

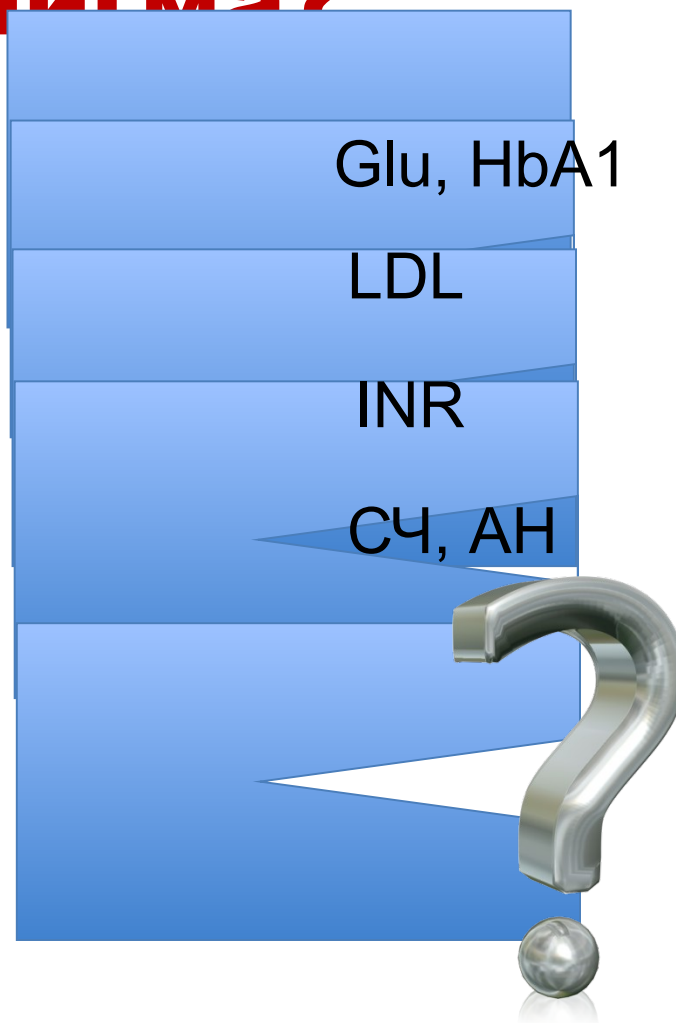


# Ниво на тромбоцитна инхибиция и връзка с дългосрочната прогноза при ОКС

**А. Постаджиян**  
**УМБАЛ "Света Анна"**  
**София**  
**[armanp@abv.bg](mailto:armanp@abv.bg)**

# Смяна на терапевтичната парадигма?

- Инсулин
- Статини
- Антикоагуланти
- В-блокери
- Антиагреганти



# Как да се оптимизира антиагрегантната терапия

- Мониторирани за ефикасност –  
резистентност
- Мониторирани за безопасност и  
превенция на кървенето
- Намиране баланса ефикасност-  
безопасност

# Как да се оптимизира антиагрегантната терапия

- Мониторинг на **резистентност** **чрез изследване на тромбоцитна реактивност**
- Мониторинг за безопасност и превенция на кървенето
- Намиране баланса ефикасност-безопасност



A.Colombo  
Operator techniques to  
reduce stent thrombosis

**The stool stands only if each leg is solid: one leg with extra strength does not compensate for the broken one**

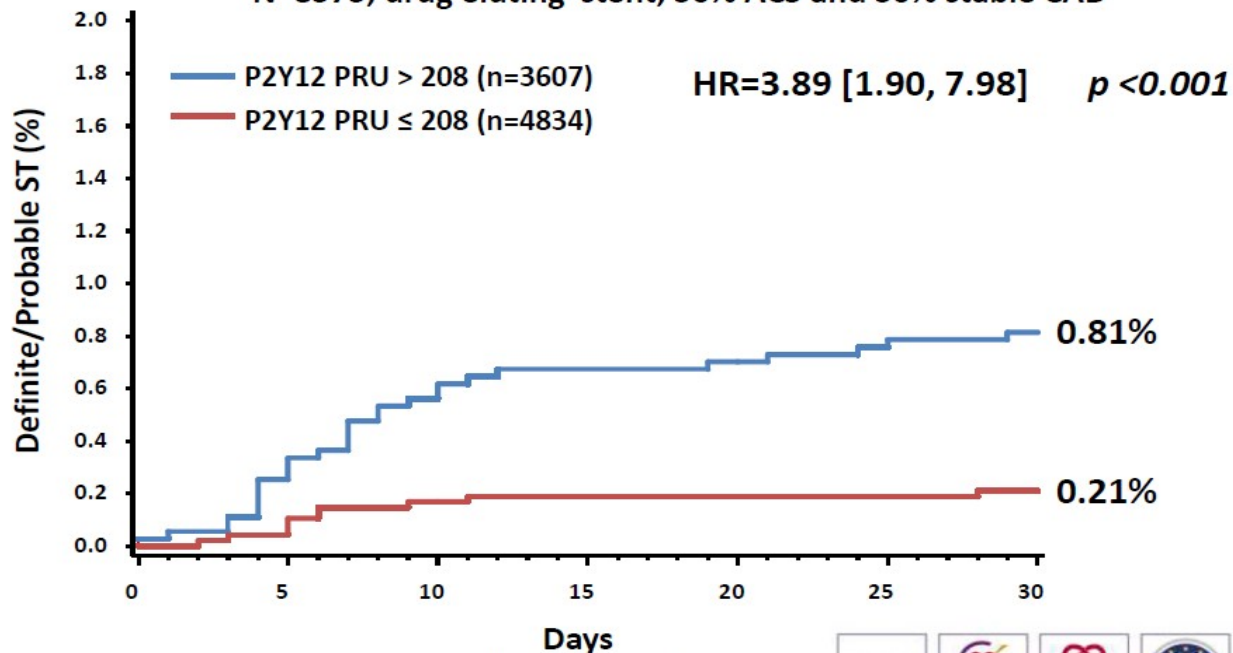
- **Lumen Leg:** optimal MLD
- **Run off leg:** TIMI 3 flow
- **Blood leg:** optimal antiplatelet therapy

# ADAPT DES – Стент тромбоза и тромбоцитна реактивност



## Stent thrombosis and platelet reactivity

N=8575, drug eluting stent, 50% ACS and 50% stable CAD



ADAPT-DES study, Stone et al, TCT 2011



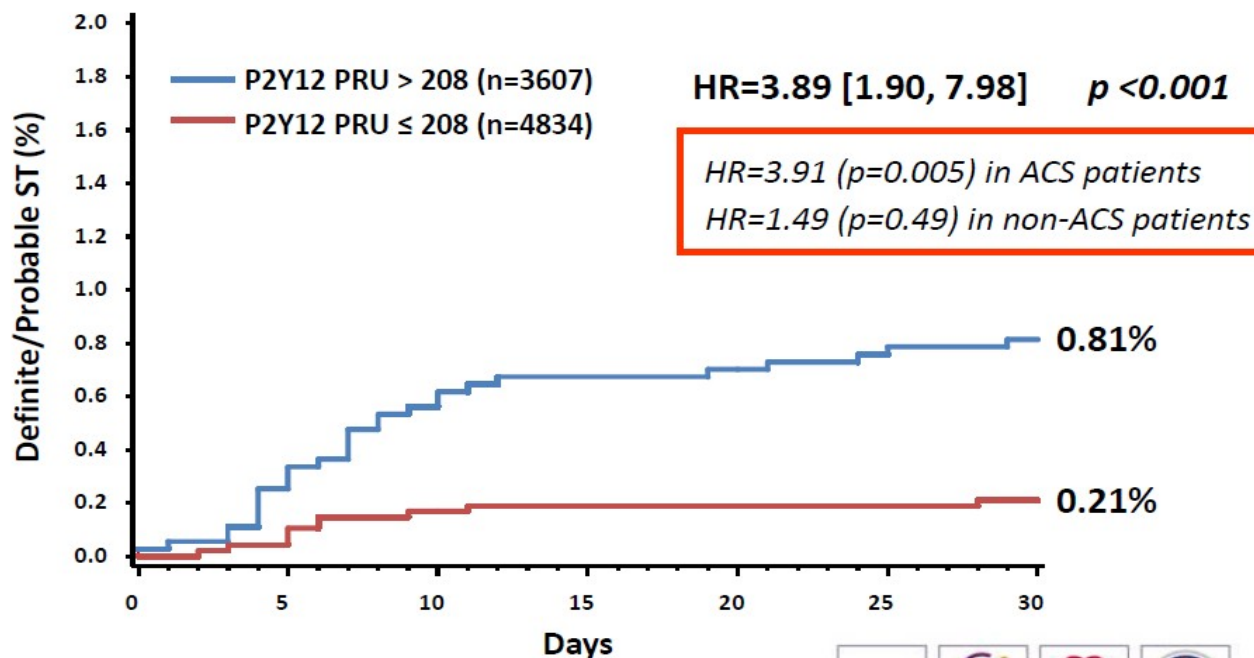
# ADAPT DES – Стент тромбоза и тромбоцитна реактивност – връзка при високорисковите

