


РЕАЛНАТА КЛИНИЧНА ПРАКТИКА СРЕЩУ  
ПРЕПОРЪКИТЕ НА ESC ОТ 2012 ЗА  
ПРОФИЛАКТИКА НА ИНСУЛТА ПРИ  
ПАЦИЕНТИ С ПМ: ДАННИ ОТ  
ПРОУЧВАНИЯ И РЕГИСТРИ

Доц. д-р Е. Манов,  
КПВБ, МУ-София





В ИЗЛОЖЕНИЕТО СА ИЗПОЛЗВАНИ  
ДОСТЪПНИ ЗА УПОТРЕБА  
СЛАЙДОВЕ НА ESC

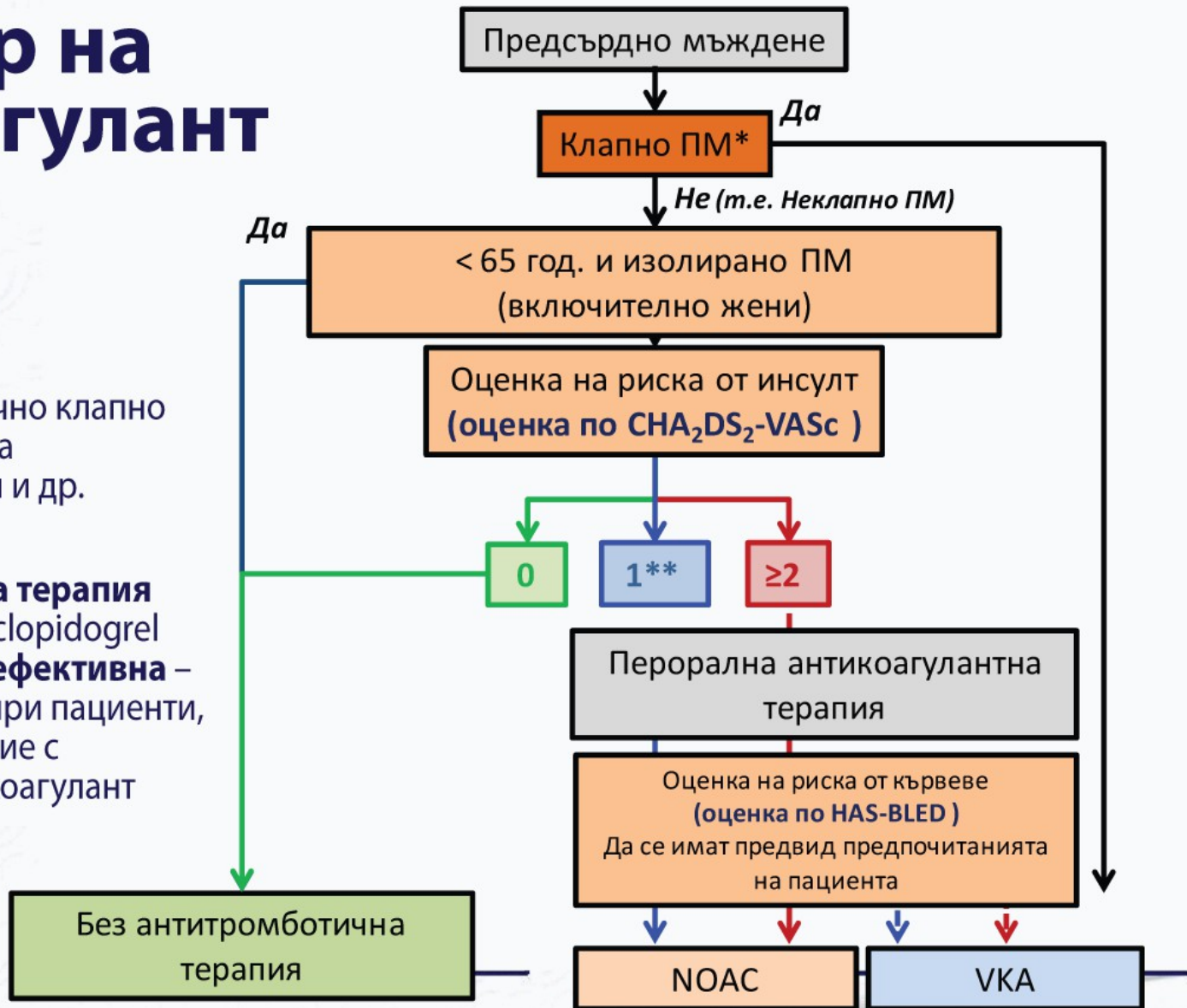
# 2012 focussed update of the ESC Guidelines for the Management of Atrial Fibrillation

## An update of the 2010 ESC Guidelines for the Management of Atrial Fibrillation

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

**Authors/Task Force Members:** A. John Camm (Chairperson) (UK), Gregory Y. H. Lip (UK), Raffaele De Caterina (Italy), Irene Savelieva (UK), Dan Atar (Norway), Stephan H. Hohnloser (Germany), Gerhard Hindricks (Germany), Paulus Kirchhof (Germany/UK)

# Избор на антикоагулант




• Включва ревматично клапно ПМ, хипертрофна кардиомиопатия и др.

\*\* Антиагрегантна терапия с аспирин плюс clopidogrel или – **по-слабо ефективна** – **само аспирин**, при пациенти, отказващи лечение с перорален антикоагулант

