ОКС и трудни ситуации в ежедневната практика

ОКС и Захарен диабет

Доц. Д Трендафилова
СБАЛССЗ " Св. Екатерина"

Дефиниция за подходяща коронарна реваскуларизация

Коронарната реваскуларизация е **подходяща**, когато очакваните ползи като преживяемост или здравен статус (симптоматика,функционално състояние и/или качество на живот) надвишават очакваните негативни последствия от процедурата.

Клас индикация

- Appropriate (7-9):

Процедурата е всеобщо приета и е разумен подход като индикация

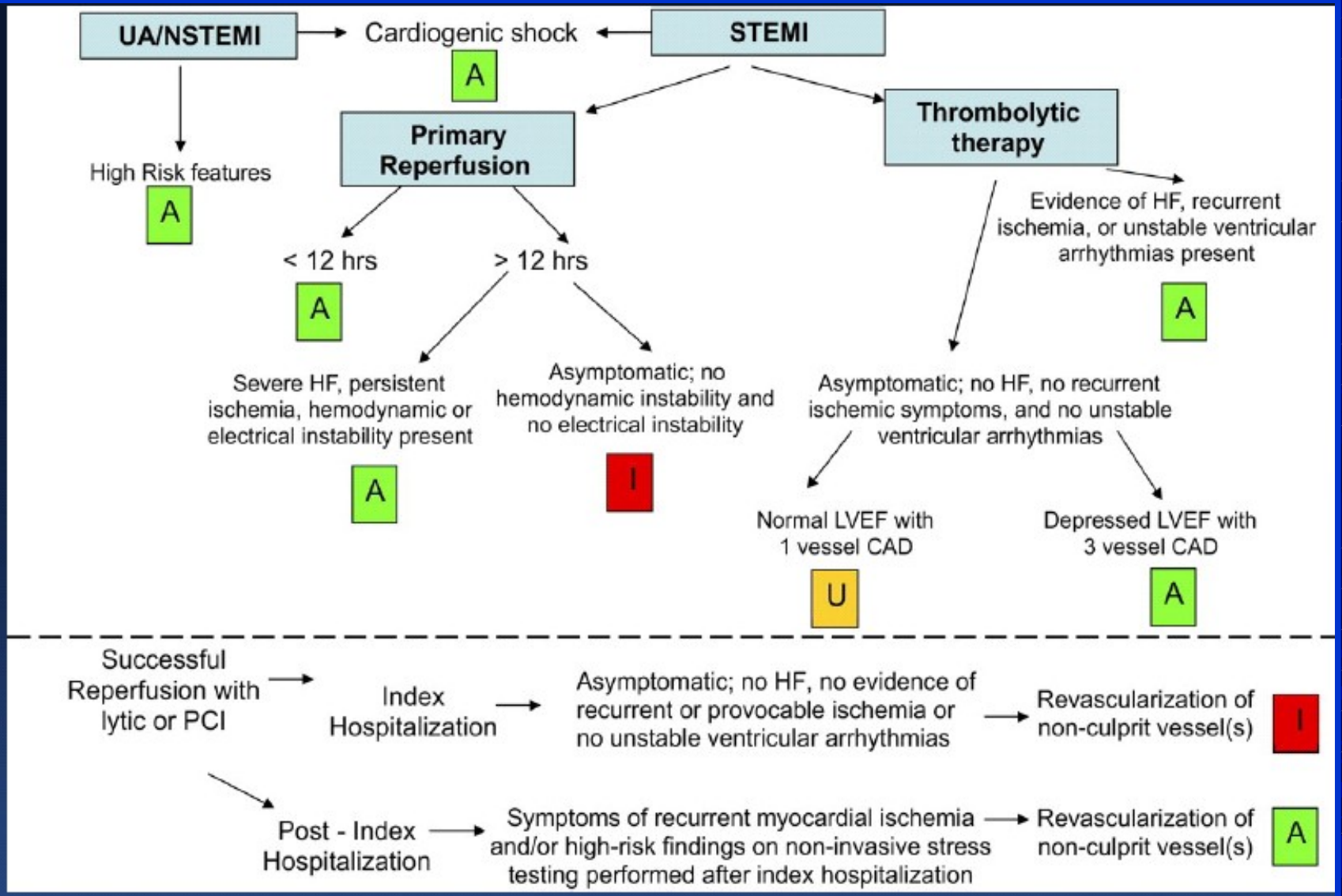
- Uncertain (4-6):

Процедурата може да е приемлива и може да бъде разумен подход като индикация

- Inappropriate (1-3):

Процедурата не е всеобщо приета и не е разумен подход като индикация

Остър коронарен синдром



Развитие – ACS и STEMI

2013

- **ACS**
  - New Guidelines
  - Diagnostic/prognostic testing
  - Antiplatelet Therapy
  - Anti Thrombin Therapy
  - Special groups
- **STEMI**
  - New Guidelines
  - Access to Care
  - Optimal Therapy
  - Special groups

2012 Updated Guidelines

2013

PRACTICE GUIDELINE

2012 ACCF/AHA Focused Update of the Guideline for the Management of Patients With Unstable Angina/ Non–ST-Elevation Myocardial Infarction (Updating the 2007 Guideline and Replacing the 2011 Focused Update)

A Report of the American College of Cardiology Foundation/ American Heart Association Task Force on Practice Guidelines

Developed in Collaboration With the American College of Emergency Physicians, Society for Cardiovascular Angiography and Interventions, and Society of Thoracic Surgeons

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European Heart Journal (2012) 33, 2569–2619
doi:10.1093/eurheartj/ehs215

ESC GUIDELINES

ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation

The Task Force on the management of ST-segment elevation acute myocardial infarction of the European Society of Cardiology

Authors/Task Force Members: Ph. Gabriel Steg (Chairperson) (France)*, Stefan K. James (Chairperson) (Sweden)*, Dan Atar (Norway), Luigi P. Badano (Italy), Carina Blomstrom Lundqvist (Sweden), Michael A. Borger (Germany), Carlo Di Mario (United Kingdom), Kenneth Dickstein (Norway), Gregory Ducrocq (France), Francisco Fernandez-Aviles (Spain), Anthony H. Gershlick (United Kingdom), Pantaleo Giannuzzi (Italy), Sigrun Halvorsen (Norway), Kurt Huber (Austria), Peter Juni (Switzerland), Adnan Kastrati (Germany), Juhani Knuuti (Finland), Mattie J. Lenzen (Netherlands), Kenneth W. Mahaffey (USA), Marco Valgimigli (Italy), Arnoud van't Hof (Netherlands), Petr Widimsky (Czech Republic), Doron Zahger (Israel).

