News on DOACs in the elderly

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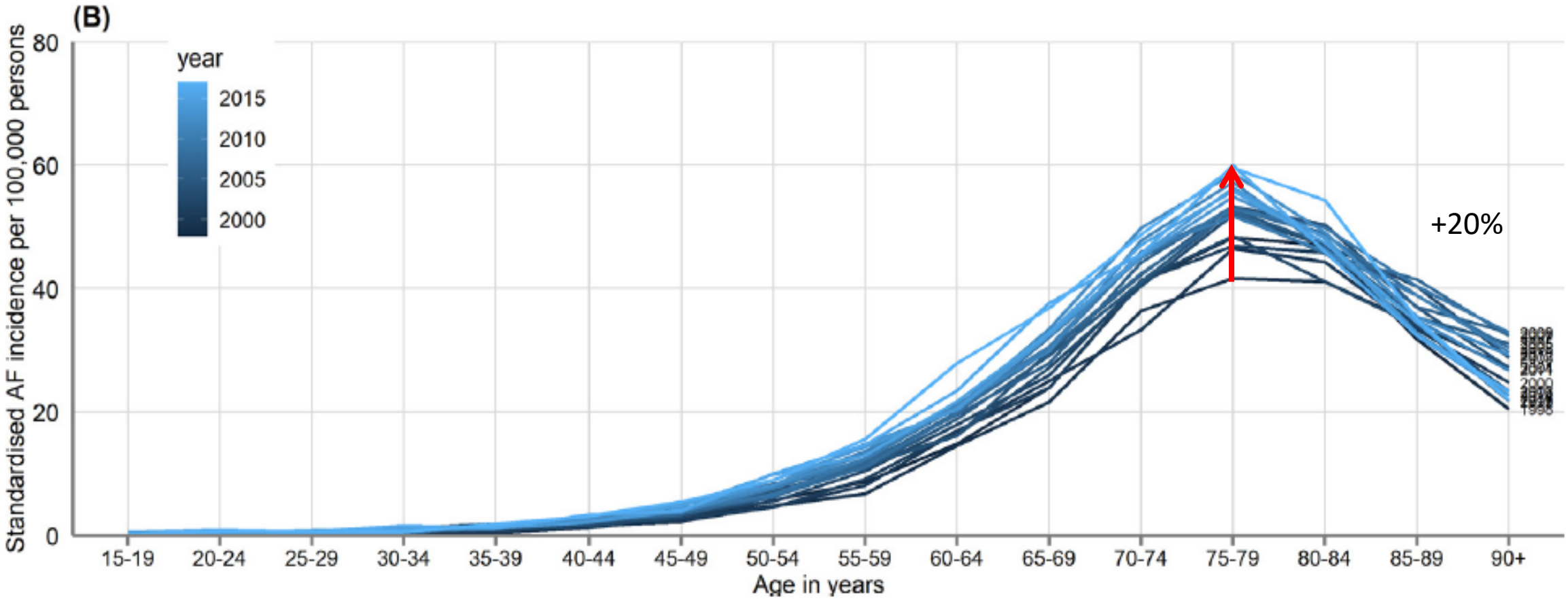
No COI to declare for this talk

Outline

1. Atrial fibrillation in the elderly: recent epidemiology and OAC use
2. Bleeding scores, are they adequate?
3. DOAC, VKA or nothing?
4. Measuring?

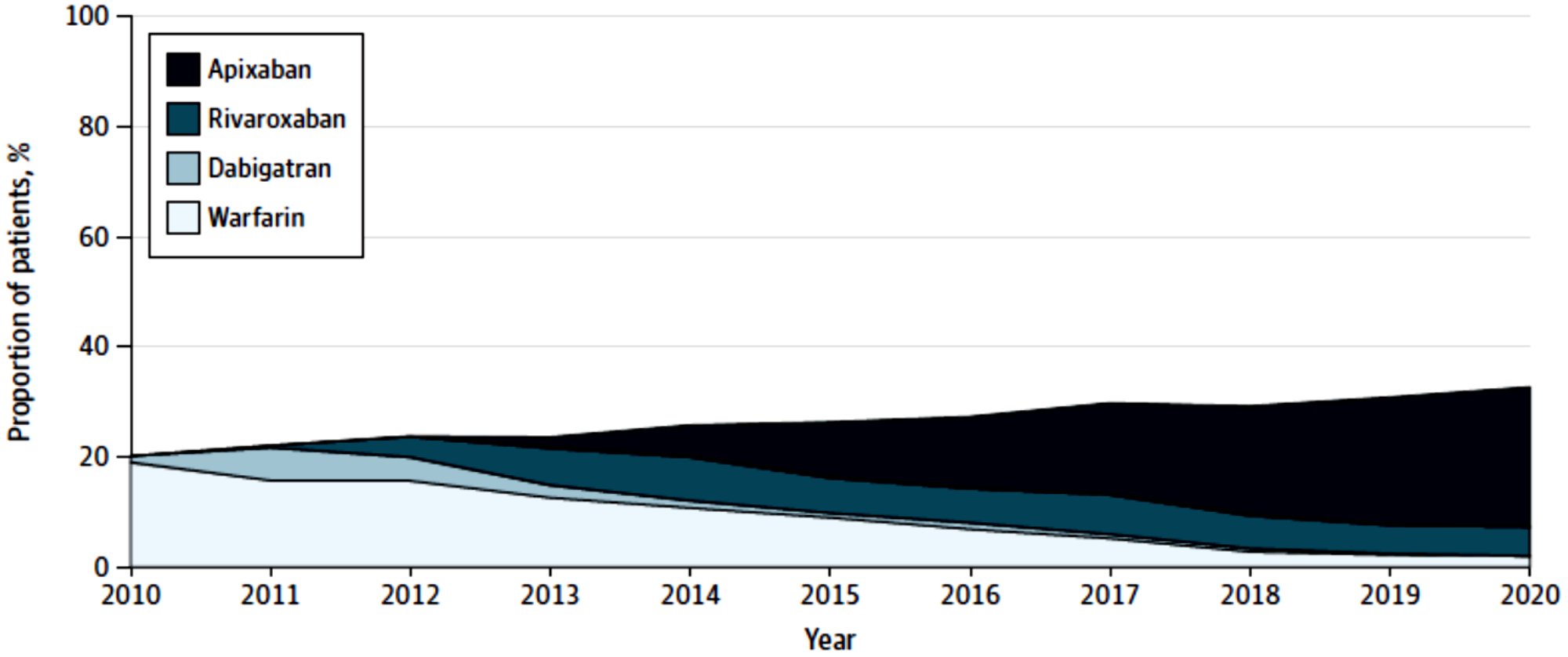
Afib in the elderly is on the rise over the past decades



