09:50-10:30 **Meet the Expert**

SFATARE I MITI SUL TRATTAMENTO ANTICOAGULANTE DEL PAZIENTE ANZIANO

Moderatore: *Mauro Cacciafesta (Roma), Agostino Virdis (Pisa)*

- E nell'anziano fragile? Facciamo chiarezza - *Mario Bo (Torino)*

SOCIETÀ ITALIANA DI GERONTOLOGIA E GERIATRIA

Roma, 30 novembre - 3 dicembre 2022
UNIVERSITÀ CATTOLICA DEL SACRO CUORE

Age and Ageing 2021; **50:** 772–779

Atrial fibrillation and oral anticoagulation in older people with frailty: a nationwide primary care electronic health records cohort study

58.204 patients, mean age 80,
30.916 (**53.1%**) OAT-treated

Canadian Journal of Cardiology 38 (2022) 77–84

Clinical Research

The Introduction of Direct Oral Anticoagulants Has Not Resolved Treatment Gaps for Frail Patients With Nonvalvular Atrial Fibrillation

74.650 patients, mean age 78,
36.269 (**50.1%**) OAT-treated

J Am Geriatr Soc. 2022;70:2386–2392.

Oral anticoagulants and outcomes in adults ≥80 years with atrial fibrillation: A global federated health network analysis

763.627 patients, mean age 82,
335.154 (**43.9%**) OAT-treated

Journal of Thrombosis and Thrombolysis (2022) 54:616–624

Prescribing of anticoagulation for atrial fibrillation in primary care

5.253 patients, mean age 75,
2.481 (**47.0%**) OAT-treated

Bo M, Fumagalli S, Marchionni N, Degli Esposti L

170.404 patients, mean age 78,
63.1 % OAT-treated

Malpractice, inerzia terapeutica o incertezze cliniche?

Non-Vitamin K Oral Anticoagulants in Comparison to Phenprocoumon in Geriatric and Non-Geriatric Patients with Non-Valvular Atrial Fibrillation

Christopher Hohmann[1] Stefan H. Hohnloser[2] Josephine Jacob[3] Jochen Walker[3] Stephan Baldus[1] Roman Pfister[1]

Thromb Haemost 2019;119:971–980.

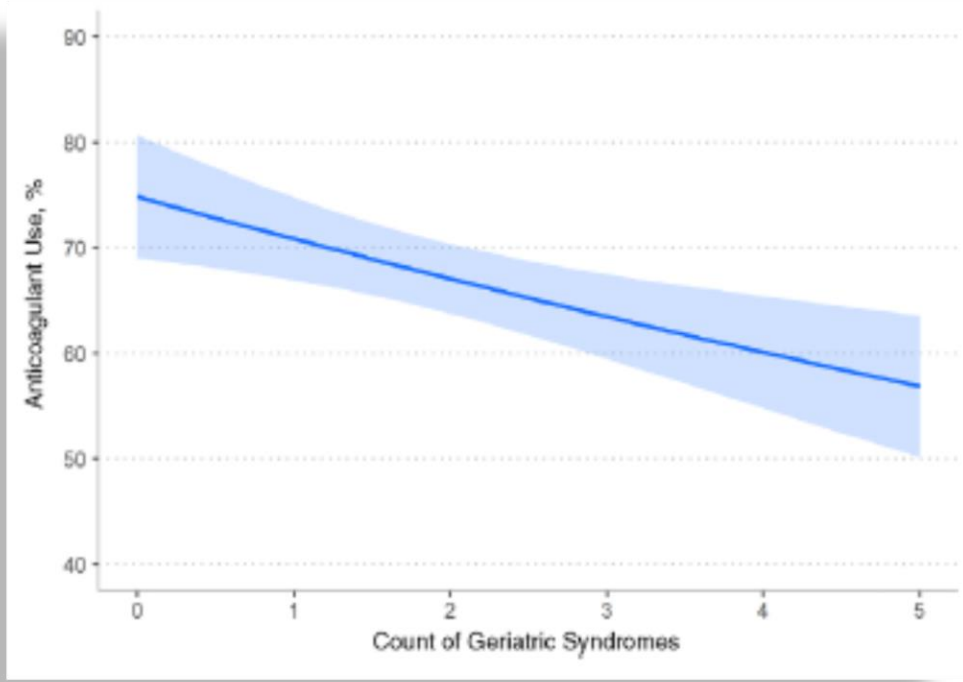
>**800000** real world **AF** patients,
mean age **78 years**,
52% frail
31% CCS>4
44% polypharmacy

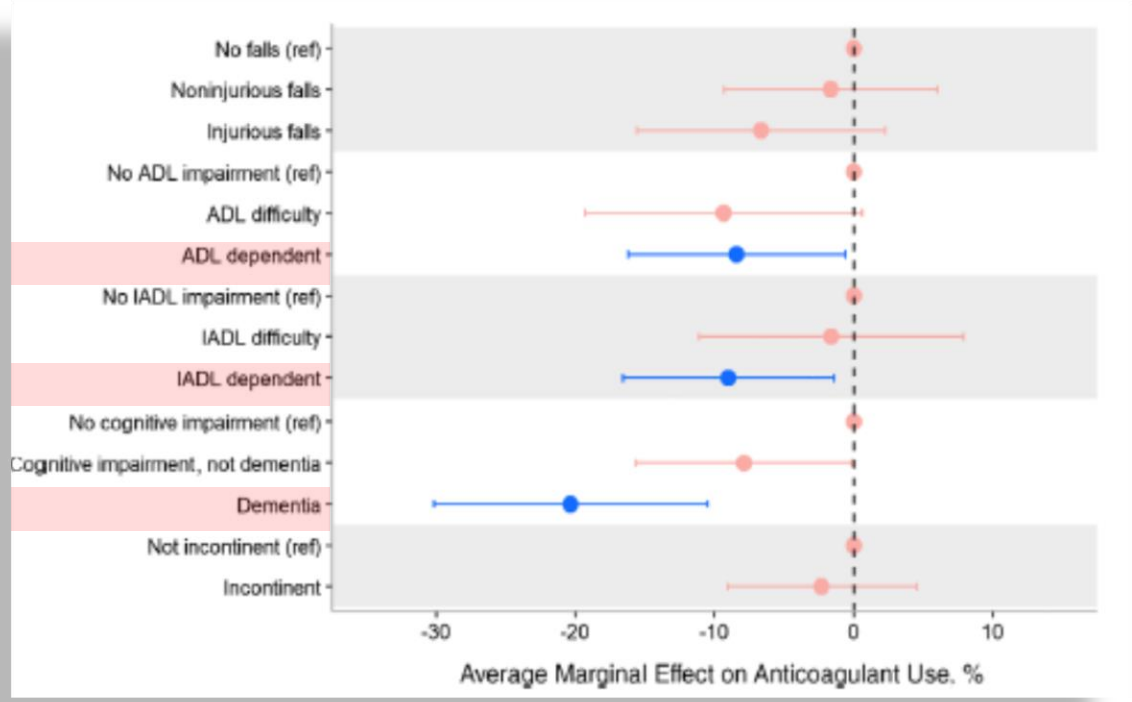
Multicenter study (Pisa, Torino, Cuneo) including 4230 AF older in-patients

	Overall N=4230
Gender (F) (%)	2426 (57.4)
Age mean (± SD)	85.8 (± 6.1)
ADL median(IQR)	3(0-5)
≤ 3	2401(57.3)
> 3	1787 (42.7)
SPMSQ median	3(1-6)
MILD	1884(45.7)
MODERATE	1418(34.4)
SEVERE	818 (19.9)
History of bleeding (%)	859(20.3)
History of stroke (%)	974(23)
CCI	3.9 (±1.9)
CHA2DS2Vasc	5 (4-6)
≤ 3	828(19.7)
> 3	3379(80.3)
HASBLED	2(1-2)
≤ 3	4000(95,1)
> 3	206(4.9)
EGFR mean (± SD)	52.8(±22.8)
OAC	2461 (58.2)

Geriatric Syndromes and Atrial Fibrillation: Prevalence and Association with Anticoagulant Use in a National Cohort of Older Americans

J Am Geriatr Soc 69:349- 356, 2021.





GL recommended OAC use: 97%

Effective OAC use: 61%

(Am J Cardiol 2016;117:590–595)

Effects of Oral Anticoagulant Therapy in Medical Inpatients ≥65 Years With Atrial Fibrillation

Mario Bo, PhD[a], Irene Sciarrillo, MD[a], Federica Li Puma, MD[a], Marco Badinella Martini, MD[a], Yolanda Falcone, MD[a,*], Marina Iacovino, MD[a], Enrica Grisoglio, MD[a], Elena Menditto, MD[a], Gianfranco Fonte, MD[a], Enrico Brunetti, MD[a], Guido Maggiani, MD[a], Giovanni Carlo Isaia, MD[a], :

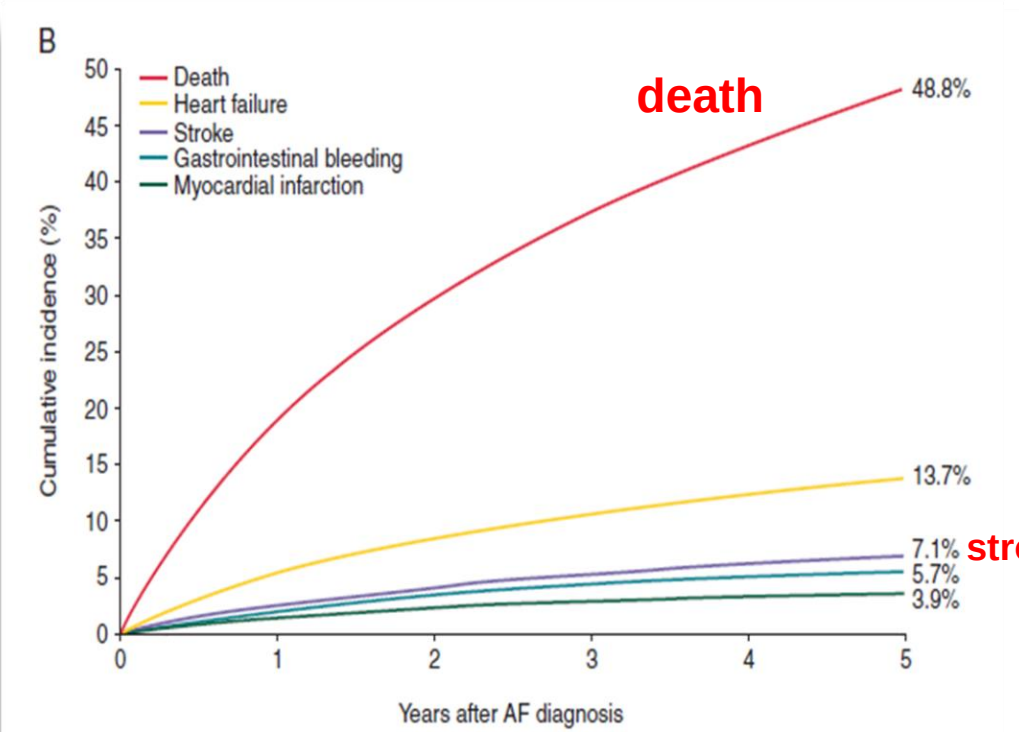
Clinical variables associated with overall mortality and non-fatal events: results of multivariate analysis