# Антитромбозна терапия при ПМ

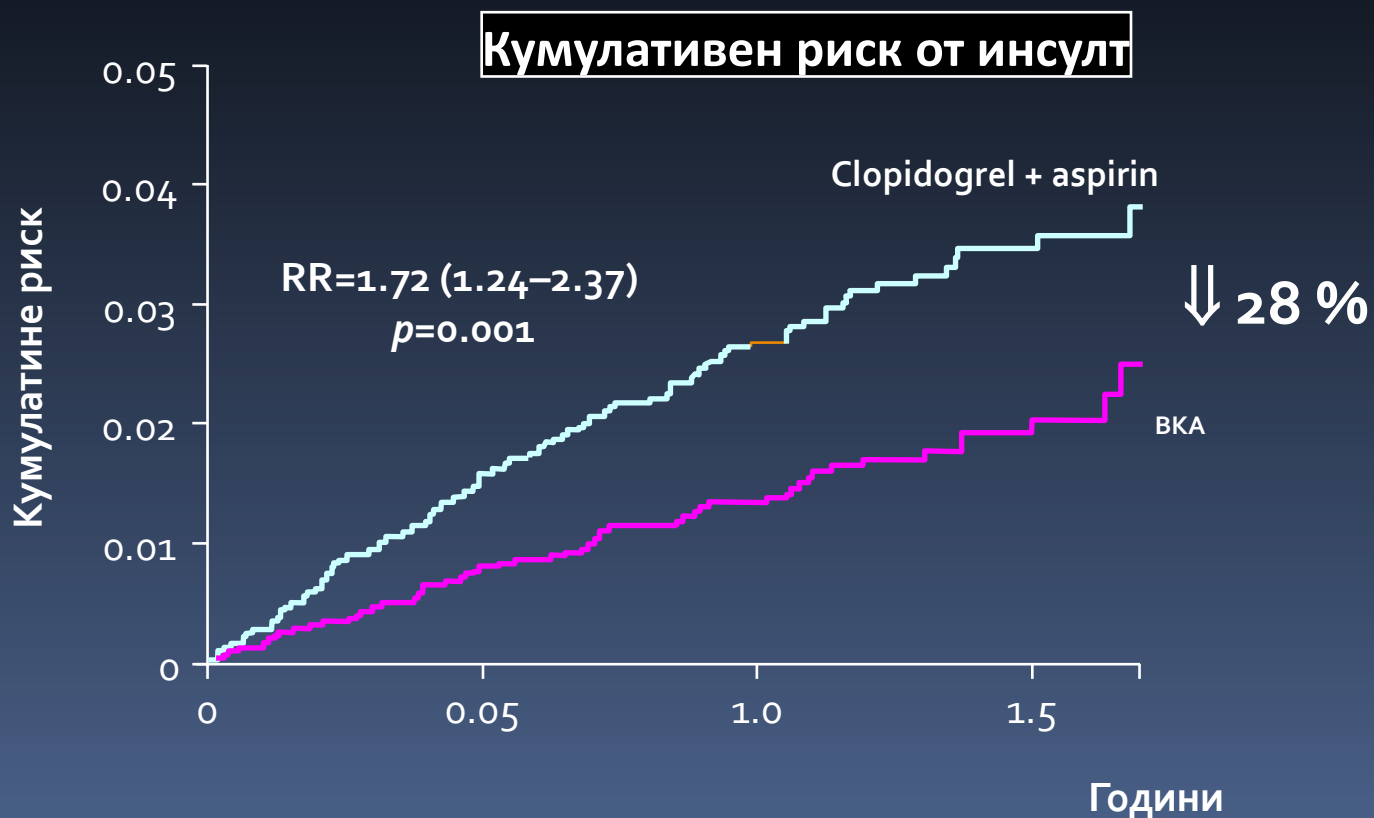




# СРАВНИТЕЛНИ ПРОУЧВАНИЯ МЕЖДУ РАЗЛИЧНИТЕ ГРУПИ АНТИТРОМБОТИЧНИ АГЕНТИ

# ВКА са по - ефективни от ДАТ


ACTIVE W – сравнение на ОАК срещу аспирин с клопидогрел



Connolly *et al*, 2006







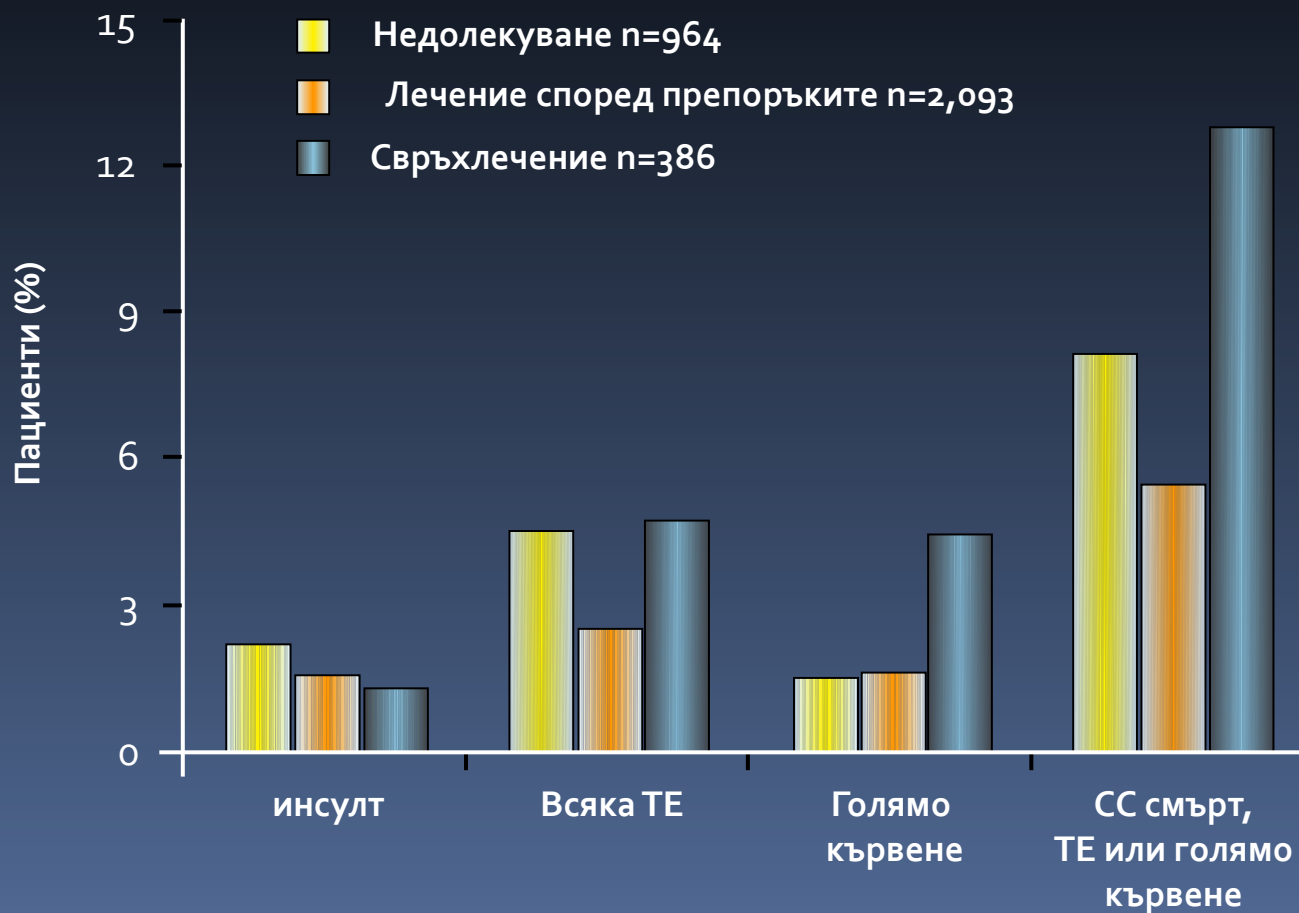
# УПОТРЕБА НА АНТИТРОМБОТИЧНИТЕ АГЕНТИ ПРЕДИ ПРЕПОРЪКИТЕ ОТ 2012 ГОДИНА

Според Euro Heart Survey 2003-2004 антиагрегантите остават широко използвани при пациенти с ПМ: 15 -20%, въпреки че:

- Проучванията сочат, че аспирин е по-малко ефективен от VKA за профилактика на инсульта
- ACTIVE A: двойната антиагрегантна терапия е по-ефективна от самостоятелния прием на аспирин
- ACTIVE W: двойната антиагрегантна терапия е по-малко ефективна от VKA за превенция на съдови събития

