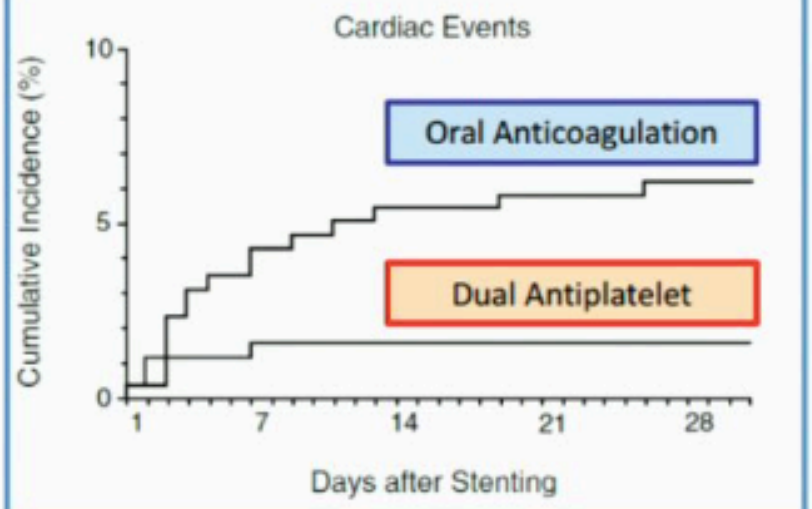
Terapia di combinazione anticoagulante e antiaggregante nei pazienti con fibrillazione atriale e coronaropatia: dati dal mondo reale