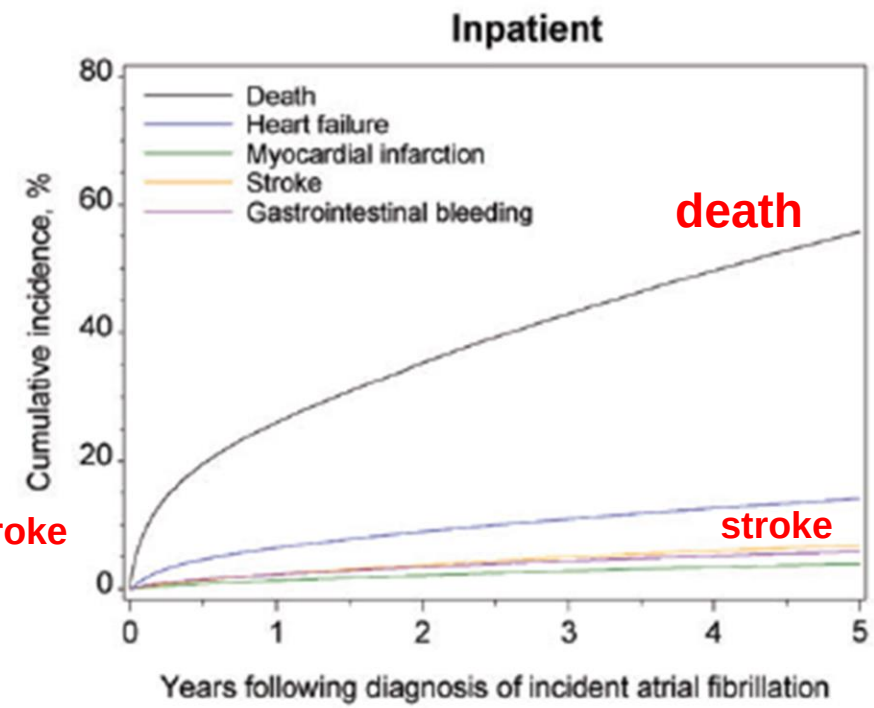
	p Value	OR (95% CI)
Mortality		
Intermediate or long-term care facility discharge	.0003	2.29 (1.47 - 3.57)
Creatinine	.0137	1.37 (1.07 - 1.75)
Charlson comorbidity index	.000	1.19 (1.11 - 1.28)
Anticoagulant therapy at discharge	.0000	0.52 (0.39 – 0.71)
Functional dependence in ADL	.0020	1.60 (1.19 – 2.16)
Age	.0000	1.07 (1.04 – 1.09)
Ischemic stroke		
CHAD2S2VASC	.0040	1.27 (1.08 - 1.49)
Hemoglobin level	.0016	1.20 (1.07 – 1.35)
Dementia	.0007	2.43 (1.46 – 4.05)
Hemorrhagic stroke	-	-
Major Bleeding events		
Female gender	.0163	0.45 (0.24 – 0.86)
Known atrial fibrillation	.0036	0.34 (0.16 – 0.70)
Permanent atrial fibrillation	.0407	1.73 (1.02 - 2.93)
HAS-BLED	.0053	1.35 (1.09 – 1.66)
Hemoglobin level	.0255	0.83 (0.17 – 4.14)
Re-hospitalizations	.0050	1.15 (1.04 – 1.28)

Clinical course of atrial fibrillation in older adults: the importance of cardiovascular events beyond stroke

European Heart Journal (2014) **35**, 250–256

186461 Medicare beneficiaries >=65 years (**mean age 79.5 years**) with AF; outcomes mortality and hospitalization





CHA2DS2-VASC score	Thromboembolism rate during the 1st year
9	15.2%
8	6.7%
7	9.6%
6	9.8%
5	6.7%
4	4.0%
3	3.2%
2	2.2%
1	1.3%
0	0.0%

European Heart Journal (2018) **39**, 1322–1329

'Ten Commandments' of the EHRA Guide for the Use of NOACs in AF

Do not undertreat frail and elderly patients.

2020 ESC Guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association of Cardio-Thoracic Surgery (EACTS)

"**frailty**, comorbidities, and increased risk of falls **do not outweigh the benefits of OAC**"

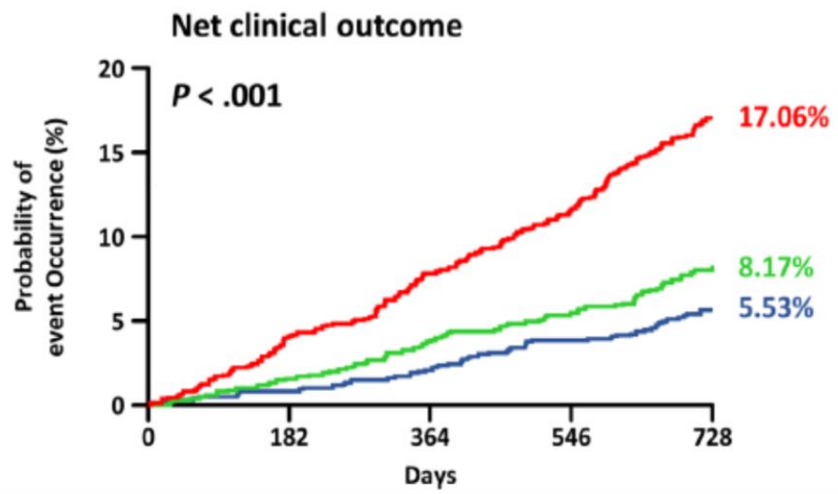
2021 European Heart Rhythm Association Practical Guide on the Use of Non-Vitamin K Antagonist Oral Anticoagulants in Patients with Atrial Fibrillation Europace (2021) **23**, 1612–1676

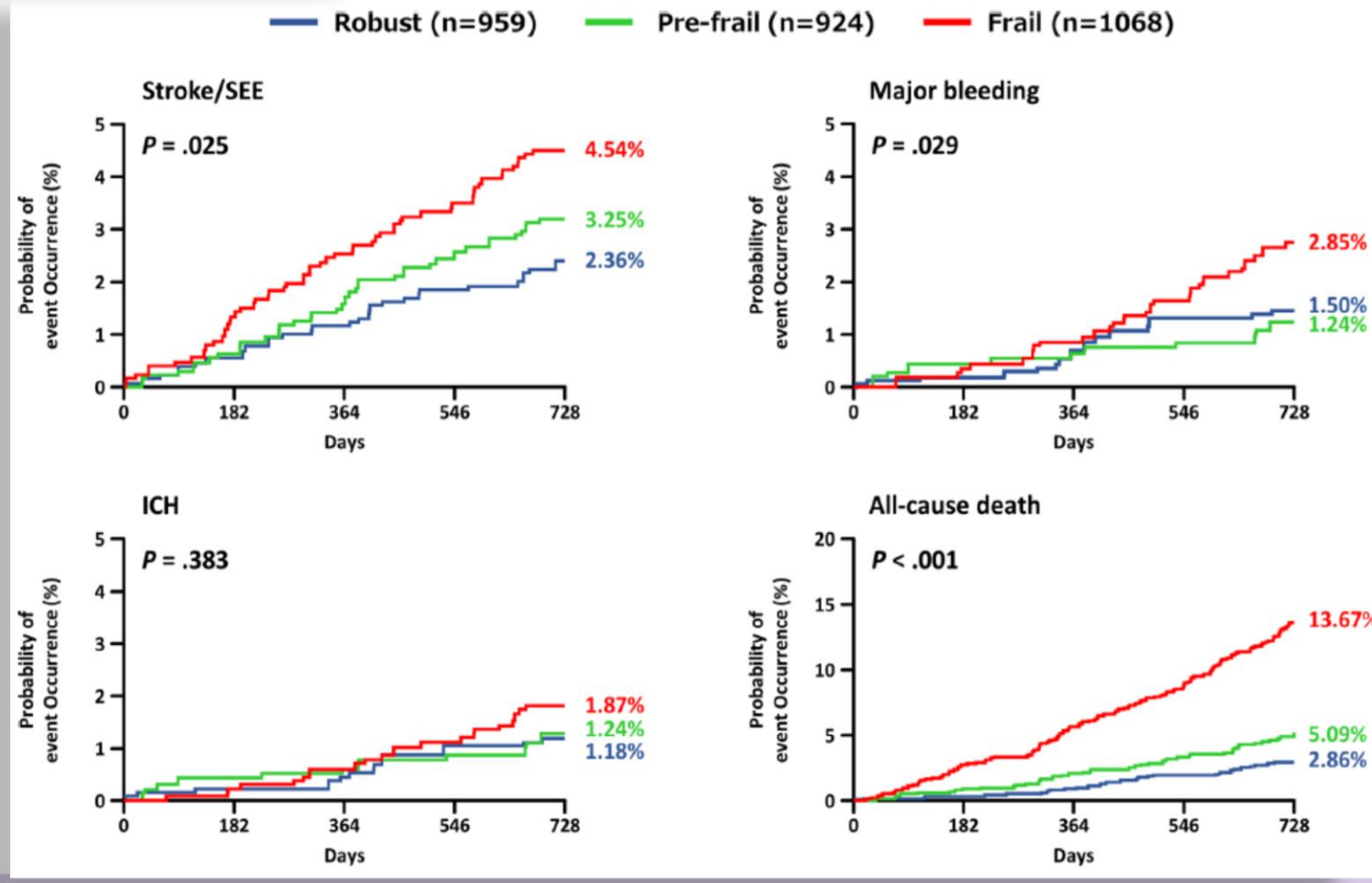
"*there may be* ***no benefit to OAC*** *in states of* ***severe frailty*** *or where* ***life expectancy is likely to be limited***"

Frailty and outcomes in older adults with non-valvular atrial fibrillation from the ANAFIE registry

Archives of Gerontology and Geriatrics 101 (2022) 104661

The Kihon Checklist for older adults, a validated screening tool widely used in Japan and Asian countries, was used to estimate frailty status in this study. It comprises 25 yes/no questions to evaluate physical strength, nutrition, eating, socialization, memory, mood, and lifestyle, for a total of seven categories. Each question is rated as 0 or 1, with the total score ranging from 0 to 25, and 0 indicating no frailty and 25, severe frailty. (Fukutomi, Okumiya & Wada, 2015; Satake, Senda & Hong, 2016) Patients with a score of 0 to 3 points are considered robust; those with a score of 4 to 7 points are pre-frail; and those with a score ≥8 points are frail.





