Conoscere e Curare il Cuore 2019

DOMENICA 3 MARZO

CHE NESSO C'È TRA FIBRILLAZIONE ATRIALE, TERAPIA ANTICOAGULANTE E DEMENZA ?

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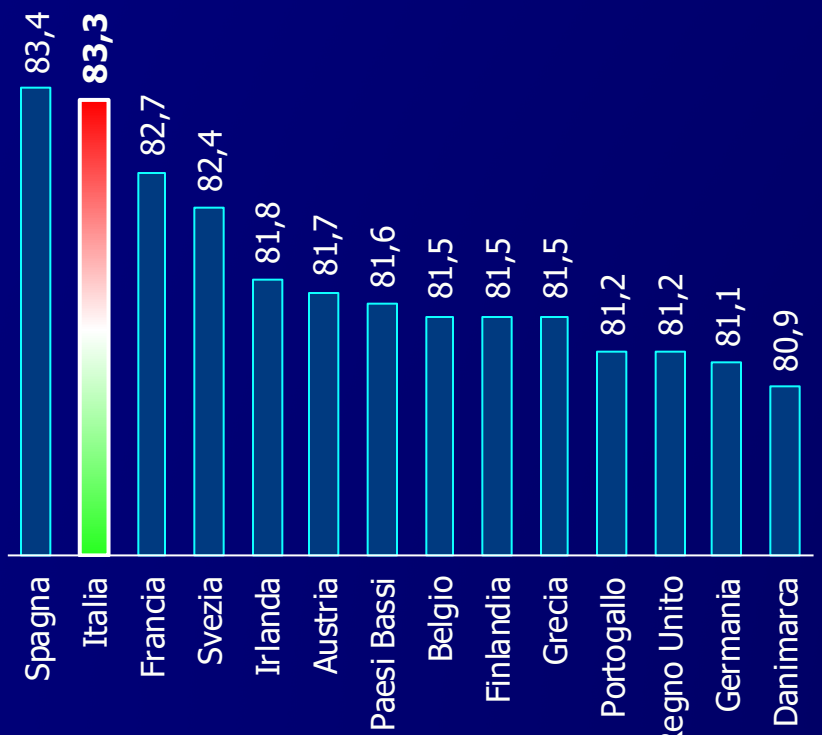
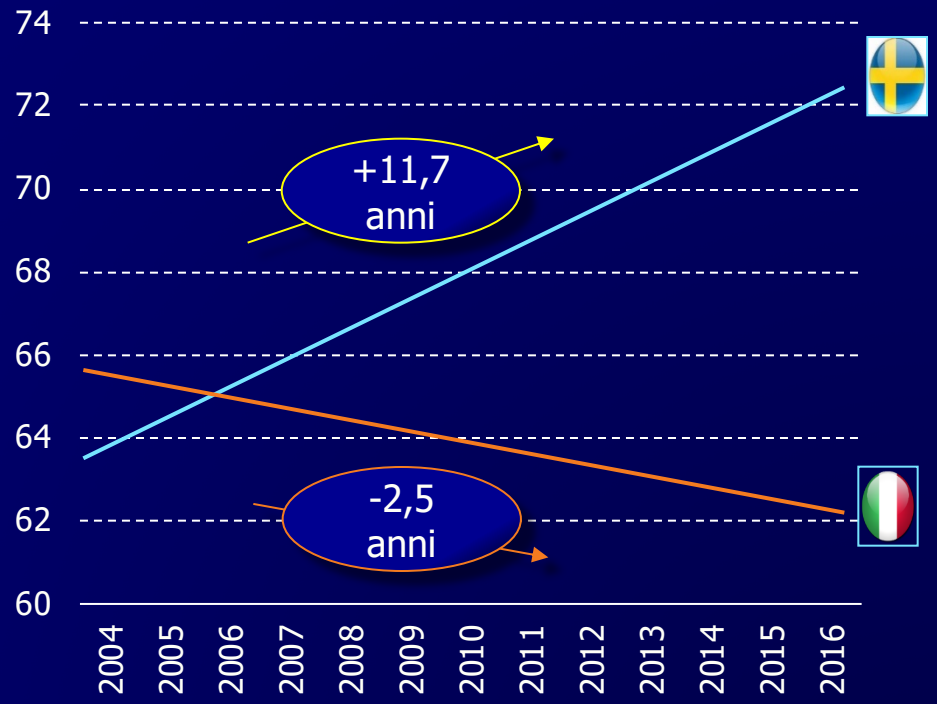
Speranza di vita ed Anni in buona salute

ISTAT 16.5.2018
84,9 anni donne
80,6 anni uomini





Multidimensional frailty indexes

List of variables used by the Canadian Study of Health and Aging to construct the 70-item CSHA Frailty Index

- Changes in everyday activities
- Head and neck problems
- Poor muscle tone in neck
- Bradykinesia, facial
- Problems getting dressed
- Problems with bathing
- Problems carrying out personal grooming
- Urinary incontinence
- Toileting problems
- Bulk difficulties
- Rectal problems
- Gastrointestinal problems
- Problems cooking
- Sucking problems
- Problems going out alone
- Impaired mobility
- Musculoskeletal problems
- Bradykinesia of the limbs
- Poor muscle tone in limbs
- Poor limb coordination
- Poor coordination, trunk
- Poor standing posture
- Irregular gait pattern
- Falls
- Mood problems
- Feeling sad, blue, depressed
- History of depressed mood
- Tiredness all the time
- Depression (clinical impression)
- Sleep changes
- Restlessness
- Memory changes
- Short-term memory impairment
- Long-term memory impairment
- Changes in general mental functioning
- Onset of cognitive symptoms
- Clouding or delirium
- Paranoid features
- History relevant to cognitive impairment or loss
- Family history relevant to cognitive impairment or loss
- Impaired vibration
- Tremor at rest
- Postural tremor
- Intention tremor
- History of Parkinson's disease
- Family history of degenerative disease
- Seizures, partial complex
- Seizures, generalized
- Syncope or blackouts
- Headache
- Cerebrovascular problems
- History of stroke
- History of diabetes mellitus
- Arterial hypertension
- Peripheral pulses
- Cardiac problems
- Myocardial infarction
- Arrhythmia
- Congestive heart failure
- Lung problems
- Respiratory problems
- History of thyroid disease
- Thyroid problems
- Skin problems
- Malignant disease
- Breast problems
- Abdominal problems
- Presence of snout reflex
- Presence of the palmomental reflex
- Other medical history

CSHA Clinical classification

1 *Very fit* — robust, active, energetic, well motivated and fit; these people commonly exercise regularly and are in the most fit group for their age