The Clinical Challenge in Patients with AF Undergoing PCI

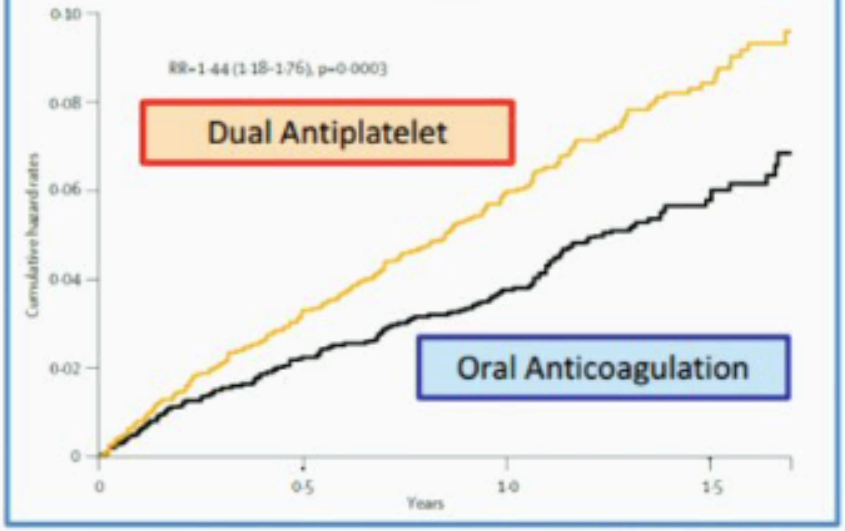
Coronary stent implantation



ISAR, NEJM 1996

+

Atrial fibrillation



ACTIVE-W Lancet 2006

= Dual Antiplatelet + Oral Anticoagulation

DAPT > OAC
for Stent Thrombosis prevention

OAC > DAPT
for Stroke prevention

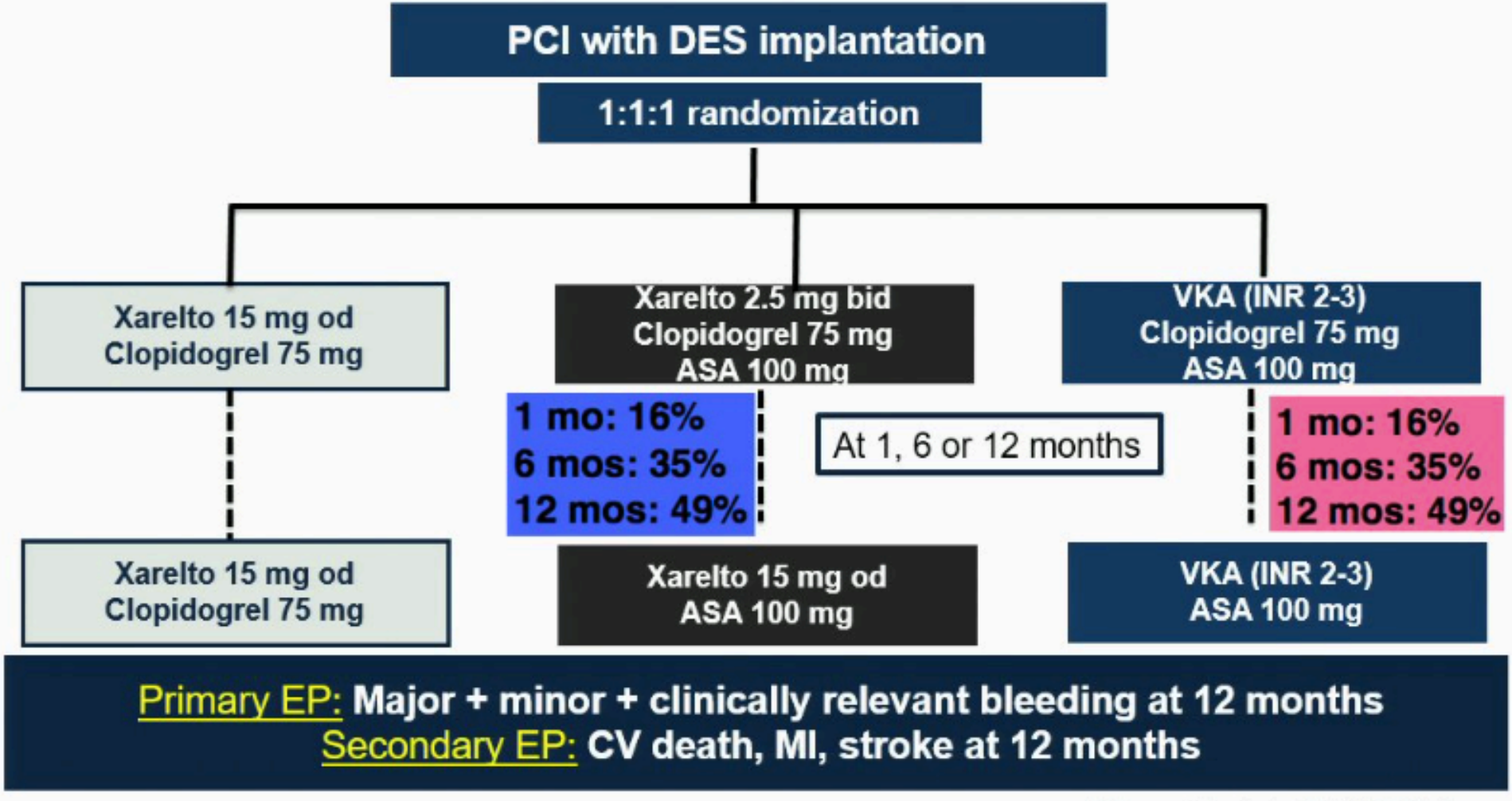
TRIPLE THERAPY

↓

BLEEDING

The PIONEER AF-PCI Trial

2124 pts with NVAF, coronary Stent (51% ACS)
No Prior stroke/TIA , GI bleeding or CrCl<30 ml/min
International, multicenter, randomized, open-label

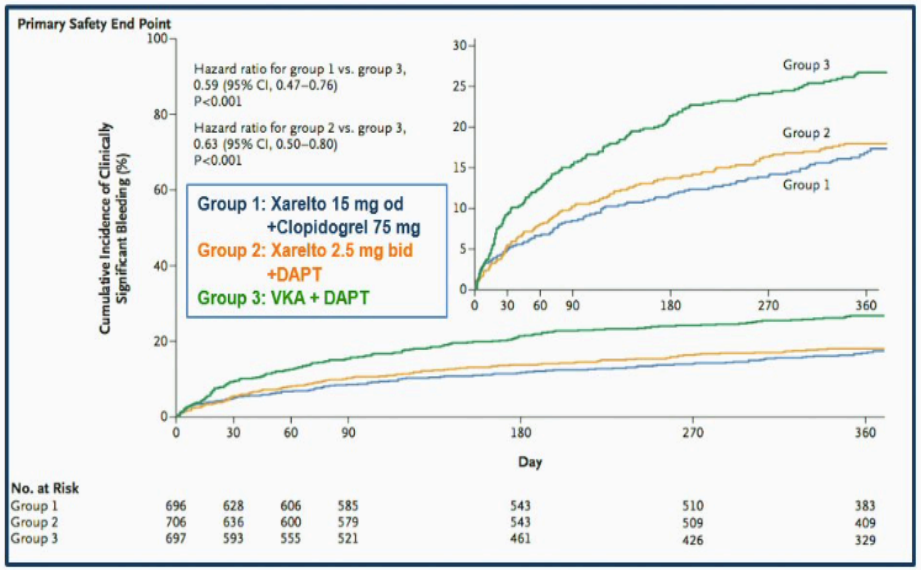


Primary EP: **Major + minor + clinically relevant bleeding at 12 months**
Secondary EP: **CV death, MI, stroke at 12 months**

