With Warfarin in Relation to Baseline Renal Function in Patients With Atrial Fibrillation

A RE-LY (Randomized Evaluation of Long-term Anticoagulation Therapy) Trial Analysis

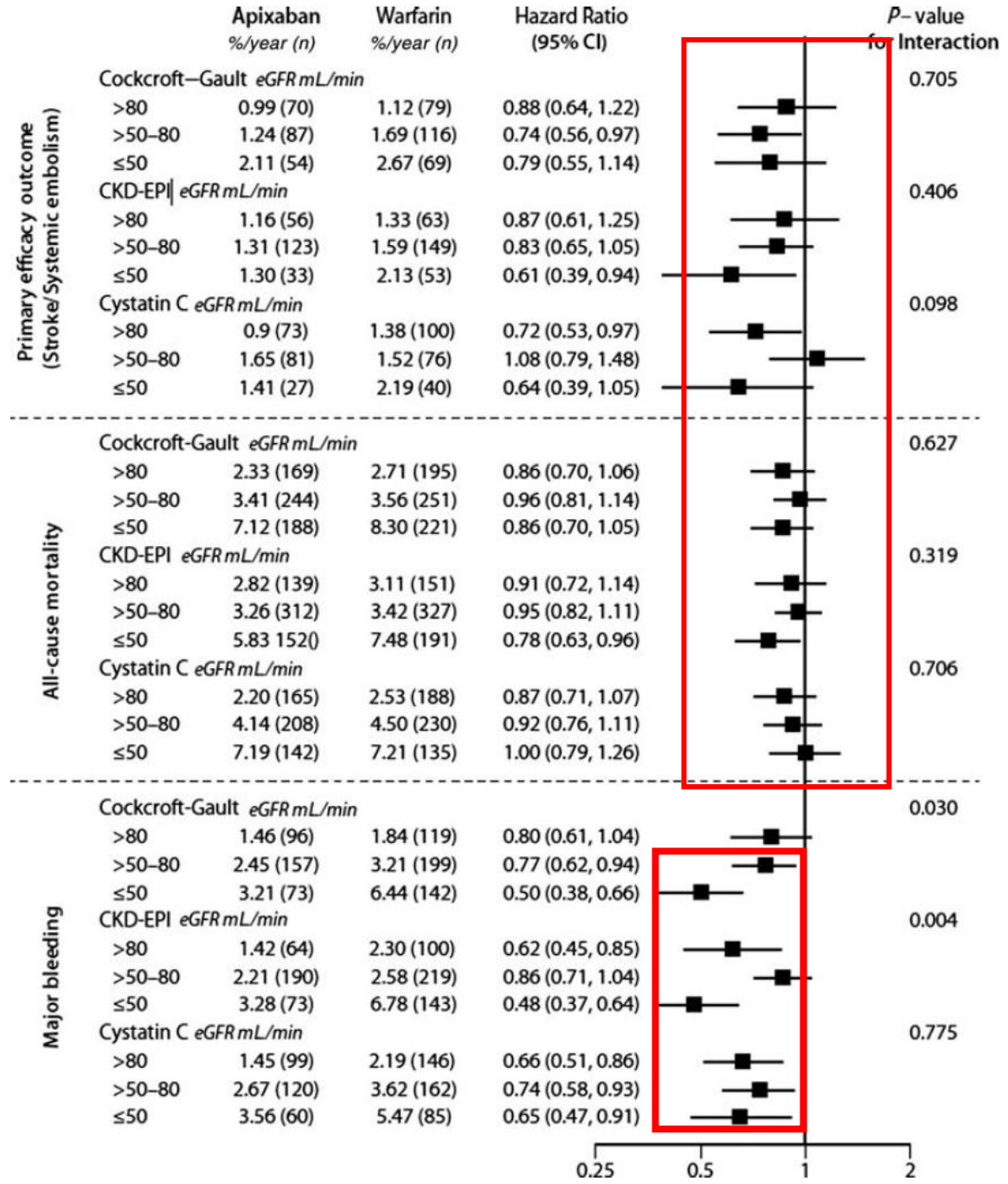
Outcome According to Renal Function Level (in mL/min)	Events, n (%/y)			Dabigatran 110 mg BID vs Warfarin		Dabigatran 150 mg BID vs Warfarin		Dabigatran 150 vs Dabigatran 110 mg BID	
	Dabigatran 110 mg BID Events/n (%/y)	Dabigatran 150 mg BID Events/n (%/y)	Warfarin Events/n (%/y)	HR (95% CI)	PValue (Inter)	HR (95% CI)	PValue (Inter)	HR (95% CI)	PValue (Inter)
Stroke or systemic embolism									0.8337
≥80	35/1958 (0.88)	28/1945 (0.71)	41/1941 (1.05)	0.84 (0.54–1.32)	0.9108	0.67 (0.42–1.09)	0.7522	0.80 (0.49–1.32)	
50 to <80	94/2803 (1.69)	70/2852 (1.25)	103/2898 (1.83)	0.93 (0.70–1.23)		0.68 (0.50–0.92)		0.73 (0.54–1.00)	
<50	52/1196 (2.32)	36/1232 (1.53)	57/1126 (2.70)	0.85 (0.59–1.24)		0.56 (0.37–0.85)		0.66 (0.43–1.01)	
All-cause mortality									0.1941
≥80	89/1958 (2.24)	81/1945 (2.04)	97/1941 (2.48)	0.90 (0.68–1.20)	0.0074	0.82 (0.61–1.11)	0.3610	0.91 (0.68–1.23)	
50 to <80	175/2803 (3.15)	198/2852 (3.53)	244/2898 (4.32)	0.72 (0.60–0.88)		0.81 (0.67–0.98)		1.12 (0.91–1.37)	
<50	176/1196 (7.86)	159/1232 (6.77)	143/1126 (6.77)	1.16 (0.93–1.44)		1.00 (0.80–1.25)		0.86 (0.69–1.07)	
Major bleed									0.3439
≥80	59/1958 (1.48)	81/1945 (2.04)	95/1941 (2.43)	0.61 (0.44–0.84)	0.0607	0.84 (0.62–1.13)	0.6393	1.38 (0.99–1.93)	
50 to <80	158/2803 (2.84)	188/2852 (3.35)	209/2898 (3.70)	0.76 (0.62–0.94)		0.91 (0.75–1.11)		1.19 (0.96–1.47)	
<50	122/1196 (5.45)	129/1232 (5.50)	116/1126 (5.49)	0.99 (0.77–1.28)		1.01 (0.79–1.30)		1.02 (0.79–1.30)	
Life-threatening bleed									0.2565
≥80	17/1958 (0.43)	31/1945 (0.78)	50/1941 (1.28)	0.33 (0.19–0.58)	0.0169	0.61 (0.39–0.95)	0.4254	1.83 (1.01–3.30)	
50 to <80	74/2803 (1.33)	87/2852 (1.55)	107/2898 (1.90)	0.70 (0.52–0.94)		0.82 (0.62–1.08)		1.17 (0.86–1.59)	
<50	56/1196 (2.50)	60/1232 (2.56)	61/1126 (2.89)	0.86 (0.60–1.24)		0.88 (0.62–1.26)		1.02 (0.71–1.47)	
Intracranial bleed									0.2113
≥80	2/1958 (0.05)	7/1945 (0.18)	15/1941 (0.38)	0.13 (0.03–0.57)	0.4022	0.46 (0.19–1.13)	0.6930	3.52 (0.73–16.92)	
50 to <80	14/2803 (0.25)	22/2852 (0.39)	49/2898 (0.87)	0.29 (0.16–0.52)		0.45 (0.27–0.74)		1.56 (0.80–3.05)	
<50	11/1196 (0.49)	9/1232 (0.38)	26/1126 (1.23)	0.40 (0.20–0.80)		0.31 (0.14–0.66)		0.78 (0.32–1.88)	
Net clinical benefit*									0.3042
≥80	186/1958 (4.68)	182/1945 (4.59)	207/1941 (5.29)	0.88 (0.72–1.07)	0.1252	0.87 (0.71–1.06)	0.8534	0.98 (0.80–1.20)	
50 to <80	376/2803 (6.77)	396/2852 (7.05)	453/2898 (8.03)	0.84 (0.73–0.96)		0.88 (0.77–1.01)		1.05 (0.91–1.21)	
<50	291/1196 (12.99)	269/1232 (11.46)	260/1126 (12.31)	1.05 (0.89–1.24)		0.93 (0.78–1.10)		0.88 (0.75–1.04)	

On-Treatment Outcomes in Patients With Worsening Renal Function With Rivaroxaban Compared With Warfarin

Insights From ROCKET AF



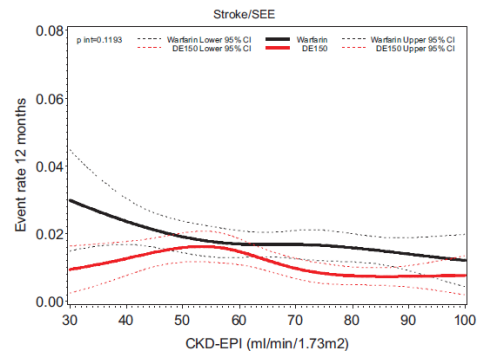
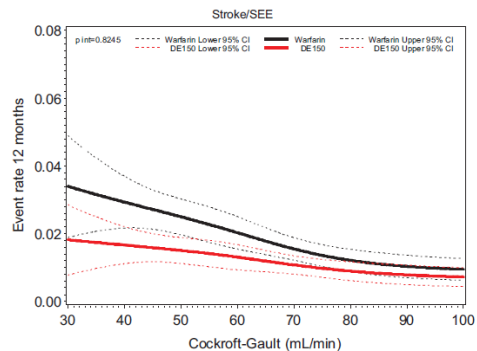
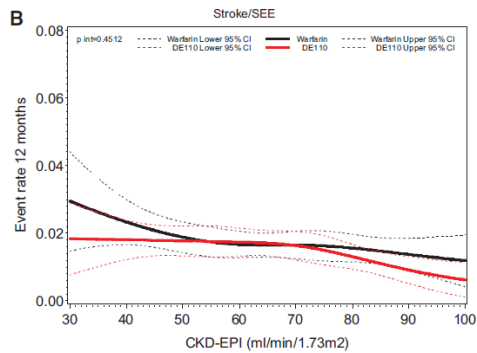
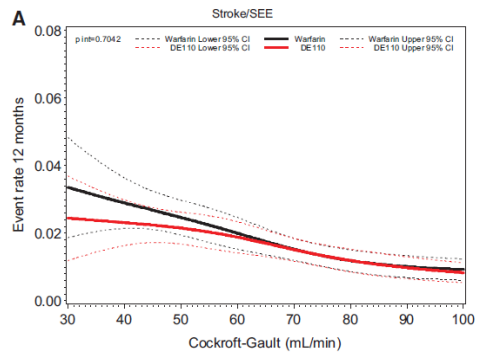
Efficacy of apixaban when compared with warfarin in relation to renal function in patient with atrial fibrillation: insights from the ARISTOTLE trial



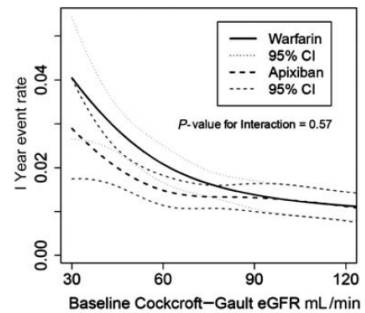
Definition of CKD

Method	Equation	Additional Variables
Cockroft and Gault	$\text{GFR (ml/min)} = \frac{(140 - \text{age}) \times \text{weight (kg)}}{7.2 \times \text{SCr (mg/dl)}}$	× 0.085 if female
MDRD 4-Variable study equation	$\text{GFR (ml/min/1.73 m}^2\text{)} = 186 \times \text{SCr (mg/dl)}^{-1.154} \times \text{age}^{-0.203} \times 0.742 \text{ (if female)}$	× 1.21 if Black-American × 0.763 if Japanese × 1.233 if Chinese
MDRD 4-Variable study equation (IDMS traceable)	$\text{GFR (ml/min/1.73 m}^2\text{)} = 175 \times \text{SCr (mg/dl)}^{-1.154} \times \text{age}^{-0.203} \times 0.742 \text{ (if female)}$	× 1.21 if Black-American × 0.763 if Japanese × 1.233 if Chinese
CKD - EPI creatinine equation	$\text{GFR} = 141 \times \min\left(\frac{\text{SCr}}{\kappa}, 1\right)^\alpha \times \max\left(\frac{\text{SCr}}{\kappa}, 1\right)^{-1.209} \times 0.993^{\text{age}}$	× 1.018 if female × 1.159 if Black

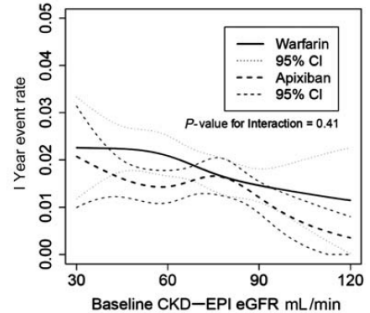
$\alpha = -0.329$ if female, -0.411 if male
 $\kappa = 0.7$ if female, 0.9 if male
 min = the minimum of $\frac{\text{SCr}}{\kappa}$ or 1
 max = the maximum of $\frac{\text{SCr}}{\kappa}$ or 1



