Debate: Είναι αναγκαία τα αντιπηκτικά στην Κολπική Μαρμαρυγή σε ασθενείς σε ΑΚ και ποια να χρησιμοποιήσουμε;

Ναι. Άλλωστε υπάρχουν εγκεκριμένα από τον FDA

Κανταρτζή Κωνσταντία
Παν. Νεφρολογική Κλινική
Αν. Καθηγ. Νεφρολογίας ΔΠΘ

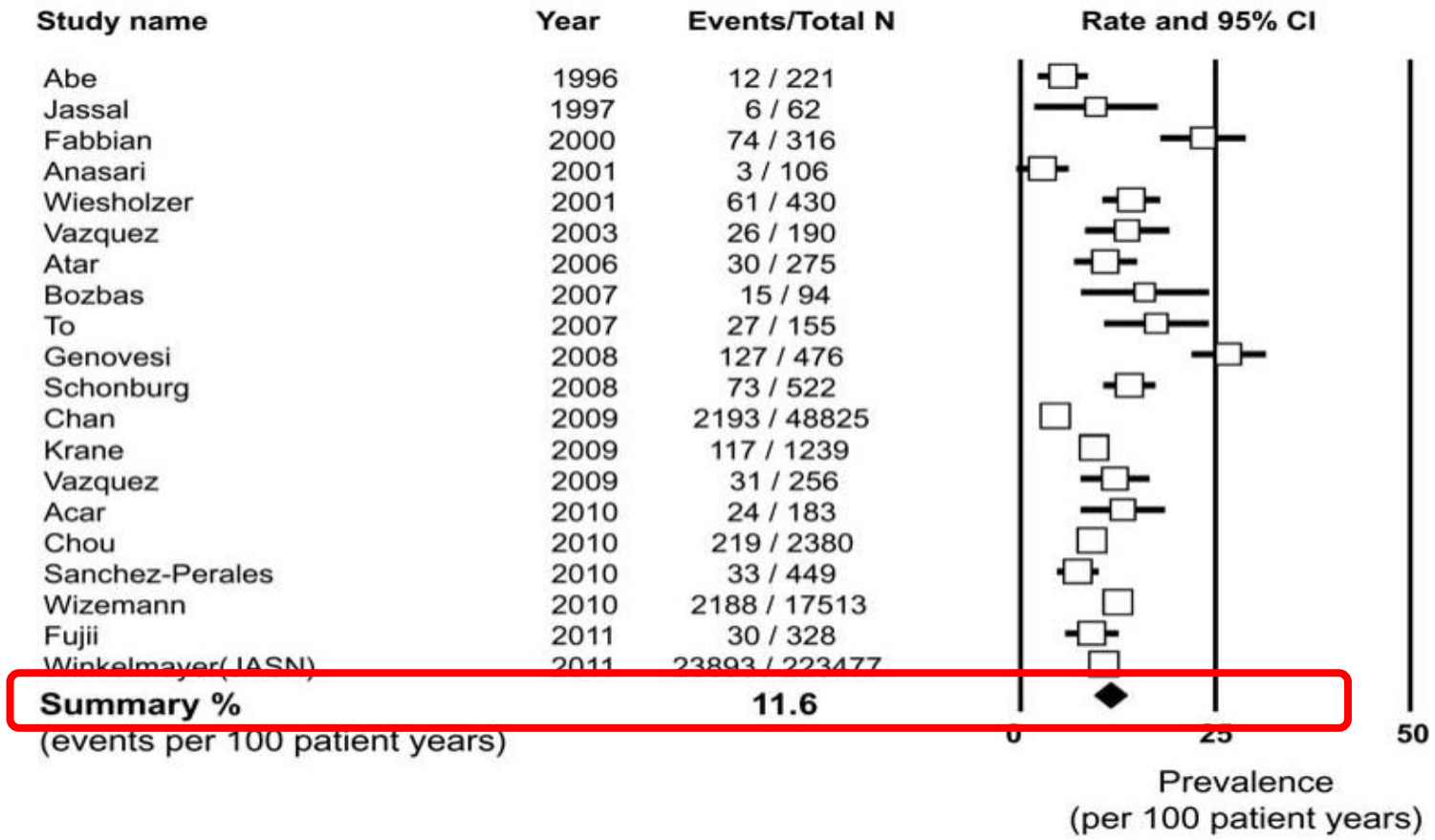
Χρειάζονται οι ΑΚ ασθενείς αντιπηκτικά για ΚΜ???

Nephrol Dial Transplant (2012) 27: 3816–3822
doi: 10.1093/ndt/gfs416

NDT
Nephrology Dialysis Transplantation

Original Articles

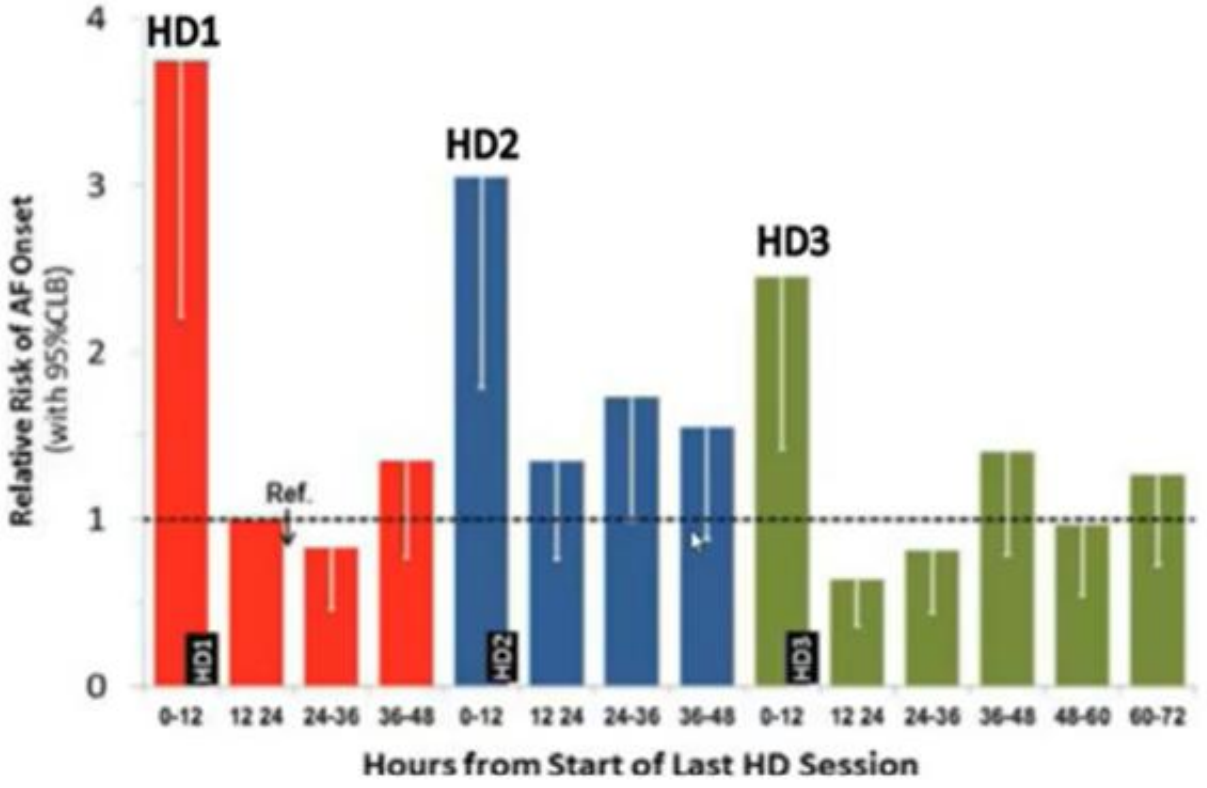
Systematic review and meta-analysis of incidence, prevalence and outcomes of atrial fibrillation in patients on dialysis

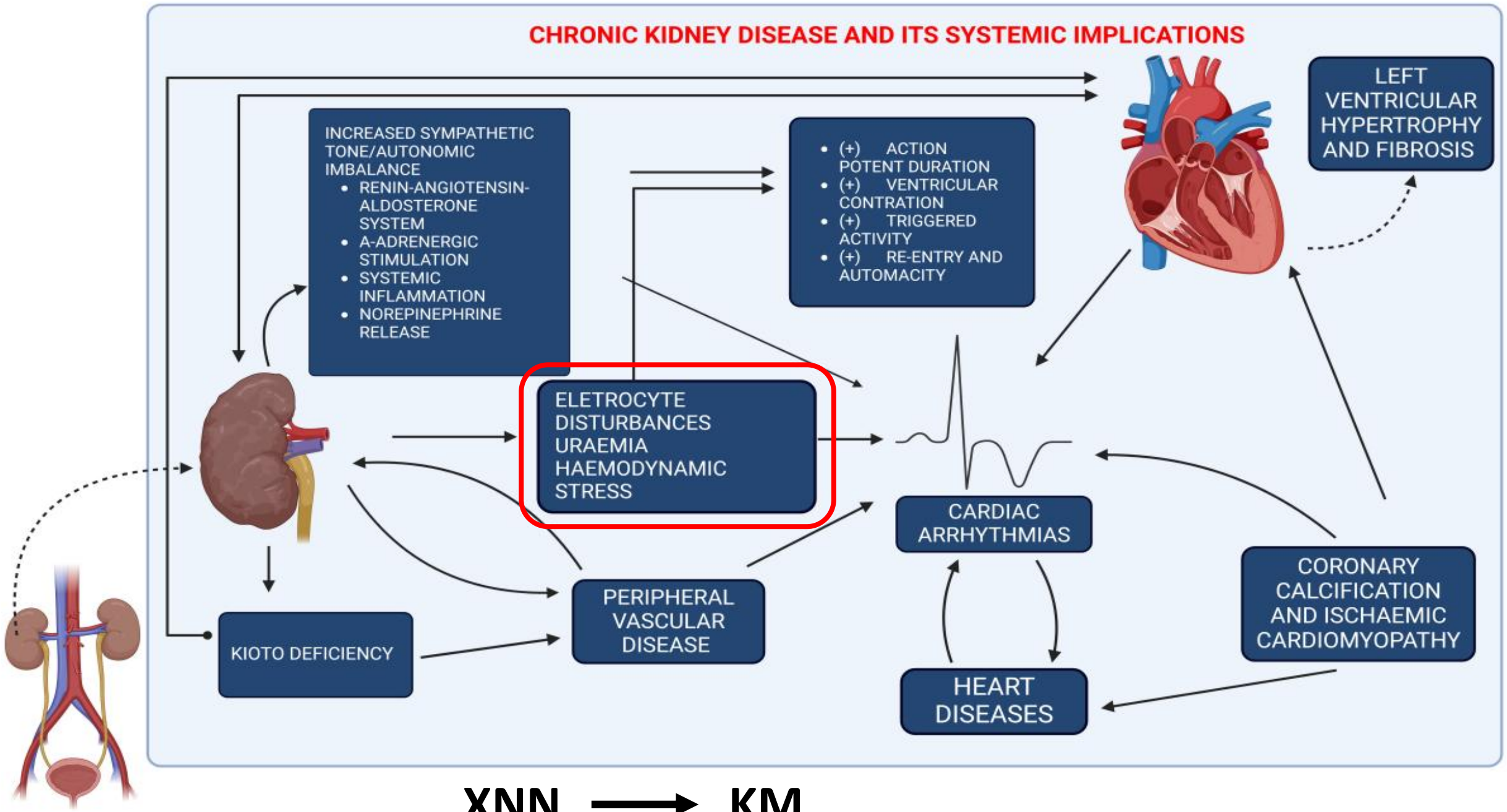


Η επεμβατική παρακολούθηση του καρδιακού ρυθμού καταδεικνύει ότι η συχνότητα εμφάνισης κολπικής μαρμαρυγής είναι υψηλότερη από ό,τι πιστεύαμε

Table 2 | Arrhythmias during follow-up

	6 mo		
Arrhythmia type	Incidence *N*	Rate % (n/N)	Event rate (95% CI)
CSA	1678	66.7% (44/66)	4.48 (2.51, 7.98)
CSA subtypes			
VT	1	1.5% (1/66)	0.00 (0.00, 0.02)
Bradycardia	1461	19.7% (13/66)	3.90 (1.04, 14.63)
Asystole	14	9.1% (6/66)	0.04 (0.01, 0.11)
Patient Marked	196	57.6% (38/66)	0.52 (0.34, 0.80)
RCA	12480	97.0% (64/66)	33.74 (23.36, 48.74)
RCA subtypes			
Atrial arrhythmia	7488	90.9% (60/66)	20.11 (13.43,30.12)
Ventricular arrhythmia	913	77.3% (51/66)	2.45 (1.60, 3.74)
Bradycardia	1770	25.8% (17/66)	4.74 (1.53, 14.69)
Asystole		10.6% (7/66)	0.08 (0.03, 0.26)
Sinus tachycardia	6065	80.3% (53/66)	16.59 (10.26, 26.83)
Reveal detected AF	4419	40.9% (27/66)	11.88 (4.92, 28.73)





XNN ⟶ KM

Rev. Cardiovasc. Med. 2025

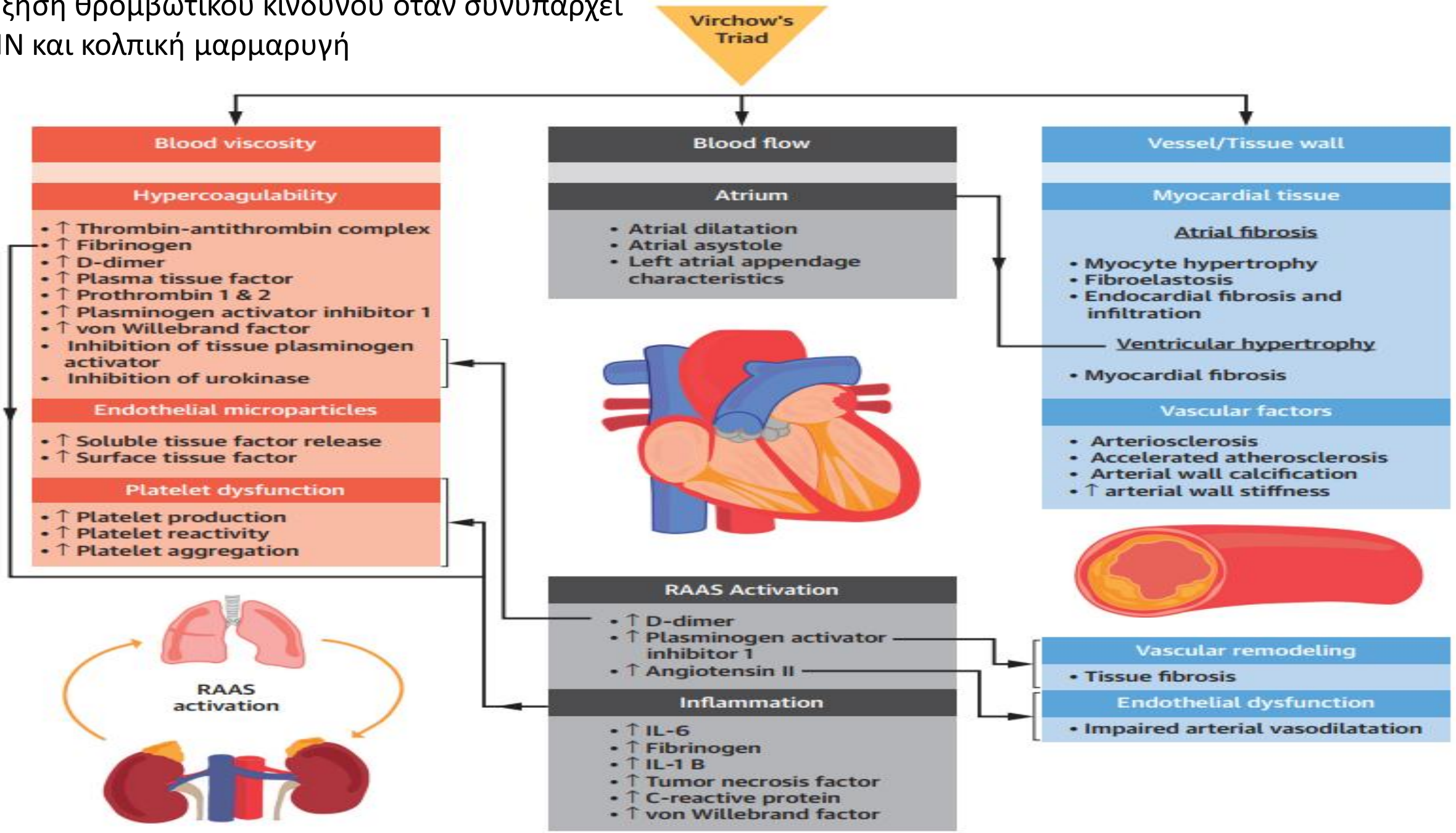
Εκβάσεις που σχετίζονται με την ΚΜ

AF-Related Outcome	Frequency in AF	Mechanism(s)
Death 	1.5 - 3.5 fold increase	Excess mortality related to: • HF, comorbidities • Stroke
Stroke 	20-30% of all ischaemic strokes, 10% of cryptogenic strokes	• Cardioembolic, or • Related to comorbid vascular atheroma
LV dysfunction / Heart failure 	In 20-30% of AF patients	• Excessive ventricular rate • Irregular ventricular contractions • A primary underlying cause of AF
Cognitive decline / Vascular dementia 	HR 1.4 / 1.6 (irrespective of stroke history)	• Brain white matter lesions, inflammation, • Hypoperfusion, • Micro-embolism
Depression 	Depression in 16-20% (even suicidal ideation)	• Severe symptoms and decreased QoL • Drug side effects
Impaired quality of life 	>60% of patients	• Related to AF burden, comorbidities, psychological functioning and medication • Distressed personality type
Hospitalizations 	10-40% annual hospitalization rate	• AF management, related to HF, MI or AF related symptoms • Treatment-associated complications

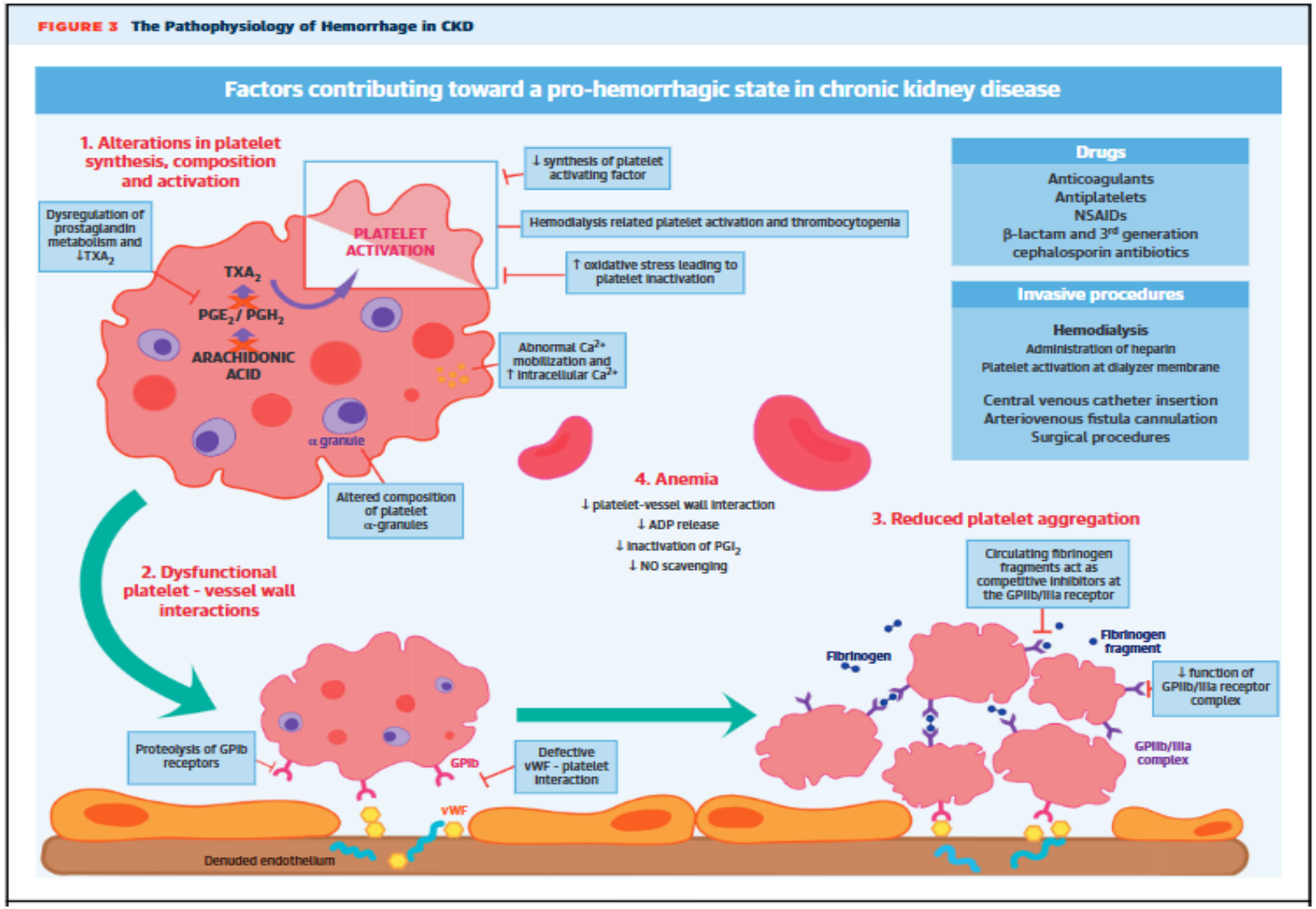
Hindricks et al. European Heart Journal 2021

Η ΚΜ είναι παράγοντας κινδύνου για ΑΕΕ σε ασθενείς υπό αιμοκάθαρση?

