



HILTON SORRENTO PALACE
(SORRENTO-NA)

10-13 OTTOBRE 2019



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FIBRILLAZIONE NELL'ANZIANO, AL DI LA' DI UNA SEMPLICE ARITMIA

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Syncope Unit – Centro Ipertensione
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Firenze

Syncope
Unit
Florence



Syncope
Unit
Florence

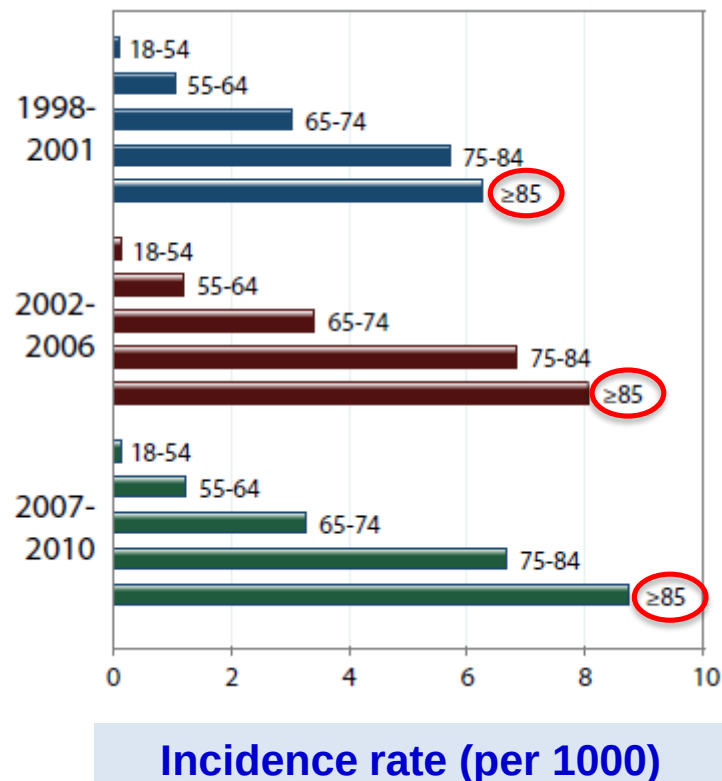


Table 8 Cardiovascular and other conditions independently associated with atrial fibrillation

Characteristic/comorbidity	Association with AF
Genetic predisposition (based on multiple common gene variants associated with AF) ⁶⁴	HR range 0.4–3.2
Older age ¹⁹	HR:
50–59 years	1.00 (reference)
60–69 years	4.98 (95% CI 3.49–7.10)
70–79 years	7.35 (95% CI 5.28–10.2)
80–89 years	9.33 (95% CI 6.68–13.0)

Temporal Trends in Incidence, Prevalence, and Mortality of Atrial Fibrillation in Primary Care

Incidence rate of AF by age-group and year of diagnosis (the UK Clinical Practice Research Datalink, a primary care database – GOLD – N=57 818 patients with incident AF)



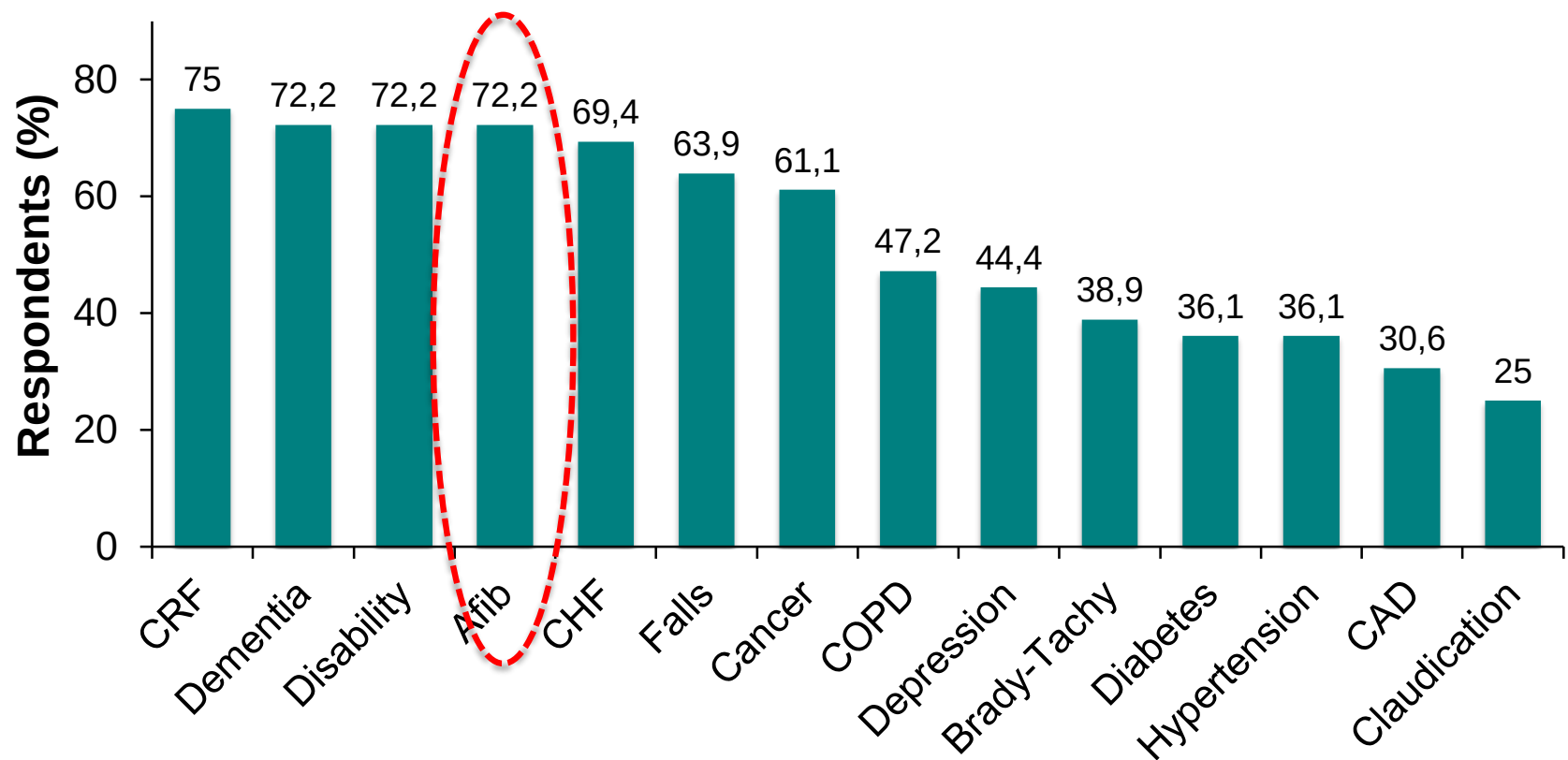
Recommendations for screening for atrial fibrillation

Recommendations for screening for atrial fibrillation

Recommendations	Class ^a	Level ^b	Ref ^c
Opportunistic screening for AF is recommended by pulse taking or ECG rhythm strip in patients >65 years of age.	I	B	130, 134, 155
(AHRE). Patients with AHRE should undergo further ECG monitoring to document AF before initiating AF therapy.	I	B	27, 127
Systematic ECG screening may be considered to detect AF in patients aged >75 years, or those at high stroke risk.	IIb	B	141, 156
aged >75 years, or those at high stroke risk.	IIb	B	18, 128
			30, 135, 157

**Frailty syndrome: an emerging clinical problem
in the everyday management of clinical
arrhythmias: results of the European Heart
Rhythm Association survey**

Comorbidities most frequently associated to the **frailty syndrome**



Afib: atrial fibrillation; **Brady-Tachy:** bradycardia tachycardia syndrome; **CAD:** coronary artery disease; **CRF:** chronic renal failure



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Ma chi è l'anziano fragile ?



Definitions

Comorbidity definition

the presence of one or more additional diseases or disorders co-occurring with a primary disease (eg. HF) or disorder.

Disability definition

the loss of autonomy and the consequent dependence in one or more global activities of daily living.

Frailty definition

Definitions

Comorbidity definition

the presence of one or more additional diseases or disorders co-occurring with a primary disease (eg. HF) or disorder.

Disability definition

the loss of autonomy and the consequent dependence in one or more global activities of daily living.

Frailty definition

??

Fragilità: definizione

- Sindrome multifattoriale, determinata dalla riduzione della fisiologica riserva funzionale e della capacità di resistere a eventi stressanti ambientali (capacità di omeostasi)
- Comporta un aumentato rischio di eventi clinici: disabilità, ospedalizzazione, istituzionalizzazione, morte
- Condizione complessa e dinamica, della quale si sono proposti numerosi modelli

Definizione operativa di fragilità in popolazione anziana generale: Cardiovascular Health Study

1. Forza (handgrip) nel quintile inferiore
2. Velocità del cammino nel quintile inferiore
3. Perdita di peso non intenzionale $\geq 4,5$ kg nell'ultimo anno
4. Facile esauribilità
5. Livello di attività fisica nel quartile inferiore



PHENOTYPE FRAILTY INDEX

Fragile: ≥ 3 componenti

Intermedio (prefragile): 1 o 2 componenti

Non fragile (robusto): 0 componenti

Short Physical Performance Battery (SPPB)

Test dell'equilibrio



Posizione piedi uniti
per 10 sec → 1 punto

NO

tempo: ____ sec
<10 secondi → 0 punti

SI



Posizione semitandem
per 10 sec → 1 punto

NO

tempo: ____ sec
<10 secondi → 0 punti

SI

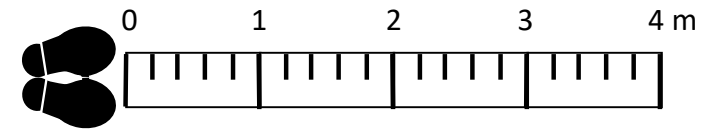


Posizione tandem
tempo: ____ sec
per 10 sec → 2 punti
3-9.9 sec → 1 punto
<3 sec → 0 punti

Punteggio totale: 0-12

Test della marcia

Tempo per percorrere 4 metri di passo normale: ____ sec
(tempo migliore di 2 prove)
<4.8 sec → 4 punti
4.8-6.2 sec → 3 punti
6.3-8.7 sec → 2 punti
>8.7 sec → 1 punto
incapace → 0 punti



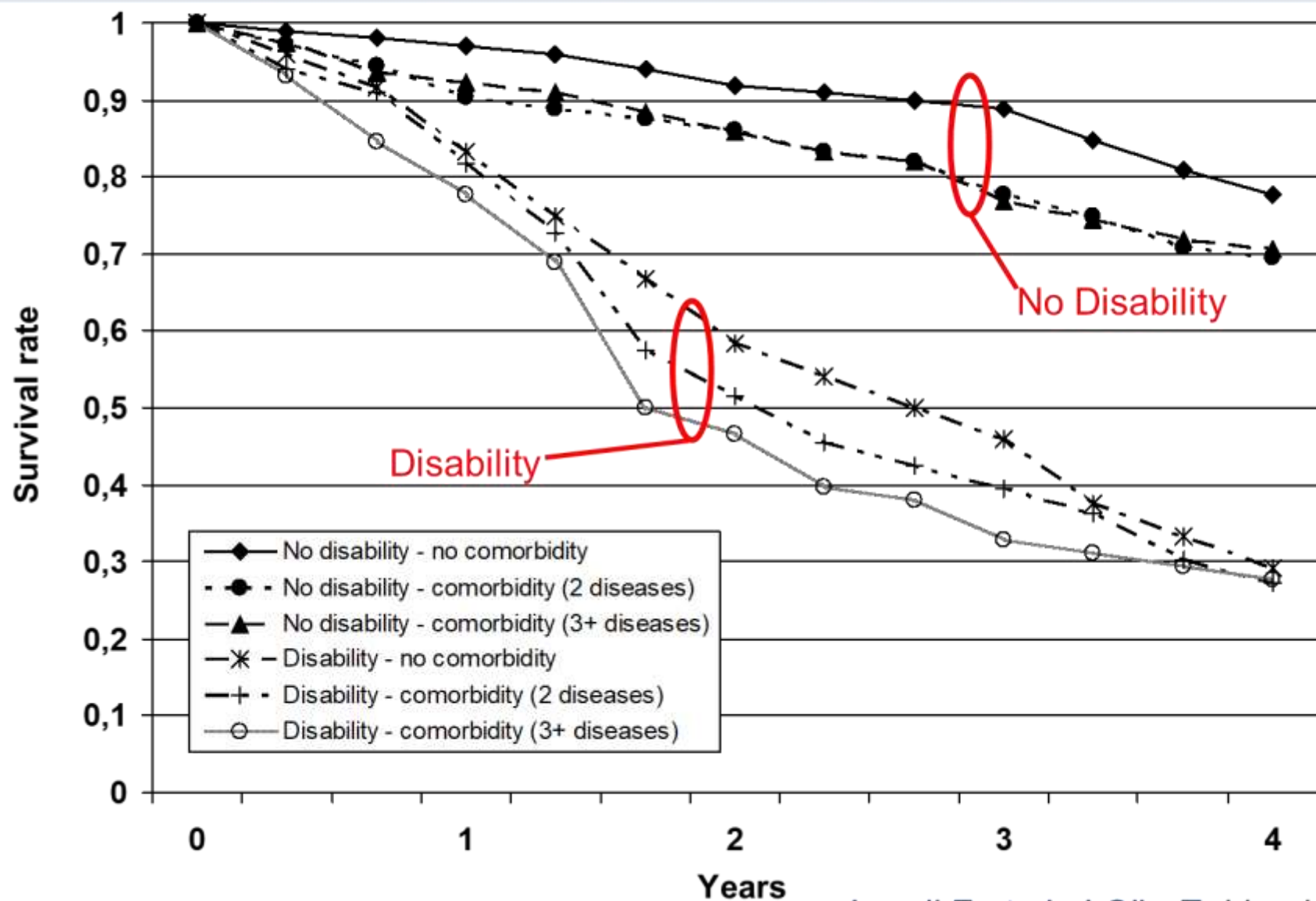
Test della sedia



Capace

Alzarsi e sedersi per 5 volte più velocemente possibile a braccia incrociate
<11.2 sec → 4 punti
11.2-13.7 sec → 3 punti
13.8-16.7 sec → 2 punti
16.8-60 sec → 1 punto
>60 sec o incapace → 0 punti