# Неспазването на терапевтичния прозорец води до неблагоприятни събития

## Euro Heart Survey



# ISAM2: Европа: Субоптимален контрол на INR в клиничната практика

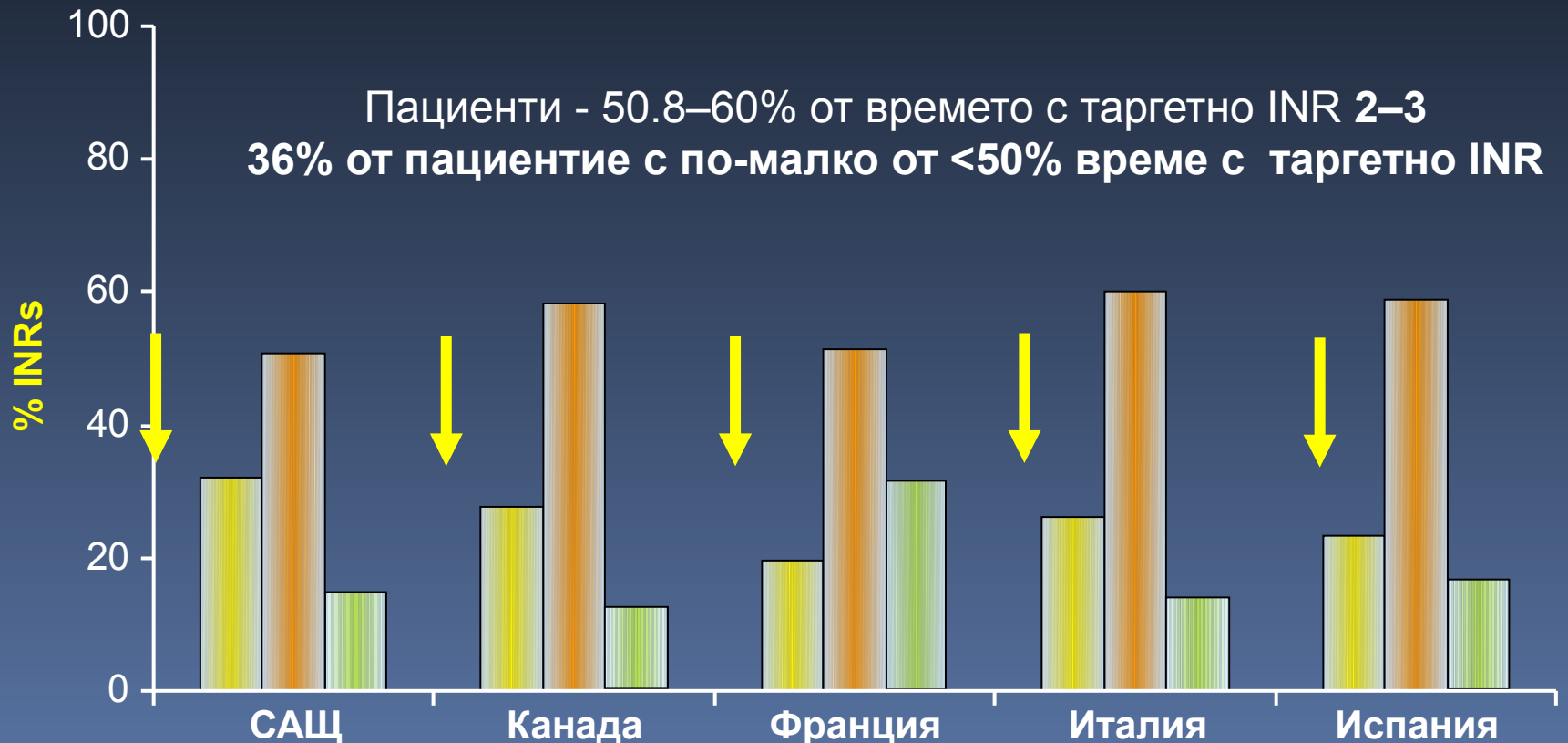
гистърът ISAM: Ретроспективно, многоцентрово кохортно проучване (ISAM)