euro  
PCR

ALL  
you need  
to KNOW

## Relationship in High Risk Patients

N=8575, drug eluting stent, 50% ACS and 50% stable CAD



ADAPT-DES study, Stone et al, TCT 2011

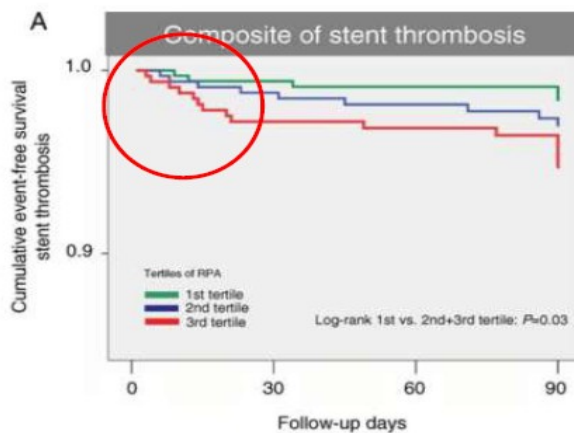


# Персистиращо висока тромбоцитна реактивност - връзка с ранната дефинитивна стент тромбоза

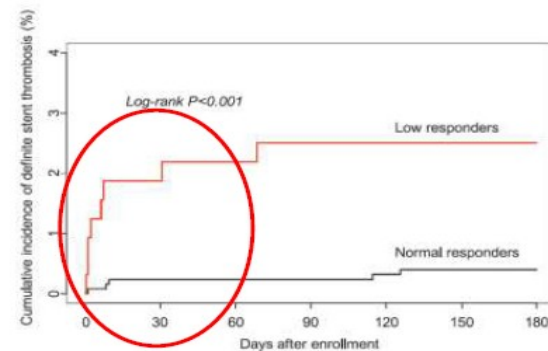
euro  
PCR

Relationship for early events

ALL  
you need  
to KNOW



Geisler et al, EHJ 2010



Sibbing et al, TH 2010

HTPR is good predictor of early thrombotic events

PCR

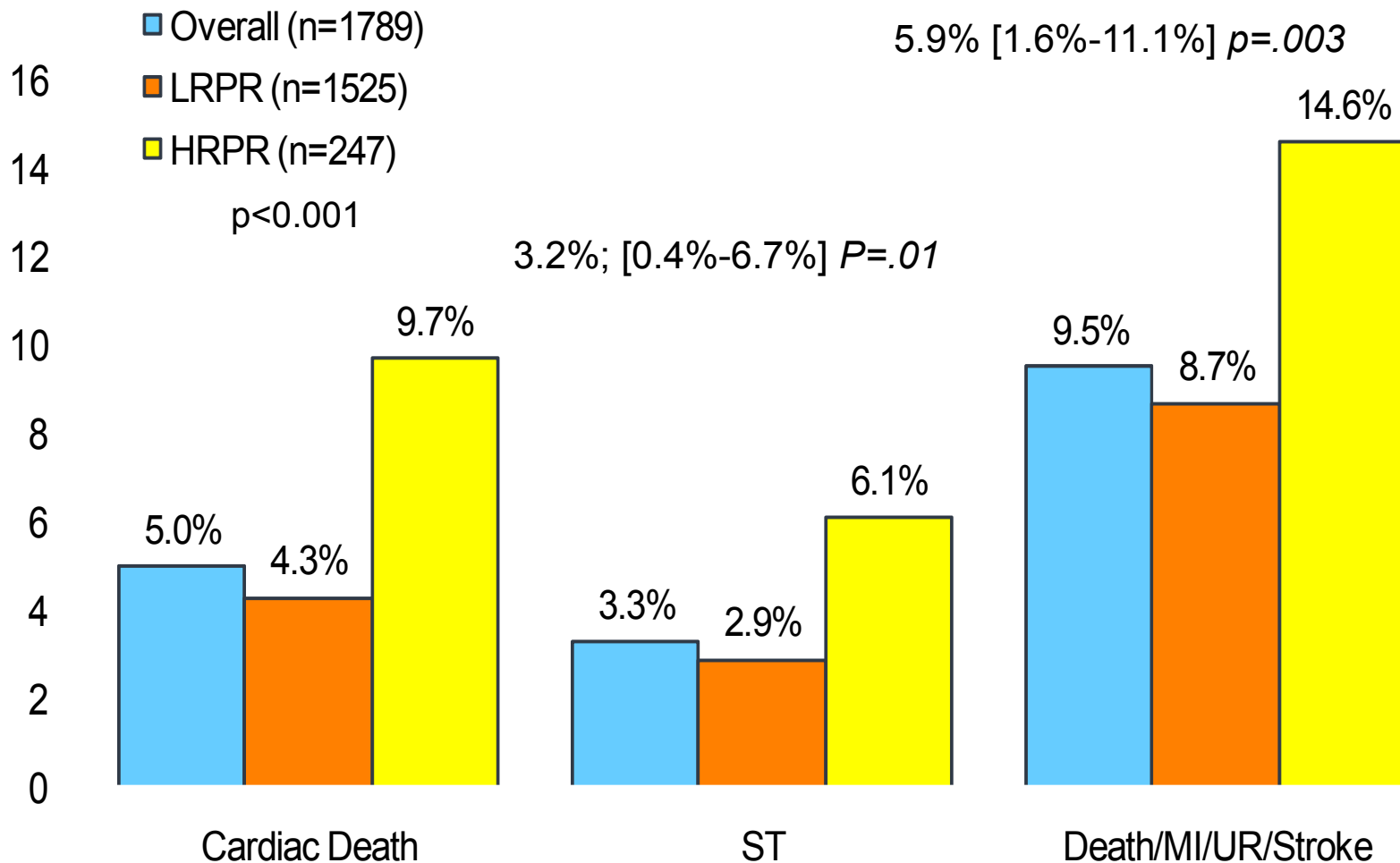
EAPCI

EUROPEAN  
SOCIETY OF  
CARDIOLOGY

EACTS



# The RECLOSE Study СМЪРТНОСТ



HRPR: независимо корелира със смъртност HR, 1.81; [1.18-2.76;] P=.006

# **Мониторирание за ефикасност – резистентност**

- Ясна връзка за ранните тромботични инциденти
- Ясна връзка при високорисковите пациенти
- ...Не означава, че тестването и оптимизирането на терапията е свързано с подобряване на прогнозата...
- ...Доказателства към 2014 год

# Концепцията за индивидуализираната терапия с тестване в клиничните проучвания

PCR Issues in clinical practice: 1 x

www.pcronline.com/Lectures/2013/Issues-in-clinical-practice-tailoring-treatment-to-individual-patients

22761 07:49 Steps

**НЕГАТИВНО**

**CONCEPT OF INDIVIDUALIZED THERAPY**

**НЕГАТИВНО**

**СПРЯНО**

Genotyping for PCI	NCT01177592	PCI (1500)	non-guided	Urgent revascularization, ST	(LD+MD) vs prasugrel (LD+MD)
ARCTIC (2012) Double Randomization of a Monitoring Adjusted Antiplatelet Treatment Versus		Elective PCI, DES	Use of Vorixa New™ M	12 months Composite end point of	Therapy based on

**НЕГАТИВНО**

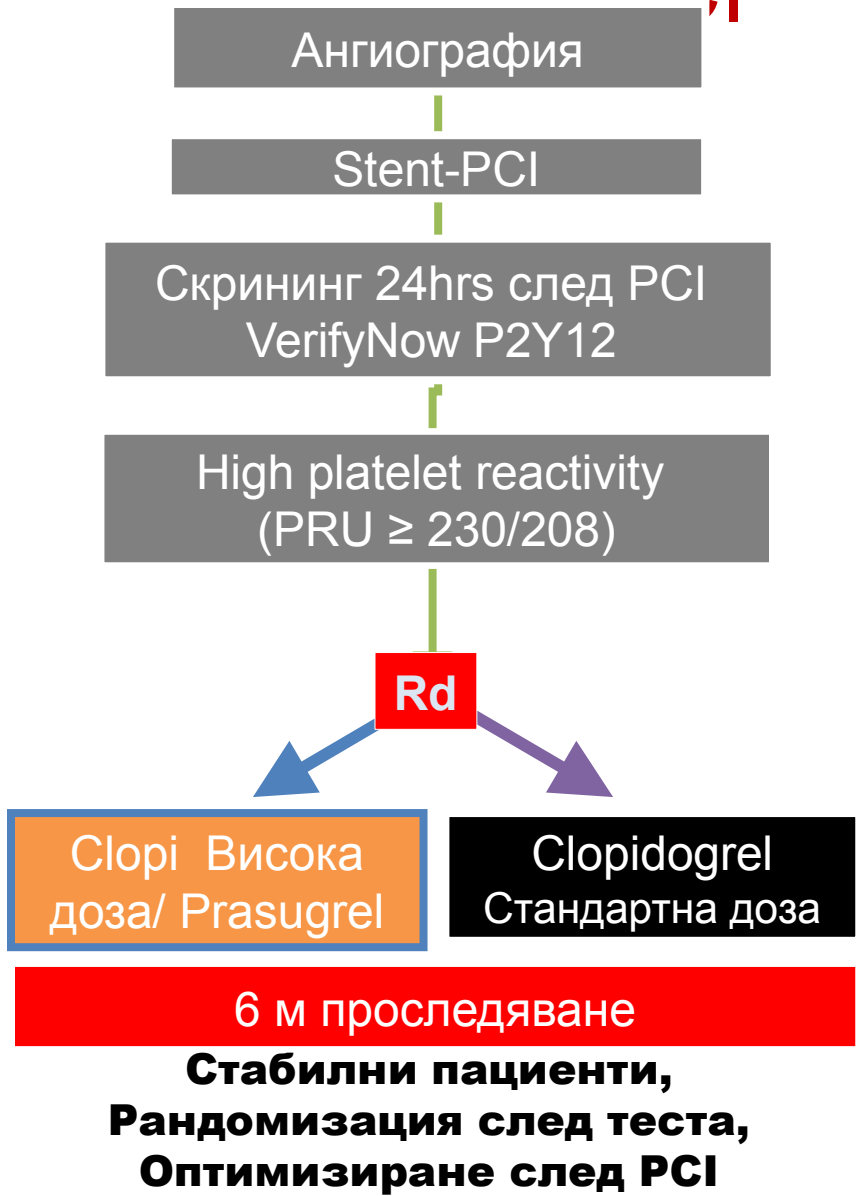
**СТАТУС НЕИЗВЕСТЕН 422 ПАЦИЕНТИ**

**READ AND SHARE**

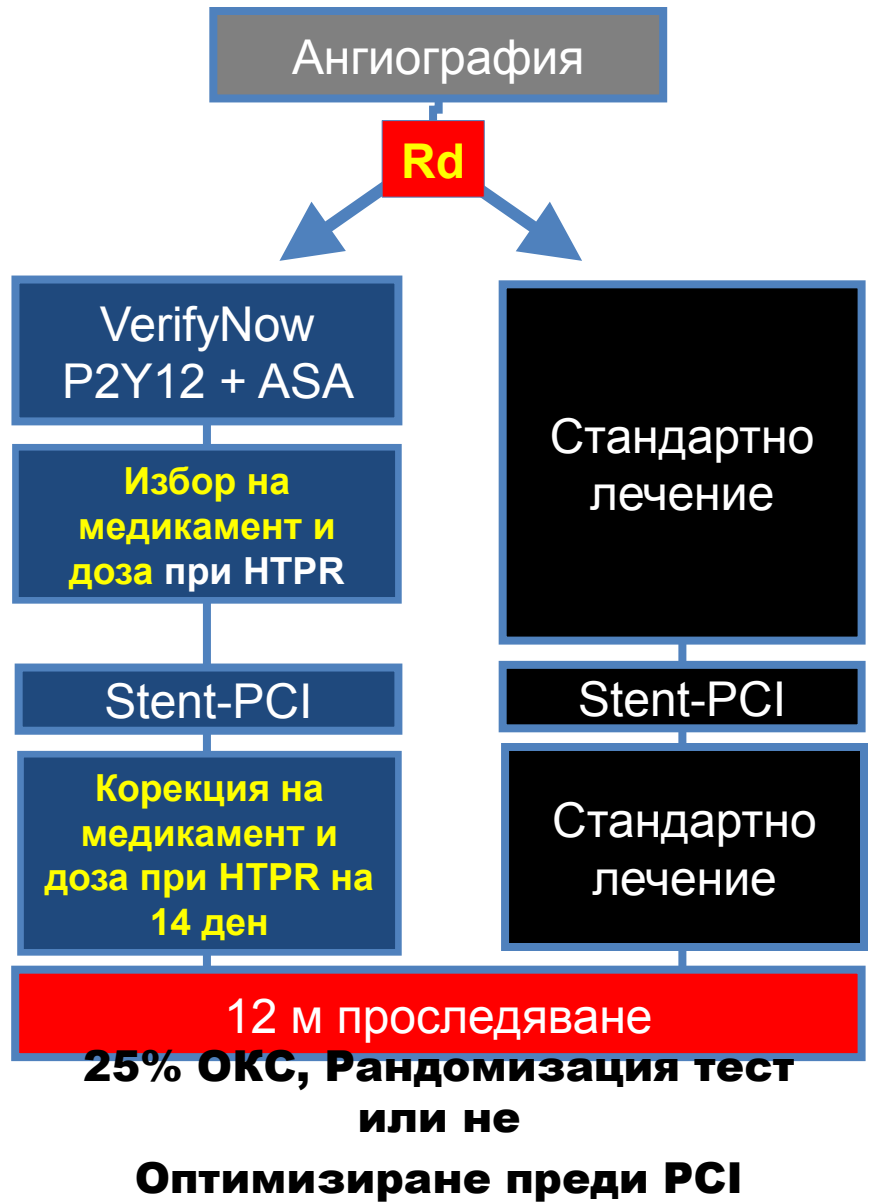
- ▶ A complex and complicated TAVI case
- ▶ Advanced coronary and carotid disease in a patient undergoing non-cardiac surgery
- ▶ Coronary stenoses are stented: who cares about
- ▶ 41-year old female with hypertension and obstructive sleep apnea
- ▶ MVD and primary PCI: which