2 *Well* — without active disease, but less fit than people in category 1

3 *Well, with treated comorbid disease* — disease symptoms are well controlled compared with those in category 4

4 *Apparently vulnerable* — although not frankly dependent, these people commonly complain of being "slowed up" or have disease symptoms

5 *Mildly frail* — with limited dependence on others for instrumental activities of daily living

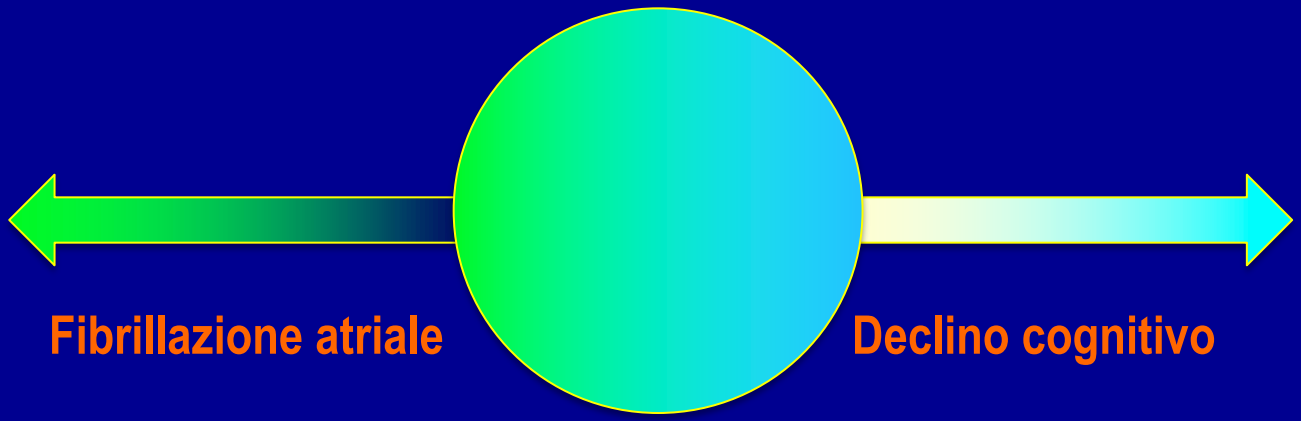
6 *Moderately frail* — help is needed with both instrumental and non-instrumental activities of daily living

7 *Severely frail* — completely dependent on others for the activities of daily living, or terminally ill

Note: CSHA = Canadian Study of Health and Aging.

Esiste un nesso ?

Esiste un nesso ?



Dementia and Atrial Fibrillation - cross-sectional, prospective and retrospective studies

Study (year)	Number of patients	Age (years)	Diagnosis screening of dementia or CI	Results
Ott et al. (1997)	6,584 (195 with AF)	69.2	MMSE score < 26	Positive associations of AF with both dementia (odds ratio 2.3) and CI (1.7)
Jozwiak et al. (2006)	2,314 (hospitalized)	76	MMSE score < 24	Positive association of AF with CI (odds radio 1.56)
Elias et al. (2006)	1,011 men (59 with AF)	61	Neuropsychological testing	Significantly lower mean levels of cognitive performance in men with AF.
Kawabata-Yoshihara et al. (2012)	1,524 (37 with AF)	> 65	DSM-IV criteria	Odds ratio for dementia in participants with AF was 2.8
Di Nisio et al. (2015)	784 (103 with AF)		DSM-IV	AF was associated with 2.0-fold increase in vascular dementia and 1.72-fold increase in AD
Alonso et al. (2017)	6,432 (611 with AF)	76 (no AF); 79 (with AF)	Neurocognitive battery	AF was associated with increased odds of dementia (2.25) and CI (1.28).

Study (year), design	N	Age (years)	Diagnosis screening of dementia or CI	Follow-up (years)	Results
Tilvis et al. (2004), prospective	650	>75	MMSE and CDR	up 10	Five-years decline was predicted by AF (risk of 2.8)
Forti et al. (2007), prospective	611	75.2	Neurocognitive battery and MMSE	3.8	AF associated with dementia with a risk of 4.63 among those with mild cognitive impairment
Peters et al. (2009), prospective	3,336	≥80	longitudinal MMSE scores	2	No relationship of AF with annual change in MMSE (multivariate analysis)
Bunch et al. (2010), prospective	37,025	60.6	ICD-9 codes	5	AF was independently associated with all forms of dementia
Dublin et al. (2011), prospective	3,045	74.3	Cognitive abilities screening instrument	6.8	AF was associated with a 40 to 50% higher risk of both AD and all-cause dementia, independent of stroke.
Marengoni et al. (2011), prospective	685	>75	MMSE	6	AF was not associated with dementia
Haring et al. (2013), prospective	6,455 women	65–79	MMSE and neurocognitive examination	8.4	No significant association between AF and CI
Marzona et al. (2012), prospective	31,506	66.5	MMSE	4.66	AF was associated with an increased risk of CI (hazard ratio 1.14) and new dementia (1.30)
Thacker et al. (2013), prospective	5,150	73	MMSE	7	AF was associated with CI in the absence of clinical stroke
Rusanen et al. (2014), prospective	1,510	65–79	ICD and DSM-IV	7.8	AF in late-life was an independent risk factor for dementia (risk 2.610
de Bruijn et al. (2015), longitudinal community-based study	6,514	68.3 without AF; 75.7 with AF	DSM-III	20	AF was associated with an increased risk of dementia, independent of clinical stroke
Liao et al. (2015), longitudinal community-based study	332,665	70.3	ICD	14	AF was significantly associated with the occurrence of dementia (risk 1.42)
Marzona et al. (2016), retrospective	1,600,200 (without AF); 27,431 (hospitalized for AF)	75.2 (without AF); 78.4 (with AF)	ICD	10	AF was associated with a higher risk of dementia (17%)
Singh-Manoux et al. (2017), prospective	10,538 (for analysis of incident dementia)	45–85	Serial battery of cognitive tests	26.6	AF had 87% excess risk of dementia
Nishtala et al. (2018), cross-sectionally and longitudinally	2,682	72	Neurocognitive battery	6	AF was significantly associated with CI
Chen et al. (2018), prospective	12,515	56.9	Cognitive tests	20	AF was associated with an increased risk of dementia (risk 1.23) independent of ischemic stroke