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www.escardio.org/guidelines

European Heart Journal (2012) 33, 2569–2619
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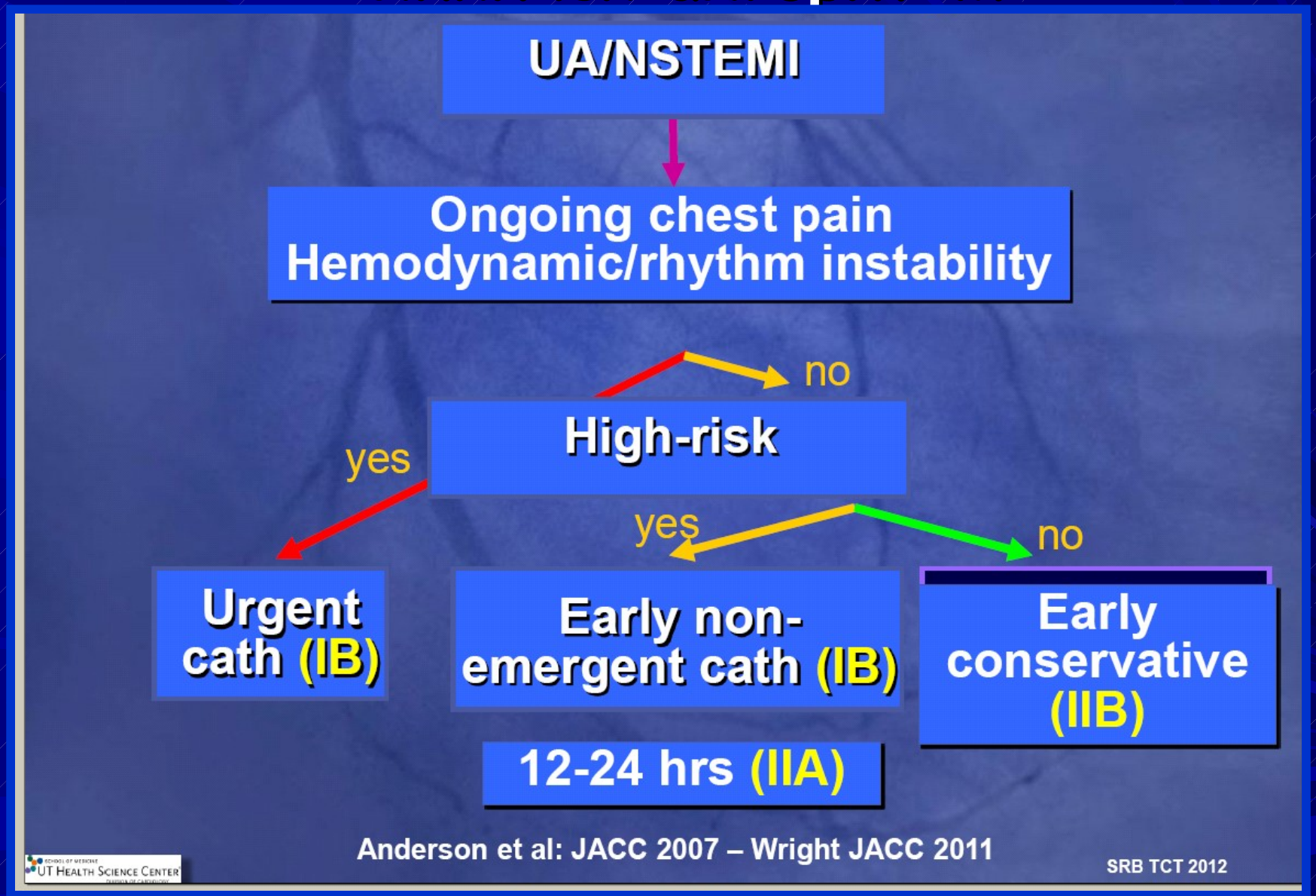
Клиничен алгоритъм



2012 US Updated Guidelines ACCF/AHA Focused Update

- Новите препоръки включват Ticagrelor(Brilinta, Astra Zeneca) и Prasugrel (Effient, Lilly) като терапевтична опция в допълнение с Clopidogrel.
- Pts, подложени на инвазивна процедура трябва да получават двойна антитромбоцитна Th - aspirin и друг антитромботичен медикамент.
- Pts, подложени само на медикаментозно лечение трябва да получават Aspirin и Clopidogrel или Ticagrelor за 12 месеца.
- Aspirin - 81 мг дневна поддържаща доза се предпочита пред по-високите дневни дози.
- При хоспитализирани пациенти с НАП или NSTEMI се препоръчва инсулинов режим за достигане на дневни нива на кр. захар под 180 mg/dl и избягване на хипогликемия.