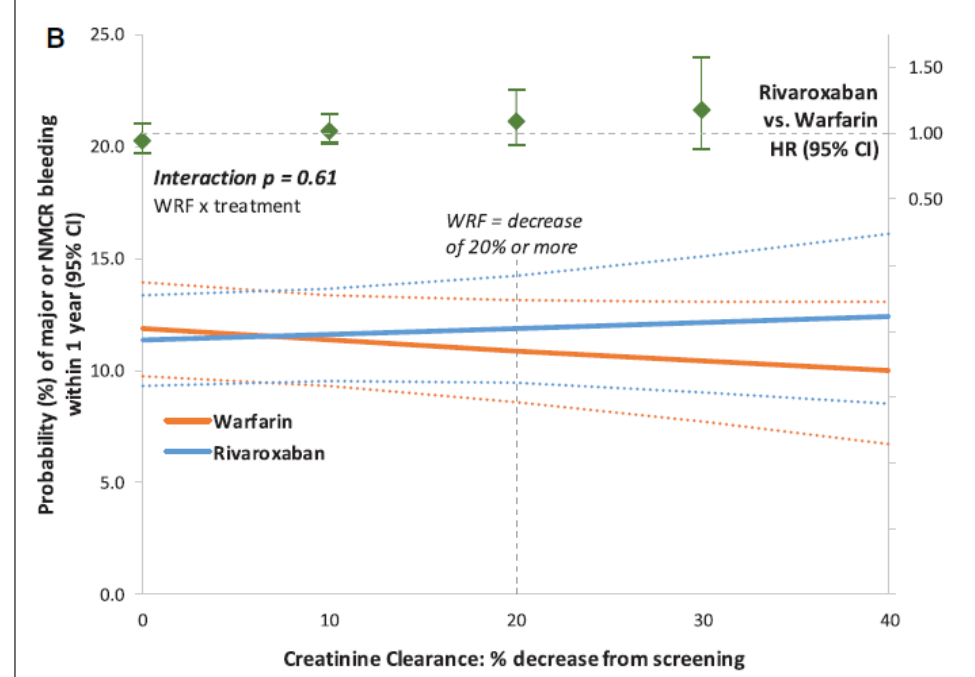
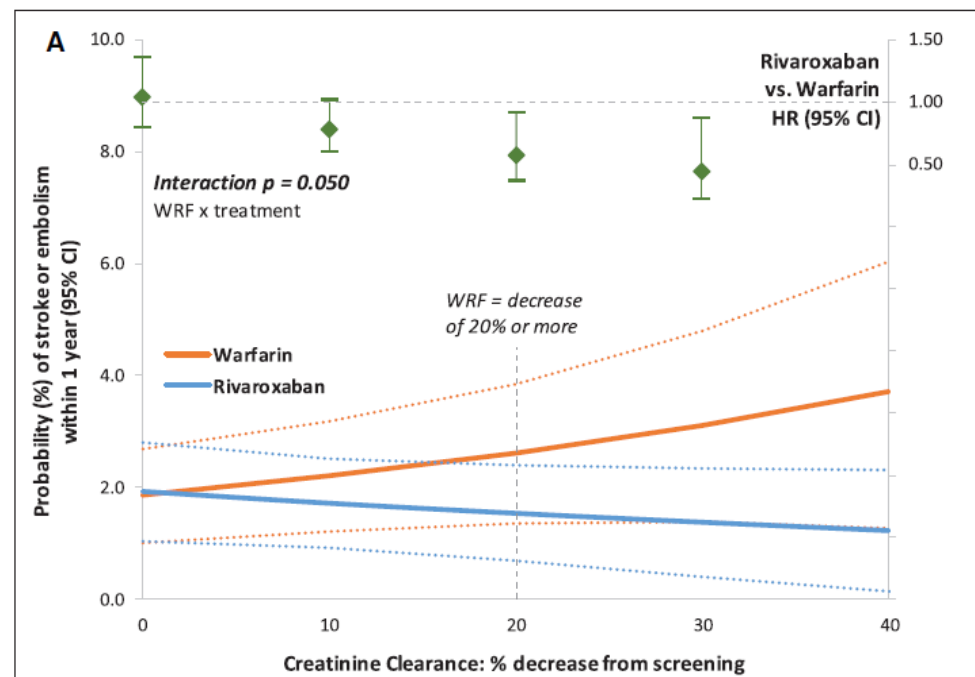
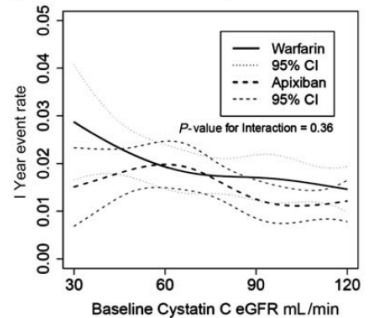
A Outcome: Stroke or Systemic Embolism



B Outcome: Stroke or Systemic Embolism

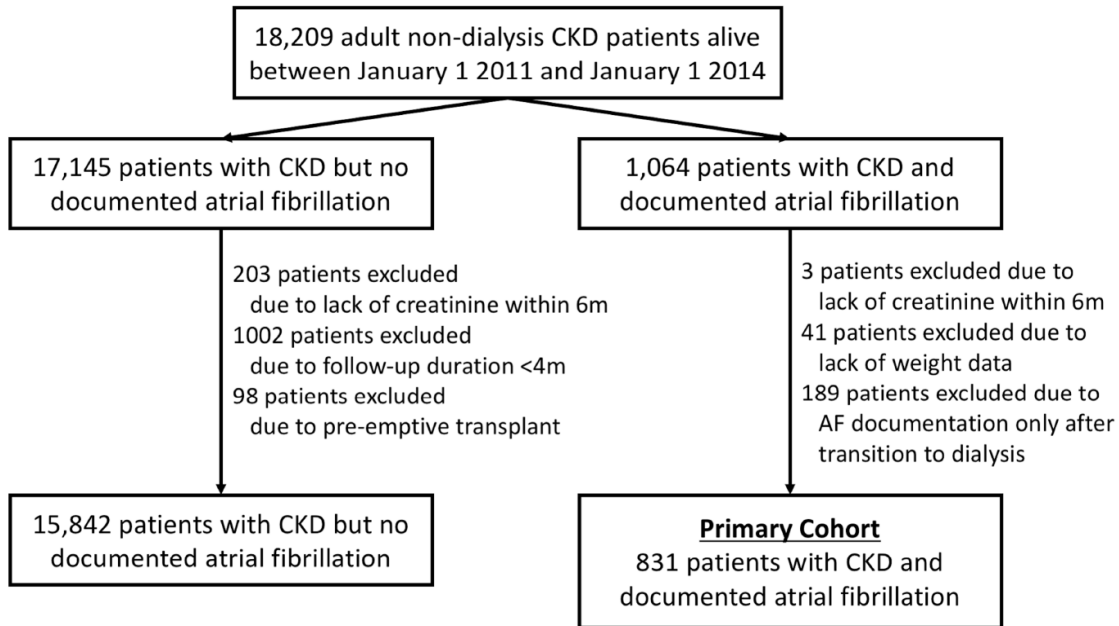


C Outcome: Stroke or Systemic Embolism



Variability In NOAC Dose Adjustment In Atrial Fibrillation Patients With Renal Dysfunction: The Influence Of Renal Function Estimation Formulae

Jason G. Andrade, MD, Nathaniel M. Hawkins, MD, Christopher B. Fordyce, MD MHS MSc, Marc W. Deyell, MSc MD, Lee Er, Ognjenka Djurdjev, Laurent Macle, MD, Sean A. Virani, MD MSc MPH, Adeera Levin, MD



CG	MDRD			Total
	<30	30-50	>50	
<30	318	60	3	381 (46%)
30-50	110	167	14	291 (35%)
>50	14	100	45	159 (19%)
Total	442 (53%)	327 (39%)	62 (7%)	831

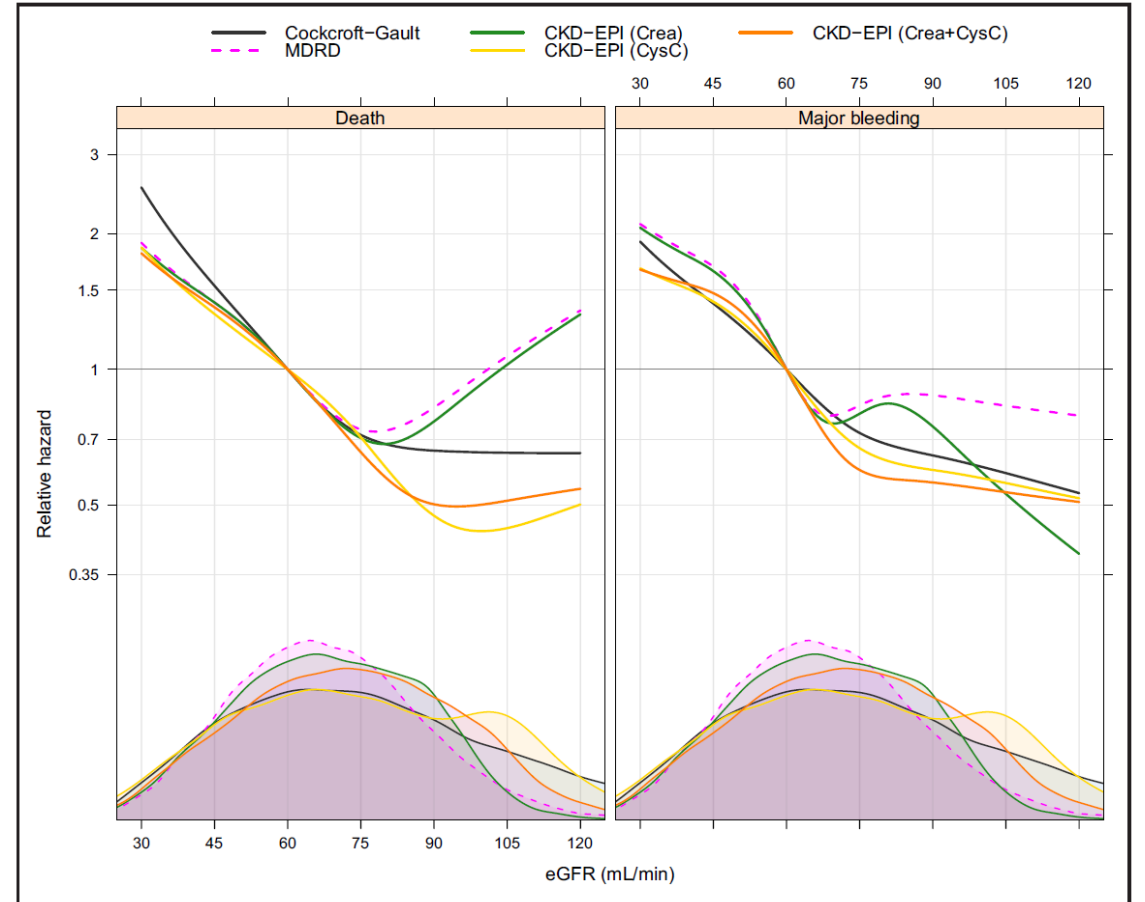
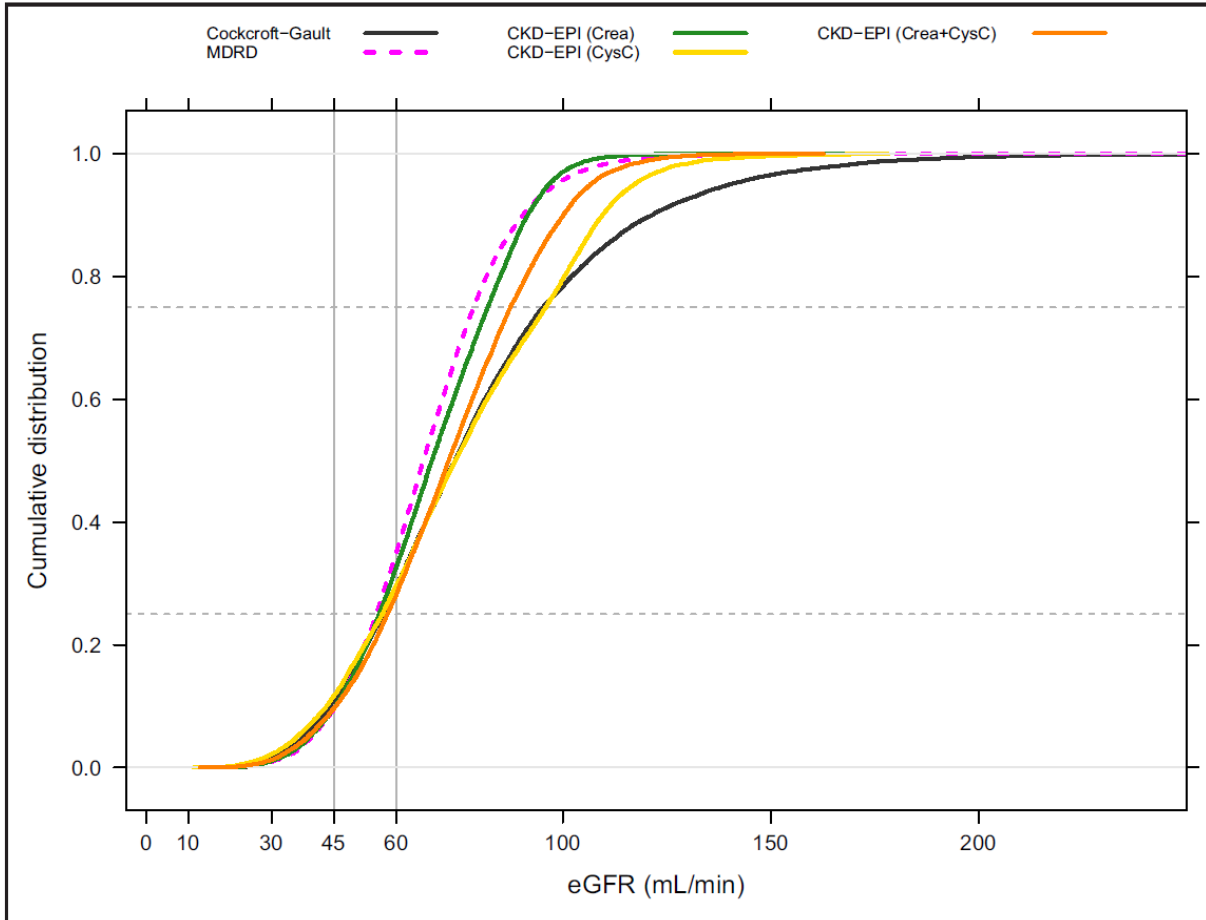
Agreement=63.8% [95% CI: 59.6%, 67.7%]

