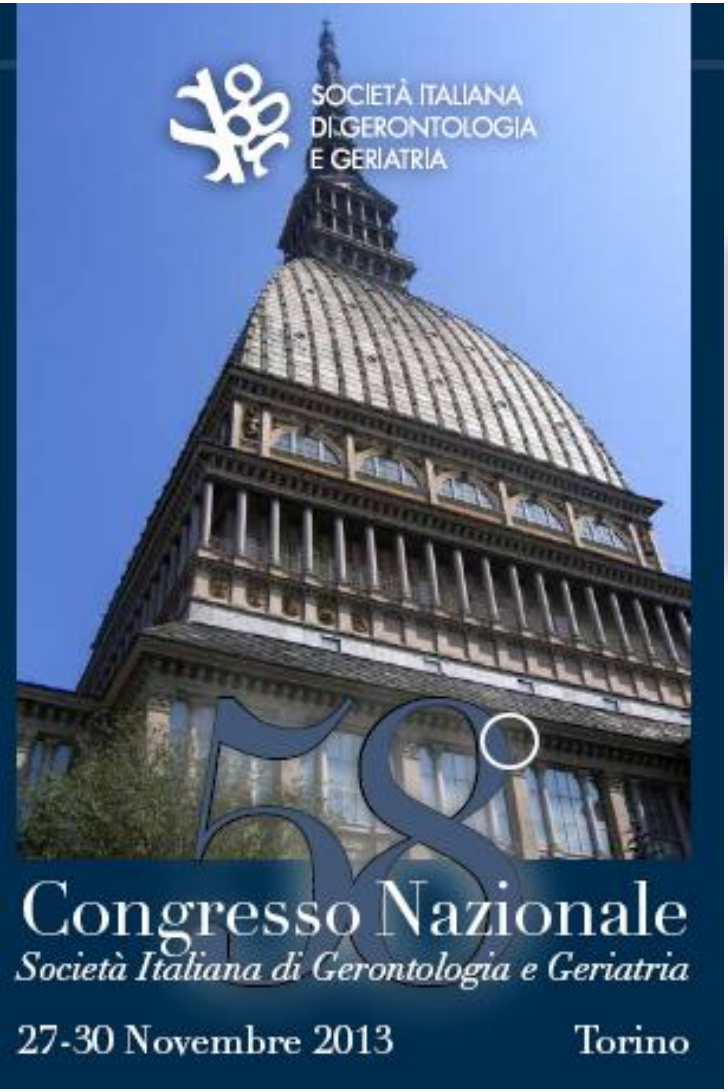

Simposio
I nuovi Anticoagulanti Orali: nella Fibrillazione Atriale

Stratificazione del Rischio Embolico ed Emorragico nell'Anziano

Niccolò Marchionni

Cattedra di Geriatria, Università di Firenze

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Società Italiana di Cardiologia Geriatrica (SICGe)

Epidemiologia e fattori di rischio di FA

Key point

- **L'età avanzata è uno dei principali fattori di rischio di FA**

Development of a risk score for atrial fibrillation (Framingham Heart Study): a community-based cohort study

Schnabel RB et al, Lancet 2009

Age (years)	45-49	-3 – 1
	50-54	-2 – 2
	55-59	0 – 3
	60-64	1 – 4
	65-69	3 – 5
	70-74	4 – 6
	75-79	6 – 7
	80-84	7 – 7
	≥85	8 – 8
BMI (Kg/m^2)	<30	0
	≥30	1
SBP (mmHg)	<160	0
	≥160	1
PR (ms)	<160	0
	160 – 199	1
	≥200	2
Age / Cardiac murmur	45-54	5
	55-64	4
	65-74	2
	75-84	1
	≥85	0
Age / HF	45-54	10
	55-64	6
	65-74	2
	≥75-84	0
Tx Hypertension	No	0
	Yes	1

Women / **Men**; **Age / Cardiac murmur:** Age at which significant cardiac murmur developed; **Age / HF:** Age of heart failure

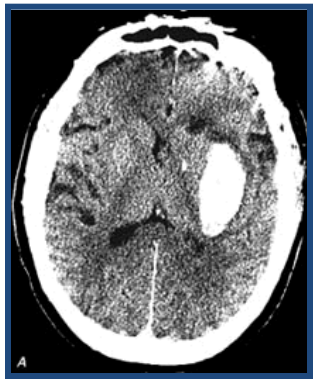
Tipi di ictus e ruolo della FA

Key points

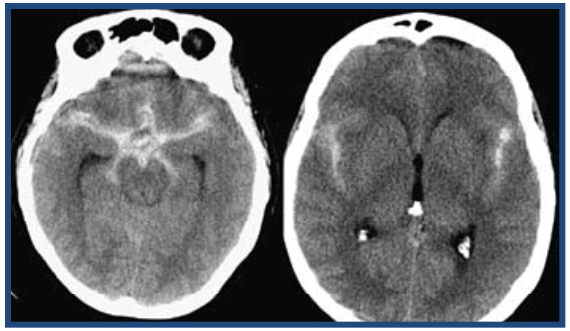
- **La FA è il principale fattore di rischio per ictus cardioembolico**
  - **Quale è la proporzione di ictus ischemici attribuibile a cardioembolismo?**

Cerebrovascular Disease: Stroke Subtype

Hemorrhagic stroke (17%)