Disability, more than multimorbidity, was predictive of mortality among older persons aged 80 years and older



EDITORIAL COMMENTARY

Frailty: It's hard to define, but you know it when you see it

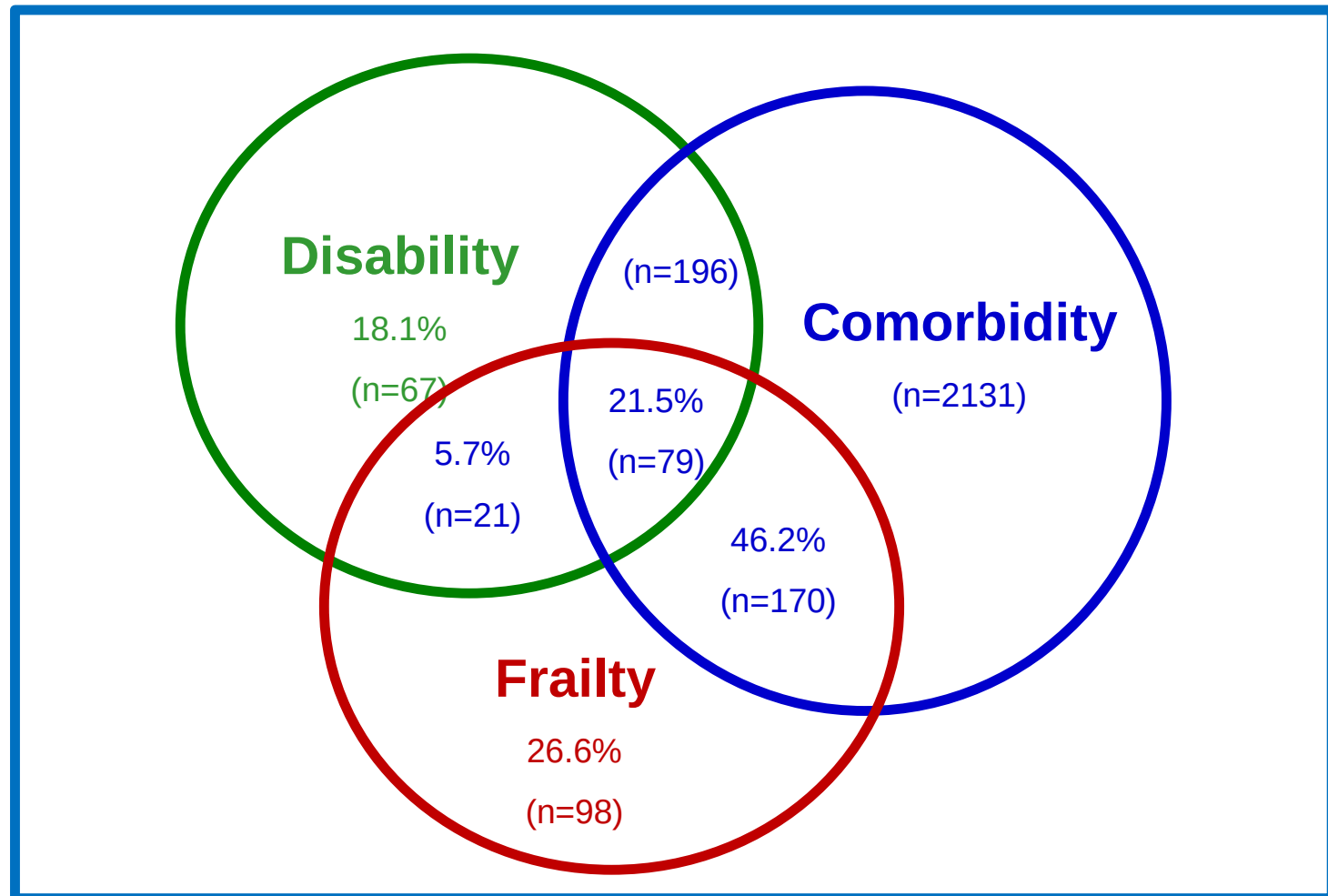
Keith B. Allen, MD

J Thorac Cardiovasc Surg. 2014;148:3117-8



Frailty concept: two 78-year-old patients with severe degenerative mitral valve regurgitation and **comparable Logistic Euro-Score (12%)**

Relationship between comorbidity, disability and **frailty** according to the Phenotype Frailty Index



Winter 1507-1508

IN QUESTO ANTICO OSPEDALE NEI PRIMI ANNI DEL MILLECINQUECENTO

LEONARDO DA VINCI

GENIO UNIVERSALE DEL RINASCIMENTO
ESEGUIÌ LE DISSEZIONI CON CUI DAVA AVVIO ALLO STUDIO AUTOPTICO
SISTEMATICO DELLA ANATOMIA UMANA

E QUESTO VECCHIO, DI POCHE ORE INNANZI LA SUA MORTE, MI DISSE LUI PASSARE I CENTO ANNI,
E CHE NON SI SENTIVA ALCUN MANCAMENTO NE LA PERSONA, ALTRO CHE DEBOLEZZA;
E COSÌ STANDOSI A SEDERE SOPRA UNO LETTO NELLO SPEDALE DI SANTA MARIA NOVA DI FIRENZE,
SANZA ALTRO MOVIMENTO O SEGNO D'ALCUNO ACCIDENTE, PASSÒ DI QUESTA VITA.
E IO NE FECI NOTOMIA, PER VEDERE LA CAUSA DI SÌ DOLCE MORTE.

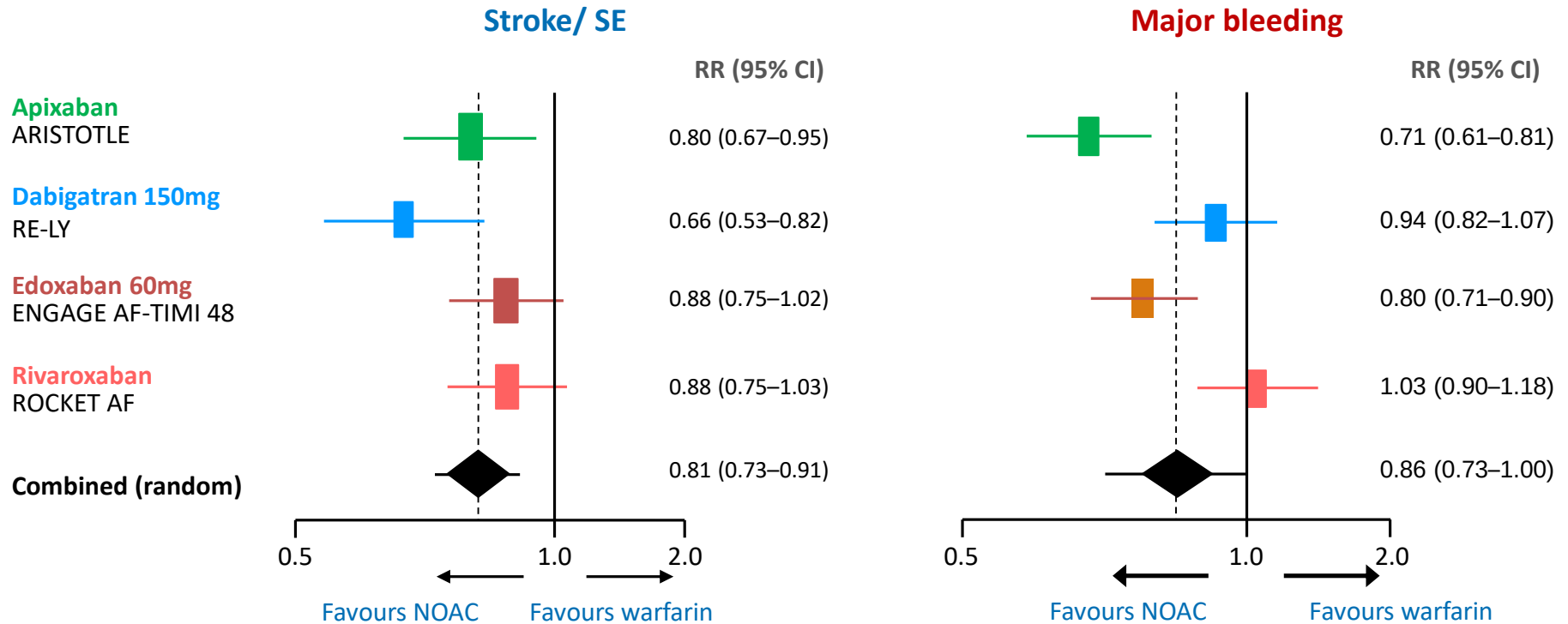
LA FONDAZIONE SANTA MARIA NUOVA ONLUS POSE NELL'ANNO 2017





**.... MS, 96 aa; Non assume farmaci
Dal 1948 non perde un angelus....**

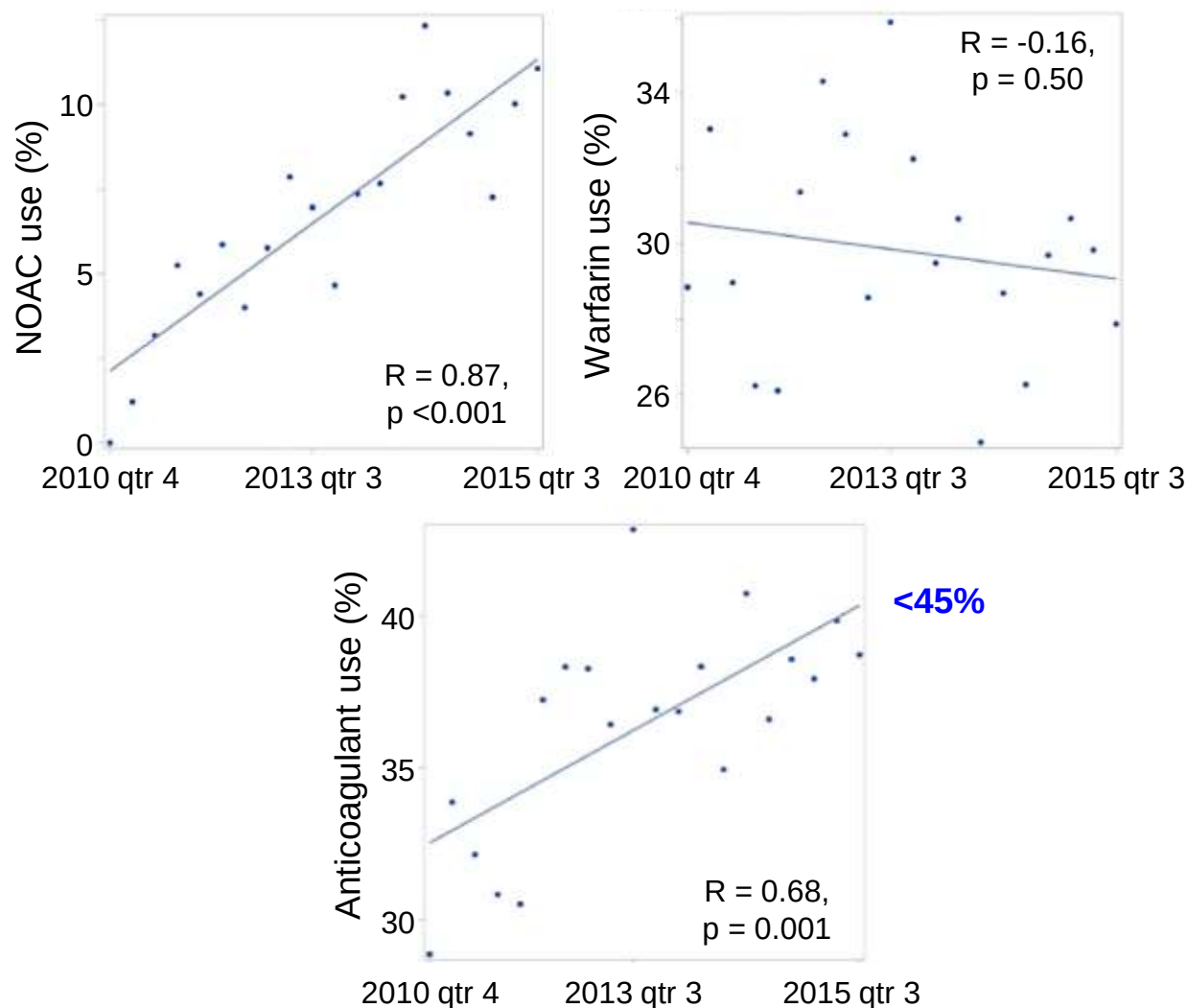
NOACs: main outcomes in AF



Modified from Ruff *et al. Lancet* 2014;383:955-62

Effect of New Oral Anticoagulants on Prescribing Practices for Atrial Fibrillation in Older Adults