Време в терапевтичен обхват

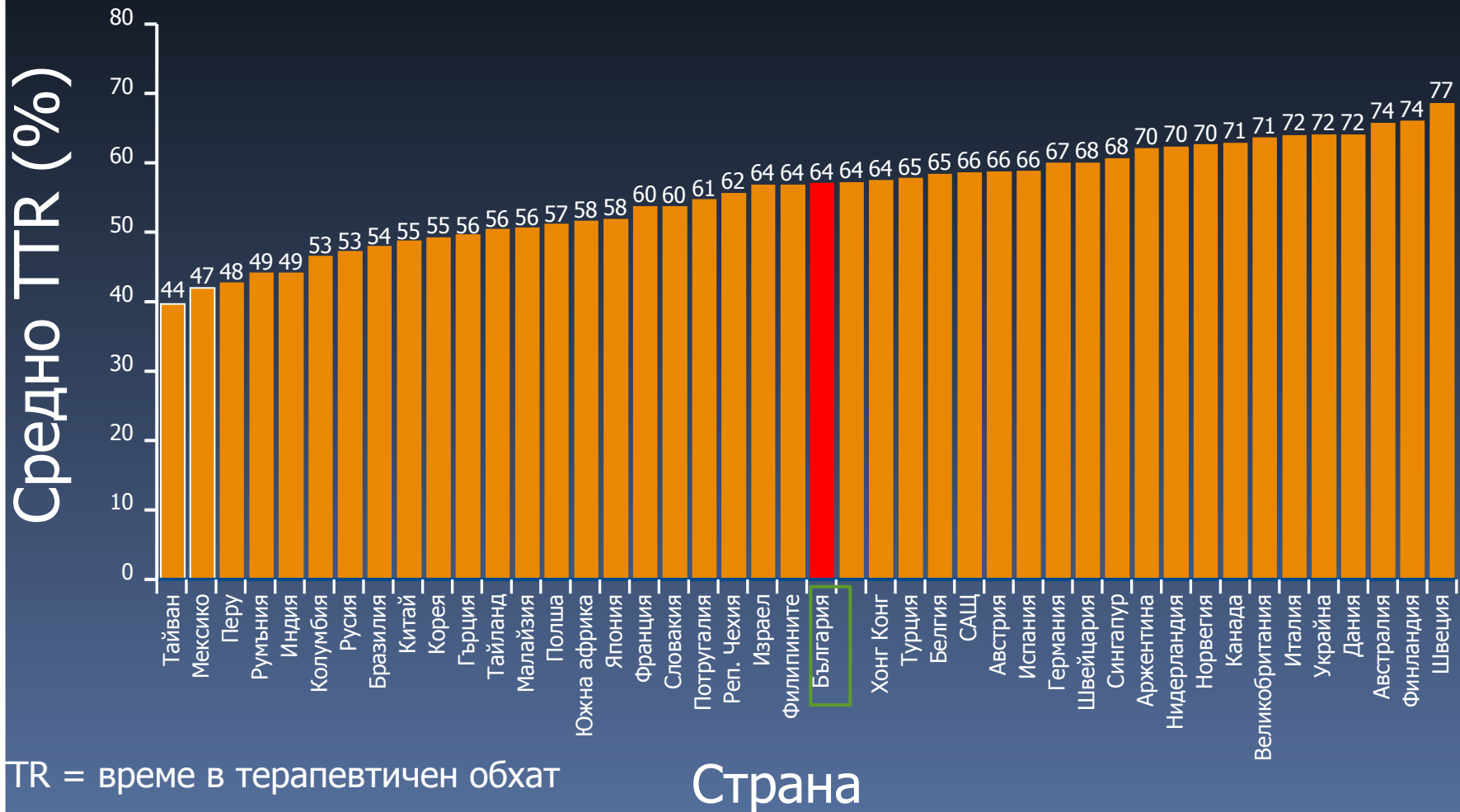
■ INR <2

■ INR 2–3

■ INR >3



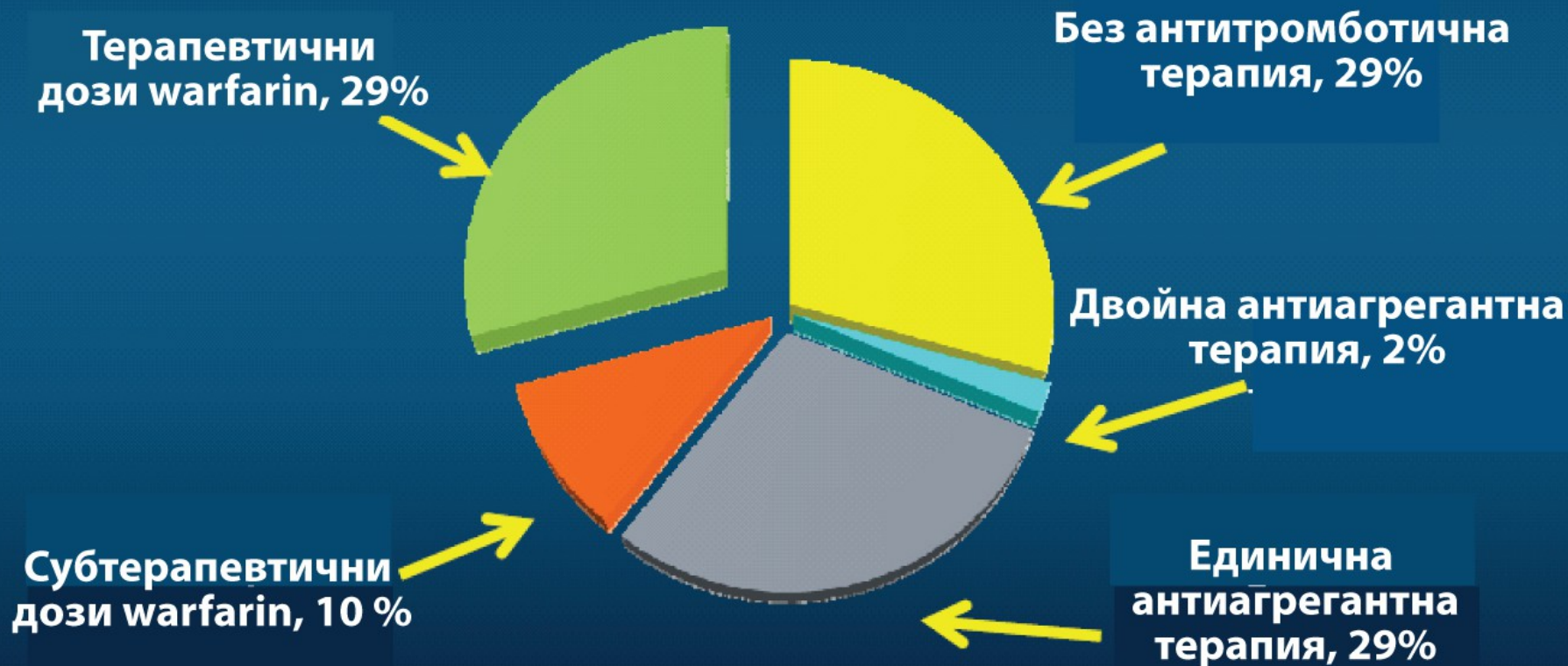
# Анализ на подгрупата с TTR: средно TTR по страни




TTR = време в терапевтичен обхват

# Пропуснати възможности за превенция на инсулт при предсърдно мъждене

Прилагани терапии преди хоспитализацията при пациенти с доказано предсърдно мъждене, хоспитализирани с остър исхемичен инсулт (кохорта с висок риск, n= 597)





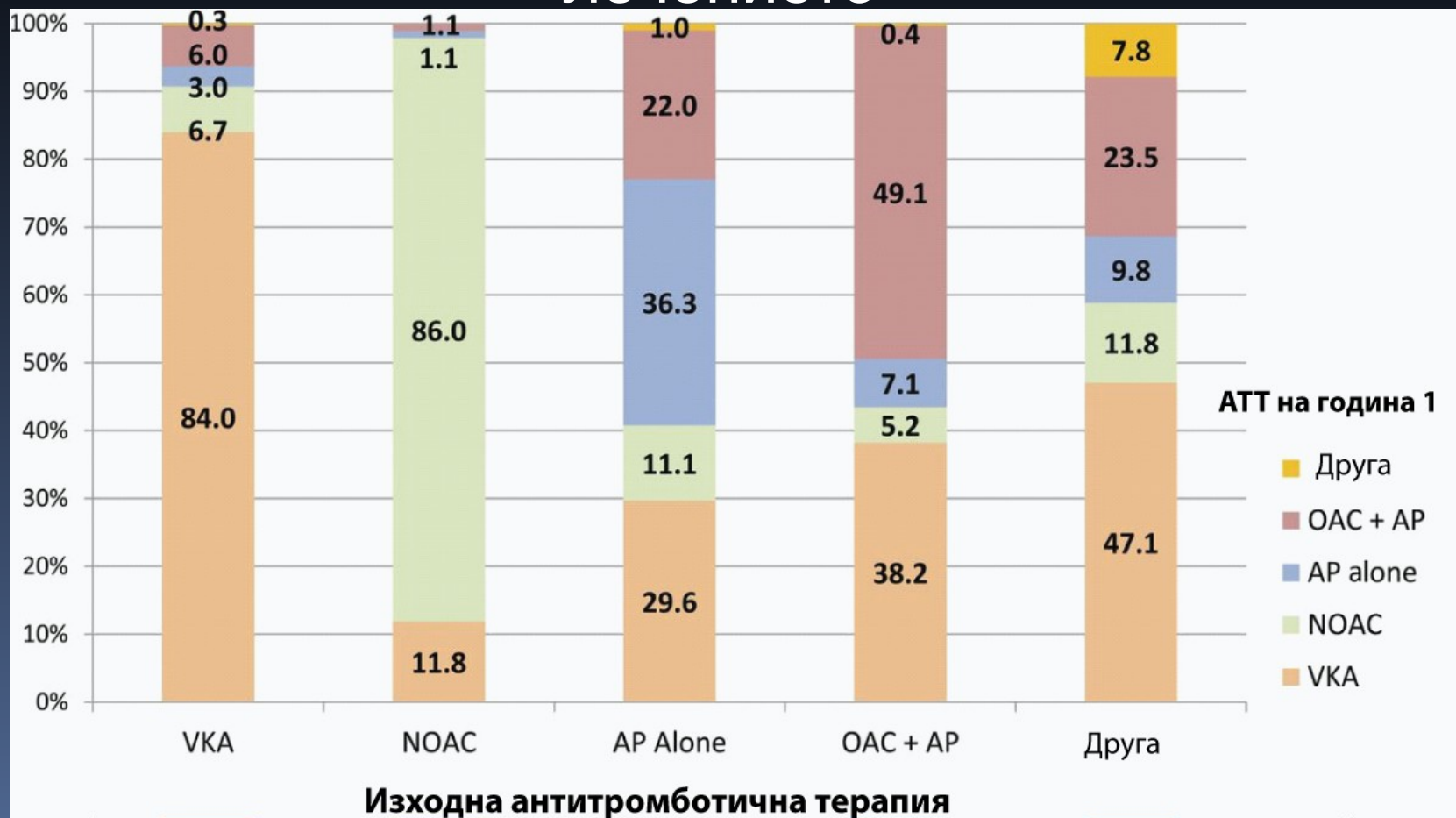
УПОТРЕБА НА  
АНТИТРОМБОТИЧНИТЕ  
АГЕНТИ СЛЕД ПОЯВАТА  
НА НОАК И  
ПРЕПОРЪКИТЕ ОТ 2012  
ГОДИНА

# Prognosis and treatment of atrial fibrillation patients by European cardiologists: One Year Follow-up of the EURObservational Research Programme-Atrial Fibrillation General Registry Pilot Phase (EORP-AF Pilot registry)

**Gregory Y.H. Lip<sup>1\*</sup>, Cécile Laroche<sup>2</sup>, Popescu Mircea Ioachim<sup>3</sup>, Lars Hvilsted Rasmussen<sup>4</sup>, Laura Vitali-Serdoz<sup>5</sup>, Lucian Petrescu<sup>6</sup>, Dan Darabantiu<sup>7</sup>, Harry J.G.M. Crijns<sup>8</sup>, Paulus Kirchhof<sup>9</sup>, Panos Vardas<sup>10</sup>, Luigi Tavazzi<sup>11</sup>, Aldo P. Maggioni<sup>12,13</sup>, and Giuseppe Boriani<sup>14</sup>**