Wu et al., The Lancet Regional Health – Europe, 2022;17: 100386

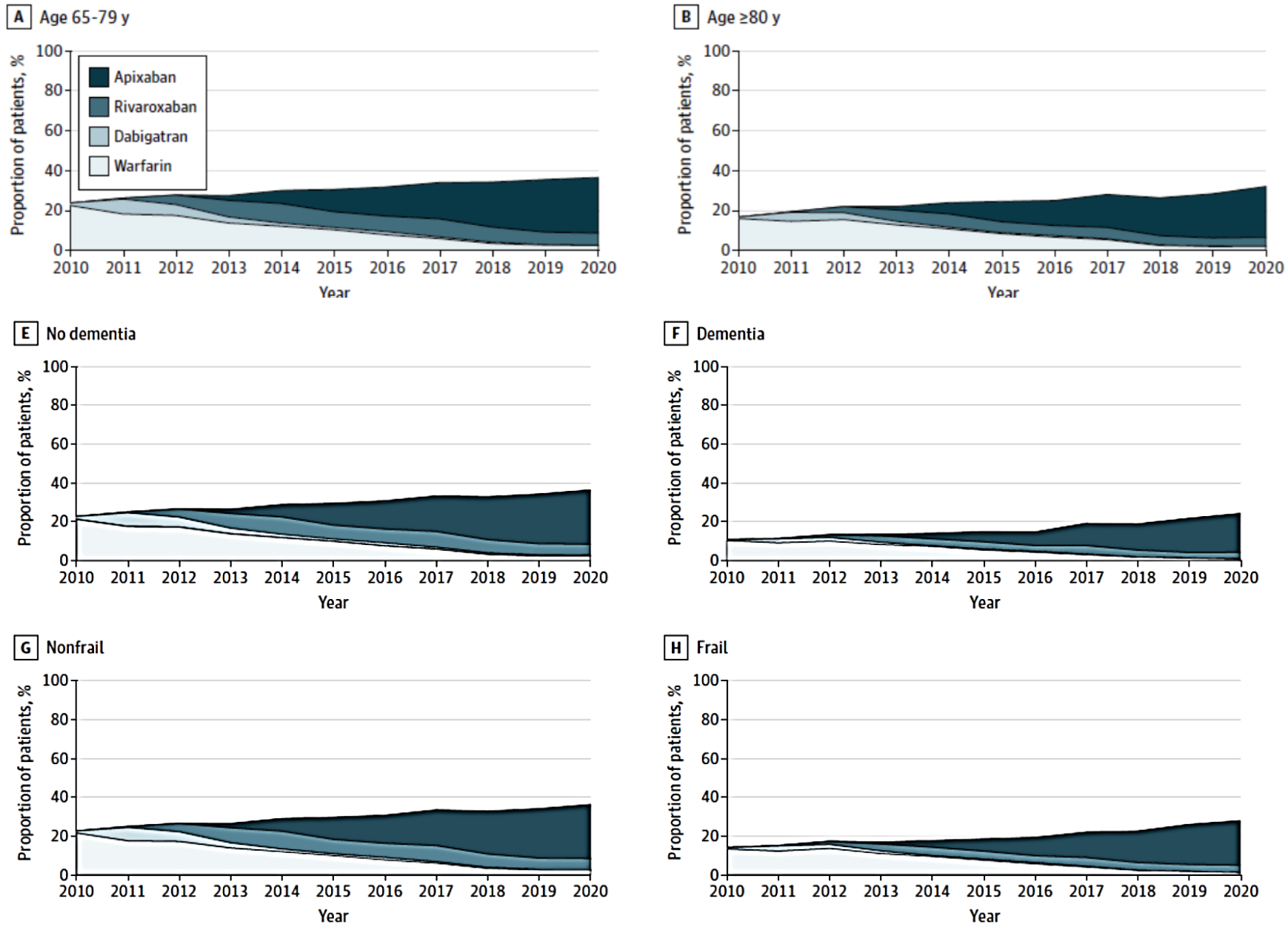
Trend in prescription of Oral Anticoagulant Drugs (2010-2020) from a US MediCare Registry in patients >65 years with AF

Figure 2. Oral Anticoagulant (OAC) Initiation and Direct OAC Uptake in 2010-2020



Ko et al., JAMA Network Open. 2022;5(11):e2242964

Older age, frailty and dementia: barriers to OAC prescription



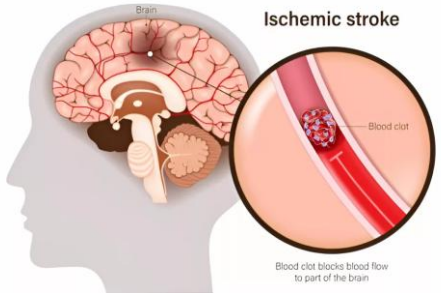
Ko et al., JAMA Network Open. 2022

AGE in

Old BLEEDING SCORES: Which threshold?

AGE in

Old THROMBOTIC SCORES: How much weight?



HASBLEED age >**65** years, 1 pt out of 9

HEMORR2HAGES age >**65** years 1 pt; Elderly >**75** years 1 pt out of 11

ATRIA age ≥**75**, 2 pt out of 10

ORBIT age >**74**, 1 pt out of 7

CHA_2DS_2-VA <65 0 pt; **65-74** 1 pt; **75+** 2 pt out of 8

CHA_2DS_2-VASc <65 0 pt; **65-74** 1 pt; **75+** 2 pt out of 11

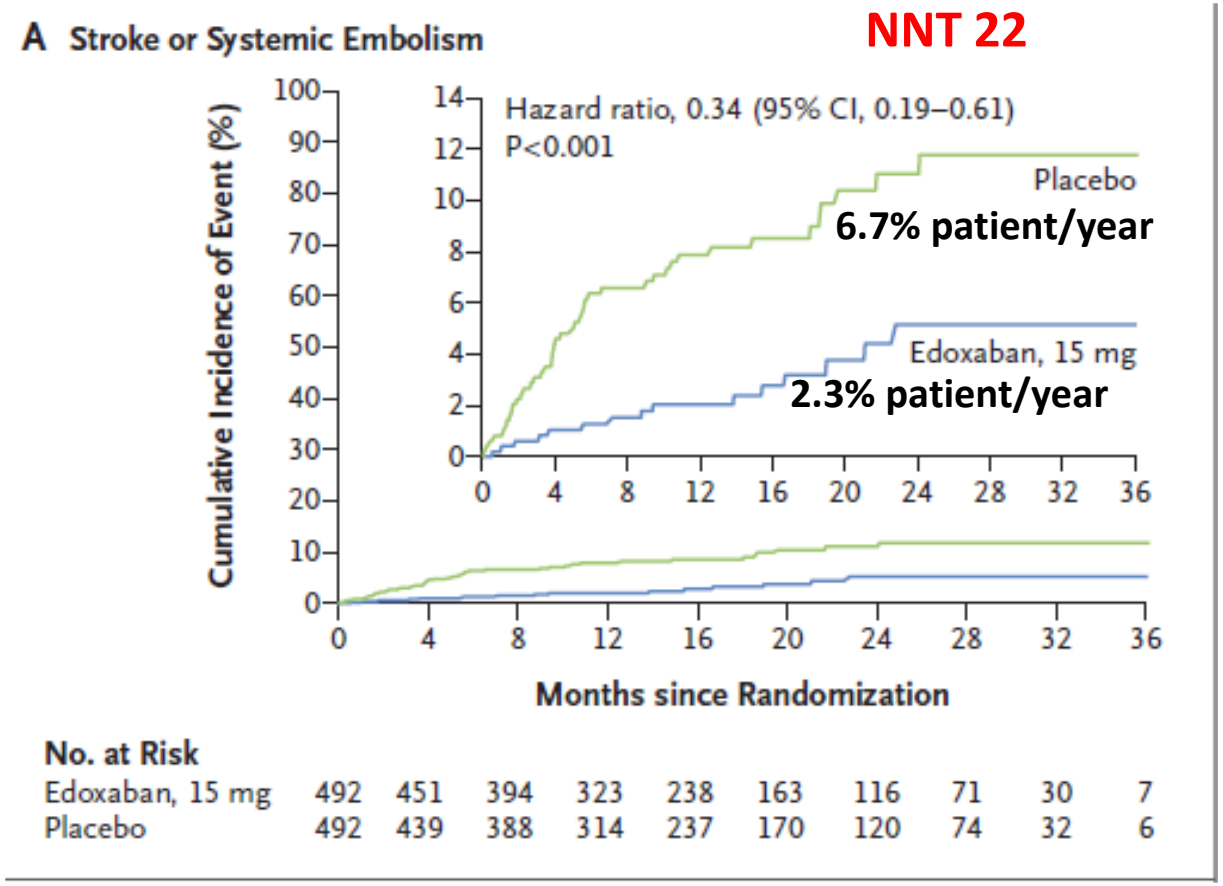
VKA, DOAC, either one or none?

