



# CardioAlessandria

2a Edizione

Alessandria 12-13 giugno 2015



**Come i NAO stanno cambiando il rischio embolico ed emorragico nella FA**

**Cimminiello C- Vimercate (MB)**



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# CURRENT APPROACH TO THE CARDIOEMBOLIC AND HAEMORRHAGIC RISK RELATED TO AF



The impact of changes in guidelines



The situation in the real world



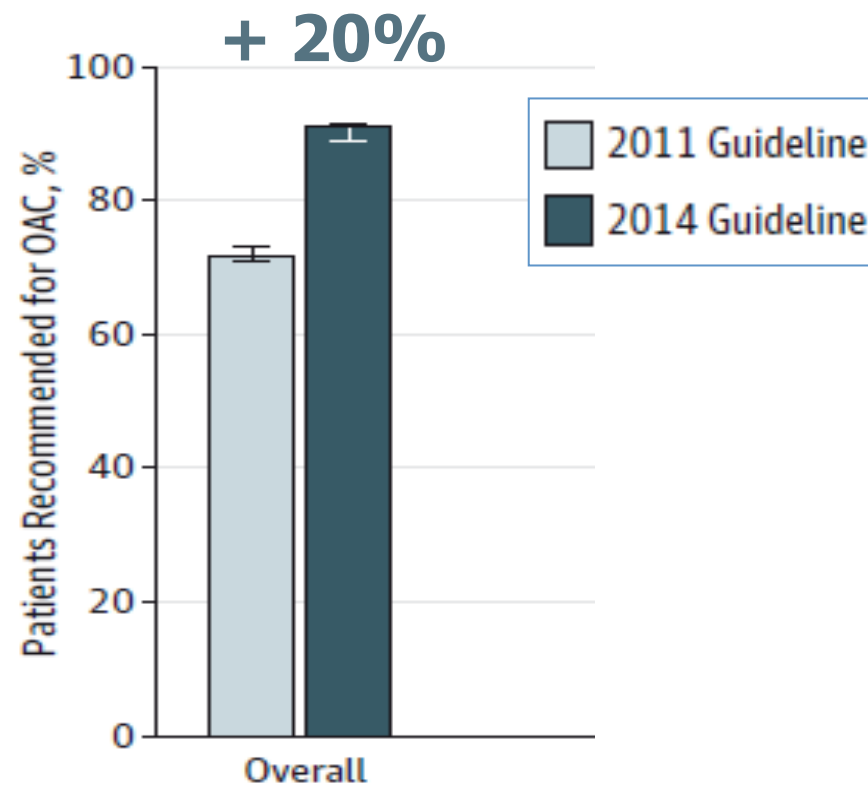
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## Change in the Percentage of Patients Recommended for Oral Anticoagulation (OAC) Under New vs Old Atrial Fibrillation Treatment Guidelines



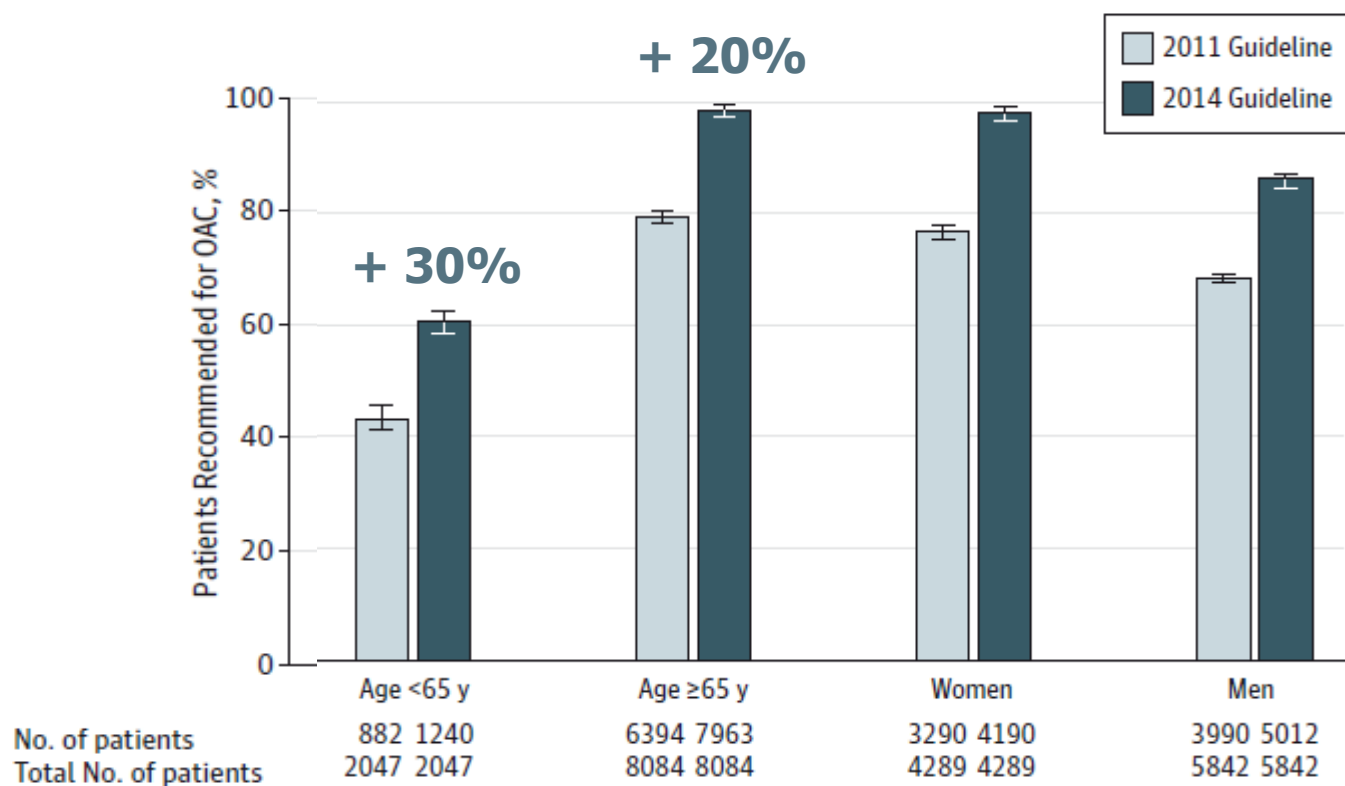
No. of patients	7274	9199
Total No. of patients	10131	10131