Impact of frailty on all-cause mortality and major bleeding in patients with atrial fibrillation: A meta-analysis

Ageing Research Reviews 73 (2022) 101527

Lian He [a], Rong He [a], Jiabin Huang [a], Chen Zou [b,*], Yu Fan [a,*]

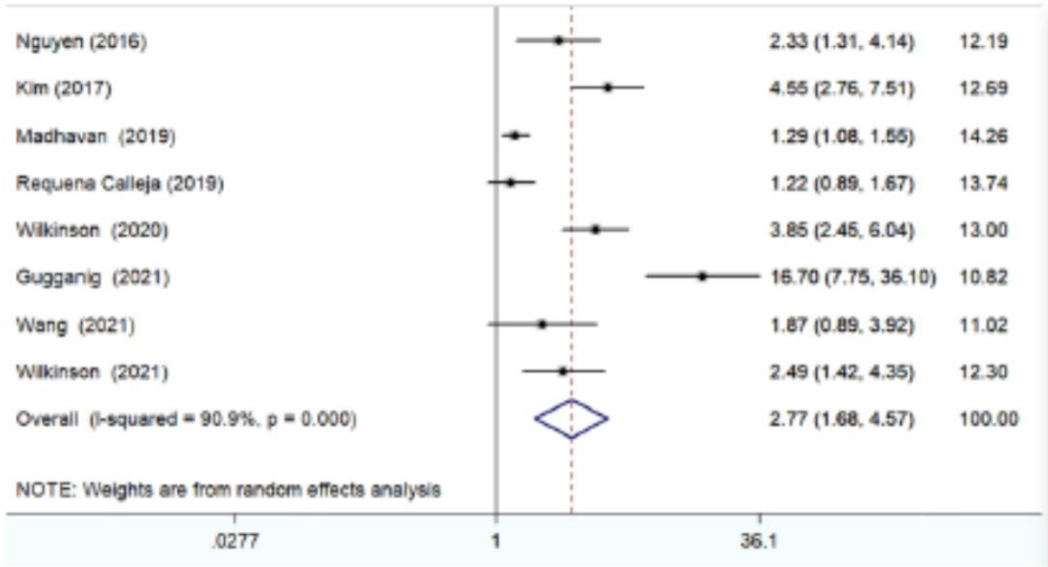


Fig. 2. Forest plots showing the pooled RR with 95% CI of all-cause mortality for the frail vs. nonfrail patients.

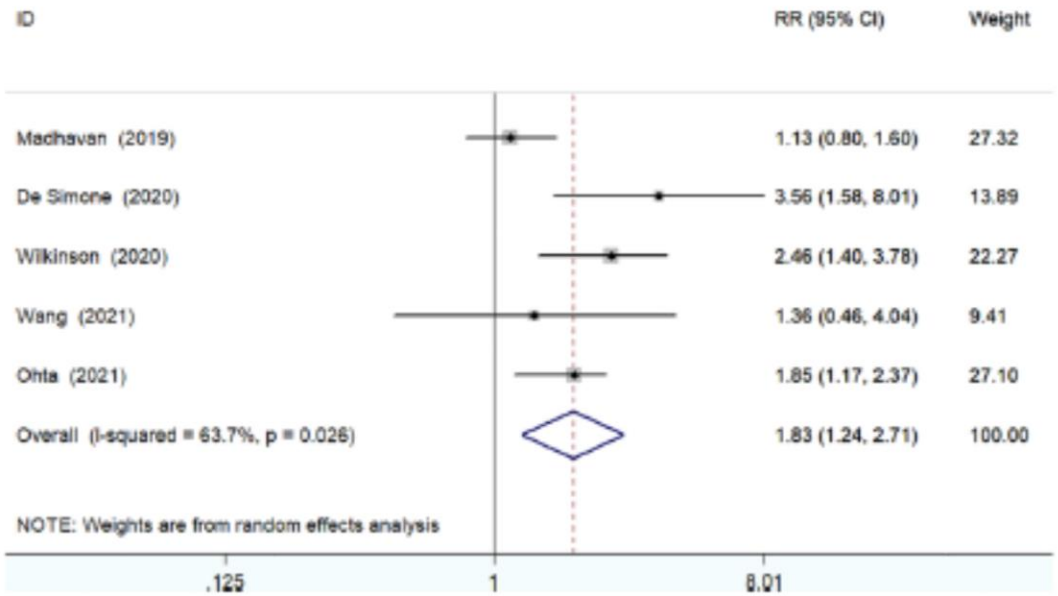
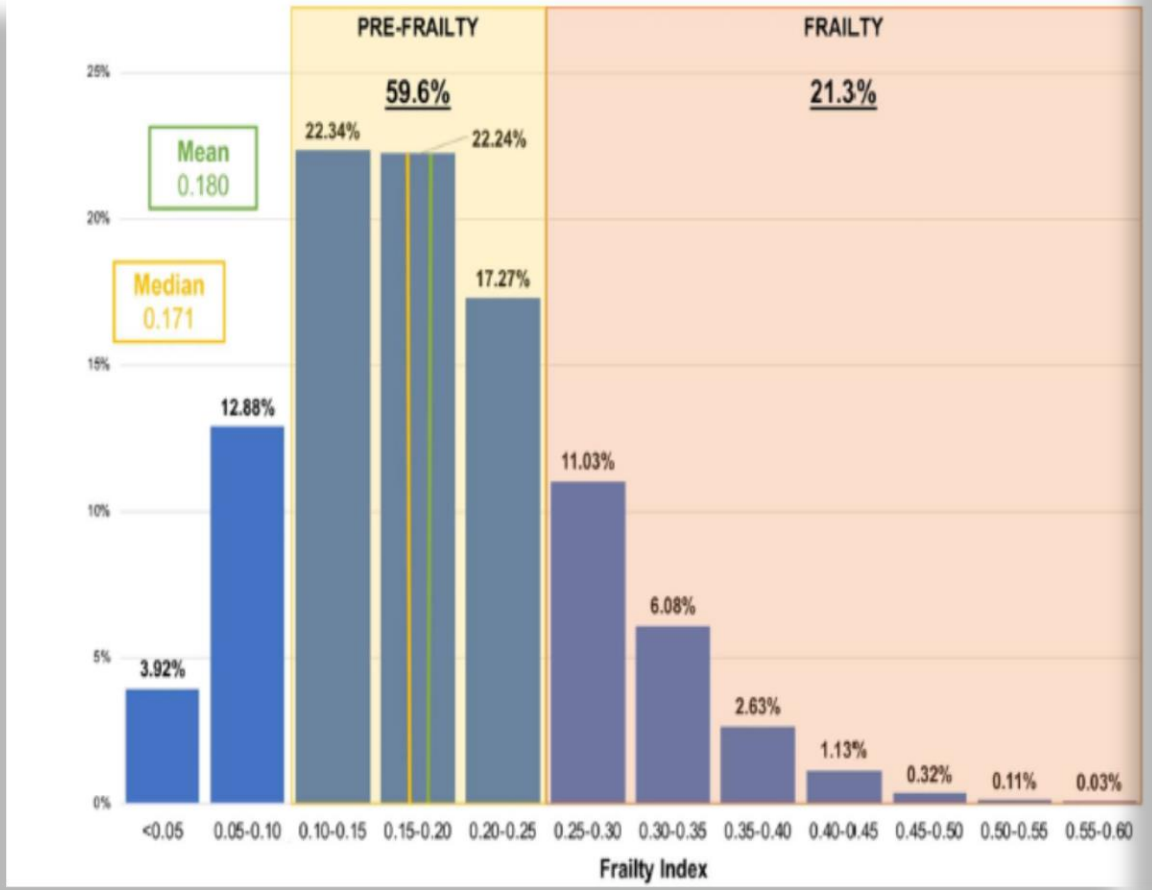


Fig. 3. Forest plots showing the pooled RR with 95% CI of major bleeding for the frail vs. nonfrail patients.