Under-treated=26.9% [95% CI: 23.3%, 30.9%]

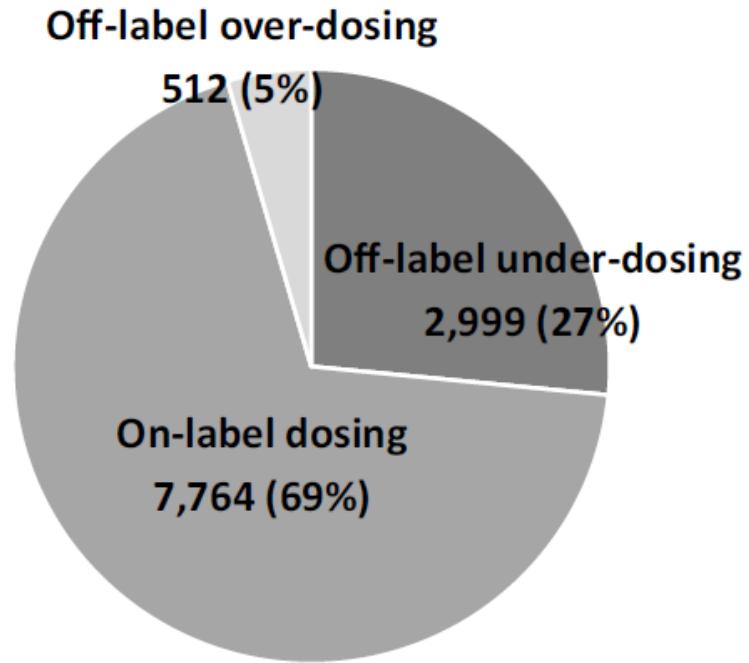
Over-treated=9.3% [95% CI: 7.1%, 12.0%]

Association of Different Estimates of Renal Function With Cardiovascular Mortality and Bleeding in Atrial Fibrillation

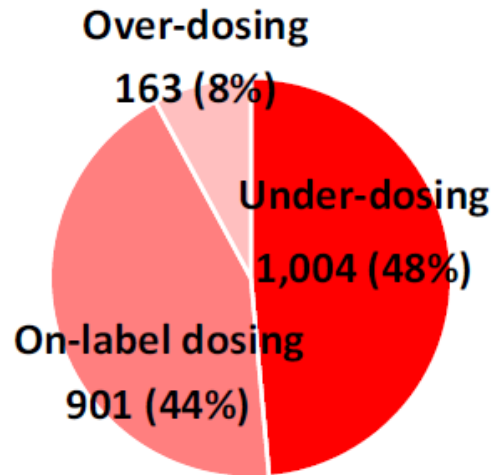
Ziad Hijazi ^{ID}, MD, PhD; Christopher B. Granger, MD; Stefan H. Hohnloser ^{ID}, MD; Johan Westerbergh, MSc; Johan Lindbäck ^{ID}, MSc; John H. Alexander ^{ID}, MD, MHS; Matyas Keltai, MD, DSc; Alexander Parkhomenko, MD, PhD; José L. López-Sendón, MD, PhD; Renato D. Lopes, MD, PhD; Agneta Siegbahn, MD, PhD; Lars Wallentin, MD, PhD



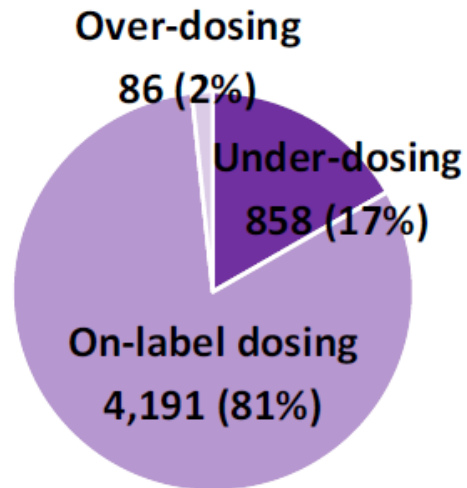
All NOACs 11,275



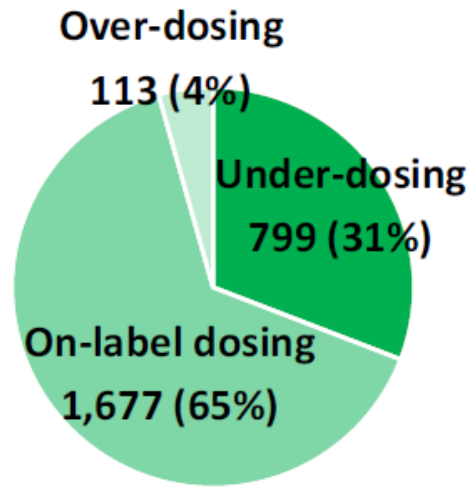
Dabigatran 2,068



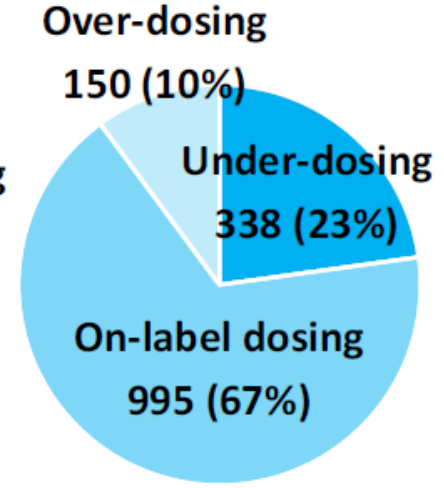
Rivaroxaban 5,135

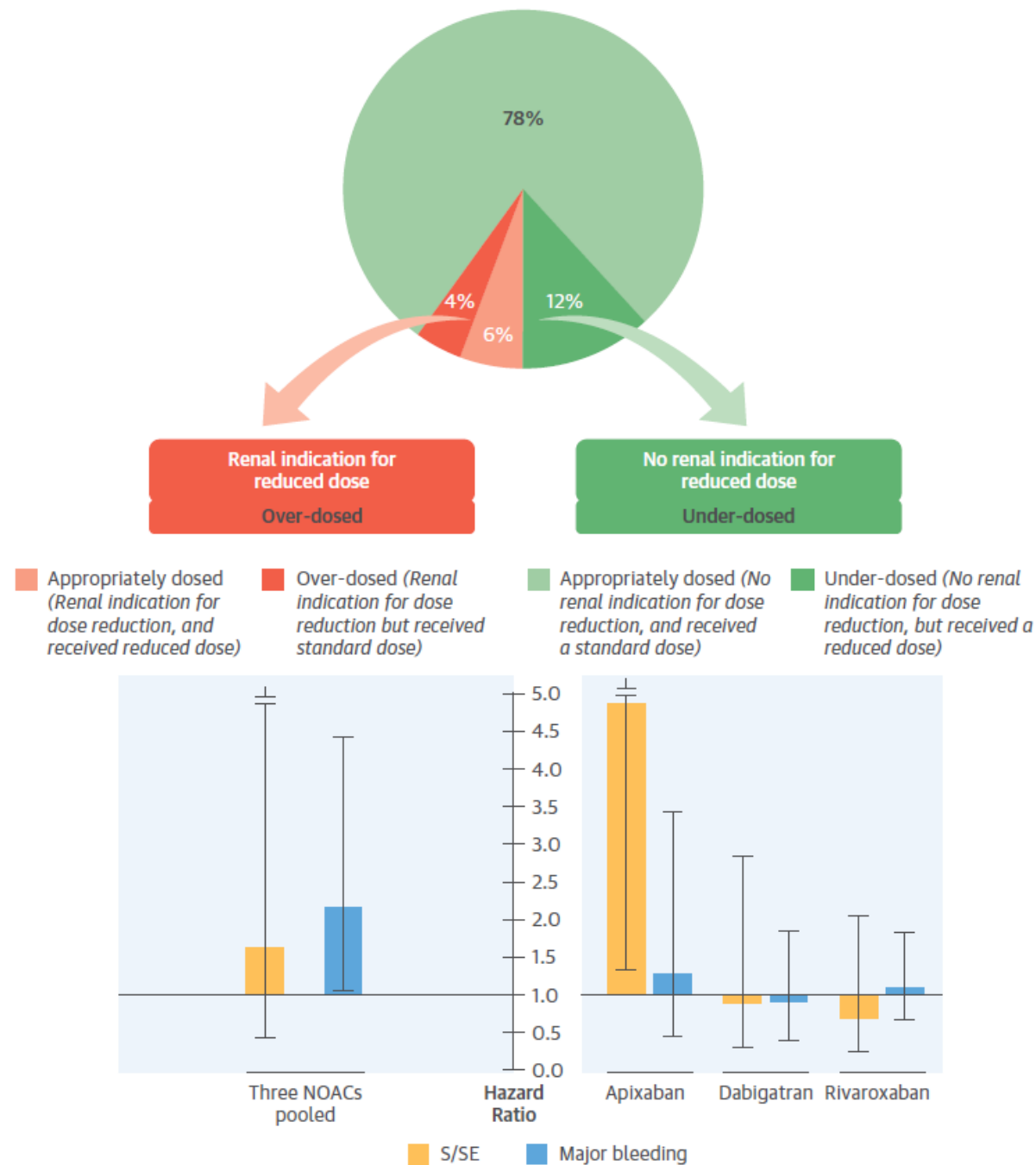
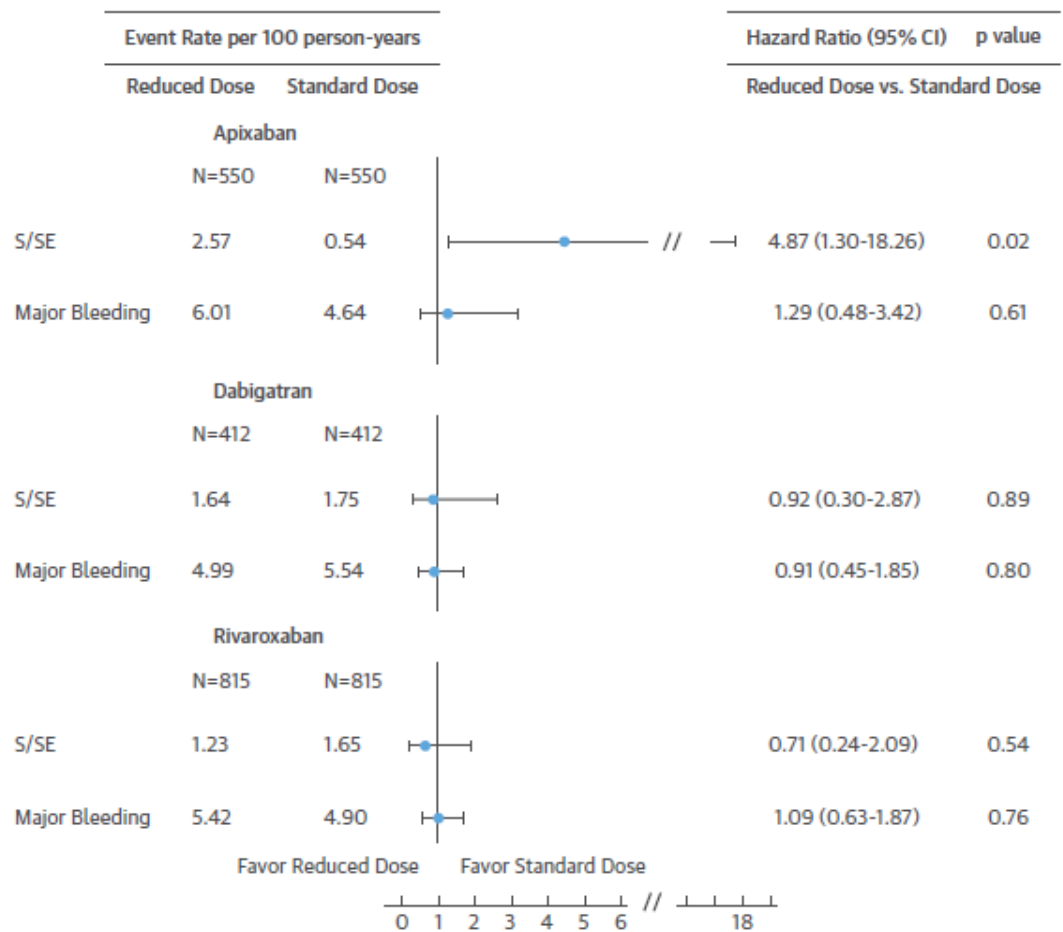
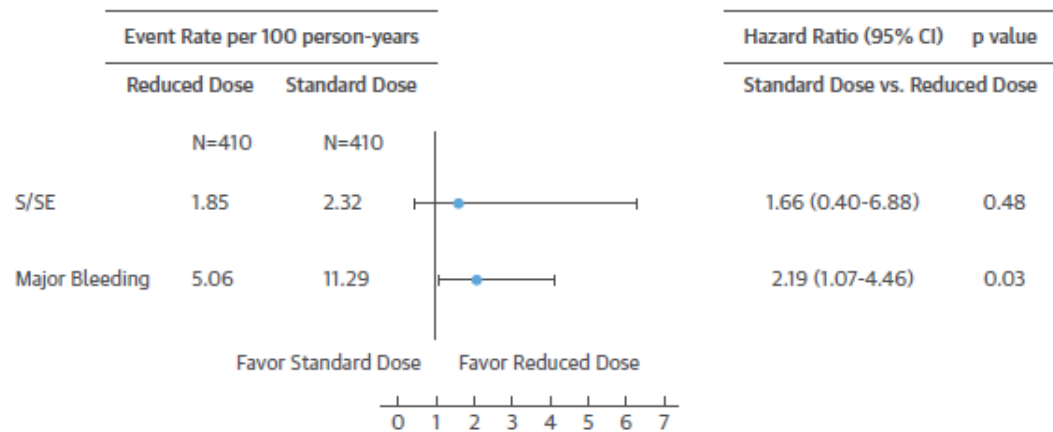