Quarterly trend in anticoagulants use (N=6568; age ≥ 75 years)
(the Clinical Investigation Data Exploration Repository - CIDER, Washington University)



2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS

The Task Force for the management of atrial fibrillation of the European Society of Cardiology (ESC)

13. Specific situations

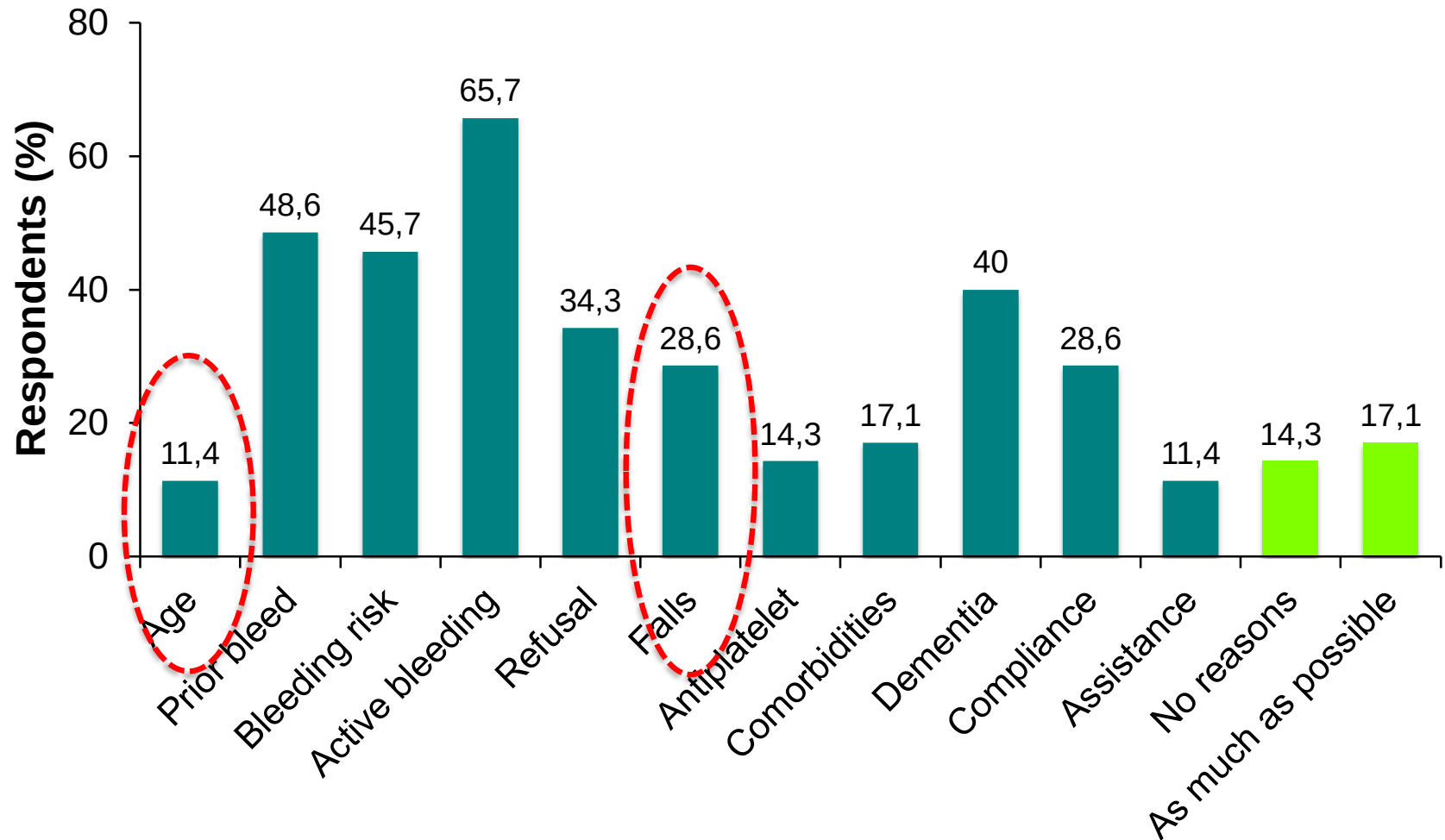
13.1 Frail and 'elderly' patients

- ✓ Many AF patients present at **older age** (e.g. >75 or >80 years)
- ✓ There are **no studies** suggesting that cardiovascular risk reduction is **less effective** in these 'elderly' AF patients than in younger patients
- ✓ Rather, **age** is one of the strongest predictors/risk factors for **ischaemic stroke** in AF
- ✓ Good data are available to support the use of **anticoagulants** in older patients
- ✓ Elderly AF patients are at higher risk of stroke and, thus, are more likely to benefit from OAC than younger patients, and yet **OAC is still underutilized** in the elderly

Frailty syndrome: an emerging clinical problem in the everyday management of clinical arrhythmias: results of the European Heart Rhythm Association survey

Fumagalli S et Al.,
EP Europace 2017

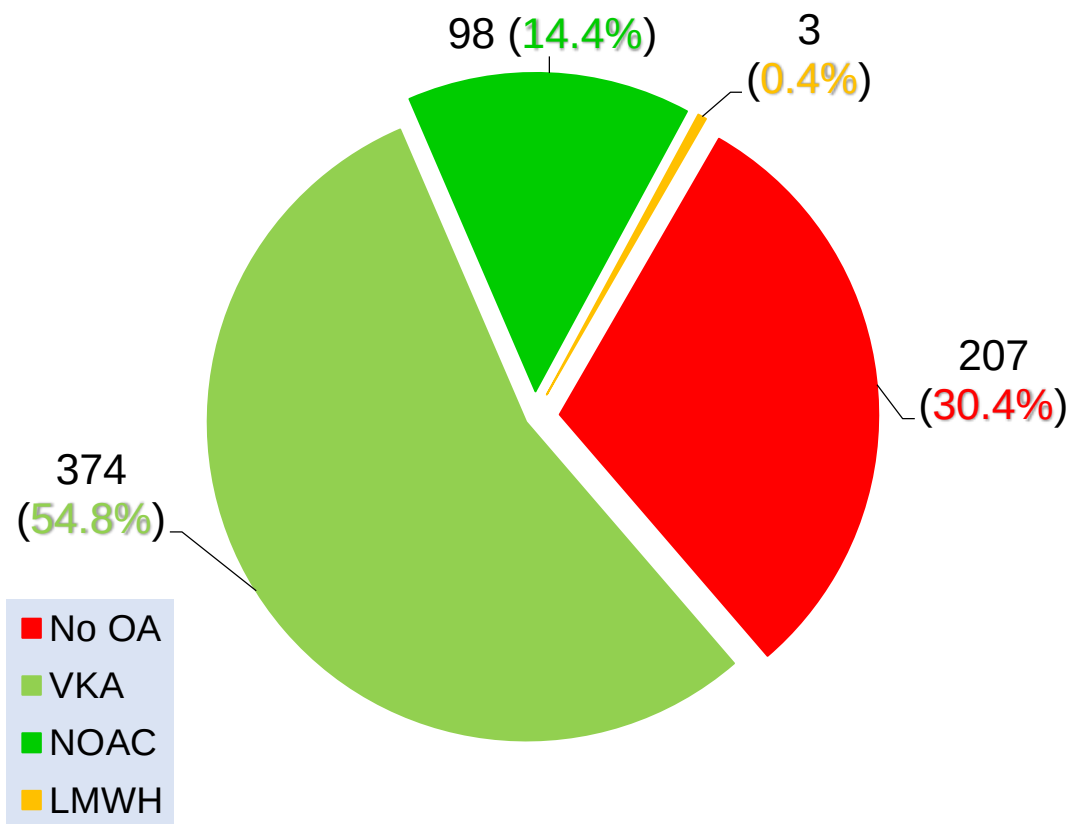
Reasons not to prescribe OAs to a frail patient with AF (light green bars indicate responses that are in favour of the use of Oas)



The Effect of Bleeding Risk and Frailty Status on Anticoagulation Patterns in Octogenarians With Atrial Fibrillation: The FRAIL-AF Study



Anticoagulant use in 682 hospitalized patients ≥ 80 years with AF/AFL
(Age: 85.9; 3 academic hospitals; Montreal, Quebec; 2012-2013)



The most common reasons for not prescribing an OA:

1. Hx of bleeding (15.5%)
2. Active bleeding (15.5%)
3. Risk of falls (14%)
4. Patient refusal (8.7%)
5. No justification provided (15%)

Arrhythmias in elderly and frailty syndrome

AF Antithrombotic management – Consensus statements

All AF patients with non-sex-related CHA₂DS₂-VASc stroke risk factor should be considered for OAC therapy, irrespective of their frailty status

Frail AF patients require a detailed assessment of their baseline stroke /bleeding risk profile and consideration of their personal values / preferences with regards to AF management

Frail AF patients taking OAC need a frequent, regular clinical follow-up for treatment effects monitoring and stroke / bleeding risk re-assessment

The advantages of NOACs relative to VKAs are likely consistent in frail and non-frail AF patients, but frail AF patients may have a greater benefit from NOACs owing to a higher absolute risk of TE events

Aspirin should not be used for stroke prevention in frail AF patients, since it is essentially ineffective and associated to similar risk of bleeding compared to NOACs / VKAs

2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS

The Task Force for the management of atrial fibrillation of the European Society of Cardiology (ESC)