PCR

- GRAVITAS / TRIGGER\_PCI



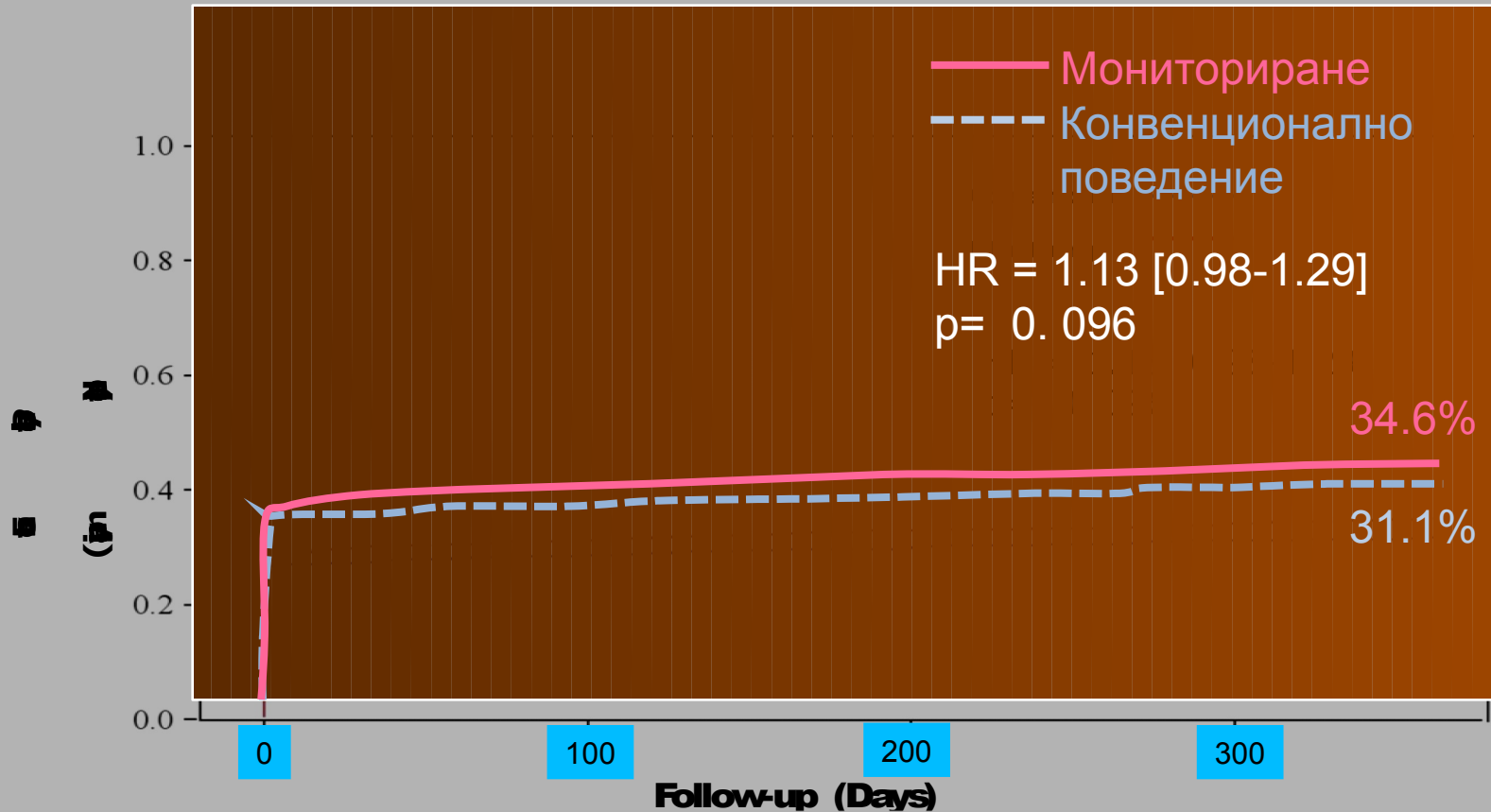
- ARCTIC



# ARCTIC – първична крайна точка 1

Смърт/МИ/ Инсулт/стент тромбоза/спешна реваascularизация

Год



N at risks

Conventional

1227

835

801

767

Monitoring

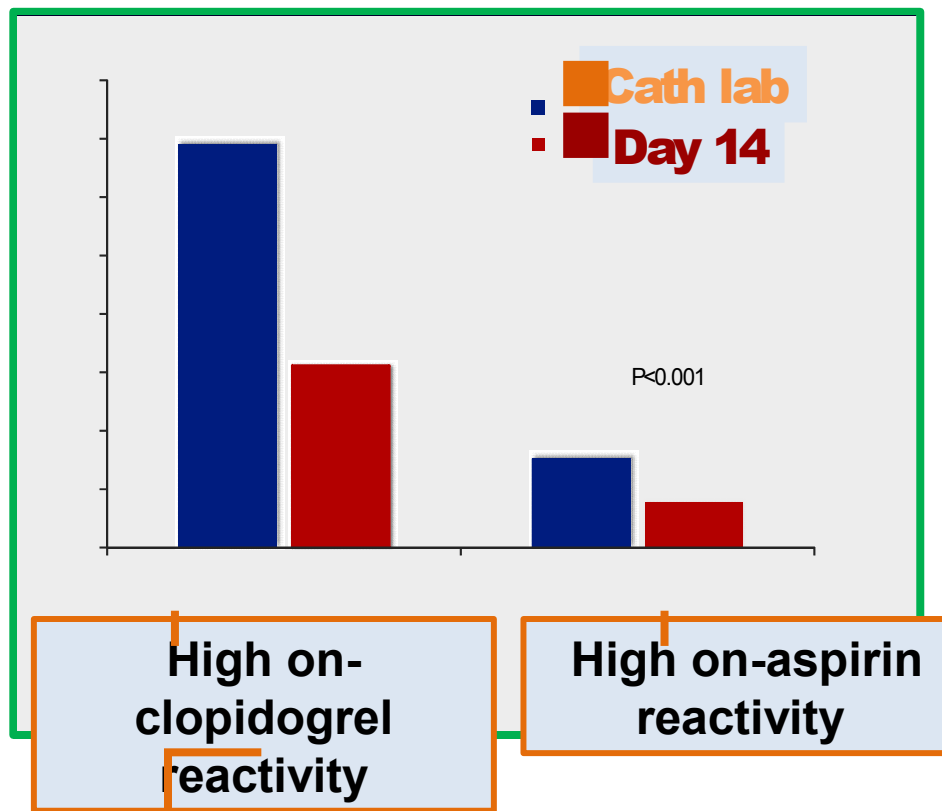
1213

790

762

730

# Оптимизирани преди PCI

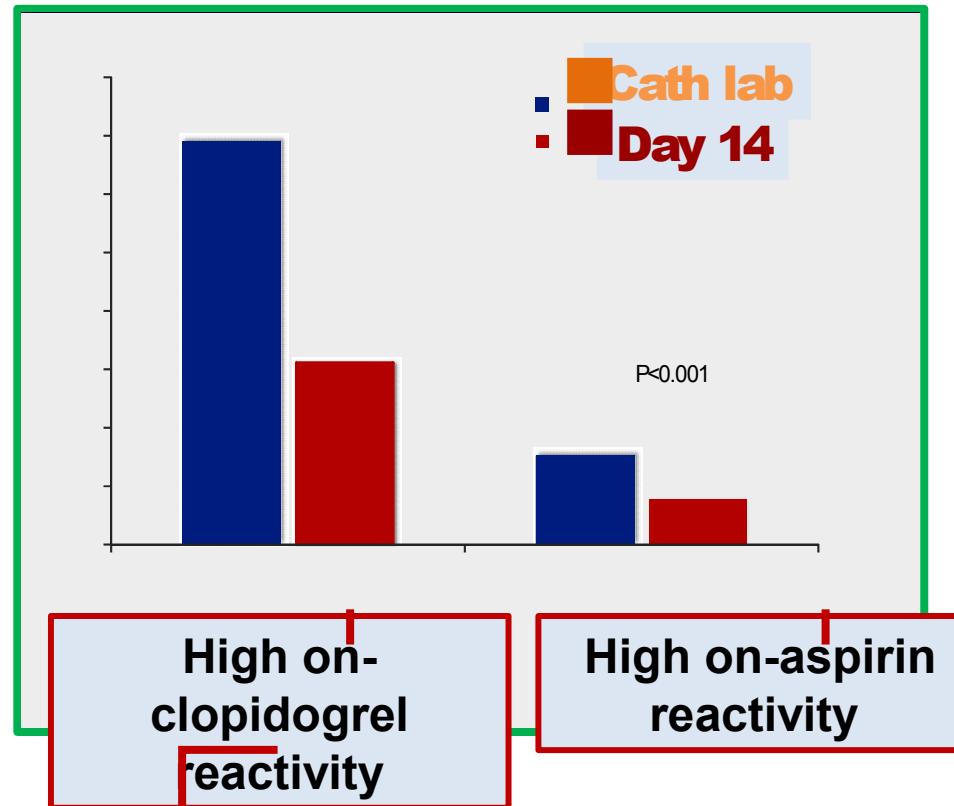


High on-clopidogrel reactivity

High on-aspirin reactivity

80% нова натоварваща доза clopidogrel преди PCI  
77% GP IIb/IIIa по време на PCI

# Оптимизиране при проследяване



43% повишаване дозата на clopidogrel  
17% prasugrel MD

# Ограничения на ARCTIC

- Само 25% от пациентите са с ОКС
- Оптимизиране – 17% prasugrel при НТТР на фона на лечение с клопидогрел

## Дизайн

- Оценка на отговора към клопидогрел
- Фокусирано върху НТТР/ превенция на исхемичните усложнения



**Тромбоцитна реактивност за**  
· Ниско ризикова  
**мониторирани за ефикасност**  
PCI/стабилни  
**– резистентност**  
пациенти  
· Високо ризикова  
PCI/ОКС

## Comparison of Prasugrel and Ticagrelor Loading Doses in ST-Segment Elevation Myocardial Infarction Patients

RAPID (Rapid Activity of Platelet Inhibitor Drugs) Primary PCI Study

Guido Parodi, MD, PhD, Renato Valenti, MD, Benedetta Bellandi, MD, Angela Migliorini, MD, Rossella Marcucci, MD, Vincenzo Comito, MD, Nazario Carrabba, MD, Alberto Santini, MD, Gian Franco Gensini, MD, Rosanna Abbate, MD, David Antoniucci, MD