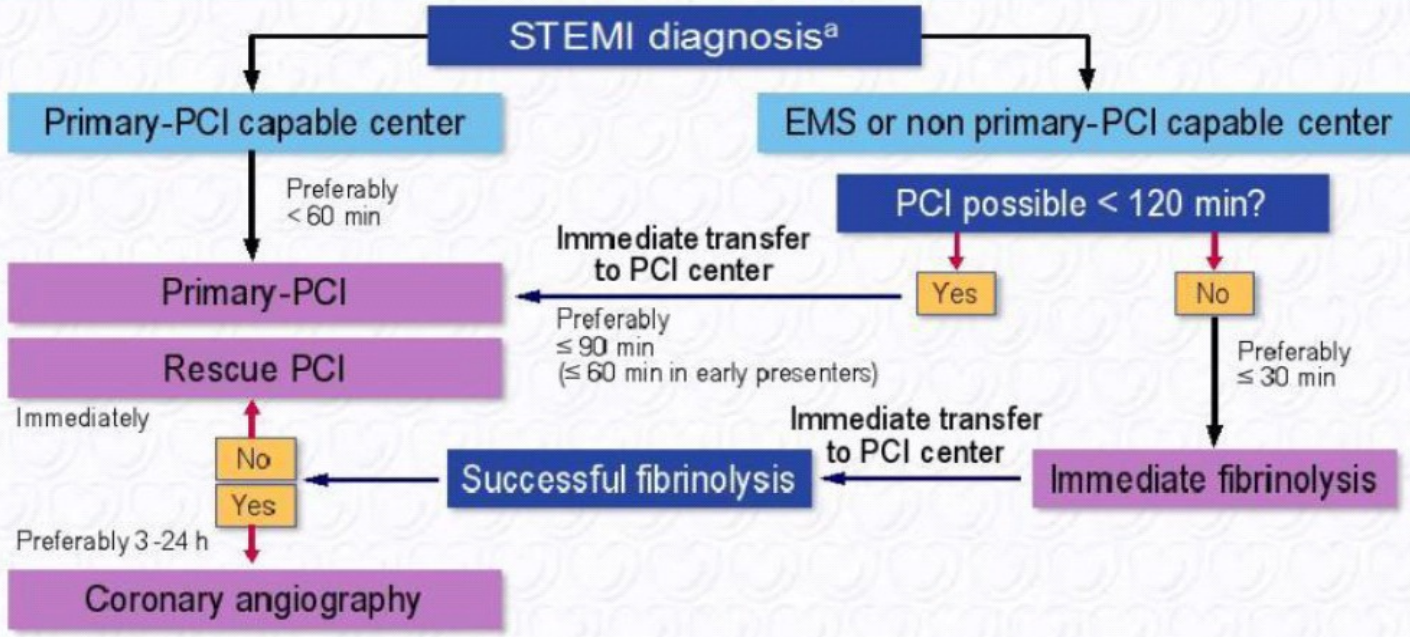
2012 US Updated Guidelines ACCF/AHA Focused Update

- Инвазивната стратегия е разумна при лека (2) и умерена (3) ст. ХБН

  Има недостатъчни данни за ползата и риска от инвазивната стратегия при Pts с НАП или NSTEMI и напреднала (4-5) степен ХБН
- Разумно е да се пристъпи към сърдечна катетеризация и възможна реваскуларизация в първите 12-24 ч от приема при първоначално стабилизирани с висок риск pts с НАП или NSEMI
- Тестове за изследване на тромбоцитната ф-ция може да бъде обсъждана при селектирана група pts с НАП или NSEMI , които са на лечение с P2Y12 рецепторни антагонисти и когато резултатите от тестовете могат да променят лечението.

STEMI - Терапевтичен алгоритъм

Prehospital and in-hospital management, and reperfusion strategies within 24 h of FMC



[a] The time point the diagnosis is confirmed with patient history and ECG ideally within 10 min from the first medical contact (FMC). All delays are related to FMC (first medical contact).

Cath = catheterization laboratory; EMS = emergency medical system; FMC = first medical contact; PCI = percutaneous coronary intervention; STEMI = ST-segment elevation myocardial infarction.

European Heart Journal (2012) 33, 2569–2619
doi:10.1093/eurheartj/ehs215

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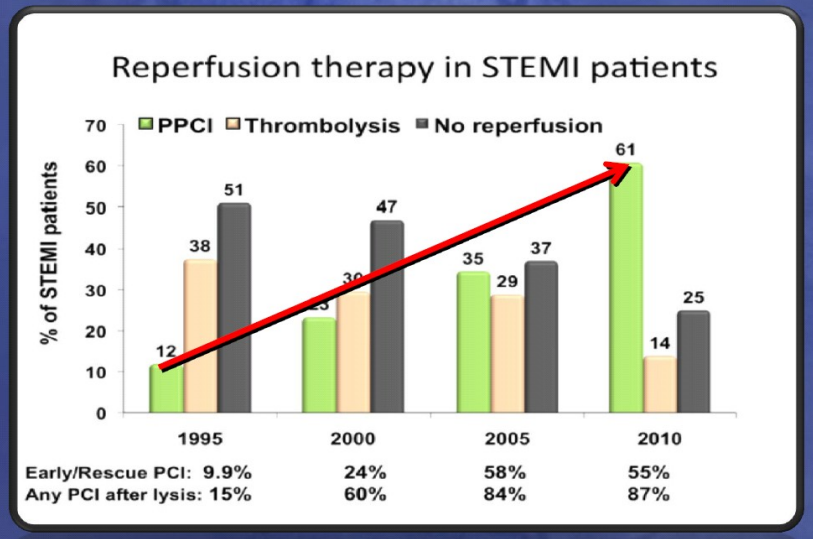
Реперфузионна терапия- прогноза

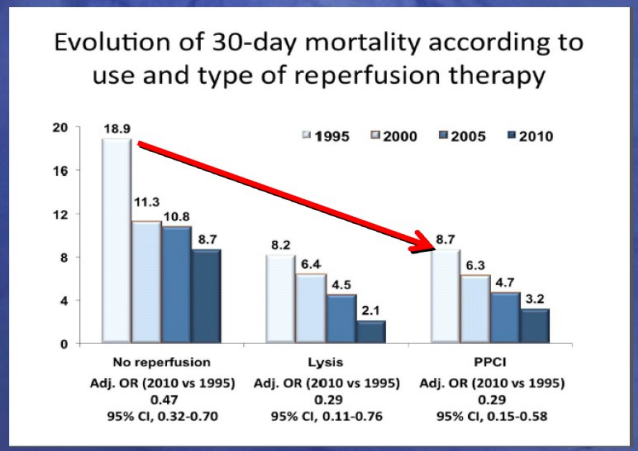
Impact of STEMI Care on Patient Outcomes