Age in the major phase III DOAC trials of AFib: over 80s poorly represented

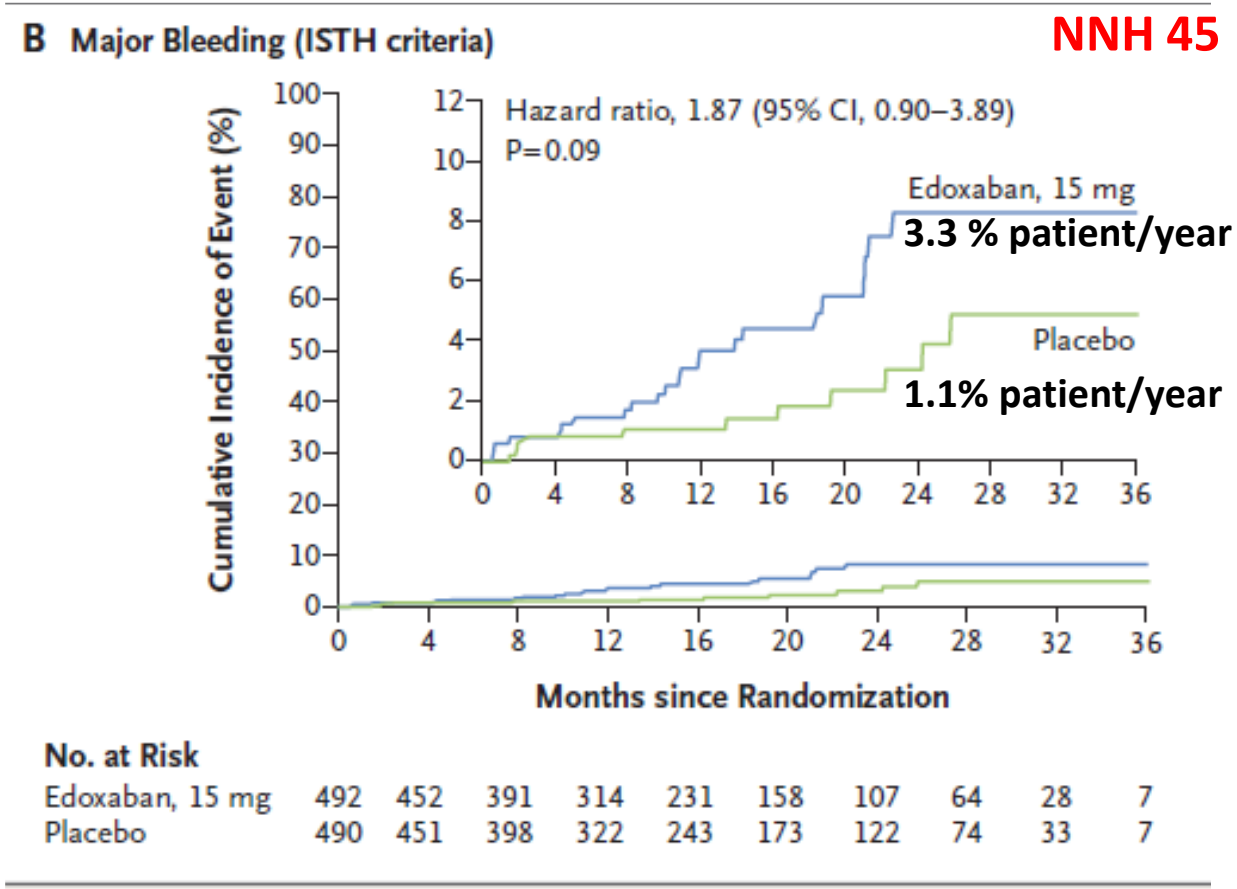
ROCKET-AF- rivaroxaban:	median	73 [IQR 65-**78**] years
ARISTOTLE- apixaban:	median	70 [IQR 63-**76**]
RELY- dabigatran	mean	71.5 ± 8.6
ENGAGE- edoxaban	median	72 [IQR 64-**78**]

ELDERCARE-AF phase III trial: reduced dose (15 mg) edoxaban vs. **placebo** in Japanese patients aged ≥80 with AF, unsuitable for OAC*

NNT 22



NNH 45



*creatinine clearance 15 to 30 ml/min, history of bleeding from a critical area or organ or gastrointestinal bleeding, body weight ≤45 kg, need for chronic NSAIDs or an antiplatelet drug.

Okumura et al., NEJM 2022

However, no apparent differences of CV death and all cause mortality and no net benefit when mortality was included