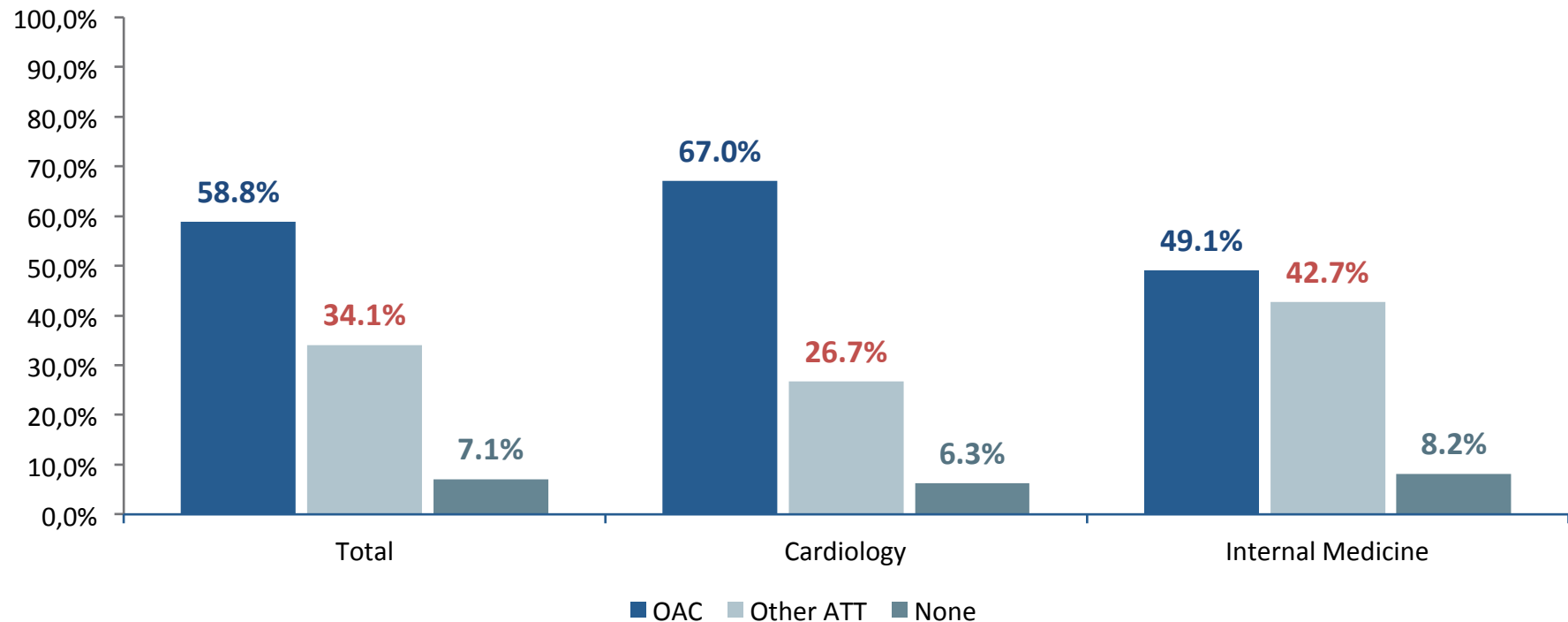
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# Current presentation and management of 7148 patients with atrial fibrillation in cardiology and internal medicine hospital centers: The ATA AF study