Gibson M et al. NEJM 2016

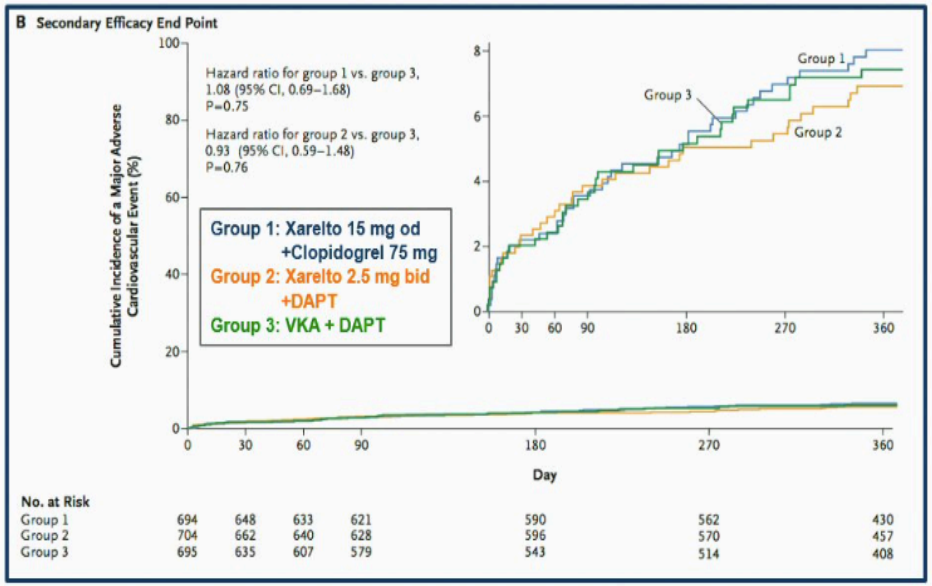
The PIONEER AF-PCI Trial

Primary Safety Endpoint: Bleeding



Gibson M, NEJM 2016

Secondary Efficacy Endpoint: CV, MI, STROKE

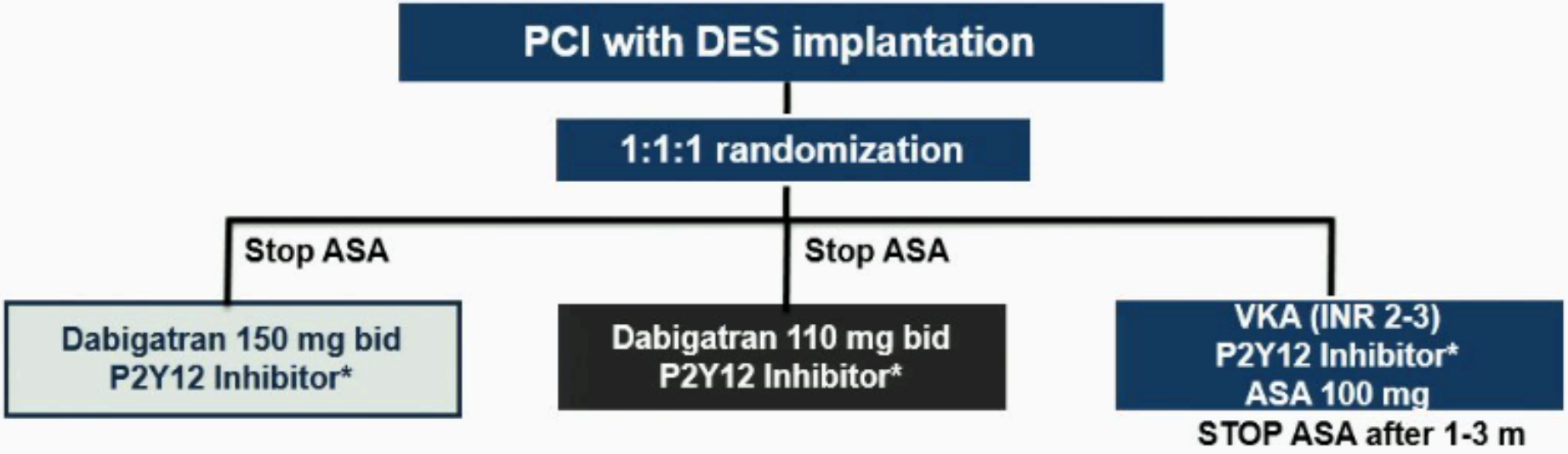


Gibson M, NEJM 2016

The RE-DUAL PCI Trial

2725 pts with NVAF+ PCI (50.5% ACS)

International, multicenter, randomized, open-label



Minimum treatment duration = 12 months

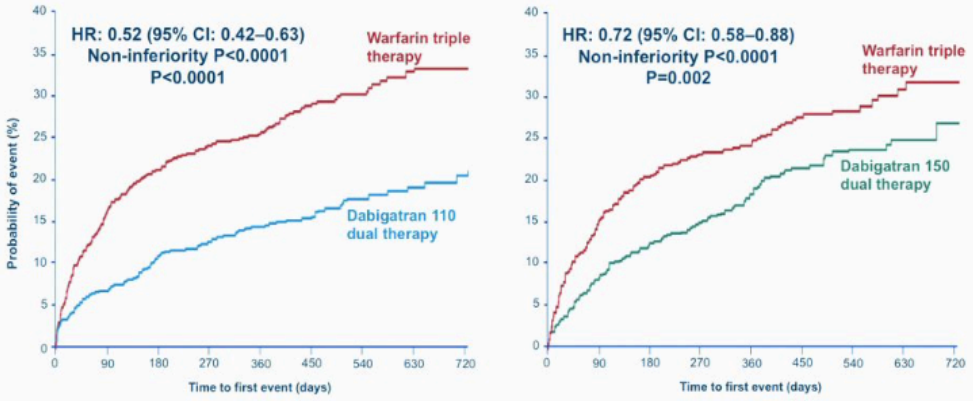
Primary EP: ISTH Major + clinically relevant bleeding
Secondary EP: CV death, MI, stroke

*P2Y12 Inhibitor: Clopidogrel or Ticagrelor (12%)