Florence, Italy

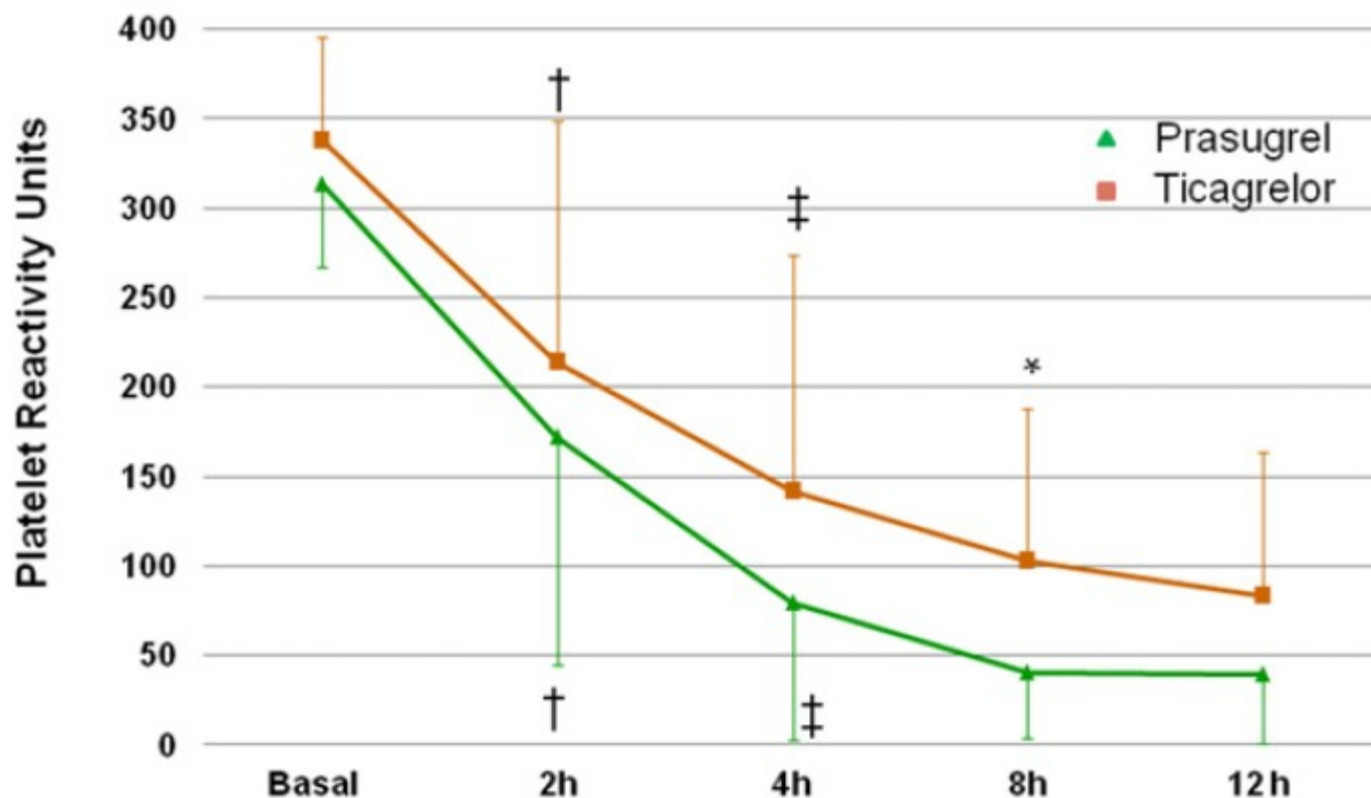
**Objectives** This study sought to compare the action of prasugrel and ticagrelor in ST-segment elevation myocardial infarction (STEMI) patients undergoing

**Background** It has been documented that platelet reactivity after loading dose (LD). However, the optimal loading dose is not provided by assessing only hea

**Methods** Fifty patients with STEMI undergoing primary PCI were randomized to receive prasugrel LD (n = 25) or 180 mg ticagrelor LD (n = 25) at baseline and 2, 4, 8, and 12 h

**Results** Platelet reactivity units (PRU) 2 h after the LD were significantly lower in the prasugrel group (305) in the prasugrel and ticagrelor groups (340). High residual platelet reactivity was observed in 10% of patients in the prasugrel group and 20% in the ticagrelor group. The mean time to achieve a PRU < 100 was 1.44 to 19.49; p = 0.012) and 1.44 to 19.49; p = 0.046).

**Conclusions** In patients with STEMI, prasugrel loading dose significantly reduced platelet reactivity 2 h after the LD in the majority of patients, and at least 4 h after the LD in half of patients. Morphine use is associated with higher platelet reactivity (MORPHINE in the Platelet Inhibitor Drugs Study, NCT01510171) (American College of Cardiology Foundation)



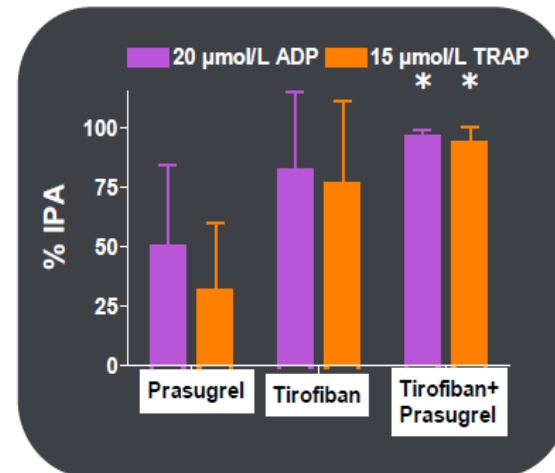
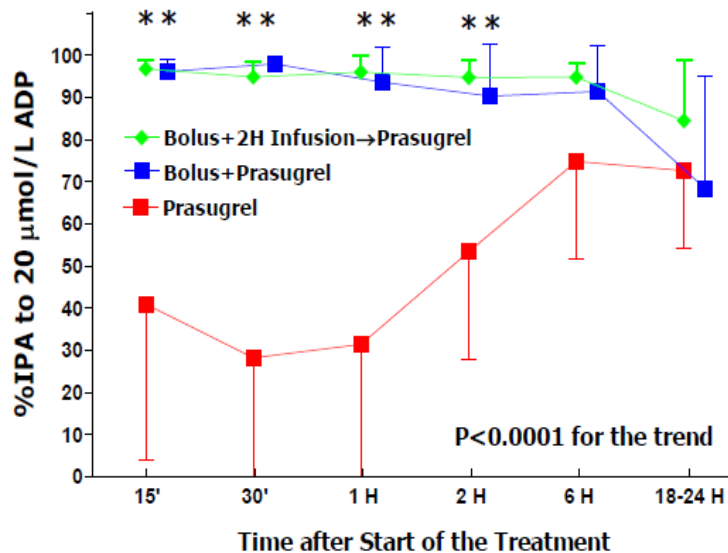
# Имаме ли нужда от интравенозни антиагреганти през 2013 год?

euro  
**PCR**  
2013

Do we still need i.v. anti-platelet Tx  
in 2013 ?

**ALL**  
you need  
to KNOW

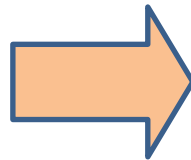
This question is relevant for our present (GPI) and future practice (Cangrelor)!



# Как да се оптимизира антиагрегантната терапия

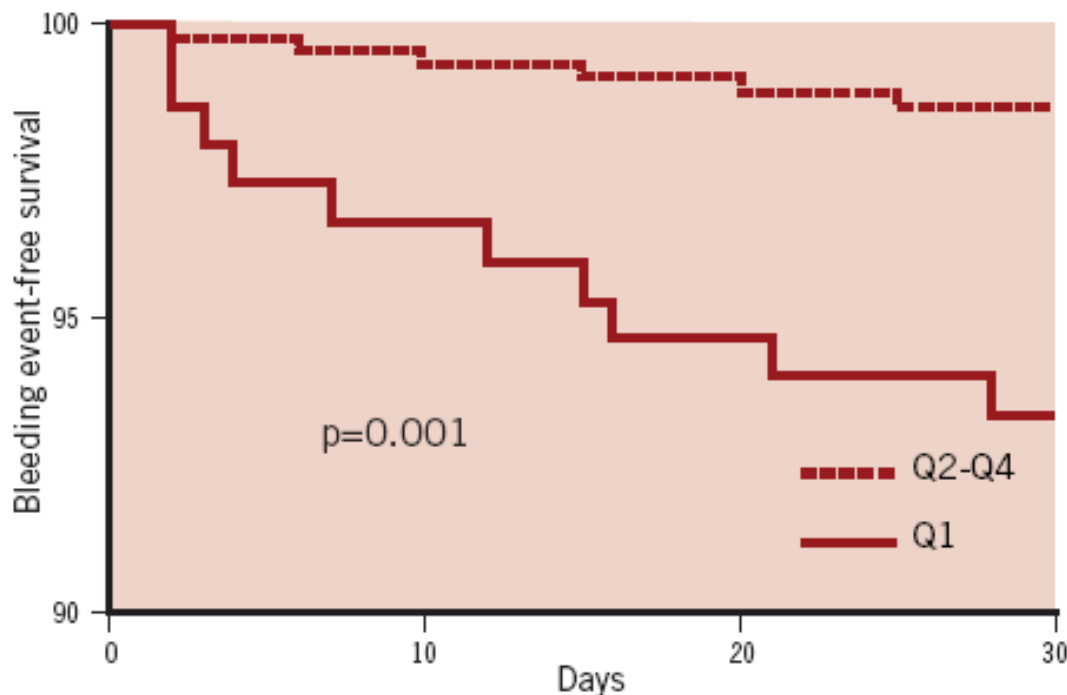
- Мониторирани за ефикасност –  
резистентност
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превенция на кървенето
- Намиране баланса ефикасност-  
безопасност

# **Промяна в парадигмата при мониториране**



# Тромбоцитна реактивност и кървене

597 NSTE ACS, clopidogrel 600 mg, Кървене след дехоспитализацията



Q1: Хиперреспондери,  
ADP-Ag < 40%  
ADP 10  $\mu\text{mol/L}$ , LTA

**Повишен отговор към клопидогрел → Висок риск от кървене**  
**HR 5.3, 95% CI 1.9 to 14.9; p < 0.01**

## ORIGINAL ARTICLE

## Bedside Monitoring to Adjust Antiplatelet Therapy for Coronary Stenting

Jean-Philippe Collet, M.D., Ph.D., Thomas Cuisset, M.D., Ph.D.,  
 Grégoire Rangé, M.D., Guillaume Cayla, M.D., Ph.D., Simon Elhadad, M.D.,  
 Christophe Pouillot, M.D., Patrick Henry, M.D., Ph.D., Pascal Motreff, M.D., Ph.D.,  
 Didier Carrié, M.D., Ziad Boueri, M.D., Ph.D., Loïc Belle, M.D.,  
 Eric Van Belle, M.D., Ph.D., Hélène Rousseau, Ph.D., Pierre Aubry, M.D.,  
 Jacques Monségu, M.D., Pierre Sabouret, M.D., Stephen A. O'Connor, M.B., B.Ch.,  
 Jérémie Abtan, M.D., Mathieu Kerneis, M.D., Christophe Saint-Etienne, M.D.,  
 Olivier Barthélémy, M.D., Farzin Beygui, M.D., Ph.D., Johanne Silvain, M.D., Ph.D.,  
 Eric Vicaut M.D., Ph.D., and Gilles Montalescot, M.D., Ph.D.,  
 for the ARCTIC Investigators\*