Apixaban 2,589

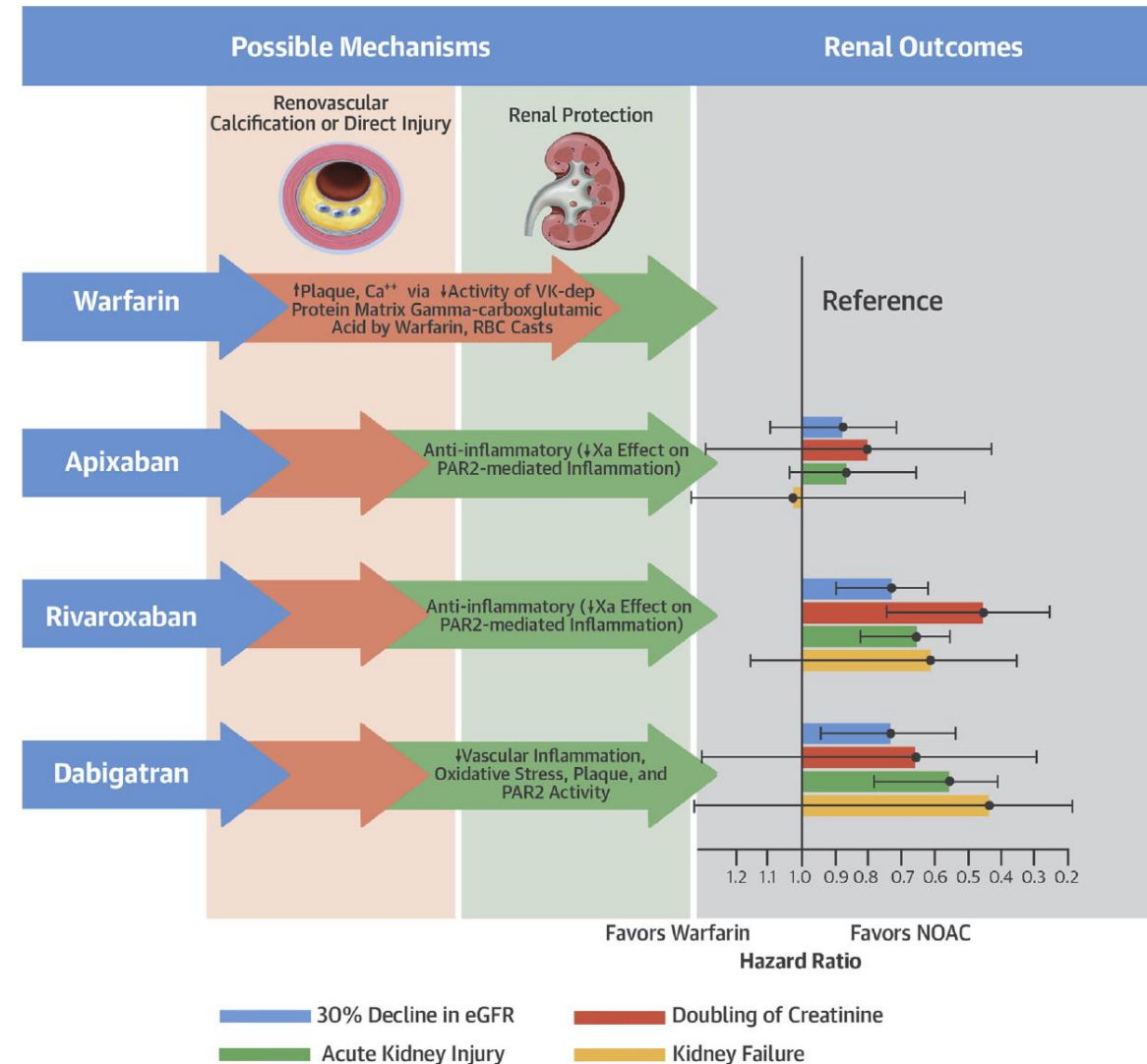
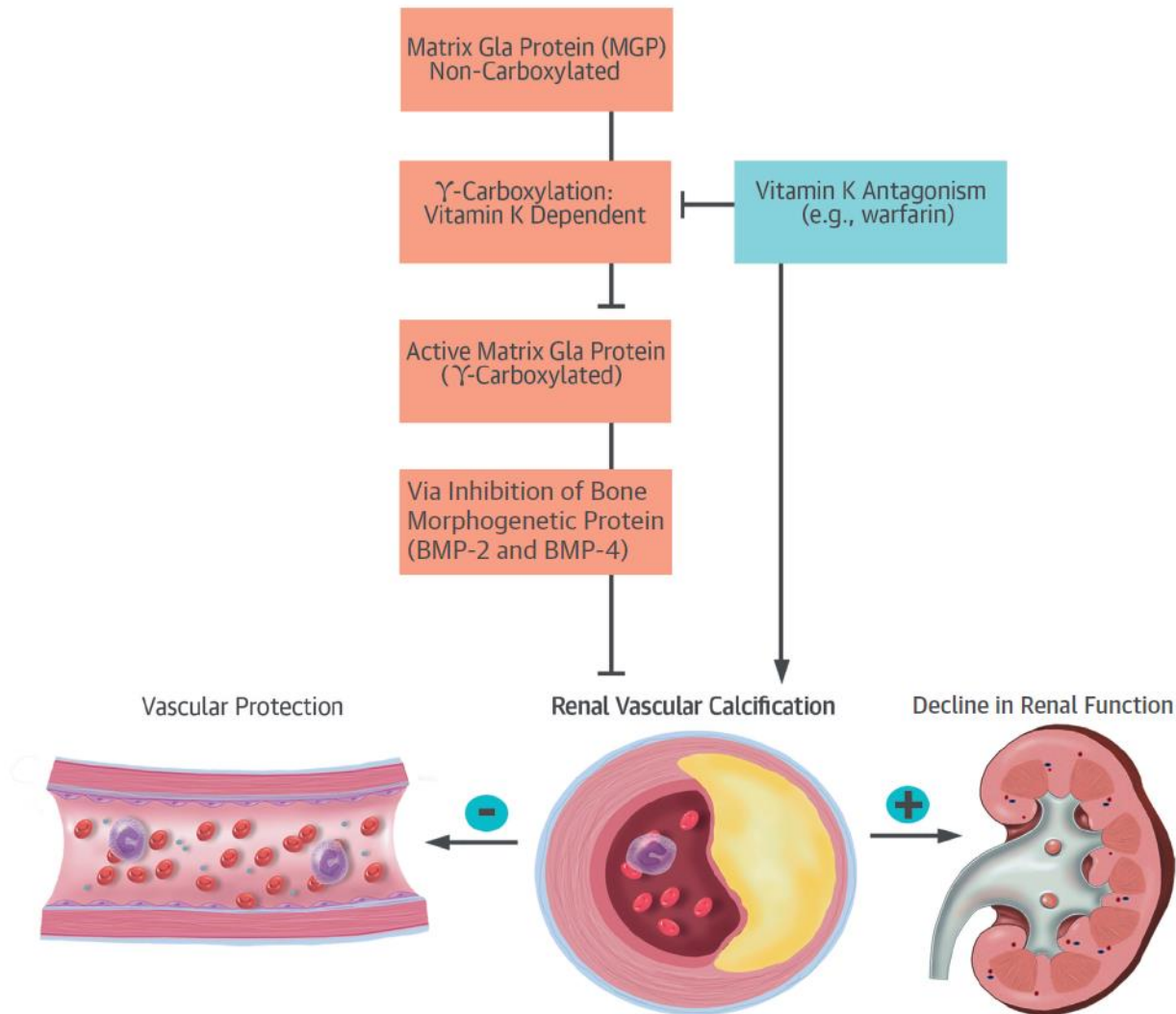


Edoxaban 1,483

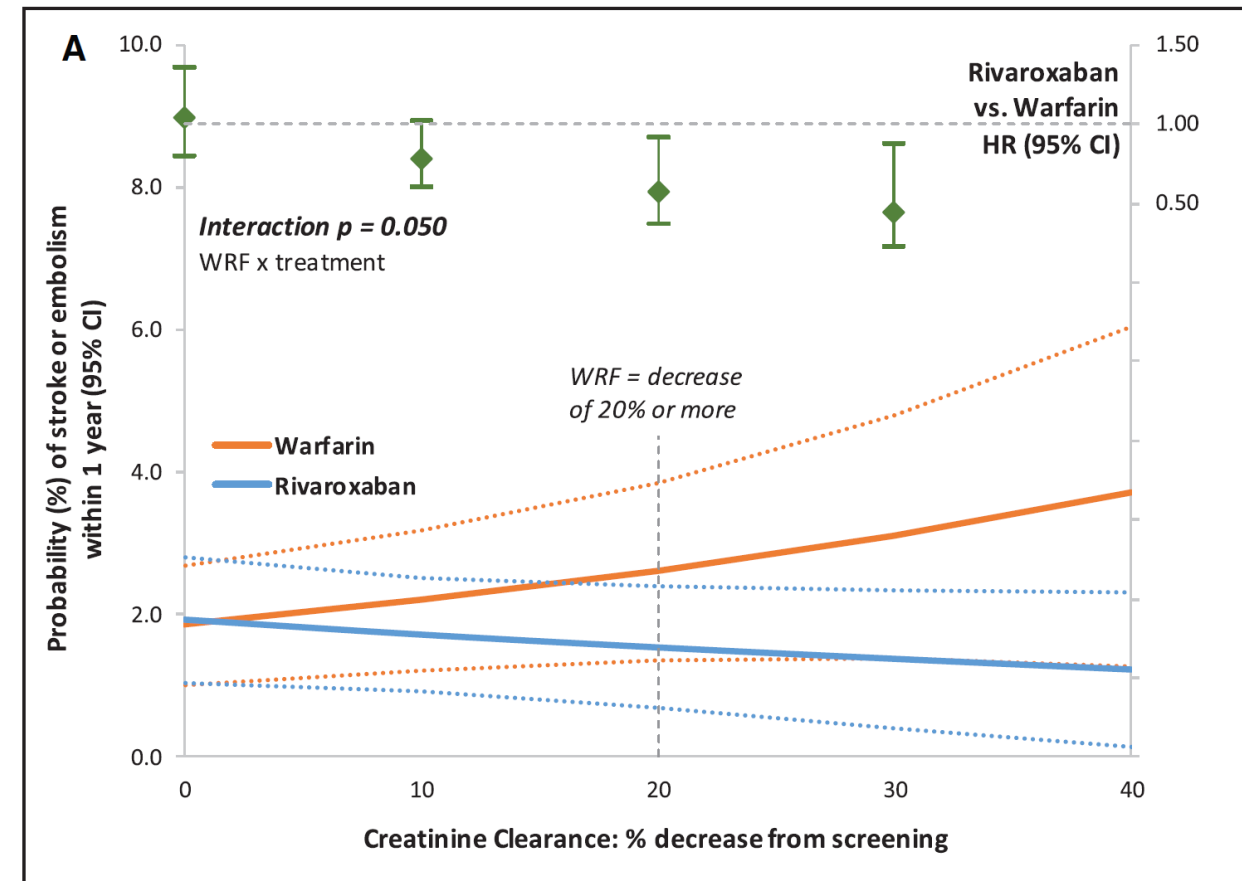
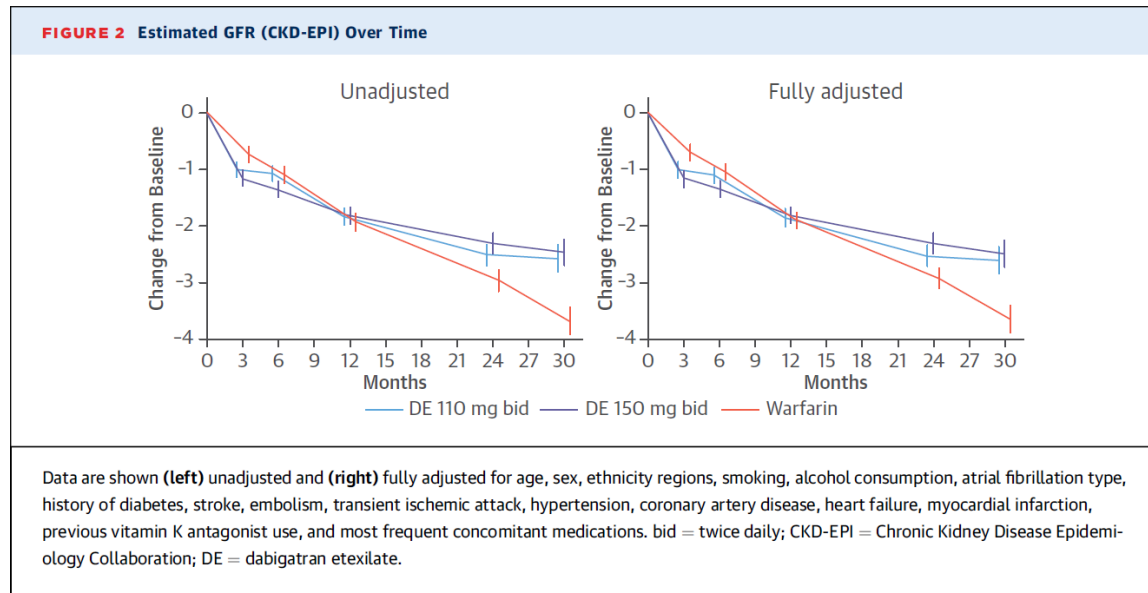