13. Specific situations

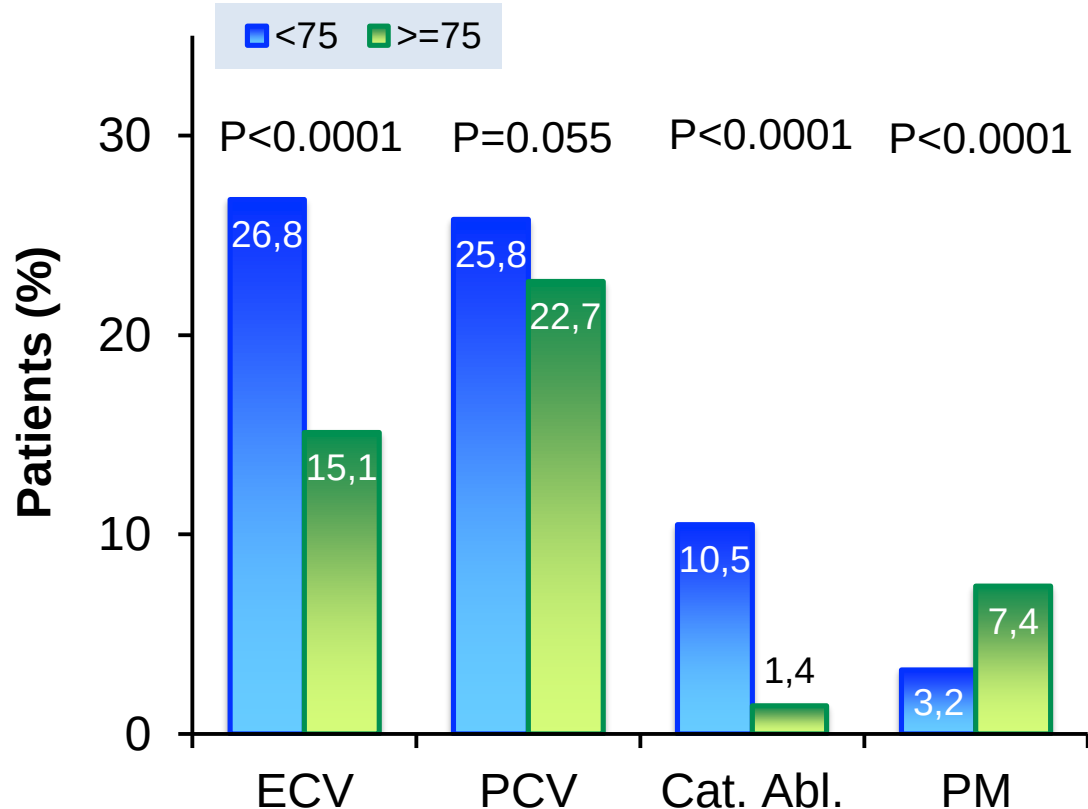
13.1 Frail and 'elderly' patients

- ✓ The available data support the use of rate and rhythm control interventions, including PMs and catheter ablation, **without justification to discriminate** by age group
- ✓ Patients at older age may present with **multiple comorbidities**. Such conditions may limit HRQL more than AF
- ✓ Impairment of **renal** and **hepatic function**, and **polypharmacy** make drug interactions and ADRs more likely
- ✓ **Integrated AF management** and careful **adaptation of drug dosing** seem reasonable to reduce the complications of AF therapy in such patients

Age-Related Differences in Presentation, Treatment, and Outcome of Patients With Atrial Fibrillation in Europe

Interventions Performed or Planned at Enrollment by Age Group in the EORP-AF General Pilot Registry

(<75 years - N=2068; age: 63±9 y; ≥75 years - N=1051; age: 81±5 y)

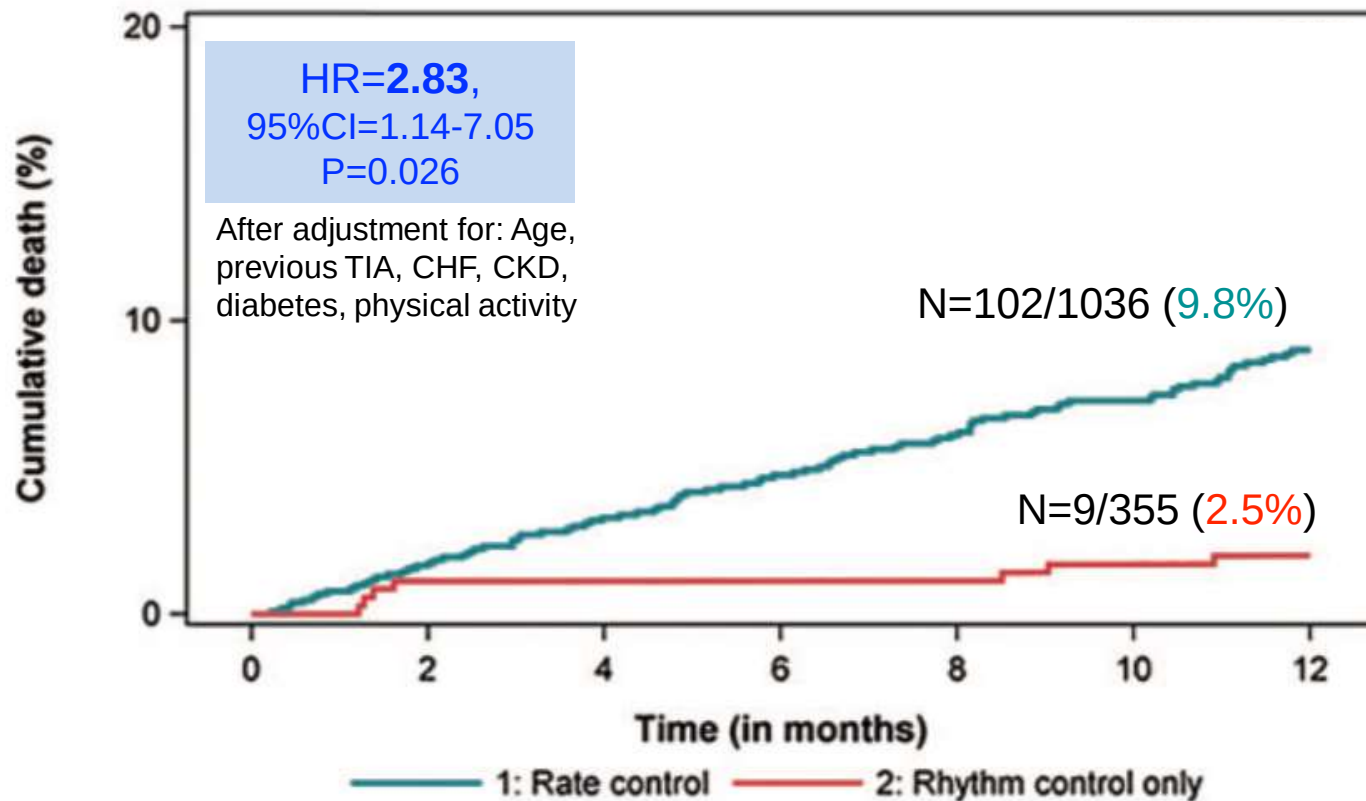


ECV / PCV: External / Pharmacological CV
Cat. Abl.: catheter ablation of AF
PM: pacemaker implantation

Rate vs. rhythm control and adverse outcomes among European patients with atrial fibrillation

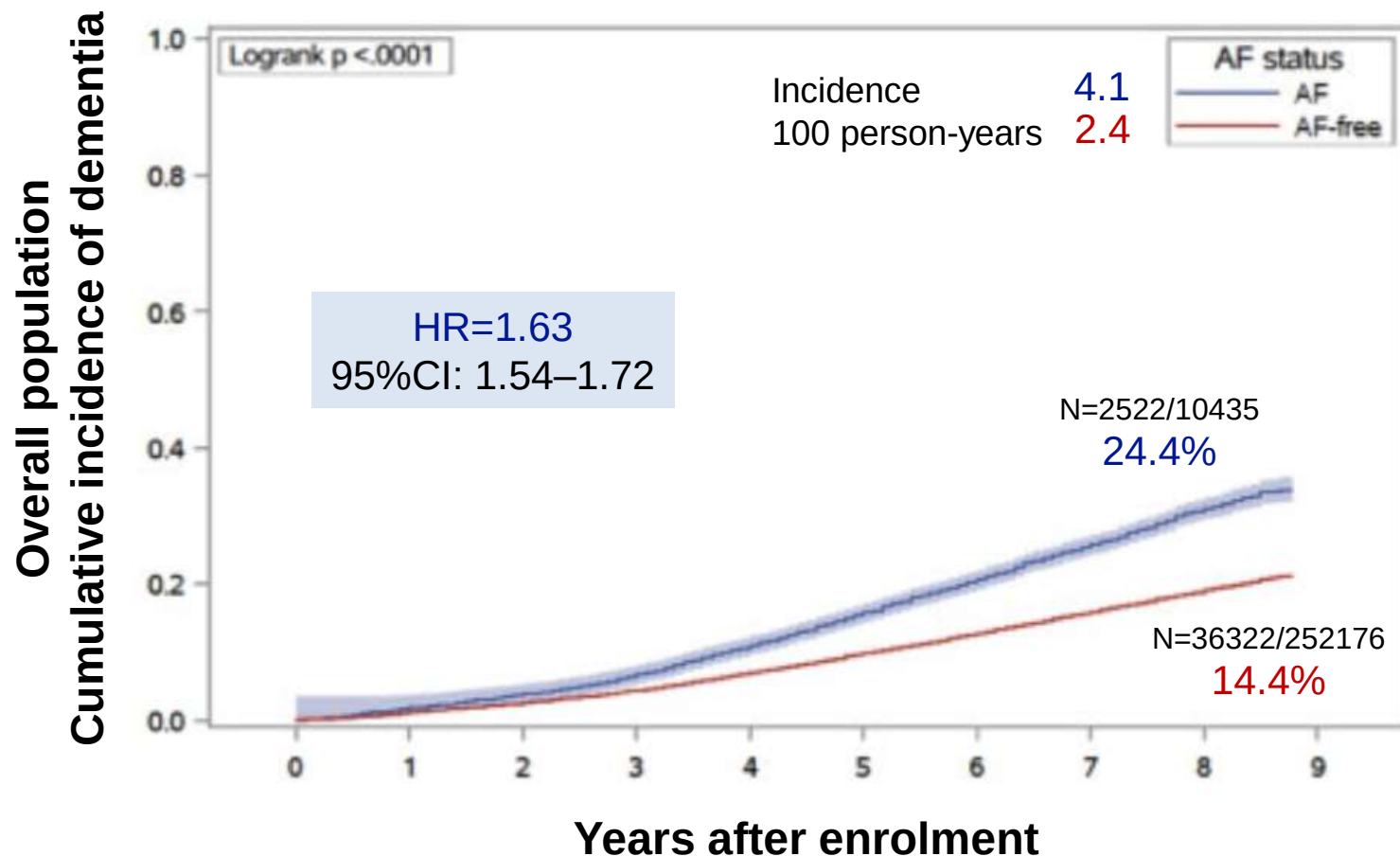
the EORP-AF General Pilot Registry Investigators

Kaplan–Meier curves for all-cause death according to baseline strategy (Rate control – 73 y, women: 40%; Rhythm control – 66 y, women: 34%)



Risk of dementia in stroke-free patients diagnosed with atrial fibrillation: data from a population-based cohort

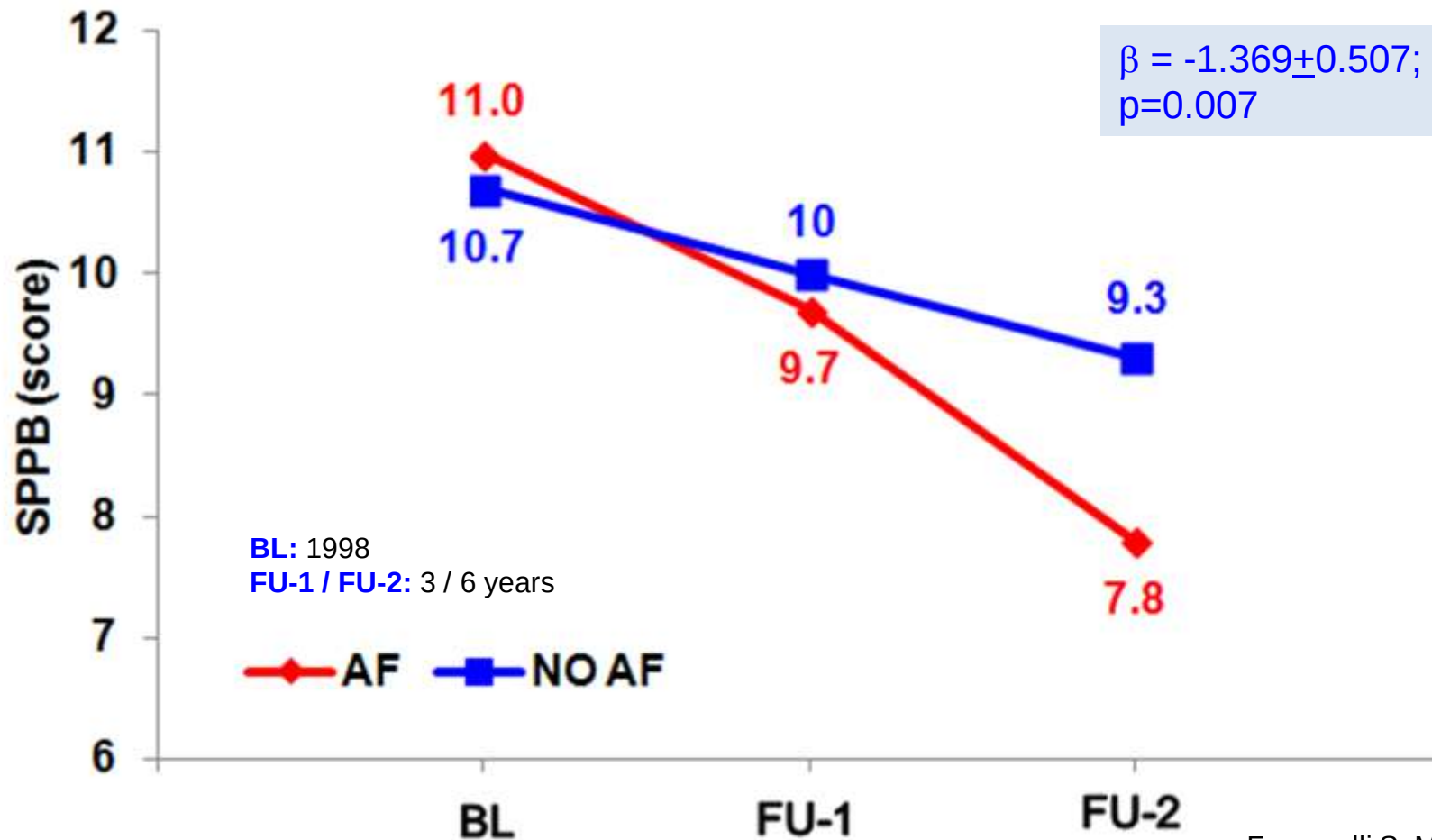
The cumulative incidence of dementia in the overall population of the Korean NHIS-Senior (2005-13; **AF-free** - 71 years, FU: 85 m; **AF** - 72 years; FU: 86 m)



Atrial fibrillation and physical function decline in an Italian elderly population: the InCHIANTI Study experience

SPPB trends by presence of AF

(N=267; AF prevalence: 4.9%; age - AF: 81±6 vs. NO AF: 77±6 years, p<0.01)





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Perchè I DOAC nell'anziano fragile?