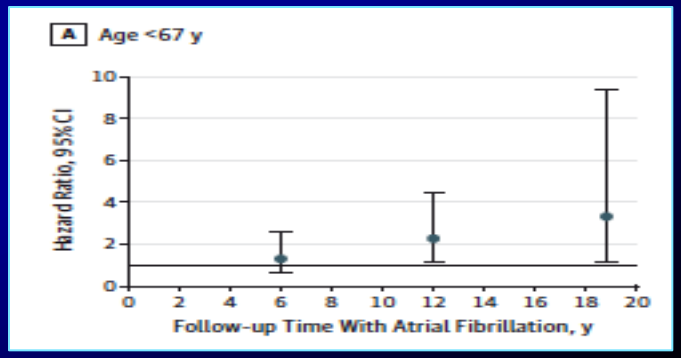
Ferrera Lisboa da Silva RM et alFront Neurosci. 2019;13:18

Incidence of dementia in the general population

Characteristic	Dementia			Alzheimer Disease		
		HR (95% CI)			HR (95% CI)	
	Cases, No. (%)	Model I[a]	Model II[b]	Cases, No. (%)	Model I[a]	Model II[b]
Including Stroke						
Atrial fibrillation						
Prevalent (n = 6514)	994 (15.3)	1.34 (1.03-1.74)	1.33 (1.02-1.73)	787 (12.1)	1.30 (0.96-1.75)	1.29 (0.95-1.75)
Incident (n = 6194)	932 (15.0)	1.13 (0.90-1.41)	1.23 (0.98-1.56)	741 (12.0)	1.09 (0.85-1.40)	1.18 (0.91-1.54)
Censored for Stroke						
Atrial fibrillation						
Prevalent (n = 6314)	844 (13.4)	1.35 (1.01-1.81)	1.33 (0.99-1.78)	705 (11.2)	1.31 (0.94-1.81)	1.28 (0.93-1.78)
Incident (n = 6019)	793 (13.2)	1.14 (0.89-1.49)	1.24 (0.96-1.61)	665 (11.0)	1.08 (0.82-1.42)	1.15 (0.87-1.54)

Characteristic	Dementia, HR (95% CI)			
	No./Total No. (%)[b]	Age, <67 y	No./Total No. (%)[b]	Age, ≥67 y
Atrial fibrillation				
Prevalent	213/3096 (6.9)	1.91 (0.85-4.26)	781/3418 (22.8)	1.28 (0.97-1.70)
Incident	206/3049 (6.8)	1.81 (1.11-2.94)	726/3145 (23.1)	1.12 (0.85-1.46)

Time with FA
In younger pts



de Bruijn RF et al JAMA Neurol. 2015;72(11):1288-94

Incidence of dementia in FA with no cognitive impairment at baseline

Variable	HR (95% CI), *P* value	
	Women	Men
Bivariable model		
IMRS: moderate vs low	1.74 (1.54–1.97), $P < .001$	1.89 (1.70–2.09), $P < .001$
IMRS: high vs low	3.09 (2.71–3.51), $P < .001$	2.70 (2.39–3.06), $P < .001$
CHA_2DS_2-VASc score: 2 vs ≤1	3.13 (2.35–4.17), $P < .001$	3.45 (2.99–3.98), $P < .001$
CHA_2DS_2-VASc score: ≥3 vs ≤1	7.77 (5.94–10.17), $P < .001$	4.75 (4.15–5.44), $P < .001$
Multivariable model		
IMRS: moderate vs low	1.75 (1.55–1.98), $P < .001$	1.72 (1.55–1.91), $P < .001$
IMRS: high vs low	3.12 (2.74–3.55), $P < .001$	2.41 (2.13–2.73), $P < .001$
CHA_2DS_2-VASc score: 2 vs ≤1	3.11 (2.34–4.14), $P < .001$	3.43 (2.97–3.97), $P < .001$
CHA_2DS_2-VASc score: ≥3 vs ≤1	7.74 (5.92–10.11), $P < .001$	4.70 (4.11–5.38), $P < .001$

Variable	HR (95% CI), *P* value	
	Women	Men
CHA_2DS_2-VASc score ≤1		
IMRS: moderate vs low	1.73 (1.03–2.92), $P = .04$	1.51 (0.76–3.03), $P = .24$
IMRS: high vs low	4.08 (1.37–14.79), $P = .03$	1.25 (0.16–9.62), $P = .83$
CHA_2DS_2-VASc score 2		
IMRS: moderate vs low	1.64 (1.25–2.16), $P < .04$	1.52 (1.25–1.84), $P < .001$
IMRS: high vs low	1.79 (1.08–2.97), $P = .02$	2.05 (1.60–2.65), $P < .001$
CHA_2DS_2-VASc score ≥3		
IMRS: moderate vs low	1.79 (1.55–2.06), $P < .001$	1.71 (1.48–1.98), $P < .001$
IMRS: high vs low	3.18 (2.75–3.68), $P < .001$	2.31 (1.96–2.72), $P < .001$

IMRS: Hct, WBC, PLT, MCV, MCHC, RDW, MPV, Na^+, K^+, Bicarbonate, Ca^{++}, Glucose, Creatinine, Age and Gender

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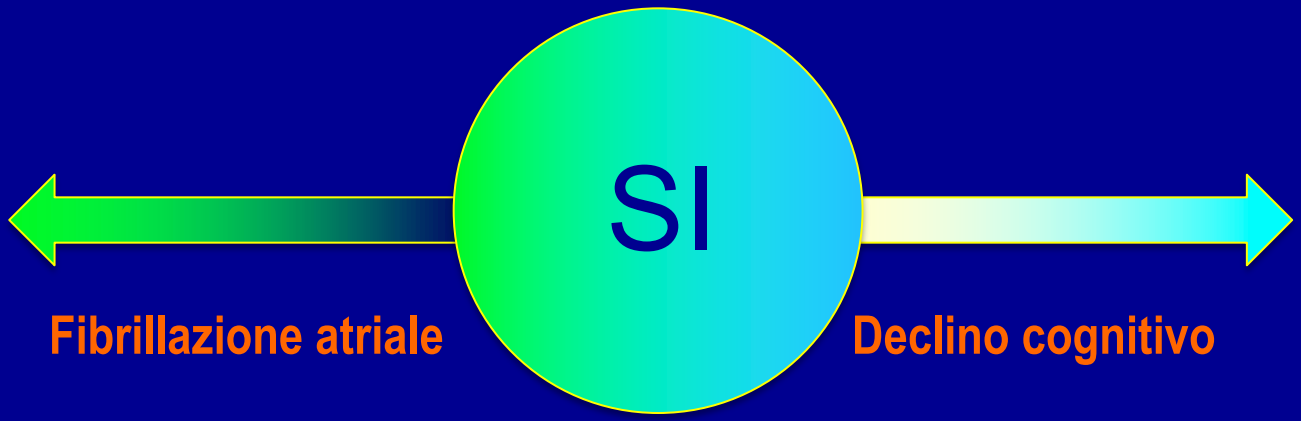
Graves KG et al Heart Rhythm. 2019;16(1):3-9

Esiste un nesso ?