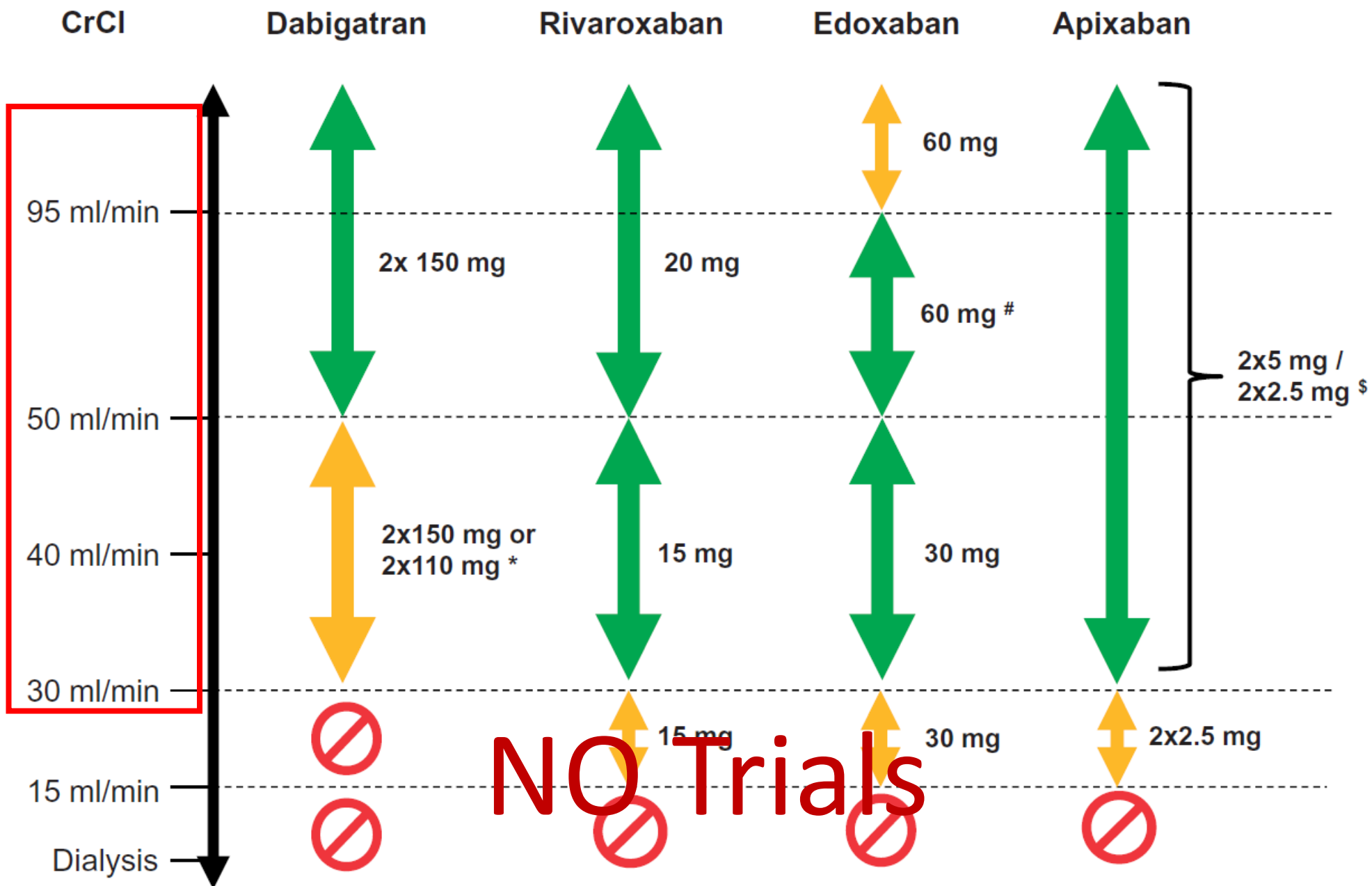


Renal monitoring in patients taking anticoagulation



Renal monitoring in patients taking anticoagulation





CrCl 15–29 ml/min	AHA/ACC/HRS (2019) (5)	Adjusted dose INR 2–3	75 mg BID	5.0 or 2.5 mg BID*	15 mg QD	Not recommended
	CHEST Guideline (2018) (4)	Adjusted dose TTR >70%	75 mg BID (U.S. only) Not recommended outside U.S.	2.5 mg BID	15 mg QD	30 mg QD
	KDIGO (2018)† (2)	Consider adjusted dose INR 2–3	Unknown (consider 75 mg BID)	Consider 2.5 mg BID	Consider 15 mg QD	Consider 30 mg QID
	EHRA practical guide (2018) (3)	Not discussed	Not recommended	2.5 mg BID	15 mg QD	30 mg QD
	ESC (2016) (1)	Adjusted dose INR 2–3	Not recommended	Not recommended if CrCl <25	Not recommended	Not recommended
CrCl <15 ml/min (Dialysis)	AHA/ACC/HRS (2019) (5)	Adjusted dose INR 2–3	Not recommended	5.0 or 2.5 mg BID*	Not recommended	Not recommended
	CHEST guideline (2018) (4)	Adjusted dose TTR >70%	Not recommended	5 mg BID‡	Not recommended	Not recommended
	KDIGO (2018)† (2)	Equipose	Not recommended	Consider 2.5 mg BID	Unknown (15 mg QD mentioned)	Not recommended
	EHRA practical guide (2018) (3)	Not discussed	Not recommended	Not recommended	Not recommended	Not recommended
	ESC (2016) (1)	Not discussed	Not recommended	Not recommended	Not recommended	Not discussed

		Dabigatran	Apixaban	Rivaroxaban	Edoxaban
CrCl 15-30 ml/min	FDA	75 mg BID	5 or 2.5 mg BID*	15 mg QD	30 mg QD
	EMA	Contraindicated	2.5 mg BID	Limited clinical data –15 mg QD	30 mg QD
CrCl < 15 ml/min	FDA	Not approved	5 mg BID	Limited clinical data–15 mg QD	Not approved
	EMA	Contraindicated	Contraindicated	Contraindicated	Contraindicated
Dialysis	FDA	Not approved	5 mg BID	Limited clinical data–15 mg QD	Not approved
	EMA	Contraindicated	Contraindicated	Contraindicated	Contraindicated

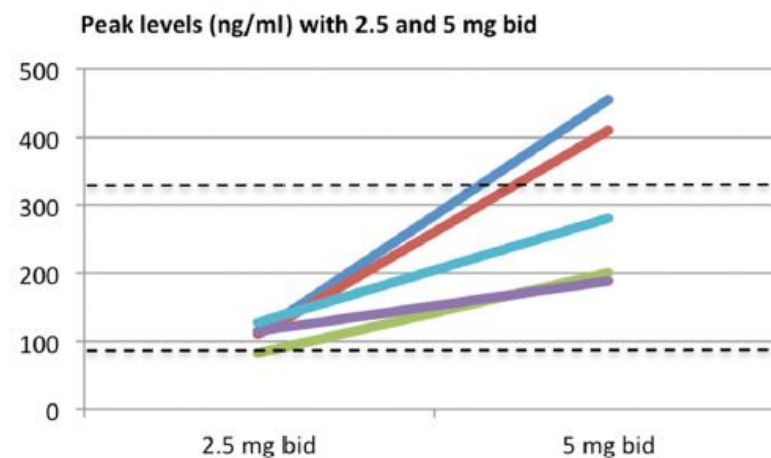
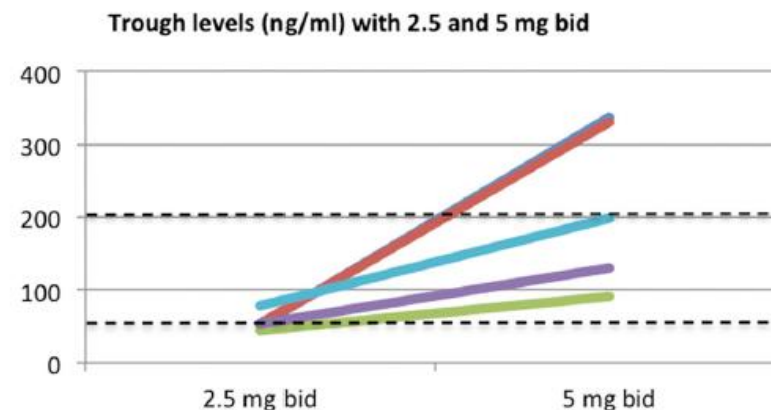
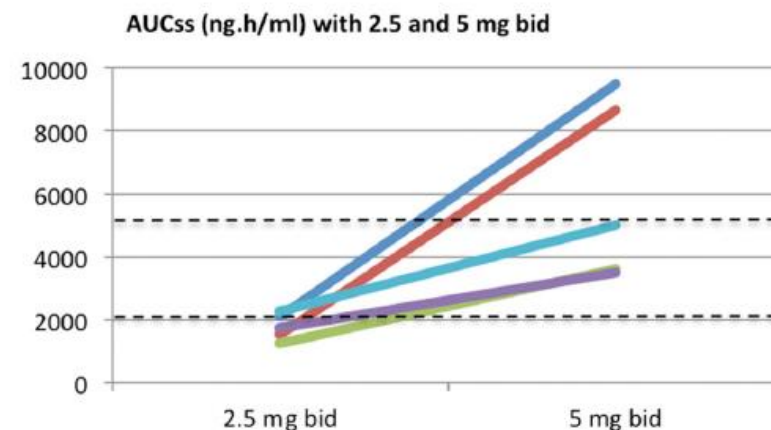
Apixaban Pharmacokinetics at Steady State in Hemodialysis Patients

Table 2. PK parameters of apixaban after administration of 5 mg twice daily for a week and comparison with expected levels in the general population

Apixaban 5 mg Twice Daily	Day 22	P Value	Reference Levels (for the 5 mg twice daily dose)
AUC ₀₋₁₂ , ng h/ml	3026.6 ± 46.6% [2770.4]	0.03	[1474–1717] ¹⁸
AUC ₀₋₂₄ , ng h/ml	6053.2 ± 46.6% (3505.5–9469.7)	0.03	3370 (2070–5250) ¹⁹
C _{max,r} , ng/ml	307.0 ± 39.4% (189.0–455.0)	0.02	171 (91–321) ²⁰
t _{max,r} , h	3.8 ± 35.6% (2.5–6.0)	0.89	—
C _{min,r} , ng/ml	217.5 ± 51.9% (91.0–337.4)	0.03	107 (56–203) ¹⁹
t _{1/2,r} , h	17.4 ± 51.3% (7.1–29.8)	0.13	—

This table shows the PK parameters of apixaban 5 mg twice daily at steady state (day 8). Results are presented as mean ± coefficient of variation (range), median (10th–90th percentile), or median (5th–95th percentile). For AUC₀₋₁₂, the geometric mean (in brackets) is also depicted. P values are comparing apixaban 5 mg twice daily (day 22) with apixaban 2.5 mg twice daily at steady state (day 8; data depicted in Table 1, column 3). t_{max,r}, Time to peak apixaban concentration.

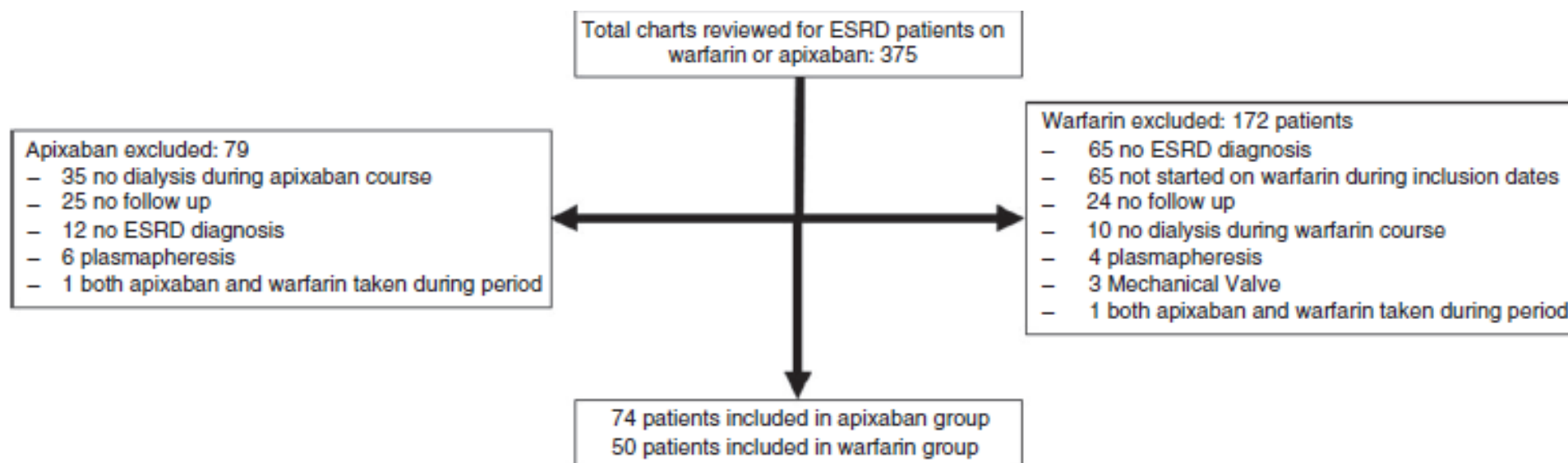
^aMedian (5th–95th percentile).