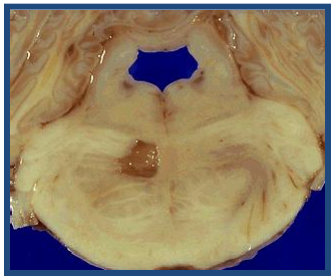


Intracerebral hemorrhage (59%)

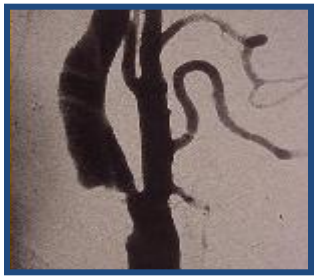


SAH (41%)

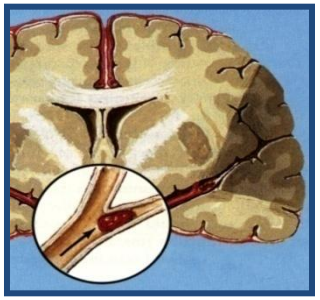
Ischemic stroke (83%)



Lacunar small vessel disease (25%)



Atherothrombotic disease (20-25%)



Embolism (20%)

Cryptogenic (30%)

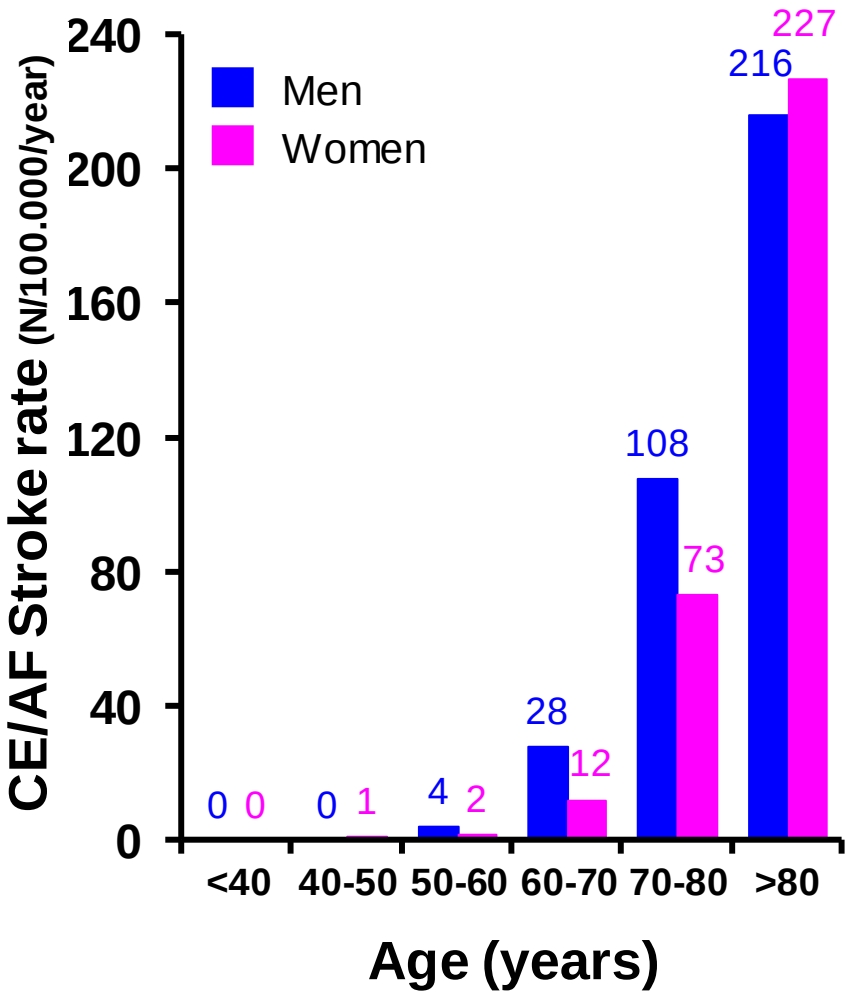
Albers GW et al. Chest. 1998;114:683S-698S.
Rosamond WD et al. Stroke. 1999;30:736-743.

Ictus cardioembolico in FA: fattori di rischio

Key point

- **L'età avanzata è uno dei principali fattori di rischio di ictus cardioembolico secondario a FA**

Epidemiology of ischemic stroke from atrial fibrillation in Dijon, France, from 1985 to 2006



NEUROLOGY

Bejot Y, 2009

CE/AF stroke = 572/3064 (18.7%)

CE/AF 80.6 vs. other strokes 73.6 years

Validation of clinical classification schemes for predicting stroke

Results from the National Registry of Atrial Fibrillation

$CHADS_2$ Risk Stratification Scheme

Risk Factors	Score
C - recent Congestive heart failure	1
H - Hypertension	1
A - Age >75 years	1
D - Diabetes mellitus	1
S_2 - History of Stroke or TIA	2

Gage, JAMA, 2001
Rockson, JACC, 2004

Linee Guida ESC per la gestione della FA

European Heart Journal (2010) 31, 2369–2429
doi:10.1093/eurheartj/ehq278

ESC GUIDELINES

Guidelines for the management of atrial fibrillation

The Task Force for the Management of Atrial Fibrillation of the European Society of Cardiology (ESC)

Developed with the special contribution of the European Heart Rhythm Association (EHRA)†

Endorsed by the European Association for Cardio-Thoracic Surgery (EACTS)

Authors/Task Force Members: A. John Camm (Chairperson) (UK)*, Paulus Kirchhof (Germany), Gregory Y.H. Lip (UK), Ulrich Schotten (The Netherlands), Irene Savelieva (UK), Sabine Ernst (UK), Isabelle C. Van Gelder (The Netherlands), Nawwar Al-Attar (France), Gerhard Hindricks (Germany), Bernard Prendergast (UK), Hein Heidbuchel (Belgium), Ottavio Alfieri (Italy), Annalisa Angelini (Italy), Dan Atar (Norway), Paolo Colonna (Italy), Raffaele De Caterina (Italy), Johan De Sutter (Belgium), Andreas Goette (Germany), Bulent Gorenek (Turkey), Magnus Heldal (Norway), Stefan H. Hohloser (Germany), Philippe Kolh (Belgium), Jean-Yves Le Heuzey (France), Piotr Ponikowski (Poland), Frans H. Rutten (The Netherlands).