Puymirat *JAMA*. 2012;308(10):1-8. doi:10.1001/2012.jama.11348

SRB TCT 2

Impact of STEMI Care on Patient Outcomes



Puymirat *JAMA*. 2012;308(10):1-8. doi:10.1001/2012.jama.11348

SRB TCT 2012

Реперфузионна терапия- прогноза

ST-Segment Resolution as a Predictor of Death and MACE after Primary PCI in STEMI: The HORIZONS-AMI Trial

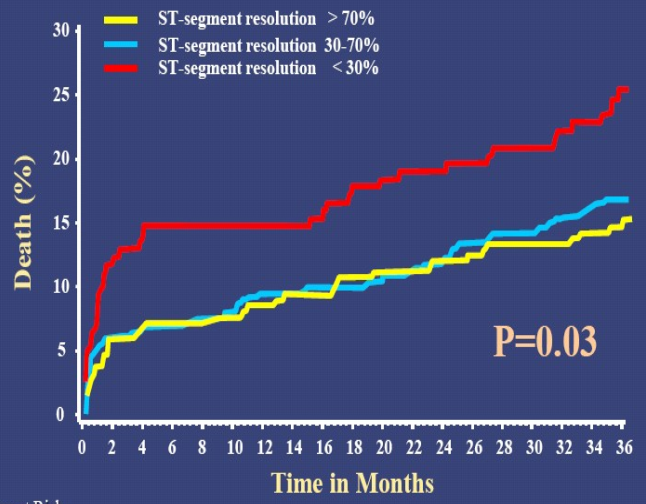
2,484 pts with interpretable baseline and 60-minute post-PCI ECGs

ST resolution at 60'

Complete (>70%)
1,258 (50.5%)

Partial (30%-70%)
712 (28.7%)

Absent (<30%)
514 (20.7%)



Number at Risk

>70%	1258	1213	1203	1188	1173	1167	1154	1129	1119	744
30-70%	712	690	682	678	669	665	659	645	641	445
<30%	514	484	483	480	465	461	457	445	443	327

Farkouh ME et al from Stone 2012.

SRB TCT 2012

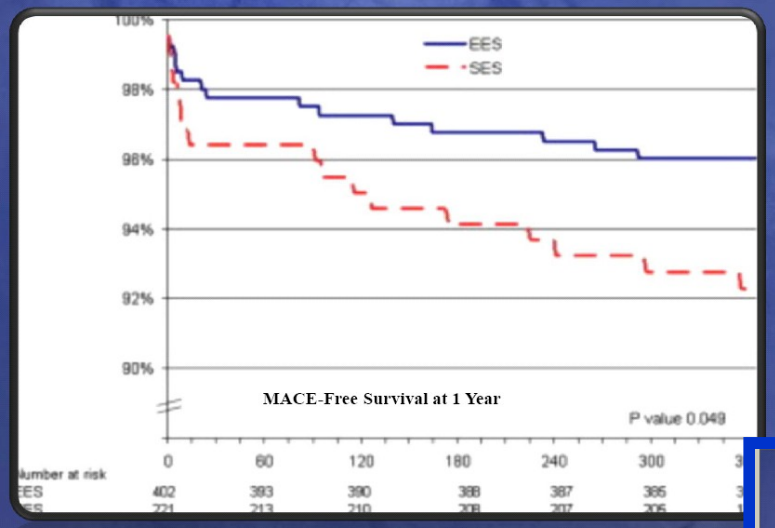
Подобряване на времената

Pain to balloon time

Door to balloon time

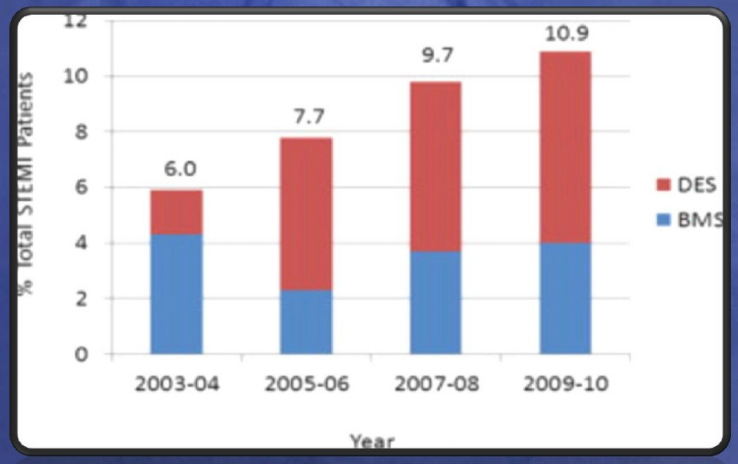
Реперфузионна терапия- прогноза

STEMI Outcomes Impact of Stent Design



J Am Coll Cardiol. 2012;60(5):381-387. doi:10.1016/j.jacc.2012.01.073

STEMI Due to Stent Thrombosis: Increasing in High-Risk Patients



Frequency of STEMI Resulting From Stent Thrombosis as a Percentage of all STEMI Patients Treated With Primary Percutaneous Coronary Intervention From 2003 Through 2010. **(n 2,086 pts)**

J Am Coll Cardiol. 2012;0:-. doi:10.1016/j.jacc.2012.07.043

SRB TCT 2012

2012 ESC Guidelines Focused Update

Important delays and treatment goals in the management of acute STEMI

Delay	Target
Preferred for FMC to ECG and diagnosis	**≤10 min**
Preferred for FMC to fibrinolysis ('FMC to needle')	**≤30 min**
Preferred for FMC to primary PCI ('door to balloon') in primary PCI hospitals	**≤60 min**
Preferred for FMC to primary PCI	**≤90 min** (≤60 min if early presenter with large area at risk)
Acceptable for primary PCI rather than fibrinolysis	**≤120 min** (≤90 min if early presenter with large area at risk) if this target cannot be met, consider fibrinolysis.