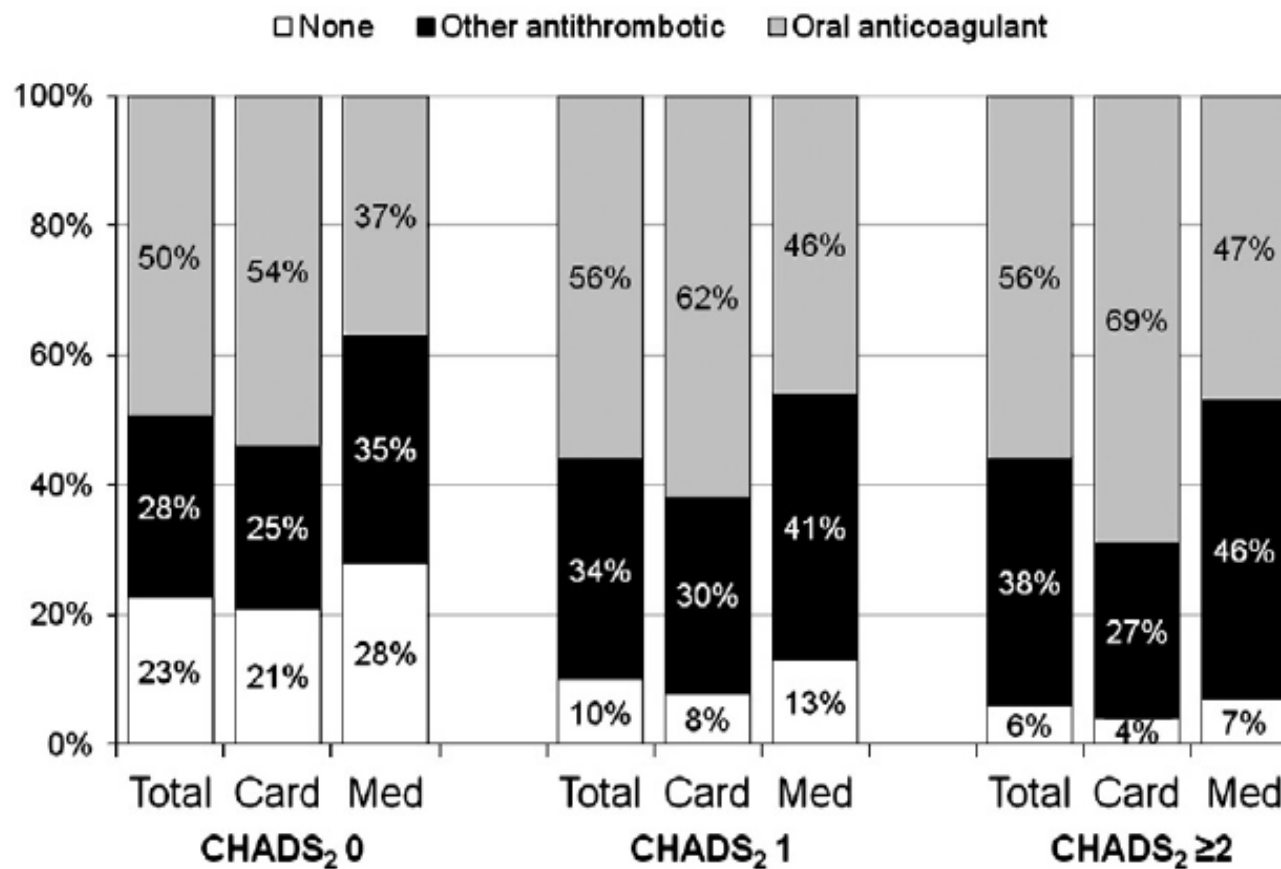


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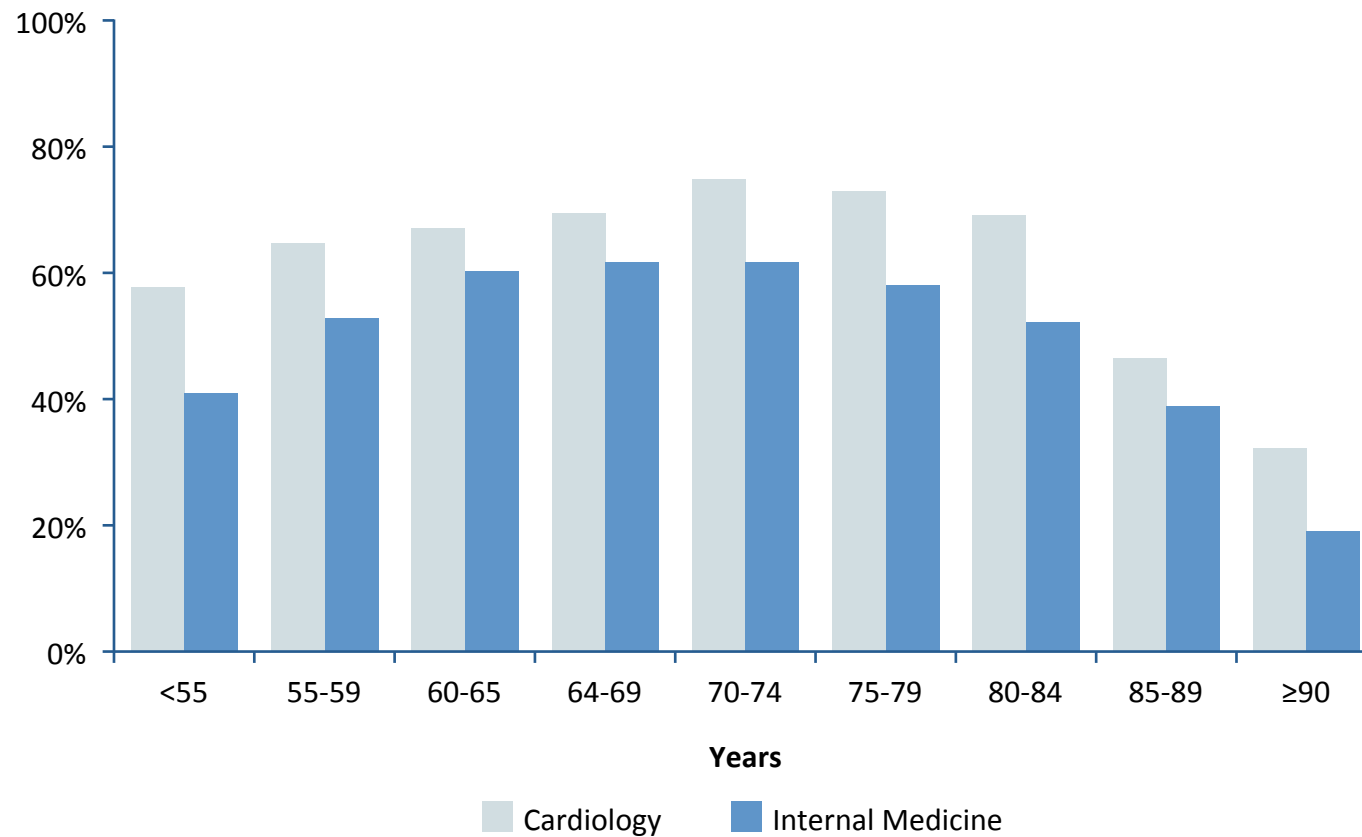
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### Antithrombotic treatment prescribed in cardiology and internal medicine according to the risk CHADS<sub>2</sub> score.



# OAC prescription at discharge from cardiology and internal medicine patients according to the age





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The impact of changes in guidelines **widens the number of candidates for treatment by increasing the number of patients at low risk of stroke: risk of increased bleeding against a low absolute number of events spared**



The situation in the real world **Patients at highest risk of stroke are less treated**



# Systematic reviews and meta-analyses on efficacy and safety of NOACs

Review	NOACs	No.of Included studies	Efficacy and safety endpoints, HR for NOACs vs warfarin (95%CI)							