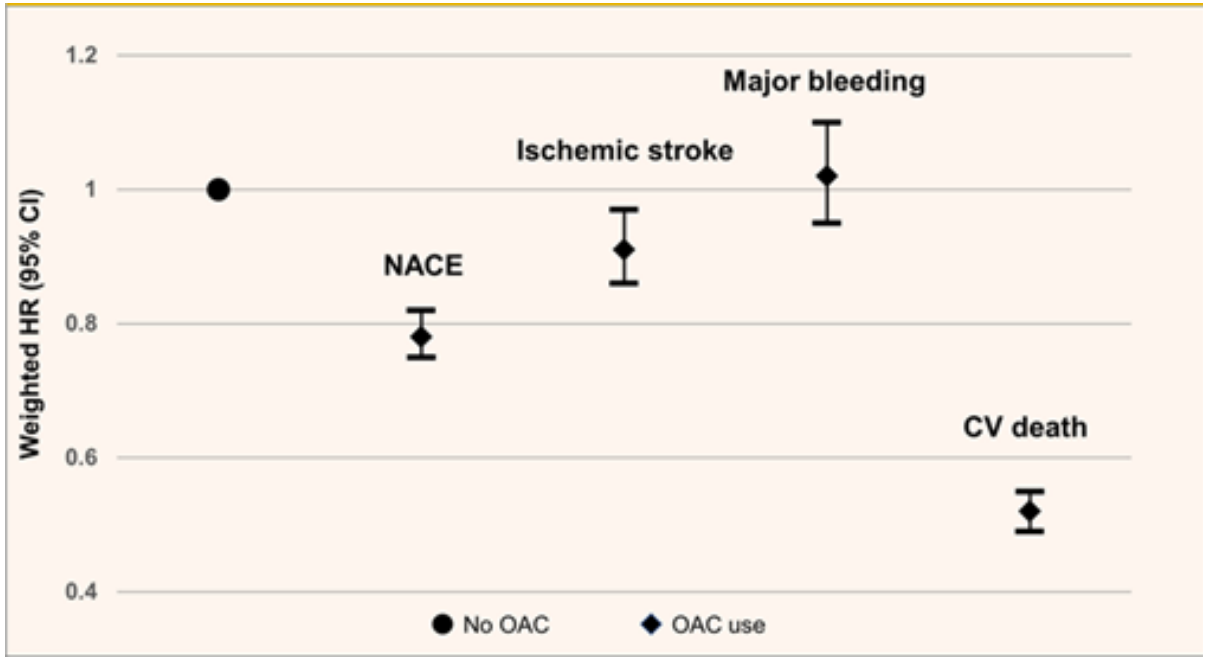
Secondary efficacy end points†			
Stroke, systemic embolism, or death from cardiovascular causes	52 (7.8)	72 (10.9)	0.72 (0.50–1.03)
Major adverse cardiovascular event‡	51 (7.7)	72 (11.0)	0.70 (0.49–1.01)
Stroke, systemic embolism, or death from any cause	74 (11.1)	98 (14.8)	0.75 (0.56–1.02)
Net clinical benefit§	87 (13.5)	103 (15.6)	0.86 (0.65–1.15)
Death from any cause	66 (9.9)	69 (10.2)	0.97 (0.69–1.36)

§ Net clinical benefit was the composite of stroke, systemic embolism, major bleeding, or death from any cause.

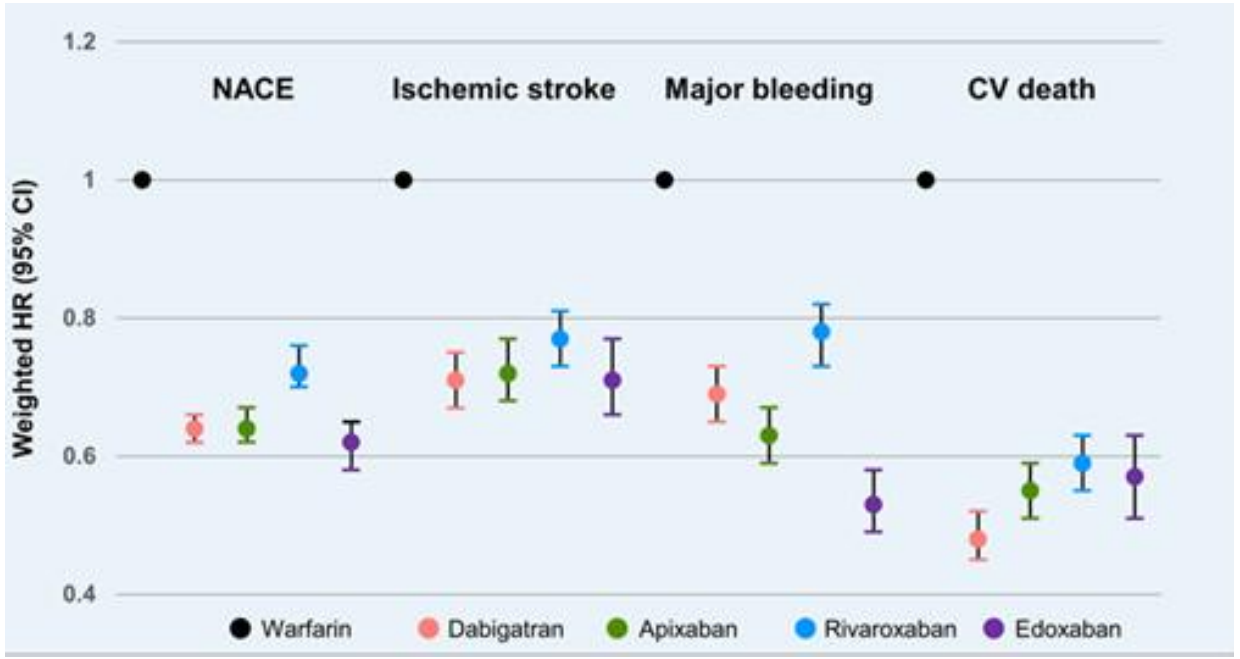
Okumura et al., NEJM 2022

Effectiveness and Safety of Anticoagulation in 83,635 Frail Patients With Atrial Fibrillation from Observational Data

OAC versus NO anticoagulation (reference)



DOAC versus VKA (reference)



mean age **78.5±7.2** years with AF and **frailty** (≥5 Hospital Frailty Risk Score)

Kim et al., Stroke 2022

Switching From a Vitamin K Antagonist to a DOAC in Frail Older Patients With Atrial Fibrillation: the FRAIL-AF Trial

- ✓ Age ≥75 years on INR-guided VKA for AF
- ✓ a Groningen Frailty Indicator (GFI) ≥3
- ✓ willing to switch to a DOAC
- ✓ eGFR ≥30 ml/min

Superiority Hypothesis: relative reduction of 20%-30% when switching to an NOAC in the incidence of major or CRNM bleeding complications on VKA (prediction 11%-15%).