FMC = first medical contact; PCI = percutaneous coronary intervention.

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Procedural aspects of primary PCI

If performed by an experienced radial operator, radial access should be preferred over femoral access.	IIa	B
If the patient has no contraindications to prolonged DAPT (indication for oral anticoagulation, or estimated high longterm bleeding risk) and is likely to be compliant, DES should be preferred over BMS.	IIa	A
Routine thrombus aspiration should be considered.	IIa	B

BMS = bare-metal stent; DAPT = dual antiplatelet therapy; DES = drug-eluting stent; IABP = intra-aortic balloon pump

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2012 ESC Guidelines Focused Update

Cardiac arrest

Recommendations	Class[a]	Level[b]
All medical and paramedical personnel caring for a patient with suspected myocardial infarction must have access to defibrillation equipment and be trained in cardiac life support.	I	C
Therapeutic hypothermia is indicated early after resuscitation of cardiac arrest patients who are comatose or in deep sedation.	I	B
Immediate angiography with a view to primary PCI is recommended in patients with resuscitated cardiac arrest whose ECG shows STEMI.	I	B

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Oral Antiplatelet Therapy

Recommendations	Class[a]	Level[b]
Antiplatelet therapy		
Aspirin oral or i.v. (if unable to swallow) is recommended	I	B
An ADP-receptor blocker is recommended in addition to aspirin. Options are:	I	A
• Prasugrel in clopidogrel-naive patients, if no history of prior stroke/TIA, age <75 years.	I	B
• Ticagrelor.	I	B
• Clopidogrel, preferably when prasugrel or ticagrelor are either not available or contraindicated.	I	C

TCT2011

2012 ESC Guidelines Focused Update

Use of Glycoprotein IIb/IIIa Receptor Antagonists in STEMI

Modified Recommendation

It is reasonable to start treatment with glycoprotein IIb/IIIa receptor antagonists at the time of primary PCI (with or without stenting) in selected patients with STEMI:

I IIa IIb III
A

abciximab

I IIa IIb III
B

tirofiban and eptifibatide

ACC/AHA 2009 Joint STEMI/PCI Guidelines Focused Update

21

Anticoagulation in primary PCI

Anticoagulants		
Bivalirudin (with use of GP IIb/IIIa blocker restricted to bailout) is recommended over unfractionated heparin and a GP IIb/IIIa blocker.	I	B
Enoxaparin (with or without routine GP IIb/IIIa blocker) may be preferred over unfractionated heparin.	IIb	B
Unfractionated heparin with or without routine GP IIb/IIIa blocker must be used in patients not receiving bivalirudin or enoxaparin.	I	C
The use of fibrinolysis before planned primary PCI is not recommended.	III	A

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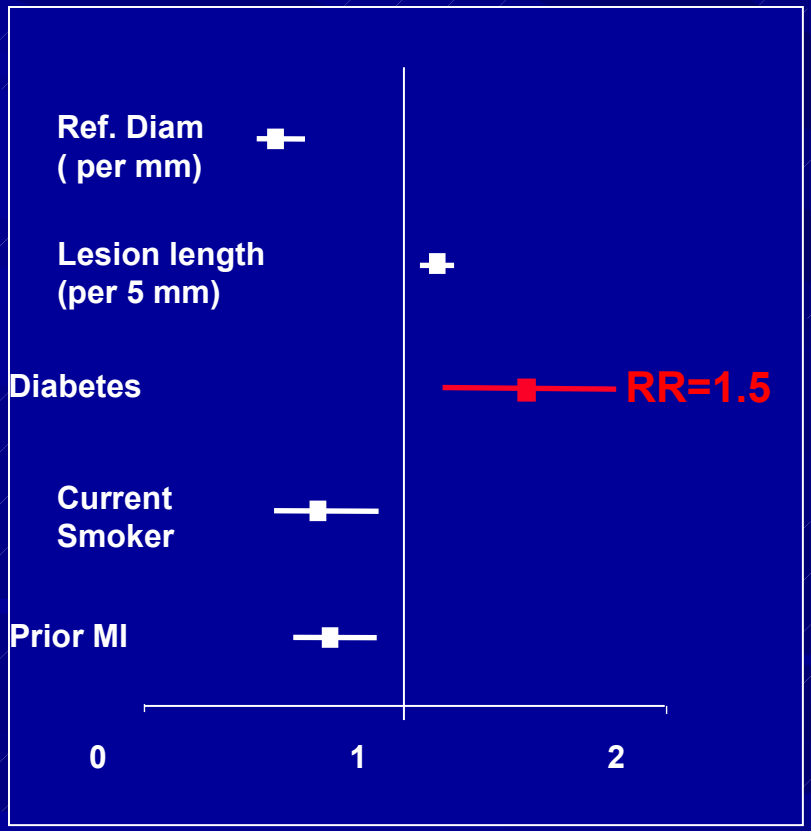
ОКС и Захарен диабет

Атеросклероза и захарен диабет Патофизиологични съображения

- Абнормна тромбоцитна ф-ция
  - ↑ активация и адхезия в отговор на shear stress
  - ↑ expression на GpIIb/IIIa receptors→ ↑ агрегация
- По-дифузна коронарна болест
  - Увреден коронарен flow reserve→ намален толеранс към емболизации
    - ↑ превалиране на богати на липиди плаки→ предразположени към руптуриране
  - Увредена възможност за развитие на колатерали→ по-голям MI
- Повишен отговор към съдова увреда
  - ↑ честота на ре-стеноза и ре-оклузия след PTCA и BMS