Cannon CP, NEJM 2017

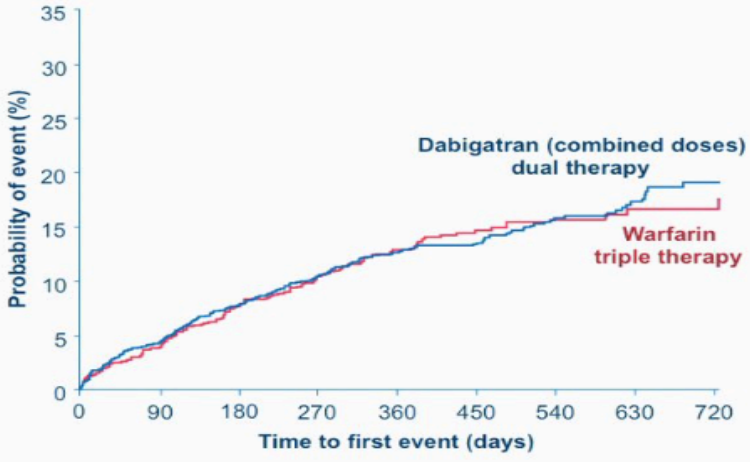
The RE-DUAL PCI Trial

Primary EP: Major + clinically relevant bleeding



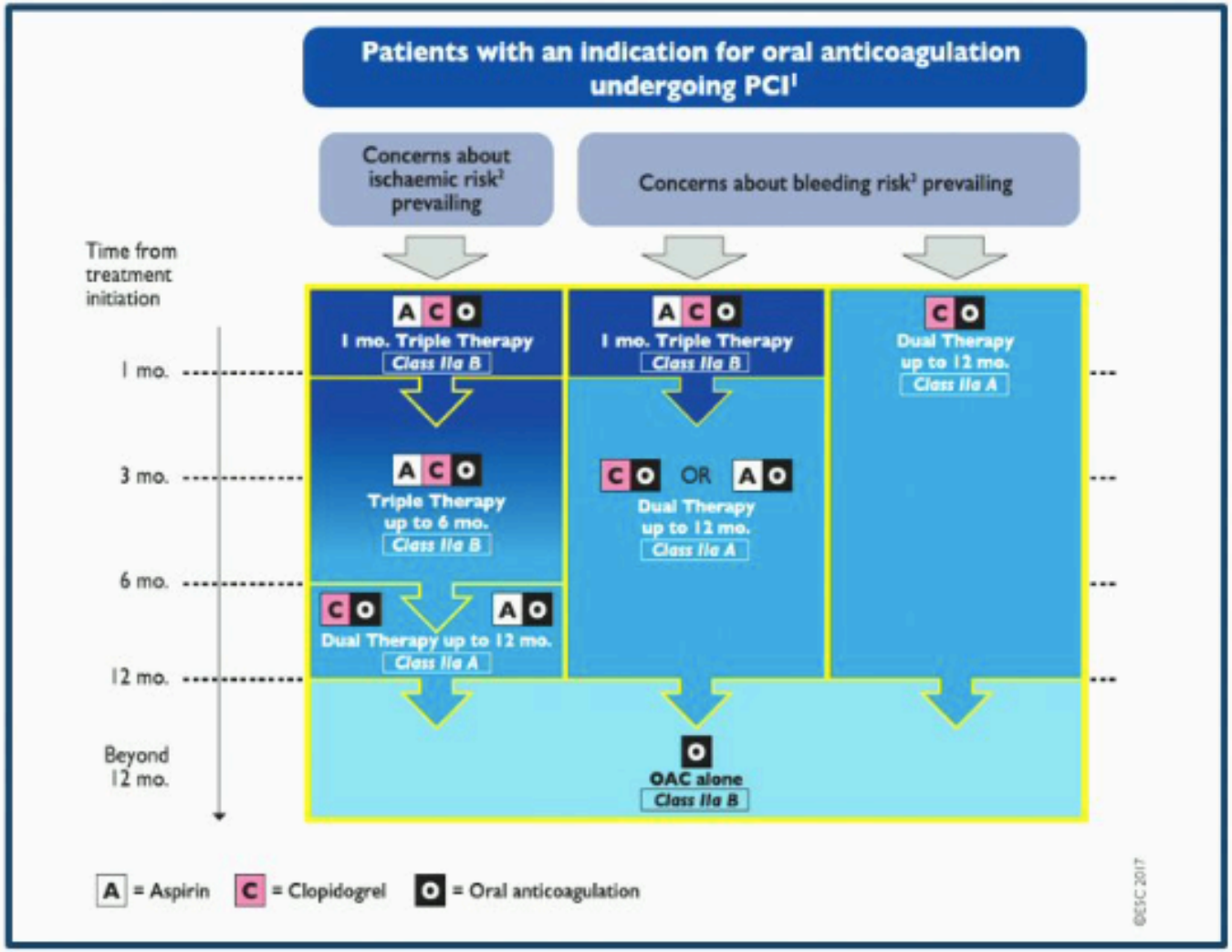
Cannon CP, NEJM 2017

Secondary efficacy EP: D, MI, stroke, Systemic embolism, unplanned revascularization



Cannon CP, NEJM 2017

2017 ESC focused update on dual antiplatelet therapy in coronary artery disease developed in collaboration with EACTS



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Combining Oral Anticoagulants With Platelet Inhibitors in Patients With Atrial Fibrillation and Coronary Disease

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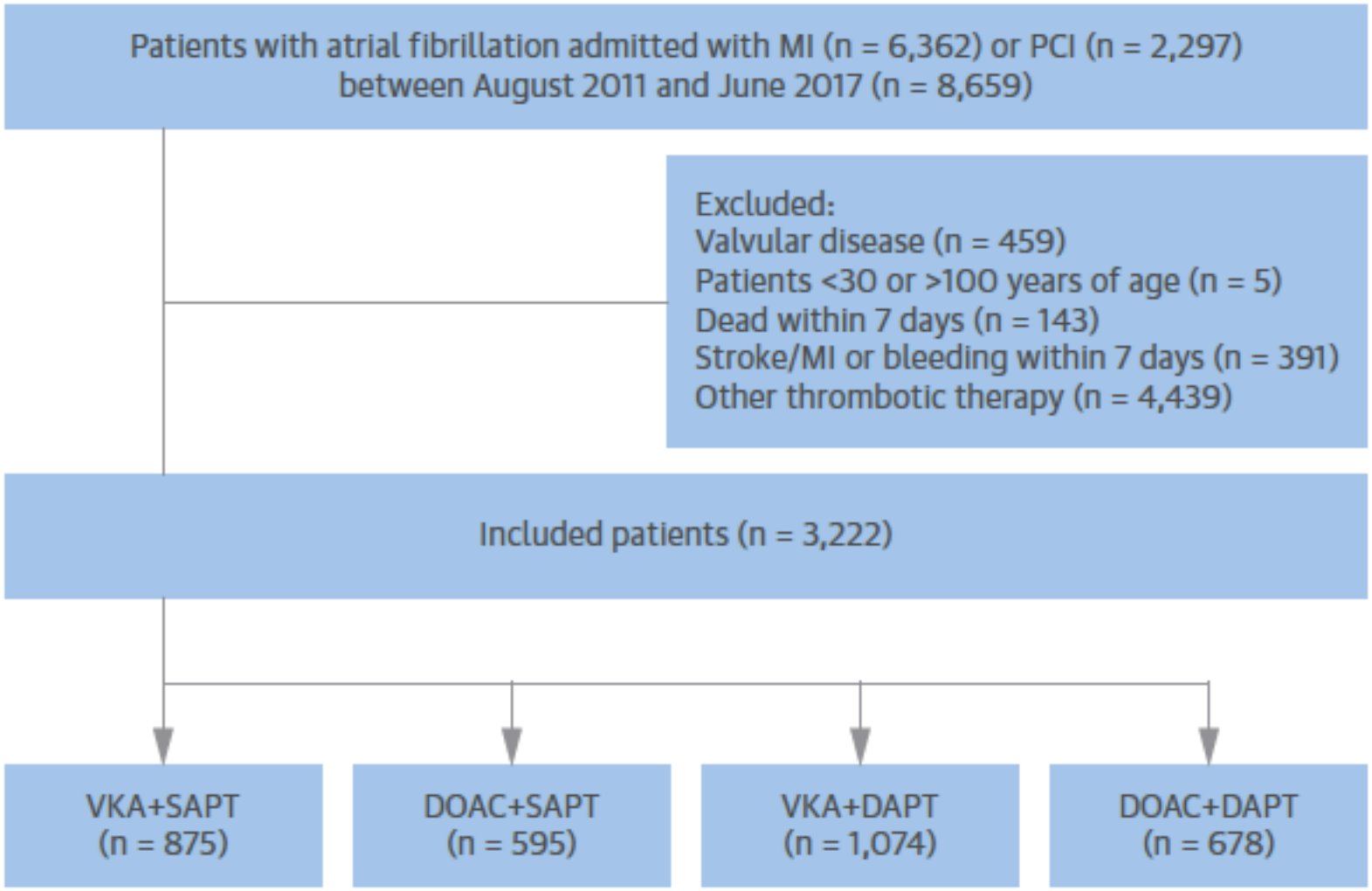
Objective

To investigate the risk of bleeding, ischemic stroke, MI, and all-cause mortality associated with direct oral anticoagulants (DOACs) compared with vitamin K antagonists (VKAs) in combination with aspirin, clopidogrel, or both in patients with AF following MI and/or PCI.