Limitations of *pharmacokinetics* study

- Small sample sizes
- Ideal patients with few comorbidities

Safety and effectiveness of apixaban compared to warfarin in dialysis patients

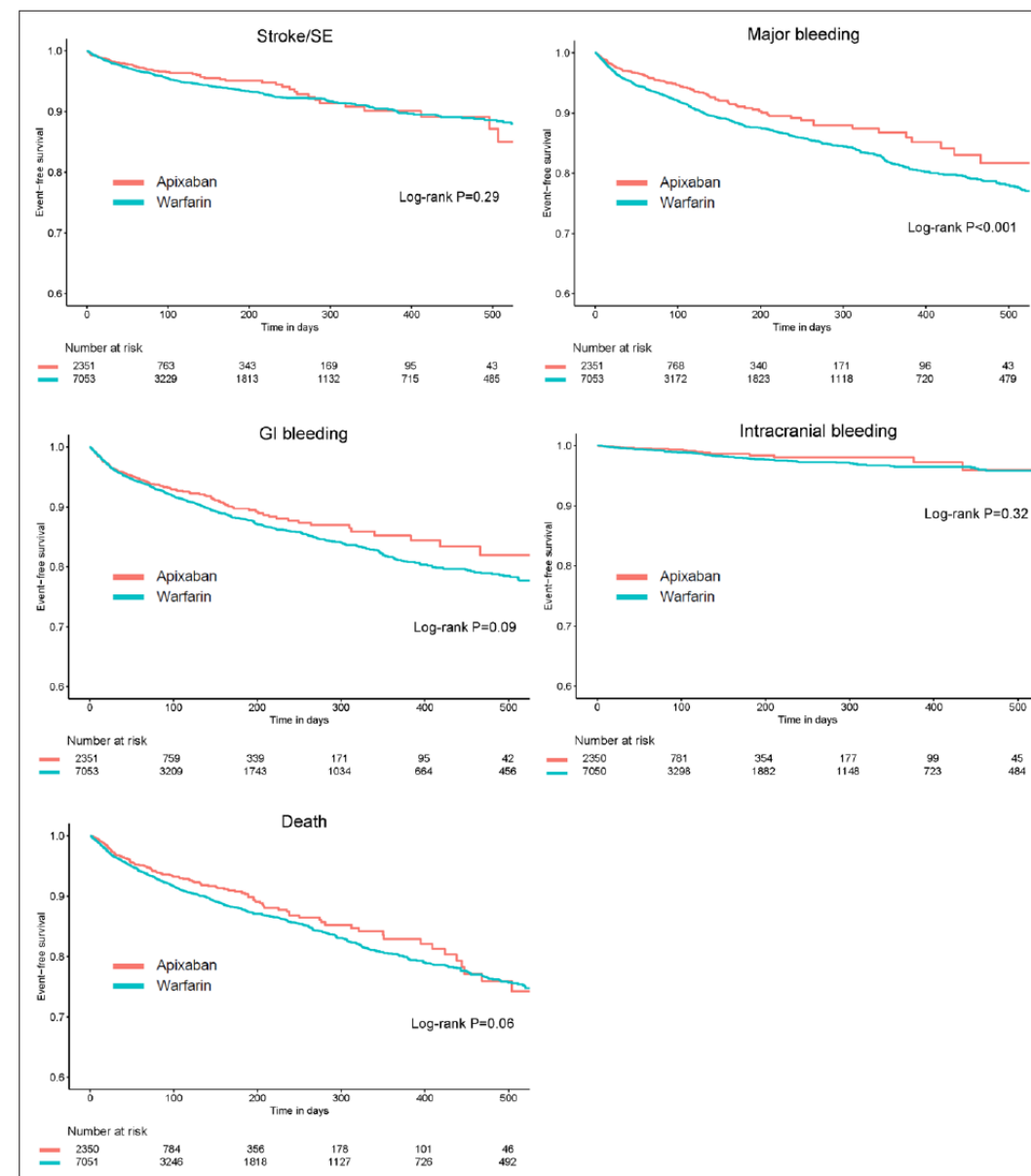


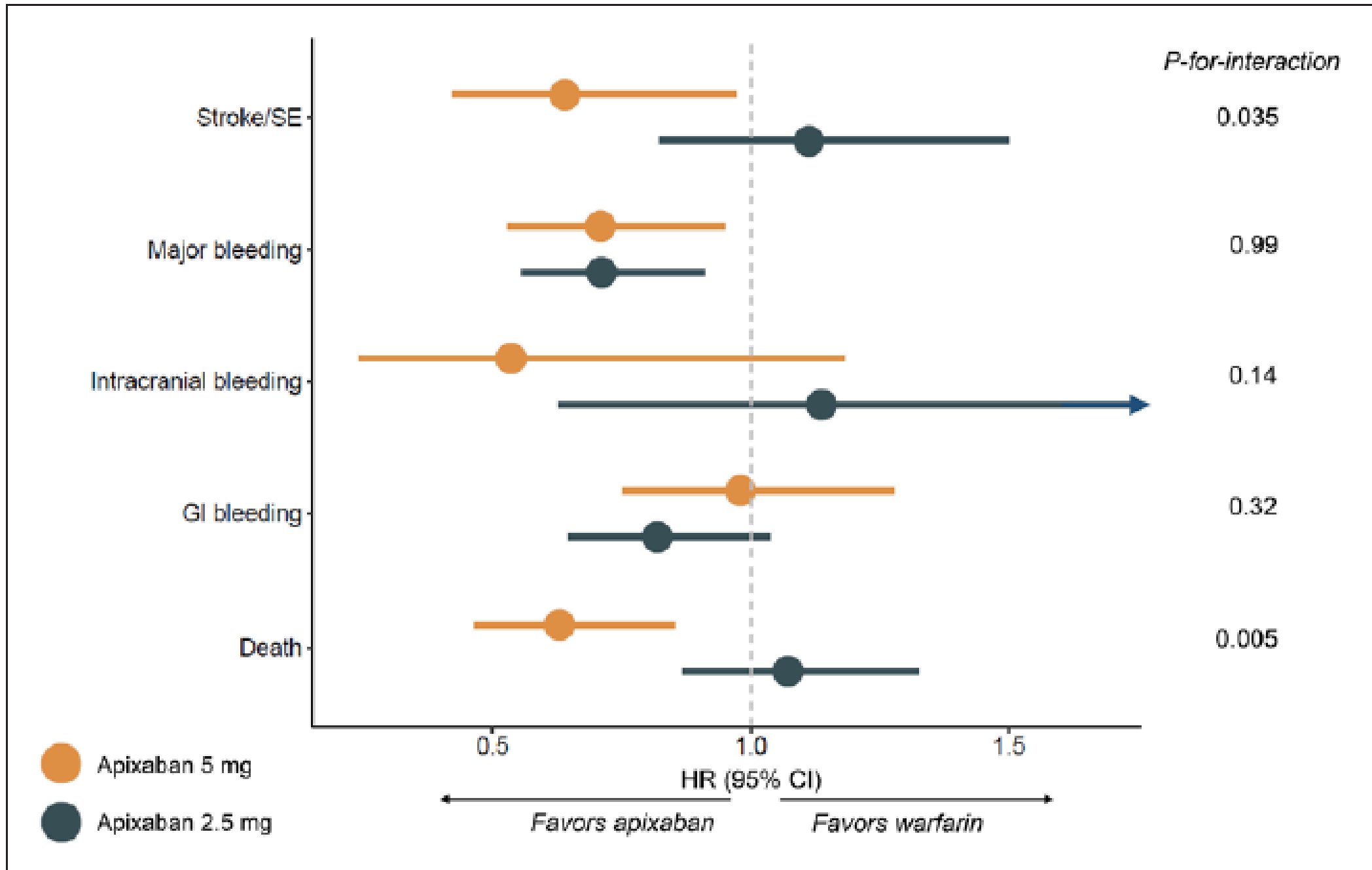
Characteristic	Apixaban	Warfarin	P-value
Bleeding event			
Any	14 (18.9%)	21 (42%)	.01
Major (among all patients)	4 (5.4%)	11 (22%)	.01
Recurrent venous thromboembolism*	2 (4.4%)	6 (28.6%)	.99



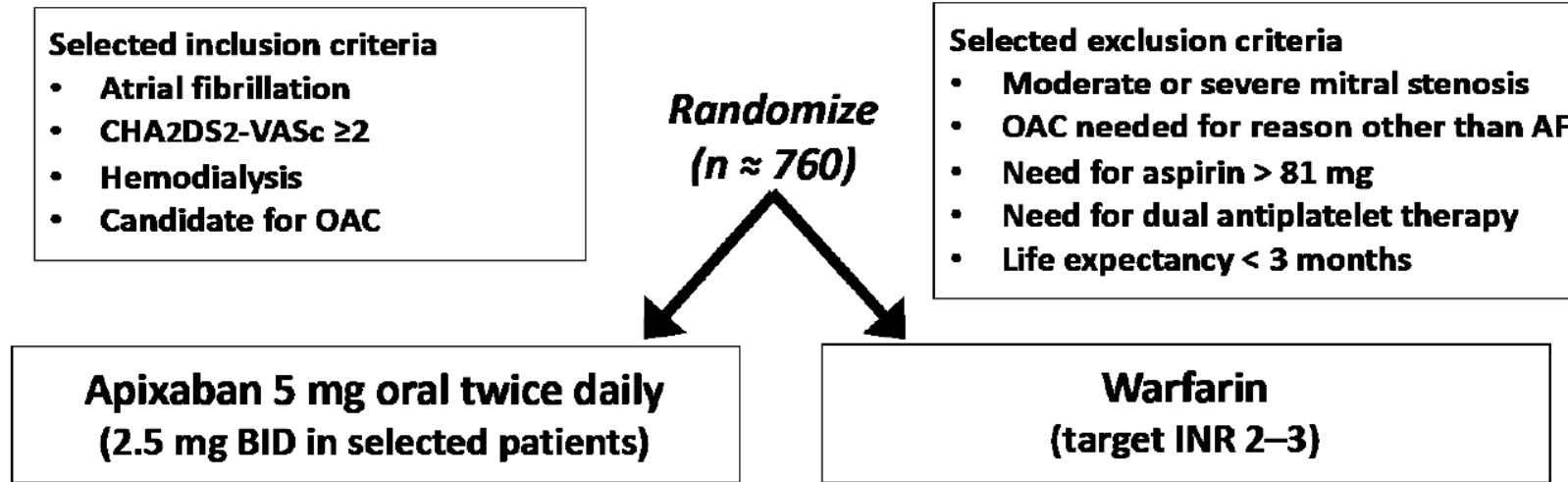
Outcomes Associated With Apixaban Use in Patients With End-Stage Kidney Disease and Atrial Fibrillation in the United States

Outcome	Overall	Apixaban	Warfarin	Hazard Ratio (95% CI)	P Value
Stroke/systemic embolism					
No. of patients	9404	2351	7053	0.88 (0.69–1.12)	0.29
No. of events	454	81	373		
Event rate per 100 PY	11.9	12.4	11.8		
Major bleeding					
No. of patients	9404	2351	7053	0.72 (0.59–0.87)	<0.001
No. of events	844	129	715		
Event rate per 100 PY	22.3	19.7	22.9		
Gastrointestinal bleeding					
No. of patients	9404	2351	7053	0.86 (0.72–1.02)	0.09
No. of events	865	155	710		
Event rate per 100 PY	23.4	23.8	23.4		
Intracranial bleeding					
No. of patients	9400	2350	7050	0.79 (0.49–1.26)	0.32
No. of events	132	21	111		
Event rate per 100 PY	3.4	3.1	3.5		
Death					
No. of patients	9404	2351	7053	0.85 (0.71–1.01)	0.06
No. of events	912	159	753		
Event rate per 100 PY	24.7	23.7	24.9		





Original Study Design



Open label with blinded event adjudication

Primary outcome: ISTH major and clinically relevant non-major bleeding

Secondary outcomes:

- PK in patients randomized to apixaban
- Stroke and systemic embolism
- Death
- Tolerability/persistence/adherence parameters

Safety and efficacy of apixaban versus warfarin in patients with end-stage renal disease: Meta-analysis

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Affiliations + expand

PMID: 29577340 DOI: 10.1111/pace.13331

Erratum in

Erratum.

[No authors listed]

Pacing Clin Electrophysiol. 2018 Jul;41(7):879. doi: 10.1111/pace.13431.

PMID: 31651055 No abstract available.