**Table 3. Study End Points at 1 Year of Follow-up.\***

End Point	Conventional Treatment (N=1227)	Monitoring (N=1213)	Hazard Ratio (95% CI)	P Value
Bleeding				
Major bleeding	40 (3.3)	28 (2.3)	0.70 (0.43–1.14)	0.15
Minor bleeding	21 (1.7)	12 (1.0)	0.57 (0.28–1.16)	0.12
Major or minor bleeding	55 (4.5)	38 (3.1)	0.69 (0.46–1.05)	0.08

98 пациента

Clopidogrel  
60 (61,2%)

Ticagrelor  
29 (29,6%)

Prasugrel  
9 (9,2%)

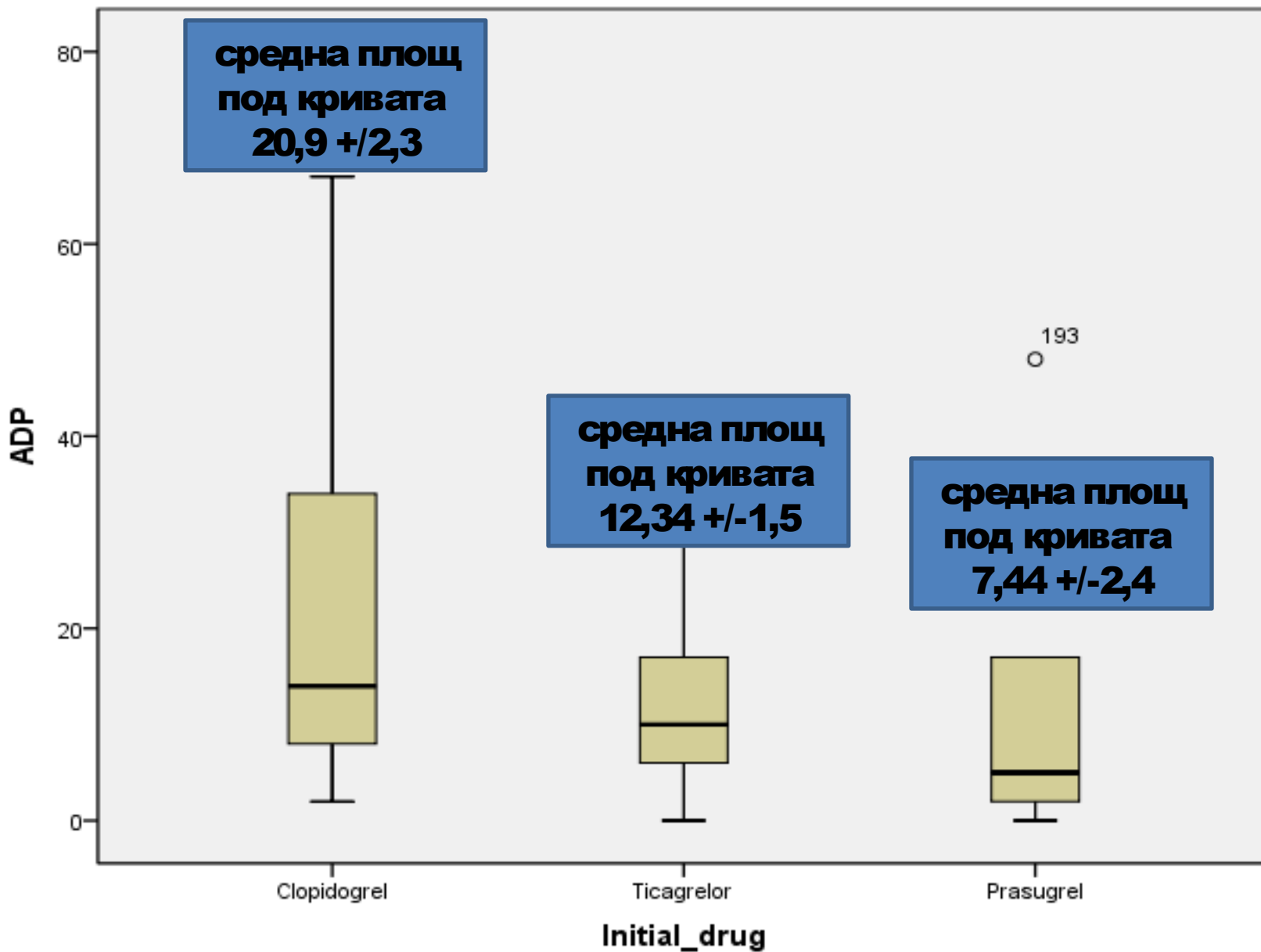
**PCI**

24-48  
ч.

ADP тест за тромбоцитна

реактивност  
Д-р Н. Стоянов, УМБАЛ Света Анна, София, Собствени резултати





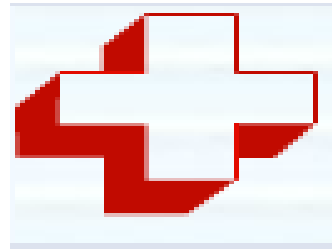
# Результати

9%

60 пацієнта

29 пацієнта

9 пацієнта



## Clinical Implications of Very Low On-Treatment Platelet Reactivity in Patients Treated With Thienopyridine

### The POBA Study (Predictor of Bleedings With Antiplatelet Drugs)

Thomas Cuisset, MD, PhD,\*†‡ Charlotte Grosdidier, PhD,†‡§  
Anderson Diendoné Loundou, PhD,|| Jacques Quilici, MD,\*†‡ Marie Loosveld, MD,†‡§  
Laurence Camoin, PhD,†§ Mathieu Pankert, MD,\*† Shirley Beguin, PhD,¶  
Marc Lambert, MD,\*†‡ Pierre Emmanuel Morange, MD, PhD,†‡§  
Jean-Louis Bonnet, MD,\*†‡ Marie-Christine Alessi, MD, PhD†‡§

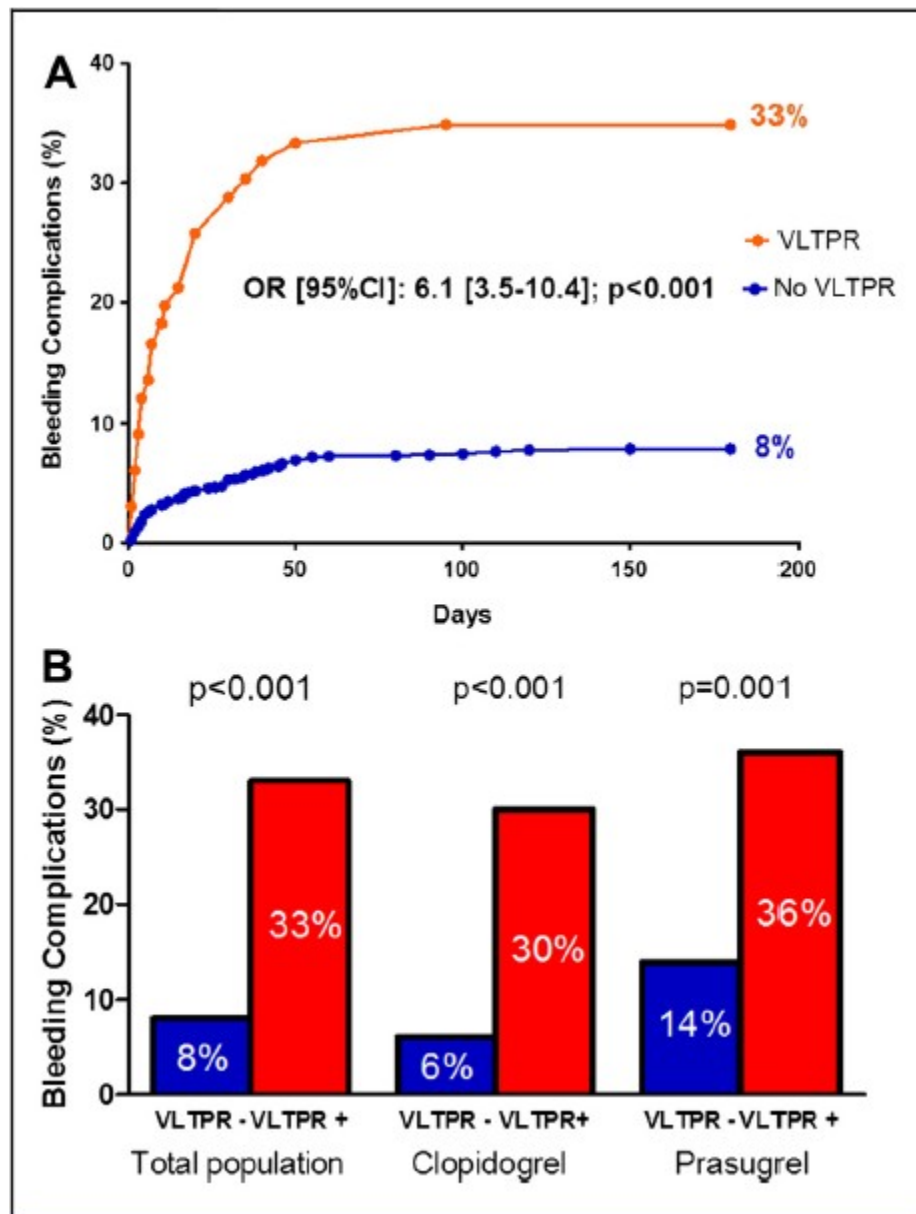
Marseille, France

**Objectives** This study was designed to define the hyperresponse to thienopyridine (very low on-treatment platelet reactivity [VLTPR]) as the most predictive threshold value of platelet reactivity index vasodilator-stimulated phosphoprotein (PRI VASP) for the prediction of non-access site-related bleeding events. We also aimed to identify predictors of bleeding and VLTPR in patients treated with thienopyridines.

**Background** New P2Y<sub>12</sub> blockers and platelet monitoring has been proposed to optimize platelet inhibition after acute coronary syndromes and improve ischemic outcomes. However, bleeding complications remain the Achilles' heel of antiplatelet therapy, and platelet monitoring could be useful to evaluate this risk.

**Methods** A total of 1,542 consecutive patients undergoing coronary stenting for ACS were included in the present study (287 taking clopidogrel 75 mg, 868 taking clopidogrel 150 mg, and 387 taking prasugrel 10 mg).

**Results** During 6-month follow-up, 9% of patients (n = 139) experienced nonaccess site-related Bleeding Academic Research Consortium bleeding complications. These patients were more often women and nondiabetic and had lower PRI VASP values than others (p < 0.001). Receiver-operating characteristic curve analysis (0.71, p < 0.01) identified a threshold value for VLTPR of PRI VASP ≤ 10% to predict bleeding events with a sensitivity of 17% and a specificity of 97%. Although prasugrel was the main predictor of VLTPR in the whole population (odds ratio: 10.2, 95% confidence interval: 3.0 to -34.2; p < 0.001), VLTPR was the strongest and independent predictor of bleeding (odds ratio: 4.7, 95% confidence interval: 2.7 to 8.3; p < 0.001).