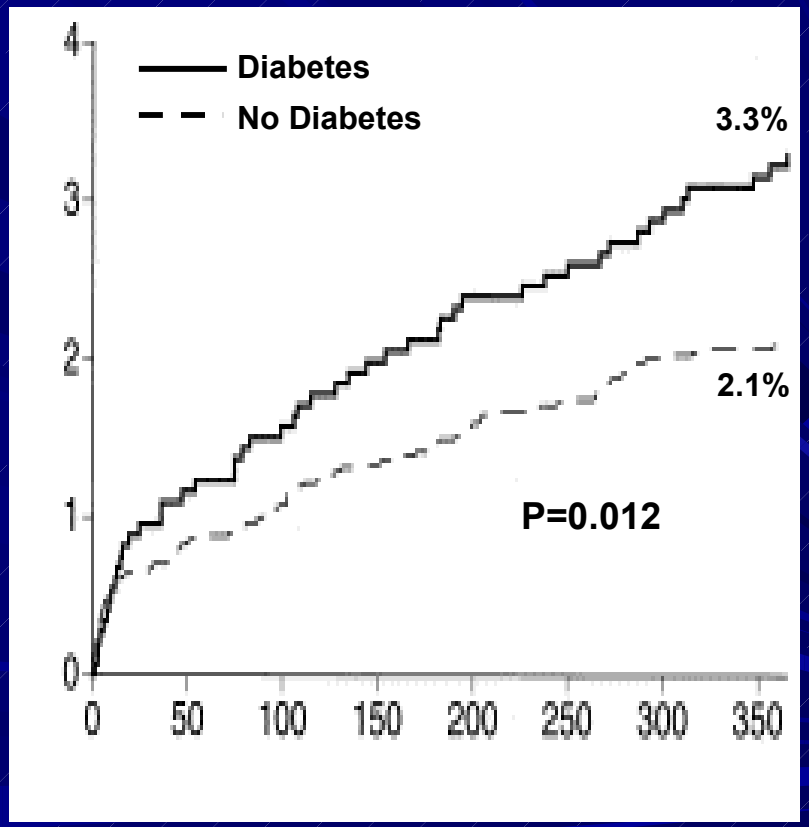
Влияние на ЗД върху краткосрочната и дългосрочната прогноза след PCI

Predictors of TLR (n=6186)



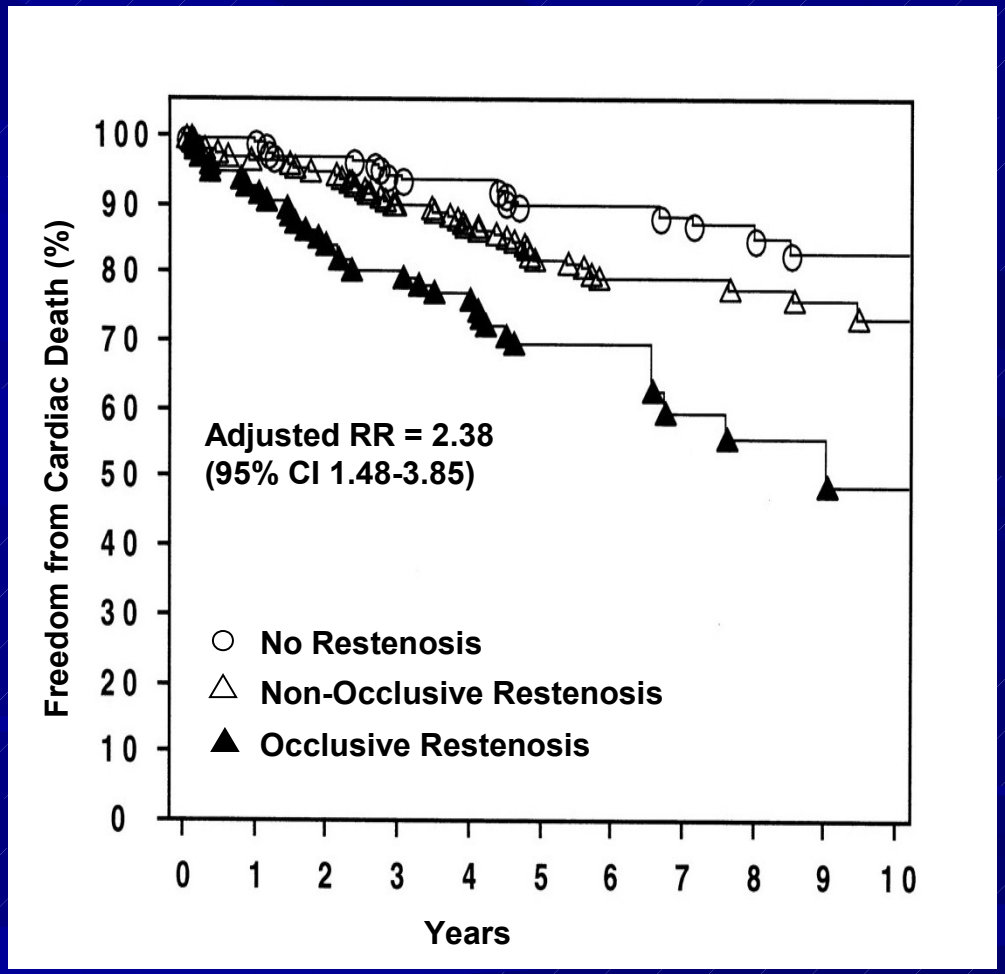
Cutlip DE et al. *JACC* 2002;40:2082-9

1-year mortality (n=6534)