Abstract

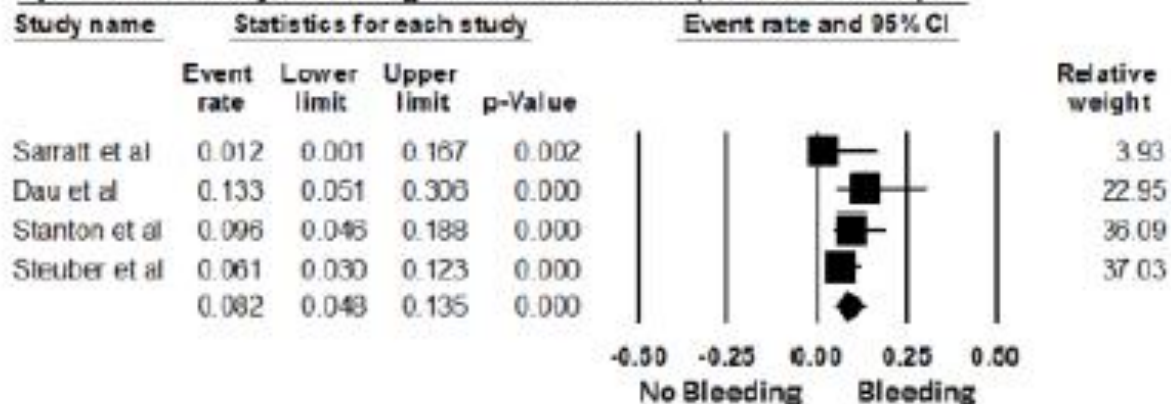
Background: At the present, apixaban is the only nonvitamin K oral anticoagulant approved by the Food and Drug Administration for use with patients with creatinine clearance <15 mL/min or end-stage renal disease (ESRD). However, the recommendations are based on pharmacokinetic and pharmacodynamic data and there was lack of clinical trial evidence. We aimed to assess safety and efficacy of apixaban in patients with advanced chronic kidney disease (CKD) or ESRD.

Methods: Databases were searched through November 2017. Studies that reported incidence or odd ratios of bleeding complications or thromboembolic events in the use of apixaban in patients with CKD stage 4-5 or ESRD on dialysis were included. Effect estimates from the individual study were extracted and combined using random-effect, generic inverse variance method of DerSimonian and Laird.

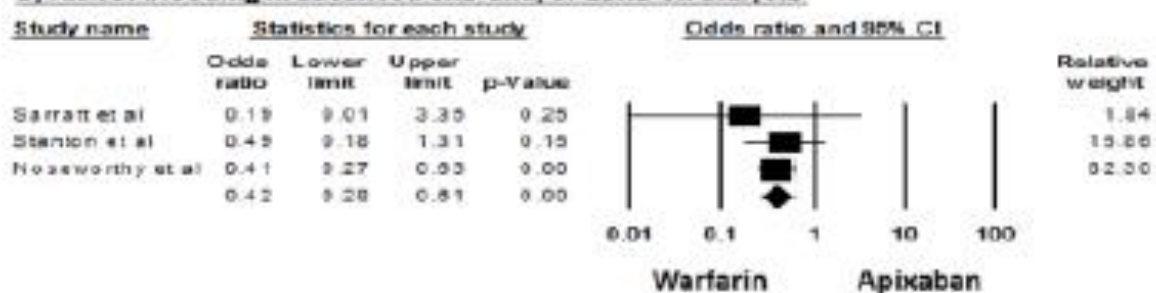
Results: Five studies were included into the analysis consisting of 43,850 patients in observational cohort studies. The majority of patients (87%) used apixaban for atrial fibrillation. The pooled estimated incidence of any bleeding complications on apixaban was 17.4% (95% confidence interval [CI]: 13.0%-23.0%). Compared to warfarin, apixaban was significantly associated with reduced risk of major bleeding (pooled odds ratio [OR], 0.42; 95% CI, 0.28-0.61). In studies in ESRD patients on dialysis, the pooled OR of major bleeding was 0.27 (95% CI, 0.07-0.95). There was no significant difference in risk of thromboembolic events in advanced CKD or ESRD patients on apixaban versus vitamin K antagonists (pooled OR, 0.56; 95% CI, 0.23-1.39).

Conclusions: Among patients with advanced CKD and ESRD, the use of apixaban was associated with lower risk of major bleeding compared to warfarin, and was found to be relatively effective with no excess risk of thromboembolic events.

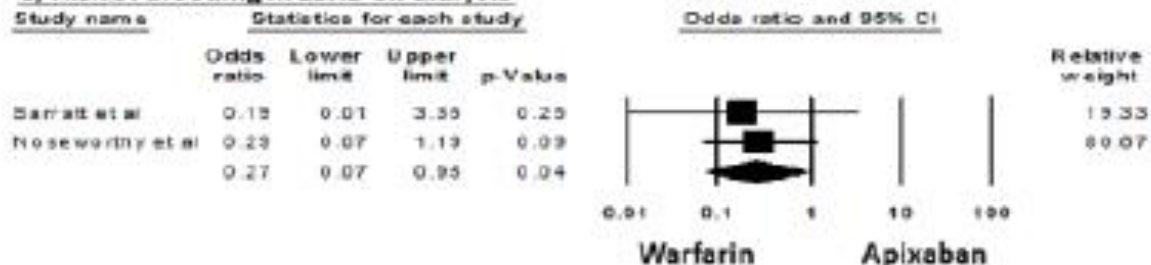
A) Incidence of major bleeding in advanced CKD and/or ESRD on dialysis



B) Risk of bleeding in advanced CKD and/or ESRD on dialysis



C) Risk of bleeding in ESRD on dialysis



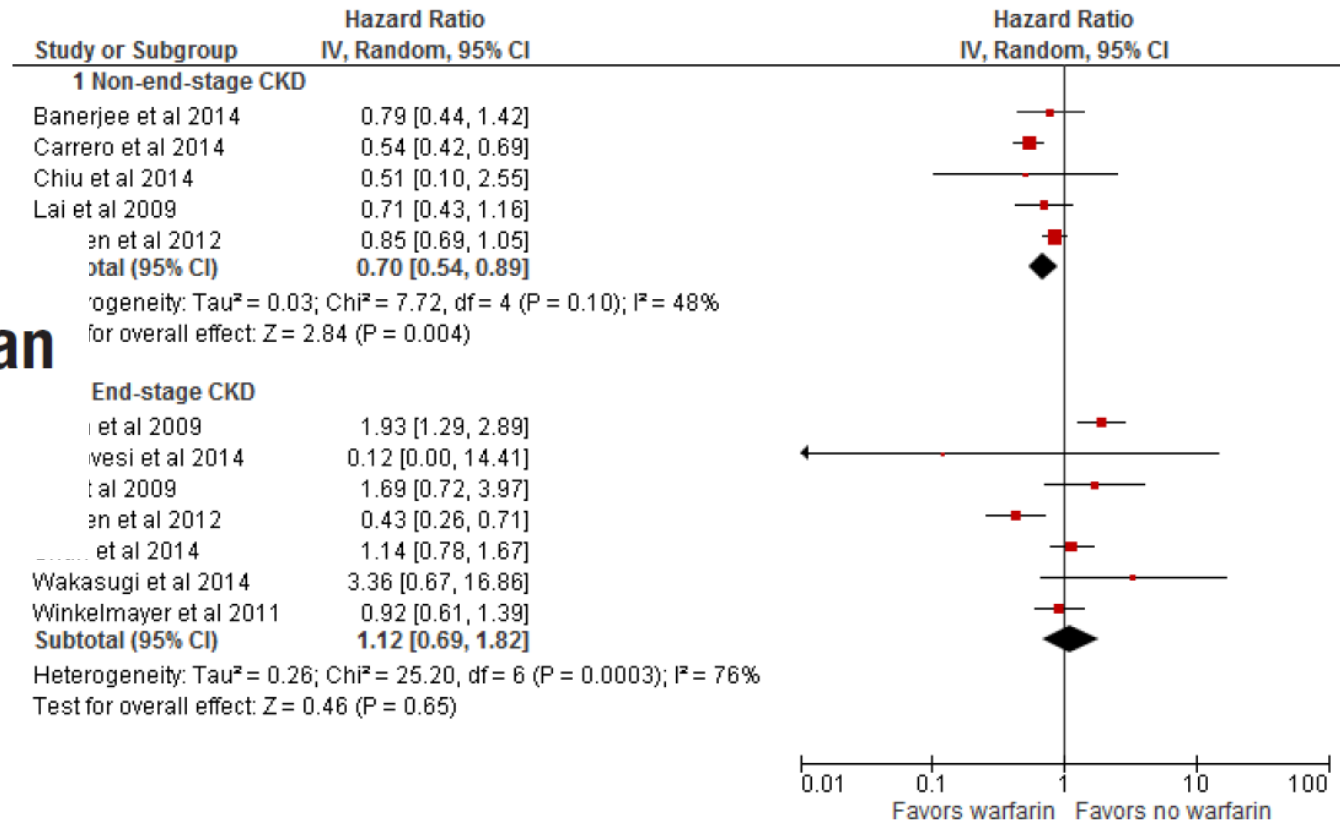


Stroke, Major Bleeding and Mortality Outcomes in Warfarin Users with Atrial Fibrillation and Chronic Kidney Disease: A Meta-analysis of Observational Studies

Khagendra Dahal, MD, Sumit Kunwar, MD, Jharendra Rijal, MD, Peter Schulman, MD, Juyong Lee, MD, PHD

Efficacy and Safety of Dabigatran Compared With Warfarin in Relation to Baseline Renal Function in Patients With Atrial Fibrillation

A RE-LY (Randomized Evaluation of Long-term Anticoagulation Therapy) Trial Analysis



On-Treatment Outcomes in Patients With Worsening Renal Function With Rivaroxaban Compared With Warfarin

Insights From ROCKET AF

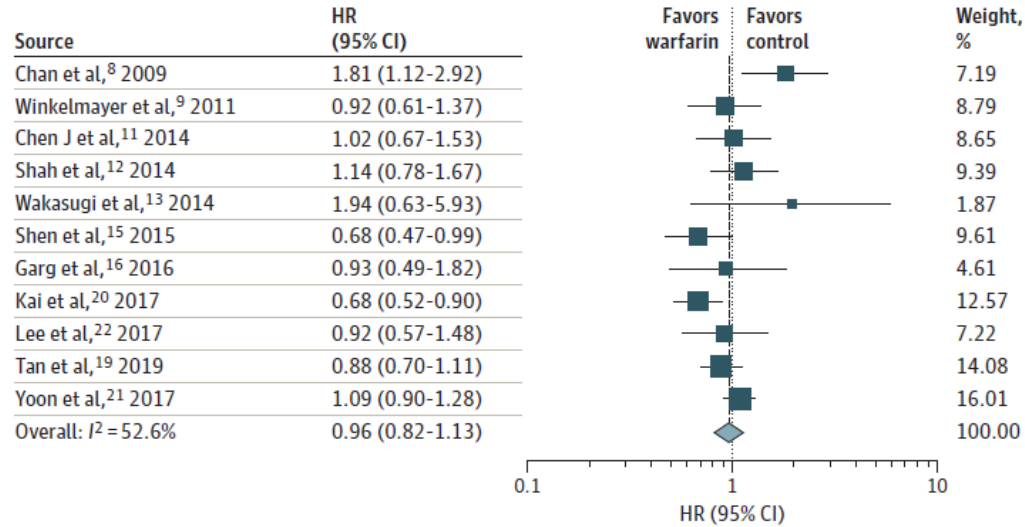
Efficacy of apixaban when compared with warfarin in relation to renal function in patients with atrial fibrillation: insights from the ARISTOTLE trial

Association Between Use of Warfarin for Atrial Fibrillation and Outcomes Among Patients With End-Stage Renal Disease

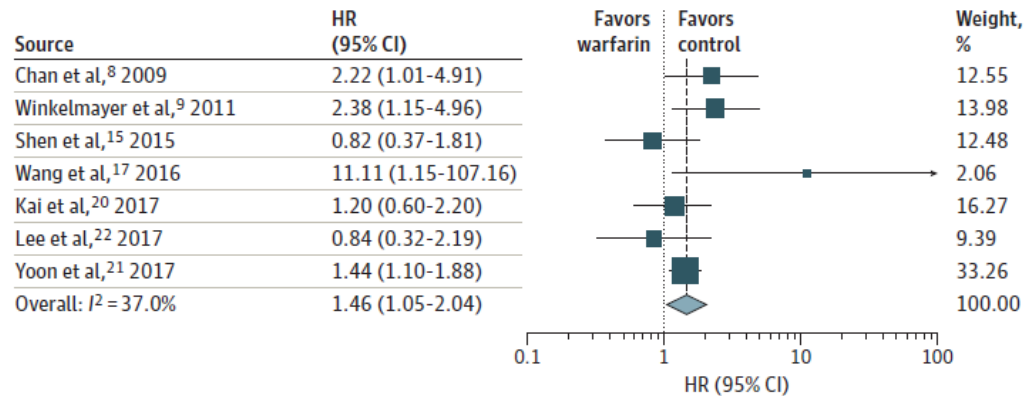
A Systematic Review and Meta-analysis

Mandeep S. Randhawa, MD; Rohanlal Vishwanath, BSc; Manoj P. Rai, MD; Ling Wang, PhD; Amritpal K. Randhawa, MD; George Abela, MD; Gaurav Dhar, MD