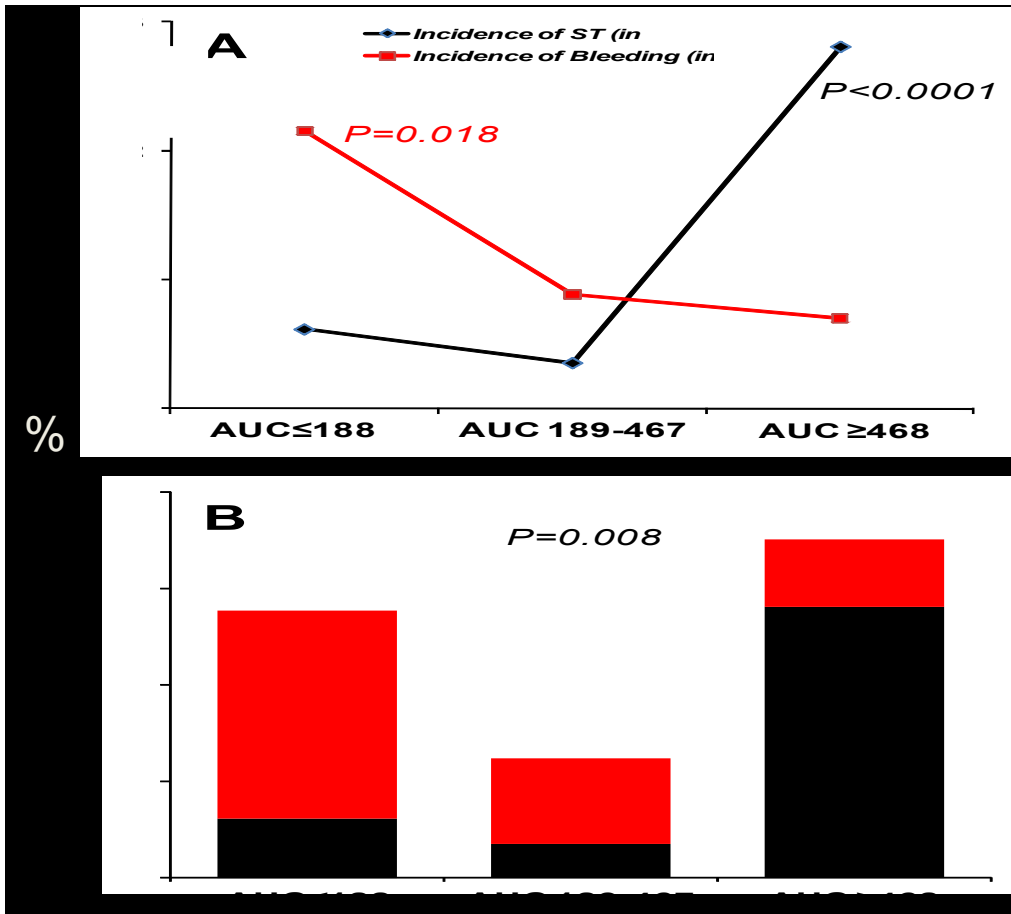
# Как да се оптимизира антиагрегантната терапия

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безопасност

# “Терапевтичен прозорец” на

антиагрегантния ефект

2533 пациенти след PCI (след 30 дни след clopidogrel LD)  
Тромбоцитната функция - Multiplate analyzer



Стент тромбоза:

n=22 – в рамките 30 дни

- 16 дефинитивна
- 6 възможна

Кървене:

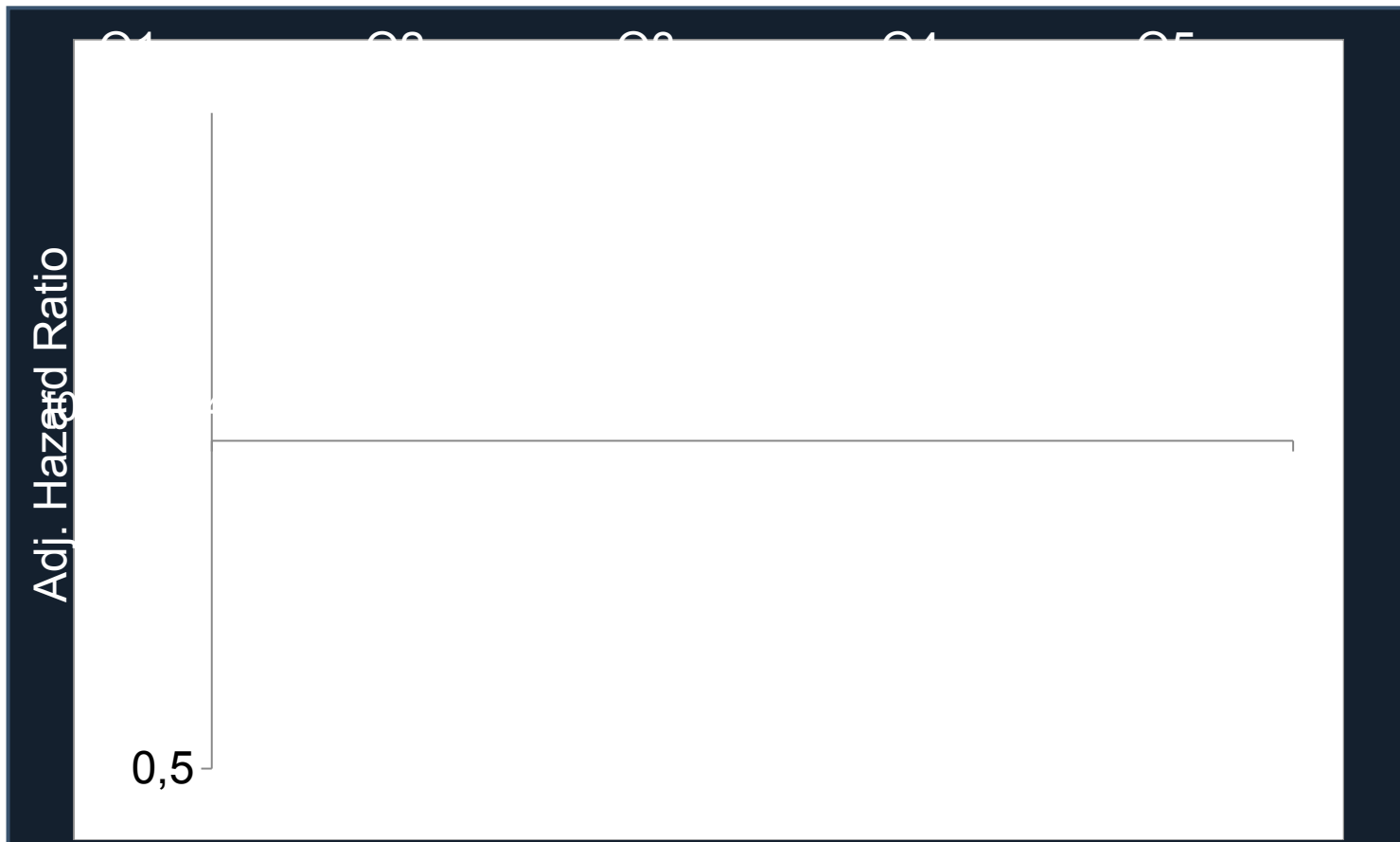
n=34 (вътреболнично)

- TIMI голямо кървене

# ADAPT DES – Едногодишен анализ

**ST:**

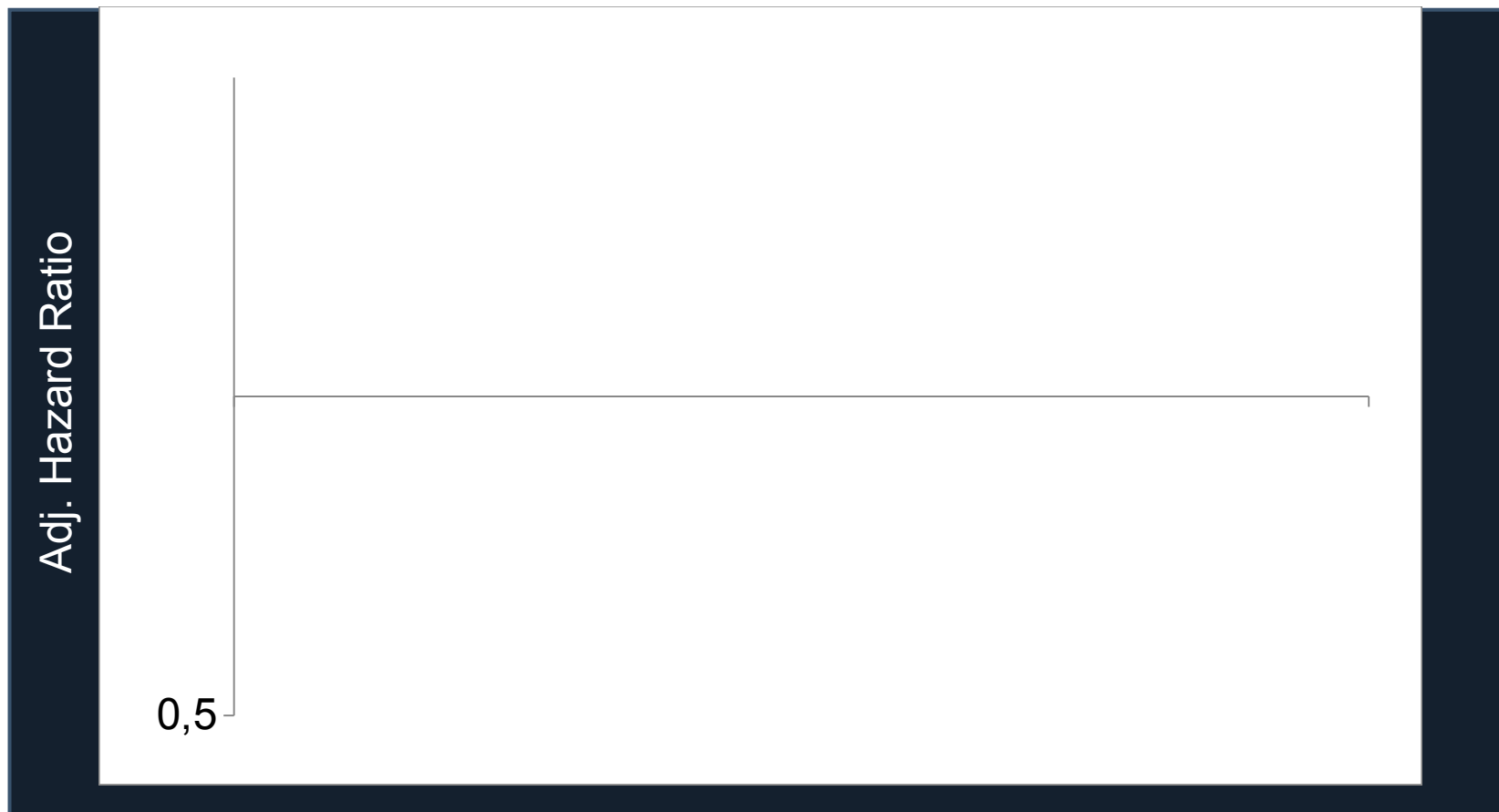
8,449 пациенти след PCI оценени с VerifyNow PRU  
след НД клопидогрел