Programma ETNA-AF Global (Edoxaban Treatment in routine clinical practice for patients with nonvalvular Atrial Fibrillation)



- L'ETNA-AF Global è il più ampio Registro con un singolo DOAC
- analizzerà l'utilizzo, la sicurezza e l'efficacia di edoxaban nella normale pratica clinica

Obiettivo primario: valutare la sicurezza di edoxaban

- L'ETNA-AF è stato disegnato per valutare in un periodo di 4 anni l'insorgenza, la durata e la severità di:
 - Sanguinamenti, incluse le emorragie intracraniche
 - Eventi avversi correlati al farmaco
 - Mortalità cardiovascolare e mortalità per tutte le cause
- Obiettivi secondari:
 - Ictus, TIA, eventi embolici sistemici, eventi cardiovascolari maggiori (MACE)
 - Eventi tromboembolici venosi
 - SCA, ospedalizzazioni per patologie cardiovascolari, *compliance* al trattamento

First 1-year follow-up snapshot analysis of over 12,500 AF patients treated with edoxaban in routine clinical practice: ETNA-AF-Europe

Introduction



- ▶ Evidence from real-world studies has demonstrated the safety of different NOACs in routine care; moreover, real-world data are currently emerging for edoxaban and will complement the findings from the randomised trials¹⁻³
- ▶ ETNA-AF-Europe (clinicaltrials.gov: NCT02944019) aims to evaluate the risk-benefit profile of edoxaban in unselected AF patients in routine clinical practice⁴

¹Steinberg BA, et al. Am J Cardiol 2017;119:1590–5.

²Eikelboom JW, Weitz JI. Thromb Haemost 2015;113:1159–61.

³Pottegard A, et al. Pharmacoepidemiol Drug Saf 2018;27:174–81.

⁴De Caterina R, et al. J Cardiovasc Med (Hagerstown) 2019;20:97–104.

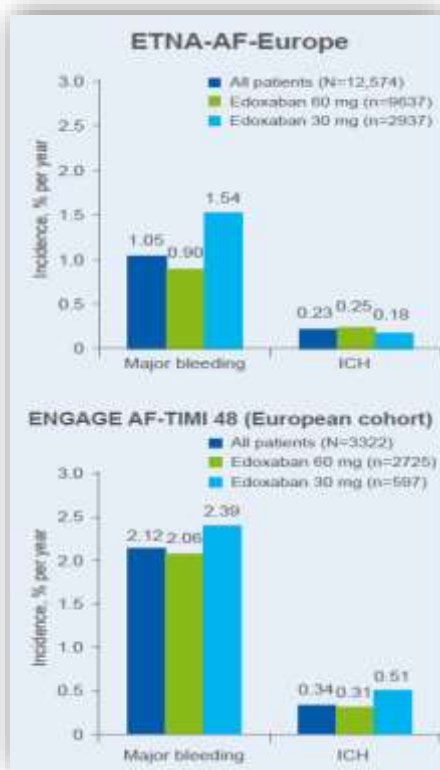
Methods



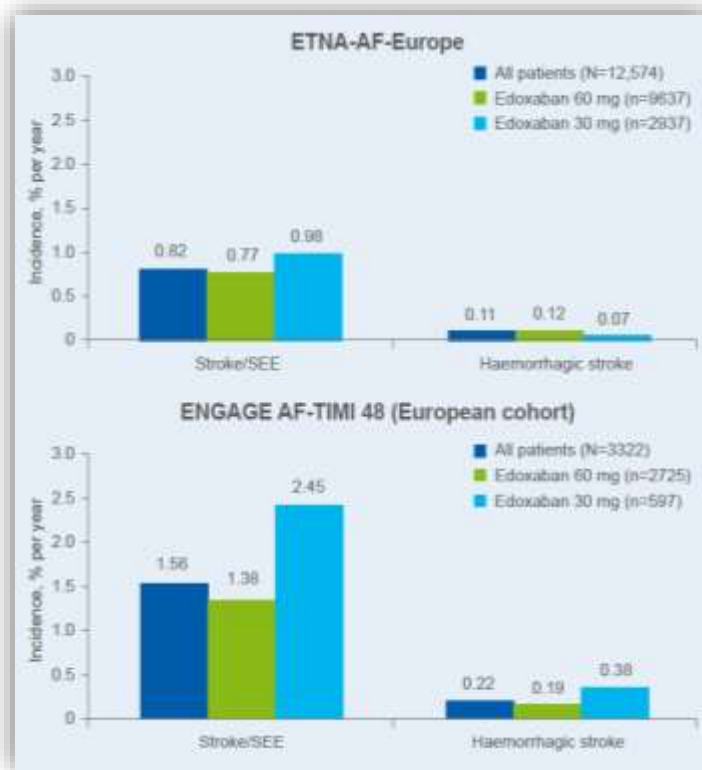
- ▶ ETNA-AF-Europe is a multinational, multicentre, observational, post-authorisation, safety study conducted in 825 sites in 10 European countries (Austria, Belgium, Germany, Ireland, Italy, The Netherlands, Portugal, Spain, Switzerland and United Kingdom)
- ▶ A total of 13,980 patients were enrolled, and will be followed for up to 4 years
- ▶ The ETNA-AF-Europe snapshot that was used for this analysis was executed on 22 April 2019

ETNA-AF Europe : Risultati al primo anno di follow up

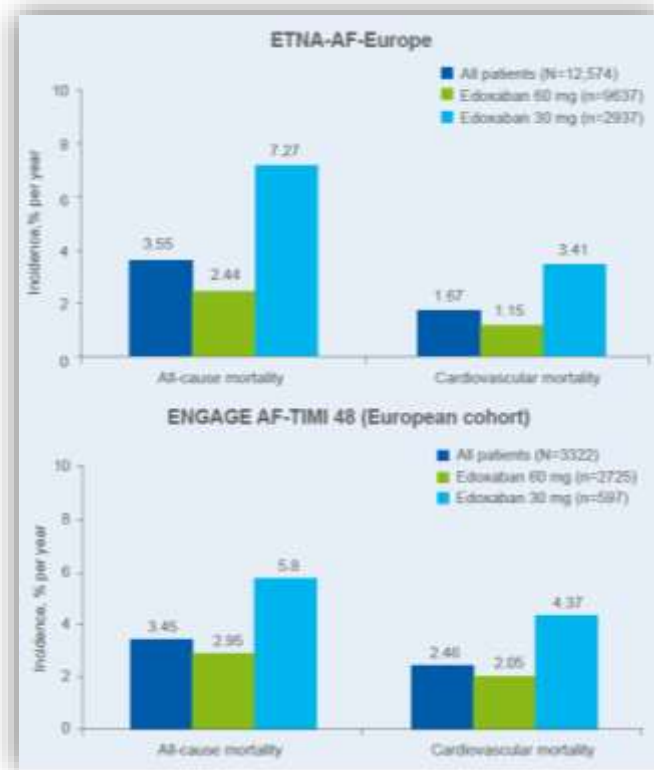
Safety events



Stroke events

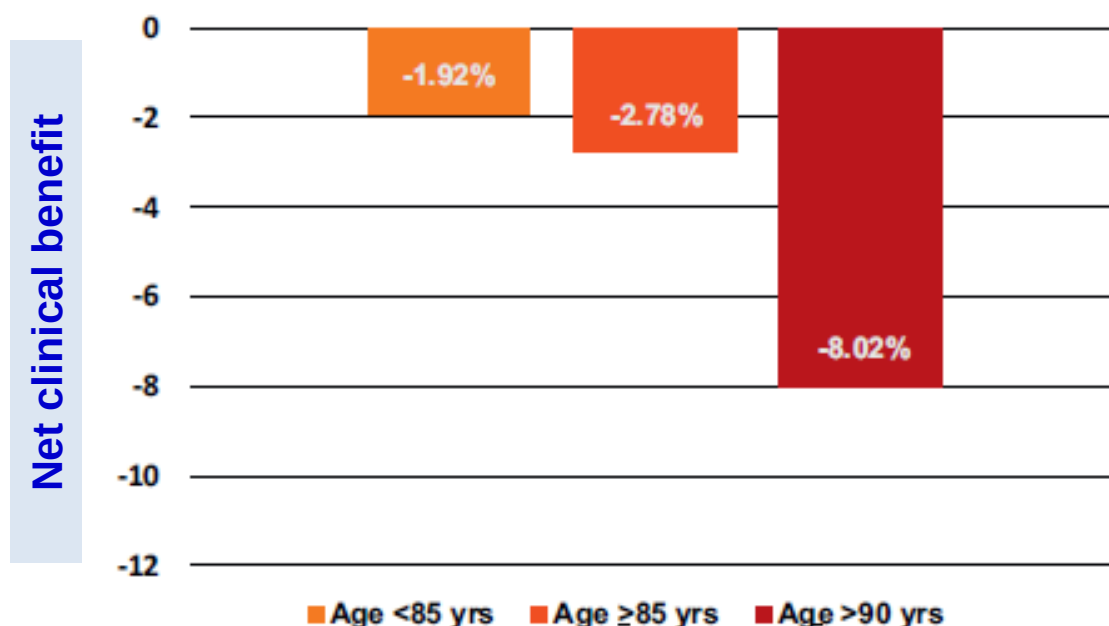


Mortality



The safety and efficacy of non-vitamin K antagonist oral anticoagulants in atrial fibrillation in the elderly

Net clinical benefit, adjusted for the risk of subsequent death, of OACs vs no OACs according to different age groups (the PREFER in AF)