# Прилагане на анти тромботична терапия в края на първата година в сравнение с началото на лечението



# GARFIELD: objective

- Describe real-life treatment patterns in newly diagnosed AF patients with at least one additional risk factor for stroke
- Measure the rate of stroke and systemic embolization
- Assess patient outcomes with specific reference to:
  - Incidence of bleeding complications
  - Therapy persistence including discontinuation, interruption and changes in therapy regimen
  - Utilization of healthcare resources
  - Impact of comorbidity management
  - For patients on VKAs: measure INR fluctuations and dose adjustments over time



# GARFIELD: methodology

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- Novel approach to outcomes research
- 50 countries
- 50,000 prospective and 5000 retrospective patients
- Patients newly diagnosed with non-valvular AF
- Five sequential cohorts
- Random site selection
- Sites representative of national AF care settings
- Consecutive patients
- Follow-up period of 2 years minimum



# Stroke risk profile: CHA<sub>2</sub>DS<sub>2</sub>VASc

CHA <sub>2</sub> DS <sub>2</sub> -VASc Risk factor	GARFIELD Cohort One (n=9288)
CHF/LV dysfunction (1)	1790 (19%)
Hypertension (1)	7236 (78%)
Age >75 years (2)	3121 (34%)
Diabetes (1)	2074 (22%)
Stroke or TIA (2)	1324 (14%)
Vascular Disease (1)	659 (7%)
Age 65–74 (1)	3115 (34%)
Sex category (1) (female sex)	4000 (43%)

CHA <sub>2</sub> DS <sub>2</sub> VASc Score	GARFIELD Cohort One (n=9288)
0	312 (3%)
1	1430 (15%)
2	2131 (23%)
3	2237 (24%)
4	1771 (19%)
5	944 (10%)
6	337 (4%)
7	94 (1%)
8	22 (0.2%)
9	3 (0%)

CHA<sub>2</sub>DS<sub>2</sub>VASc: congestive heart failure/left ventricular dysfunction (EF<40%), hypertension, age > 75y (doubled), diabetes, stroke (doubled), peripheral arterial disease, age > 65-74y, female sex



# Bleeding risk profile

Clinical characteristic (based on HAS-BLED score)	GARFIELD Cohort One (n=9288)
Hypertension	7236 (78%)
Abnormal renal function GFR < 30 ml/min	148 (1.5%)
Abnormal liver function (Cirrhosis)	47 (1%)
Stroke	891 (10%)
Bleeding history or predisposition	311 (3%)
Labile INR	n.a. <sup>1</sup>
Elderly (age >65 years)	6395 (69%)
Alcohol (heavy consumption)	191 (2%)
Drugs incl. aspirin, NSAIDs.	481 (6%)

Points <sup>2</sup>	GARFIELD Cohort One (n=9288)
0	171 (3%)
1	1356 (24%)
2	2647 (47%)
3	1265 (22%)
4	197 (3%)
5	17
6	1
7	0
8	0
9	0

HAS-BLED: hypertension, abnormal renal and/or liver function (1 point each), stroke, bleeding history /predisposition, labile INR, age > 65 y, alcohol abuse and/or concomitant use of antiplatelet agents, NSAIDs etc. (1 point each)

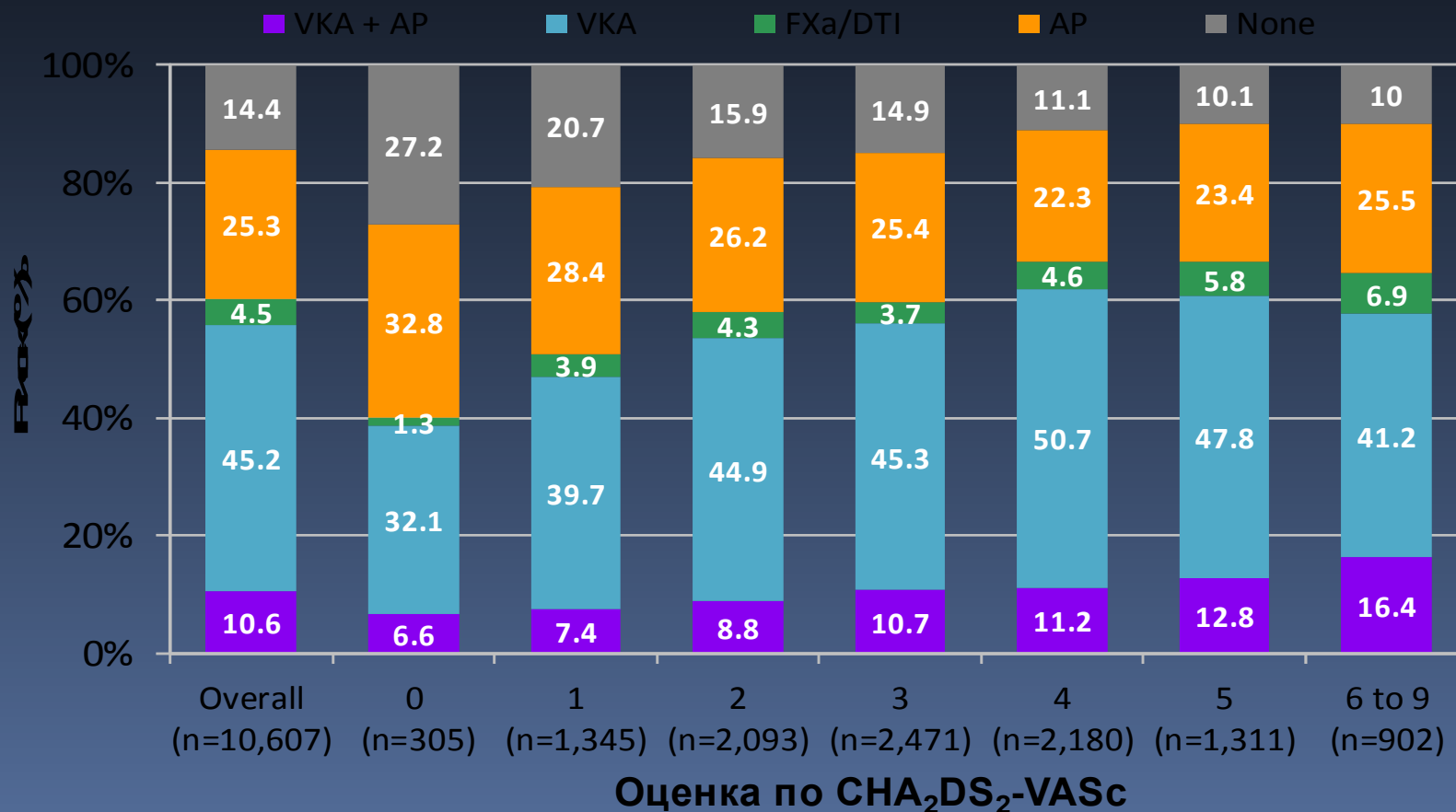


# Thromboprophylaxis and CHA<sub>2</sub>DS<sub>2</sub>VASc

Score	Anticoagulants	Antiplatelets	ACs + APs	Neither	Overall
Total (n)	4496 (48%)	2348 (25%)	1243 (13%)	1201 (13%)	9288 (100%)
0	106 (34%)	114 (37%)	21 (7%)	71 (23%)	312 (100%)
1	618 (43%)	425 (30%)	143 (10%)	244 (17%)	1430 (100%)
2	1025 (48%)	532 (25%)	279 (13%)	295 (14%)	2131 (100%)
3	1059 (47%)	577 (26%)	310 (14%)	291 (13%)	2237 (100%)
4	981 (55%)	387 (22%)	230 (13%)	173 (10%)	1771 (100%)
5	492 (52%)	213 (23%)	164 (17%)	75 (8%)	944 (100%)
6	164 (49%)	71 (21%)	69 (20%)	33 (10%)	337 (100%)
7	39 (41%)	26 (28%)	20 (21%)	9 (10%)	94 (100%)
8	10 (45%)	3 (14%)	5 (23%)	4 (18%)	22 (100%)
9	1 (33%)	0	2 (67%)	0	100%
Not recorded	1	0	0	6	7