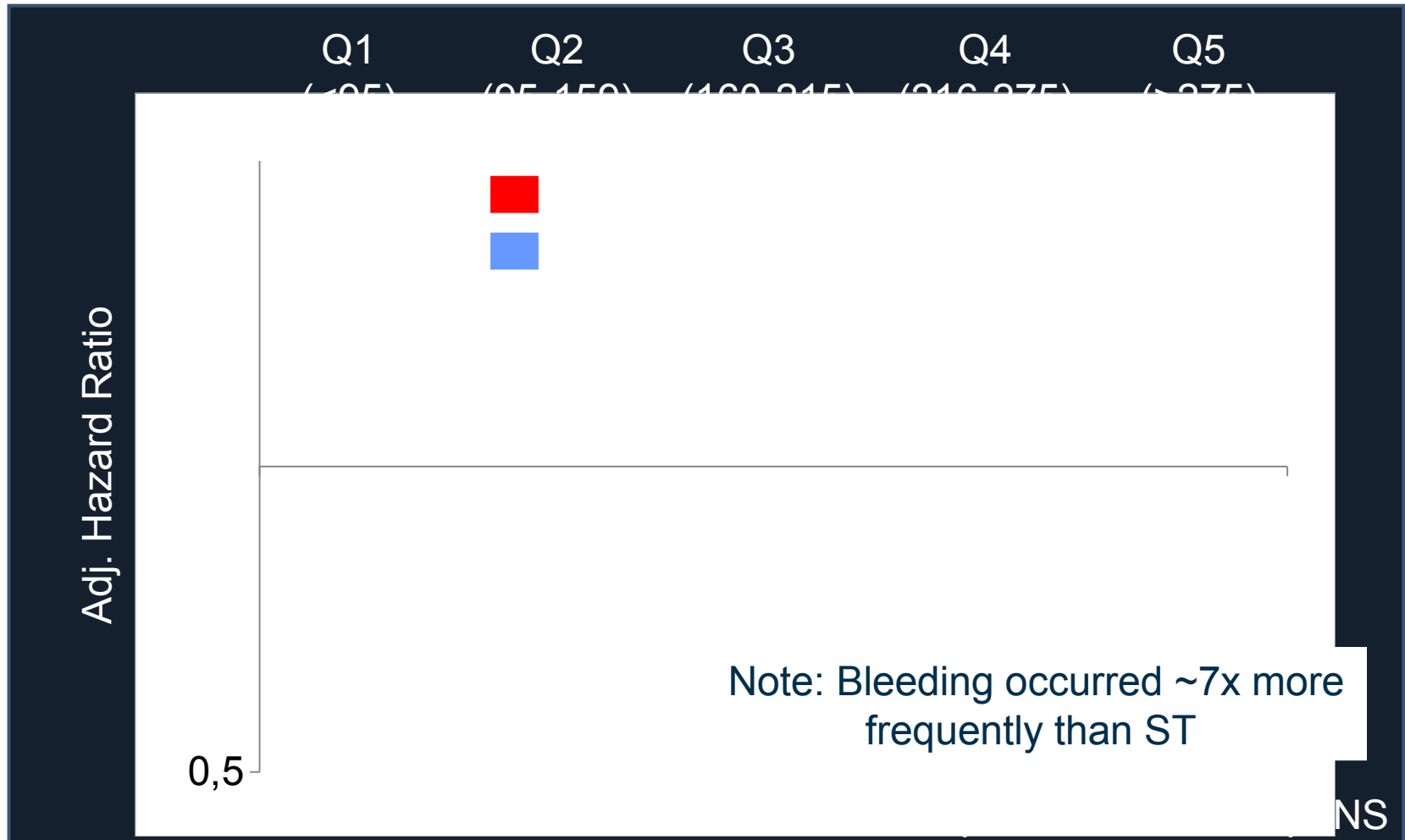
# ADAPT DES – Едногодишен анализ

## голямо кървене:

8,449 пациенти след PCI оценени с VerifyNow PRU  
след НД клопидогрел

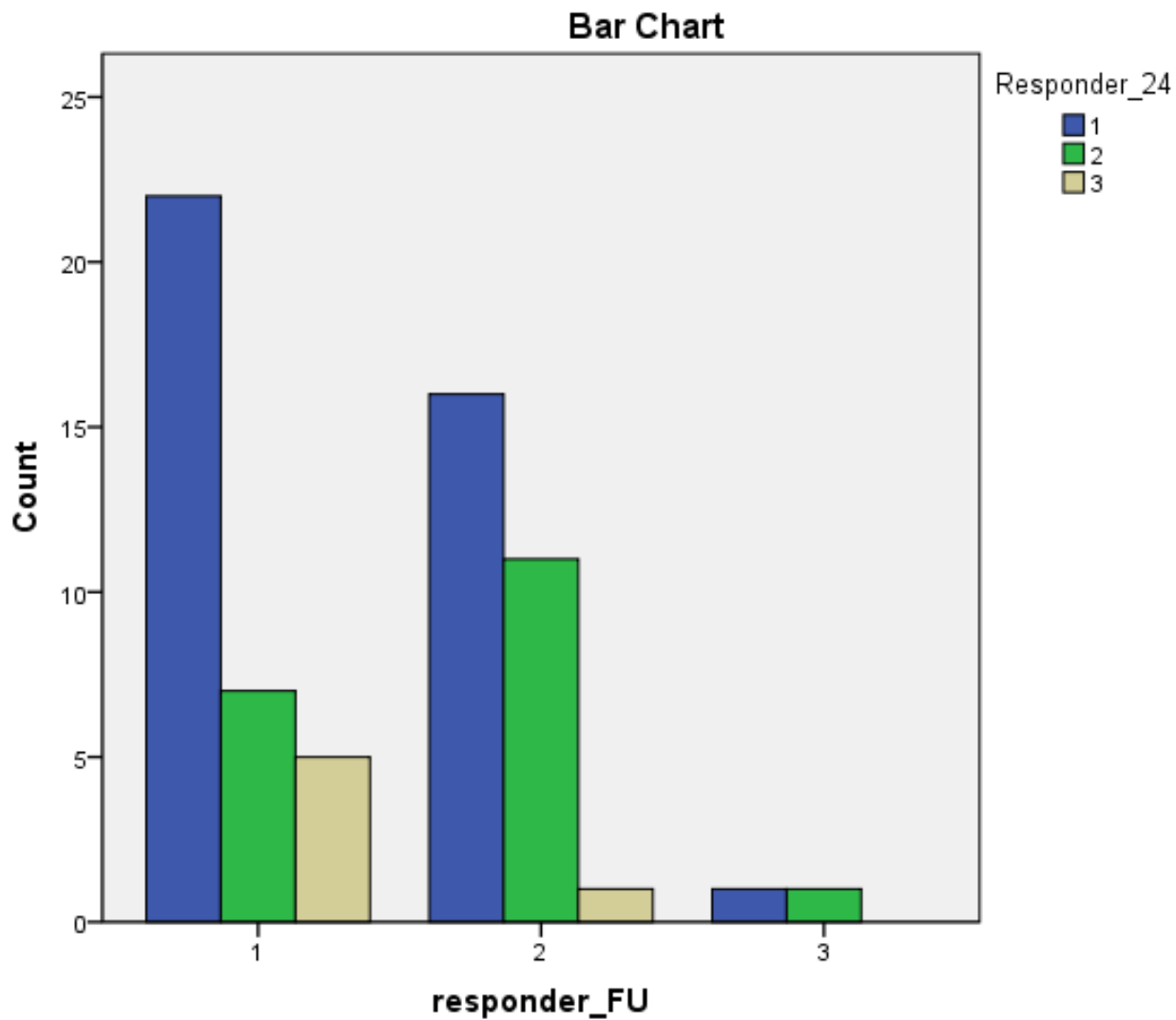


# ADAPT DES – Едногодишен анализ ST и голямо кървене





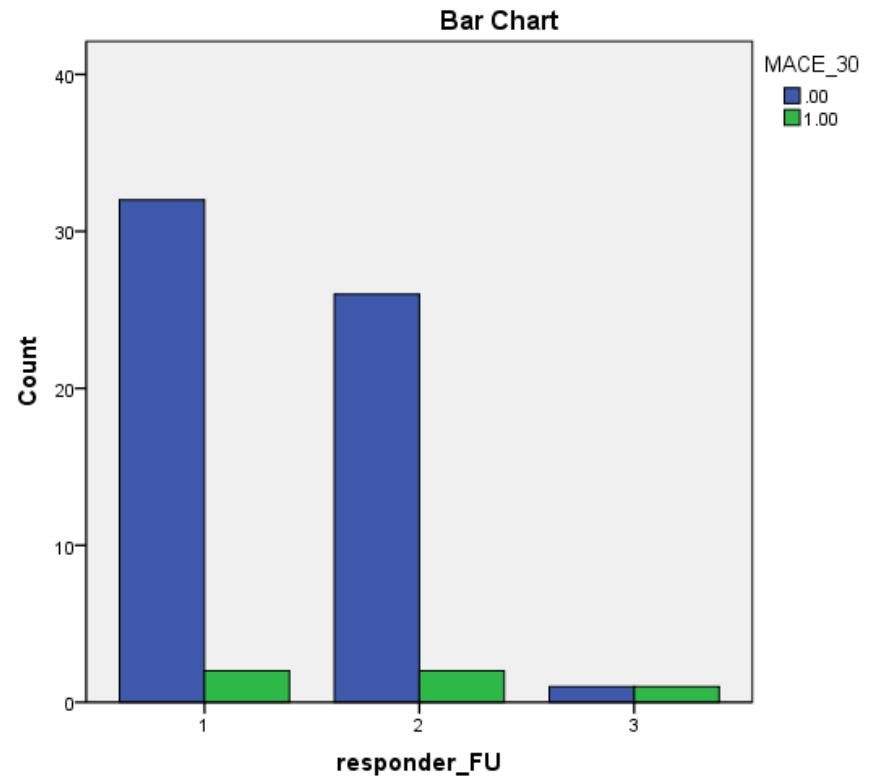
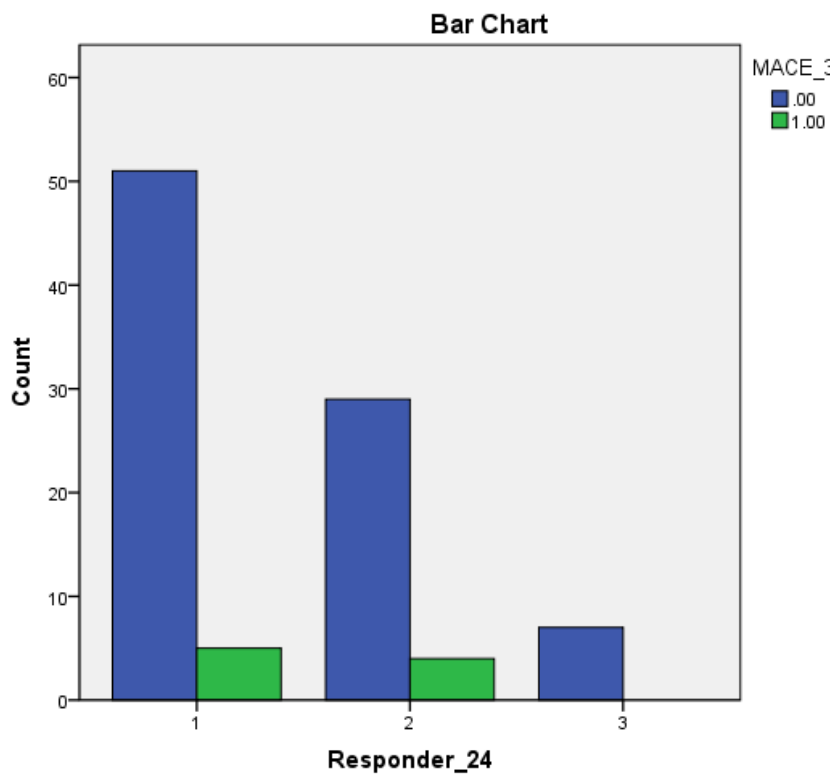
# Промяна в отговора до 30 ден