Αύξηση θρομβωτικού κινδύνου όταν συνυπάρχει ΧΝΝ και κολπική μαρμαρυγή

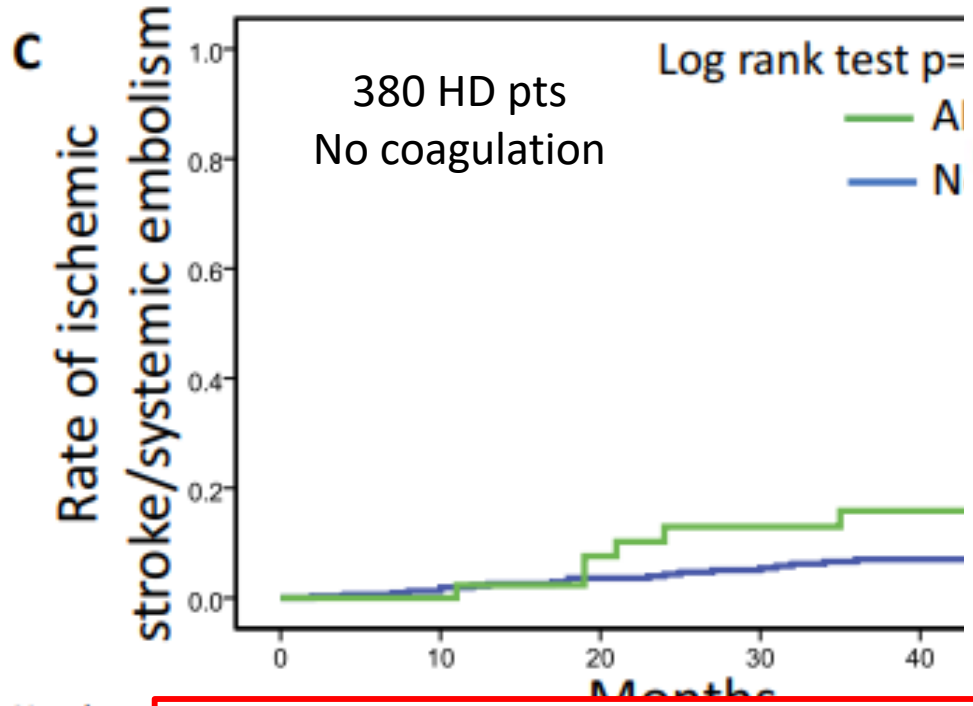


Αυξημένος κίνδυνος αιμορραγίας στα προχωρημένα στάδια ΧΝΝ

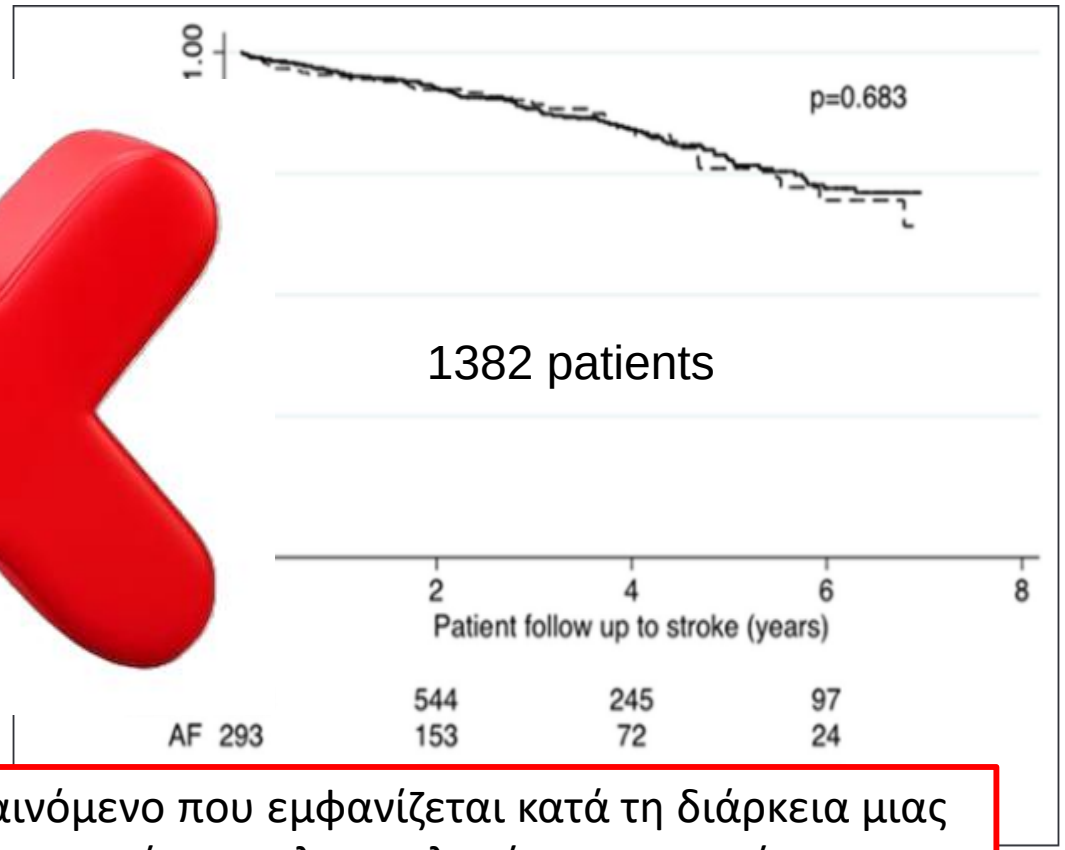


Journal of the American College of Cardiology 2019

Atrial Fibrillation had Less Impact on the Risk of Ischemic Stroke in Non-anticoagulated Patients Undergoing Hemodialysis: Insight from the RAKUEN study



Risk Factors of Ischemic Stroke and Subsequent Outcome in Patients Receiving Hemodialysis

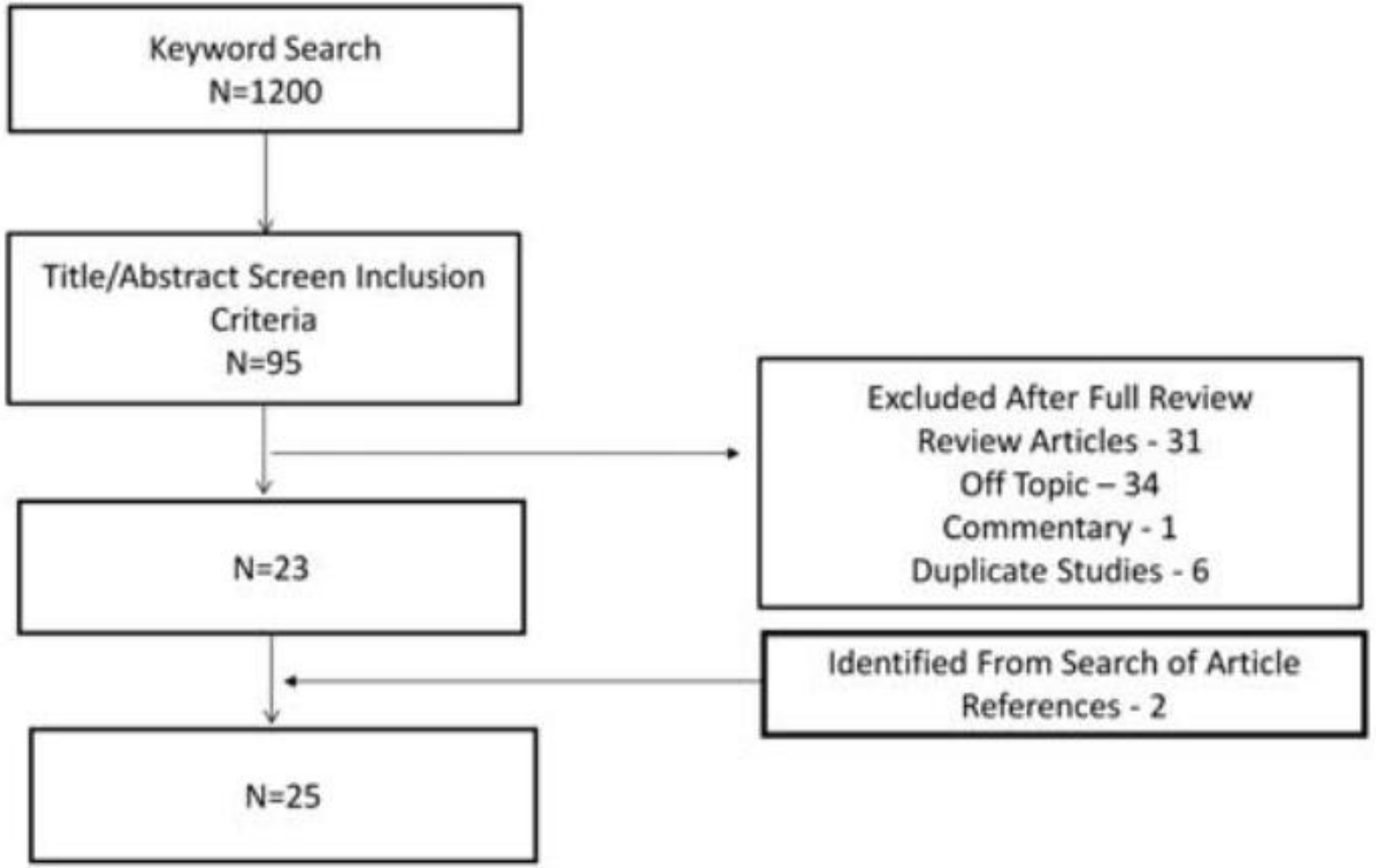


Η τυχαία κολπική μαρμαρυγή μπορεί να είναι ένα επιφαινόμενο που εμφανίζεται κατά τη διάρκεια μιας συνεδρίας αιμοκάθαρσης ως αποτέλεσμα μετατοπίσεων υγρών και ηλεκτρολυτών και μπορεί να μην σχετίζεται με αυξημένο κίνδυνο εγκεφαλικού επεισοδίου.

Intern Med Advance Publication 2018

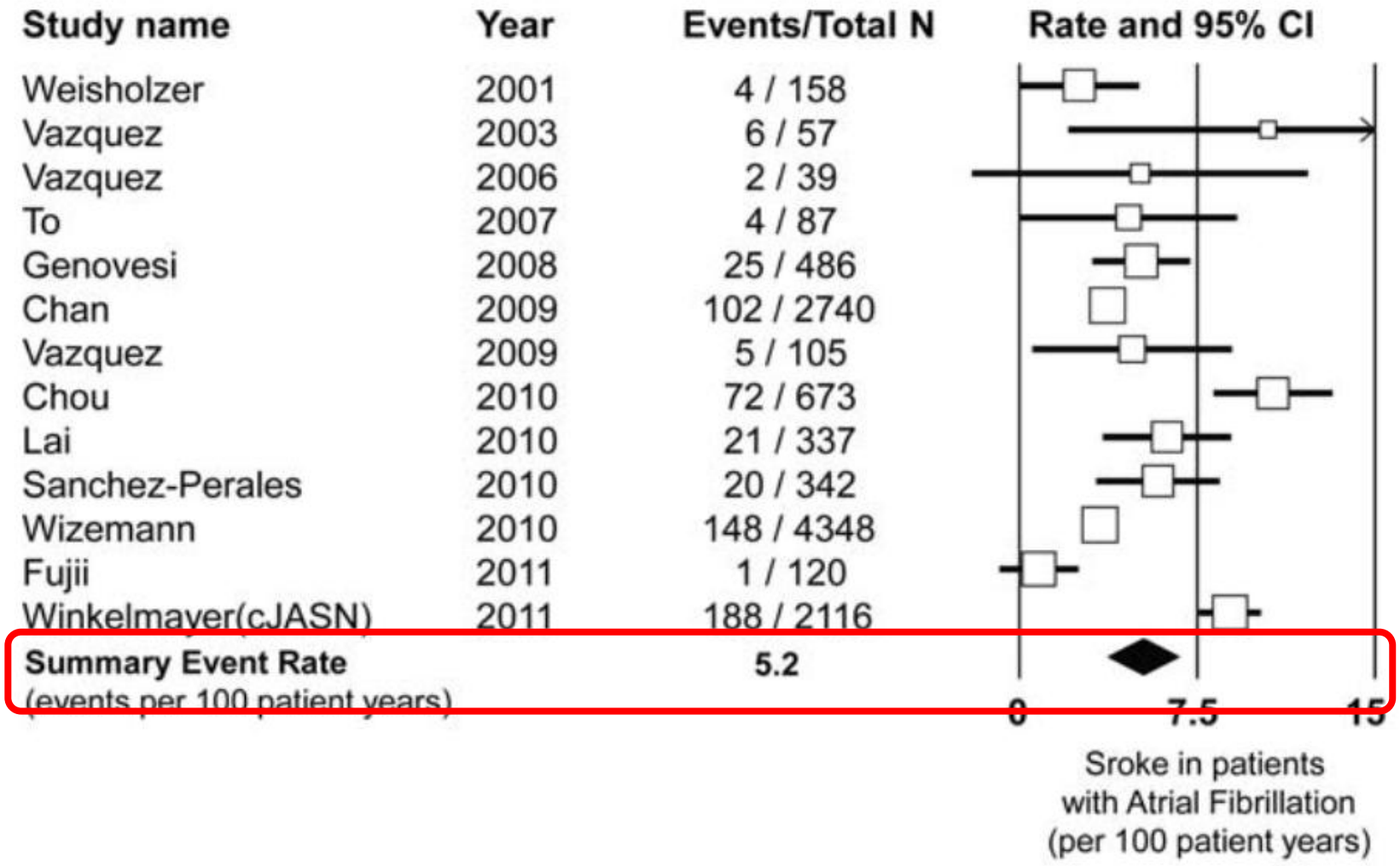
Stroke 2015

Systematic review and meta-analysis of incidence, prevalence and outcomes of atrial fibrillation in patients on dialysis



Nephrol Dial Transplant 2012

Systematic review and meta-analysis of incidence, prevalence and outcomes of atrial fibrillation in patients on dialysis



Nephrol Dial Transplant 2012

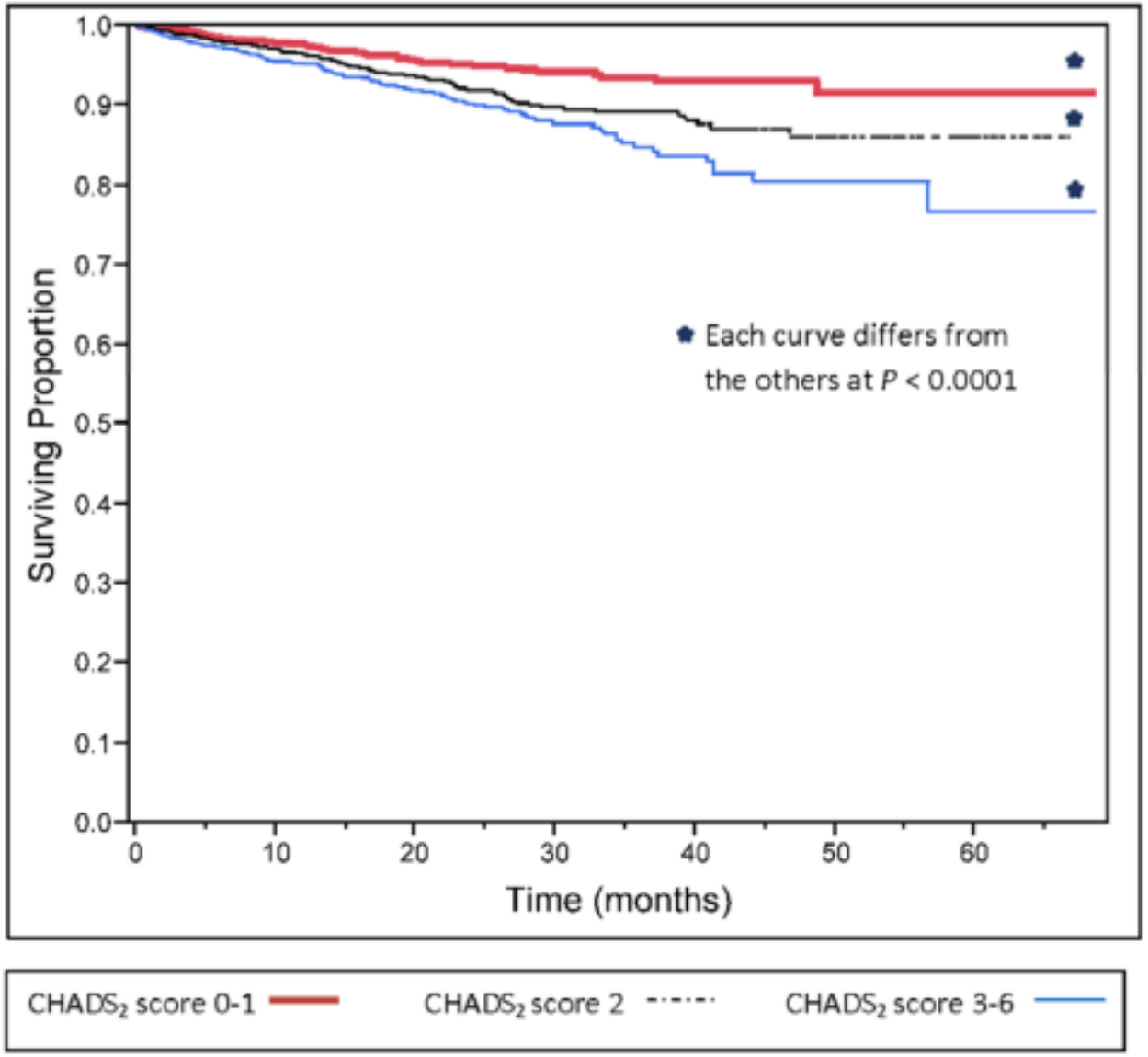
Stroke and the "Stroke Belt" in Dialysis: Contribution of Patient Characteristics to Ischemic Stroke Rate and Its Geographic Variation

Table 1. Descriptive characteristics of the Medicare-eligible cohort

Characteristic	All	Stroke	No Stroke	*P* Value[a]
Cases (*n*)	265,685	13,073	252,612	
Age (yr)	64.7±15.1	69.4±11.9	64.5±15.2	<0.0001
Male, *n* (%)	140,599 (52.9)	5406 (41.4)	135,193 (53.5)	<0.0001
Race/ethnicity, *n* (%)				<0.0001
African American	79,693 (30.0)	4336 (33.2)	75,357 (29.8)	
White	145,768 (54.9)	7030 (53.8)	138,738 (54.9)	
Hispanic	27,738 (10.4)	1248 (9.6)	26,490 (10.5)	
Other	12,486 (4.7)	459 (3.5)	12,027 (4.8)	
BMI category, *n* (%)				<0.0001
< 20 kg/m^2	25,710 (9.7)	1321 (10.1)	24,389 (9.7)	
20–24.9 kg/m^2	84,154 (31.7)	4330 (33.1)	79,824 (31.6)	
25–29.9 kg/m^2	76,043 (28.6)	3840 (29.4)	72,203 (28.6)	
30+kg/m^2	79,778 (30.0)	3582 (27.4)	76,196 (30.2)	
Smoker, *n* (%)	14,893 (5.6)	608 (4.7)	14,285 (5.7)	<0.0001
Substance abuser, *n* (%)	5,370 (2.2)	157 (1.2)	5573 (2.2)	<0.0001
Unemployed, *n* (%)	252,749 (95.1)	12,846 (98.3)	239,903 (95.0)	<0.0001
Unable to ambulate, *n* (%)	11,443 (4.3)	745 (5.7)	10,698 (4.2)	<0.0001
Unable to transfer, *n* (%)	4075 (1.5)	295 (2.3)	3780 (1.5)	<0.0001
In-center HD, *n* (%)[b]	247,584 (93.2)	12,258 (93.8)	235,326 (93.2)	0.007
Hemoglobin < 11.0 g/dl, *n* (%)	176,664 (72.9)	8759 (73.6)	167,905 (72.83)	0.05
Comorbid conditions, *n* (%)				
AF	38,619 (14.5)	2863 (21.9)	35,756 (14.2)	<0.0001
Hypertension	224,159 (84.4)	11,410 (87.3)	212,749 (84.2)	<0.0001
Diabetes mellitus	141,067 (53.1)	8050 (61.6)	133,017 (52.7)	<0.0001
Congestive heart failure	88,226 (33.2)	4990 (38.2)	83,236 (33.0)	<0.0001
Coronary artery disease	74,734 (28.1)	4302 (32.9)	70,431 (27.9)	<0.0001
Peripheral vascular disease	40,662 (15.3)	2431 (18.6)	38,231 (15.1)	<0.0001
Prior cerebrovascular accident	27,304 (10.3)	3055 (23.4)	24,249 (9.6)	<0.0001
Liu comorbidity index score	5.1±2.8	5.8±2.8	5.01±2.8	<0.0001
Cause of ESRD, *n* (%)				<0.0001
Diabetes	125,220 (47.2)	7178 (54.9)	118,042 (46.7)	
Hypertension	70,117 (26.4)	3480 (26.6)	66,637 (26.4)	
GN	22,817 (8.6)	604 (4.6)	225,213 (8.8)	
Other	47,531(17.9)	1811 (13.9)	465,720 (18.1)	

J Am Soc Nephrol 2013

Atrial fibrillation and risk of stroke in dialysis patients



- Οι ασθενείς υπό HD και ΚΜ είχαν λιγότερο χρόνο μέχρι το ΑΕΕ
- Υψηλότερο CHADS2 score - γρηγορότερα το ΑΕΕ

Ann Epidemiol. 2013

Risks of Death and Stroke in Patients Undergoing Hemodialysis With New-Onset Atrial Fibrillation