			Stroke/SE	Ischemic stroke	Hemorrhagic stroke	All-cause death	Myocardial infarction	Major bleeding	ICH	GI bleeding
Adam et al	Dabigatran Rivaroxaban Apixaban	3	NA	0.89 (0.78–1.02)	0.48 (0.36–0.62)	0.88 (0.82–0.96)	NA	0.80 (0.63–1.01)	NA	1.3 (0.97–1.73)
Dentali et al.	Dabigatran Rivaroxaban Apixaban Edoxaban	12	0.77 (0.70–0.86)	0.92 (0.81–1.04)	NA	0.89 (0.83–0.96)	0.99 (0.85–1.15)	0.80 (0.63–1.01)	0.46 (0.39–0.56)	NA
Lip et al	Dabigatran Rivaroxaban Apixaban	3	0.86 (0.77–0.95)	0.98 (0.87–1.12)	0.49 (0.37–0.63)	0.89 (0.83–0.96)	0.95 (0.81–1.12)	0.83 (0.77–0.90)	0.47 (0.38–0.57)	NA
			0.79 (0.71–0.88)	0.88 (0.77–1.00)	0.47 (0.36–0.62)	0.88 (0.82–0.95)	0.95 (0.81–1.12)	0.88 (0.81–0.95)	0.49 (0.40–0.60)	NA
Ruff et al.	Dabigatran Rivaroxaban Apixaban Edoxaban	4	0.81 (0.73–0.91)	0.92 (0.83–1.02)	0.49 (0.38–0.64)	0.90 (0.85–0.95)	0.86 (0.78–1.20)	0.88 (0.73–1.00)	0.48 (0.39–0.59)	1.25 (1.01–1.55)