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The disclosure forms of the authors and reviewers are available on the ESC website www.escardio.org/guidelines

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2010

4.1.1 Risk stratification for stroke and thrombo-embolism

The identification of various stroke clinical risk factors has led to the publication of various stroke risk schemes. Most have (artificially) categorized stroke risk into 'high', 'moderate', and 'low' risk strata. The simplest risk assessment scheme is the **$CHADS_2$ score**, as shown in *Table* 7. The $CHADS_2$ [cardiac failure, hypertension, age, diabetes, stroke (doubled)] risk index evolved from the AF Investigators and Stroke Prevention in Atrial Fibrillation (SPAF) Investigators criteria, and is based on a point system in which 2 points are assigned for a history of stroke or TIA and 1 point each is assigned for age >75 years, a history of hypertension, diabetes, or recent cardiac failure.[50]

Thus, the $CHADS_2$ stroke risk stratification scheme should be used as an initial, rapid, and easy-to-remember means of assessing stroke risk. In patients with a $CHADS_2$ score ≥2, chronic OAC therapy with a VKA is recommended in a dose-adjusted approach to achieve an international normalized ratio (INR) target of 2.5

Limiti del $CHADS_2$

- Statistica C: 0.60 → discriminazione modesta
- Pazienti classificati "a basso rischio" hanno una non trascurabile, effettiva incidenza di ictus

… quindi …

la predittività complessiva è poco soddisfacente

Lip GYH, et al. *Lancet* 2012

Refining Clinical Risk Stratification for Predicting Stroke and Thromboembolism in Atrial Fibrillation Using a Novel Risk Factor-Based Approach - The Euro Heart Survey on Atrial Fibrillation

Stroke Risk Assessment in AF: the CHA_2DS_2-VASc Score

Stroke Risk Factor	Score
Congestive Heart Failure / LV Dysfunction	1
Hypertension	1
Age ≥75 years	**2**
Diabetes mellitus	1
Stroke / TIA / TE	2
Vascular Disease (MI, PAD, aortic plaque)	1
Age 65-74 years	1
Sex category (female)	1

Maximum score = 9; Score >1 – OAC; **Score = 1** – ASA (75-325 mg) or OAC (preferred);
Score = 0 - ASA (75-325 mg) or None (preferred)

Lip, Chest, 2010

Linee guida ESC per la gestione della FA

European Heart Journal (2010) 31, 2369–2429
doi:10.1093/eurheartj/ehq278

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Table 9 Approach to th[illegible]mboprophylaxis in patients with AF

Risk category	CHA_2DS_2-VASc score	Recommended antithrombotic therapy
One 'major' risk factor or ≥2 'clinically relevant non-major' risk factors	≥2	OAC[a]
One 'clinically relevant non-major' risk factor	1	Either OAC[a] or aspirin 75–325 mg daily. Preferred: OAC rather than aspirin.
No risk factors	0	Either aspirin 75–325 mg daily or no antithrombotic therapy. Preferred: no antithrombotic therapy rather than aspirin.