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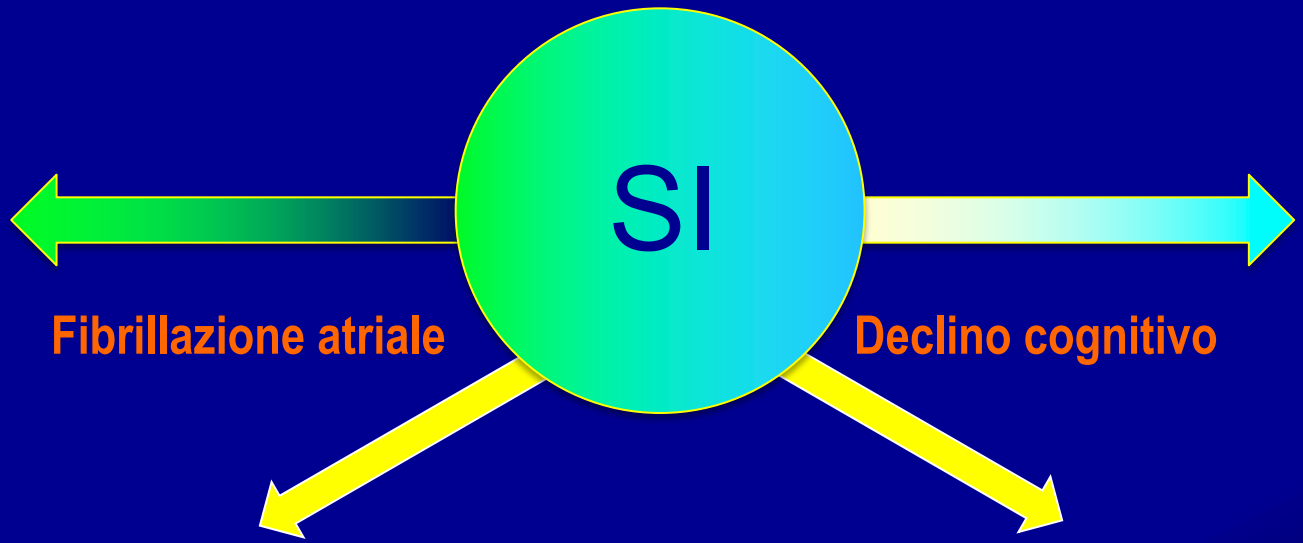
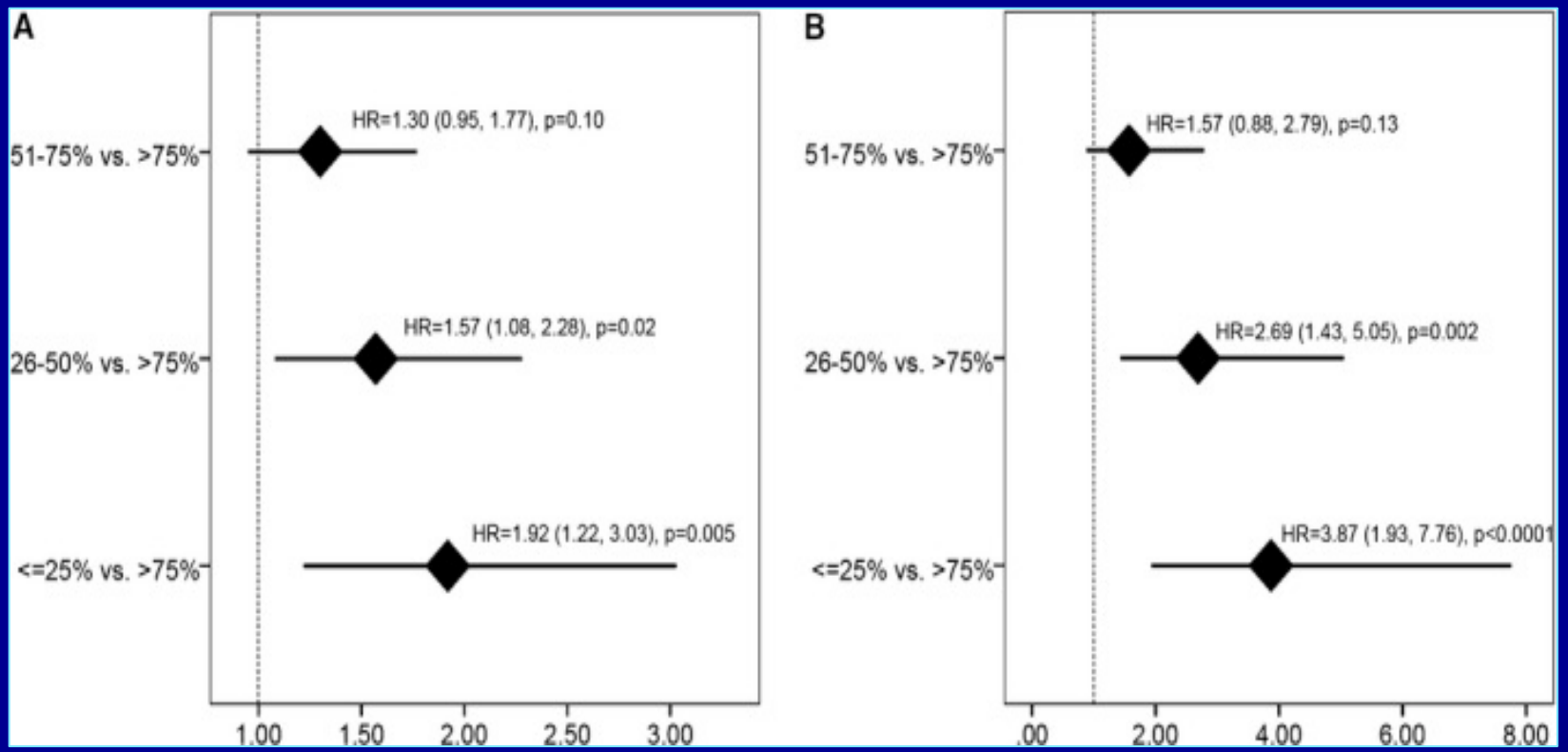
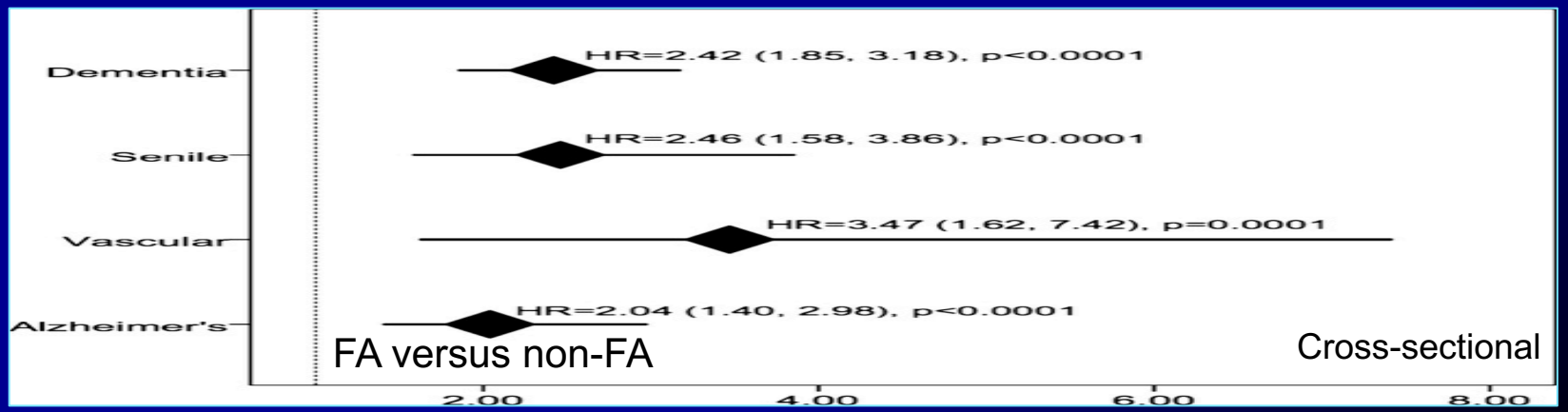