Bhatt et al. *JACC* 2000;35:922-8

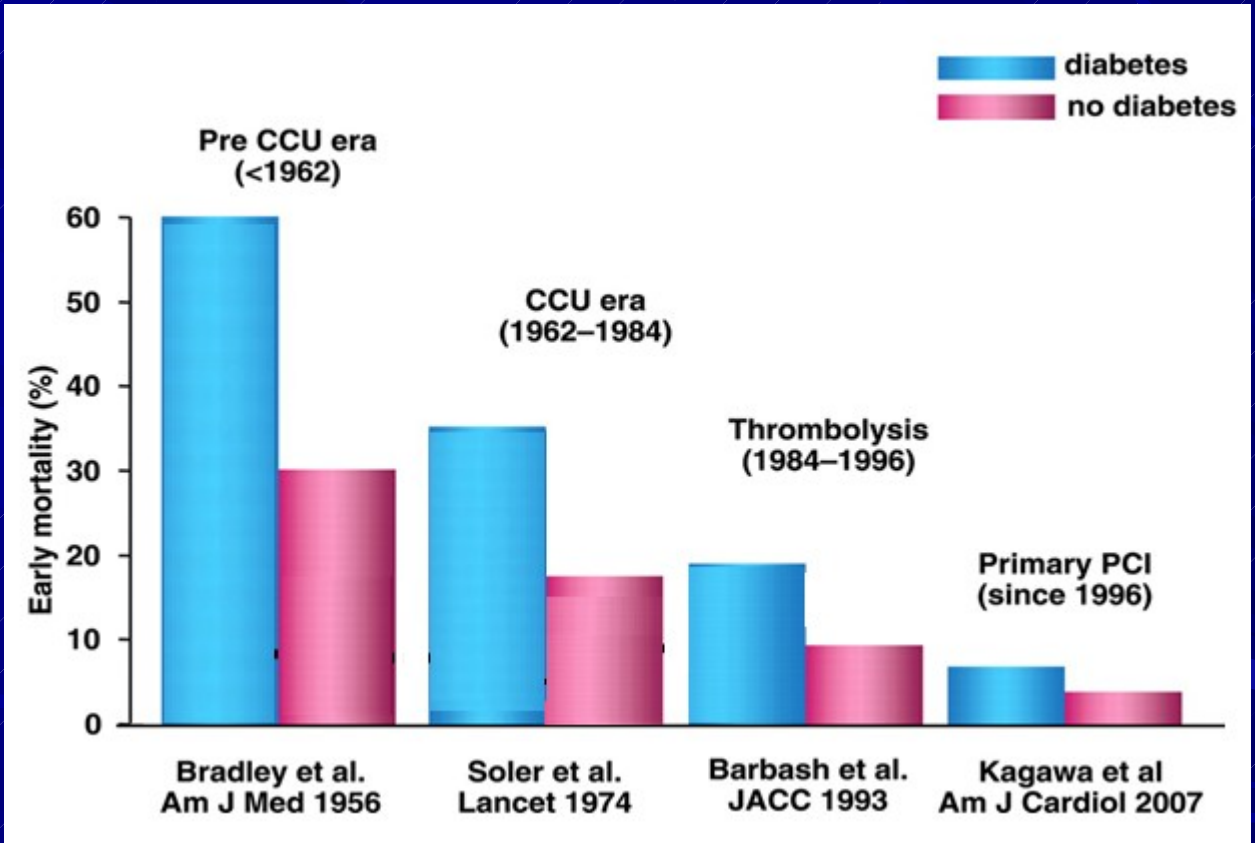
Връзка м/у ре-стеноза и смъртност при пациенти със ЗД



- 513 diabetic pts underwent 6 month f/u angio and long-term clincal f/u
- 10-yr survival
  - No restenosis: 24%
  - Non-occlusive: 35%
  - Occlusive: 59%
- Occlusive (but not non-occlusive) restenosis associated with strong, independent risk of 10-year mortality (RR 2.4)

Van Belle E et al. Circulation 001;103:1218-24

ACS Mortality in Diabetes vs. No Diabetes: Еволюция



Всички пациенти със ЗД и ОКС трябва да получат същото лечение като тези без ЗД ……

с някои разлики

Оптимизиране на PCI резултатите при диабетици

- Drug-eluting stents– кой стент за кой пациент?
- Какъв е оптималния антитромботичен режим?
- Селекция на пациентите : PCI vs. CABG ?
- Болнично лечение и вторична профилактика ?

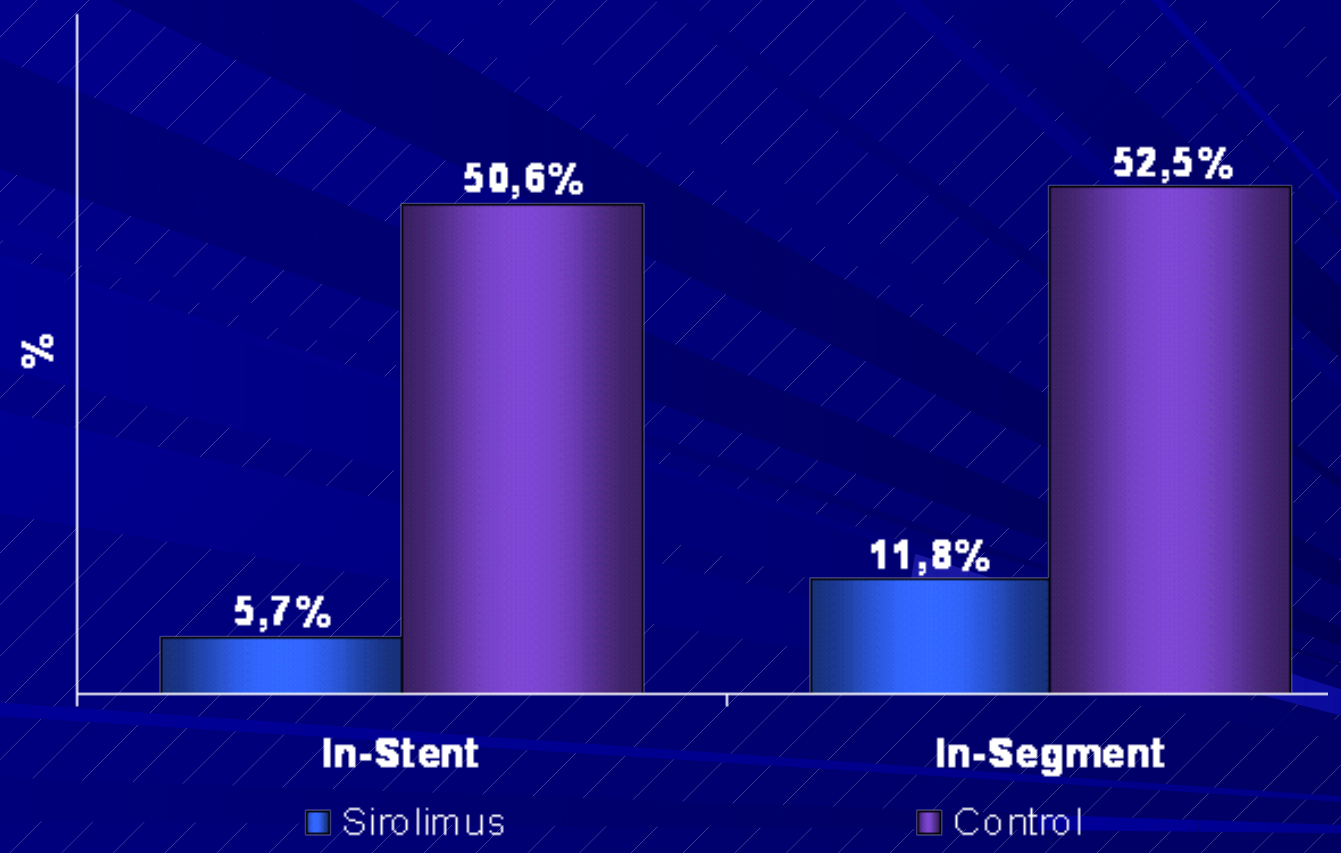
Оптимизиране на PCI резултатите при диабетици