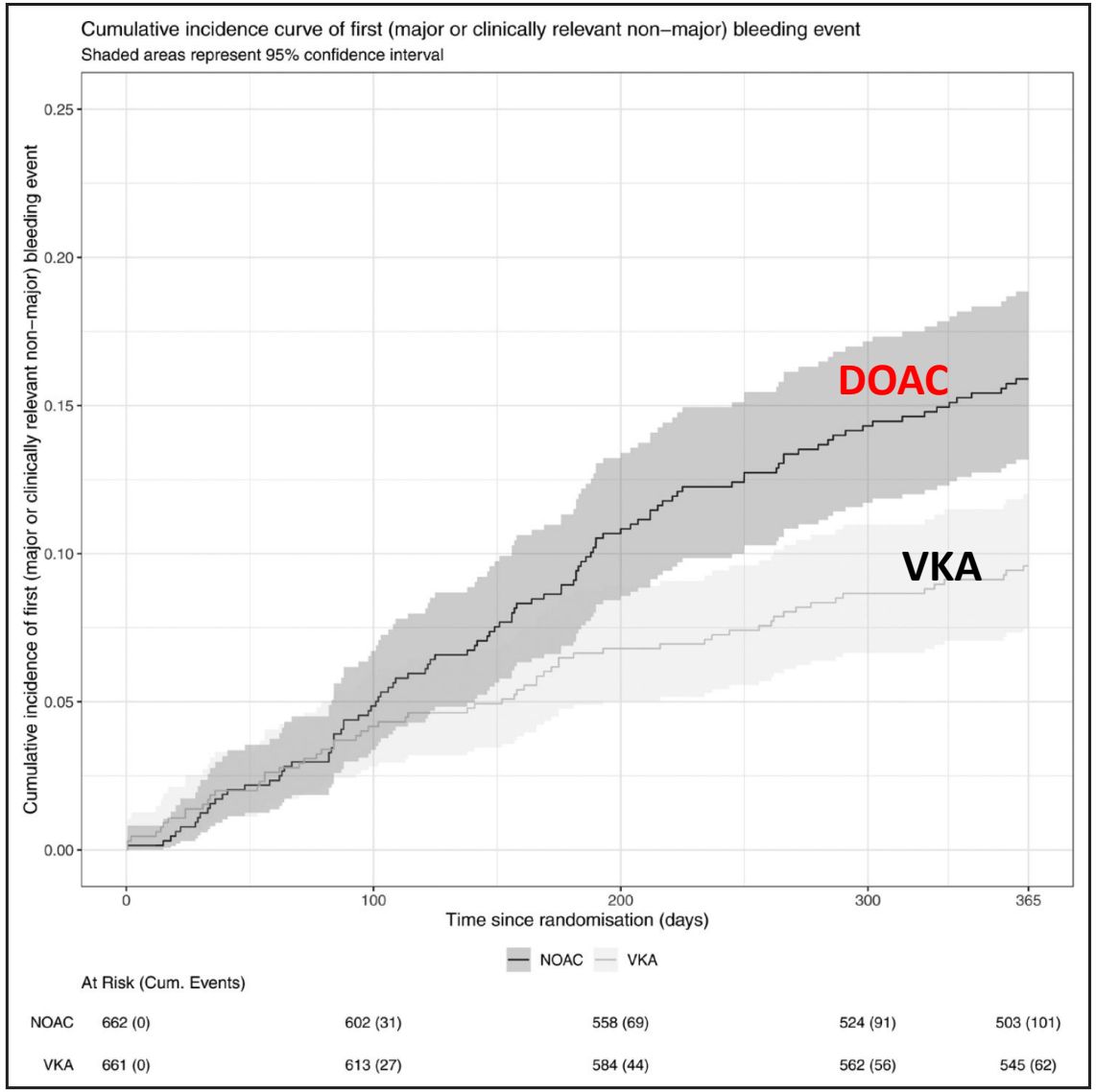
Primary outcome: a major or clinically relevant nonmajor (CRNM) bleeding-ISTH definition

1323 patients, mean age: 83±5 years

Halted for futility following the advice of the DSMB and in accordance with a prespecified protocol

Joosten et al, Circulation 2024

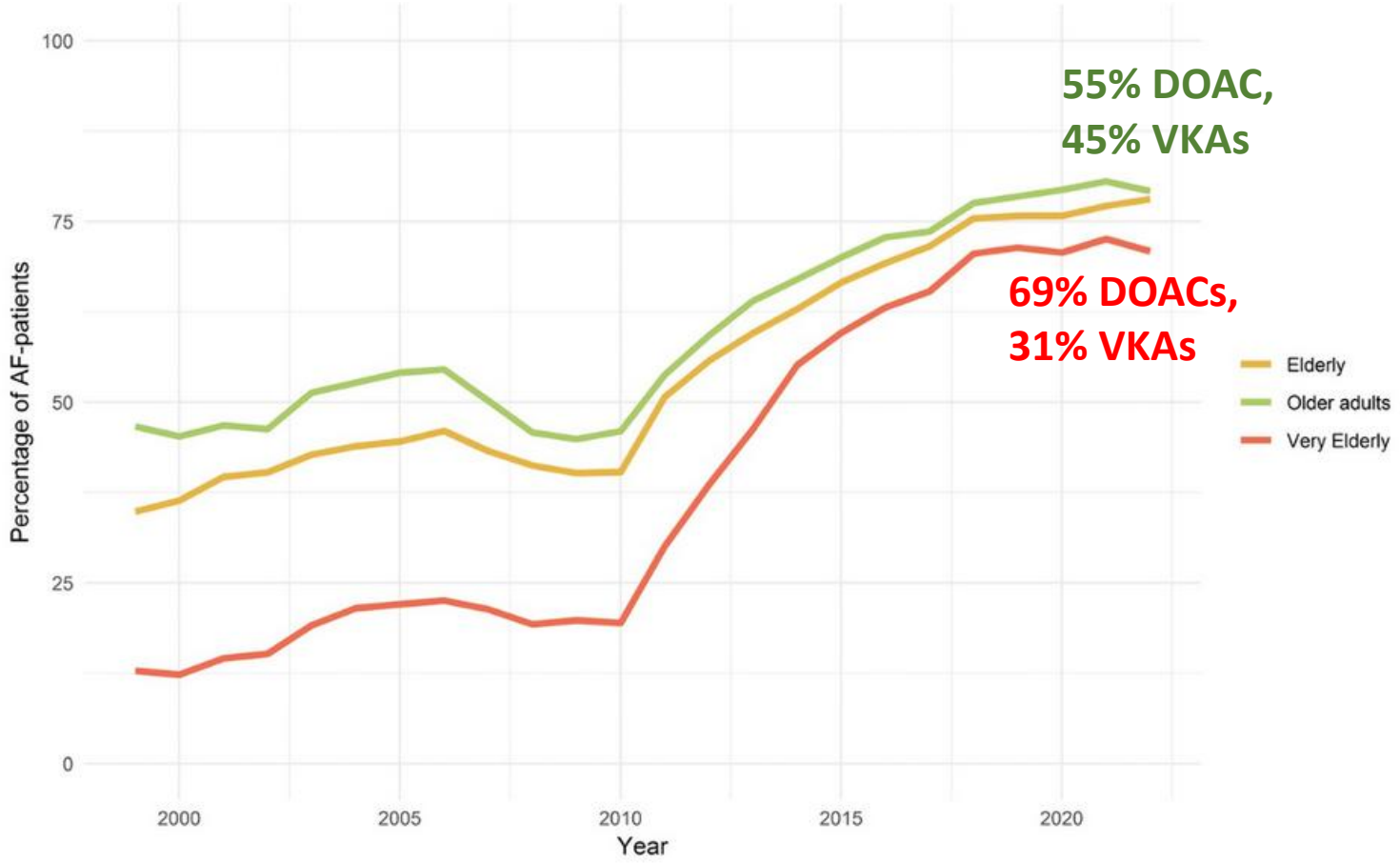
Higher rate of ISTH-defined major bleeding after switching to a DOAC