Esiste un nesso ?

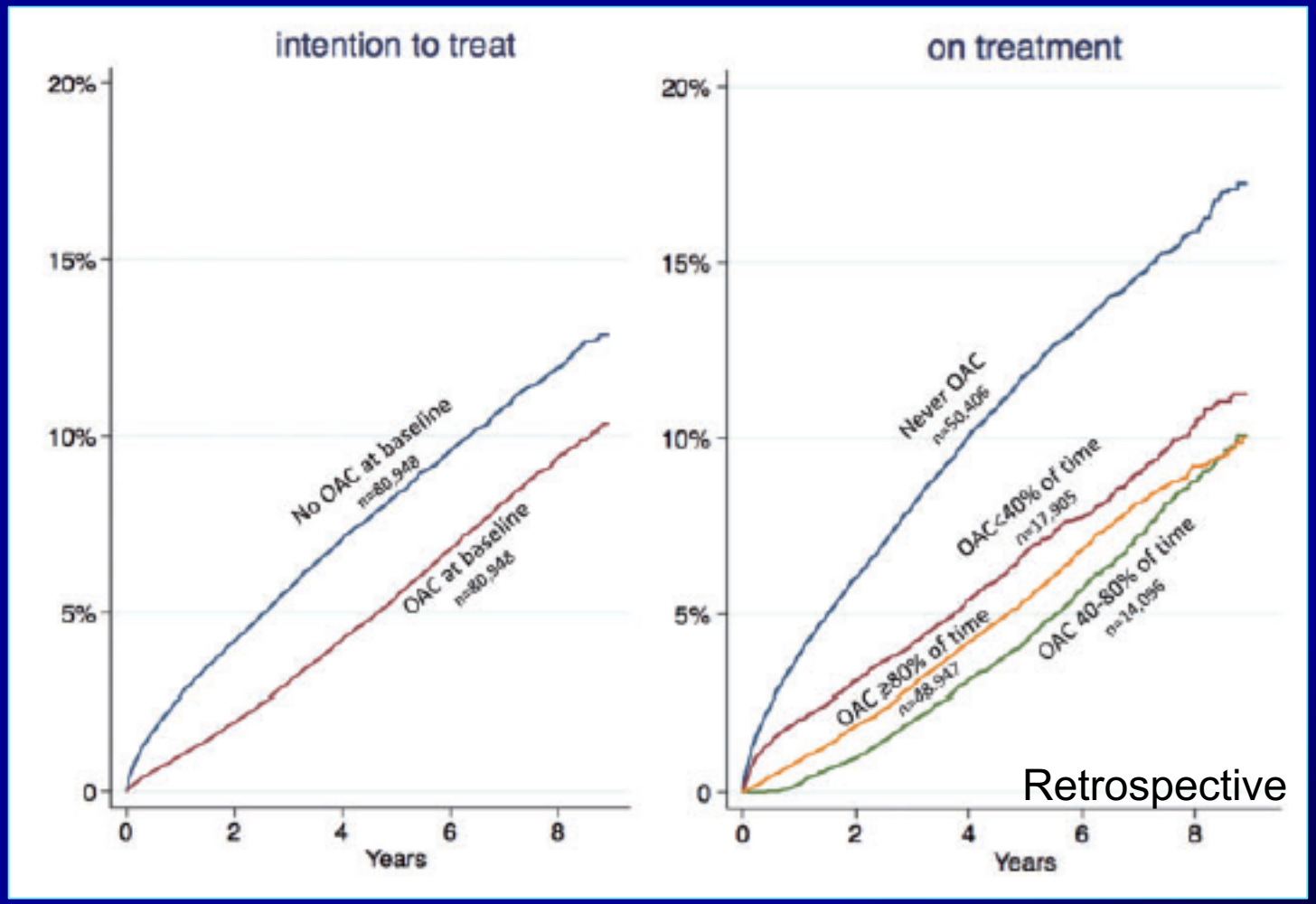
VKA in FA patients and non-FA patients with NO history of dementia