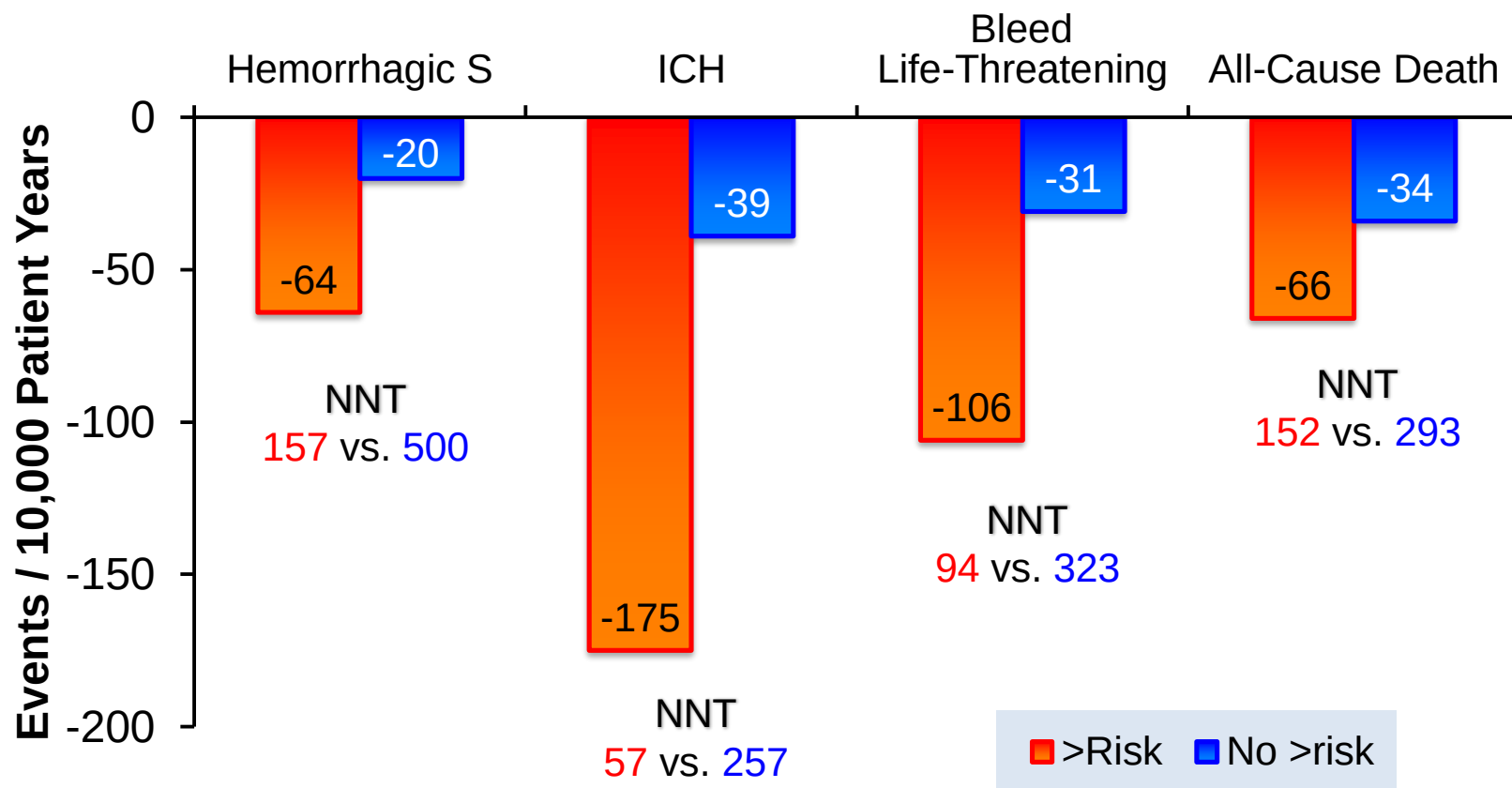
VKAs or NOACs led to a 36% risk reduction of TE events vs. antiplatelet or no treatment; notably, OACs did not increase the risk of major bleeding compared to antiplatelet therapy

Edoxaban Versus Warfarin in Atrial Fibrillation Patients at Risk of Falling

ENGAGE AF-TIMI 48 Analysis



Absolute Risk Reduction of HD Edoxaban Regimen Compared With Warfarin in Patients at Increased Versus Not at Increased Fall Risk



Clinical Outcomes and History of Fall in Patients with Atrial Fibrillation Treated with Oral Anticoagulation: Insights From the ARISTOTLE Trial

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MEDICINE®



**753 patients
with vs 15738
without history
of falling**

Characteristics	Fall(s) Within 1 Year		P-Value
	Yes (n = 753)	No (n = 15,738)	
Age, median (25th, 75th), years	75 (67, 79)	70 (63, 76)	< .0001
Age ≥75 years, n (%)	379 (50.3%)	4787 (30.4%)	< .0001
Female sex, n (%)	357 (47.4%)	5438 (34.6%)	< .0001
BMI, median (25th, 75th), kg/m ²	29.1 (25.6, 33.8)	28.4 (25.2, 32.4)	< .001
CHA2DS2-VASC score, mean (SD)	4.19 (1.65)	3.43 (1.51)	<.001
Prior stroke, TIA, SE	28.3%	20.9%	<.001
Prior bleeding	35.1%	16.0%	<.001

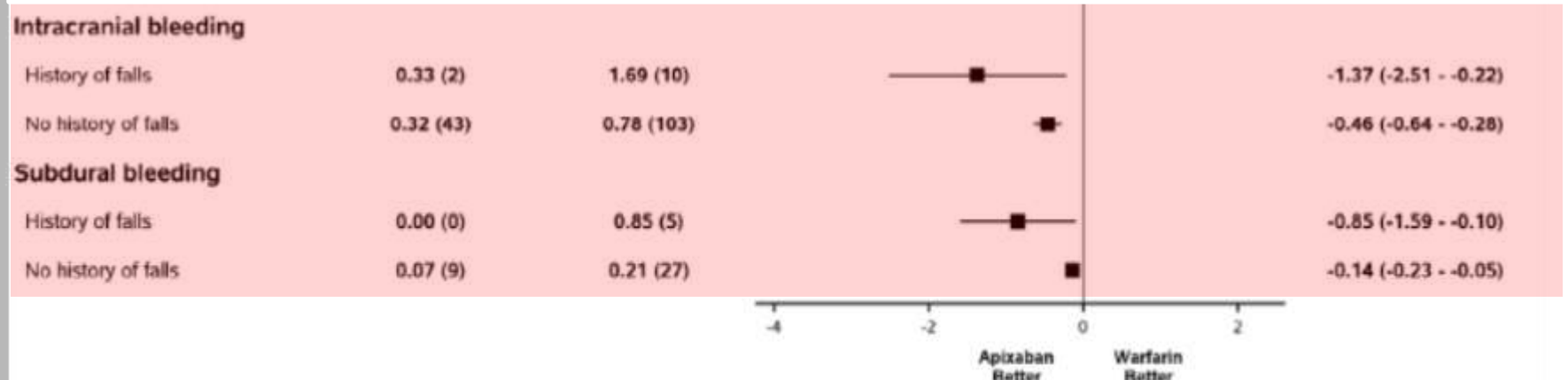
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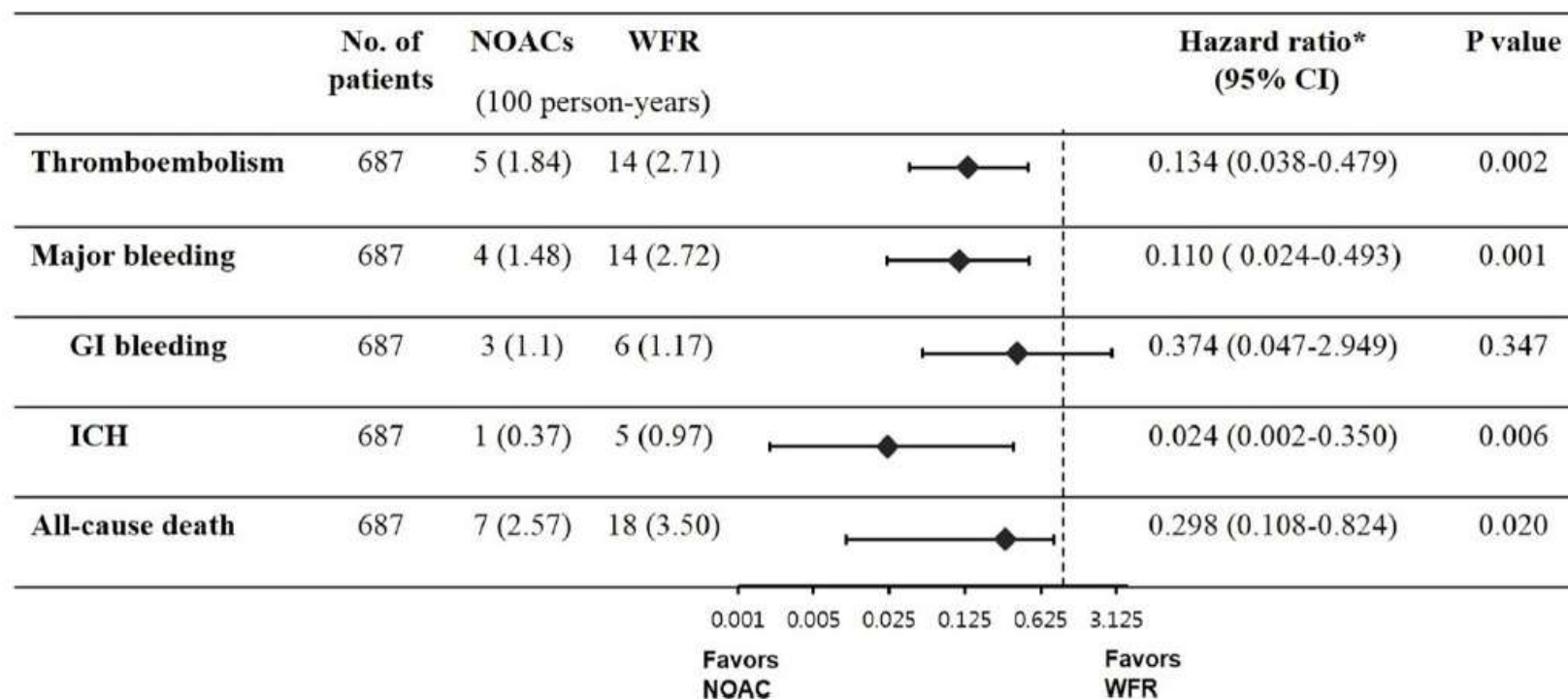
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Effectiveness and safety of non-vitamin K antagonist oral anticoagulants in octogenarian patients with non-valvular atrial fibrillation

PLOS ONE | <https://doi.org/10.1371/journal.pone.0211766> March 7, 2019

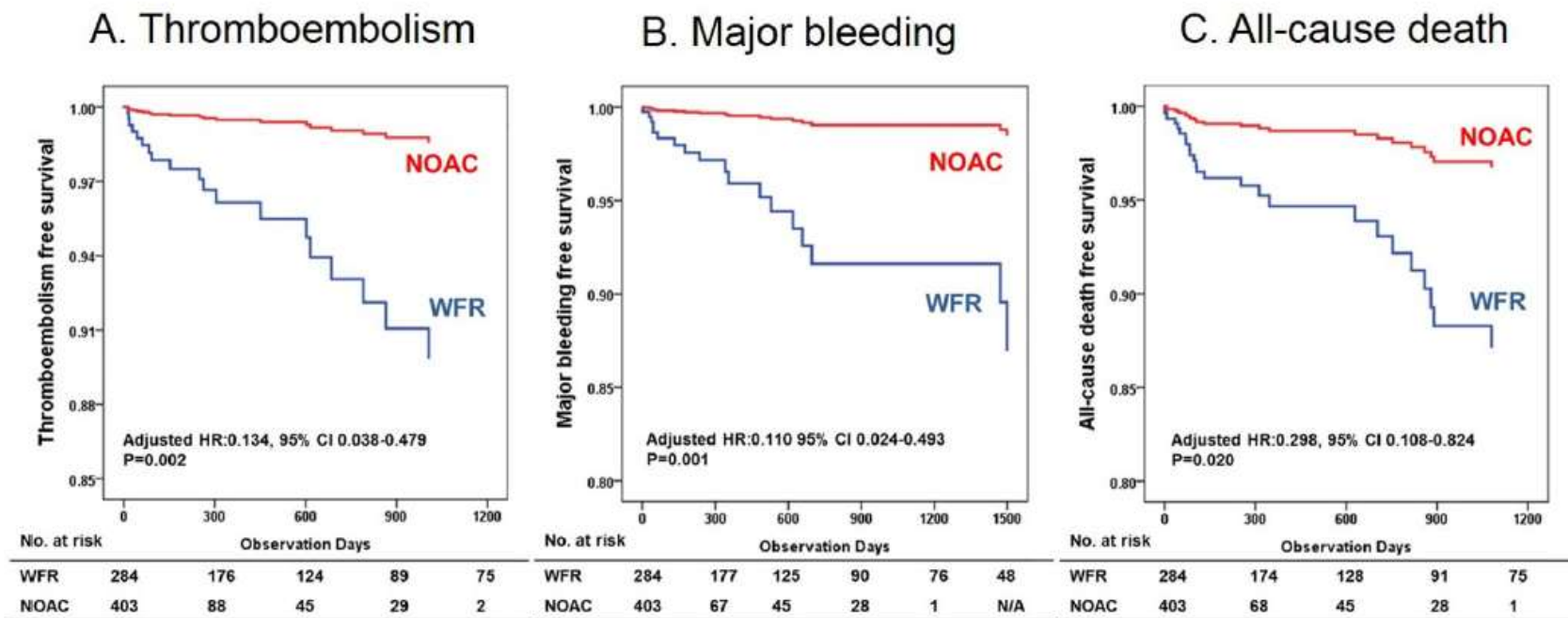
Hyue Mee Kim^{1,2}, Eue-Keun Choi^{1*}, Chan Soon Park¹, Myung-Jin Cha¹, Seo-Young Lee¹, Joon-Myung Kwon³, Seil Oh¹