# Comparison of non-vitamin k oral anticoagulant phase III clinical trials

	RE-LY	ROCKET AF	ARISTOTLE
<b>Treatment groups</b>	<b>DAB 110 mg or 150 mg bid vs. dose-adjusted warfarin</b>	<b>RIV 20 mg QD vs. dose-adjusted warfarin</b>	<b>API 5 mg bid vs. dose-adjusted warfarin</b>
<b>Trial design</b>	Open label, non-inferiority (DAB doses blinded)	Double blind, double dummy non-inferiority	Double blind double dummy non-inferiority
<b>Study participants</b>	NVAF with at least one risk factor for stroke N: 6015 vs 6076 vs 6022	NVAF with at least two risk factor for stroke N: 7131 vs 7133	NVAF with at least one risk factor for stroke N: 9120 vs 9081
<b>Age years</b>	71	73	70
<b>Mean CHADS2 score</b>	2.1	3.5	2.1
<b>Prior VKAs treatment %</b>	50	62	57
<b>Mean time in therapeutic range (warfarin)</b>	64	55	62.2



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# Joint use of cardio-embolic and bleeding risk scores in elderly patients with atrial fibrillation

Data from REPOSI study (543 pts)

## Risk stratification according to cardio-embolic and bleeding scores

### CHA<sub>2</sub>DS<sub>2</sub>-VASc

Score	Number of patients	%
Low 0	0	0
Intermediate 1	9	1.7
High $\geq 2$	534	98.3

### HAS-BLED

Score	Number of patients	%
Low 0	0	0
Intermediate 1-2	258	51.2
High $\geq 3$	265	58.8

Oral antithrombotic therapy with VKAs:

**43%**

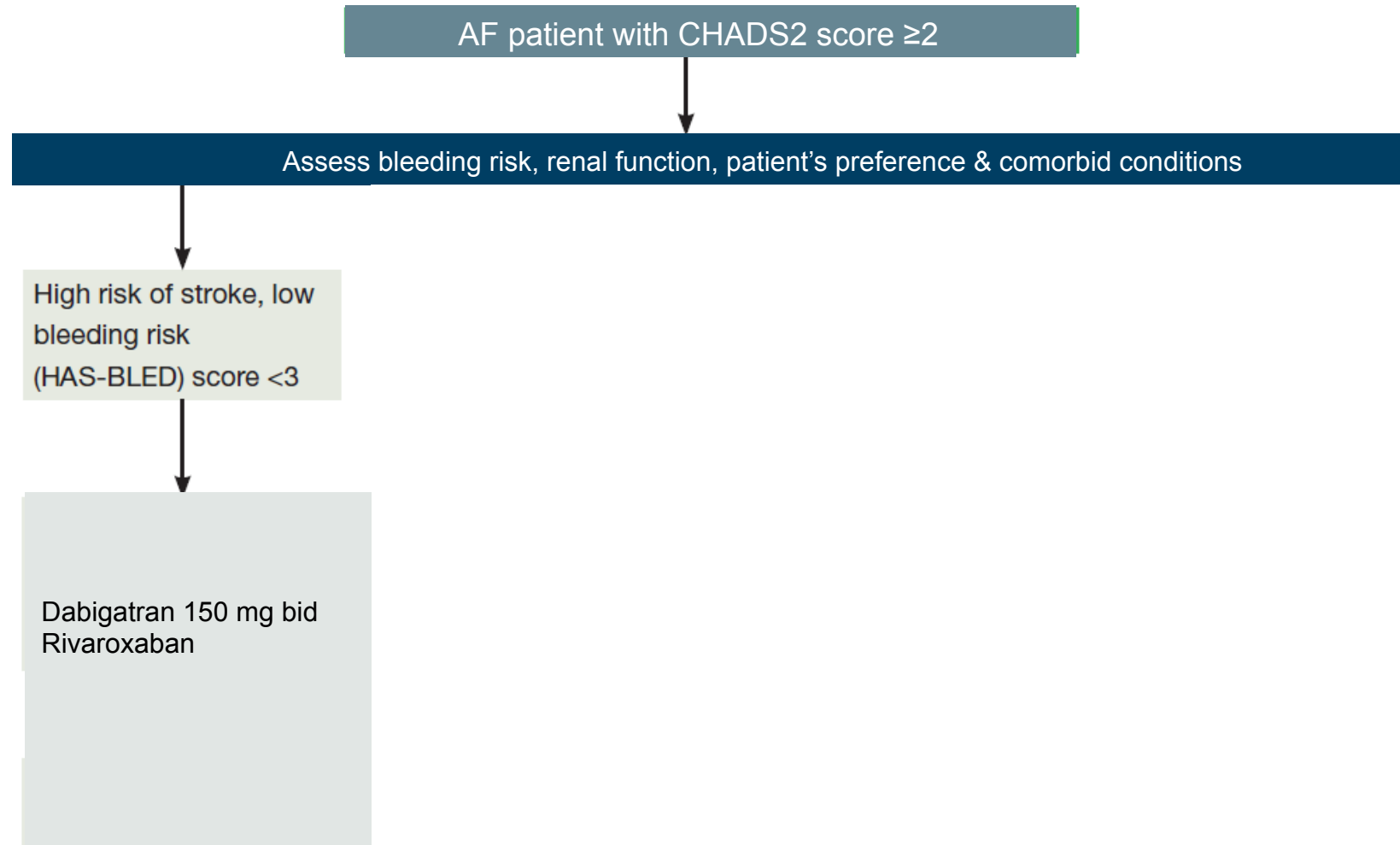


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### Proposed algorithm to aid in the selection of NOACs in patients with non-valvular AF for prevention of stroke and systemic embolism



# Comparison of non-vitamin k oral anticoagulant phase III clinical trials

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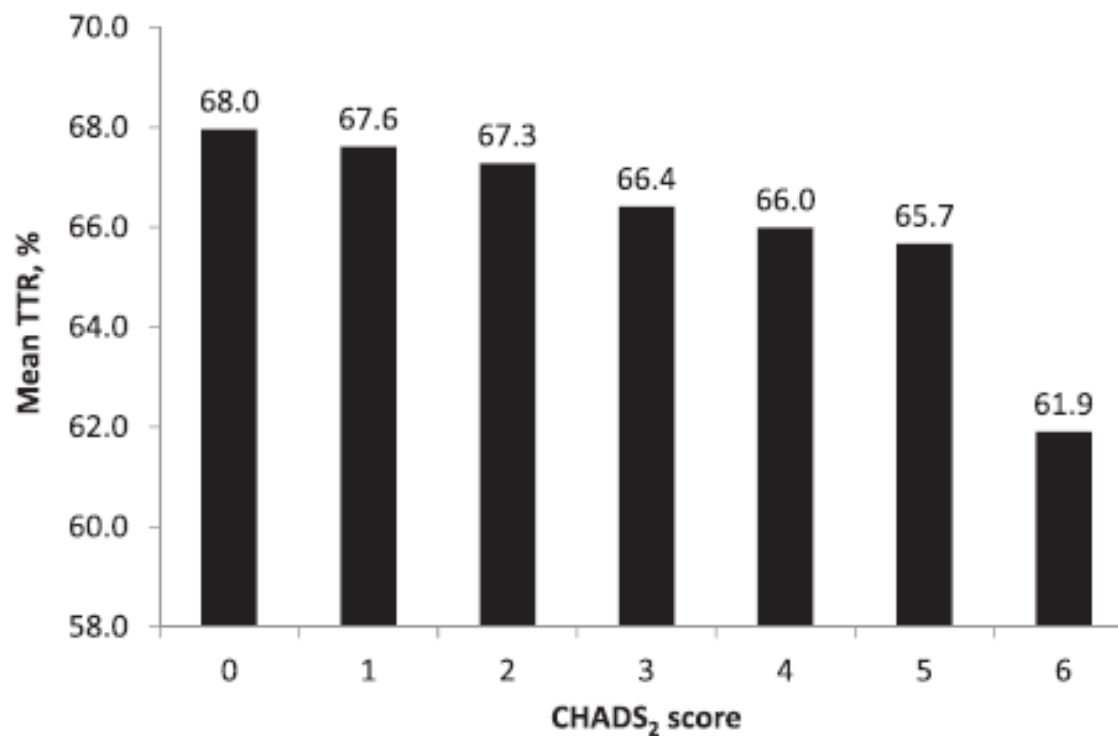