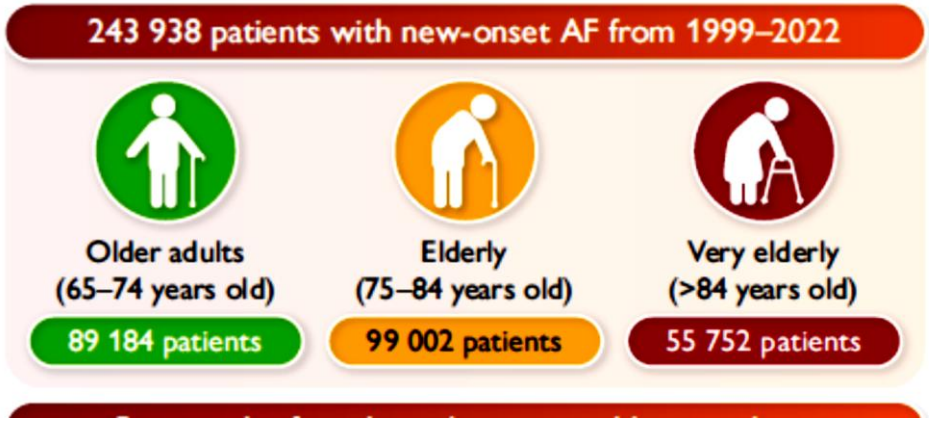


HR 1.69 for switching to an NOAC relative to continuing INR-guided VKA (95% CI, 1.23–2.32; P=0.00112)

Joosten et al, Circulation 2024

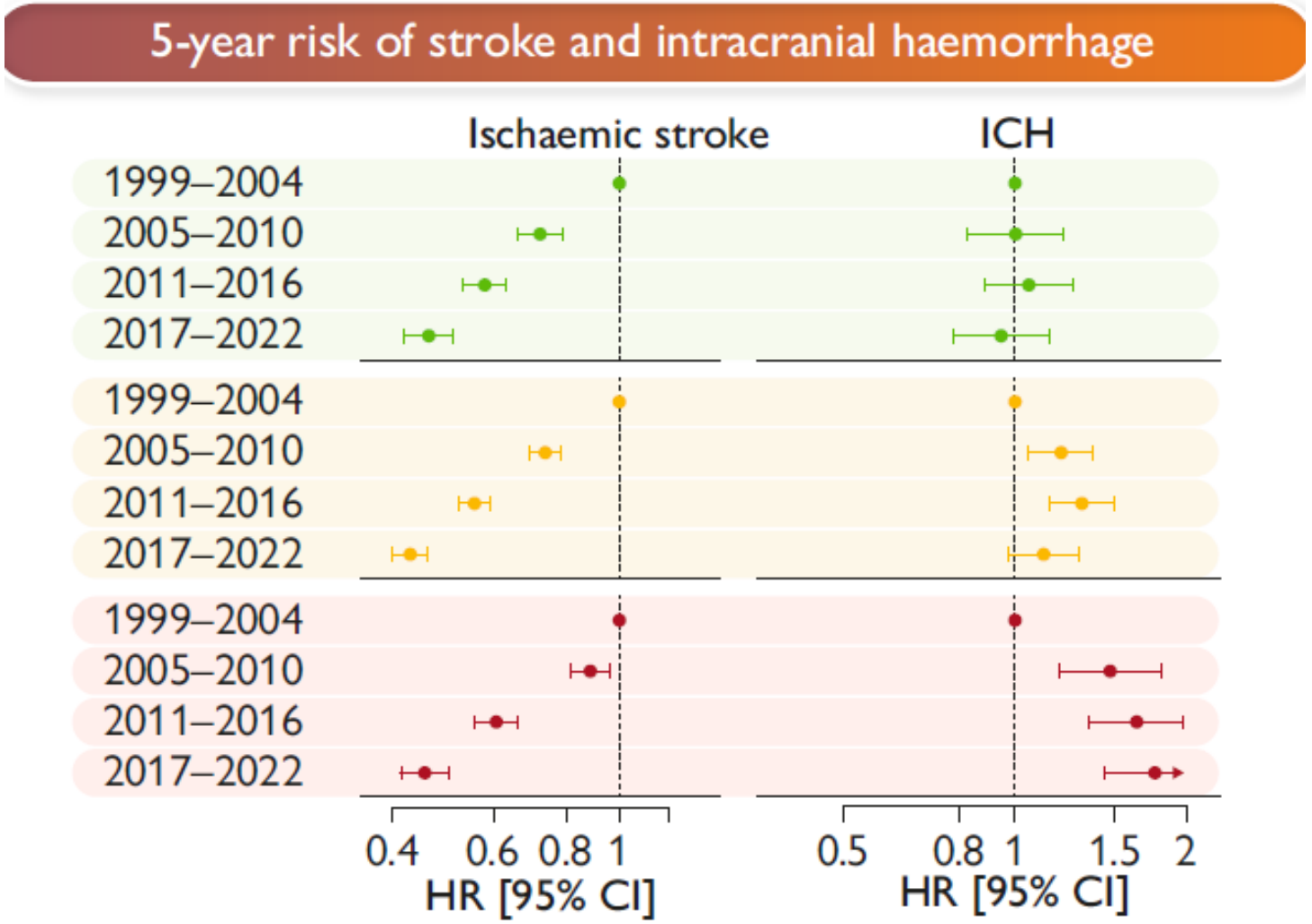
OAC prescriptions in Denmark for new-onset AF in 243,938 patients aged 65-74, 75-84 and >84 years between 2000 and 2022





Bianding et al., EHJ 2025

Significant increase in intracranial bleeding couterbalancing ischemic stroke reduction in AF patients aged >84 years versus 1999-2004