2010

European Heart Journal
doi:10.1093/eurheartj/ehs253
ESC GUIDELINES

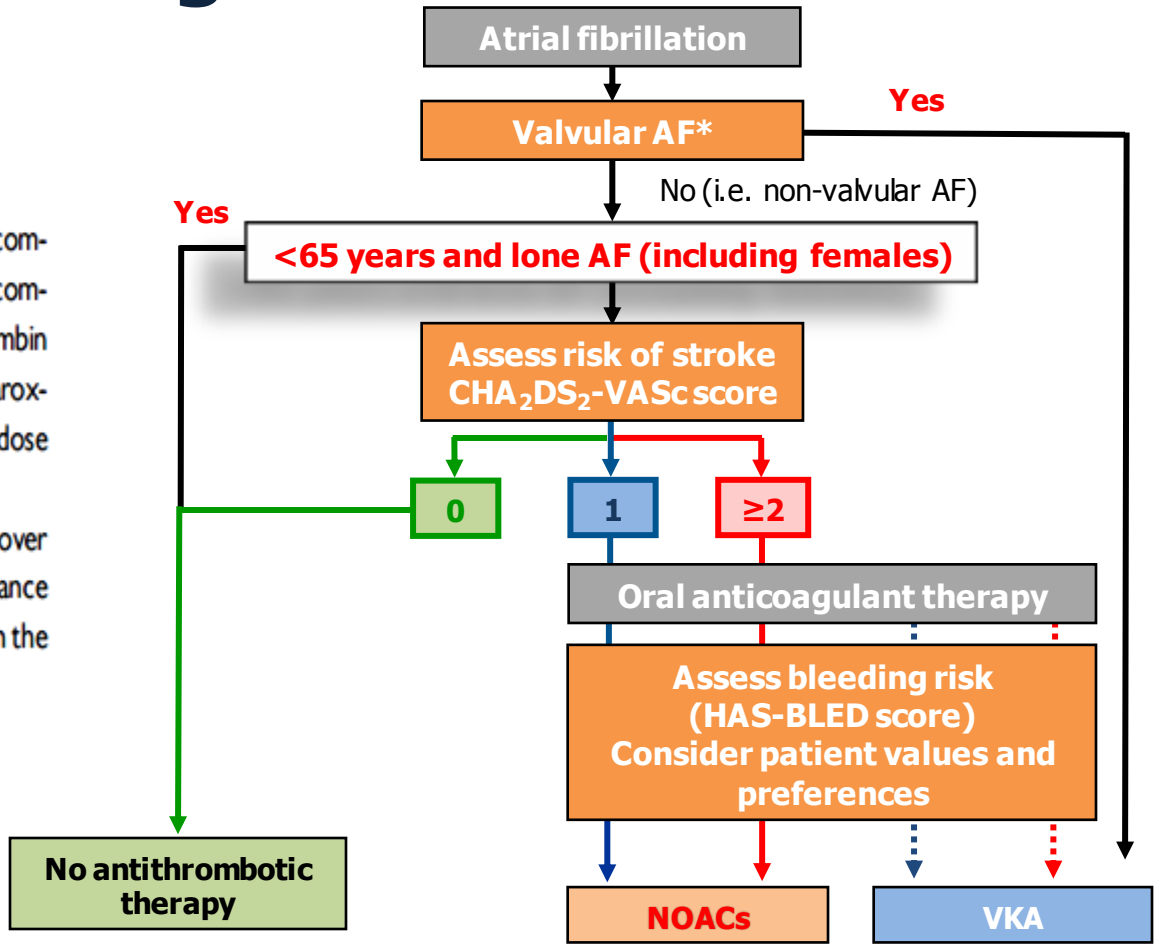
2012 focused update of the ESC Guidelines for the management of atrial fibrillation

An update of the 2010 ESC Guidelines for the management of atrial fibrillation
Developed with the special contribution of the European Heart Rhythm Association

Choice of anticoagulant

- The NOACs offer better efficacy, safety, and convenience compared with OAC with VKAs. Thus, where an OAC is recommended, one of the NOACs—either a direct thrombin inhibitor (dabigatran) or an oral factor Xa inhibitor (e.g. rivaroxaban, apixaban)—should be considered instead of adjusted-dose VKA (INR 2–3) for most patients with AF.
- There is insufficient evidence to recommend one NOAC over another, although some patient characteristics, drug compliance and tolerability, and cost may be important considerations in the choice of agent.

2012



Antiplatelet therapy with ASA plus clopidogrel or – less effectively – ASA only, should be considered in patients who refuse any OAC or cannot tolerate anticoagulation for reasons unrelated to bleeding. If there are contraindications to OAC or antiplatelet therapy, left atrial appendage occlusion, closure or excision may be considered
Colour CHA_2DS_2-VASc: green = 0, blue = 1, red ≥2; line: solid = best option; dashed = alternative option
*Includes rheumatic valvular disease and prosthetic valves; ASA = acetylsalicylic acid; NOAC = novel oral anticoagulant; VKA = vitamin K antagonist

Camm AJ et al. Eur Heart J doi:10.1093/eurheartj/ehs253

Prevenzione dell'ictus cardioembolico nell'anziano con FA

Key points

- Secondo CHA_2DS_2-VASC gli anziani sono a rischio di ictus cardioembolico almeno moderato, con indicazione assoluta alla TAO (in assenza di controindicazioni)
  - Quale è la effettiva utilizzazione della TAO nel mondo reale?

A novel user-friendly score (HAS-BLED) to assess one-year risk of major bleeding in atrial fibrillation patients: the Euro Heart Survey