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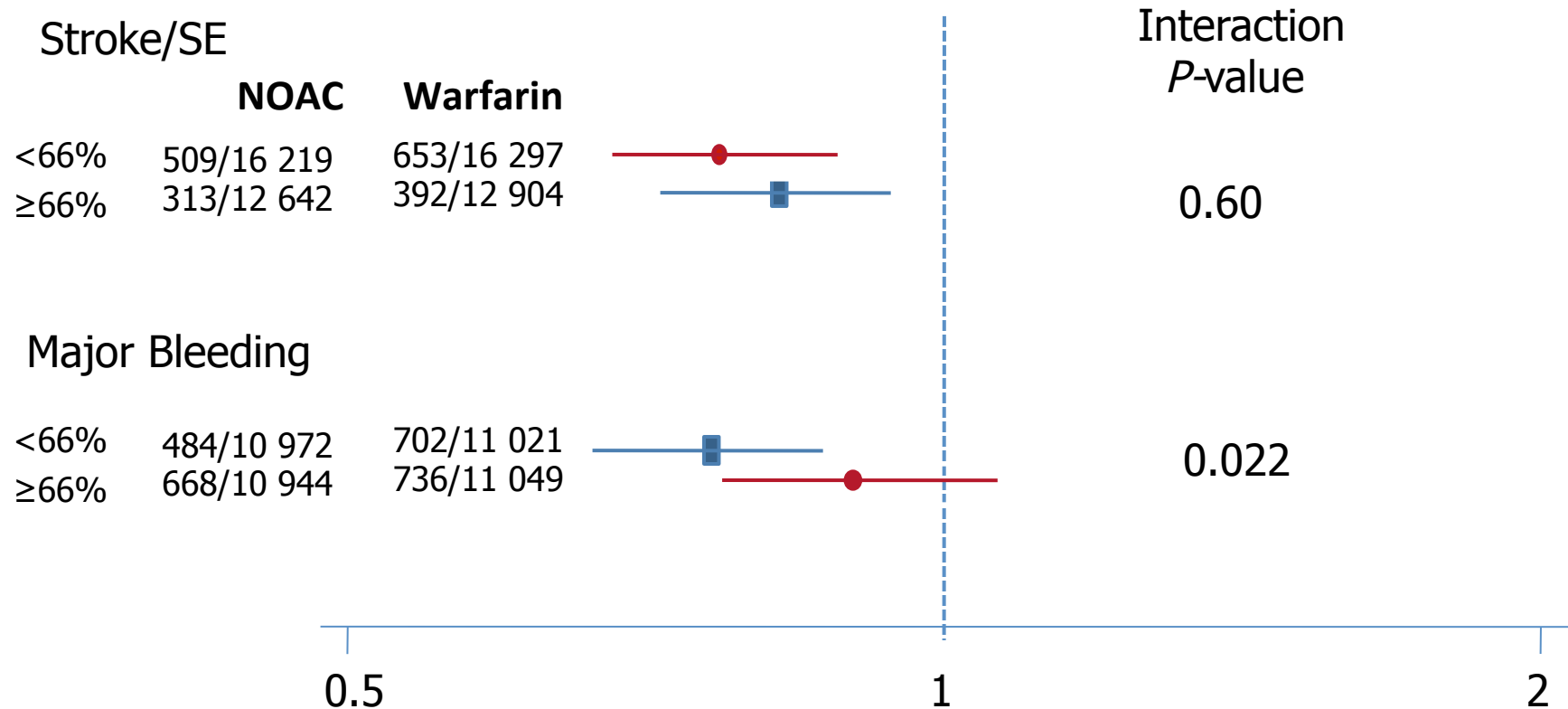
### The relation between TTR and CHADS<sub>2</sub> score (0 to 6)





## Comparison of the efficacy and safety of new oral anticoagulants with warfarin in patients with atrial fibrillation: a meta-analysis of randomised trials

### Centre-based TTR





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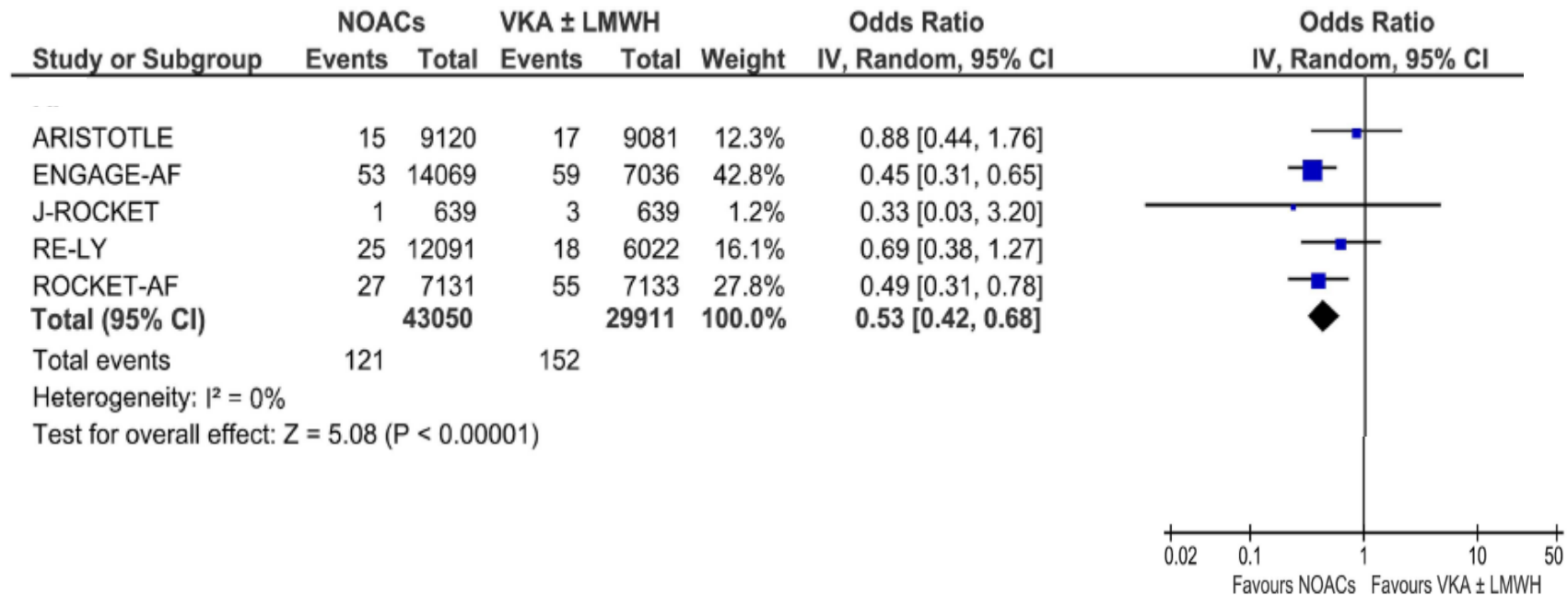