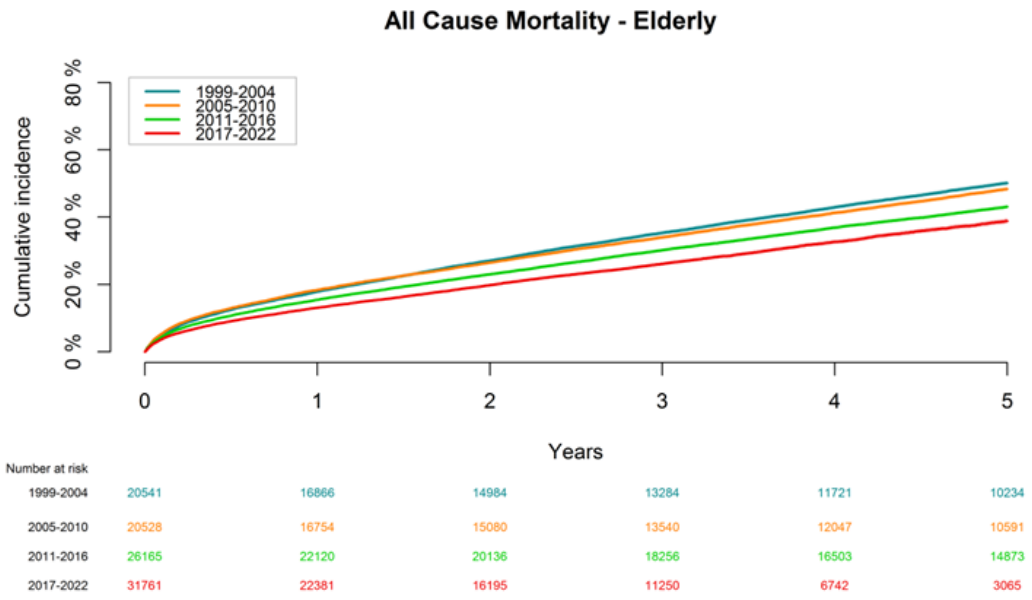
65-74 years

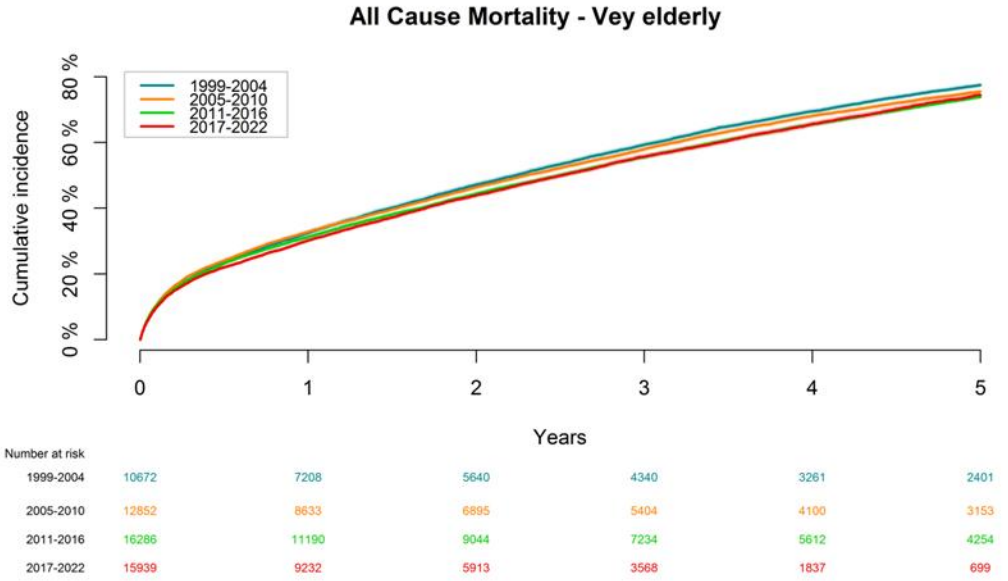
75-84 years

>84 years

Binding et al., EHJ 2025

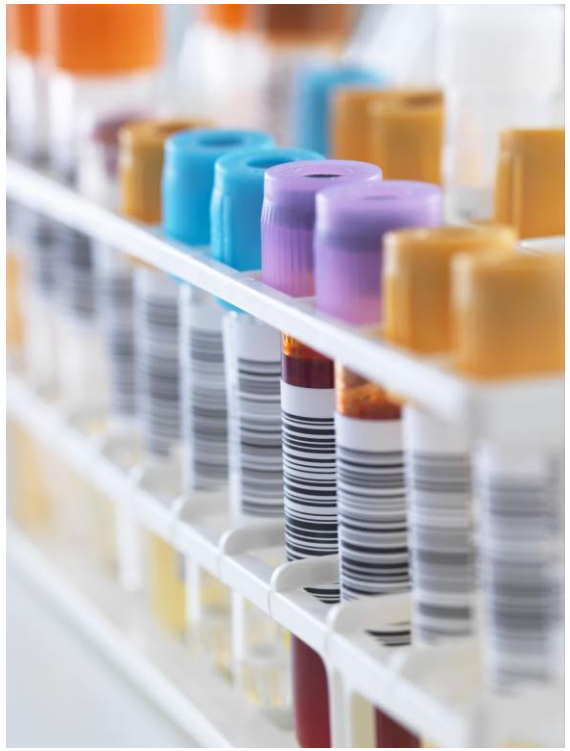
No significant reduction in 5-year mortality in AF patients aged >84 since 1999-2004





Binding et al., EHJ 2025

Current concerns about DOAC in the elderly



- In elderly/very elderly patients how predictable is the PK/PD?
- How many patients with AF are outside the “on therapy” ranges?
- Should we more often check DOAC levels to improve safety?

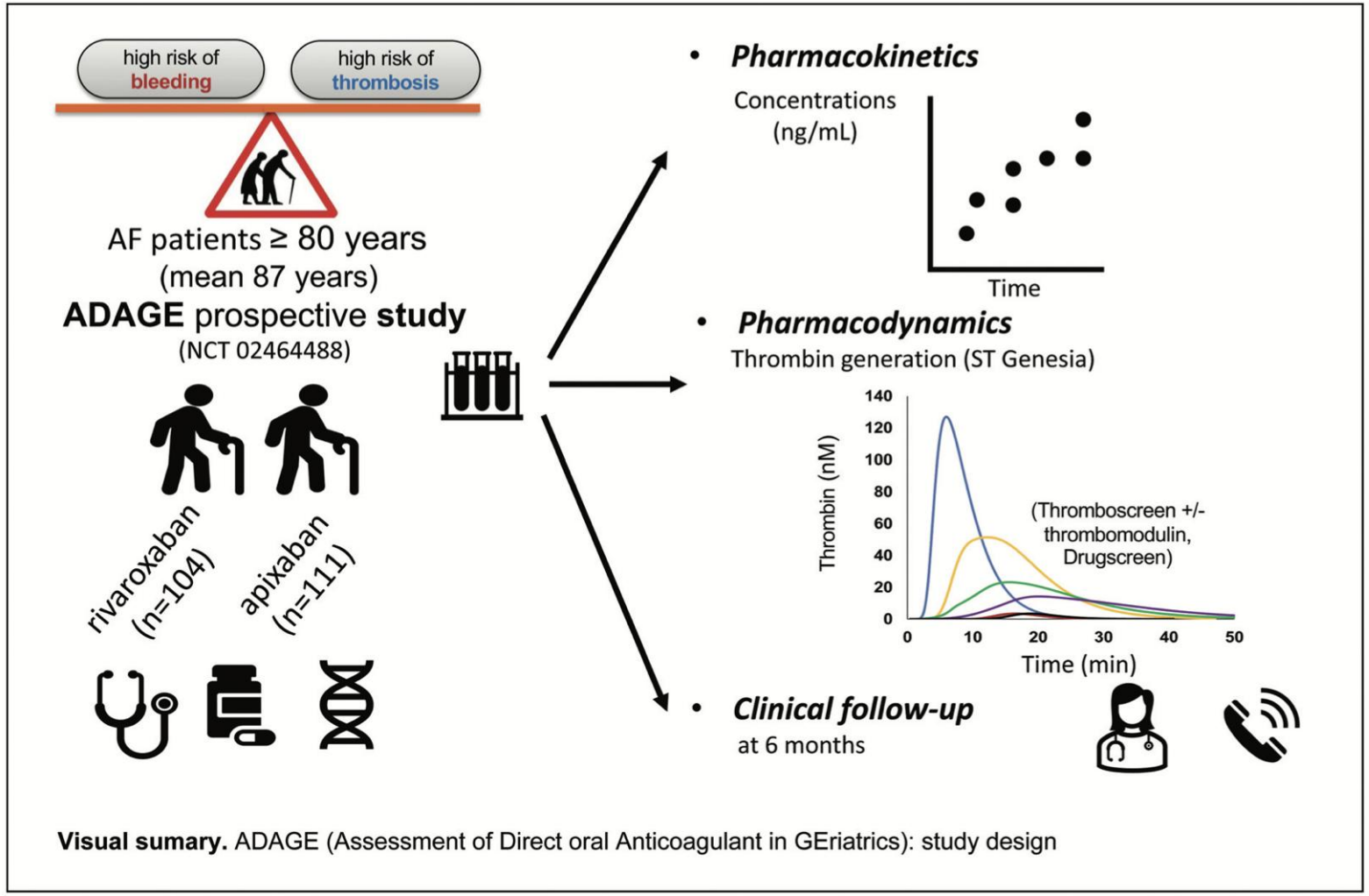
Age significantly and independently affect dabigatran plasma concentrations in patients included in the RE-LY trial