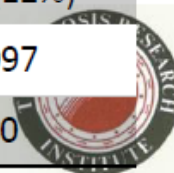
# Пероралните антикоагуланти не се прилагат в Зависимост от риска от инсулт и препоръките за профилактика

*GARFIELD* регистър кохорта 1: новодиагностицирани пациенти с ПМ  
(19 страни по цял свят, декември 2009–октомври 2011)



# Main reason VKAs not used

	Anticoagulants	Antiplatelets	ACs + APs	Neither	Overall
<b>Total (n)</b>	<b>4496</b>	<b>2348</b>	<b>1243</b>	<b>1201</b>	<b>9288</b>
Alcohol abuse	1 (0%)	9 (0%)	3 (2%)	7 (1%)	20 (1%)
Already taking antiplatelet drugs	5 (2%)	130 (7%)	16 (8%)	23 (3%)	174 (6%)
Bleeding risk	23 (10%)	128 (7%)	25 (13%)	46 (6%)	222 (7%)
Fall risk	9 (4%)	122 (7%)	7 (4%)	27 (3%)	165 (5%)
Guideline recommendation	10 (4%)	67 (4%)	14 (7%)	29 (4%)	120 (4%)
Low stroke risk	7 (3%)	267 (14%)	13 (7%)	121 (15%)	408 (13%)
Patient refusal	8 (3%)	181 (10%)	8 (4%)	43 (5%)	240 (8%)
Physician choice	81 (35%)	657 (35%)	63 (32%)	348 (43%)	1,149 (37%)
Previous bleeding event	4 (2%)	38 (2%)	3 (2%)	13 (2%)	58 (2%)
Taking medication contraindicated with VKAs	0	9 (0%)	2 (1%)	8 (1%)	19 (1%)
VKA compliance concern	12 (5%)	112 (6%)	6 (3%)	34 (4%)	164 (5%)
Other reason	71 (31%)	149 (8%)	34 (18%)	108 (13%)	362 (12%)
Unknown/not recorded	143	479	82	393	1097
Not applicable	4122	0	967	1	5090





# REgistry on Cardiac rhythm disORDers assessing the control of Atrial Fibrillation (RecordAF)

- Objective: to investigate how AF is managed in clinical cardiology settings around the world
- The first international, prospective, observational registry established to assess the burden of AF
- Launched in 2008, RecordAF was a 12-month survey (now complete) that registered 5604 patients in 532 sites across 21 countries in Europe, North America and Asia
- Results from RecordAF showed that a rhythm-control strategy (keeping patients in sinus rhythm) was significantly more effective than a rate-control strategy
- The benefit of rhythm control, was manifested in a reduced likelihood of progression to permanent AF<sup>356</sup>

## Outcomes Registry for Better Informed Treatment of Atrial Fibrillation (ORBITAF)

- Objective: to prospectively follow 10,000 patients with AF recruited from 167 outpatient practices in the United States (US) and perform follow-up for approximately 3 years
- ORBIT-AF is a multicentre, prospective, ambulatory-based registry of incident and prevalent AF launched in 2009<sup>357</sup>
- ◆ The registry will include information on:
  - ◆ The use of both antiplatelet and anticoagulant agents
  - ◆ Patient outcomes
  - ◆ Costs
  - ◆ Quality of life

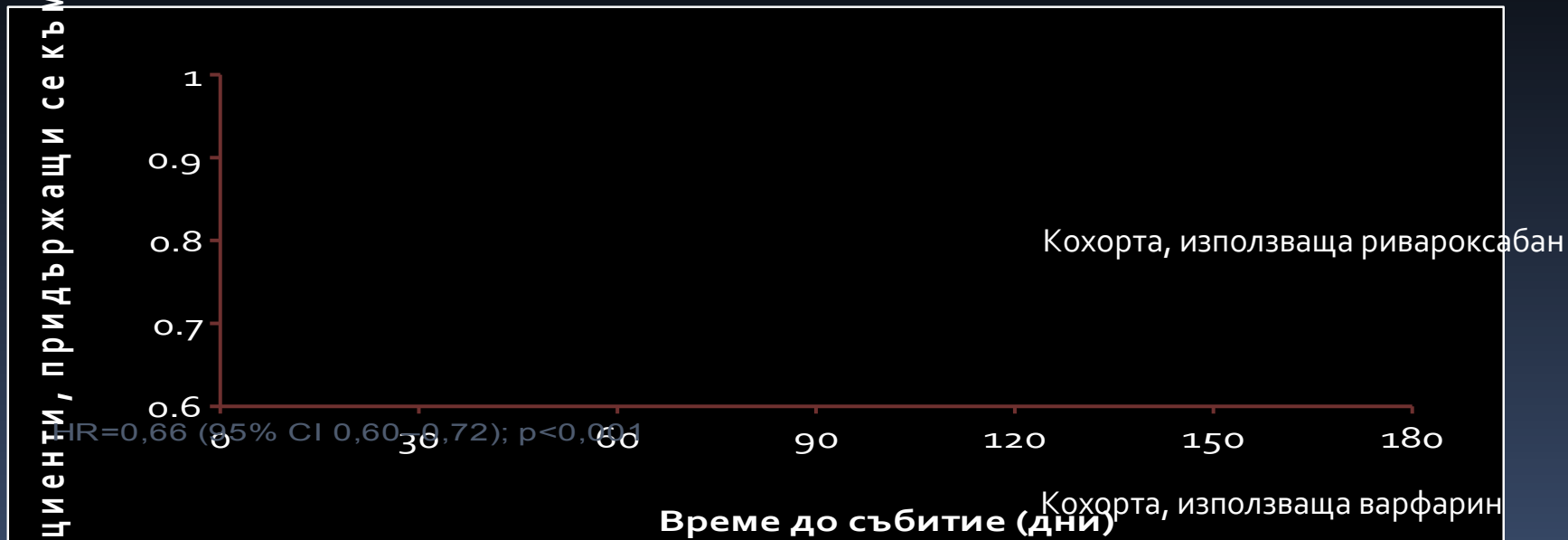
# GLOBAL Registry on long-term oral Anti-thrombotic treatment in patients with Atrial Fibrillation (GLORIATM-AF)

- ◆ Objectives: to collect real-world data in patients with non-valvular AF at risk of stroke on important outcome events, including:
  - ◆ The safety and effectiveness of antithrombotic treatments, including the vitamin K antagonist warfarin, acetylsalicylic acid and novel oral anticoagulants
  - ◆ MI
  - ◆ Life-threatening bleeding events
  - ◆ Stroke
  - ◆ All-cause death
- ◇ Recently established (2011), the GLORIA-AF registry is planned to involve 2200 sites in 50 countries
- ◆ Approximately 56,000 patients will be characterized by:
  - ◆ Age
  - ◆ Gender
  - ◆ Antithrombotic treatment choice at baseline
  - ◆ CHADS2, CHA2DS2-VASc and HAS-BLED scores