Methods

- Danish nationwide registries were used to identify patients with AF who were admitted with a MI and/or underwent PCI, between August 2011 and June 2017, treated with OAC in combination with antiplatelet(s).
- Patients were followed for 12 months or until an outcome, study end, or death.
- Standardized absolute risks were estimated on the basis of outcome-specific Cox regression models adjusted for potential confounders. Average treatment effects were obtained as standardized absolute risk differences (ARD) in risks at 3 and 12 months using the g-formula.

Flow chart on the selection process



Baseline characteristics of study population

	Total (N = 3,222)	VKA + SAPT (n = 875)	DOAC+SAPT (n = 595)	VKA+DAPT (n = 1,074)	DOAC+DAPT (n = 678)
DOAC					
Rivaroxaban	–	–	181 (30.4)	–	211 (31.1)
Dabigatran	–	–	190 (31.9)	–	209 (30.8)
Apixaban	–	–	224 (37.6)	–	258 (38.1)
Dosages					
Reduced dosage	–	–	370 (62.2)	–	460 (67.8)
Patient characteristics					
Men	2,201 (68.3)	571 (65.3)	364 (61.2)	786 (73.2)	480 (70.8)
Age, yrs	76 (69–82)	77 (70–83)	77 (70–84)	75 (69–81)	73 (67–80)
Inclusion event					
MI as inclusion event	2,092 (64.9)	637 (72.8)	448 (75.3)	589 (54.8)	418 (61.7)
PCI within 1 day	626 (19.4)	92 (10.5)	71 (11.9)	258 (24.0)	205 (30.2)
PCI within 2–7 days	192 (6.0)	42 (4.8)	13 (2.2)	89 (8.3)	48 (7.1)
PCI as inclusion event	1,130 (35.1)	238 (27.2)	147 (24.7)	485 (45.2)	260 (38.3)
With stent	999 (31.0)	192 (21.9)	121 (20.3)	449 (41.8)	237 (34.9)
CHA_2DS_2VASC					
Intermediate (n = 2)	146 (4.5)	30 (3.4)	19 (3.2)	51 (4.7)	46 (6.8)
High (n = >2)	3,076 (95.5)	845 (96.6)	576 (96.8)	1023 (95.3)	632 (93.2)
Mean $CHADS_2VASC$	4.15 (1.63)	4.39 (1.60)	4.38 (1.66)	3.99 (1.57)	3.88 (1.67)
Modified HAS-BLED					
Low	92 (2.9)	19 (2.2)	16 (2.7)	34 (3.2)	23 (3.4)
Intermediate	2,137 (66.3)	553 (63.2)	399 (67.1)	697 (64.9)	488 (72.0)
High	993 (30.8)	303 (34.6)	180 (30.3)	343 (31.9)	167 (24.6)
Mean modified HAS-BLED	2.13 (0.94)	2.22 (0.91)	2.16 (0.96)	2.14 (0.95)	1.97 (0.91)

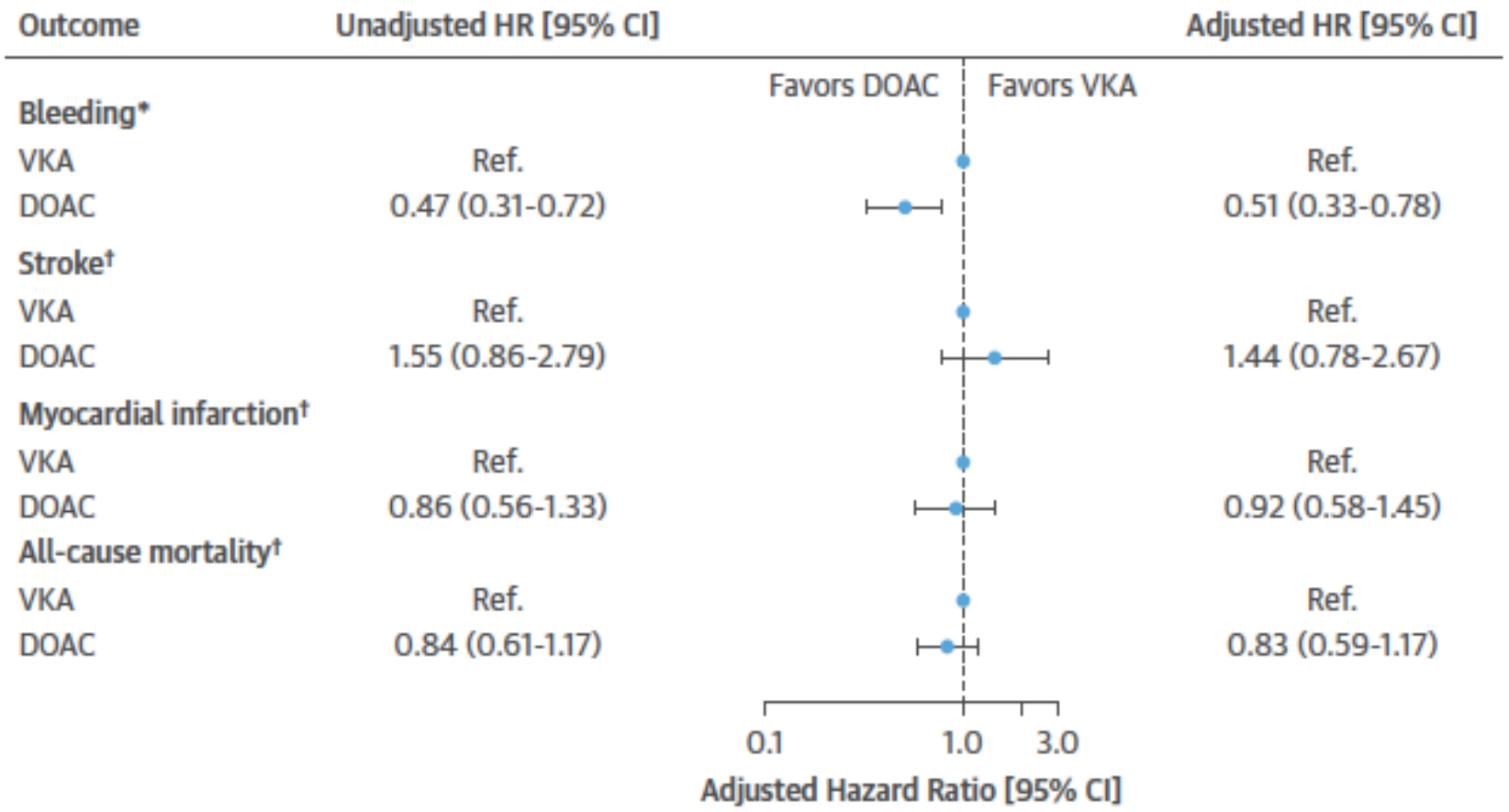
Baseline characteristics of study population