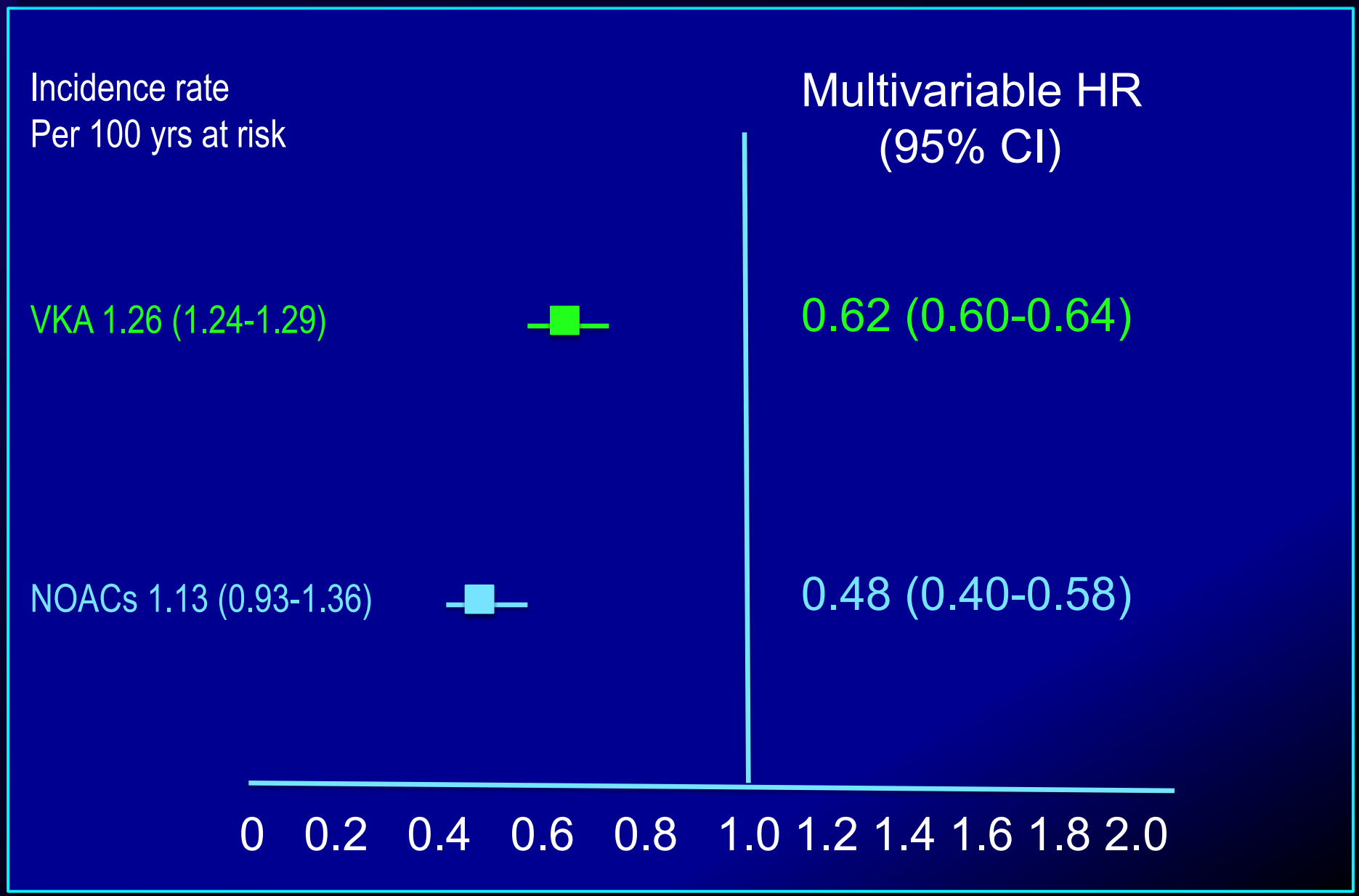
Bunch TJ et al J Am Heart Assoc. 2016 Jul 11;5(7

VKA and NOAC in FA patients



Friberg L and Rosenqvist M European Heart Journal (2018) 39, 453–460

VKA and NOAC in FA patients



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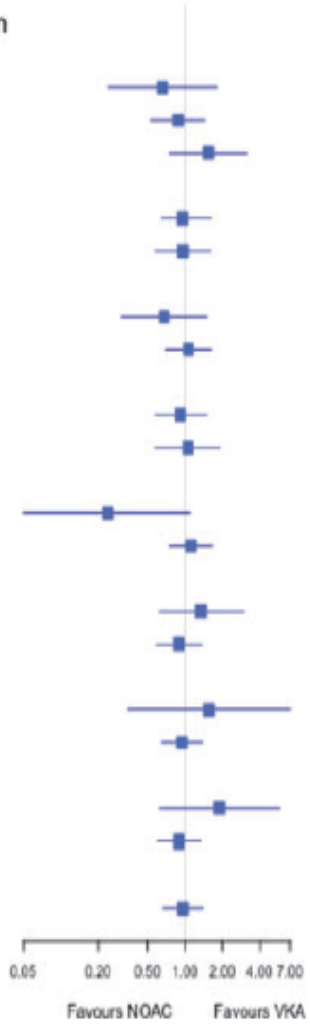
VKA and NOAC in FA patients

Subgroup	Level	HR [95%CI]	p for interaction
Age group	65-74 years	0.66 [0.24-1.79]	0.339
	75-85 years	0.88 [0.53-1.44]	
	>=85 years	1.55 [0.76-3.15]	
Gender	Male	0.96 [0.56-1.64]	0.686
	Female	0.97 [0.58-1.62]	
Heart failure	Yes	0.68 [0.31-1.49]	0.006
	No	1.07 [0.70-1.64]	
Hypertension	Yes	0.92 [0.58-1.149]	0.546
	No	1.06 [0.58-1.92]	
Diabetes	Yes	0.24 [0.05-1.09]	0.064
	No	1.12 [0.76-1.66]	
Ischaemic stroke	Yes	1.35 [0.62-2.97]	0.152
	No	0.89 [0.59-1.37]	
Bleeding hospitalization	Yes	1.56 [0.35-7.00]	0.836
	No	0.95 [0.65-1.39]	
Myocardial infarction	Yes	1.89 [0.62-5.79]	0.191
	No	0.89 [0.60-1.33]	
All patients		0.97 [0.67-1.40]	