Dose normalized plasma concentrations (ng/ml/mg) of dabigatran according to age

Age, yrs		<65 (n = 1,466)	65 to <75 (n = 3,787)	≥75 (n = 3,196)
	gMean	0.586	0.749	0.982
	gCV, %	86	75.2	76
	Median	0.595	0.761	0.994

Reilly et al, JACC 2014

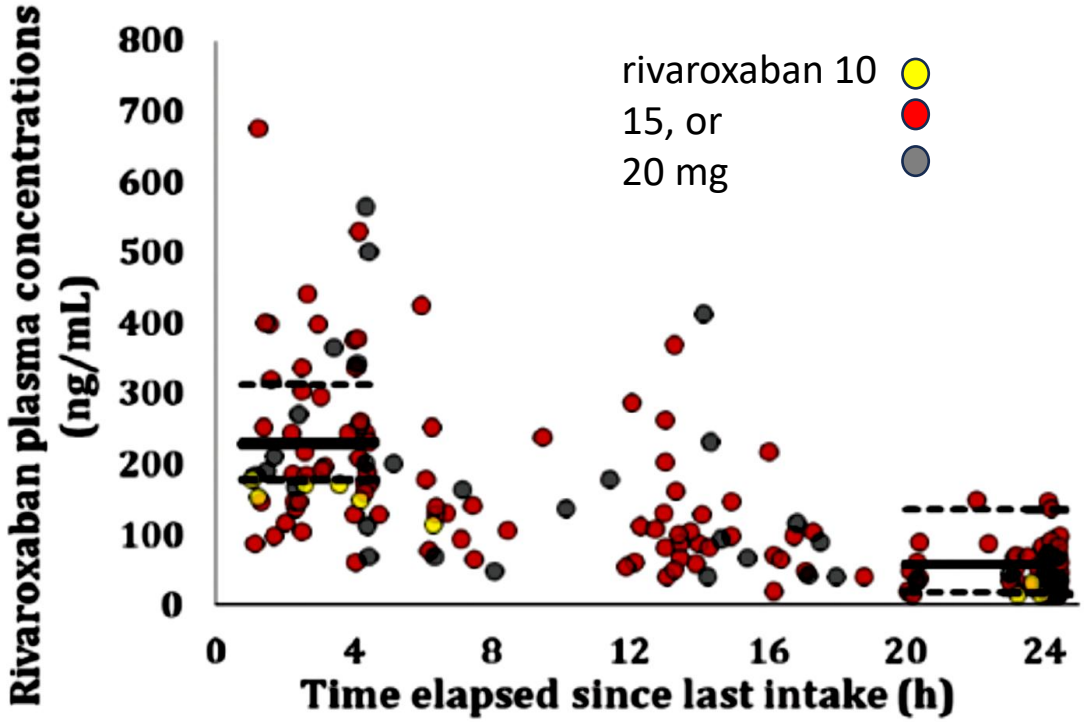
Assessment of DOAC in GEriatrics (ADAGE Study): Rivaroxaban/Apixaban Concentrations in AF Very Elderly Patients

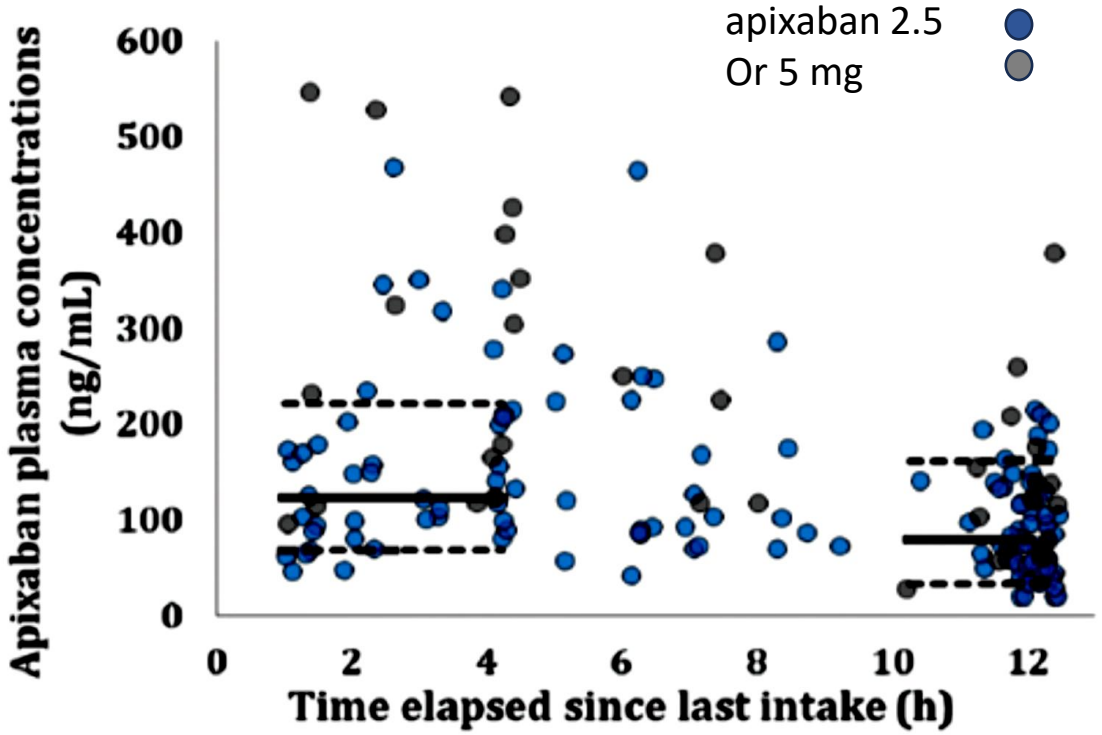


Visual sumary. ADAGE (Assessment of Direct oral Anticoagulant in GEriatrics): study design

Foulon-Pinto et al, TH 2023

Wide variability in Rivaroxaban or Apixaban Concentrations at peak and trough, outside the 'on-therapy' intervals





Foulon-Pinto et al, TH 2023

Modified from Rocca and Guasti, EHJ 2025