Pisters, Chest, 2010

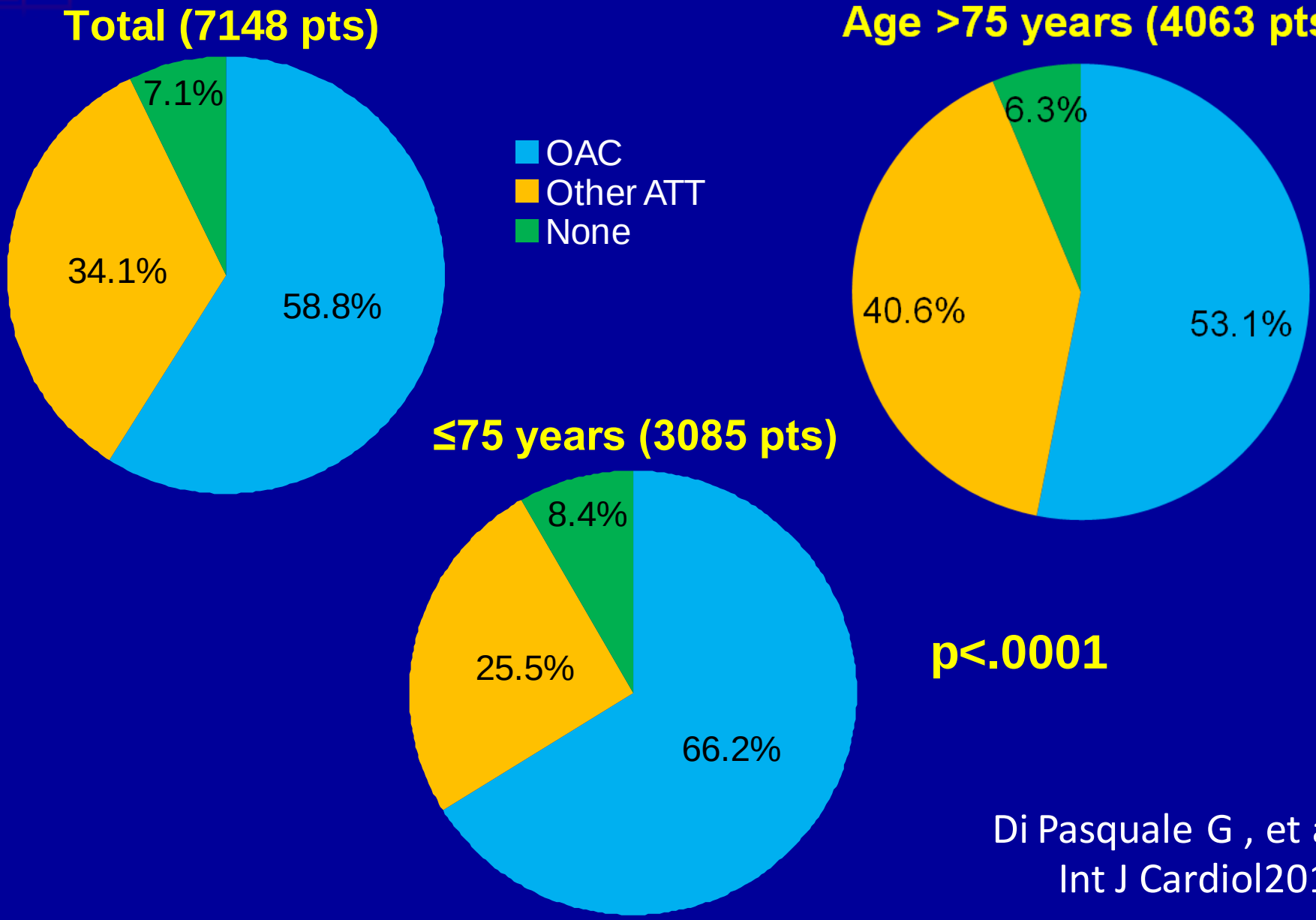
Bleeding Risk Assessment in AF: HAS-BLED Bleeding Risk Score

Letter	Clinical Characteristic	Points
H	Hypertension	1
A	Abnormal Renal / Liver Function	1
S	Stroke	2
B	Bleeding	1
L	Labile INRs	2
E	**Elderly**	**1**
D	Drugs / Alcohol	1

Maximum score = 9; Hypertension – Sap >160 mmHg; **Drugs** – antiplatelets agents or NSAIDS

Score ≥ 3 – High risk patient: Caution and regular review following the initiation of antithrombotic therapy (OAC & ASA)