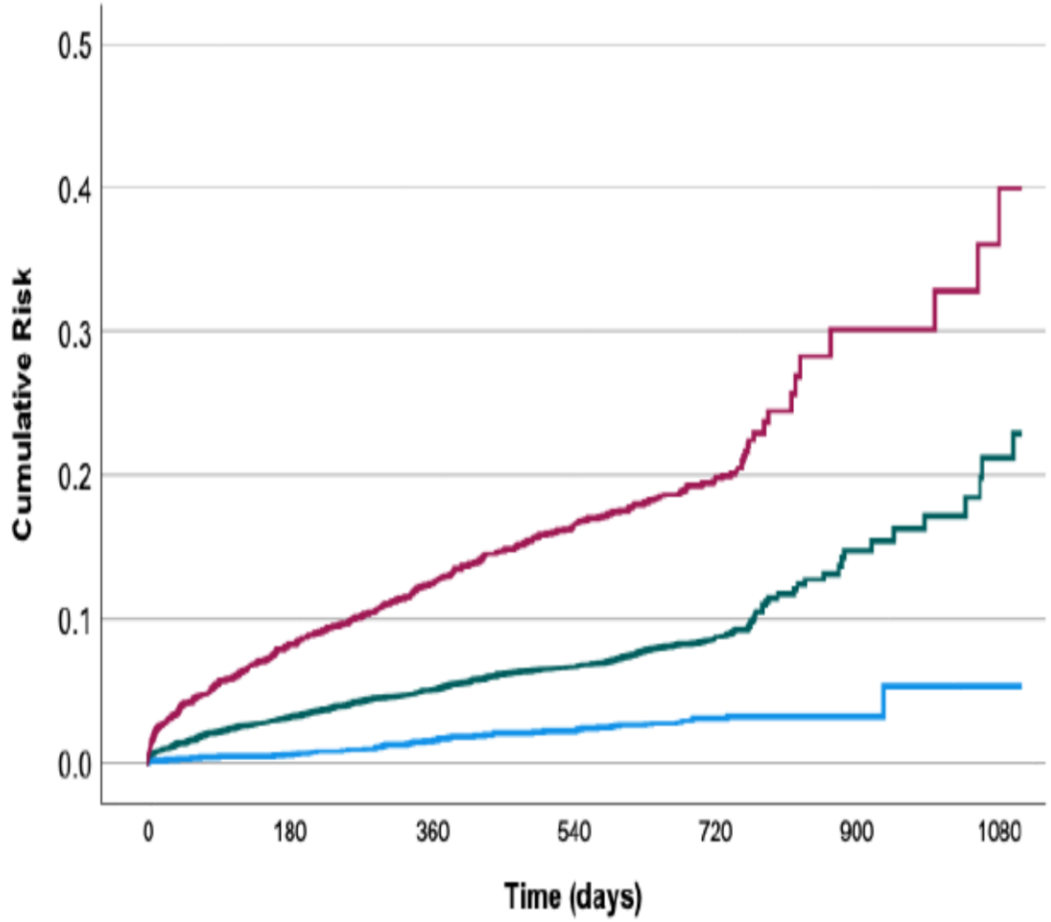
Age and Ageing 2022; **51**: 1–13

Epidemiology and impact of frailty in patients with atrial fibrillation in Europe

Marco Proietti[1,2,3,†], Giulio Francesco Romiti[1,4,†], Marco Vitolo[1,5,6], Stephanie L. Harrison[1],



Supplemental Figure 2: Kaplan-Meier Curves for All-Cause Death Cumulative Risk according to Frailty Classe

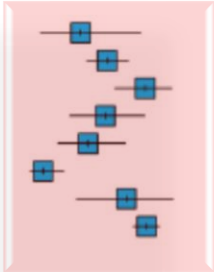


Frailty prevalence and impact on outcomes in patients with atrial fibrillation: A systematic review and meta-analysis of 1,187,000 patients

Marco Proietti[a,b,c,*,1,2,3], Giulio Francesco Romiti[d,1], Valeria Raparelli[e,f,g], Igor Diemberger[h], Giuseppe Boriani[i], Laura Adelaide Dalla Vecchia[j], Giuseppe Bellelli[k,l], Emanuele Marzetti[m,n], Gregory YH Lip[c,o,4], Matteo Cesari[a,b,4]

Ageing Research Reviews 79 (2022) 101652

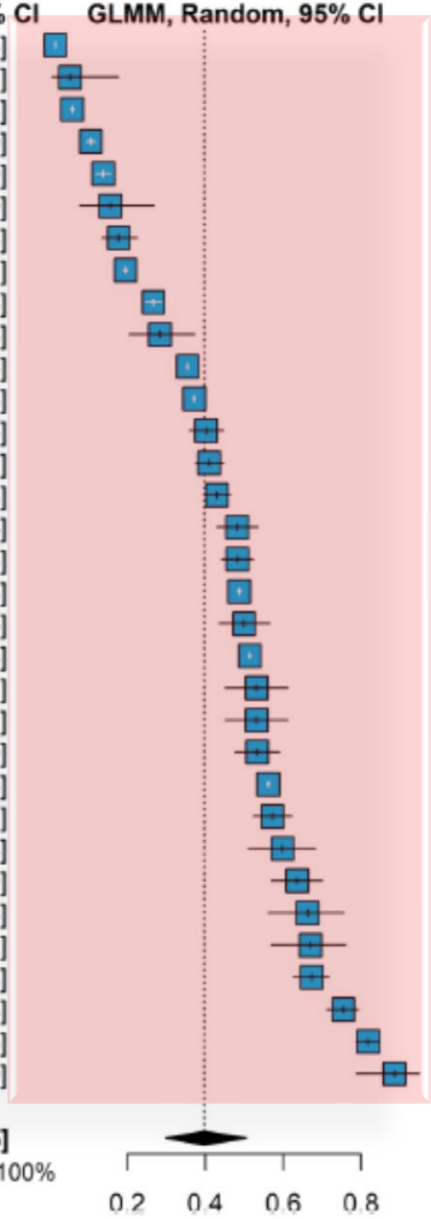
Frailty Tool			
Frailty Index	8	< 0.01	0.32 [0.12; 0.60] 100%
CFI	2		0.44 [0.35; 0.54] 100%
CFS	5		0.62 [0.48; 0.75] 98%
Edmonton	6		0.43 [0.26; 0.62] 91%
FRAIL	3		0.35 [0.21; 0.53] 97%
Frailty Phenotype	4		0.14 [0.08; 0.24] 98%
Other	3		0.53 [0.30; 0.76] 99%
TFI	2		0.63 [0.57; 0.69] 20%
Study Type			
Observational Single Centre	15	< 0.01	0.52 [0.41; 0.63] 95%
Observational Multicentre	9		0.34 [0.18; 0.56] 100%
Electronic Medical Records	5		0.44 [0.38; 0.50] 100%
RCT	1		0.20 [0.19; 0.20]
Population-based Study	3		0.09 [0.01; 0.48] 100%
Setting			
Community	10	< 0.01	0.17 [0.08; 0.32] 100%
Hospital	14		0.62 [0.53; 0.70] 97%
Other	9		0.37 [0.27; 0.48] 100%



Subgroup Analyses for the Prevalence of Frailty.

Study	Events	Total	GLMM, Random, 95% CI
Yang PS	4104	262987	0.016 [0.015; 0.016]
Yang MT	2	38	0.053 [0.006; 0.177]
Madhavan	575	9749	0.059 [0.054; 0.064]
Gugganig	252	2369	0.106 [0.094; 0.119]
Saczynski	172	1244	0.138 [0.120; 0.159]
Koca	10	64	0.156 [0.078; 0.269]
Son	53	298	0.178 [0.136; 0.226]
Wilkinson	4082	20867	0.196 [0.190; 0.201]
Pilotto	488	1827	0.267 [0.247; 0.288]
Ohta	34	120	0.283 [0.205; 0.373]
Sanghai	109475	308664	0.355 [0.353; 0.356]
Lip	150487	404798	0.372 [0.370; 0.373]
Liu	201	500	0.402 [0.359; 0.446]
De Simone	300	731	0.410 [0.374; 0.447]
Mostaza	360	837	0.430 [0.396; 0.464]
Kim	176	365	0.482 [0.430; 0.535]
Gullon	297	615	0.483 [0.443; 0.523]
Campitelli	17778	36466	0.488 [0.482; 0.493]
Yamamoto	120	240	0.500 [0.435; 0.565]
Hohmann	36267	70501	0.514 [0.511; 0.518]
Jankowska-Polanska	84	158	0.532 [0.451; 0.611]
Slawuta	84	158	0.532 [0.451; 0.611]
Nguyen	161	302	0.533 [0.475; 0.590]
Wilkinson 2	34382	61177	0.562 [0.558; 0.566]
Annoni	231	403	0.573 [0.523; 0.622]
Mlynarska	79	132	0.598 [0.510; 0.683]
Perera	140	220	0.636 [0.569; 0.700]
Wojszel	65	98	0.663 [0.561; 0.756]
Uchmanowicz	67	100	0.670 [0.569; 0.761]
Induruwa	282	419	0.673 [0.626; 0.718]
Bo	341	452	0.754 [0.712; 0.793]
Lefebvre	558	682	0.818 [0.787; 0.846]
Polidoro	62	70	0.886 [0.787; 0.949]
Total (95% CI)		**1187651**	**0.397 [0.299; 0.505]**

Heterogeneity: $Tau^2 = 1.6066$; $Chi^2 = 77852.42$, df = 32 (P = 0); $I^2 = 100\%$

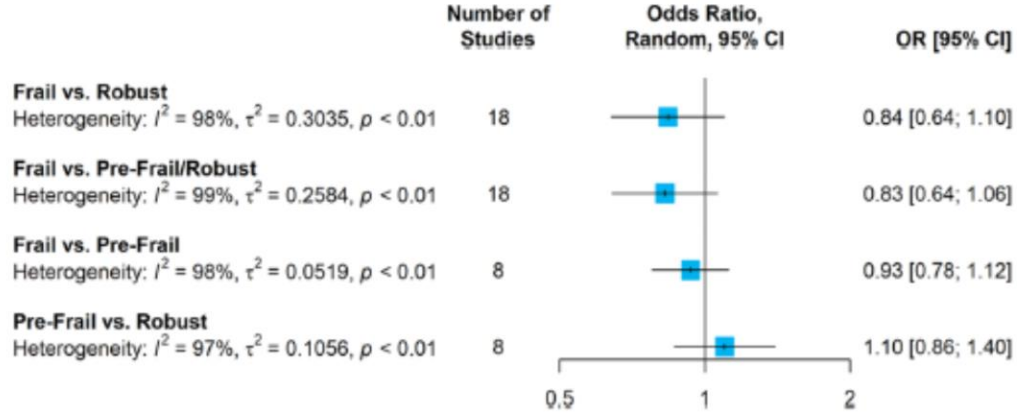


Prevalence of Frailty in patients with Atrial Fibrillation.