	Total (N = 3,222)	VKA + SAPT (n = 875)	DOAC+SAPT (n = 595)	VKA+DAPT (n = 1,074)	DOAC+DAPT (n = 678)
Comorbidity					
Previous bleeding	702 (21.8)	226 (25.8)	130 (21.8)	236 (22.0)	110 (16.2)
Stroke	553 (17.2)	159 (18.2)	121 (20.3)	154 (14.3)	119 (17.6)
Heart failure	1,288 (40.0)	395 (45.1)	219 (36.8)	442 (41.2)	232 (34.2)
Chronic kidney disease	319 (9.9)	102 (11.7)	43 (7.2)	131 (12.2)	43 (6.3)
Liver disease	47 (1.5)	14 (1.6)	13 (2.2)	12 (1.1)	8 (1.2)
Hypertension	2408 (74.7)	655 (74.9)	425 (71.4)	835 (77.7)	493 (72.7)
Diabetes	732 (22.7)	202 (23.1)	137 (23.0)	245 (22.8)	148 (21.8)
Cancer	503 (15.6)	148 (16.9)	102 (17.1)	172 (16.0)	81 (11.9)
COPD	490 (15.2)	152 (17.4)	83 (13.9)	164 (15.3)	91 (13.4)
Concomitant medication					
Beta-blockers	2,685 (83.3)	726 (83.0)	486 (81.7)	906 (84.4)	567 (83.6)
Calcium channel blockers	1,092 (33.9)	320 (36.6)	182 (30.6)	381 (35.5)	209 (30.8)
RAS	2,162 (67.1)	578 (66.1)	377 (63.4)	762 (70.9)	445 (65.6)
Loop diuretics	1,611 (50.0)	512 (58.5)	285 (47.9)	527 (49.1)	287 (42.3)
PPI	1,514 (47.0)	377 (43.1)	274 (46.1)	532 (49.5)	331 (48.8)
Digoxin	873 (27.1)	267 (30.5)	159 (26.7)	303 (28.2)	144 (21.2)
Statins	2,624 (81.4)	679 (77.6)	437 (73.4)	926 (86.2)	582 (85.8)
NSAID	278 (8.6)	69 (7.9)	61 (10.3)	72 (6.7)	76 (11.2)

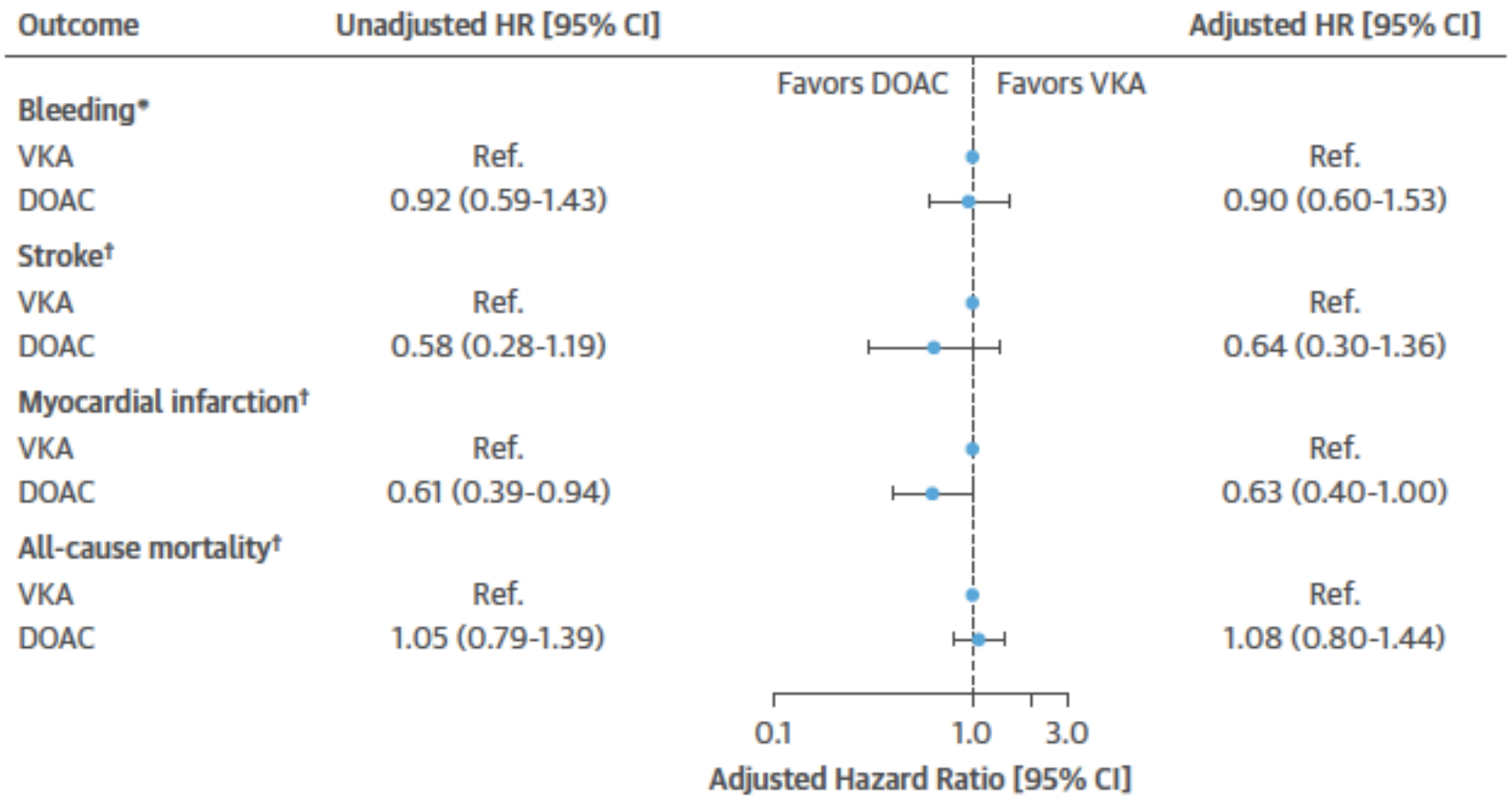
Standardized absolute risks of outcomes at 3 and 12 months