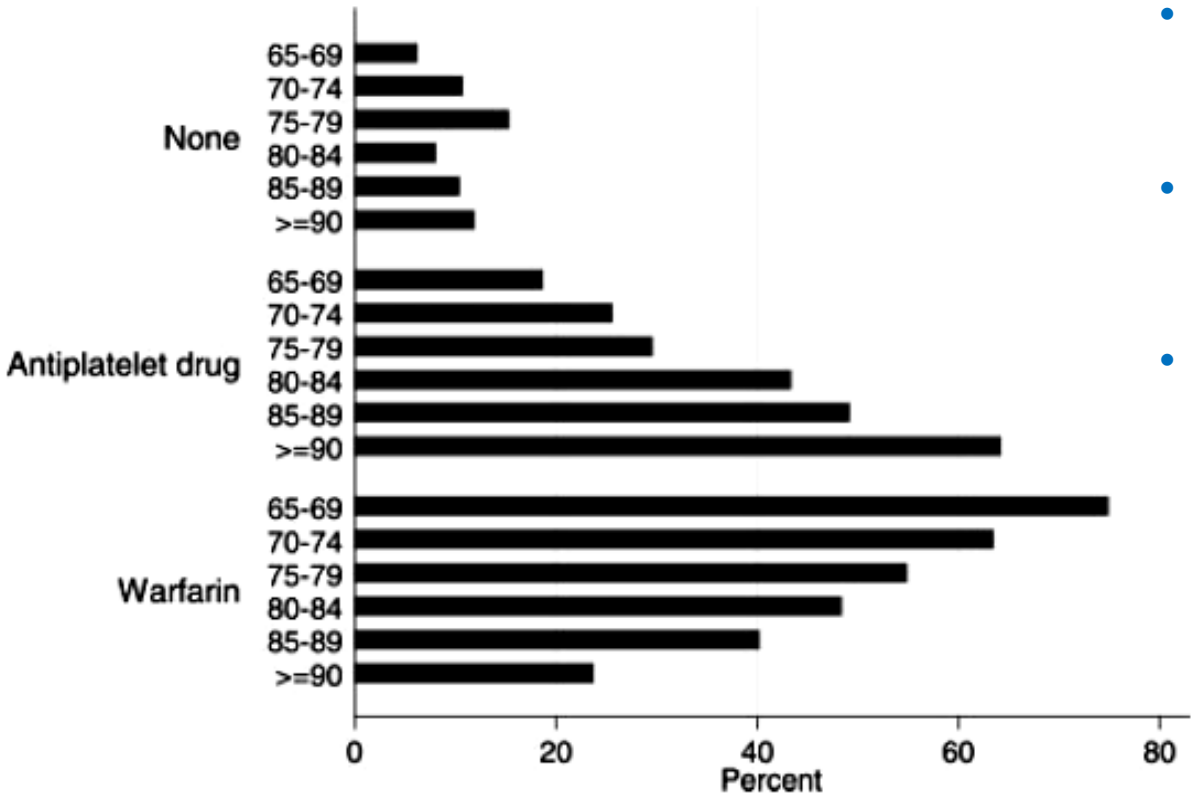
Antithrombotic Treatment by Age



Di Pasquale G , et al.
Int J Cardiol2012

Antithrombotic Prophylaxis in AF Patients by Age & Risk Category

405 patients with AF , OAC therapy naïve on admission



Antithrombotic therapy at hospital discharge by patient age.

- only 51% (n=206) discharged on warfarin
- of others 199, 83% had 2+ stroke risk factors
- risk of falling and of intracranial hemorrhage 2 most commonly cited reasons for not prescribing warfarin to patients older than 80 years

American Heart Association | American Stroke Association

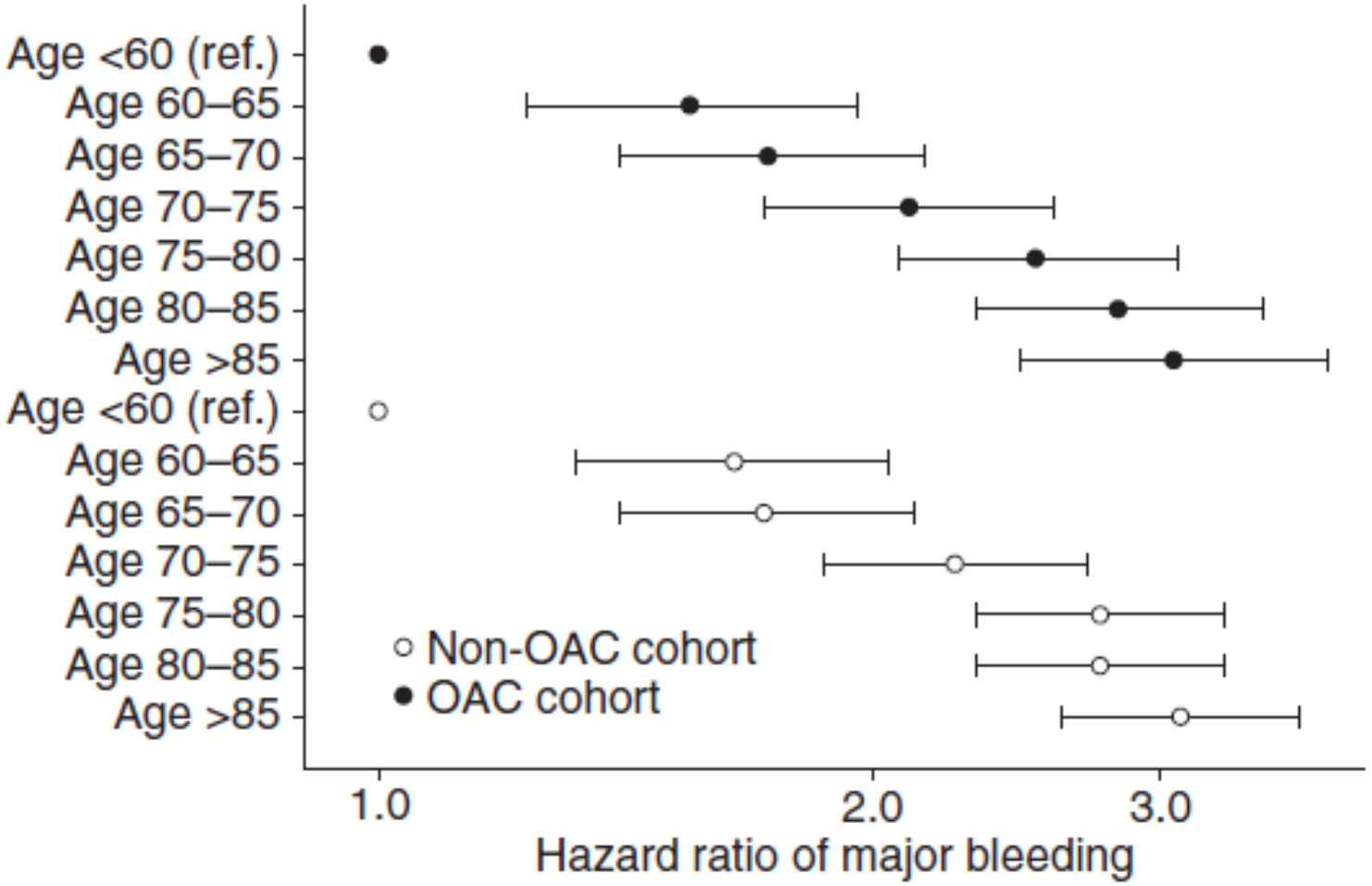
Hylek E M et al. Stroke 2006;37:1075-1080

Prevenzione dell'ictus cardioembolico nell'anziano con FA

Key points

- **Il rischio della TAO aumenta con l'età, ma [forse] anche il suo beneficio**
  - **Quale è il beneficio NETTO?**