Ageing Research Reviews 79 (2022) 101652

Frailty prevalence and impact on outcomes in patients with atrial fibrillation: A systematic review and meta-analysis of 1,187,000 patients

Marco Proietti [a,b,c,*,1,2,3], Giulio Francesco Romiti [d,1], Valeria Raparelli [e,f,g], Igor Diemberger [h], Giuseppe Boriani [i], Laura Adelaide Dalla Vecchia [j], Giuseppe Bellelli [k,l], Emanuele Marzetti [m,n], Gregory YH Lip [c,o,4], Matteo Cesari [a,b,4]



OAC Prescription according to Frailty status.

Management of atrial fibrillation for older people with frailty: a systematic review and meta-analysis

Age and Ageing 2019; **48:** 196–203

Key Points

- Older people with frailty and AF are at risk of worse clinical outcomes.
- Anticoagulation of older people with frailty and AF is an under-researched area.
- Frailty is associated with lower rates of anticoagulation in patients with AF who are admitted to hospital.

Although anticoagulation is largely initiated and managed in primary care, there is a lack of evidence to guide optimal care in this setting for patients with AF and frailty.

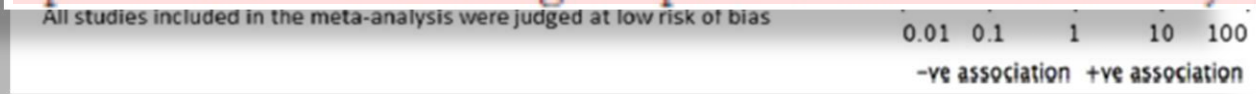


Figure 2. Forest plot to show association between frailty and anticoagulation status at admission, at discharge and in the community

*"there may be **no benefit to OAC** in states of **severe frailty** or where **life expectancy is likely to be limited**"*

Practical use of Direct Oral Anti Coagulants (DOACs) in the older persons with atrial fibrillation. European Journal of Internal Medicine 71 (2020) 32–38

Mario Bo (MD, PhD)[a,1,*], Niccolò Marchionni (MD, PhD)[b,1,2]

Table 1. MPI Score Assigned to Each Domain Based on the Severity of the Problems

	Problems		
	No	Minor	Severe
Assessment	(Value=0)	(Value=0.5)	(Value=1)
ADL*	6–5	4–3	2–0
Instrumental ADL*	8–6	5–4	3–0
Short portable mental status questionnaire†	0–3	4–7	8–10
Comorbidity index (cumulative illness rating scale-CI)‡	0	1–2	≥3
Mini nutritional assessment§	≥24	17–23.5	<17
Exton-smith scale¶	16–20	10–15	5–9
No. of medications	0–3	4–6	≥7
Social support network	Living with family	Institutionalized	Living alone

*No. of active functional activities.
†No. of errors.
‡No. of diseases.
§Mini Nutritional Assessment score: ≥24, satisfactory nutritional status; 17–23.5, at risk of malnutrition; <17, malnutrition.
¶Exton-Smith Scale score: 16–20, minimum risk; 10–15, moderate risk; 5–9 high risk of developing scores.

Pilotto A. et Al. Circ.Heart Fail.2010;3.14-20



Main frailty tools for practical use.

CHS Frailty Scale – Frailty phenotype	«physical» frailty tools, not including disability and disease burden
SOF Frailty Scale	
SPPB & Gait speed	
Green score	
Frail Scale	«hybrid» frailty tools, including measures of disease burden
Vulnerable Elders Survey-13	
Groningen Frailty Indicator (GFI)	
Clinical Frailty Scale	«Deficit accumulation» tools, identifying frail and vulnerable patient of
Frailty Index	deficits and psycho-social variables


2-year all-cause mortality:

10%

40-50%




Studies reporting the association between frailty and anticoagulation status by frailty model (RQ #1).

Deficit accumulation		
Campitelli et al. (2021)	36 466	Less use
Denoël et al. (2014)	142	No difference
Gugganig et al. (2021)	2 369	No difference
Induruwa et al. (2017)	419	Less use
Lefebvre et al. (2016)	682	Less use
Orlandi et al. (2022)	75 796	Less use
Sanghai et al. (2022)	308 664	Less use
Wilkinson et al. (2021)	61 177	More use
Wojszel and Kasiukiewicz (2020)	95	Less use

Frail phenotype		
Doucet et al. (2008)	209	No difference
Ekerstad et al. (2018)	408	No difference
Ferguson et al. (2017)	137	No difference
Gullón et al. (2019)	557	No difference
Madhavan et al. (2019)	9 479	Less use
Mailhot et al. (2020)	1 244	No difference
Saczynski et al. (2020)		No difference
Requena Calleja et al. (2019)	596	Less use
Tan et al. (2022)	150	No difference

Hybrid		
Akishita et al. (2022)	2 951	No difference
Bo et al. (2015)	550	No difference
Kim et al. (2017)	365	No difference
Nguyen et al. (2016a)	302	No difference
Perera et al. (2009)	220	Less use
Pilotto et al. (2016)	1 827	Less use
Tan et al. (2022)	150	No difference

Impact of frailty models on the prescription of oral anticoagulants and on the incidence of stroke, bleeding, and mortality in older patients with atrial fibrillation: a systematic review

Ageing Research Reviews 82 (2022) 101761

Roberto Presta [a,*,1,2], Enrico Brunetti [b,c,1,3], Maria Cristina Polidori [d,e,4], Mario Bo [a,5]

Studies reporting the association between frailty and all-cause mortality (c) by frailty model

Deficit accumulation				
Gugganig et al. (2021)	2 369	24	Higher risk	aHR 14.52 (5.03–41.90) VKA aHR 32.34 (7.04–148.50) DOAC[2]
Kusano et al. (2021)	5 717	24 (6)	Higher risk	aHR 2.09 (1.42–3.08)
Wilkinson et al. (2020)	20 867	33.6	Higher risk[3]	aHR 4.97 (3.42–7.23) severely frail aHR 3.13 (2.48–3.95) mildly-moderately frail
Yamamoto et al. (2019)	240	9.2 (1.5–25.5)	Higher risk	n.s.[4]

Frail phenotype				
Doucet et al. (2008)	209	3	No difference	n.a.
Gullón et al. (2019)	557	12	Higher risk	n.a.
Madhavan et al. (2019)	9 479	30.6 (22.0–35.8)	No difference[5]	n.s.
Ohta et al. (2021)	120	17.0	n.s.	
Wang et al. (2021)	1 244	12	Higher risk	aHR 3.87 (1.96–7.65)

Multidimensional				
Bo et al. (2017b)	452	9.9 (2.0)	Higher risk	aOR 2.77 (95% CI n.s.)
de Simone et al. (2020)	731	28.1 (13.6)	n.s.	

Impact of frailty models on the prescription of oral anticoagulants and on the incidence of stroke, bleeding, and mortality in older patients with atrial fibrillation: a systematic review

Ageing Research Reviews 82 (2022) 101761

Roberto Presta[a,*,1,2], Enrico Brunetti[b,c,1,3], Maria Cristina Polidori[d,e,4], Mario Bo[a,5]

ONE SIZE FITS ALL?

Influence of Competing Risks on Estimating the Expected Benefit of Warfarin in Individuals with Atrial Fibrillation Not Currently Taking Anticoagulants: The Anticoagulation and Risk Factors in Atrial Fibrillation Study J Am Geriatr Soc 65:35–41, 2017

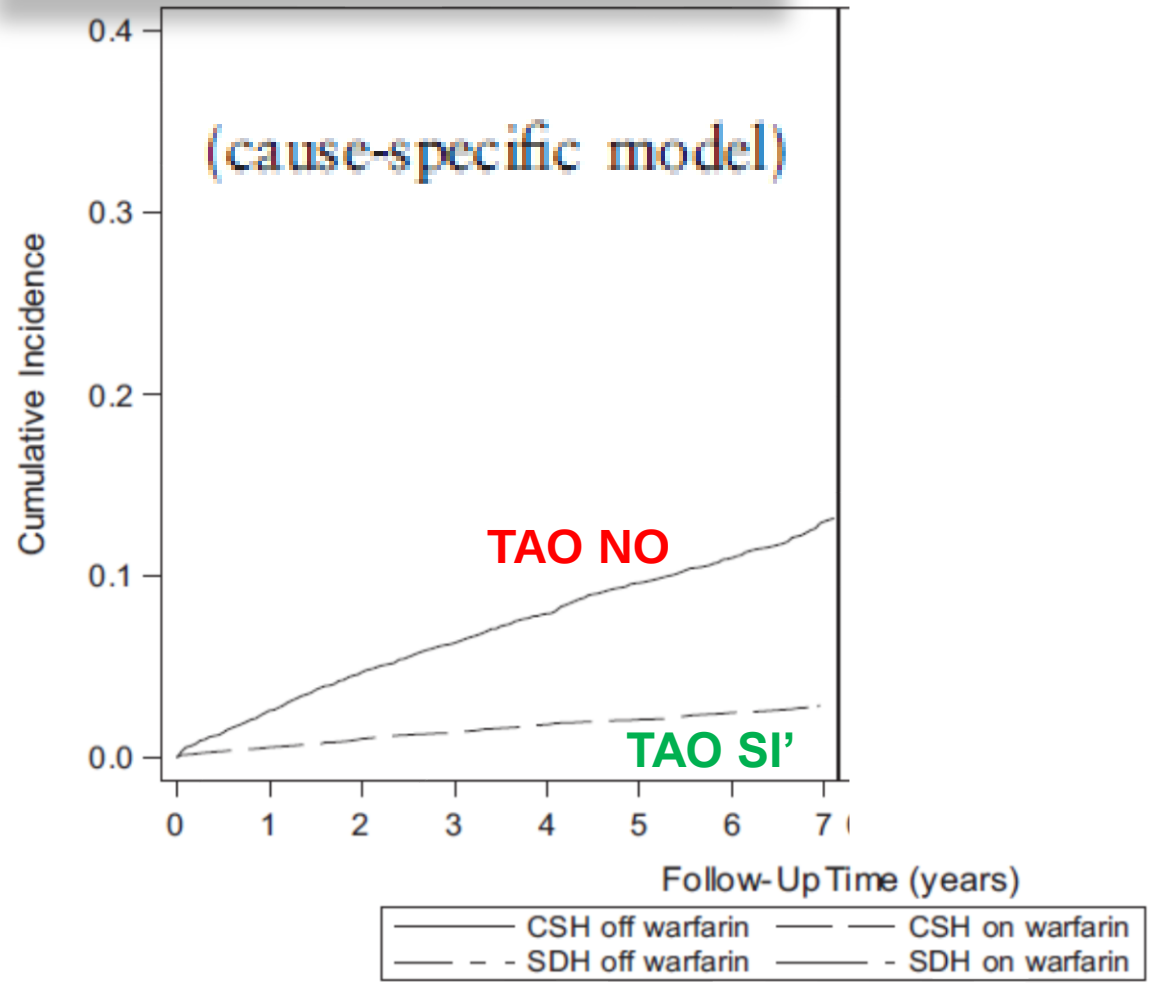


Table 4. Association Between Time-Varying Warfarin Use and Thromboembolism in Adults with Atrial Fibrillation According to Age (Cause-Specific and Subdistribution Hazards)