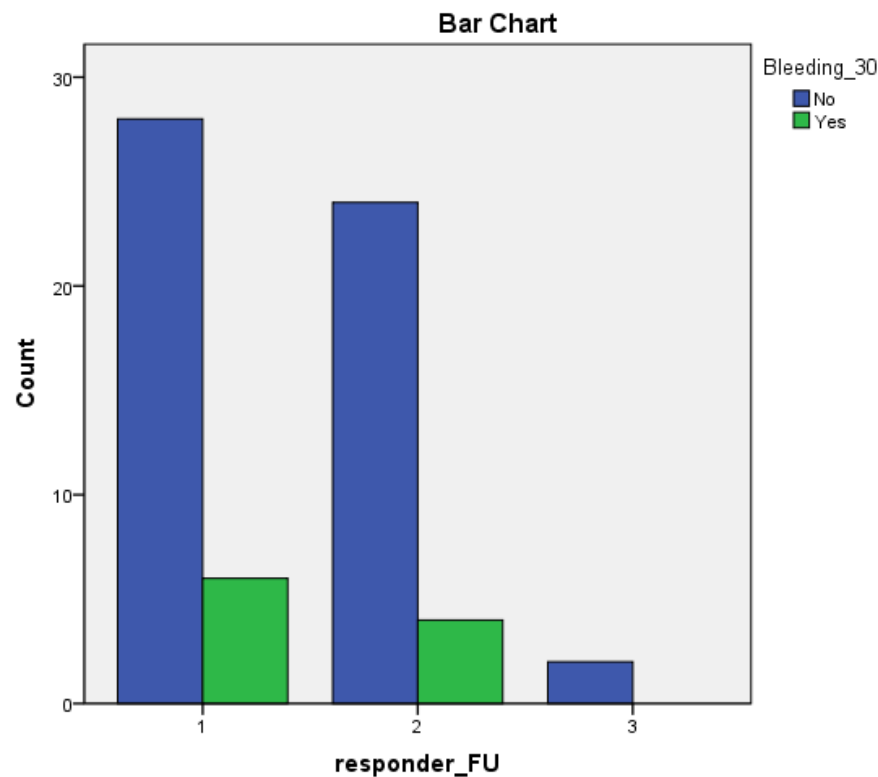
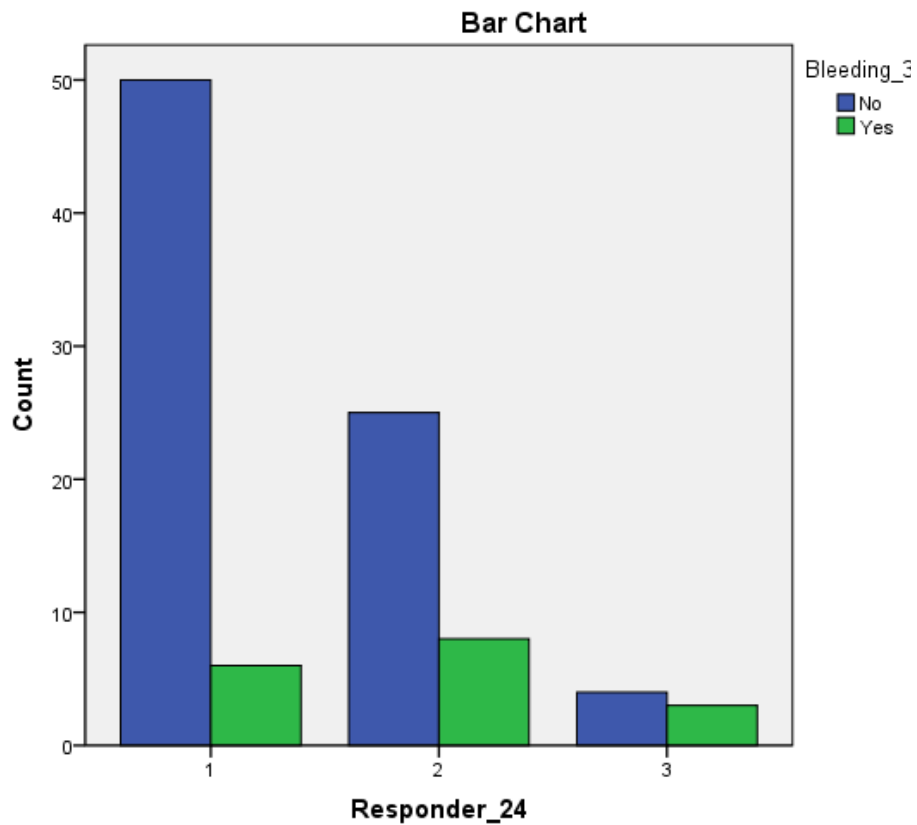
# Инциденти в хода на проследяването

Събития	Брой	Процент
СС смърт	2	2.2
Миокарден	2	2.2
ST	1	1.1
MACE	9	9,4
Кървене	9	9.4

# МАСЕ при пациенти в отделни групи отговор към терапията



# Кървене при пациенти в отделни групи отговор към терапията



# Резултати след корекция в групата на хиперреспондерите

	Хиперреспондери	Sweet point	Нонреспондери	Общо
Clopidogrel	9	11	1	21
Ticagrelor	9	2	0	11
Prasugrel	3	3	0	6
Общо	21	16	1	38

# Резултати след корекция в групата на sweet point

	Хиперреспондери	Sweet point	Нонреспондери	Total
Clopidogrel	5	4	1	10
Ticagrelor	1	6	0	7
Prasugrel	1	1	0	2
Total	7	11	1	19



A.Colombo  
Operator techniques to  
reduce stent thrombosis

**The stool stands only if each leg is solid: one leg with extra strength does not compensate for the broken one**

- **Lumen Leg:** optimal MLD
- **Run off leg:** TIMI 3 flow
- **Blood leg:** optimal antiplatelet therapy

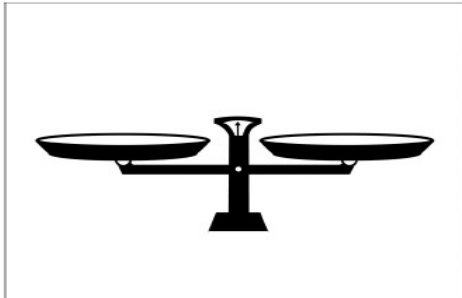
# Антиагрегантната терапия винаги е индивидуализирана – избор на медикамент и продължителност на терапията


Cuisset\_keynote.pdf (SECURED) - Adobe Reader  
File Edit View Window Help  
5 / 30 77.6% Tools Sign Comment

**Assistance Publique Hôpitaux de Marseille** **PÔLE CARDIO-VASCULAIRE ET THORACIQUE**

## Antiplatelet Therapy always Individualized !!

**Исхемичен риск**  Ischemic Risk

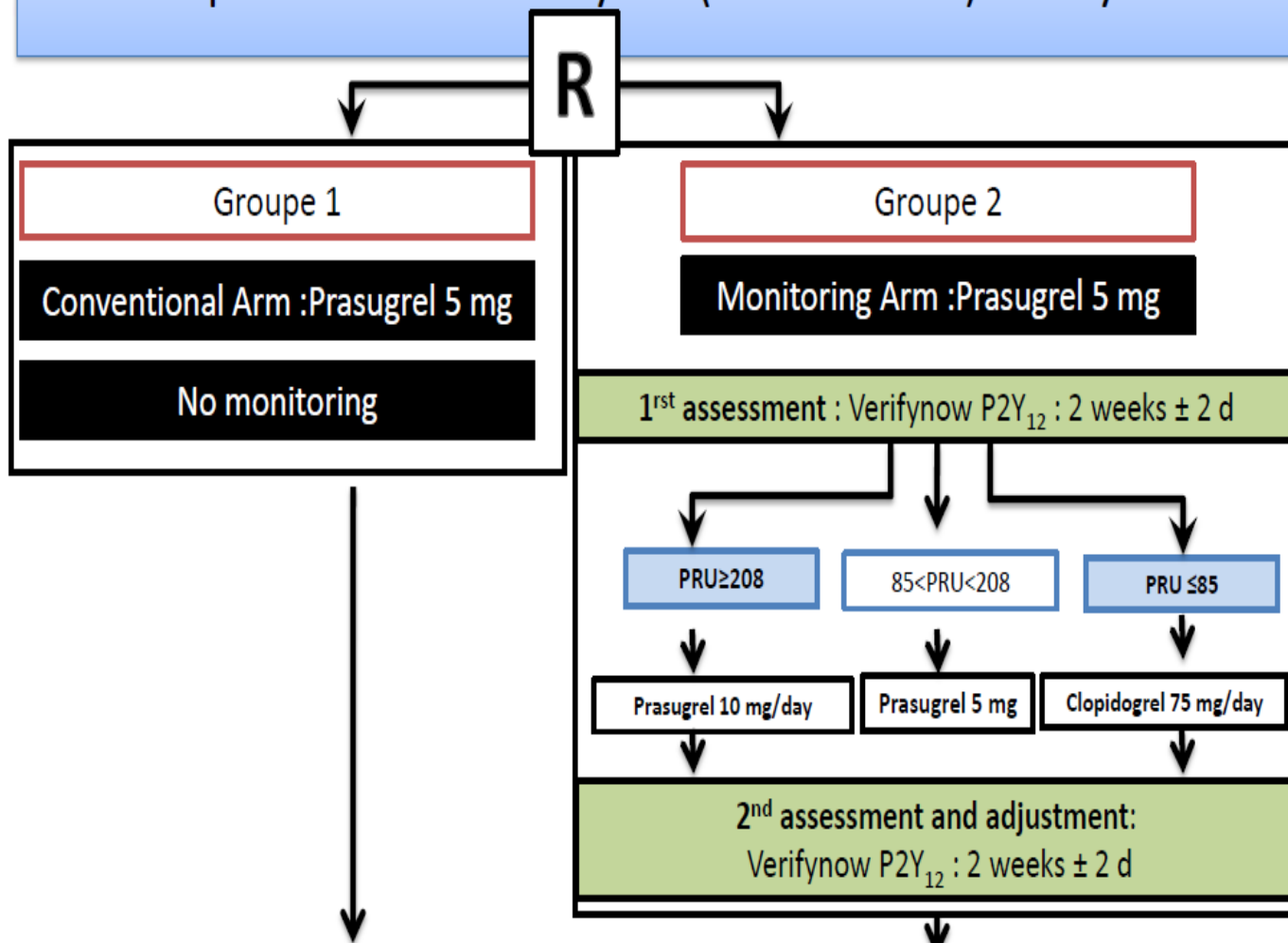


**Хеморагичен риск**  Bleeding Risk

### Impact Drug Choice / Therapy Duration



ACS patients treated by PCI(BMS or DES)  $\geq 75$  years



**Assessment of the primary end point (net clinical benefit) over 12 months**  
Bleeding type 2,3,5 of the BARC definition *and*  
MACE : CV death, MI, urgent revascularisation, stent thrombosis, stroke



# PRU-MATRIX

NCT01433627

High-risk NSTEMI or STEMI who underwent PCI  
After-PCI and Before Discharge



**Customized DAPT  
Selection**

**Liberal DAPT  
selection**

Platelet function testing with VerifyNow P2Y12 Assay



Dose and type of P2Y12 i  
adjudged based on PRUs



Clopidogrel  
Prasugrel  
Ticagrelor