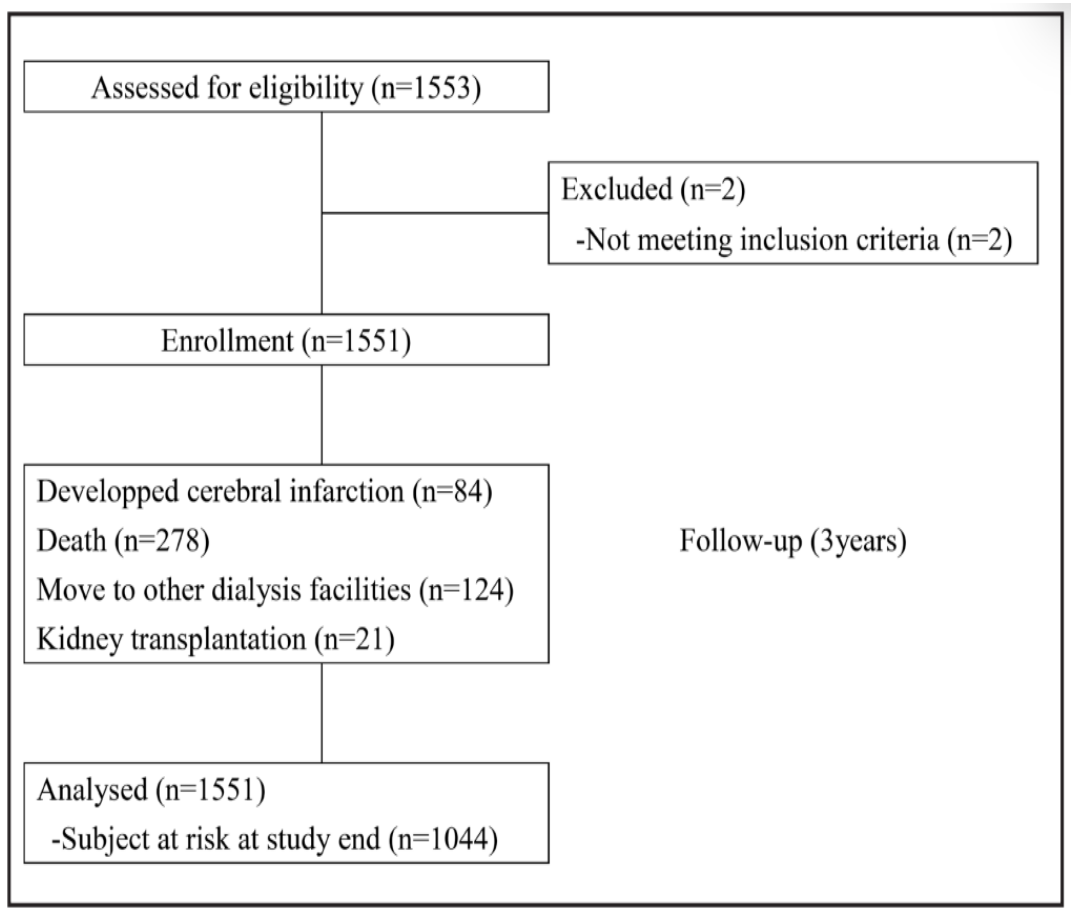
A Competing-Risk Analysis of a Nationwide Cohort

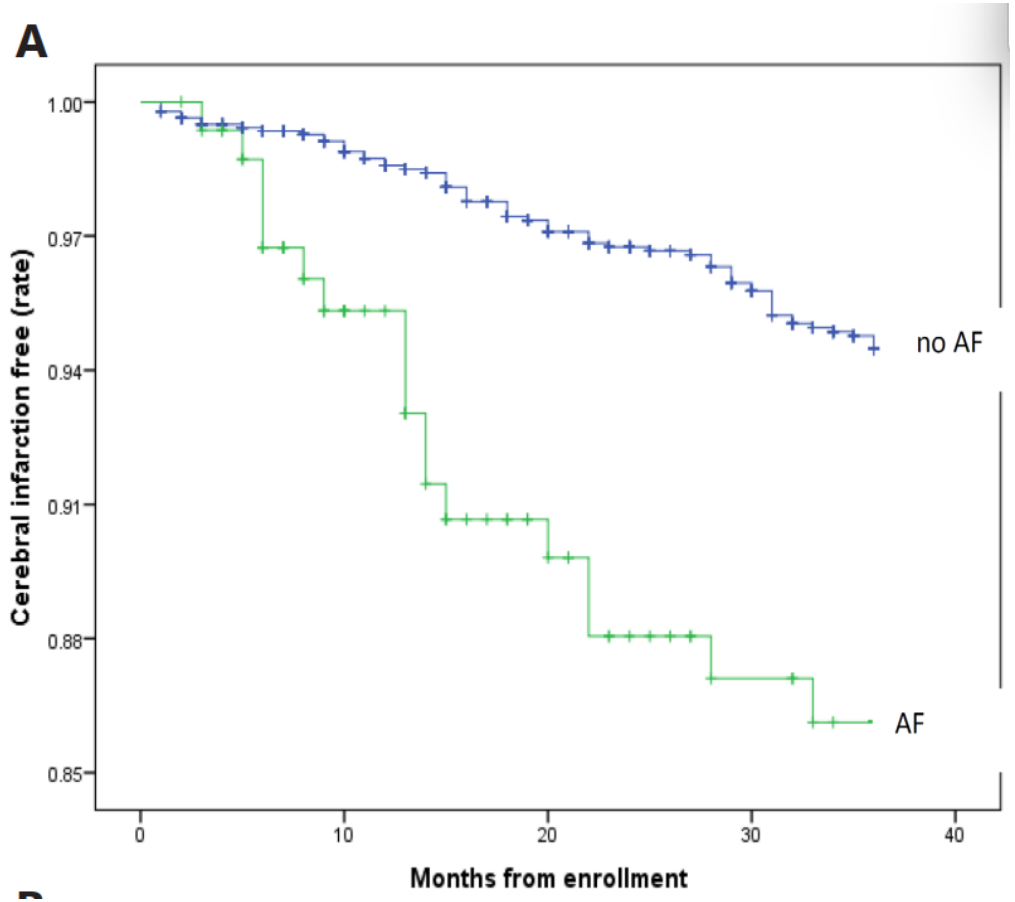
Table 2. Incidence and Risk of Stroke, Myocardial Infarction, and Major Bleeding Among Hemodialysis Patients With and Without AF

	AF		Non-AF		Crude		Adjusted*		Competing Risk†	
	No. of Events	Annual Rate	No. of Events	Annual rate	Hazard Ratio (95% CI)	*P* Value	Hazard Ratio (95% CI)	*P* Value	Hazard Ratio (95% CI)	*P* Value
Before propensity score matching										
All-cause death	4642	24.72	22 008	9.56	2.57 (2.49–2.66)	<0.001	1.64 (1.59–1.70)	<0.001	–	
In-hospital cardiovascular death	2461	13.11	10 403	4.52	2.88 (2.76–3.01)	<0.001	1.89 (1.80–1.99)	<0.001	1.71 (1.63–1.80)	<0.001
Ischemic stroke	600	3.35	3963	1.77	1.88 (1.73–2.05)	<0.001	1.25 (1.15–1.37)	<0.001	.03 (0.94–1.12)	0.558
Hemorrhagic stroke	278	1.40	2101	0.92	1.52 (1.34–1.72)	<0.001	1.28 (1.12–1.46)	<0.001	1.03 (0.90–1.18)	0.683
Myocardial infarction	517	2.84	3312	1.46	1.94 (1.76–2.12)	<0.001	1.30 (1.18–1.44)	<0.001	1.14 (1.03–1.27)	0.010
Hospitalization for heart failure	1719	10.88	7822	3.58	2.95 (2.80–3.11)	<0.001	1.95 (1.84–2.06)	<0.001	1.63 (1.54–1.72)	<0.001
After propensity score matching										
All-cause death	4380	24.33	3548	14.84	1.59 (1.52–1.66)	<0.001	1.59 (1.52–1.67)	<0.001	–	
In-hospital cardiovascular death	2,322	12.90	1,629	6.81	1.82 (1.71–1.94)	<0.001	1.83 (1.71–1.94)	<0.001	1.65 (1.55–1.76)	<0.001
Ischemic stroke	563	3.28	573	2.50	1.27 (1.13–1.42)	<0.001	1.27 (1.13–1.43)	<0.001	1.01 (0.90–1.14)	0.832
Hemorrhagic stroke	245	1.38	254	1.07	1.24 (1.04–1.49)	0.015	1.24 (1.04–1.48)	0.015	0.99 (0.83–1.18)	0.882
Myocardial infarction	499	2.86	483	2.07	1.33 (1.18–1.51)	<0.001	1.33 (1.17–1.51)	<0.001	1.06 (0.94–1.21)	0.327
Hospitalization for heart failure	1636	10.77	1153	5.25	1.90 (1.76–2.05)	<0.001	1.90 (1.76–2.05)	<0.001	1.56 (1.45–1.68)	<0.001

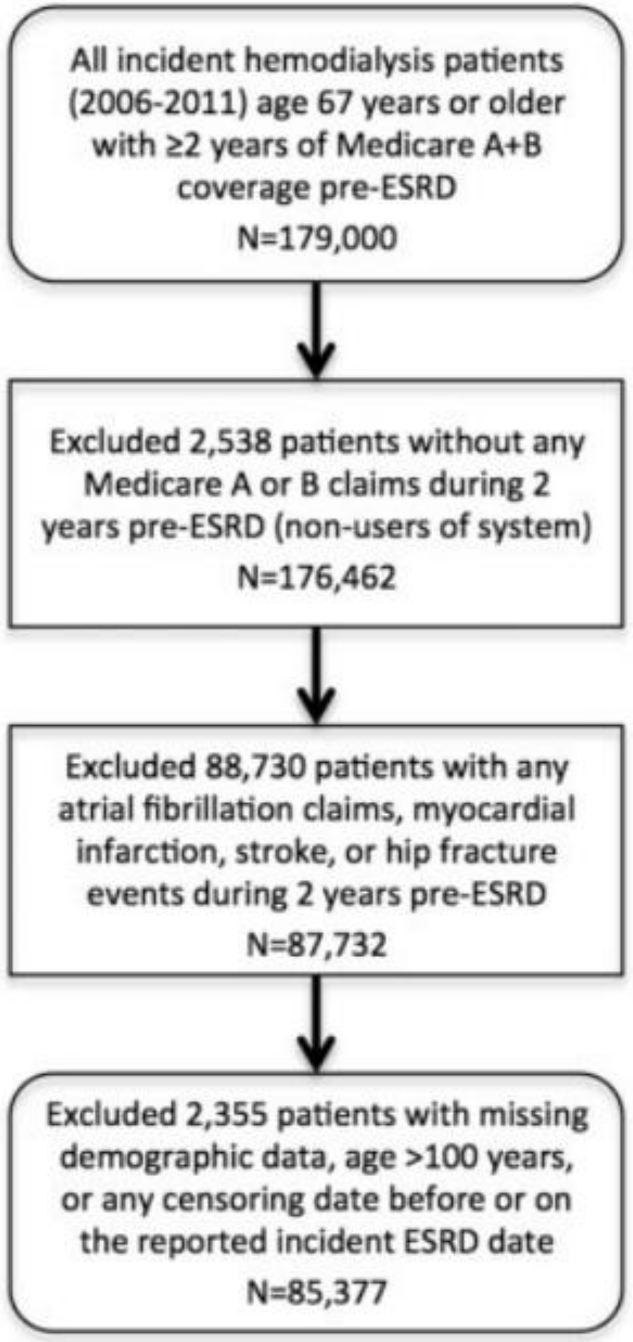
Circulation. 2016

Risk of Cerebral Infarction in Japanese Hemodialysis Patients: Miyazaki Dialysis Cohort Study (MID study)





Kidney Blood Press Res 2016

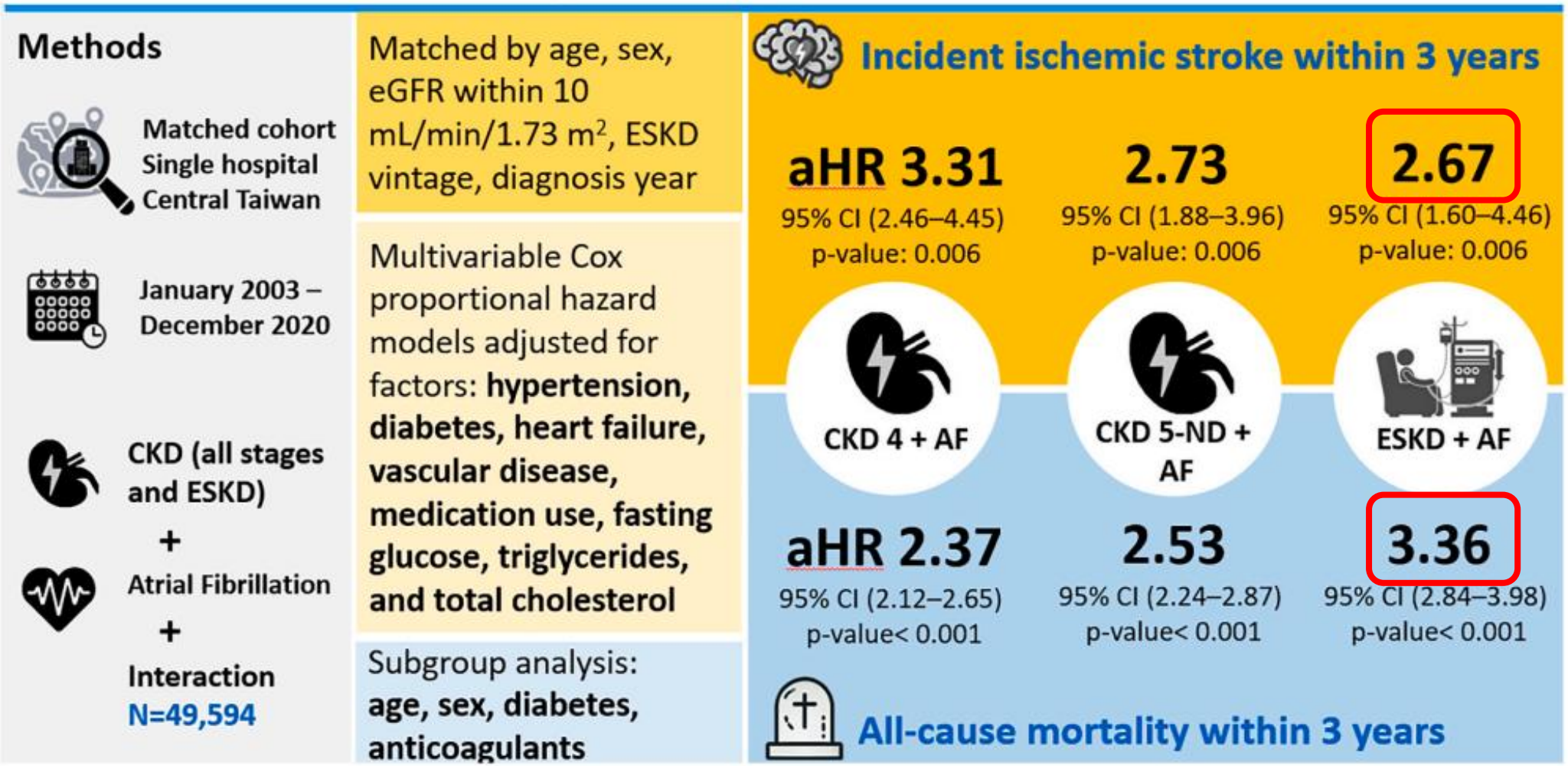


Risk profiles for acute health events after incident atrial fibrillation in patients with end-stage renal disease on hemodialysis

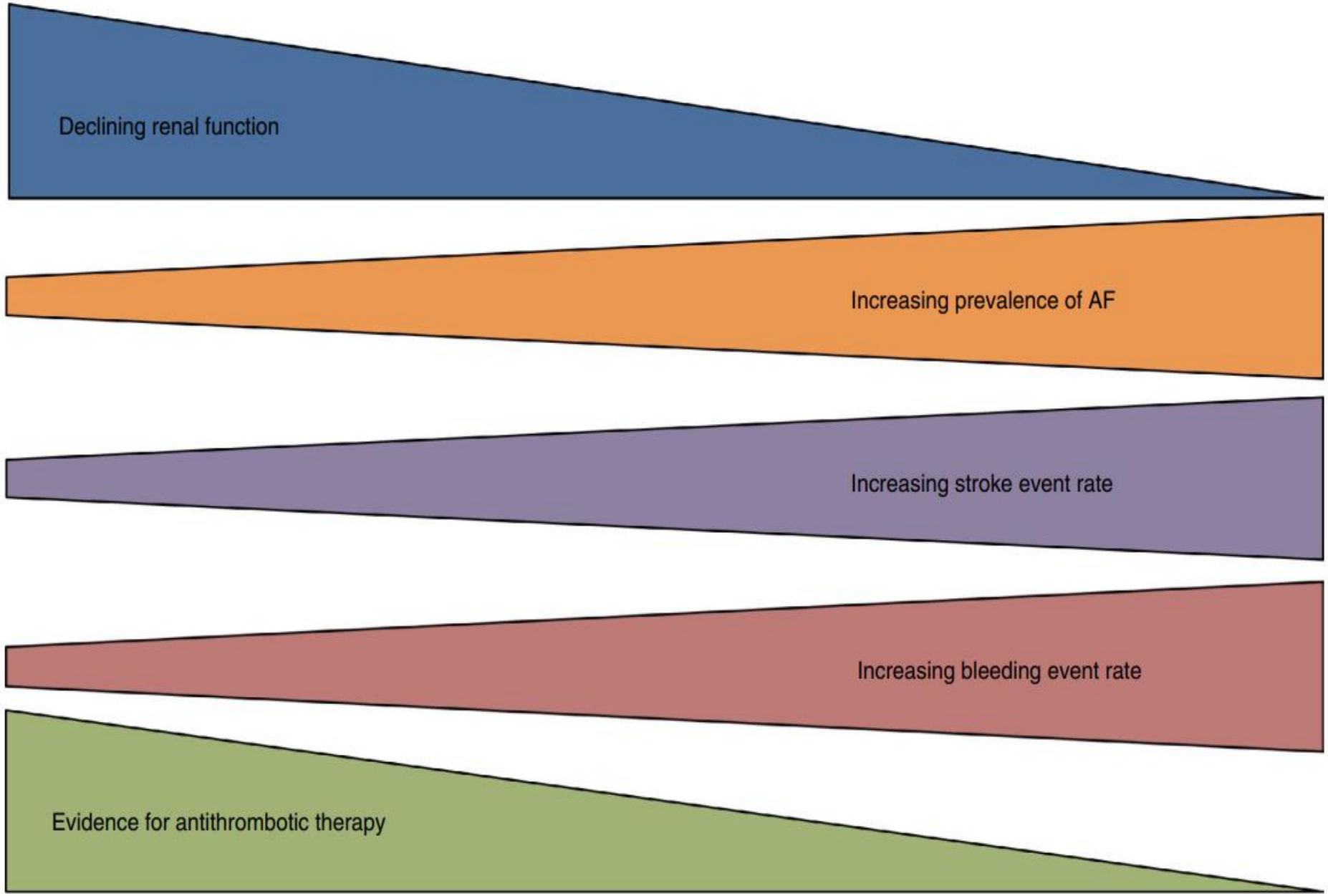
Outcome Time since AF	Unadjusted		Demographics-adjusted		Demographics + comorbidities-adjusted	
	HR	95% CI	HR	95% CI	HR	95% CI
Ischemic stroke						
No AF	1.0	Referent	1.0	Referent	1.0	Referent
≤30 days	2.21	1.72–2.85	2.16	1.68–2.78	2.10	1.63–2.70
31–90 days	2.57	2.12–3.11	2.53	2.09–3.07	2.47	2.03–2.99
>90 days	1.52	1.36–1.71	1.53	1.37–1.72	1.51	1.34–1.69
Myocardial infarction						
No AF	1.0	Referent	1.0	Referent	1.0	Referent
0–30 days	1.86	1.53–2.25	1.77	1.46–2.15	1.69	1.39–2.04
>30–90 days	2.37	2.06–2.72	2.28	1.98–2.62	2.17	1.89–2.49
>90 days	1.34	1.23–1.45	1.30	1.20–1.41	1.25	1.15–1.36
Hip fracture						
No AF	1.0	Referent	1.0	Referent	1.0	Referent
0–30 days	1.26	0.86–1.85	1.11	0.76–1.64	1.09	0.74–1.60
>30–90 days	1.54	1.17–2.03	1.39	1.05–1.83	1.36	1.03–1.79
>90 days	1.35	1.18–1.53	1.24	1.09–1.41	1.22	1.07–1.39
Death						
No AF	1.0	Referent	1.0	Referent	1.0	Referent
0–30 days	10.41	9.97–10.85	9.69	9.29–10.11	9.17	8.79–9.57
>30–90 days	5.07	4.83–5.33	4.78	4.55–5.02	4.55	4.33–4.78
>90 days	2.42	2.34–2.50	2.30	2.23–2.38	2.21	2.14–2.29

Nephrol Dial Transplant 2018

Interaction between chronic kidney disease and atrial fibrillation on incident stroke and all-cause mortality: Matched cohort study of 49,594 patients



Res Pract Thromb Haemost. 2019



Res Pract Thromb Haemost. 2019

Τελικά τι φταίει????

Ποικιλία στους ορισμούς της κολπικής μαρμαρυγής

Όρος	Όρος	Ορισμός
AF burden	Επιβάρυνση ΚΜ	Το ποσοστό του χρόνου σε ΚΜ κατά τη διάρκεια μιας συγκεκριμένης περιόδου παρακολούθησης
Paroxysmal AF	Παροξυσμική ΚΜ	ΚΜ που τερματίζεται αυθόρμητα ή με παρέμβαση εντός 7 ημερών από την έναρξή της
Persistent AF	Επίμονη ΚΜ	Συνεχής ΚΜ που διαρκεί > 7 ημέρες
Long-standing persistent AF		Συνεχής ΚΜ διάρκειας > 12 μηνών
Permanent AF	Μόνιμη ΚΜ	Αποδοχή ΚΜ από τον ασθενή και τον κλινικό ιατρό Λαμβάνεται κοινή απόφαση για τη διακοπή περαιτέρω προσπαθειών αποκατάστασης ή/και διατήρησης του φλεβοκομβικού ρυθμού
First diagnosed AF	Πρώτη διάγνωση ΚΜ	ΚΜ που δεν είχε διαγνωστεί στο παρελθόν, ανεξάρτητα από τη διάρκεια της αρρυθμίας ή την παρουσία και τη σοβαρότητα των σχετικών συμπτωμάτων

European Heart Journal 2024

Όρος	Όρος	Ορισμός
Device-detected subclinical AF	Υποκλινική ΚΜ που ανιχνεύεται από συσκευή	Ασυμπτωματικά επεισόδια ΚΜ που ανιχνεύονται σε συσκευές συνεχούς παρακολούθησης. Εμφυτευμένες καρδιακές ηλεκτρονικές συσκευές, φορητές συσκευές συνεχούς παρακολούθησης. Προγνωστικός παράγοντας μελλοντικής κλινικής ΚΜ

European Heart Journal (2024

KI REPORTS
KIReports.org

Implantable Loop Recorder Monitoring and the Incidence of Previously Unrecognized Atrial Fibrillation in Patients on Hemodialysis

Kidney International Reports 2022

- 66 pts HD: 59 (90%) χωρίς διάγνωση ΚΜ
- ΚΜ διάρκειας 6 min ανιχνεύτηκε στο 31% (18/59) χωρίς προηγούμενη διάγνωση ΚΜ
- 71% (5/7) με προηγούμενη διάγνωση ΚΜ
- Στους 23 pts με ΚΜ, τα επεισόδια καταγράφηκαν στο 16% pts days
- Στους pts με AF > 6 min, 83% (19/23) είχαν CHA2DS2-VASc score >2

Conclusion: New AF was detected in approximately one-third of patients with KF-HD. AF affects a substantial proportion of patient days and may be an underappreciated cause of stroke in KF-HD.