	3 Months			12 Months		
	Events, n	Standardized Absolute Risk	Absolute Risk Difference	Events, n	Standardized Absolute Risk	Absolute Risk Difference
Bleeding, %*						
VKA+DAPT	45	3.93 (2.93 to 5.33)	Ref.	98	9.39 (7.75 to 11.31)	Ref.
DOAC+DAPT	10	1.98 (1.30 to 2.84)	**−1.94 (−3.46 to −0.88)**	27	4.89 (3.34 to 6.59)	**−4.50 (−7.16 to −2.24)**
VKA+SAPT	25	3.16 (2.14 to 4.09)	Ref.	54	6.16 (4.42 to 7.77)	Ref.
DOAC+SAPT	20	3.12 (2.04 to 4.65)	−0.04 (−1.17 to 1.53)	31	6.05 (4.35 to 8.52)	−0.11 (−2.33 to 2.56)
Stroke, %†						
VKA+DAPT	9	0.79 (0.39 to 1.26)	Ref.	24	2.38 (1.37 to 3.27)	Ref.
DOAC+DAPT	7	1.17 (0.60 to 1.80)	0.38 (−0.22 to 0.97)	21	3.51 (2.06 to 4.93)	1.13 (−0.57 to 3.04)
VKA+SAPT	13	1.44 (0.82 to 2.29)	Ref.	28	3.14 (2.21 to 4.19)	Ref.
DOAC+SAPT	5	0.94 (0.33 to 1.66)	−0.51 (−1.50 to 0.33)	10	2.03 (0.78 to 3.46)	−1.11 (−2.88 to 0.65)
MI, %†						
VKA+DAPT	31	2.96 (2.15 to 3.90)	Ref.	62	5.75 (4.49 to 7.32)	Ref.
DOAC+DAPT	18	2.73 (1.76 to 4.11)	−0.23 (−1.38 to 1.31)	31	5.35 (3.63 to 7.56)	−0.40 (−2.63 to 2.48)
VKA+SAPT	37	4.19 (2.91 to 5.47)	Ref.	72	8.35 (6.32 to 10.23)	Ref.
DOAC+SAPT	15	2.66 (1.60 to 3.66)	**−1.53 (−3.08 to −0.11)**	28	5.36 (3.35 to 6.92)	**−2.99 (−5.90 to −0.19)**
All-cause mortality, %†						
VKA+DAPT	41	4.14 (3.20 to 5.01)	Ref.	108	10.48 (8.64 to 12.38)	Ref.
DOAC+DAPT	26	3.44 (2.50 to 4.67)	−0.70 (−1.73 to 0.53)	52	8.79 (6.92 to 11.00)	−1.69 (−4.25 to 1.30)
VKA+SAPT	41	4.82 (3.65 to 6.04)	Ref.	125	14.56 (12.37 to 17.06)	Ref.
DOAC+SAPT	31	5.29 (3.94 to 6.76)	0.47 (−0.74 to 2.08)	80	15.82 (13.03 to 19.10)	1.26 (−1.95 to 5.60)

Outcome-specific HRs for oral anticoagulation therapy in combination with **dual** antiplatelet therapy



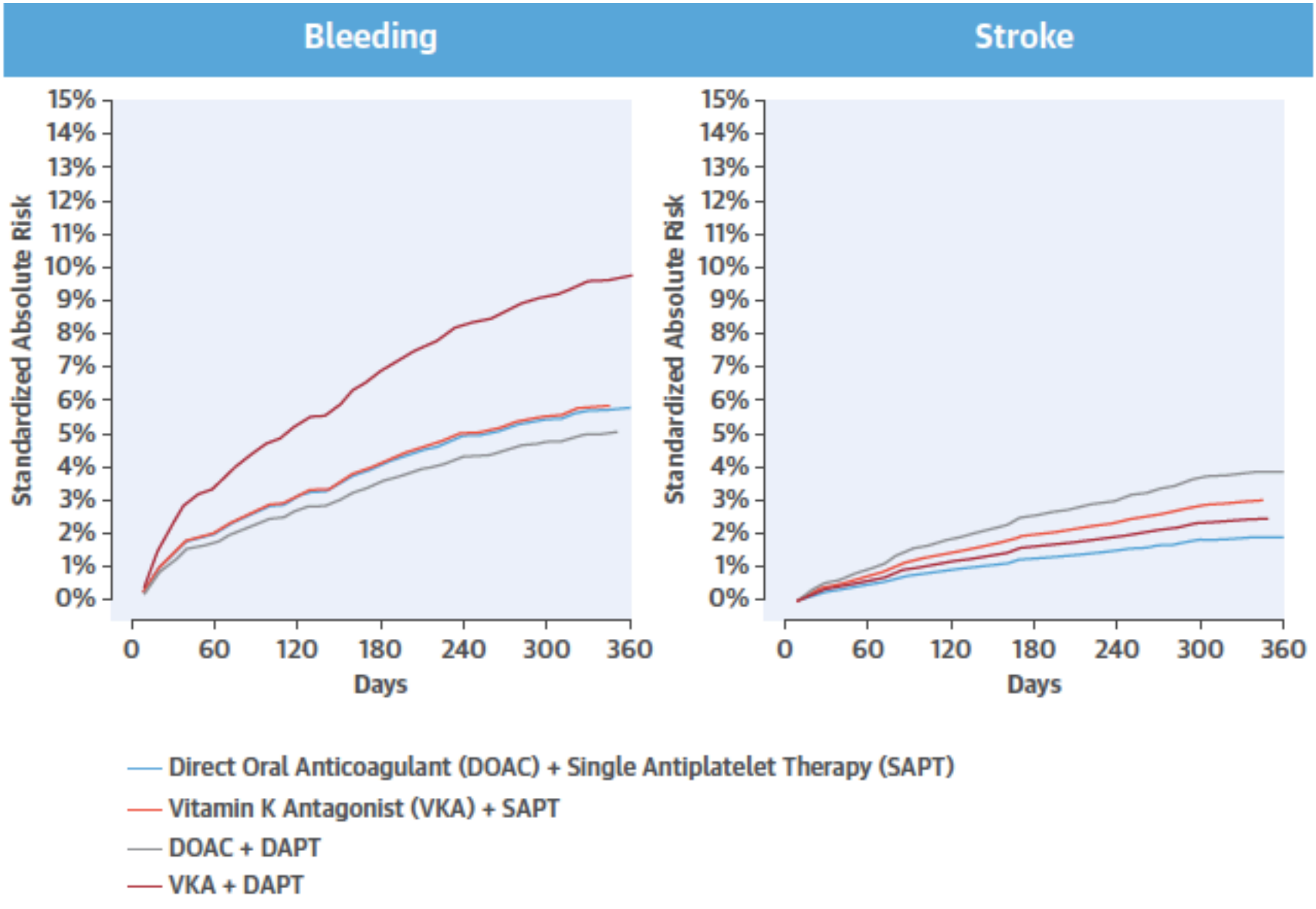
Outcome-specific HRs for oral anticoagulation therapy in combination with **single** antiplatelet therapy