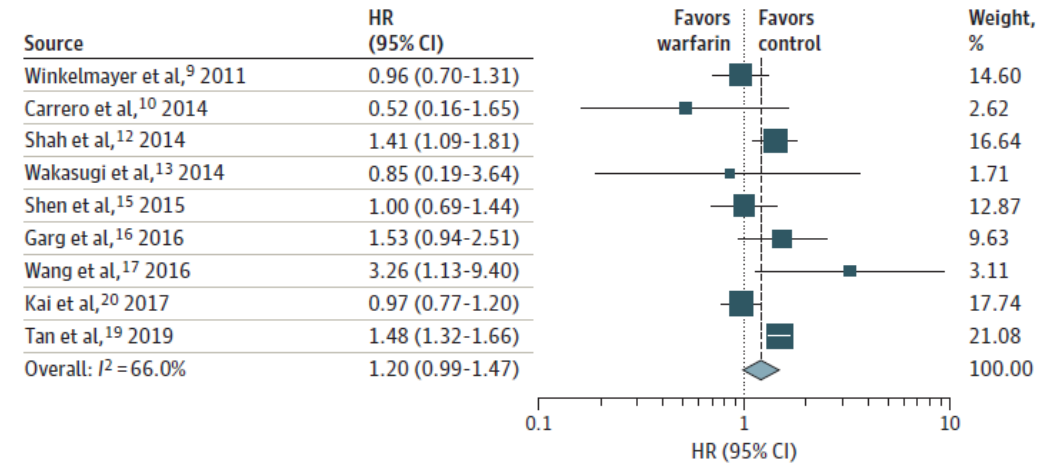
A Ischemic stroke



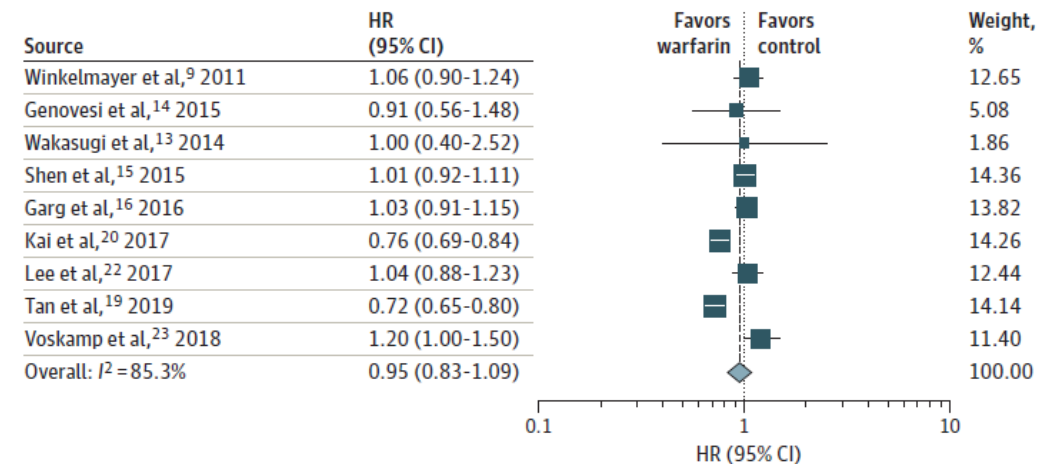
B Hemorrhagic stroke



A Major bleeding



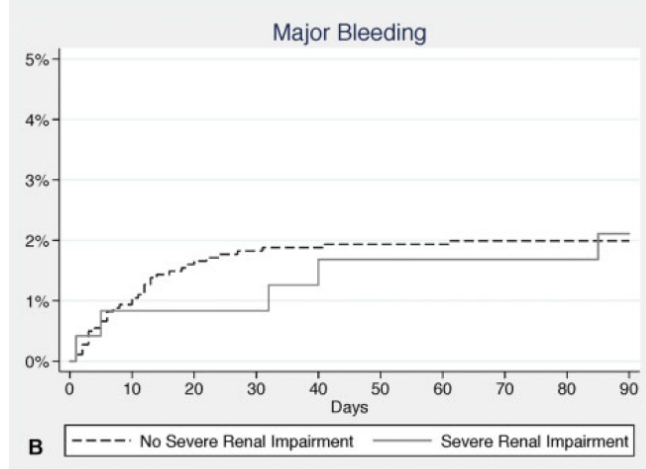
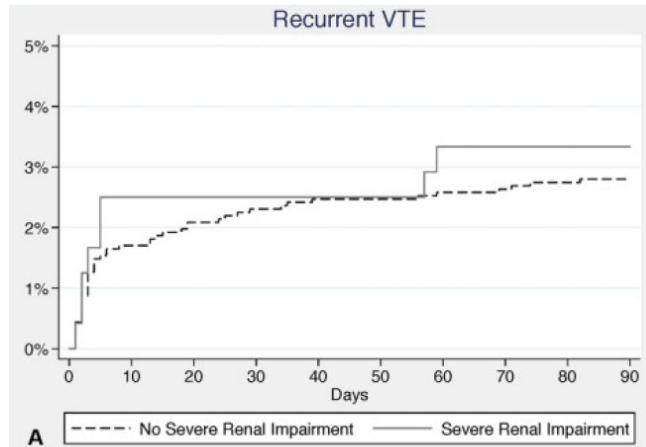
B Mortality



Venous Thromboembolism and Renal Impairment: Insights from the SWISS Venous ThromboEmbolic Registry (SWIVTER)

David Spirk, MD¹ Tim Sebastian, MD² Martin Banyai, MD² Jürg H. Beer, MD³ Lucia Mazzolai, MD⁴
 Thomas Baldi, MD⁵ Drahomir Aujesky, MD, MSc⁶ Daniel Hayoz, MD⁷ Rolf P. Engelberger, MD⁷
 Thomas Kaeslin, MD⁸ Wolfgang Korte, MD⁹ Robert Escher, MD¹⁰ Marc Husmann, MD²
 Annette Mollet, PhD¹¹ Thomas D. Szucs, MD¹¹ Nils Kucher, MD²

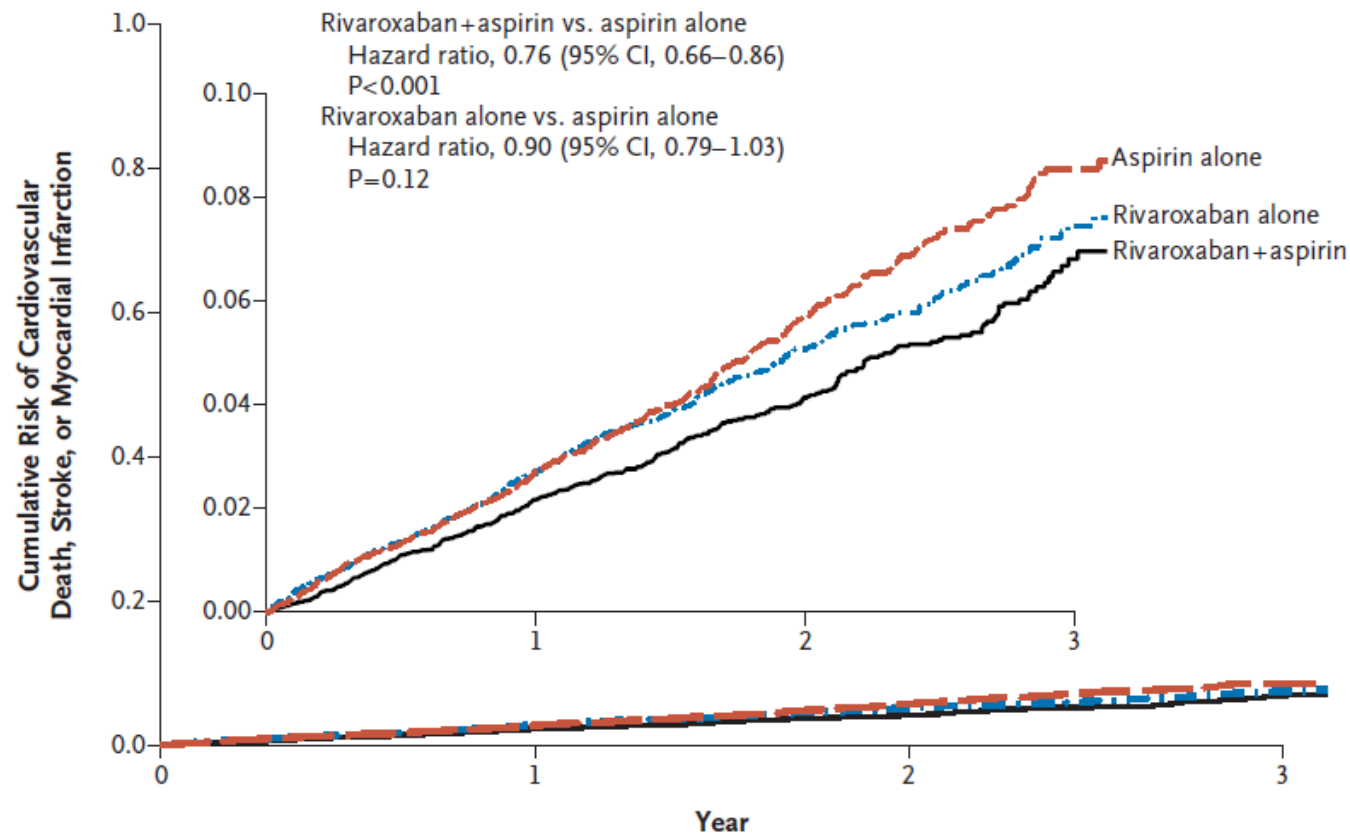
	No severe RI N = 1,822		Severe RI N = 240		HR	95% CI	p ^a
Mortality, n (%)	76	4.2	22	9.2	2.27	1.41–3.65	0.001
VTE related, n (%)	20	1.1	4	1.7	1.54	0.53–4.50	0.43
Bleeding related, n (%)	3	0.2	2	0.8	5.25	0.88–31.42	0.07
Nonfatal recurrent VTE, n (%)	31	1.7	4	1.7	0.98	0.35–2.77	0.97
Nonfatal recurrent PE, ^b n (%)	20	1.1	4	1.7	1.52	0.52–4.45	0.44
Nonfatal recurrent DVT, ^b n (%)	18	1.0	3	1.2	1.27	0.37–4.31	0.70
Nonfatal major bleeding, n (%)	33	1.8	3	1.3	0.69	0.21–2.25	0.53
Nonfatal bleeding requiring medical attention, n (%)	64	3.6	9	3.8	1.06	0.53–2.14	0.86
Recurrent VTE, n (%)	51	2.8	8	3.3	1.19	0.57–2.52	0.64
Major bleeding, n (%)	36	2.0	5	2.1	1.05	0.41–2.68	0.92
Bleeding requiring medical attention, n (%)	67	3.7	11	4.6	1.24	0.66–2.35	0.50



Rivaroxaban with or without Aspirin in Stable Cardiovascular Disease

J.W. Eikelboom, S.J. Connolly, J. Bosch, G.R. Dagenais, R.G. Hart, O. Shestakovska, R. Diaz, M. Alings, E.M. Lonn, S.S. Anand, P. Widimsky, M. Hori, A. Avezum, L.S. Piegas, K.R.H. Branch, J. Probstfield, D.L. Bhatt, J. Zhu, Y. Liang, A.P. Maggioni, P. Lopez-Jaramillo, M. O'Donnell, A.K. Kakkar, K.A.A. Fox, A.N. Parkhomenko, G. Ertl, S. Störk, M. Keltai, L. Ryden, N. Pogossova, A.L. Dans, F. Lanas, P.J. Commerford, C. Torp-Pedersen, T.J. Guzik, P.B. Verhamme, D. Vinereanu, J.-H. Kim, A.M. Tonkin, B.S. Lewis, C. Felix, K. Yusoff, P.G. Steg, K.P. Metsarinne, N. Cook Bruns, F. Misselwitz, E. Chen, D. Leong, and S. Yusuf, for the COMPASS Investigators*

COMPASS Trial



No. at Risk

Aspirin alone	9126	7808	3860	669
Rivaroxaban alone	9117	7824	3862	670
Rivaroxaban+aspirin	9152	7904	3912	658

Characteristic	Rivaroxaban plus Aspirin (N = 9152)	Rivaroxaban Alone (N = 9117)	Aspirin Alone (N = 9126)
Coronary artery disease — no. (%)‡	8313 (90.8)	8250 (90.5)	8261 (90.5)
Peripheral arterial disease — no. (%)§	2492 (27.2)	2474 (27.1)	2504 (27.4)
Estimated GFR — no. (%)¶			
<30 ml/min	77 (0.8)	80 (0.9)	86 (0.9)
30 to <60 ml/min	1977 (21.6)	2028 (22.2)	2028 (22.2)
≥60 ml/min	7094 (77.5)	7005 (76.8)	7012 (76.8)
Race — no. (%)			
White	5673 (62.0)	5672 (62.2)	5682 (62.3)
Black	76 (0.8)	94 (1.0)	92 (1.0)
Asian	1451 (15.9)	1421 (15.6)	1397 (15.3)
Other	1952 (21.3)	1930 (21.2)	1955 (21.4)
Geographic region — no. (%)			
North America	1304 (14.2)	1305 (14.3)	1309 (14.3)
South America	2054 (22.4)	2036 (22.3)	2054 (22.5)
Western Europe, Israel, Australia, or South Africa	2855 (31.2)	2845 (31.2)	2855 (31.3)
Eastern Europe	1607 (17.6)	1612 (17.7)	1604 (17.6)
Asia–Pacific	1332 (14.6)	1319 (14.5)	1304 (14.3)
Medication — no. (%)			
ACE inhibitor or ARB	6475 (70.7)	6581 (72.2)	6462 (70.8)
Calcium-channel blocker	2413 (26.4)	2374 (26.0)	2482 (27.2)
Diuretic	2727 (29.8)	2666 (29.2)	2746 (30.1)
Beta-blocker	6389 (69.8)	6401 (70.2)	6394 (70.1)
Lipid-lowering agent	8239 (90.0)	8204 (90.0)	8158 (89.4)
NSAID	531 (5.8)	466 (5.1)	473 (5.2)
Nontrial PPI	3268 (35.7)	3266 (35.8)	3264 (35.8)