Εκτίμηση του κινδύνου εμφάνισης ΑΕΕ σε ΚΜ

Clinical Kidney Journal, 2024

ESC European Society of Cardiology

Europace (2021) **23**, 665–673
doi:10.1093/europace/euaa287

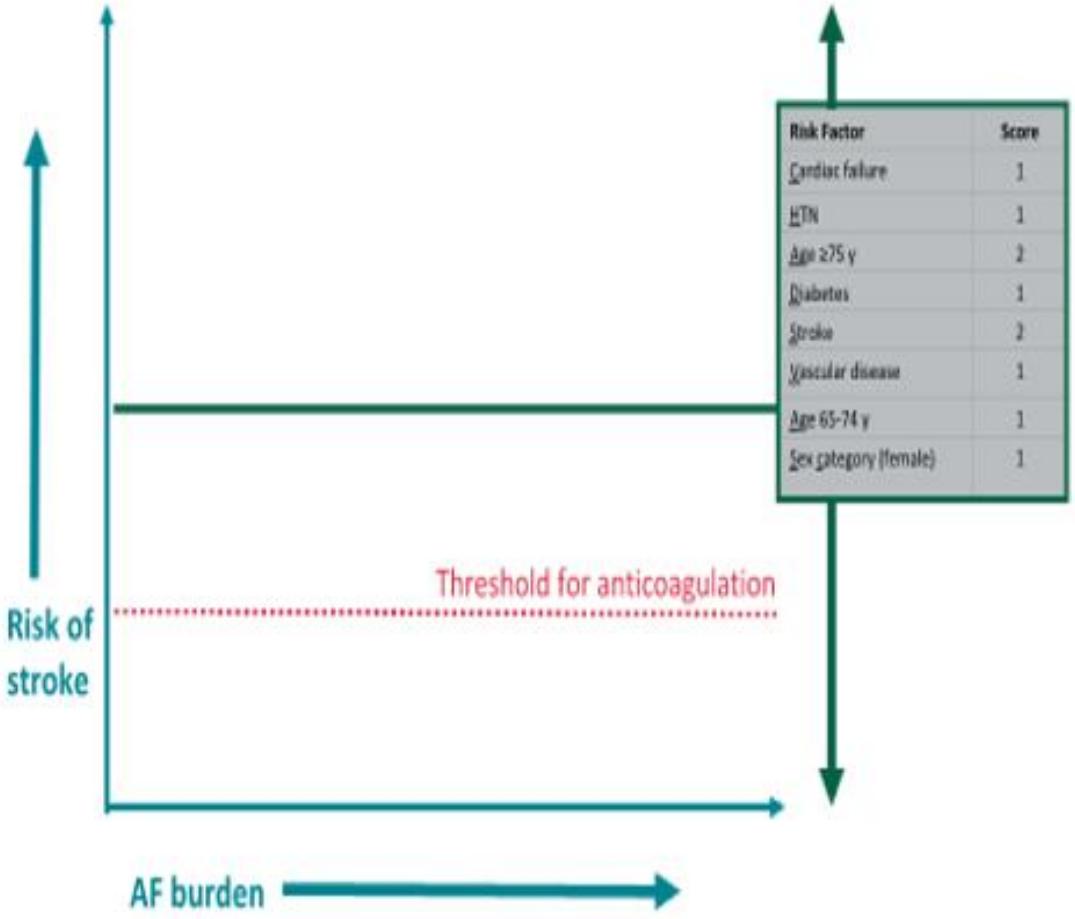
REVIEW

Atrial fibrillation burden: an update—the need for a CHA_2DS_2-VASc-AFBurden score

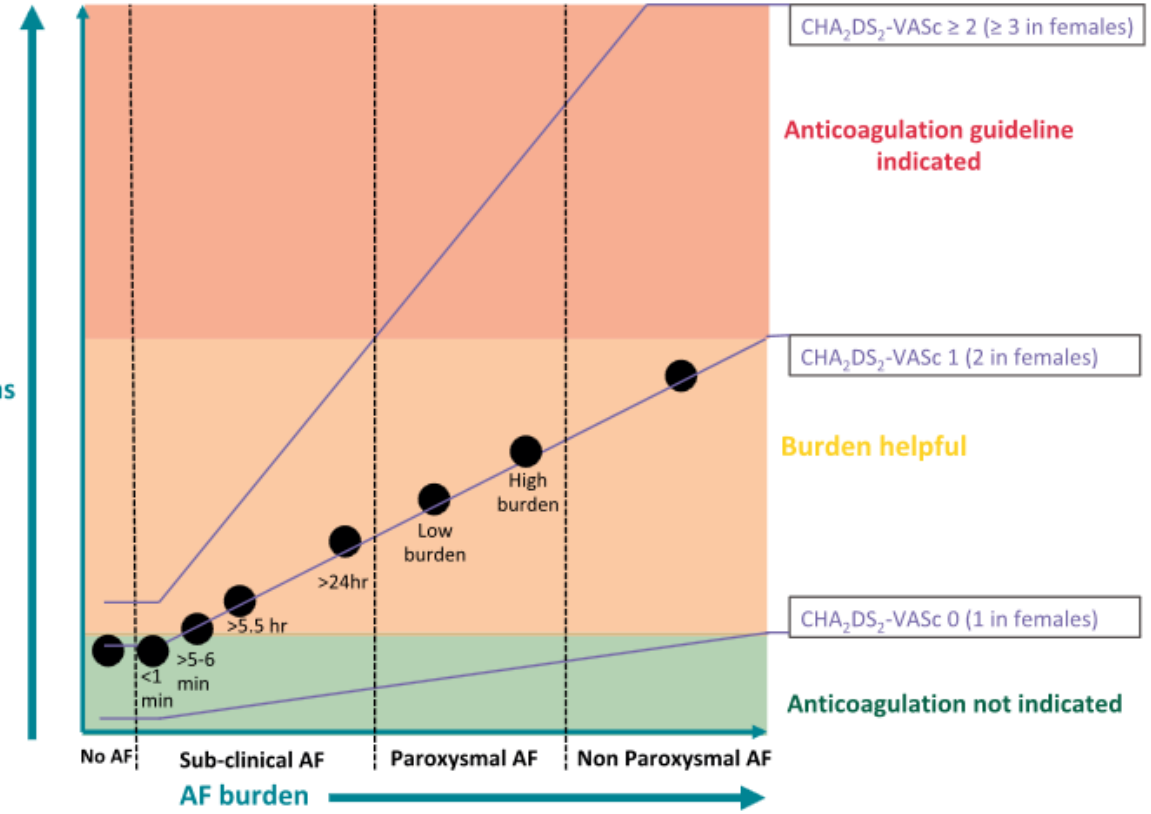
Kathryn D. Tiver [1], Jing Quah[1,2], Anandaroop Lahiri[1], Anand N. Ganesan[1,2], and Andrew D. McGavigan[1,2]*

[1]Department of Cardiovascular Medicine, Flinders Medical Centre, Bedford Park, South Australia 5042, Australia; and [2]College of Medicine and Public Health, Flinders University of South Australia, Bedford Park, South Australia 5042, Australia

Παλαιότερα …..
Κίνδυνος ισχαιμικού ΑΕΕ ΚΜ, καθορίζεται μόνο τη βαθμολογία CHA_2DS_2-VASc, ανεξάρτητα από το φορτίο της κολπικής μαρμαρυγής



Προτείνεται …
Υποθετικό σχήμα που περιγράφει τη σχέση μεταξύ του φορτίου της ΚΜ, των παραγόντων κινδύνου σε επίπεδο ασθενούς και του κινδύνου εγκεφαλικού επεισοδίου



CHA_2DS_2-VASC SCORE

CHA_2DS_2-VASc risk factor	Points
Congestive heart failure Signs/symptoms of heart failure or objective evidence of reduced left-ventricular ejection fraction	+1
Hypertension Resting blood pressure >140/90 mmHg on at least two occasions or current antihypertensive treatment	+1
Age 75 years or older	+2
Diabetes mellitus Fasting glucose >125 mg/dL (7 mmol/L) or treatment with oral hypoglycaemic agent and/or insulin	+1
Previous stroke, transient ischaemic attack, or thromboembolism	+2
Vascular disease Previous myocardial infarction,peripheral artery disease, or aortic plaque	+1
Age 65–74 years	+1
Sex category (female)	+1

Validation of risk scores for ischaemic stroke in atrial fibrillation across the spectrum of kidney function

Graphical Abstract

Weighing stroke and bleeding risk is essential for individualized medicine

Classic risk factors for ischaemic stroke

Atrial fibrillation (AF) + Hypertension + Dyslipidaemia + Atherosclerosis + Demographics

Attenuated in chronic kidney disease (CKD)

= **Ischaemic stroke risk** + **Bleeding risk**

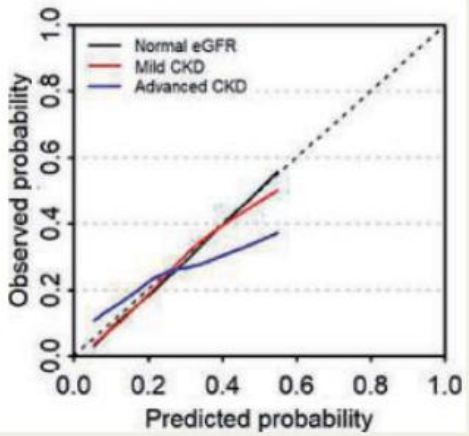
Unclear predictive performance in patients with CKD: risk of misclassification and over- or undertreatment

Six scores validated: AFI, $CHADS_2$, Modified $CHADS_2$, CHA_2DS_2-VASc, ATRIA, and GARFIELD-AF

Modified $CHADS_2$ showed consistent and good predictive discrimination:

Kidney function	C-statistic (95% CI)
Normal eGFR	0.78 (0.77-0.79)
Mild CKD	0.73 (0.71-0.74)
Advanced CKD	0.74 (0.69-0.79)

... and **reasonable calibration**, largely independent of kidney function



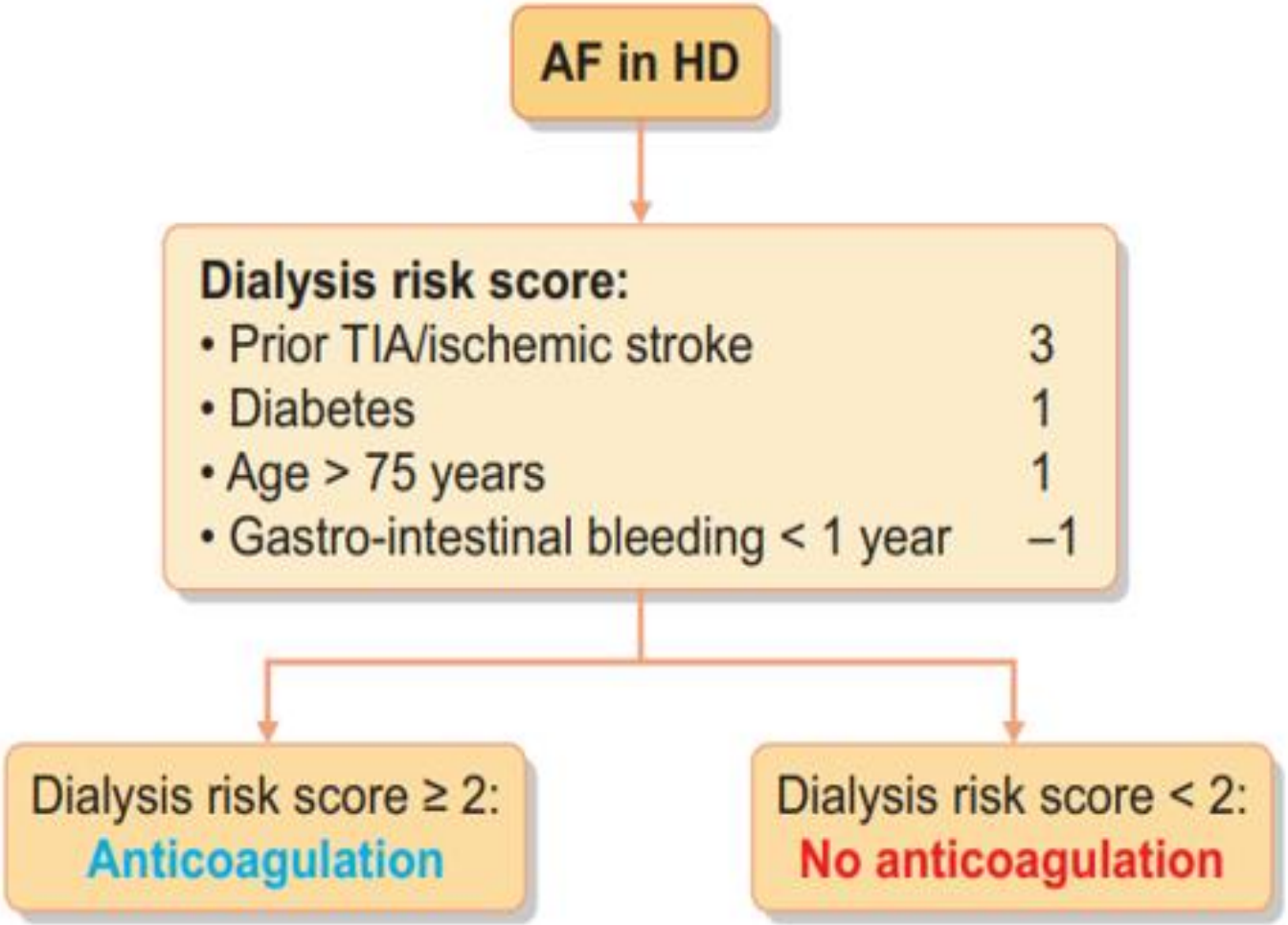
36 004 participants with AF included

European Heart Journal 2021

Προγνωστική απόδοση έξι επικυρωμένων βαθμολογιών κινδύνου

Study	Outcome	Risk score characteristics		Validation								
		Timeframe (validated)	Original c-statistic	Normal eGFR			Mild CKD			Advanced CKD		
				C-statistic	Obs.	Pred.	C-statistic	Obs.	Pred.	C-statistic	Obs.	Pred.
AFI[20]	IS, TIA, SE	NS (2.3 y)	—	0.68 (0.67–0.69)	0.076	0.114	0.58 (0.57–0.59)	0.130	0.147	0.55 (0.51–0.59)	0.127	0.150
$CHADS_2$[21]	IS, TIA	NS (1.0 y)	0.82	0.78 (0.77–0.80)	0.047	0.039	0.70 (0.68–0.72)	0.084	0.055	0.71 (0.66–0.76)	0.086	0.063
Modified-$CHADS_2$[22]	IS, HS	5 y (5 y)	0.72	0.78 (0.77–0.79)	0.124	0.150	0.73 (0.71–0.74)	0.204	0.231	0.74 (0.69–0.79)	0.225	0.238
CHA_2DS_2-VASc[23]	IS, TIA, SE	1 y (1 y)	0.61	0.70 (0.69–0.71)	0.043	0.022	0.60 (0.58–0.62)	0.074	0.027	0.58 (0.52–0.64)	0.065	0.028
ATRIA[24]	IS, SE	NS (2.4 y)	0.73	0.78 (0.76–0.79)	0.078	0.055	0.68 (0.66–0.70)	0.133	0.097	0.66 (0.60–0.72)	0.130	0.120
GARFIELD-AF[25]	IS, TIA, SE	1 y (1 y)	0.69	0.76 (0.75–0.77)	0.047	0.029	0.67 (0.65–0.69)	0.084	0.104	0.70 (0.64–0.76)	0.086	0.108

Ανάγκη για νέα αξιόπιστα εργαλεία εκτίμησης του κινδύνου ΑΕΕ

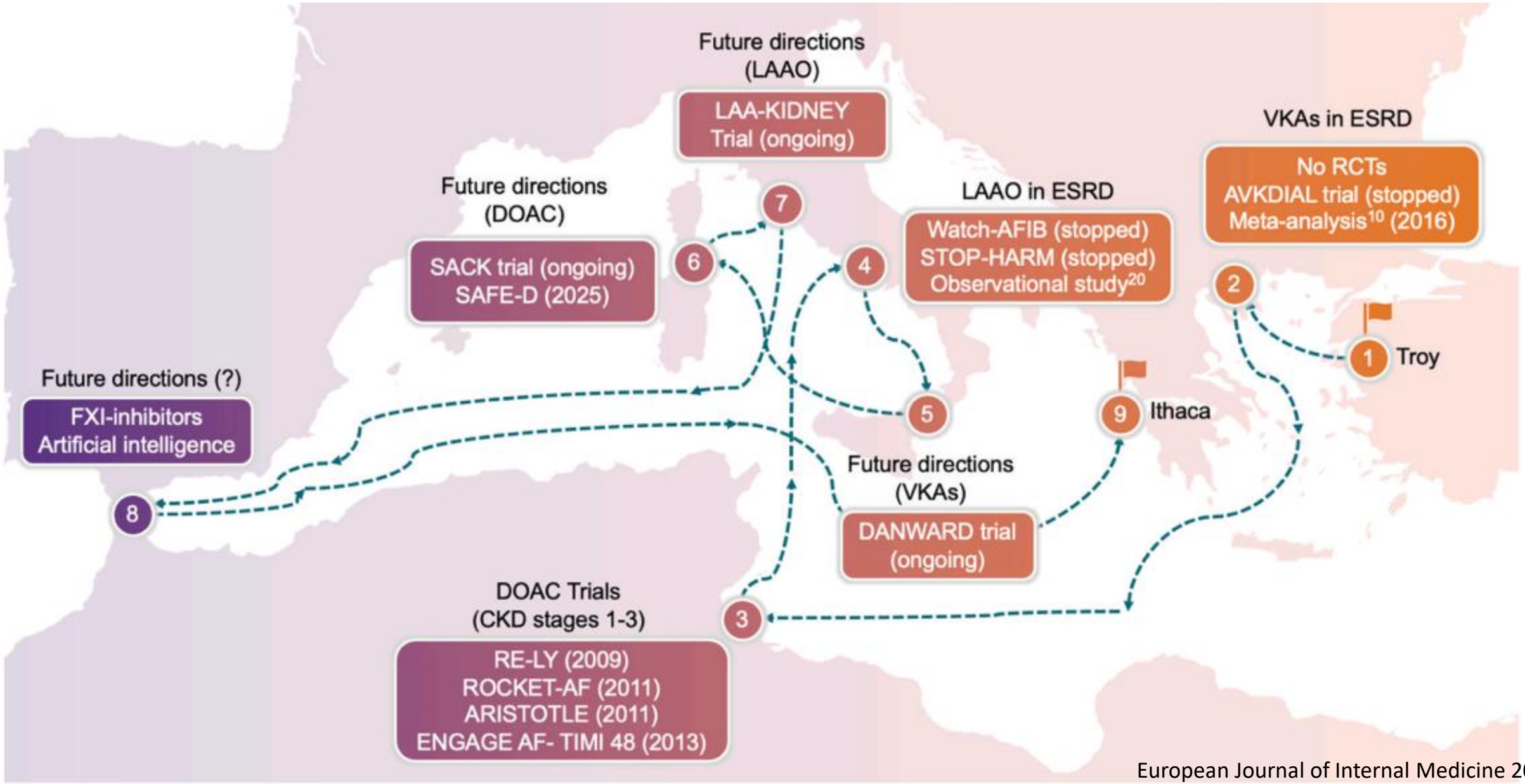


Nephrol Dial Transplant 2022

Υπάρχουν ασθενείς υπό ΑΚ με ΚΜ που θα ωφεληθούν από τα νεότερα αντιπηκτικά

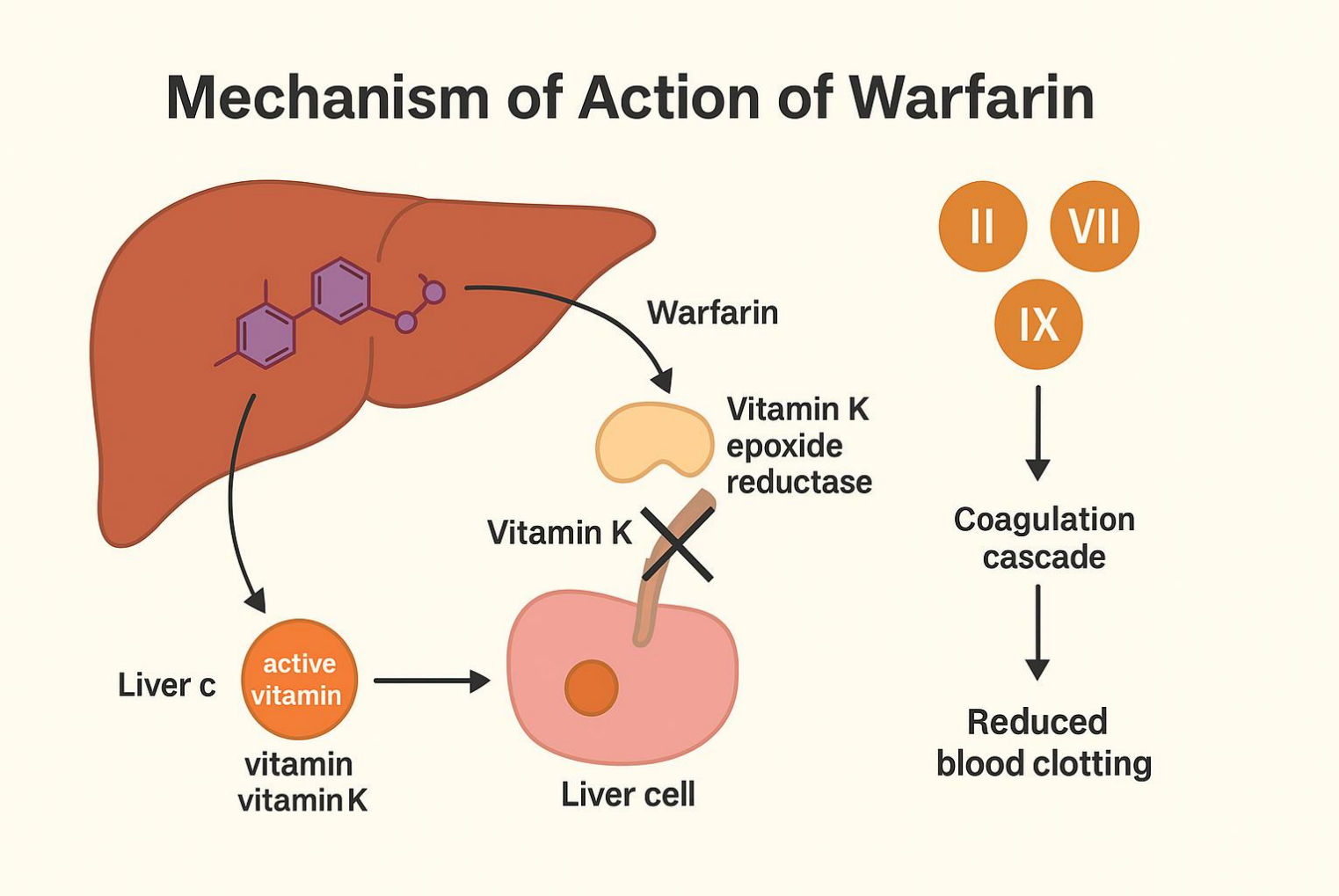
Clinical Kidney Journal, 2024

Stroke prevention in atrial fibrillation patients with end-stage renal disease: **how far from Ithaca after a long Odyssey?**