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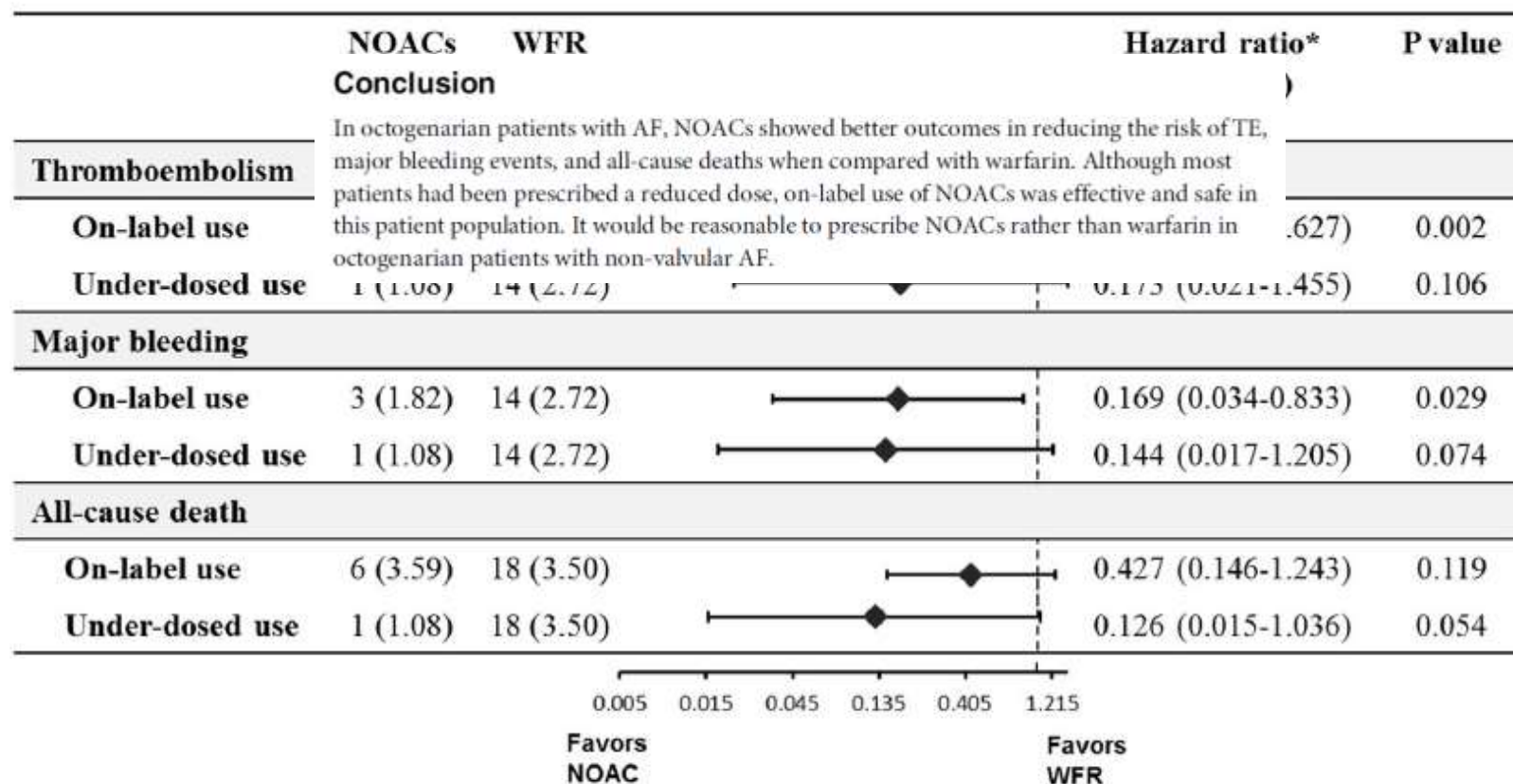
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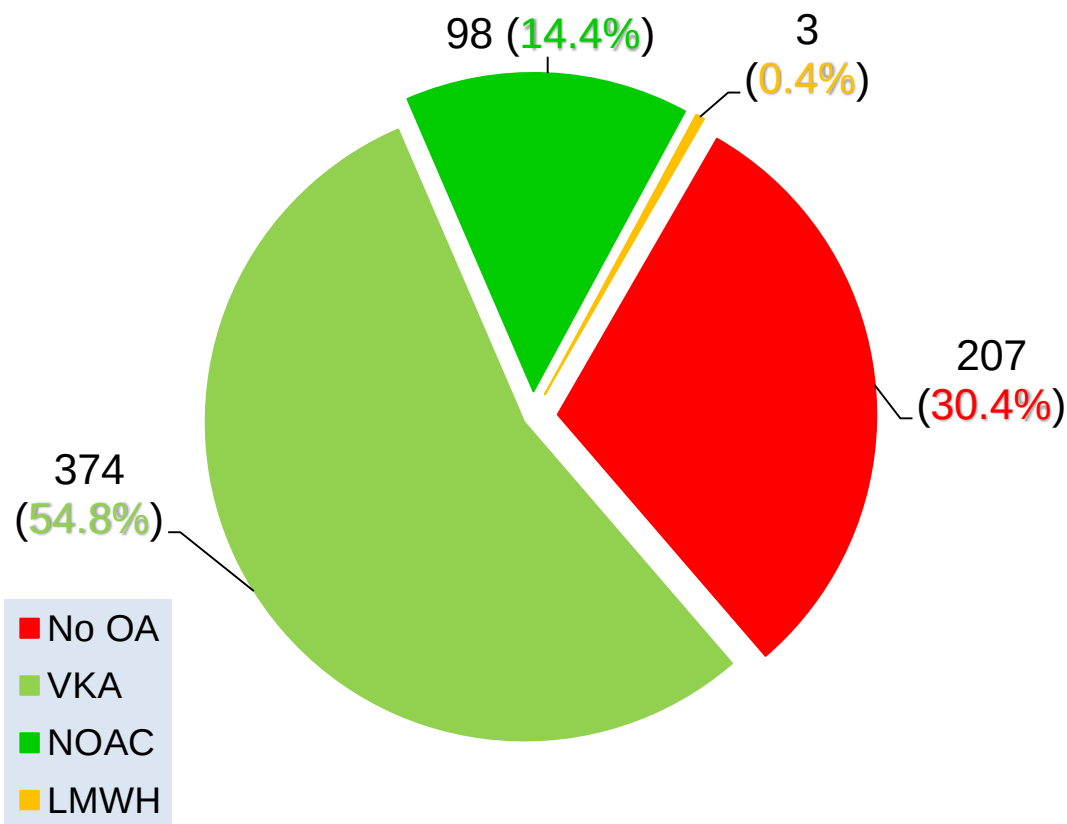
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The Effect of Bleeding Risk and Frailty Status on Anticoagulation Patterns in Octogenarians With Atrial Fibrillation: The FRAIL-AF Study



Anticoagulant use in 682 hospitalized patients ≥ 80 years with AF/AFL
(Age: 85.9; 3 academic hospitals; Montreal, Quebec; 2012-2013)



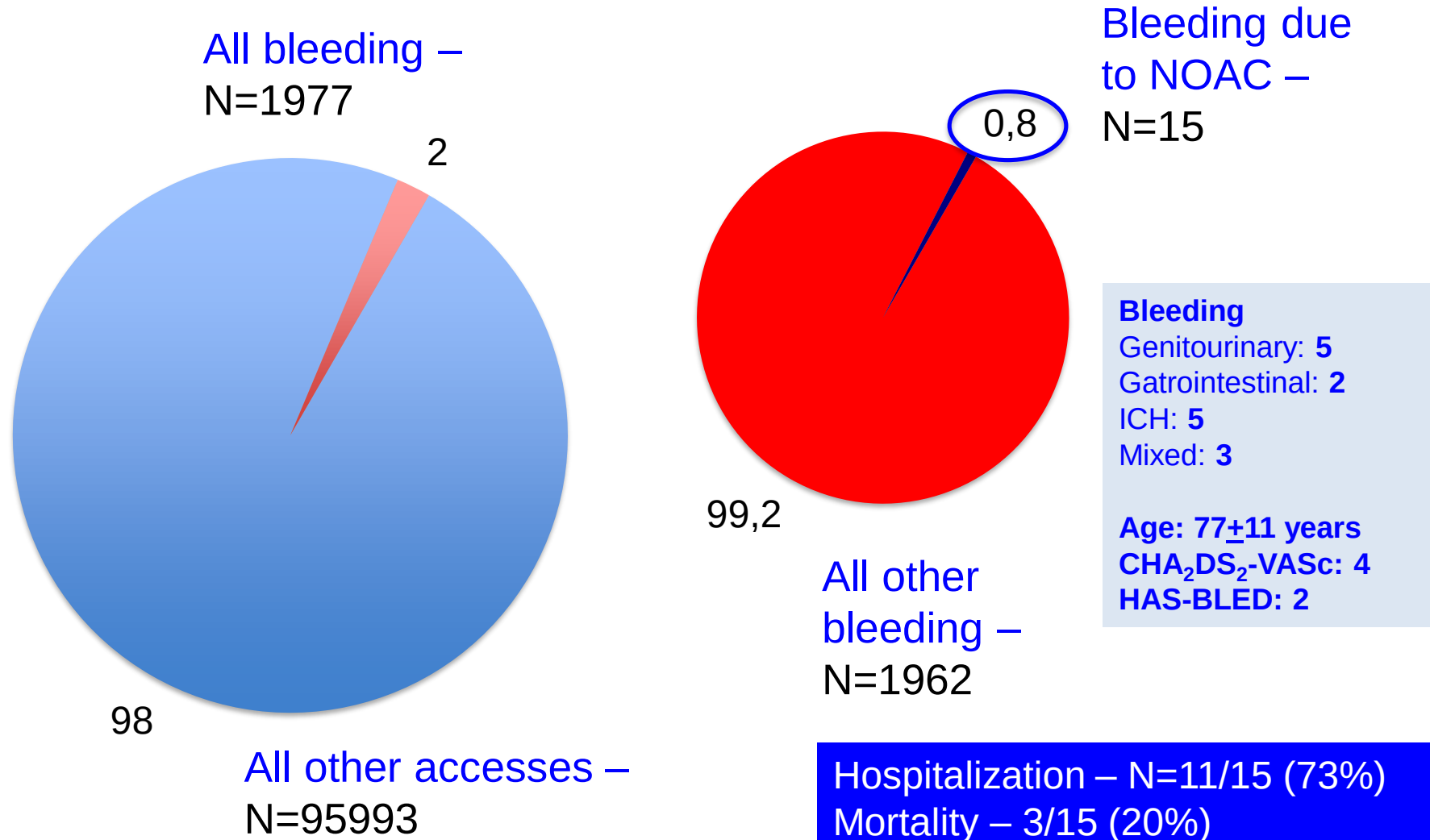
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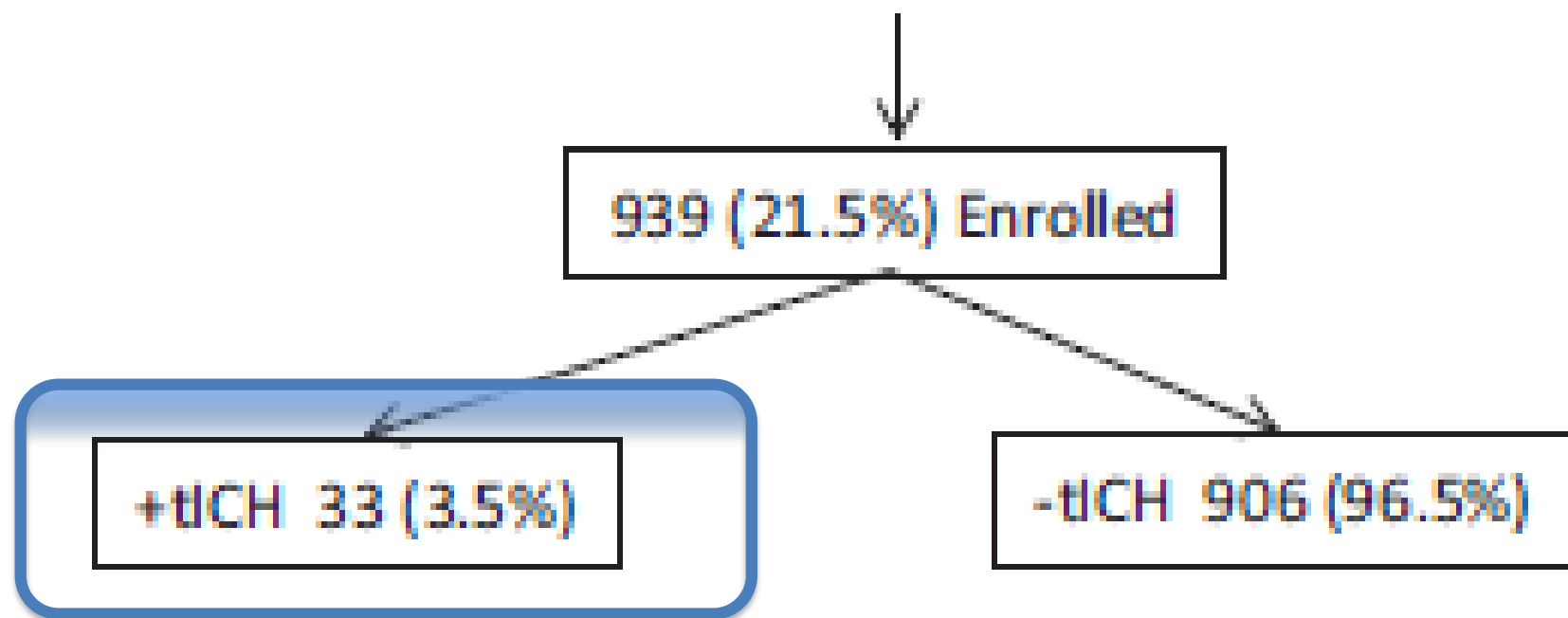
Bleeding related to non-vitamin K antagonist oral anticoagulants in emergency department: A “Real-world” snapshot from Southern Italy
On behalf of MIRC-NOAC study group

Salzano A,
Eur J Intern Med 2017

Clinical characteristics of patients with bleeding (year 2015; people potentially referring to the ED: N=3.000.000)



GLF = ground-level fall and tICH = traumatic intracranial hemorrhage and taking and antiplatelet or anticoagulants.