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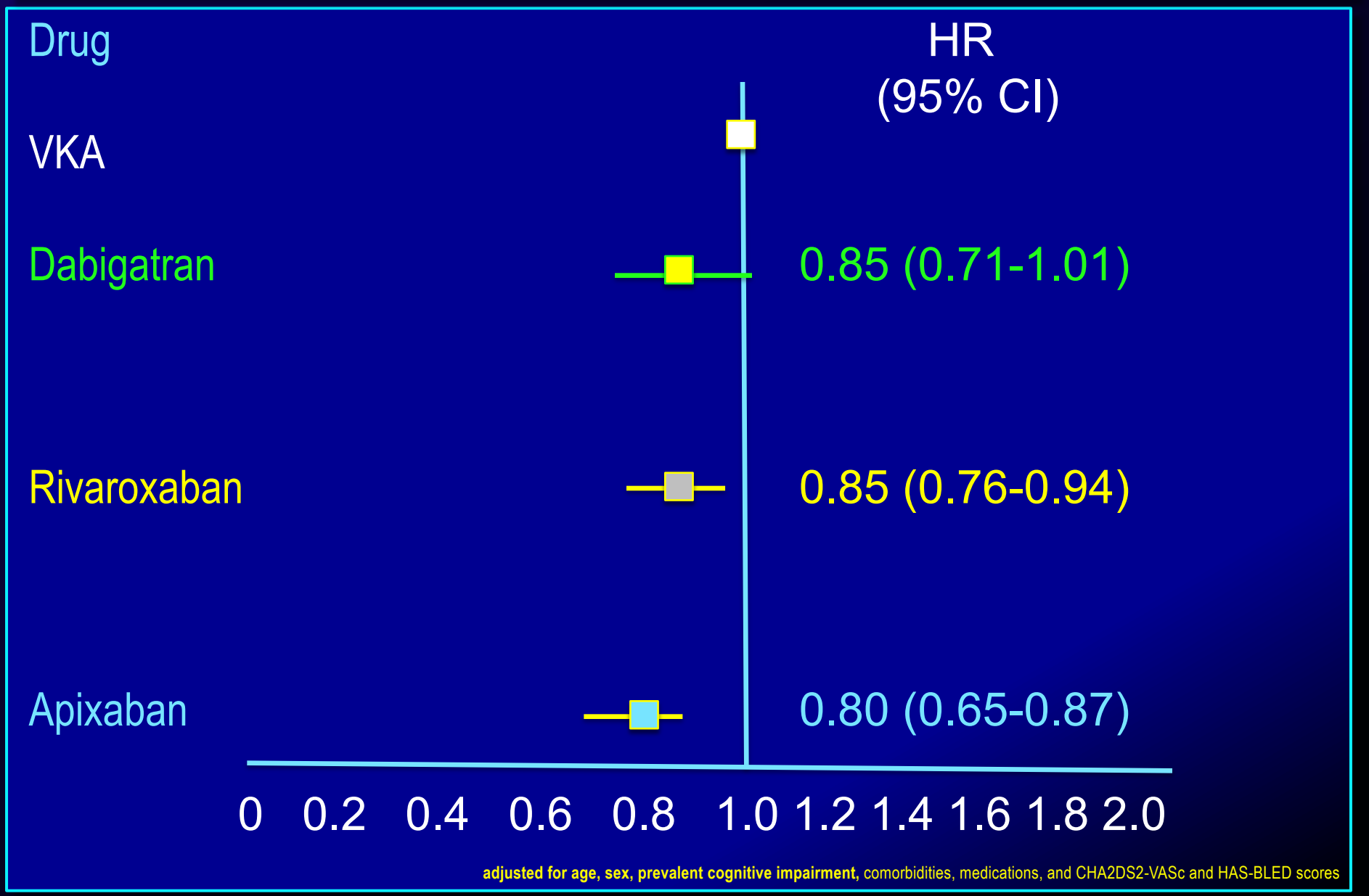
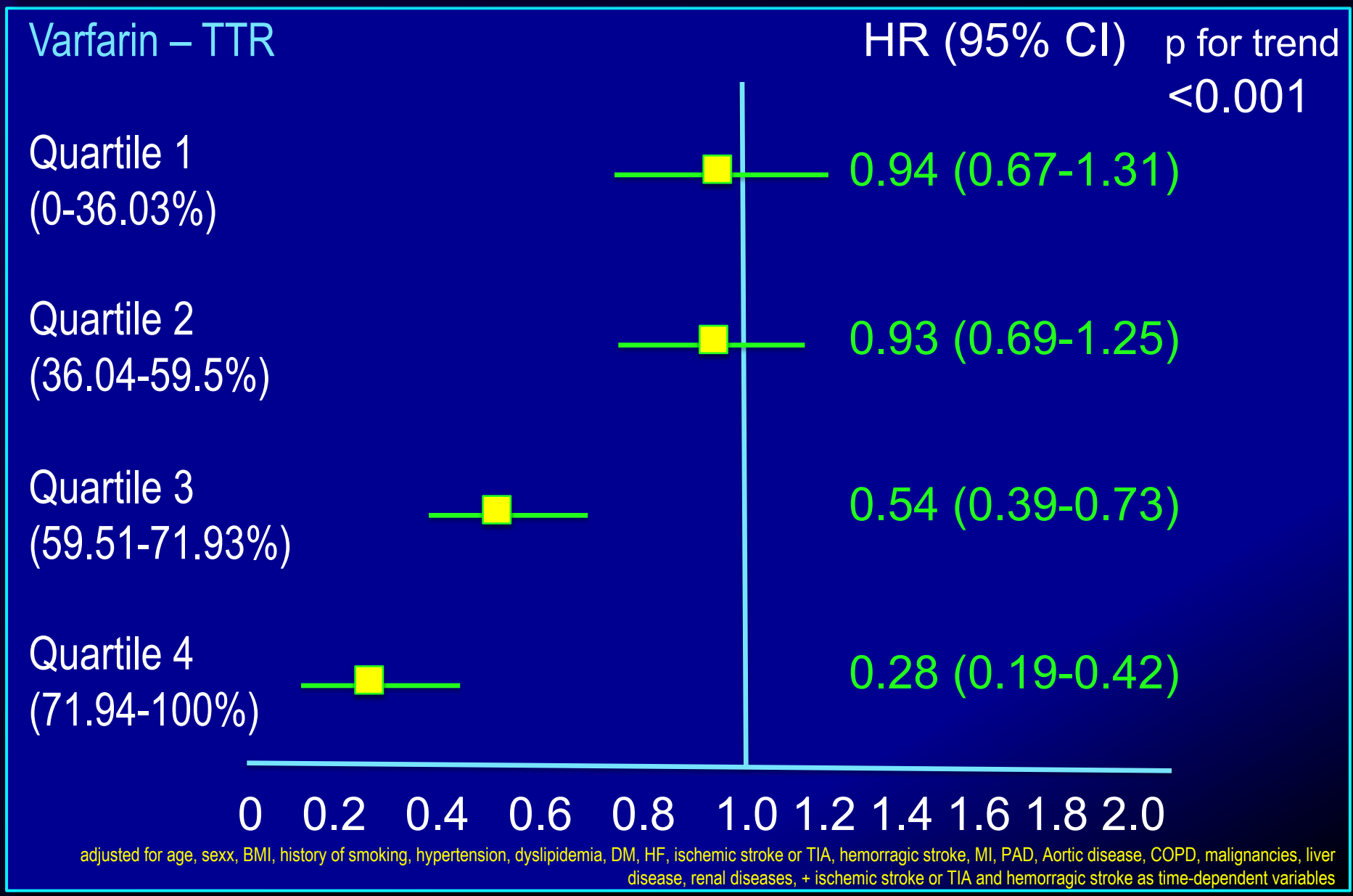