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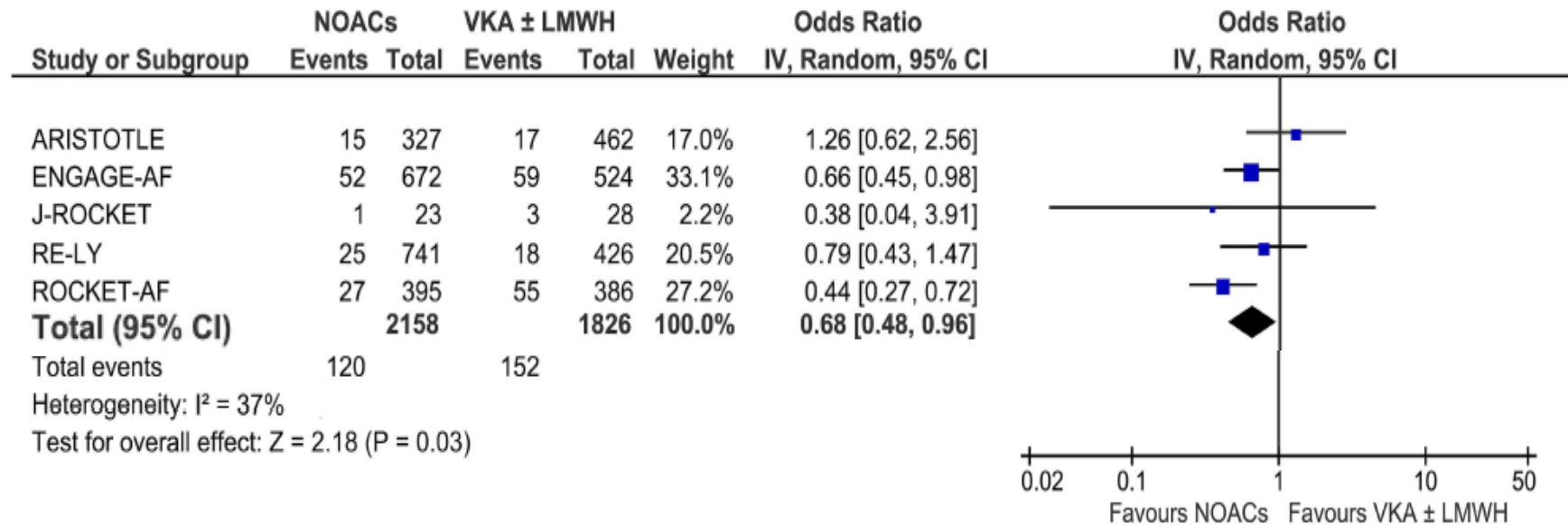
# Non-vitamin K antagonist oral anticoagulants and major bleeding-related fatality in patients with atrial fibrillation: a systematic review and meta-analysis





# Non-vitamin K antagonist oral anticoagulants and major bleeding-related fatality in patients with atrial fibrillation: a systematic review and meta-analysis

## Fatal bleeding in Phase III AF studies





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# CONCLUSIONS

**Indications for treatment with OAC<sub>s</sub> dictated by new guidelines expand the eligible population. AF patients at lower risk (than before) will be treated**



**Risk of reduced absolute benefit against unchanged risk of bleeding**

**Case-fatality due to bleeding for NOAC<sub>s</sub> is not as high as for VKAs**

**Substantial proportions of AF patients at highest risk are still not treated in clinical practice. To treat them more would lead to significant benefits in terms of absolute benefit**

**Patients at both high risk of stroke/SE and increased risk of bleeding may benefit from the use NOAC<sub>s</sub>**