Età e rischio di sanguinamento

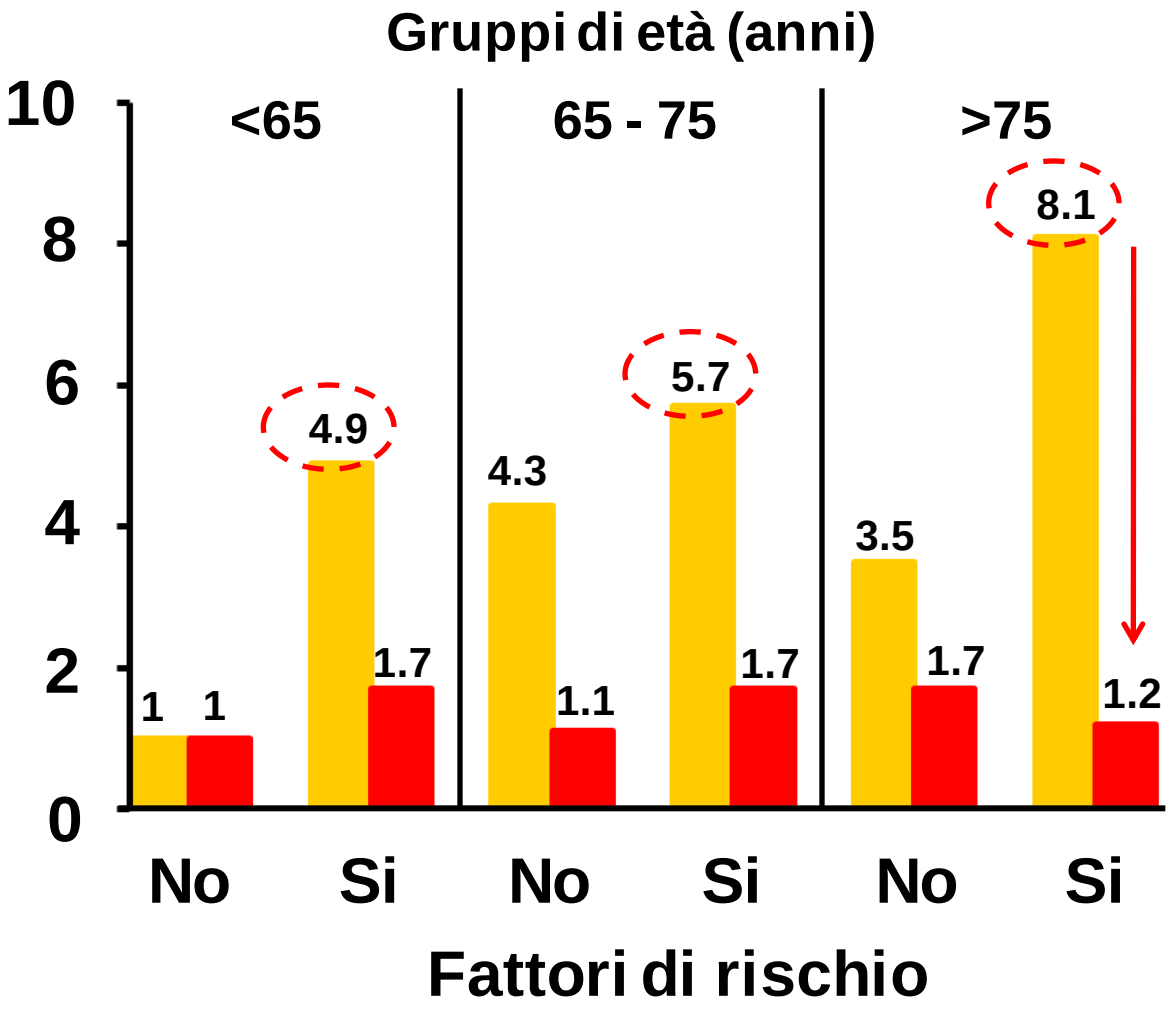


J Thromb Haemost. 2011;9:1460-7

Rischio annuale di ictus in pazienti con fibrillazione atriale, per gruppi di età

The Atrial Fibrillation Investigators

AFI, Arch Int Med, 1994
Rockson, JACC, 2004



Fattori di rischio: diabete, ipertensione, storia di ictus/TIA

Placebo

Warfarin

Beneficio clinico netto della tromboprofilassi nella FA: rischio tromboembolico *vs.* rischio emorragico

- ***Net clinical benefit*** = (incidenza ictus ischemico in assenza di terapia – incidenza ictus ischemico in presenza di terapia) – 1.5 x (incidenza emorragia intracranica in presenza di terapia – incidenza emorragia intracranica in assenza di terapia) (n=132,372)

	VKA	
	HAS-BLED score	
	Score ≤2	Score ≥3
$CHADS_2$		
Score 0	–0.02 (-0.09 to 0.06)	0.19 (-1.39 to 1.77)
Score 1	0.84 (0.70 to 0.99)	0.56 (0.16 to 0.95)
Score 2–6	1.95 (1.70 to 2.20)	2.68 (2.33 to 3.04)

Values >0 favours treatment. If less than 200 person-years in treatment in a cell the net clinical benefit was not calculated. ASA: acetylsalicylic acid; $CHADS_2$, CHA_2DS_2-VASc, and HAS-BLED: see text; VKA: vitamin K antagonist.