## Real-life global survey evaluating patients with Atrial Fibrillation (RealiseAF)

- Objective: to determine AF rhythm control strategies
- Launched in 2009
- Contains data from >10,000 patients with AF across 26 countries<sup>359</sup>
- ◆ Assesses:
  - ◆ AF management strategies
  - ◆ Cardiovascular risk profiles of enrolled patients
- ◆ Will also contains details of:
  - ◆ Demographic factors, including risk factors for cardiovascular events
  - ◆ Cardiovascular and bleeding event rates
  - ◆ Anticoagulant and antithrombotic therapy prescription rates stratified by CHADS2 stroke risk scores
  - ◆ AF guidelines compliance
- ◆ Initial data suggests that:
  - ◆ Rate, rather than rhythm control, is the most frequently chosen therapeutic strategy; however, rhythm control was shown to be the most effective
  - ◆ Substantial proportions of patients with controlled AF have symptoms, regardless of rate or rhythm control strategy
  - ◆ Prescription of antithrombotic therapy for ischaemic stroke prophylaxis in the real world deviates from guideline recommendations

Данни от реалната практика показват по-добро спазване на терапевтичния режим с ривароксабан в сравнение с варфарин<sup>1\*</sup>



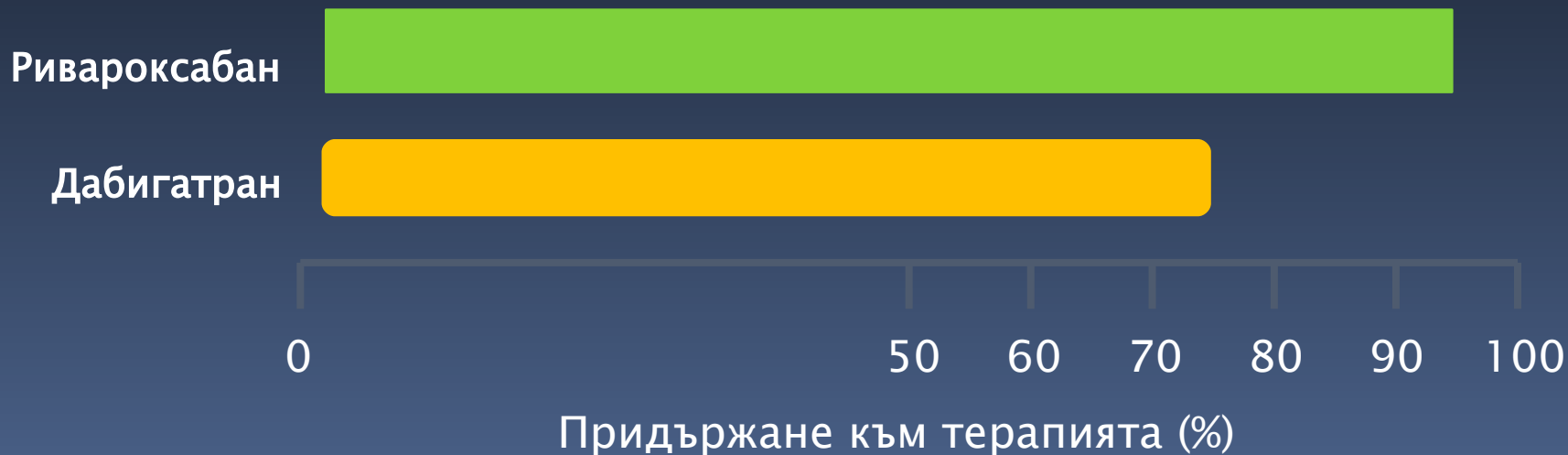
„...съществуват доказателства, че фиксираните дози без редовна корекция след проследяване може да допринесат за подобро придържане към лечението, особено в дългосрочен план“<sup>2</sup>

\*След 90 и 180 дни.

1. Laliberté F, et al. *Curr Med Res Opin.* 2014;**30**:1317–1325;
2. Ewen S, et al. *Clin Res Cardiol.* 2014;**103**:173–182.

Данни от реалната практика показват по-добро спазване на лечебния режим с ривароксабан 1х дн. спрямо дабигатран 2х дн.

- ◆ Резултати от регистъра DRESDEN показват, че 90,7% от пациентите, приемащи rivaroxaban, продължават лечението към 9 месец в сравнение със 73,6% от пациентите на дабигатран



# Methods

**An international (26 countries) large scale  
(more than 10 000 Pts) cross-sectional survey, (2010)**



**An international (35 countries) large scale (more than 5 000 Pts) multi-  
centre prospective observational study, (2003-2004)**



EURO HEART SURVEY

# Patients and AF characteristics

	Total N=15,523
Lone AF*	5.1
<b>Time since AF diagnosis</b>	
< 3 months	20.6
3 to 6 months	6.3
6 to 12 months	10.2
> 12 months	62.9
<b>Type of AF</b>	
Paroxysmal	24.8
Persistent	22.3
Permanent	46.4
Unable to assign (first episode)	6.4

REALISE AF

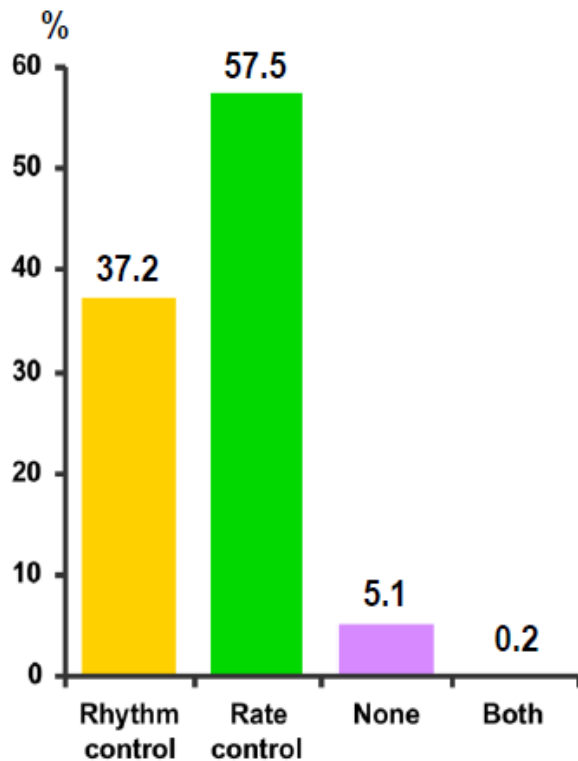
	Total N=5,333
Lone AF*	9.9
<b>Time since AF diagnosis</b>	
< 3 months	-
3 to 6 months	-
6 to 12 months	-
> 12 months	-
<b>Type of AF</b>	
Paroxysmal	28.4
Persistent	21.8
Permanent	28.9
Unable to assign (first episode)	18.3

EURO HEART SURVEY



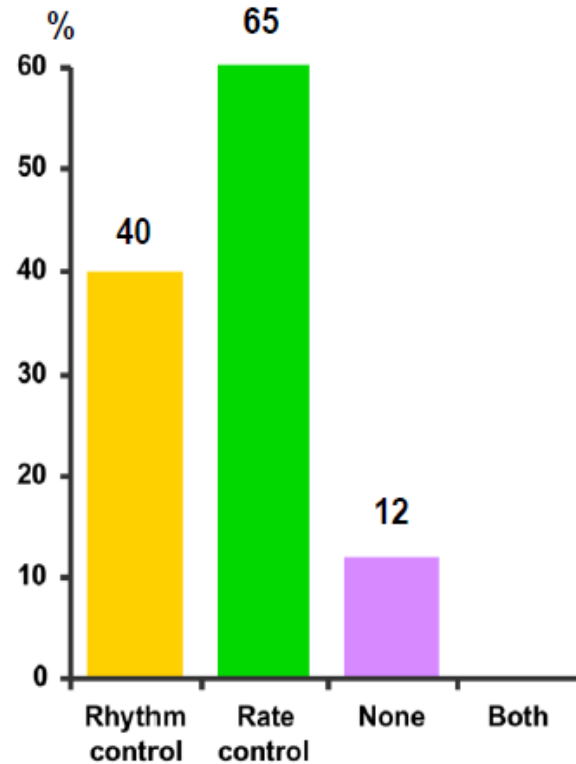
# Rate control was the strategy most frequently chosen