	Cause-Specific	Subdistribution
Age	Hazard Ratio (95% Confidence Interval)[a]	
<65	1.08 (0.90–1.30)	1.07 (0.73–1.57)
65–74	0.66 (0.59–0.73)	0.96 (0.77–1.20)
75–84	0.57 (0.52–0.62)	0.76 (0.63–0.92)
≥85	0.62 (0.53–0.72)	0.91 (0.63–1.31)

Conclusions:..analyses accounting for competing death events may provide a more realistic estimate of OAC benefit…and highlight the **importance of accounting for the individual's life expectancy in weighing the benefits and the harms of long-term OAC**

Percorso clinico decisionale nel paziente anziano fragile con fibrillazione atriale: la proposta di un gruppo di lavoro multidisciplinare

Niccolò Marchionni[1], Stefano Fumagalli[2], Mario Bo[3], Alessandro Boccanelli[4], Giuseppe Boriani[5], Andrea Rubboli[6], Francesco Violi[7], Giuseppe Di Pasquale[8]

Fit, completa autonomia

RACCOMANDATA
Indipendentemente dall'età

Fenotipo fragile o pre-fragile, CFS <5
Autonomia preservata (B-ADL <2)
Impairment cognitivo (MMSE >18/30)
MPI 0.33-0.66
DA CONSIDERARE

Severo deterioramento cognitivo (MMSE <18) e/o perdita di autonomia (B-ADL >2) e/o ridotta spettanza di vita (CFS >6)
Nessuna evidenza di beneficio clinico
MPI >0.66
NO EVIDENCE







ABC — **OPTIONS??**

Europace (2022) **24**, 1065–1075

Impact of oral anticoagulation on the association between frailty and clinical outcomes in people with atrial fibrillation: nationwide primary care records on treatment analysis

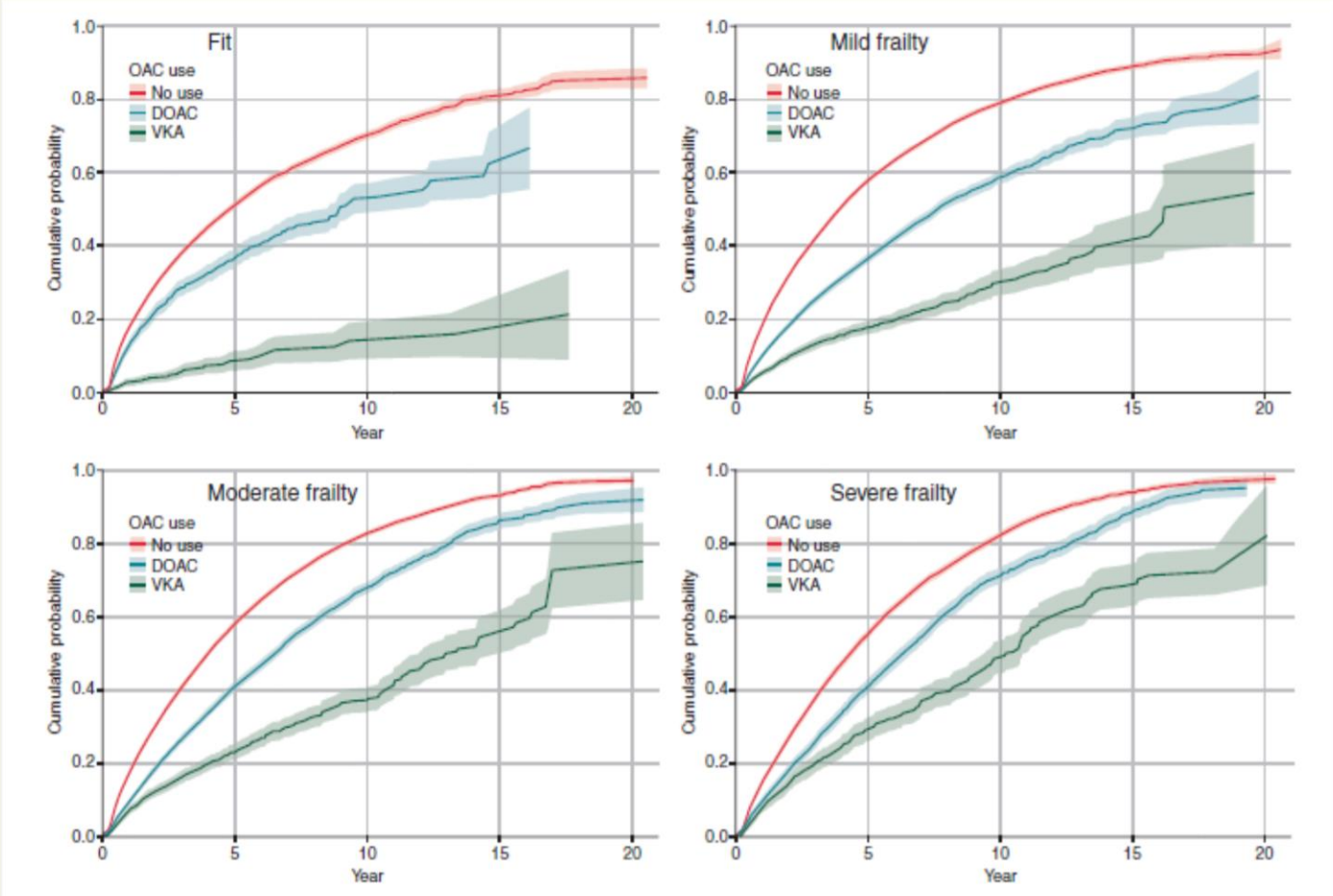


Figure 1 Cumulative incidence function for composite outcome (death, stroke, systemic embolism, gastrointestinal, or intra-cranial haemorrhage) by frailty category and time-varying anticoagulation status (with 95% confidence intervals).

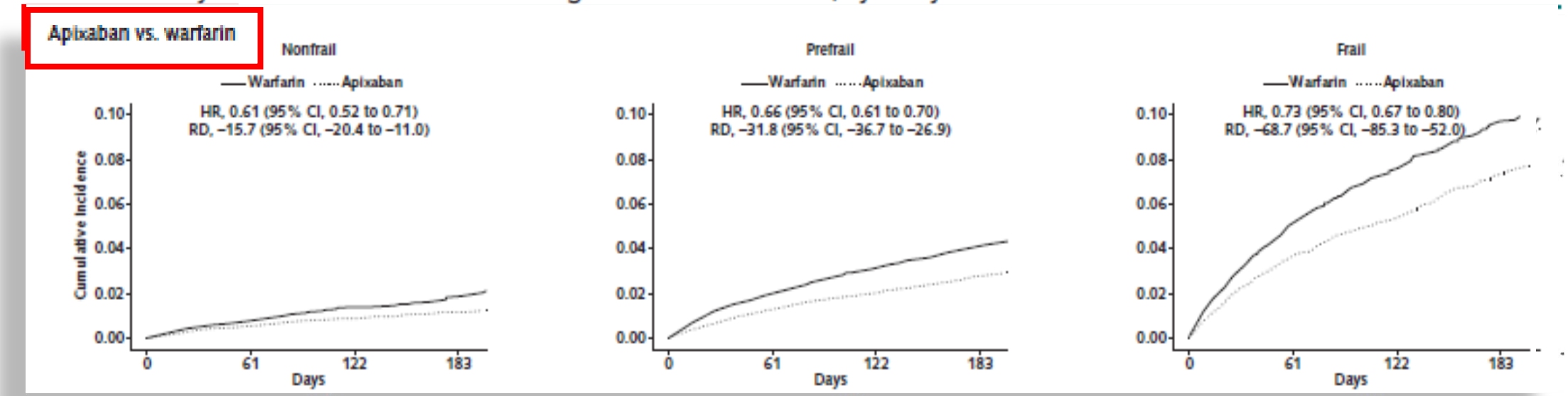
Frailty and Clinical Outcomes of Direct Oral Anticoagulants Versus Warfarin in Older Adults With Atrial Fibrillation

A Cohort Study

Ann Intern Med. doi:10.7326/M20-7141

1:1 PSM analysis AF Medicare beneficiaries (mean age 76 years) with frailty (CFI) who initiated warfarin or DOACs

Figure. Cumulative incidence plots of a composite end point of death, ischemic stroke, or major bleeding in older adults with atrial fibrillation newly treated with direct oral anticoagulants versus warfarin, by frailty level.