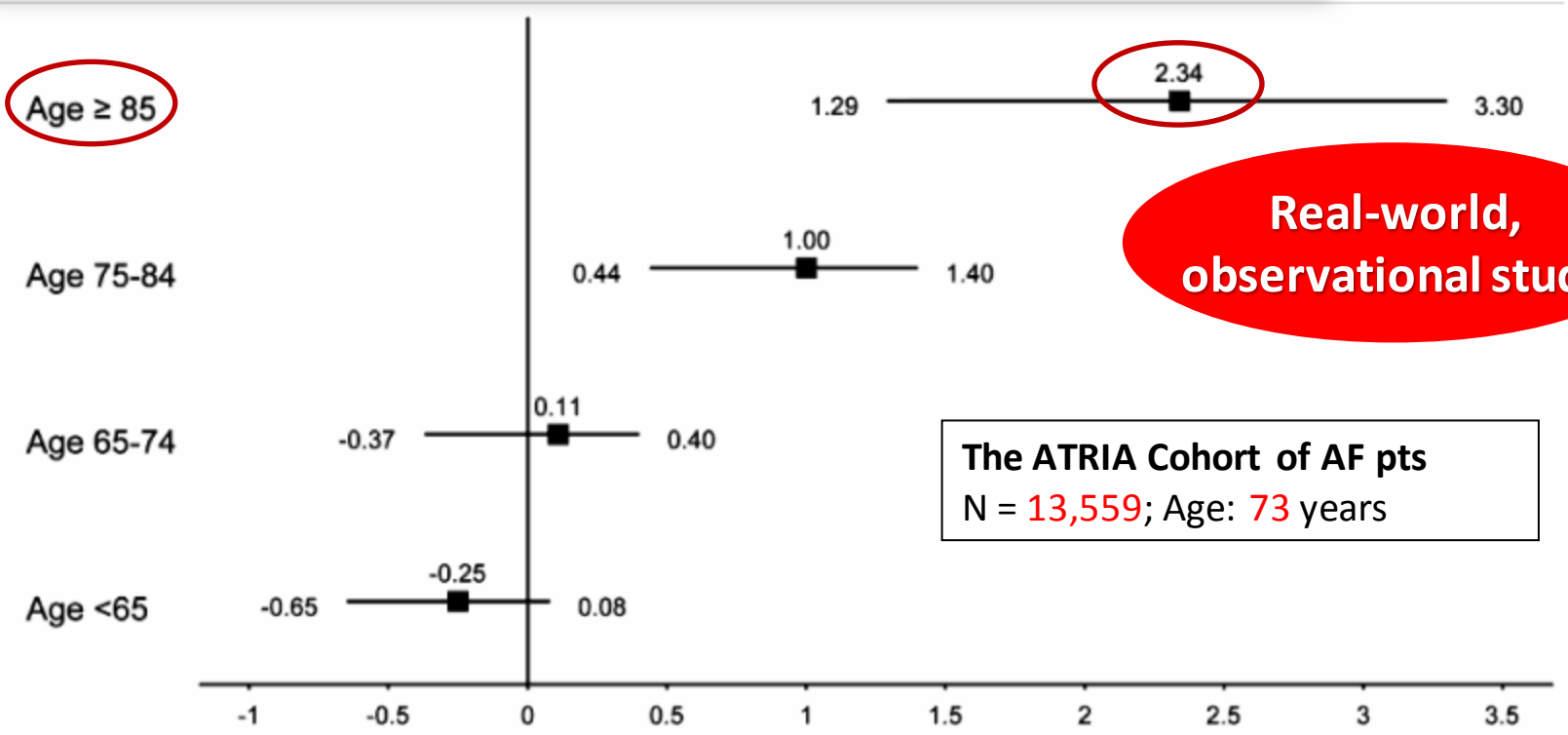
Olesen JB, et al. *Thromb Haemost* 2011

Annals of Internal Medicine | ARTICLE

The Net Clinical Benefit of Warfarin Anticoagulation in Atrial Fibrillation

Ann Intern Med. 2009;151:297-305.

Daniel E. Singer, MD; Yuchiao Chang, PhD; Margaret C. Fang, MD, MPH; Leila H. Borowsky, MPH; Niela K. Pomernacki, RD; Natalia Udaltsova, PhD; and Alan S. Go, MD



Real-world, observational study

The ATRIA Cohort of AF pts
N = 13,559; Age: 73 years

Net Clinical Benefit :

(annual rate of ischemic strokes / systemic emboli prevented by warfarin) **minus** (intracranial hemorrhages due to warfarin) * impact weight. The impact weight was 1.5, reflecting the greater clinical impact of intracranial hemorrhage versus thromboembolism

STATE-OF-THE-ART PAPER

Age as a Risk Factor for Stroke in Atrial Fibrillation Patients

Implications for Thromboprophylaxis

Ricarda Marinigh, MD,*† Gregory Y. H. Lip, MD,* Nicola Fiotti, PHD,‡ Carlo Giansante, PHD,‡ Deirdre A. Lane, PHD*

Birmingham, United Kingdom; and Trieste, Italy

2010

Conclusions

1. Physicians may be apprehensive about prescribing OAC to elderly patients, given concerns about a higher risk of hemorrhage.
2. However, age alone should not prevent prescription of OAC in elderly patients, given the potential greater net clinical benefit among such patients.
3. Appropriate stroke and bleeding risk stratification and choice of antithrombotic therapy are essential.
4. Once OAC is initiated, good INR control (at least 65% TTR) and the provision of a health care infrastructure to support such INR therapeutic targets are crucial to prevent warfarin-associated complications.

2012: NOACs preferable!!