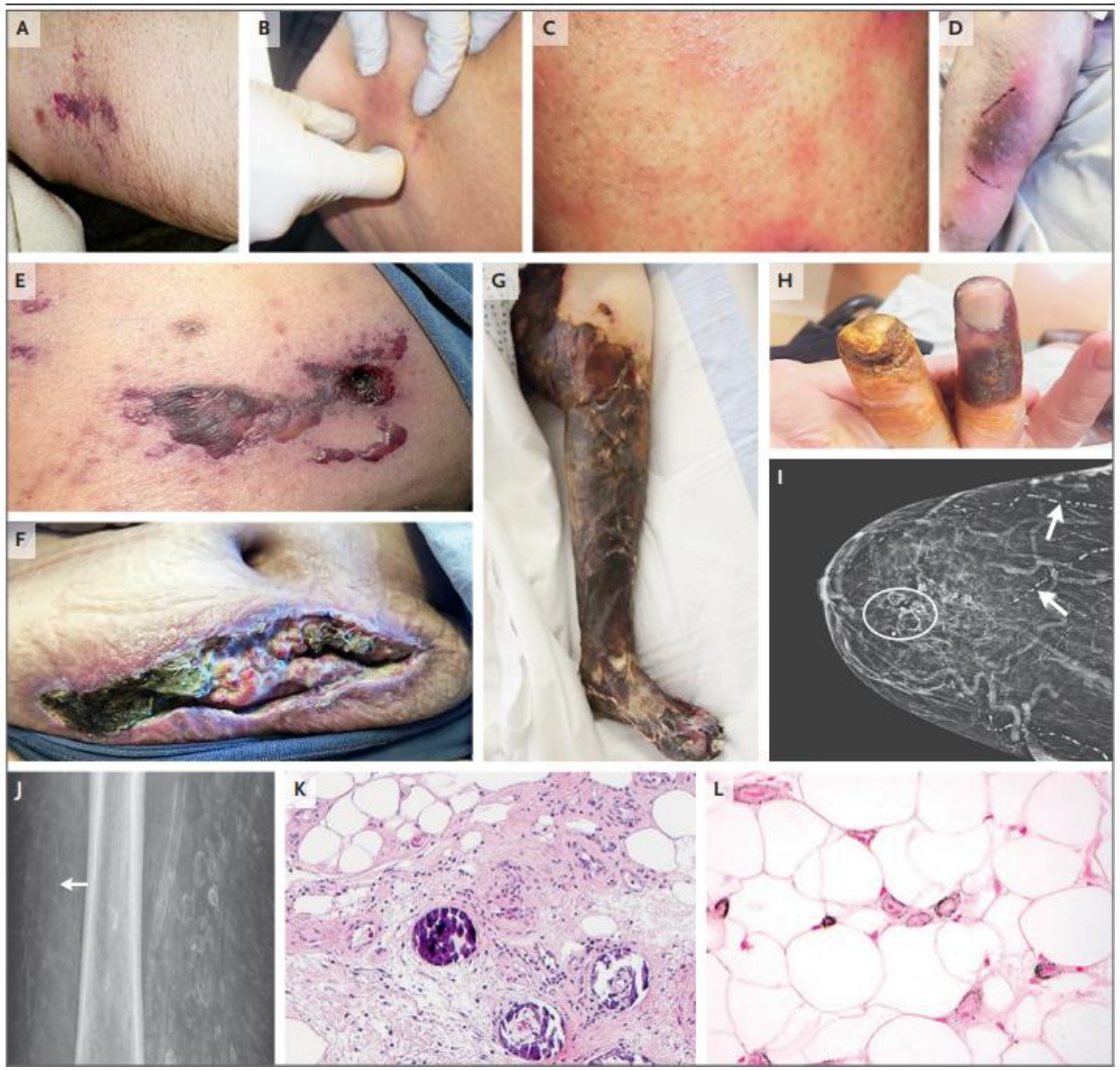


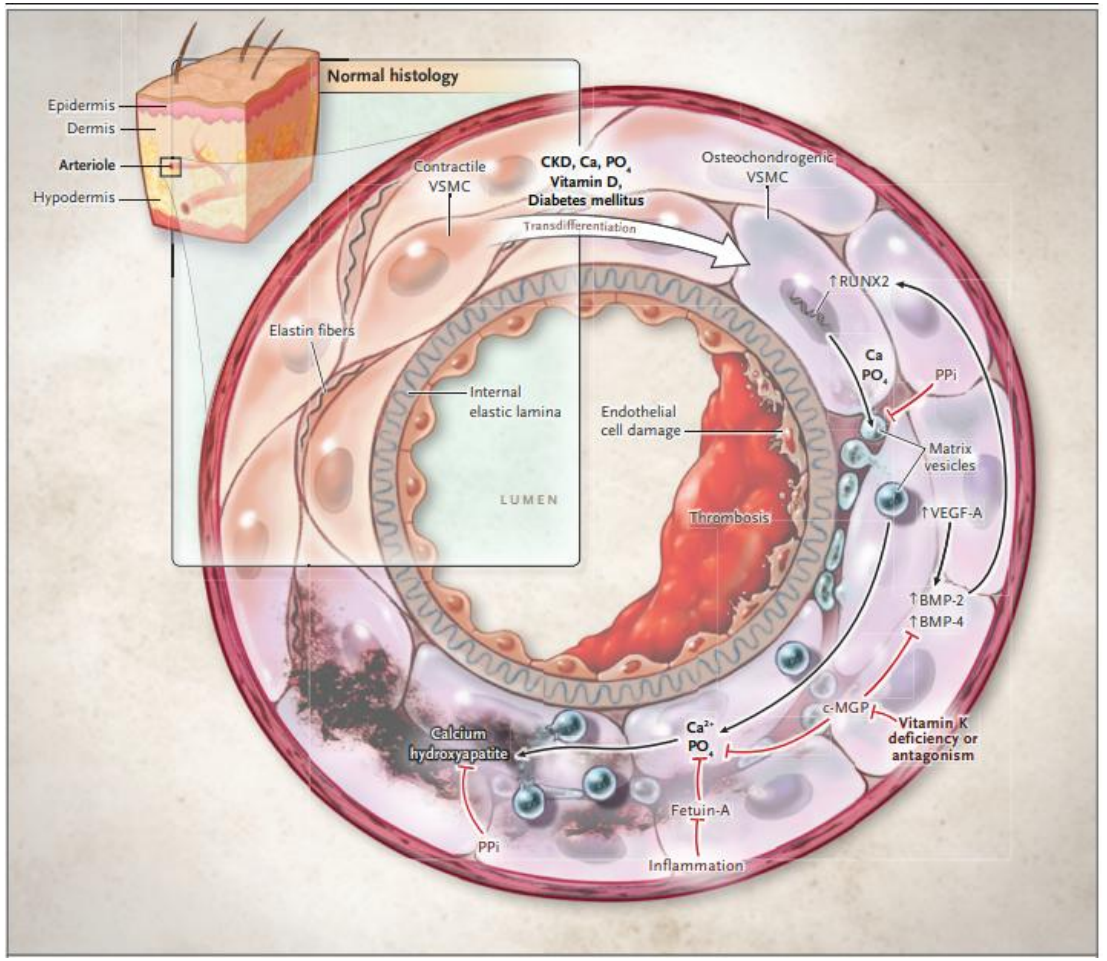
European Journal of Internal Medicine 2025

VKAs για την ΚΜ σε ασθενείς υπό ΑΚ?



Καλσιφύλαξη: σπάνιο, απειλητικό για τη ζωή σύνδρομο

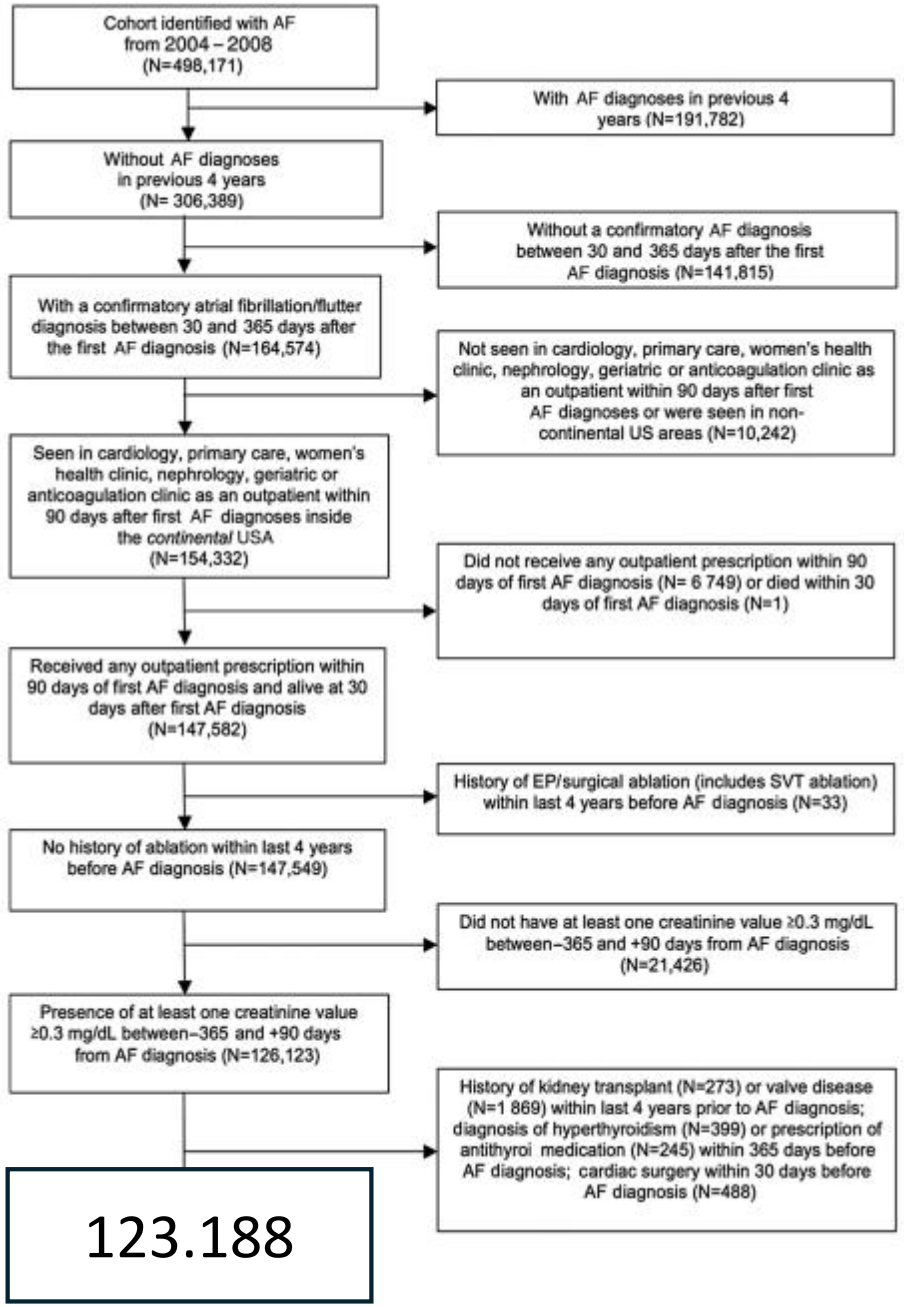


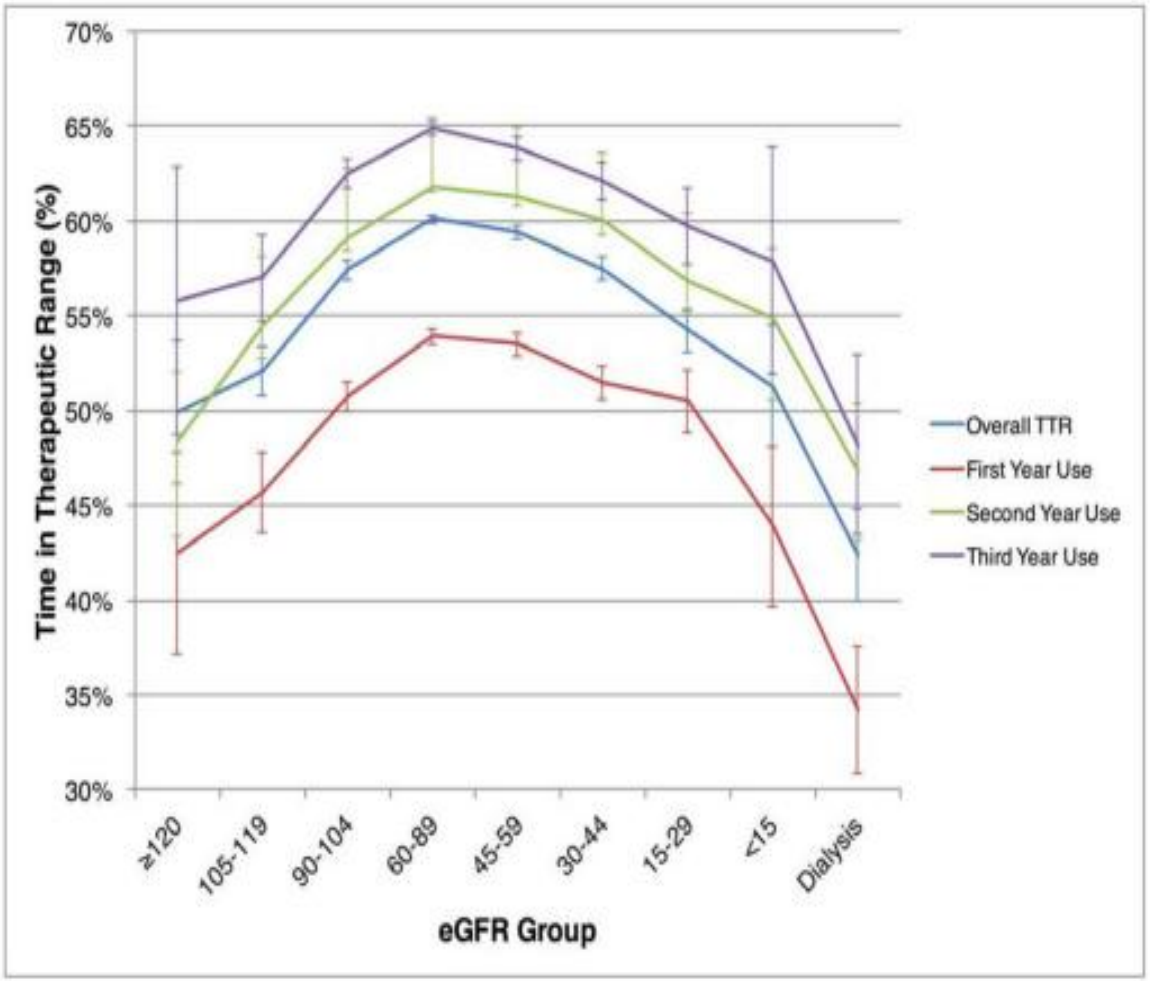


N Engl J Med 2018

ORIGINAL ARTICLE

Warfarin utilisation and anticoagulation control in patients with atrial fibrillation and chronic kidney disease



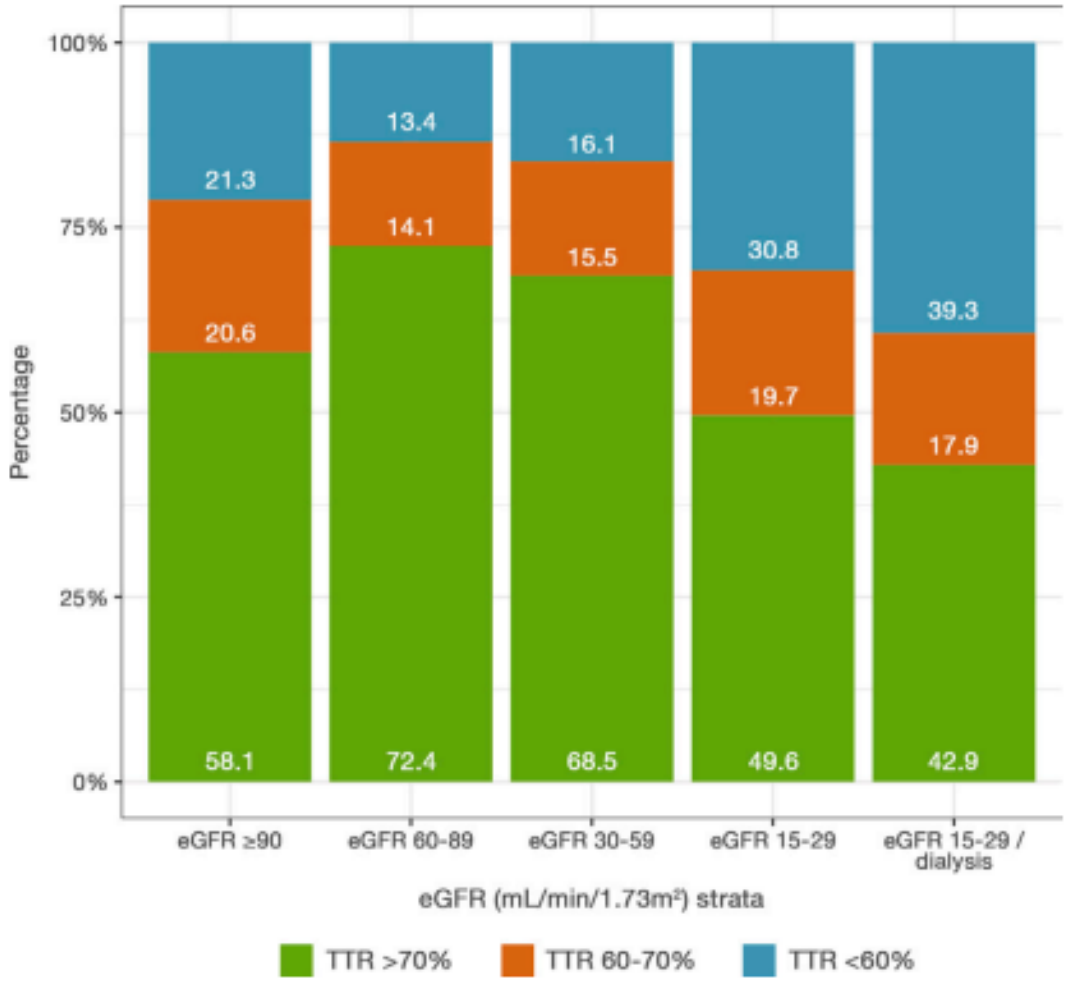


Heart 2018

Oral anticoagulants, time in therapeutic range and renal function over time in real-life patients with atrial fibrillation and chronic kidney disease

Table 2 Predictors of poor TTR

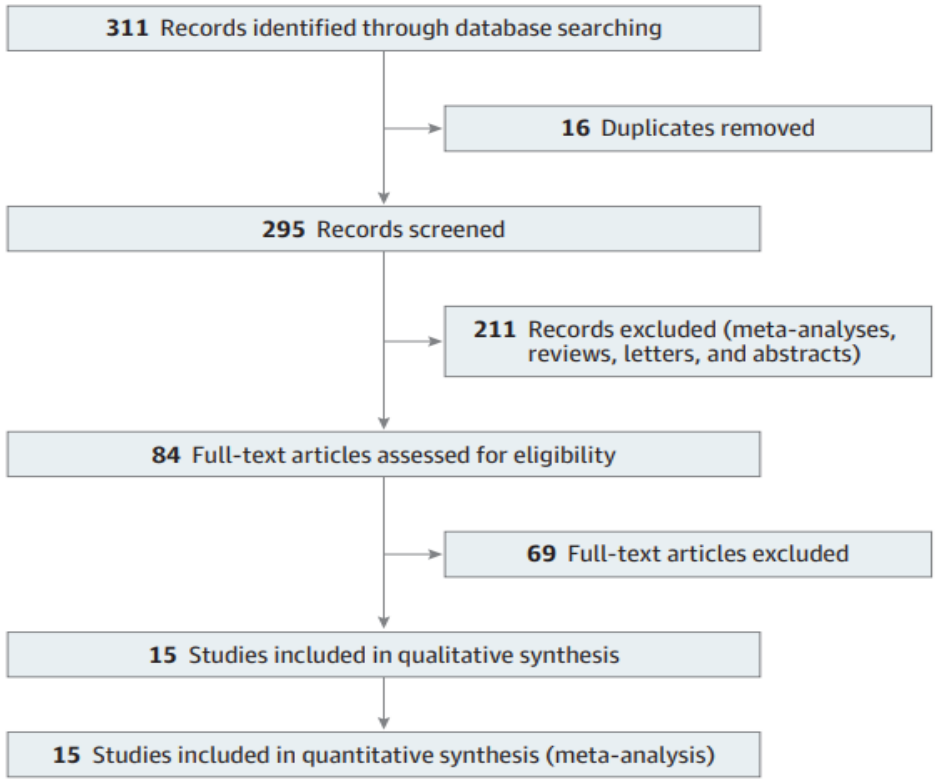
Characteristics	Coefficient (95% CI)	P value
CKD stages		
eGFR ≥90	Reference	
eGFR 60–89	3.9 (2.2 to 5.6)	<0.001
eGFR 30–59	3.0 (1.1 to 5.0)	0.002
eGFR 15–29	−0.9 (−4.0 to 2.2)	0.58
eGFR <15/dialysis	−5.5 (−11.0 to 0.1)	0.05
Age (/10 years)	0.4 (−0.1 to 1.0)	0.12
Sex, female	−0.7 (−1.6 to 0.2)	0.14
Hypertension	0.2 (−0.8 to 1.1)	0.70
Diabetes mellitus	−2.1 (−3.4 to −0.9)	<0.001
Prior stroke/TIA/systemic embolism	0.6 (−0.7 to 1.9)	0.34
Prior MI	0.7 (−1.3 to 2.6)	0.50
Prior PCI or CABG	0.2 (−1.5 to 1.9)	0.82
Heart failure	−3.5 (−4.9 to −2.2)	<0.001
Peripheral vascular disease	−1.8 (−3.9 to 0.3)	0.10
COPD	−6.3 (−8.2 to −4.5)	<0.001
Cancer (within 3 years)	−0.2 (−2.1 to 1.8)	0.86
Prior major bleeding	−1.6 (−3.4 to 0.2)	0.08
Acetylsalicylic acid	−1.5 (−2.6 to −0.4)	0.01
$P2Y_{12}$ inhibitor	0.5 (−2.5 to 3.5)	0.74