SOCIETÀ ITALIANA DI GERONTOLOGIA E GERIATRIA

67° CONGRESSO NAZIONALE SIGG

LA LONGEVITÀ DECLINATA AL FEMMINILE

Percorso clinico decisionale nel paziente anziano fragile con fibrillazione atriale: la proposta di un gruppo di lavoro multidisciplinare

Niccolò Marchionni[1], Stefano Fumagalli[2], Mario Bo[3], Alessandro Boccanelli[4], Giuseppe Boriani[5], Andrea Rubboli[6], Francesco Violi[7], Giuseppe Di Pasquale[8]

Fit, completa autonomia

RACCOMANDATA
Indipendentemente dall'età

Fenotipo fragile o pre-fragile, CFS <5
Autonomia preservata (B-ADL <2)
Impairment cognitivo (MMSE >18/30)

MPI 0.33-0.66
DA CONSIDERARE

Severo deterioramento cognitivo (MMSE <18) e/o perdita di autonomia (B-ADL >2) e/o ridotta spettanza di vita (CFS >6)
Nessuna evidenza di beneficio clinico

MPI >0.66
NO EVIDENCE







ABC **OPTIONS??**

Geriatric Care 2016; volume 2:6120

Antiplatelet therapy is not a safer alternative to oral anticoagulants, even in older hospital-discharged patients with atrial fibrillation

Mario Bo,[1] Yolanda Falcone,[1] Enrica Grisoglio,[1] Margherita Marchetti,[1] Federica Li Puma,[1] Marina Iacovino,[1] Enrico Brunetti,[1] Gianfranco Fonte[2]

[1]Department of Geriatrics, Città della Salute e della Scienza - Molinette Hospital, University of Torino; [2]Unit of Post-Acute Care, Città della Salute e della Scienza, University of Torino, Italy

Clinical events	OAT (n=520)	APT (n=442)	P
Overall mortality, n (%)	155 (29.8%)	229 (51.8%)	0.00000
Total ischemic stroke, n (%)	26 (5.0%)	40 (9.0%)	0.01327
Fatal ischemic stroke, n (%)	10 (1.9%)	18 (4.1%)	0.0425
Ischemic events, other sites, n (%)	25 (4.8%)	25 (5.7%)	0.55467
Hemorrhagic stroke/intracranial bleeding, n (%)	6 (1.15%)	3 (0.68%)	0.44556
Major extra-cranial bleeding, n (%)	25 (4.8%)	15 (3.4%)	0.27357
Major bleeding, total, n (%)	31 (6.0%)	18 (4.1%)	0.18414
Fatal bleeding, n (%)	6 (1.1%)	5 (1.1%)	0.9738
Minor bleeding, n (%)	37 (7.1%)	19 (4.3%)	0.06296

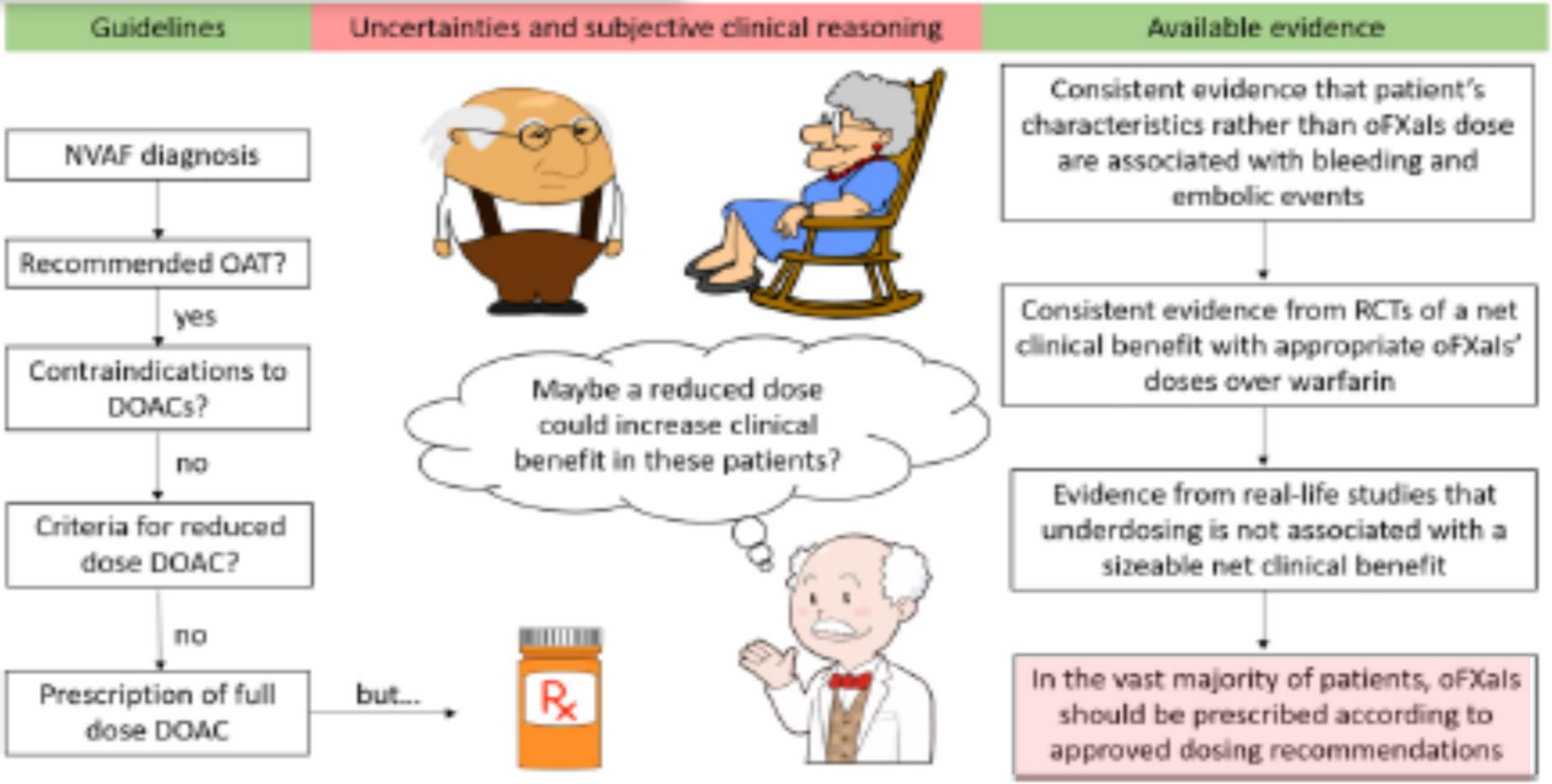
OAT, oral anticoagulant therapy; APT, anti platelet therapy.

…among real-world older AF in-patients with poor health status, those **treated with aspirin had higher incidence of stroke and similar risk of major bleeding** compared with patients treated with OAT…

Off-label use of reduced dose direct oral factor Xa inhibitors in subjects with atrial fibrillation: a review of clinical evidence

Mario Bo [1]*, Alberto Corsini [2,3], Enrico Brunetti [1], Gianluca Isaia[1], Maddalena Gibello[1], Nicola Ferri [4], Daniela Poli[5], Niccolò Marchionni [6], Gaetano Maria De Ferrari [7]

European Heart Journal - Cardiovascular Pharmacotherapy (2021) **7**, 334–345



Age and Ageing 2017; **46:** 600–607

STOPPFrail (Screening Tool of Older Persons Prescriptions in Frail adults with limited life expectancy): consensus validation

STOPPFrail is a list of potentially inappropriate prescribing indicators designed to assist physicians with stopping such medications in older patients (≥65 years) who meet ALL of the criteria listed below:

(1) End-stage irreversible pathology
(2) Poor one year survival prognosis
(3) Severe functional impairment or severe cognitive impairment or both
(4) Symptom control is the priority rather than prevention of disease progression

Special Communication | LESS IS MORE *JAMA Intern Med.* 2015;175(5):827-834.

Reducing Inappropriate Polypharmacy The Process of Deprescribing

We define *deprescribing* as the systematic process of identifying and discontinuing drugs in instances in which existing or potential harms outweigh existing or potential benefits within the context of an individual patient's care goals, current level of functioning, life expectancy, values, and preferences. Deprescribing is part of the good prescribing continuum, which spans therapy initiation, dose titration, changing or adding drugs, and switching or ceasing drug therapies.

Nei pazienti ospedalizzati con FA nota in TAO all'ingresso abbiamo valutato:

le variabili cliniche associate alla decisione di sospendere la TAO alla dimissione

l'incidenza di morte, ictus e sanguinamenti maggiori in relazione alla prosecuzione/sospensione della TAO

4059 pazienti ≥ 75 anni ricoverati in Geriatria (2289 Pisa, 986 Torino,784 Cuneo) con **diagnosi primaria o secondaria di FA**

Variabili	Tutte le FA (note+nuove) (n=4059)	Nuove FA (n=737)
Età media (sesso)	86.2 ± 5.4 anni (F 58.3%)	86.8 ± 5.8 anni (F 63%)
Classificazione FA	67.7% persistente/permanente	55.5% persistente/permanente
CHA_2DS_2VASc	4.7 ± 1.4	4.5 ± 1.3
HAS-BLED	2 ± 0.88	1.9 ± 0.83
Anamnesi sanguinamenti	20%	20%
Charlson Comorbidity Index	3.9 ± 1.9	3.3 ± 2
Deterioramento cognitivo	35.5% moderato-severo	36.3% moderato-severo
ADL	70% parz / tot dipendente	70.5% parz / tot dipendente
IADL	90% parz / tot non autonomo	85% parz / tot non autonomo
eGFR	52.4 ml/min ± 22.6	54.5 ml/min ± 23.4

Bo M, Brunetti E, Presta R., submitted

FA note in terapia anticoagulante al ricovero

Variabile (anamnestica)	Totale (n=1578)	TAO deprescritta in dimissione n=341 (21,6%)	TAO confermata in dimissione n=1237 (78,4%)	p
Età, anni, mediana (25°-75°)	86 (82-89)	86 (83-90)	85 (81-89)	0.0004
Sesso maschile, n (%)	690 (43.7)	145 (42.5)	545 (44.1)	0.6126
Tipo di FA n (%):				<0.0001
- Parossistica	374 (23.7)	110 (32.3)	264 (21.3)	
- Cronica	1204 (76.3)	231 (67.7)	973 (78.7)	
CHA2DS2-VASc, m±ds	4.7±1.4	4.7±1.4	4.7±1.3	0.8618
Storia di ictus, n (%)	361 (22.9)	92 (27)	269 (21.8)	0.0416
HAS-BLED, m±ds	1.9±0.85	2.3±0.91	1.8±0.81	<0.0001
Storia di sanguinamenti, n (%)	282 (17.9)	111 (32.6)	171 (13.8)	<0.0001
Charlson Comorbidity Index, m±ds	3.5±1.7	3.9±1.5	3.4±1.8	<0.0001
ADL, numero di funzioni conservate, m±ds	3.4±2.3	2.5±2.4	3.6±2.2	<0.0001
IADL, numero di funzioni conservate, m±ds	2.6±2.6	2.1±2.5	2.8±2.6	<0.0001
SPMSQ, numero di errori, m±ds	3.5±3.2	4.4±3.7	3.2±3.0	<0.0001