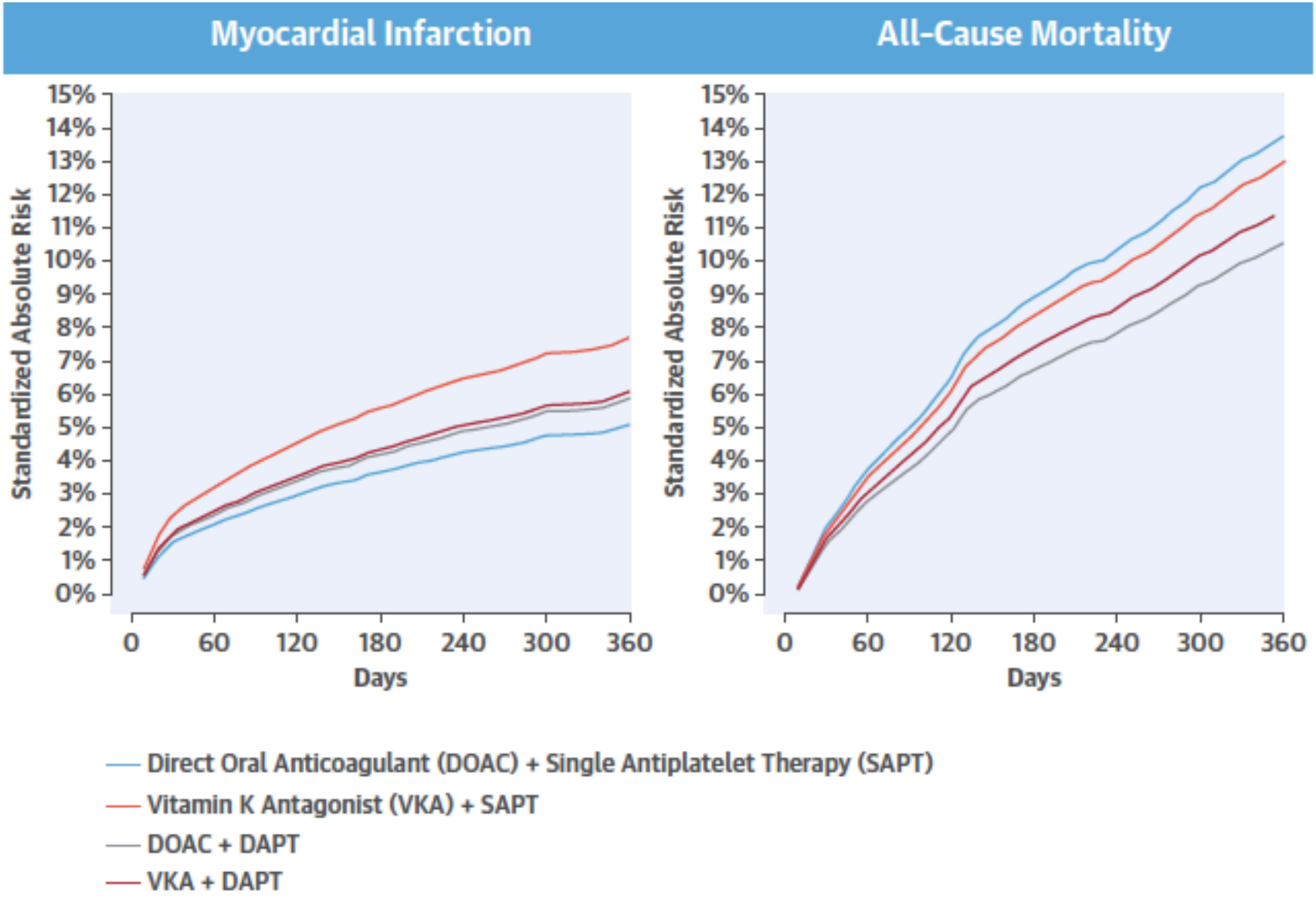
Sensitivity analyses, time-dependent analysis based on multiple-adjusted Cox regression models

	OAC+DAPT	OAC + SAPT
	Time Dependent	Time Dependent
Bleeding*		
VKA	Ref.	Ref.
DOAC	0.39 (0.20–0.76)	0.93 (0.59–1.47)
Stroke†		
VKA	Ref.	Ref.
DOAC	1.19 (0.38–3.64)	1.09 (0.58–2.06)
MI†		
VKA	Ref.	Ref.
DOAC	0.85 (0.49–1.50)	0.75 (0.48–1.16)
All-cause mortality†		
VKA	Ref.	Ref.
DOAC	1.19 (0.75–1.88)	1.35 (0.96–1.93)

CENTRAL ILLUSTRATION Anticoagulants and Antiplatelets in AF: Standardized Absolute Risks



CENTRAL ILLUSTRATION Anticoagulants and Antiplatelets in AF: Standardized Absolute Risks



Conclusions

- In a nationwide cohort of AF patients following MI, PCI, or both, DOAC+DAPT was associated with a significantly decreased risk of bleeding compared with VKA+DAPT.
- No significant differences in the risk of ischemic stroke, MI, or all-cause mortality were found between VKA+DAPT and DOAC+DAPT.
- Despite lack of trial evidence on the safety and effectiveness of DOAC versus VKA in combination with antiplatelets, DOACs seem safe and effective in real-world AF patients following MI or PCI.