Open Heart 2022

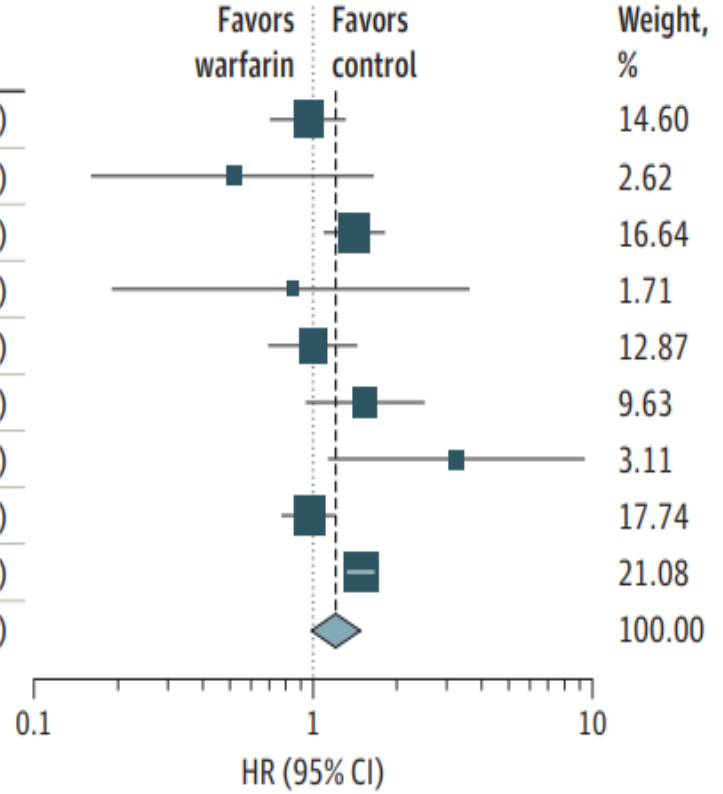
Association Between Use of Warfarin for Atrial Fibrillation and Outcomes Among Patients With End-Stage Renal Disease

A Systematic Review and Meta-analysis



A Major bleeding

Source	HR (95% CI)	Weight, %
Winkelmayer et al,[9] 2011	0.96 (0.70-1.31)	14.60
Carrero et al,[10] 2014	0.52 (0.16-1.65)	2.62
Shah et al,[12] 2014	1.41 (1.09-1.81)	16.64
Wakasugi et al,[13] 2014	0.85 (0.19-3.64)	1.71
Shen et al,[15] 2015	1.00 (0.69-1.44)	12.87
Garg et al,[16] 2016	1.53 (0.94-2.51)	9.63
Wang et al,[17] 2016	3.26 (1.13-9.40)	3.11
Kai et al,[20] 2017	0.97 (0.77-1.20)	17.74
Tan et al,[19] 2019	1.48 (1.32-1.66)	21.08
Overall: I^2 = 66.0%	1.20 (0.99-1.47)	100.00



47.480 ασθενείς με ΚΜ και ΧΝΑΤΣ και ΑΚ
10.445 (22,0%) VKAs
Μέση περίοδος παρακολούθησης 2,6 (1,4) έτη

JAMA Network Open. 2020

DOACs για την ΚΜ σε ασθενείς υπό ΑΚ?

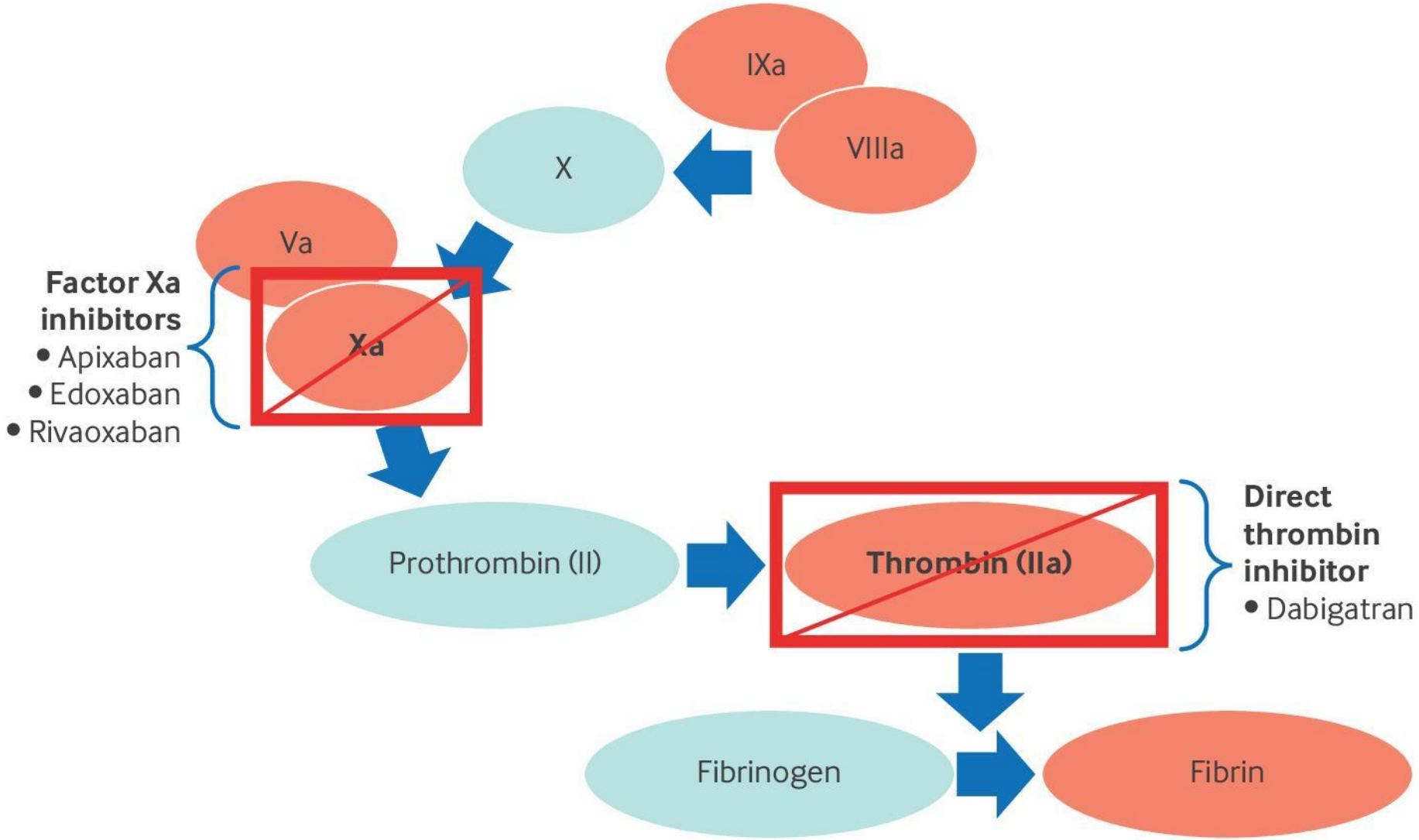
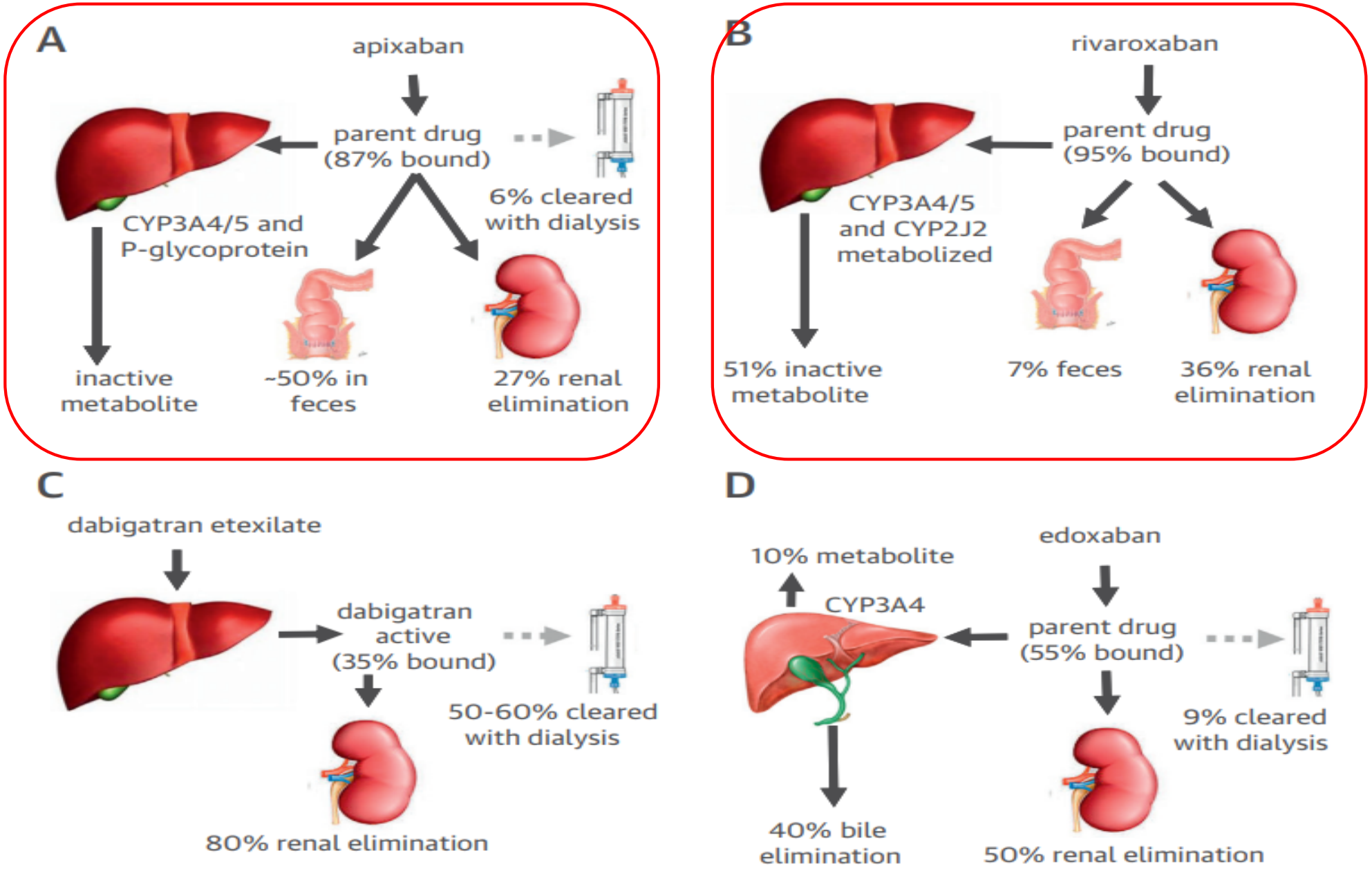


FIGURE 4 **Pharmacokinetics of Nonvitamin K-Dependent Oral Anticoagulant Agents**



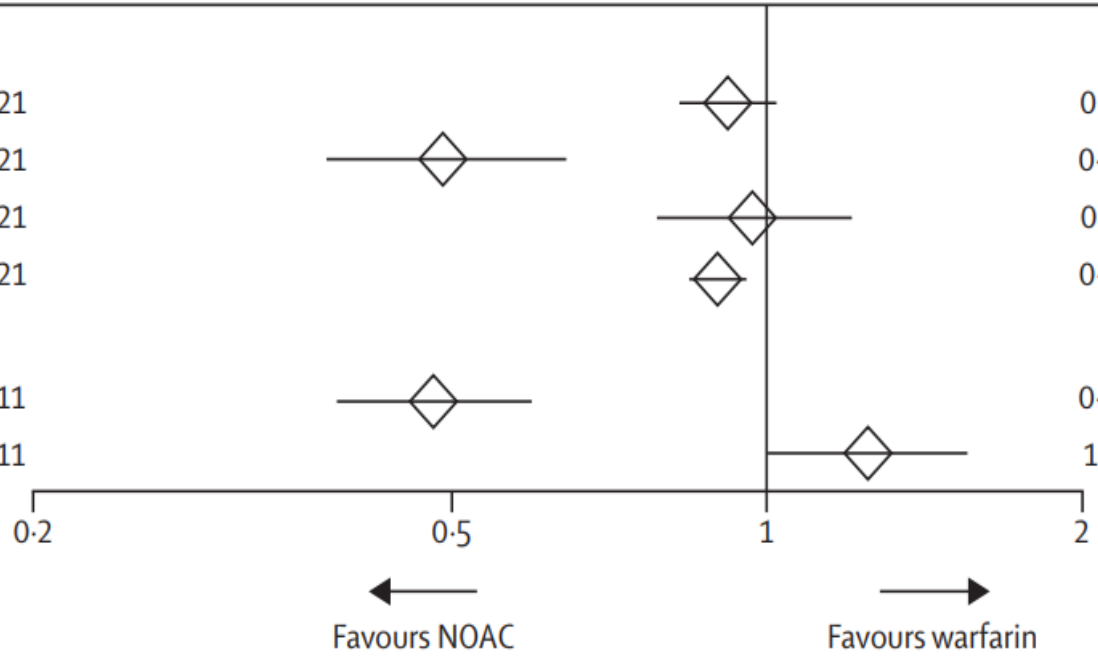
Μελέτες φάσης 3: DOACs vs VKAs

	RELY	ROCKET	ARISTOTLE	ENGAGE-AF
Sample size	18.113	14.266	18.201	21.500
New treatment	Dabigatran 110mg BID Dabigatran 150mgBID	Rivaroxaban 20mg QD	Apixaban 5mg bid	Edoxaban 30mgQD Edoxaban 60mg QD
design	Non inferiority PROBE	Non inferiority Double blind	Non inferiority Double blind	Non inferiority Double blind
Patients	AF + CHADS2>1	AF + CHADS2>2	AF + CHADS2>1	AF + CHADS2>2
Renal Exclusion	CrCl < 30 ml/min	CrCl < 30 ml/min	CrCl < 25 ml/min	CrCl < 30 ml/min
Primary outcome	Stroke (ischemic or hemorragic) or systemic embolism	Stroke (ischemic or hemorragic) or systemic embolism	Stroke (ischemic or hemorragic) or systemic embolism	Stroke (ischemic or hemorragic) or systemic embolism
Safety outcome	Primary: Major bleeding Seconary: major bleeding + CRNM	Primary: Major bleeding Seconary: major bleeding + CRNM	Primary: Major bleeding Seconary: major bleeding + CRNM	Primary: Major bleeding Seconary: major bleeding + CRNM

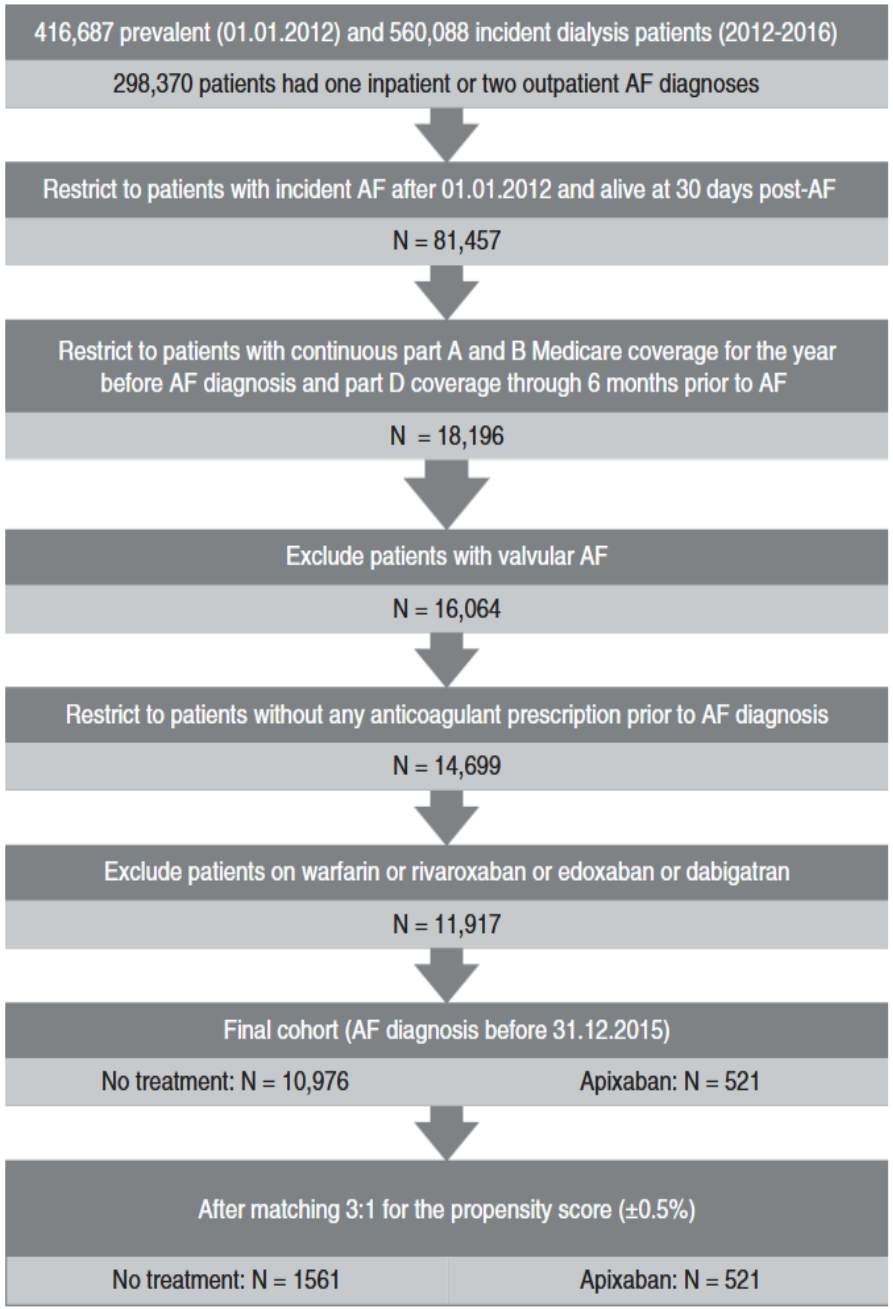
Comparison of the efficacy and safety of new oral anticoagulants with warfarin in patients with atrial fibrillation: a meta-analysis of randomised trials

71.683 pts
NOACs: 42 411 pts
VKAs: 29 272 pts

	Pooled NOAC (events)	Pooled warfarin (events)	RR (95% CI)	p
Efficacy				
Ischaemic stroke	665/29 292	724/29 221	0·92 (0·83–1·02)	0·10
Haemorrhagic stroke	130/29 292	263/29 221	0·49 (0·38–0·64)	<0·0001
Myocardial infarction	413/29 292	432/29 221	0·97 (0·78–1·20)	0·77
All-cause mortality	2022/29 292	2245/29 221	0·90 (0·85–0·95)	0·0003
Safety				
Intracranial haemorrhage	204/29 287	425/29 211	0·48 (0·39–0·59)	<0·0001
Gastrointestinal bleeding	751/29 287	591/29 211	1·25 (1·01–1·55)	0·043



Lancet 2014



Apixaban versus No Anticoagulation in Patients Undergoing Long-Term Dialysis with Incident Atrial Fibrillation

Table 2. Clinical outcomes in the "as-treated" population (main analysis)

Outcome	Incidence in Apixaban Users	Incidence in Nonusers	Crude Hazard Ratio (95% Confidence Interval)	*P* Value	Adjusted[a] Hazard Ratio (95% Confidence Interval)	*P* Value
Any stroke, TIA, or embolism	7.5 (13)	7.0 (114)	1.24 (0.69 to 2.23)	0.47	1.29 (0.72 to 2.33)	0.39
Any stroke	5.8 (<11)	5.8 (96)	1.13 (0.58 to 2.19)	0.72	1.17 (0.60 to 2.28)	0.64
Major bleeding	4.9 (<11)	1.6 (45)	**2.74 (1.37 to 5.47)**	**0.004**	**2.76 (1.38 to 5.52)**	**0.004**
Clinically important bleeding	59.2 (77)	56.9 (695)	1.15 (0.90 to 1.47)	0.26	1.15 (0.90 to 1.46)	0.26
Ischemic stroke or MI	27.6 (43)	25.1 (373)	1.24 (0.90 to 1.71)	0.18	1.25 (0.91 to 1.72)	0.17
Ischemic stroke	3.5 (<11)	5.0 (81)	0.81 (0.35 to 1.89)	0.63	0.85 (0.36 to 1.98)	0.71
Hemorrhagic stroke	2.3 (<11)	1.3 (22)	1.89 (0.65 to 5.47)	0.24	1.89 (0.65 to 5.49)	0.24

Αναδρομική μελέτη παρατήρησης
Apixaban έναντι εικονικού φαρμάκου
Propensity score δεν κατέγραψε άλλες παραμέτρους πχ. BMI,ασπιρίνη, δόση, άλλα αντιπηκτικά ……

Apixaban Dosing Patterns Versus Warfarin in Patients With Nonvalvular Atrial Fibrillation Receiving Dialysis

Study Methods

USRDS Data

- Adult Medicare beneficiaries receiving dialysis, 2013-2018
- Nonvalvular atrial fibrillation and a new prescription for apixaban or warfarin