Risk of Intracranial Hemorrhage in Ground-level Fall With Antiplatelet or Anticoagulant Agents

Authors: Michael Ganetsky, MD, Gregory Lopez, Tara Coreanu, BSc, Victor Novack, MD, PhD, Steven Horng, MD, Nathan I. Shapiro, MD, MPH, and Kenneth A. Bauer, MD

Table 2
Subject Findings and Outcomes

Finding and Outcome	Antiplatelet Treatment, <i>n</i> = 668 (71.1%)	Anticoagulation Treatment, <i>n</i> = 180 (19.2%)	Combined Treatment, <i>n</i> = 91 (9.7%)	<i>p</i> -value*
Head strike recorded	407 (60.9)	102 (56.7)	62 (68.1)	0.19
LOC	120 (18.0)	18 (10.0)	3 (3.3)	<0.001
External signs of head trauma	277 (41.5)	62 (34.4)	28 (30.8)	0.05

Conclusion: There is a low incidence of clinically significant tICH with a ground-level fall in head trauma in patients taking an anticoagulant or antiplatelet medication. There was no statistical difference in rate of tICH between antiplatelet and anticoagulants, which is unanticipated and counterintuitive as most literature and teaching suggests a higher rate with anticoagulants. A larger data set is needed to determine if small differences between the groups exist.

Deaths				
Within 7 days	8 (1.2)	0	0	0.34
Within 30 days	23 (3.4)	3 (1.7)	4 (4.4)	0.35
tICH on CT	29 (4.3)	3 (1.7)	1 (1.1)	0.13

Data are reported as *n* (%).

ICU = intensive care unit; LOC = loss of consciousness; tICH = traumatic intracranial hemorrhage.

*Chi-square or exact test analysis.



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FIBRILLAZIONE NELL'ANZIANO, AL DI LA' DI UNA SEMPLICE ARITMIA

Come ci comportiamo?



Appropriateness of oral anticoagulant therapy prescription and its associated factors in hospitalized older people with atrial fibrillation

Carlotta Franchi^{1,†} , Stefania Antoniazzi^{2,3,†}, Marco Proietti⁴, Alessandro Nobili⁴, Pier Mannuccio Mannucci⁵ and on behalf of the SIM-AF Collaborators*

	Patients with OAC N (%)	Patients without OAC N (%)
Overall	221	107
APPROPRIATE	153 (69.2)	19 (18)
a) CHA₂DS₂-VASc ≥1 (men) and ≥2 (women) but with contraindication for OAC	–	19
b) Dose	153	–
Dabigatran	11	–
Rivaroxaban	13	–
Apixaban	22	–
Edoxaban	8	–
Warfarin	93	–
Acenocoumarol	6	–

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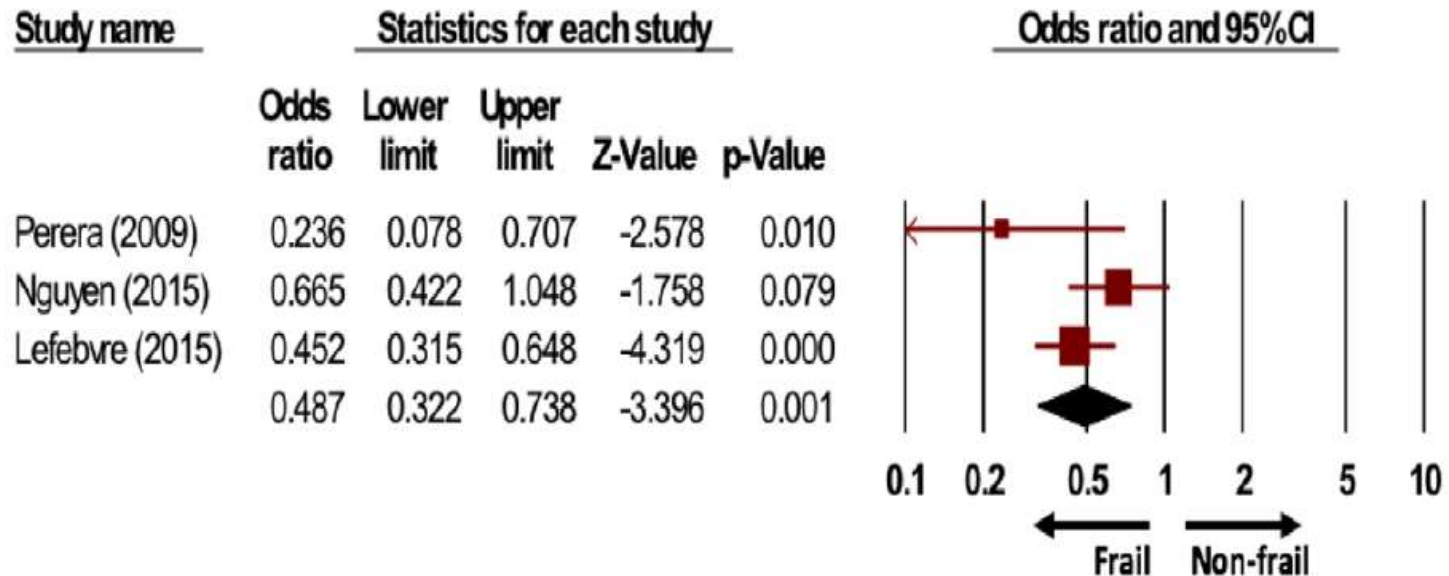
Table 3

Results from univariate and multivariable logistic regression analyses for the appropriateness of oral anticoagulant prescribing

	OR	95% CI	P-value
Univariate analysis			
Age (year)	0.97	0.94–1.00	0.030
History of falls	0.50	0.28–0.89	0.018
BMI (kg m⁻²)	1.07	1.01–1.12	0.020
BMI categories			
Underweight	0.29	0.06–1.47	0.136
Normal weight (ref.)	–	–	–
Overweight	1.69	1.02–2.82	0.043
Obesity	1.79	0.87–3.66	0.114

What is the Impact of Frailty on Prescription of Anticoagulation in Elderly Patients with Atrial Fibrillation? A Systematic Review and Meta-Analysis

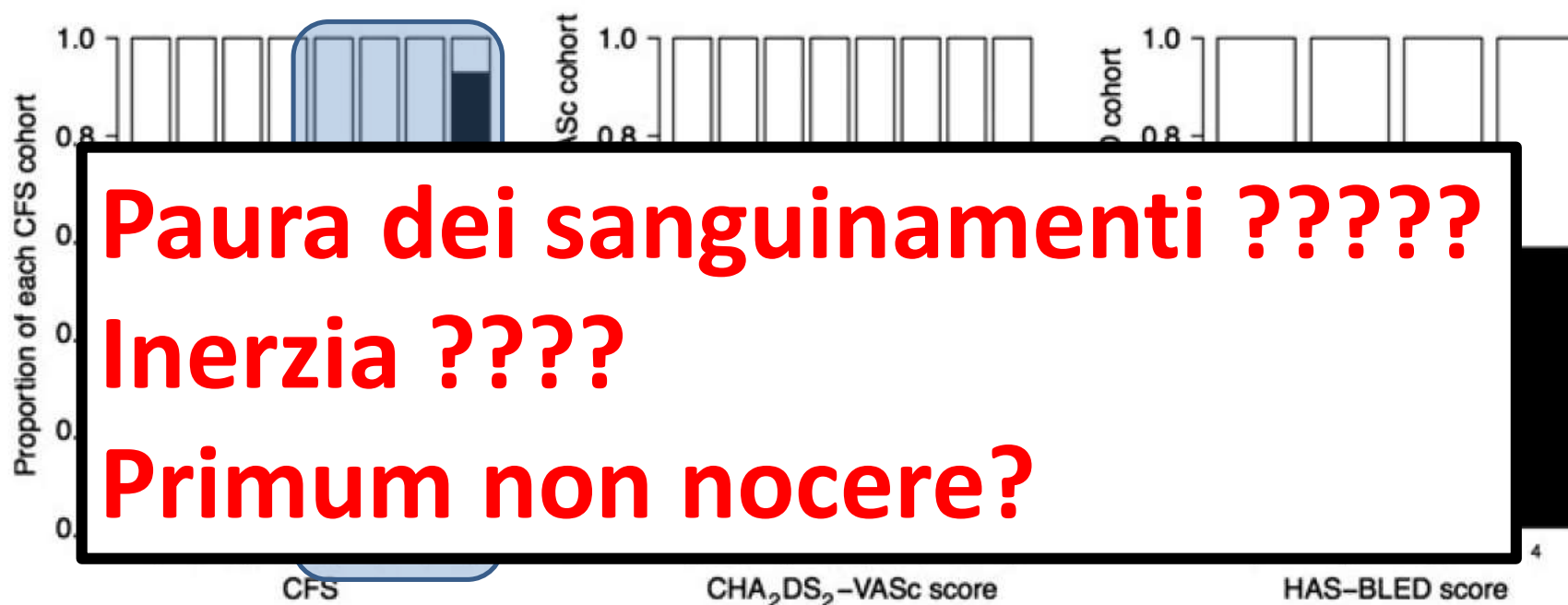
Zardasht Oqab¹, Payam Pournazari¹, Robert S Sheldon¹



Conclusions: The **prevalence** of **frailty** in hospitalized elderly patients with AF **is high**, and the **use** of OAC **is low** in these patients. Frail elderly are significantly less likely to receive OAC.

Clinical frailty is independently associated with non-prescription of anticoagulants in older patients with atrial fibrillation

The proportion of individuals not taking anticoagulants (*black*) compared with those taking anticoagulants (*white*), by Clinical Frailty Scale, CHA₂DS₂-VASc and HAS-BLED scores (N=419; anticoagulated No/Yes: 215/204)



Paura dei sanguinamenti ?????

Inerzia ?????

Primum non nocere?

Anticoagulated
Yes – Frailty: 52.5%
No – Frailty: 81.4%
P<0.001

Anticoagulated
Yes – CHA₂DS₂-VASc: 5
No – CHA₂DS₂-VASc: 4
P<0.001

Anticoagulated
Yes – Age: 83
No – Age: 87
P<0.001

Multivariate predictors
OR_{Frailty} = 0.77, p<0.001
OR_{Bleeding Risk} = 0.85, p=0.02
OR_{Age} = 0.98, p<0.001

QUESTIONI APERTE

Efficacia e sicurezza degli anticoagulanti orali nell'anziano fragile con fibrillazione atriale: problema ancora aperto

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Documento di consenso di Esperti con Metodo Delphi GIMSI-AcEMC

Utilizzo degli anticoagulanti orali nei pazienti anziani a rischio di caduta sincopale o non sincopale

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Ivo Casagrande, Andrea Ungar, Michele Brignole

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**Si agli anticoagulanti, in
particolare si ai DOACs**

**Grazie per la vostra
attenzione**



elena tempestini