Therapeutic strategy



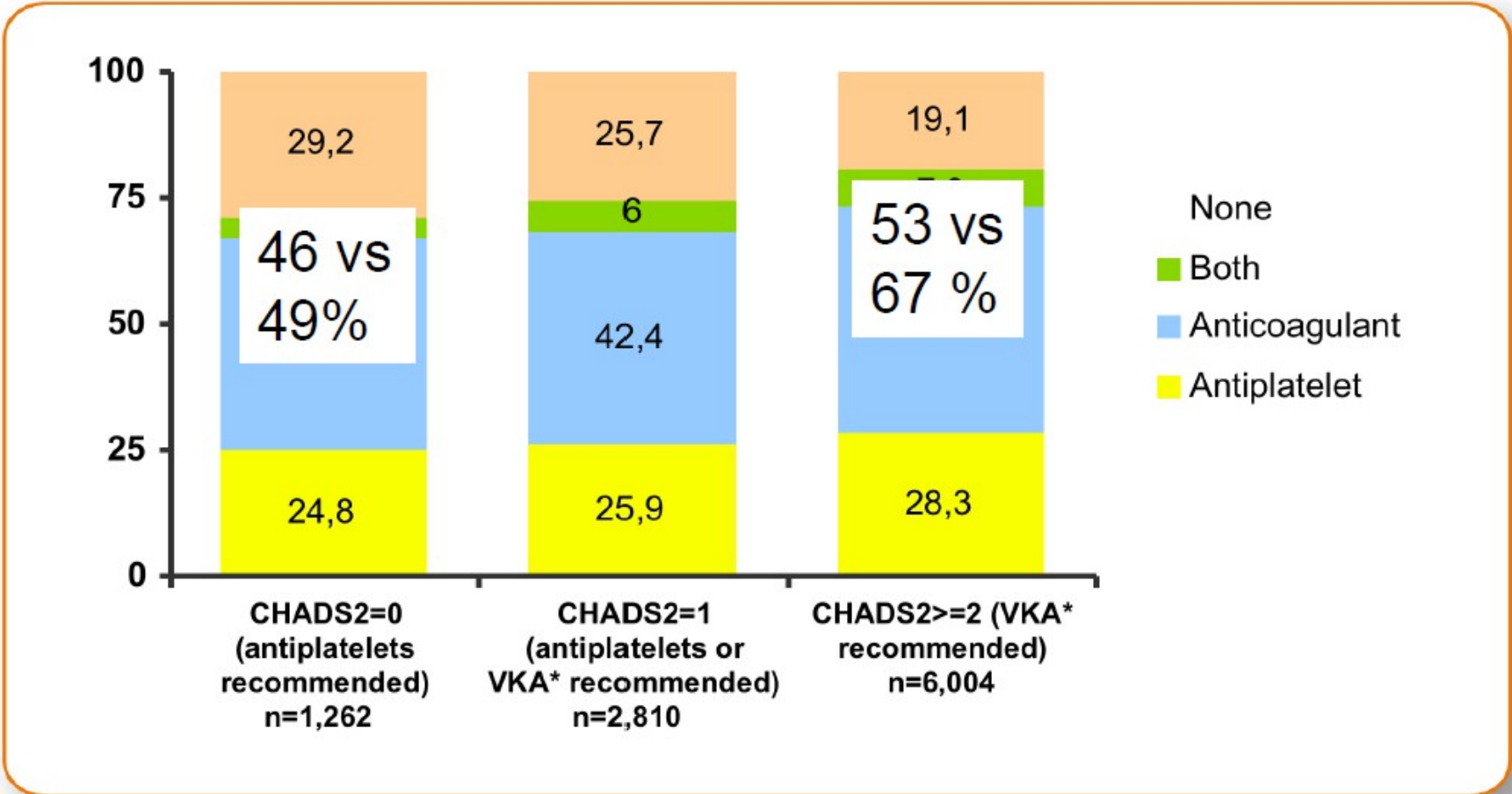
REALISE AF

Therapeutic strategy



EURO HEART SURVEY

# Management of AF in a real life setting deviates from guidelines\*



\*ACC/AHA/ESC guidelines

# Conclusions

- The Euro Heart Survey illustrates the unmet need for new safe and effective antiarrhythmic drugs to suppress symptoms in paroxysmal and persistent AF. New antithrombotic drugs or strategies including education might help to improve matters. Long term follow-up may indicate whether guideline adherence is associated with better outcome.



EURO HEART SURVEY



- The RealiseAF results highlight the need for newer therapies (antiarrhythmic and antithrombotic agents) to manage AF with a view to improve CV outcomes as well as a need for greater education to promote better adherence to guidelines.

# PREvention of thromboembolic events – European Registry in Atrial Fibrillation (PREFER in AF)

- ◆ Objectives are to assess:
    - ◆ Leading causes of stroke
    - ◆ The impact of new anticoagulant therapies for stroke prevention in patients with AF
    - ◆ Patient satisfaction with their AF management regimens
    - ◆ The impact of AF and its management on patient quality of life
    - ◆ The health economic burden of AF in Europe
  - PREFER in AF is a multi-centre, prospective registry with a one-year follow up
  - Launched in January 2012, it will collect real-life data from 5000 patients with AF across seven countries
-

## The Central Registry of the German Competence NETWORK on Atrial Fibrillation (AFNET) registry

- Objectives: to establish a nationwide patient registry on diagnostics, therapy, course and complications of AF in Germany
- AFNET is a national interdisciplinary research network funded by the German Federal Government
- The registry incorporated 9577 patients who were enrolled between 2004 and 2006 at 191 sites (either at tertiary care centres, district hospitals, by office-based cardiologists or by general practitioners/internists)
- ◆ Key results included:
  - ◆ Per guideline recommendations, younger patients and patients with non-permanent AF were more likely to receive rhythm control therapy than older patients and patients with permanent AF<sup>360</sup>
  - ◆ Despite stroke risk being similar across all centre types, enrolment at a tertiary care centre or an office-based cardiologist was associated with a significantly increased chance of receiving adequate thromboprophylaxis compared with other centre types<sup>360</sup>
- This difference was consistent irrespective of the stroke risk of the patient, as determined by both CHADS2 and CHA2DS2-VASc scores<sup>360</sup>
- ◆ Notably, anticoagulant therapy for stroke prevention was given to:<sup>361</sup>
  - ◆ 71.4% of the patients considered eligible by applicable guidelines
  - ◆ 48.4% of patients with low risk where guidelines do not recommend anticoagulation

# ЗАКЛЮЧЕНИЕ

## НАБЛЮДАВАНИ ТЕНДЕНЦИИ

Препоръките от 2012 година не променят съществено тенденциите и съотношението на различните групи използвани антитромботични агенти при ПМ;

- Прескрипцията на антикоагуланти не е в съответствие с препоръките: при показаните пациенти е относително ниска, а при нискорисковите - висока;
- Таблиците за оценка на риска не се използват адекватно в клиничната практика;
- Антиагрегантите остават широко използвани за превенция на инсулта при сходен риск от кървене;
- Употребата на NOAC остава ниска, независимо от препоръките на ESC и EHRA.

РЕАЛНАТА КЛИНИЧНА ПРАКТИКА СРЕЩУ  
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