N = 17,156

Treatments Compared

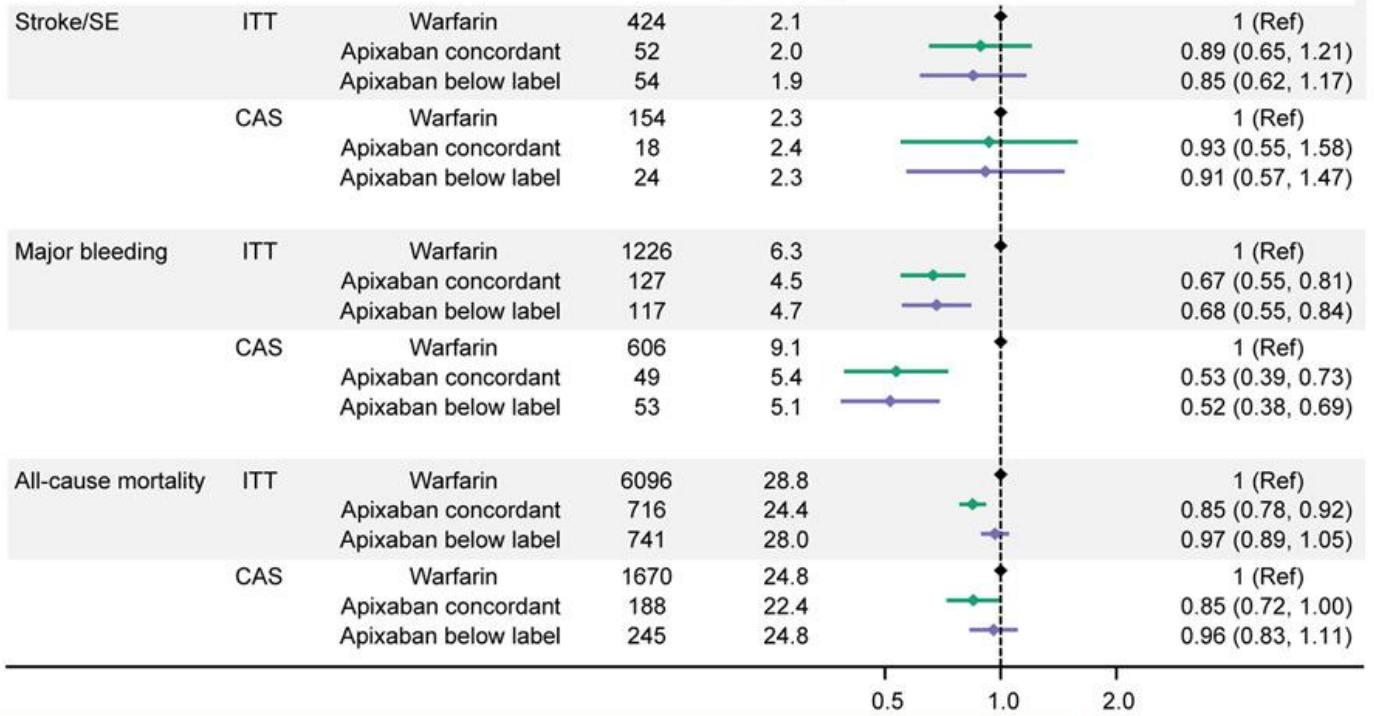
- Warfarin
- Label-concordant apixaban (5 mg, twice a day)
- Below-label apixaban (2.5 mg, when 5 mg is indicated [twice a day for both])

Clinical Outcomes

- Stroke/systemic embolism
- Major bleeding
- All-cause mortality

Results

Outcomes	Analysis	Treatment	Crude N events	Event Rate per 100 py	HR (95% CI)
Stroke/SE	ITT	Warfarin	424	2.1	1 (Ref)
		Apixaban concordant	52	2.0	0.89 (0.65, 1.21)
		Apixaban below label	54	1.9	0.85 (0.62, 1.17)
	CAS	Warfarin	154	2.3	1 (Ref)
		Apixaban concordant	18	2.4	0.93 (0.55, 1.58)
		Apixaban below label	24	2.3	0.91 (0.57, 1.47)
Major bleeding	ITT	Warfarin	1226	6.3	1 (Ref)
		Apixaban concordant	127	4.5	0.67 (0.55, 0.81)
		Apixaban below label	117	4.7	0.68 (0.55, 0.84)
	CAS	Warfarin	606	9.1	1 (Ref)
		Apixaban concordant	49	5.4	0.53 (0.39, 0.73)
		Apixaban below label	53	5.1	0.52 (0.38, 0.69)
All-cause mortality	ITT	Warfarin	6096	28.8	1 (Ref)
		Apixaban concordant	716	24.4	0.85 (0.78, 0.92)
		Apixaban below label	741	28.0	0.97 (0.89, 1.05)
	CAS	Warfarin	1670	24.8	1 (Ref)
		Apixaban concordant	188	22.4	0.85 (0.72, 1.00)
		Apixaban below label	245	24.8	0.96 (0.83, 1.11)



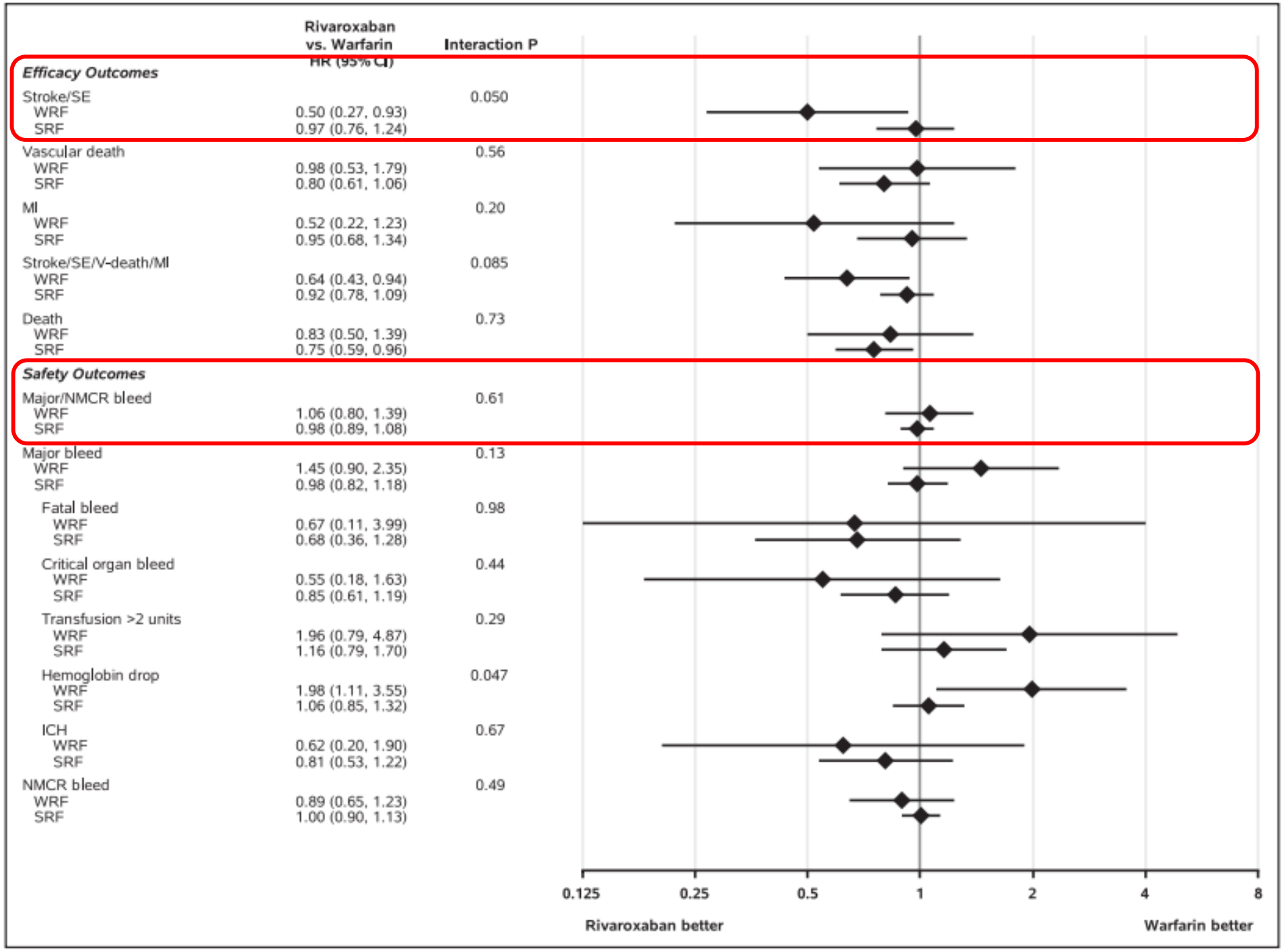
ITT: *intention-to-treat*
CAS: *censored-at-drug-switch*

CONCLUSION: Apixaban was associated with lower risk of major bleeding than warfarin, but apixaban dose was not associated with bleeding risk. Dosed according to the label, apixaban may be associated with lower mortality.

James B. Wetmore, Eric D. Weinhandl, Heng Yan, et al

@AJKDonline | DOI: 10.1053/j.ajkd.2022.03.007

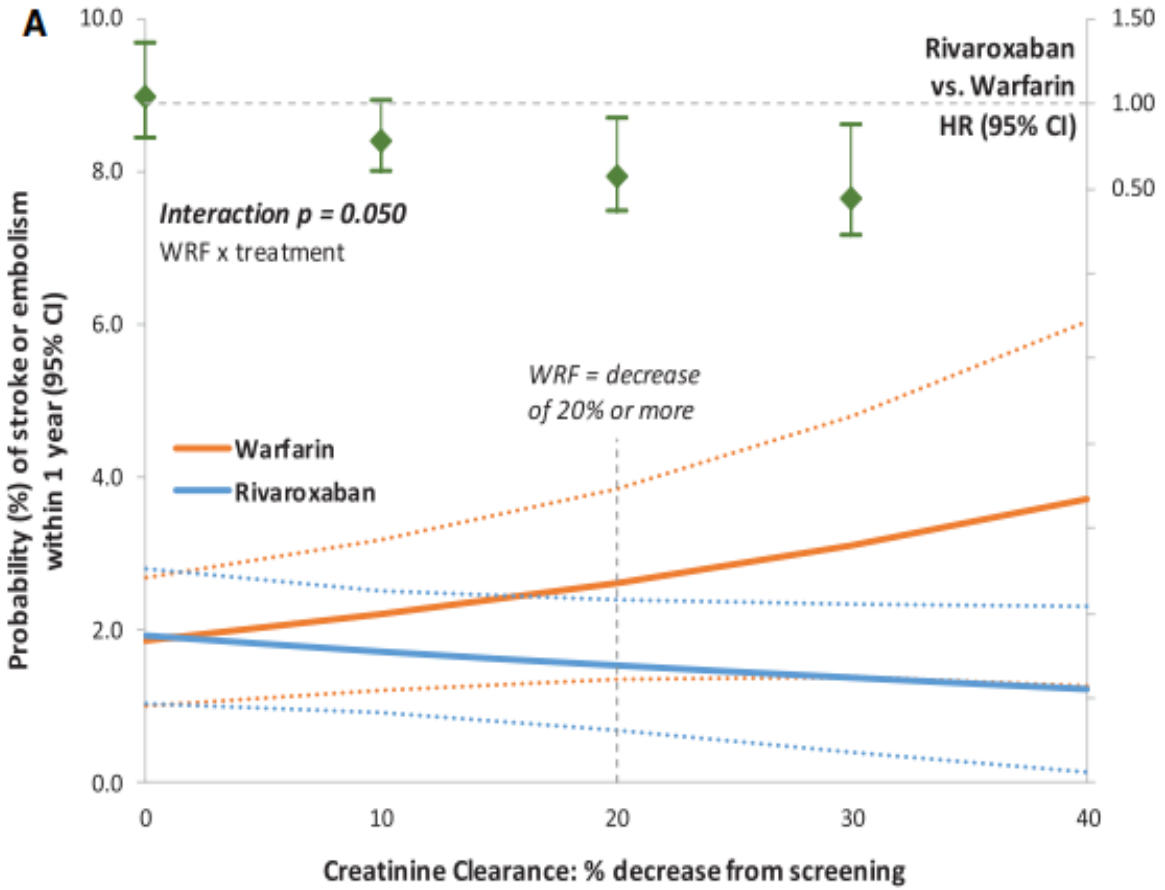
AJKD
AMERICAN JOURNAL OF KIDNEY DISEASES



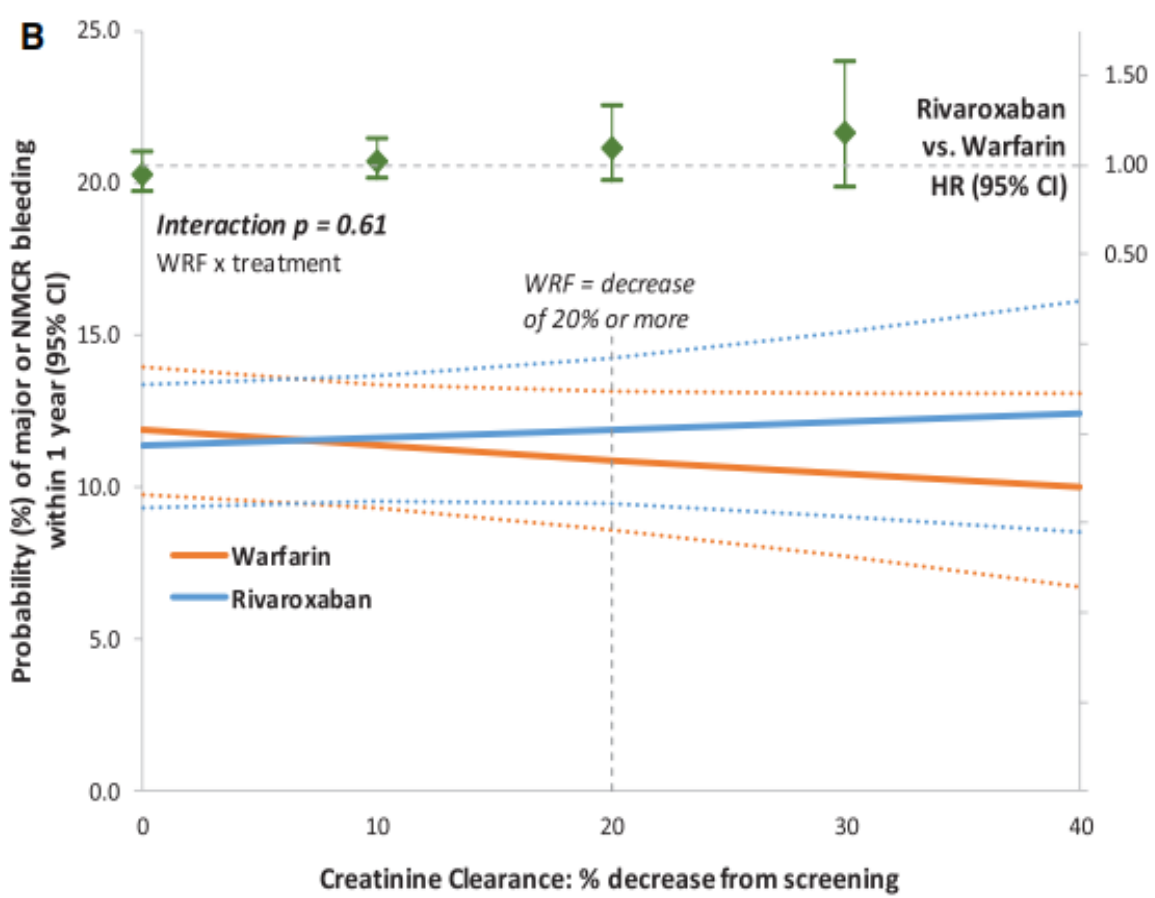
On-Treatment Outcomes in Patients With Worsening Renal Function With **Rivaroxaban** Compared With **Warfarin** Insights From ROCKET AF

Circulation 2016

Stroke/embolism less with RV vs WRF
especially in WRF (1.54 vs 3.25 events in 100 pt-years



No difference in major/non-major clinically relevant bleeding



Circulation 2016

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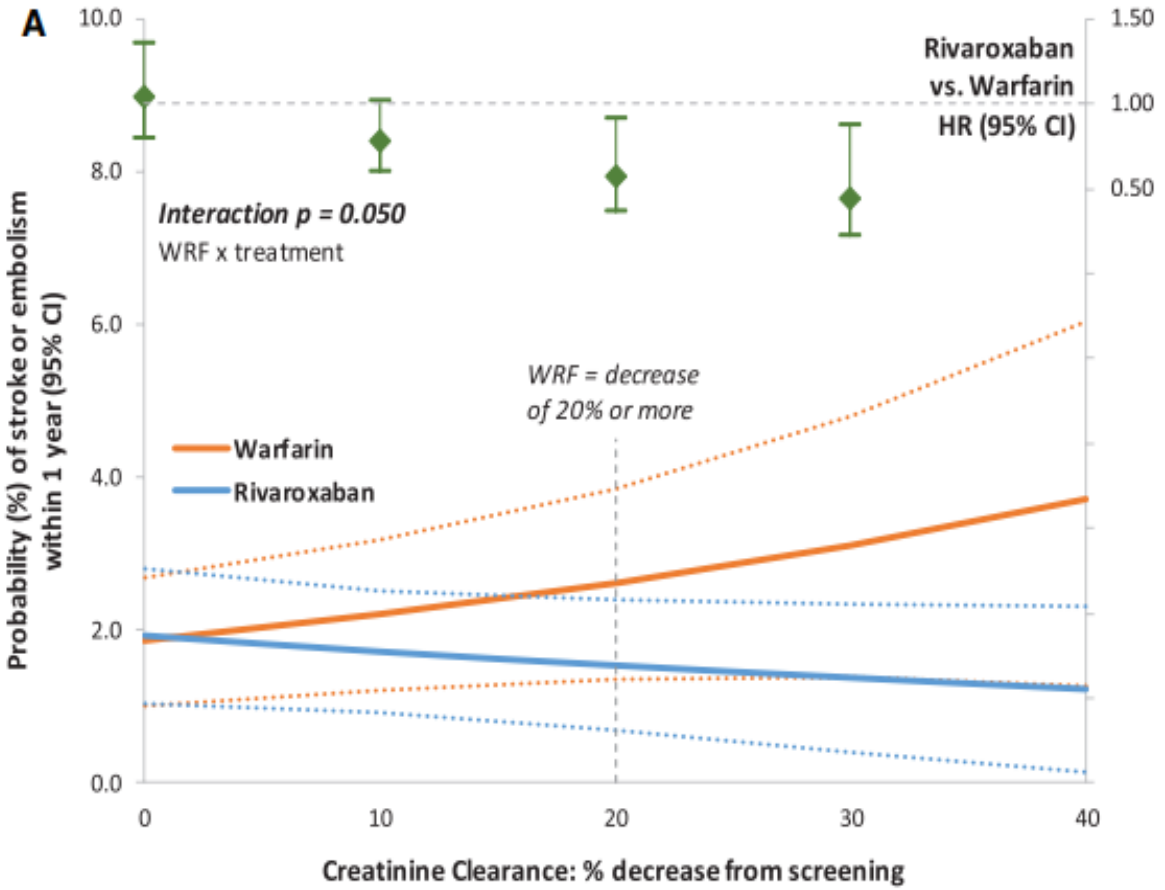
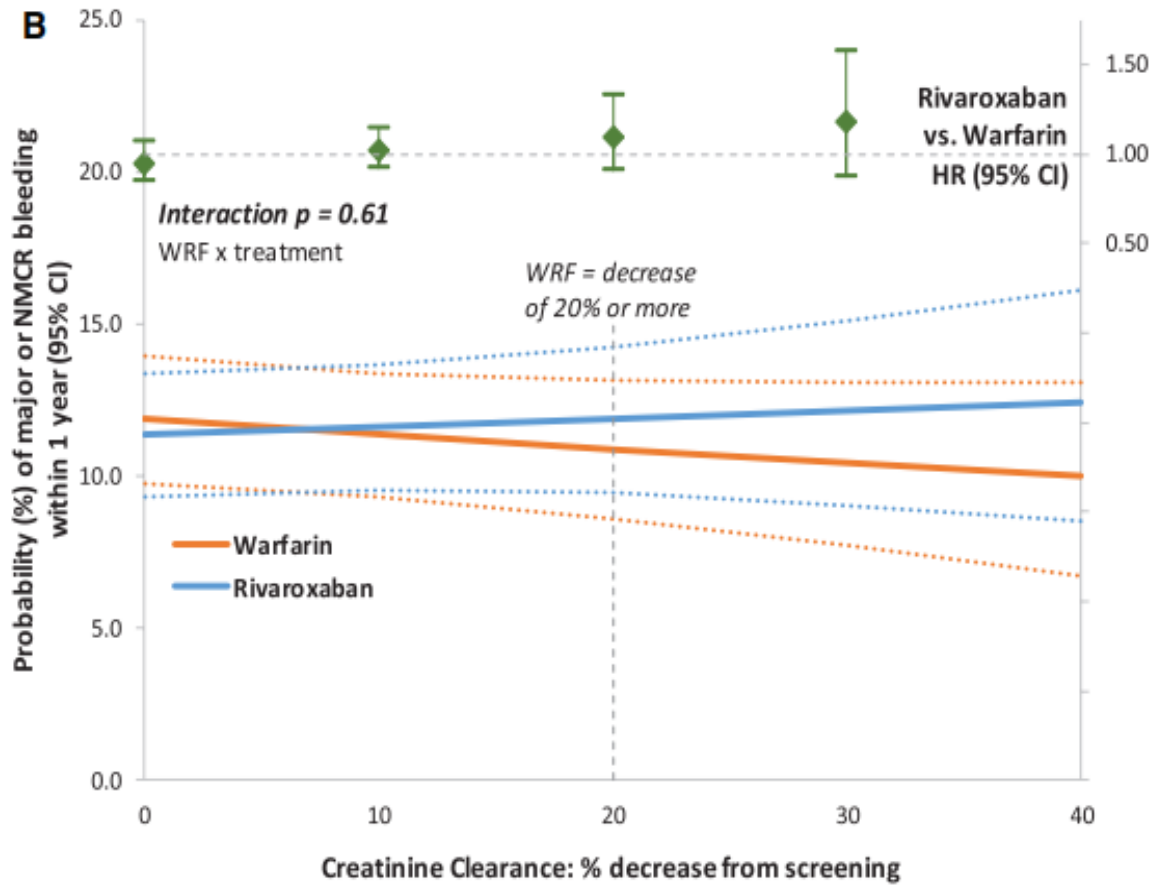


No difference in major/non-major clinically relevant bleeding



Circulation 2016

Multicenter RCT of vitamin K antagonist replacement by rivaroxaban with or without vitamin K2 in hemodialysis patients with atrial fibrillation: the Valkyrie study