Deprescrizione TAO - ANALISI MULTIVARIATA

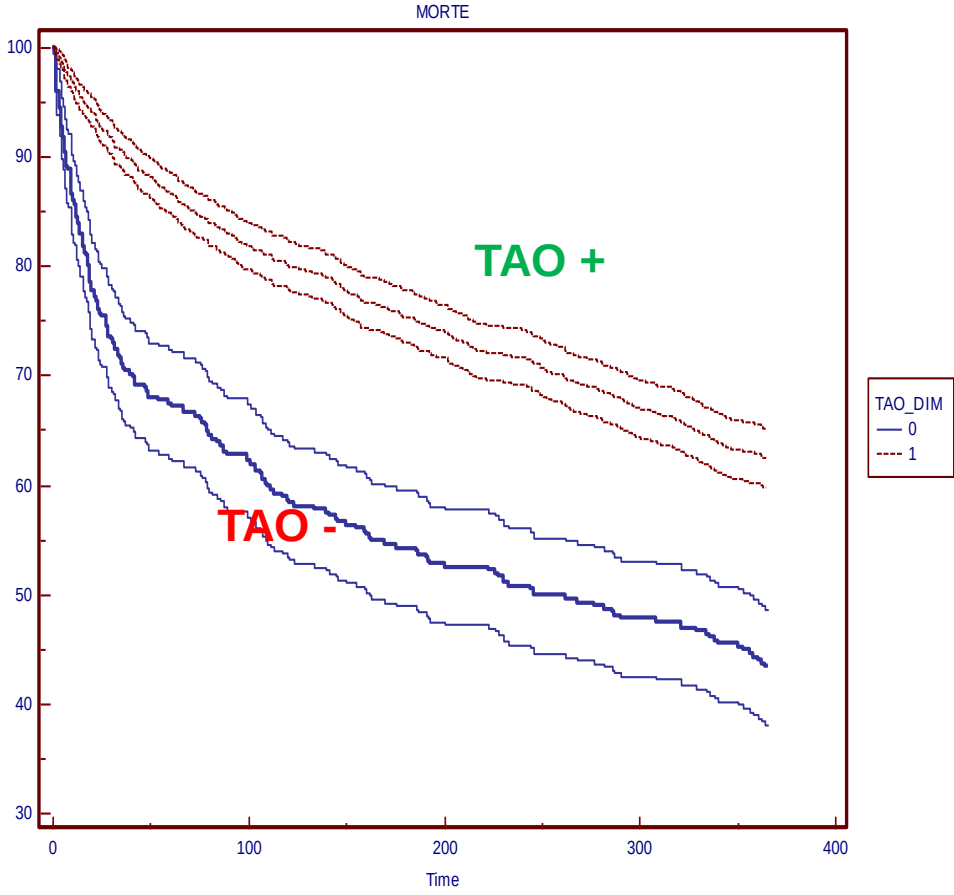
	β	OR (95% CI)
Età	0,04086	**1,0417** 1,0150 - 1,0691
FA cronica	-0,5358	**0,5852** 0,4371 - 0,7836
Storia di sanguinamenti	0,7382	**2,0923** 1,5166 - 2,8865
HAS BLED	0,3897	**1,4765** 1,2543 - 1,7379
CCI	0,0967	**1,1015** 1,0188 - 1,1910
ADL	0,3674	**1,4440** 1,2253 - 1,7018

Bo M, Brunetti E, Presta R., submitted

FA note in terapia anticoagulante al ricovero

Variabile	Campione totale n=1578	Vivi 920 (58,3%)	Morti 658 (41,7%)	p
Età, anni, mediana (25°-75°)	86 (82-89)	85 (81-88)	87 (83-90)	<.0001
Sesso maschile, n (%)	690 (43.7)	405 (44.0)	285 (43.3)	0.7796
Tipo di FA, n (%):				0.8058
- parossistica	374 (23.7)	216 (23.5)	158 (24.0)	
- cronica	1204 (76.3)	704 (76.5)	500 (76)	
CHA2DS2-VASc, m±ds	4.7±1.4	4.7±1.3	4.8±1.5	0.0732
Storia di ictus, n (%)	361 (22.9)	189 (20.5)	172 (26.1)	0.0091
HAS-BLED, m±ds	1.9±0.85	1.8±0.81	2.0±0.89	<.0001
Storia di sanguinamenti, n (%)	282 (17.9)	141 (15.3)	141 (21.4)	0.0018
eGFR sec CKD-EPI, ml/min, mediana (25°-75°)	51.6 (36.5-69.1)	52.8 (40.4-73.4)	47.1 (31.2-65.2)	<.0001
Charlson Comorbidity Index, m±ds	3.5±1.7	3.3±1.8	3.8±1.6	<.0001
ADL, numero di funzioni conservate, m±ds	3.4±2.3	4±2.1	2.6±2.2	<.0001
IADL, numero di funzioni conservate, m±ds	2.6±2.6	3.2±2.7	1.8±2.3	<.0001
SPMSQ, numero di errori, m±ds	3.5±3.2	2.9±2.9	4.4±3.4	<.0001
Deprescrizione TAO in dimissione, n (%)	341 (21.6)	148 (16.1)	193 (29.3)	<.0001

Risultati dello studio
Decesso a 12 mesi



Bo M, Brunetti E, Presta R., submitted

FA note in terapia anticoagulante al ricovero

Variabile	Totale (n=1578)	No Sanguinamenti n=1504 (95,3%)	Sanguinamenti n=74 (4,7%)	p
Età, anni, mediana (25°-75°)	86 (82-89)	86 (82-89)	85 (81-89)	0.3431
Sesso maschile, n (%)	690 (43.7)	656 (43.6)	34 (46)	0.6934
Tipo di FA, n (%):				0.8890
- Parossistica	374 (23.7)	356 (23.7)	18 (24.3)	
- Cronica	1204(76.3)	1148 (76.3)	56 (75.7)	
CHA2DS2-VASc, m±ds	4.7 ± 1.4	4.7 ± 1.3	4.7 ± 1.5	0.6261
Storia di ictus	361 (22.9)	345 (22.9)	16 (21.6)	0.7923
HAS-BLED, m±ds	1.9 ± 0.85	1.9 ± 0.85	2.1 ± 0.91	0.1339
Storia di sanguinamenti, n (%)	282 (17.9)	262 (17.4)	20 (27.0)	0.0352
eGFR sec CKD-EPI, ml/min, mediana (25°-75°)	51.6 (36.5-69.1)	51.8 (36.8-69.3)	44.7 (30.8-61.9)	0.0438
Charlson Comorbidity Index, m±ds	3.5 ± 1.7	3.5 ± 1.7	3.9 ± 1.8	0.0068
ADL, numero di funzioni conservate, m±ds	3.4 ± 2.3	3.4 ± 2.3	4±2.1	0.0343
IADL, numero di funzioni conservate, m±ds	2.6 ± 2.6	2.6 ± 2.6	3.2 ± 2.4	0.0270
SPMSQ, numero di errori, m±ds	3.5±3.2	3.5±3.2	3.1±2.8	0.5759
Deprescrizione TAO in dimissione, n (%)	341 (21.6)	327 (21.7)	14 (18.9)	0.6649

Incidenza ictus:
41/1578 (**2.6%**)
36/1237 (**2.9%**) nei pazienti con TAO
5/341 (**1.5%**) nei pazienti senza TAO

Incidenza sanguinamenti:
74/1578 (**4.7%**)
60/1237 (**4.9%**) nei pazienti con TAO
14/341 (**4.1%**) nei pazienti senza TAO

Bo M, Brunetti E, Presta R., submitted

La maggior parte dei **pazienti con FA** nel mondo clinico reale sono **anziani**, molti dei quali con **impairment cognitivo/funzionale** e con un elevato carico di **patologie e di farmaci.**

L'uso dei **DOACs è indicato e clinicamente vantaggioso per la maggior parte dei pazienti anziani con FA**, inclusi quelli con fenotipo fragile.

La **VMG** identifica quei pazienti anziani che per **perdita di autonomia funzionale**, soprattutto in associazione a **importante comorbilità** e/o **severo deterioramento cognitivo** sono più vulnerabili e con **limitata spettanza di vita**, e per i quali esistono **scarsissime evidenze di beneficio clinico netto della TAO.** Laddove la VMG non è fattibile, i nostri dati dimostrano che il riconoscimento di una **severa fragilità multidimensionale (CFS e FI)** identifica i pazienti con più alta mortalità a breve termine e scarse/assenti evidenze di beneficio dalla TAO.

In questi pazienti, in assenza di evidenze cliniche, sulla base di una **decisione clinica condivisa**, si può optare sia per un trattamento «umanitario» con DOACs sia per una **deprescrizione della TAO** che, sulla base di dati preliminari sembra **non comportare un maggior rischio di ictus fatali e non fatali** e con una tendenza ad una **minor incidenza di sanguinamenti**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European Heart Journal (2018) **39**, 1322–1329

'Ten Commandments' of the EHRA Guide for the Use of NOACs in AF

Do not undertreat frail and elderly patients.

2020 ESC Guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association of Cardio-Thoracic Surgery (EACTS)

"**frailty**, comorbidities, and increased risk of falls **do not outweigh the benefits of OAC**"

*"(...) The **complexity of AF** requires a multifaceted, **holistic, and multidisciplinary approach** ... with the goal to further **improve the structured management of AF patients, promote patient values, and finally improve patient outcomes***

2021 European Heart Rhythm Association Practical Guide on the Use of Non-Vitamin K Antagonist Oral Anticoagulants in Patients with Atrial Fibrillation

Europace (2021) **23**, 1612–1676

*"there may be **no benefit to OAC** in states of **severe frailty** or where **life expectancy is likely to be limited**"*