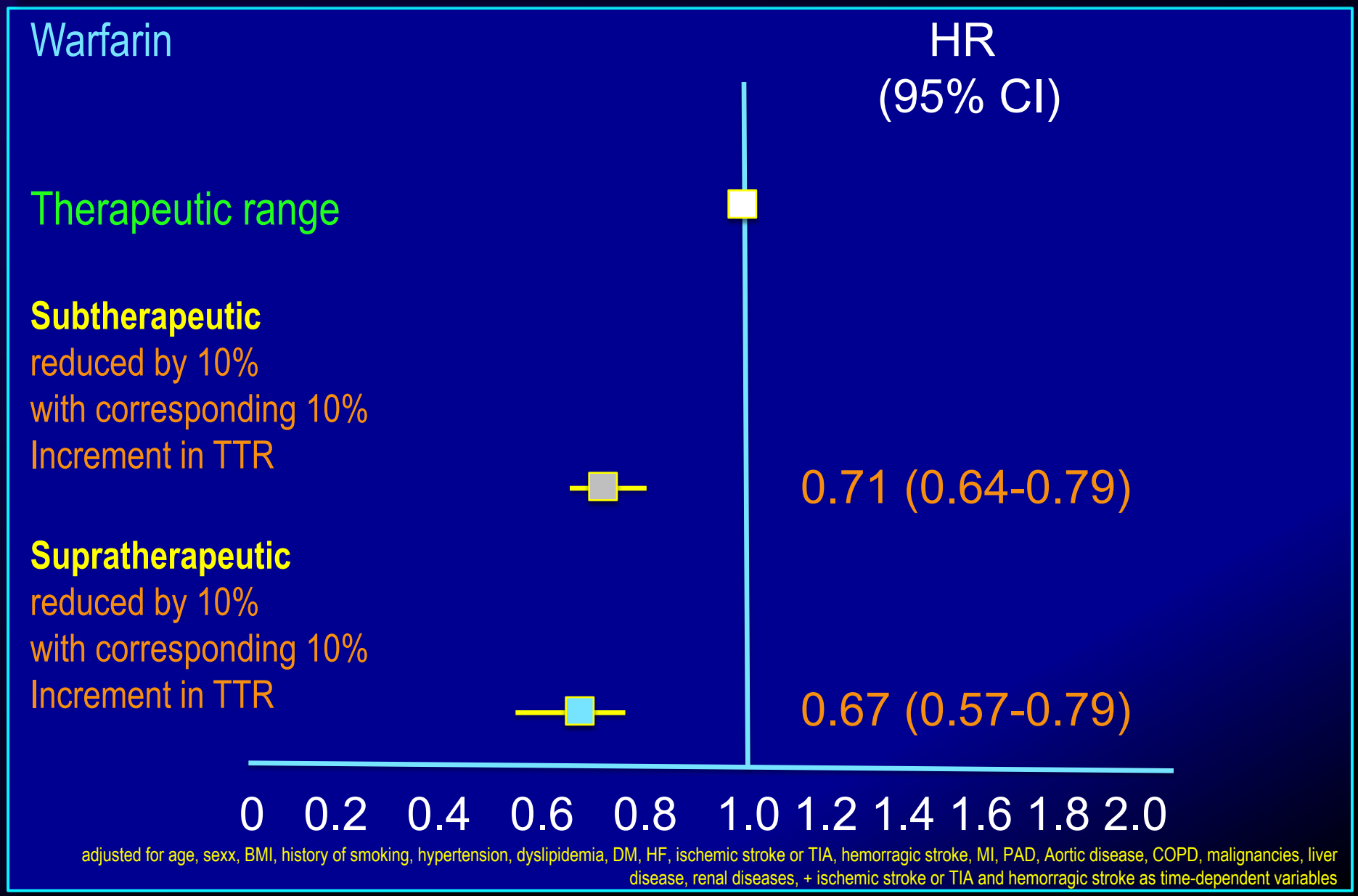
Chen L et al J Am Heart Assoc . 2018;7:e009561

VKA in FA patients – Role of TTR



Madhavan M et al Mayo Clin Prog. 2018, 93,2:145-154

VKA in FA patients – Role of TTR



adjusted for age, sexx, BMI, history of smoking, hypertension, dyslipidemia, DM, HF, ischemic stroke or TIA, hemorragic stroke, MI, PAD, Aortic disease, COPD, malignancies, liver disease, renal diseases, + ischemic stroke or TIA and hemorragic stroke as time-dependent variables

Madhavan M et al Mayo Clin Prog. 2018, 93,2:145-154

Esiste un nesso ?

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Preventive measures of cognitive dysfunction in patients with AF	Class
Appropriate anticoagulation in patients with AF and stroke risk factors should be applied for the prevention of cognitive dysfunction.	♥
Consider NOAC instead of VKA when using oral anticoagulation for the prevention of stroke in AF, which may have a beneficial effect on subsequent cognitive disorders	♥
In patients with AF managed with long-term VKA, a high anticoagulation time in therapeutic range may be beneficial for optimal prevention of new-onset dementia	♥
General health measures (prevention of smoking, hypertension, obesity and diabetes, sleep apnoea, and appropriate control of all risk factors) may reduce the concomitant risks of AF (new onset or recurrences) and stroke, with a putative benefit on cognitive function.	♥
Prevention of cognitive dysfunction in AF may include general measures proposed in vascular dementia or Alzheimer's disease.	♥
Cognitive assessment should be performed in AF patients where there is suspicion of cognitive impairment.	♥

European Heart Rhythm Association (EHRA)/Heart Rhythm Society (HRS)/Asia Pacific Heart Rhythm Society (APHRS)/Latin American Heart Rhythm Society (LAHRS) expert consensus on arrhythmias and cognitive function: what is the best practice?

Europace (2018)20, 1399–1400

Esiste un nesso ?

La FA è dementigena

portante

...F) (NCT02387229). "Impact of
...l Fibrillation (CAF)
...on cognitive function (US National Library

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OAC protegge le funzioni cognitive

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Esiste un nesso ?

La FA è dementigena

OAC protegge le funzioni cognitive

Forse i NOAC sono meglio di VKA

Sicuramente il TTR è importante

Esiste un nesso ?

DOACs: Trial of Anticoagulation to Prevent IschemicStroke and Neurocognitive Impairment in AF (BRAIN-AF)

DOACs: "Impact of AnticoagulationTherapy on the Cognitive Decline and Dementia in Patients WithNon-Valvular Atrial Fibrillation (CAF)

Secondary objective of assessing the effects of **ablation** andantiarrhythmic on cognitive function (US National Library ofMedicine, 2017b).