METHODS

N=132

VKA INR 2-3

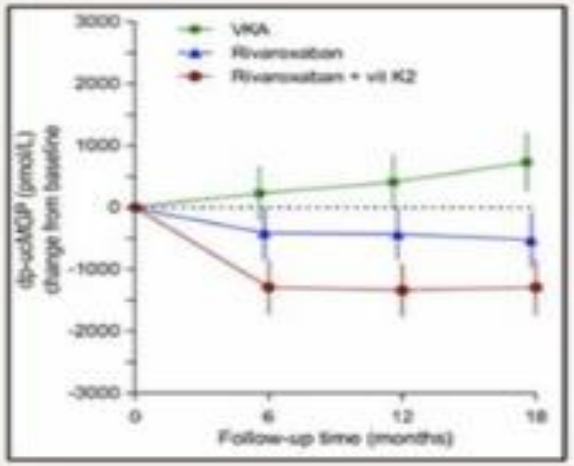
Rivaroxaban 10 mg od

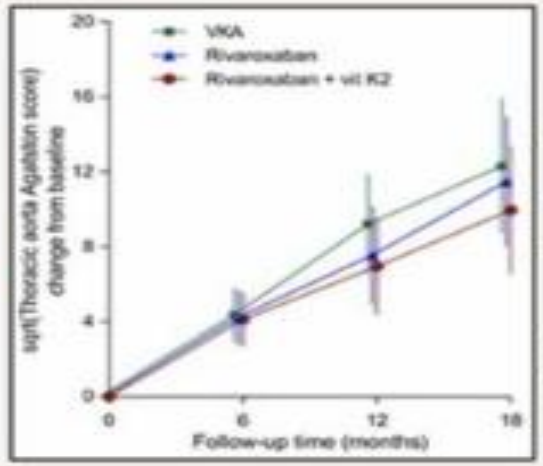
Rivaroxaban + Vit K2

0m* 6m* 12m* 18m*

*VitK status, PWV and CAC score

OUTCOME





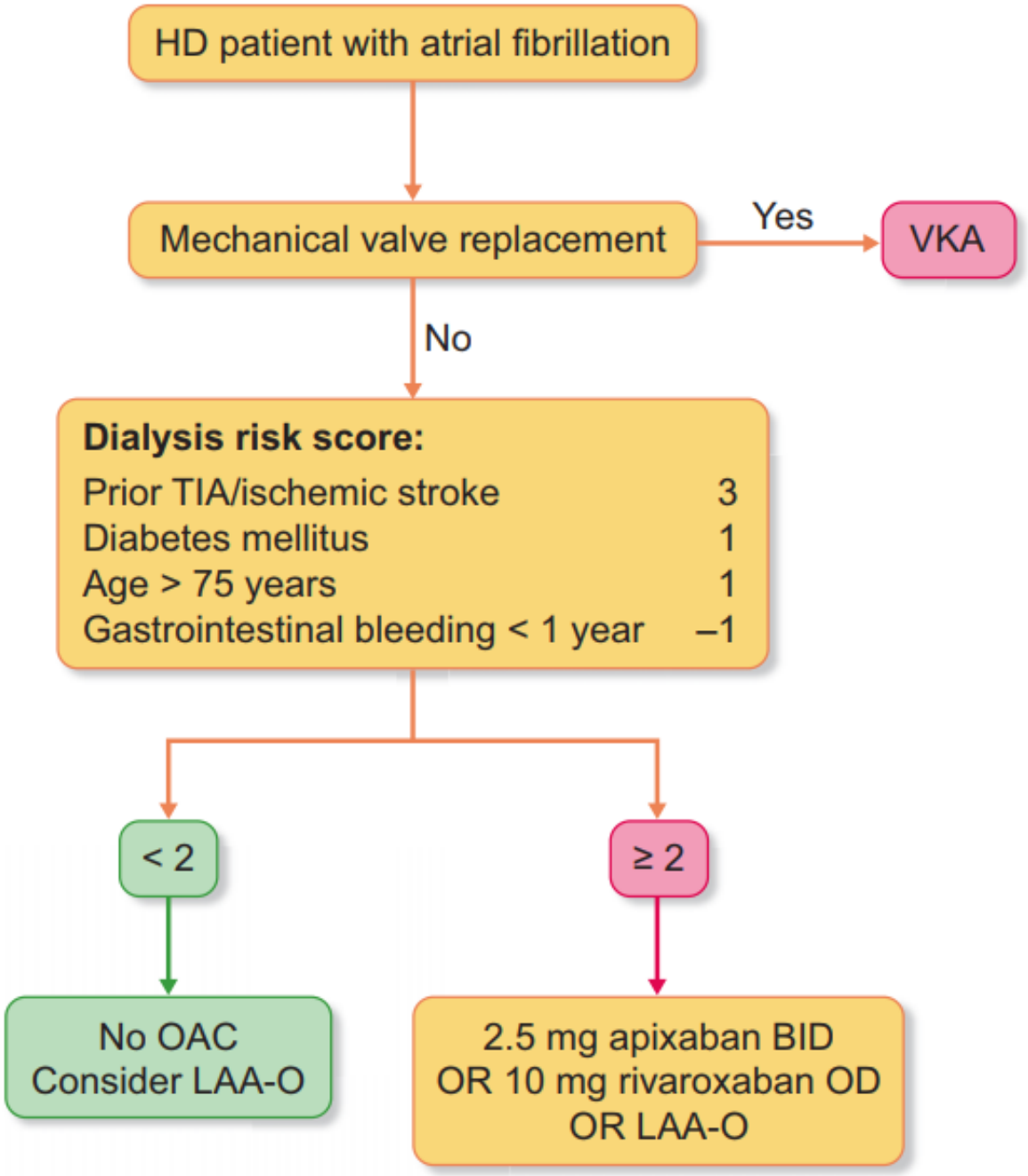
Bleeding type	Rate per 100 person-years (number)		
	VKA (n=44)	Rivaroxaban (n=46)	Rivaroxaban + VitK2 (n=42)
Life-threatening	13.3 (7)	3.5 (2)	9.5 (5)
Major	22.7 (12)	13.8 (8)	3.8 (2)
Life-threatening + major	36.0 (19)	17.3 (10)	13.2 (7)
Minor	26.5 (14)	31.1 (18)	30.3 (16)
Gastro-intestinal	22.7 (12)	17.3 (10)	24.6 (13)

CONCLUSION

Withdrawal of VKA and high-dose Vitamin K2 improve Vitamin K status in hemodialysis patients, but have no significant favorable effect on VC progression. Severe bleeding complications may be lower with rivaroxaban than with VKA.

JASN

Ανάγκη για νέα αξιόπιστα εργαλεία εκτίμησης του κινδύνου ΑΕΕ



Recommendations	Class[a]	Level[b]
Oral anticoagulation is recommended in patients with clinical AF at elevated thromboembolic risk to prevent ischaemic stroke and thromboembolism.[239,240]	I	A
A CHA_2DS_2-VA score of 2 or more is recommended as an indicator of elevated thromboembolic risk for decisions on initiating oral anticoagulation.	I	C
Oral anticoagulation is recommended in all patients with AF and hypertrophic cardiomyopathy or cardiac amyloidosis, regardless of CHA_2DS_2-VA score, to prevent ischaemic stroke and thromboembolism.[270–276]	I	B

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Nephrol Dial Transplant 2022

Συνιστώμενες δόσεις για NOACs

DOAC	Standard full dose	Criteria for dose reduction	Reduced dose only if criteria met
Apixaban	5 mg twice daily	Two out of three needed for dose reduction: (i) age ≥80 years (ii) body weight ≤60 kg (iii) serum creatinine ≥133 µmol/L.	2.5 mg twice daily
Dabigatran	150 mg twice daily	Dose reduction recommended if any apply: (i) age ≥80 years (ii) receiving concomitant verapamil. Dose reduction considered on an individual basis if any apply: (i) age 75–80 (ii) moderate renal impairment (creatinine clearance 30–50 mL/min) (iii) patients with gastritis, oesophagitis, or gastro-oesophageal reflux (iv) others at increased risk of bleeding.	110 mg twice daily
Edoxaban	60 mg once daily	Dose reduction if any apply: (i) moderate or severe renal impairment (creatinine clearance 15–50 mL/min) (ii) body weight ≤60 kg (iii) concomitant use of ciclosporin, dronedarone, erythromycin, or ketoconazole.	30 mg once daily
Rivaroxaban	20 mg once daily	Creatinine clearance 15–49 mL/min.	15 mg once daily

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European Heart Journal 2024

Recommendation 3.16.1: We recommend use of non-vitamin K antagonist oral anticoagulants (NOACs) in preference to vitamin K antagonists (e.g., warfarin) for thromboprophylaxis in atrial fibrillation in people with CKD G1–G4 *(1C)*.

Recommendations for CKD/Kidney Failure
Referenced studies that support the recommendations are summarized in the Online Data Supplement.

COR	LOE	Recommendations
1	B-R	1. For patients with AF at elevated risk for stroke and CKD stage 3, treatment with warfarin or, preferably, evidence-based doses of direct thrombin or factor Xa inhibitors (Table 19) is recommended to reduce the risk of stroke.[1–3]
2a	B-NR	2. For patients with AF at elevated risk for stroke and CKD stage 4, treatment with warfarin or labeled doses of DOACs is reasonable to reduce the risk of stroke.[4,5]
2b	B-NR	3. For patients with AF at elevated risk for stroke and who have end-stage CKD (CrCl <15 mL/min) or are on dialysis, it might be reasonable to prescribe warfarin (INR 2.0-3.0) or an evidence-based dose of apixaban for oral anticoagulation to reduce the risk of stroke.[6,7]

	CrCl (mL/min)				
DOAC	>95	51-95	31-50	15-30	<15 or on dialysis
Apixaban	5 or 2.5 mg twice daily*	5 or 2.5 mg twice daily*	5 or 2.5 mg twice daily*	5 or 2.5 mg twice daily*	5 or 2.5 mg twice daily*
Dabigatran	150 mg twice daily	150 mg twice daily	150 mg twice daily	75 mg twice daily	Contraindicated
Edoxaban	Contraindicated	60 mg once daily	30 mg once daily	30 mg once daily	Contraindicated
Rivaroxaban	20 mg once daily	20 mg once daily	15 mg once daily	15 mg once daily	15 mg once daily†

US FDA Approved Dec 2012 – except CrCL < 25
Ammended Jan 2014 to include CrCL < 25 + Dialysis pts

2024

CENTRAL ILLUSTRATION **Proposed Approach to Stroke Thromboprophylaxis in a Patient With Concomitant Chronic Kidney Disease and Atrial Fibrillation**

JAAC 2019

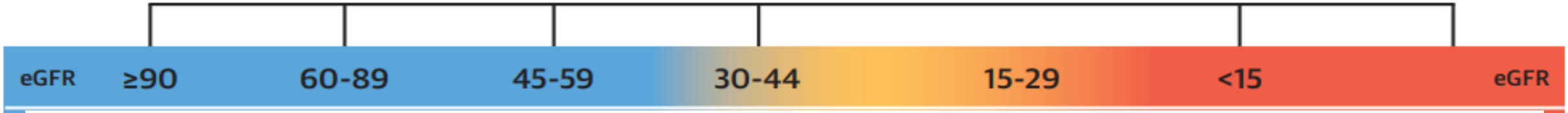
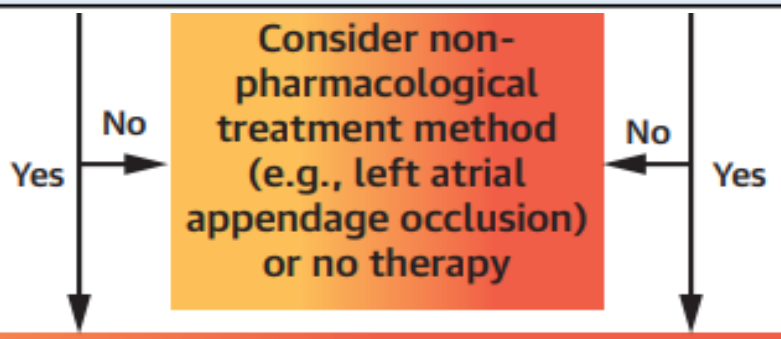


TABLE 5 **EMA/FDA Recommendation for CKD Stages 4 and 5D Patients**

		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



Registry evidence favors DOAC over vitamin K antagonist (VKA) for both efficacy and safety.
If vascular calcification, calciphylaxis or glomerular hemorrhage are a concern, avoid VKAs.
Use appropriate (usually labelled) dose of OAT.‡

CKJ REVIEW

Clinical Kidney Journal, 2024

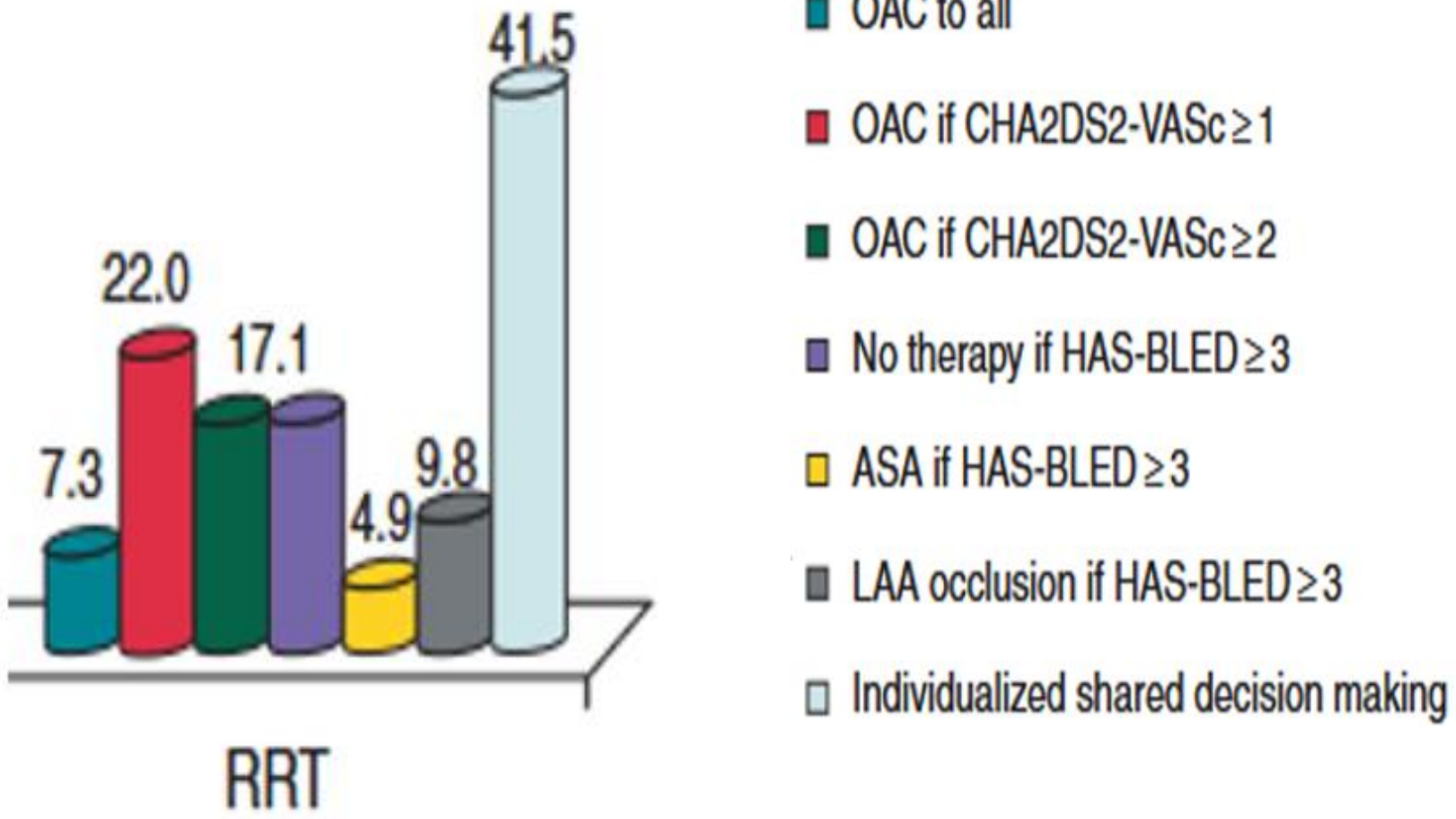
Ten tips to manage oral anticoagulation in hemodialysis patients with atrial fibrillation

Gunnar H. Heine[1,2], Carolin Schneppe[1,2], Rupert Bauersachs[3], Ingo Eitel[4], Brendon L. Neuen[5], Christian T. Ruff[6], Stephan H. Schirmer[7] and An De Vriese[8]

- Μην χρησιμοποιείτε χωρίς σκέψη το CHA2DS2-VASC score, αλλά σκεφτείτε το DIALYSIS RISK SCORE για τη διαστρωμάτωση του κινδύνου σε ασθενείς υπό HD ή τη μη χορήγηση αντιπηκτικής αγωγής
- Συμπεριλάβετε το φορτίο της ΚΜ ως επιπλέον παράγοντα κινδύνου
- Τακτική επανεκτίμηση της αντιπηκτικής αγωγής για τον κίνδυνο αιμορραγίας
- Μην χρησιμοποιείτε ανταγωνιστές της βιταμίνης Κ
- Προτιμάτε προσαρμοσμένη δόση apixaban και rivaroxaban
- Προσαρμόστε τη δόση της ΗΧΜΒ στην αιμοκάθαρση
- Εκτιμήστε τη συνολική καρδιαγγειακή κατάσταση του ασθενή υπό αιμοκάθαρση, σκεφτείτε μμικρή δόση DOAC ως προστασία των αγγείων ακόμα και σε ασθενείς χωρίς ΚΜ
- Σκεφτείτε την συγκλειση του αριστερού ωτίου
- Μην χρησιμοποιείτε ως ρουτίνα συνδυασμό αντιπηκτικών από του στόματος για μεγάλη περίοδο
- Συμπεριλάβετε ασθενείς σε αιμοκάθαρση σε μελέτες

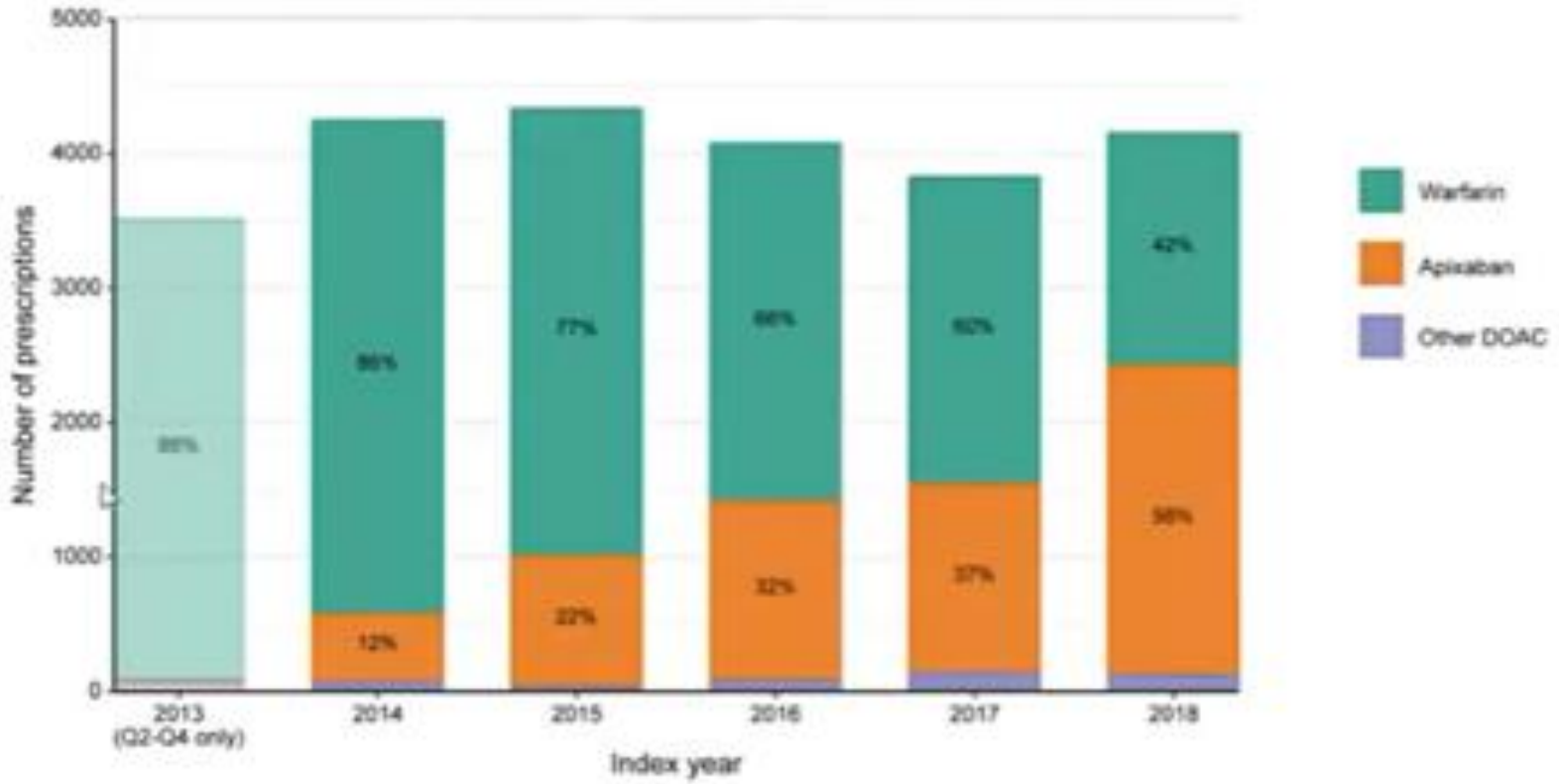
Management of atrial fibrillation in patients with chronic kidney disease in Europe Results of the European Heart Rhythm Association Survey

41 Ευρωπαϊκά κέντρα ηλεκτροφυσιολογίας



Europace 2015

Αυξάνεται η χρήση των DOACs



Weisbrod et al American Journal of Kidney Diseases 2022

Κάποιοι ΝΑΙ κάποιοι ΟΧΙ

Η ανάγκη …..

- Πρέπει να δίνουμε αντιπηκτικά?
- Ποια???

- **Ναι, υπό προϋποθέσεις**
- Όχι ανταγωνιστές της βιταμίνης Κ
- Ναι στα νεότερα αντιπηκτικά, υπό προϋποθέσεις


27ο Πανελλήνιο Συνέδριο Νεφρολογίας
Στη μνήμη του Καθηγητή Βασίλη Βαργεμέζη
20 - 23 Μαΐου 2026
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