Drug-Eluting Stents

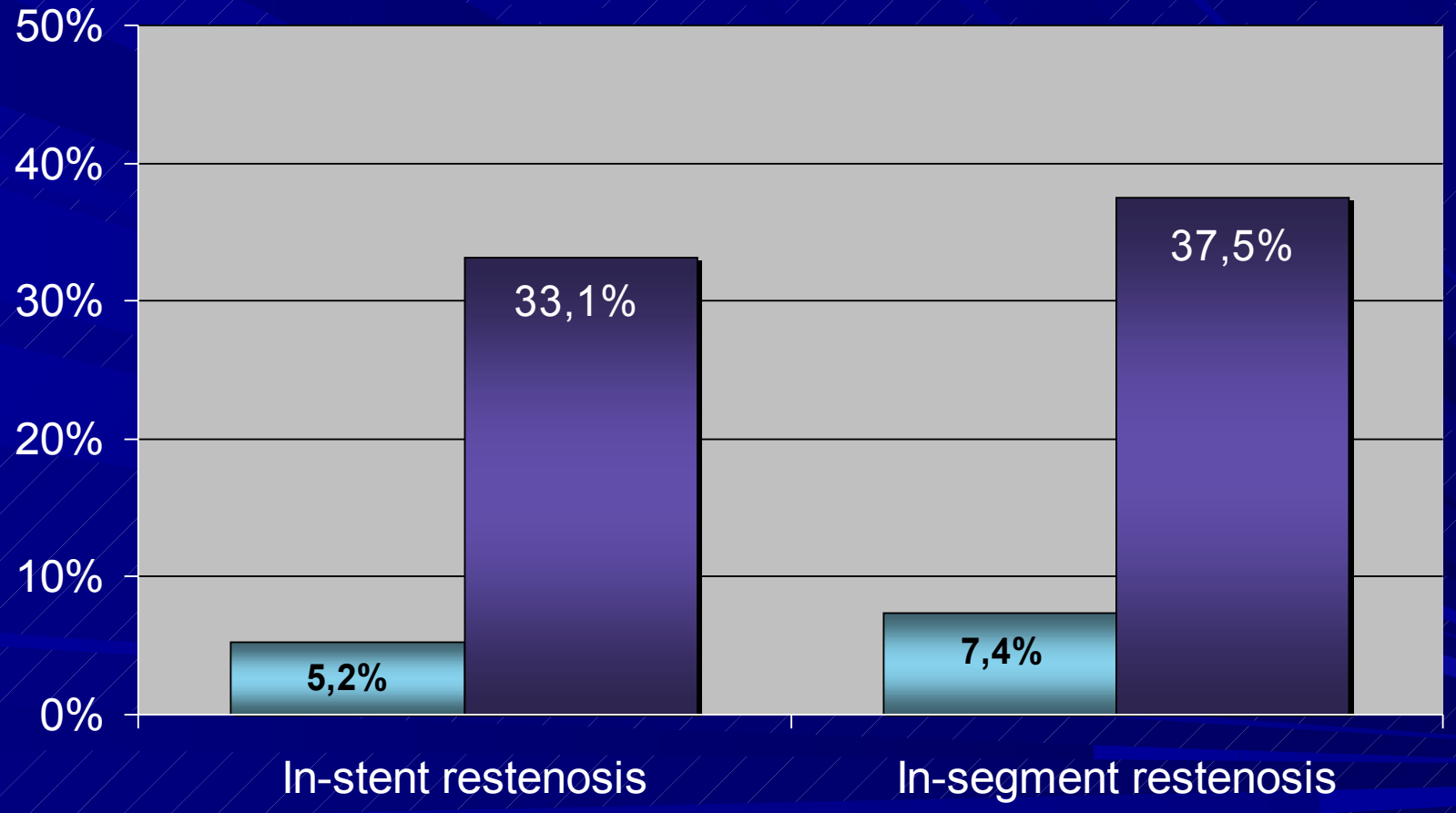
- Работят ли при пациенти с диабет?
  - Различни ефекти при ИЗТ vs. ИНЗТ ?
- Диабетът все още ли е рисков фактор за рестеноза в DES ера?
- Селекция
  - Има ли предпочитан DES за диабетични пациенти?
  - Поглед към регистрите и сравнителните проучвания

CYPHER Pooled: Diabetic Subgroup

Angiographic Restenosis

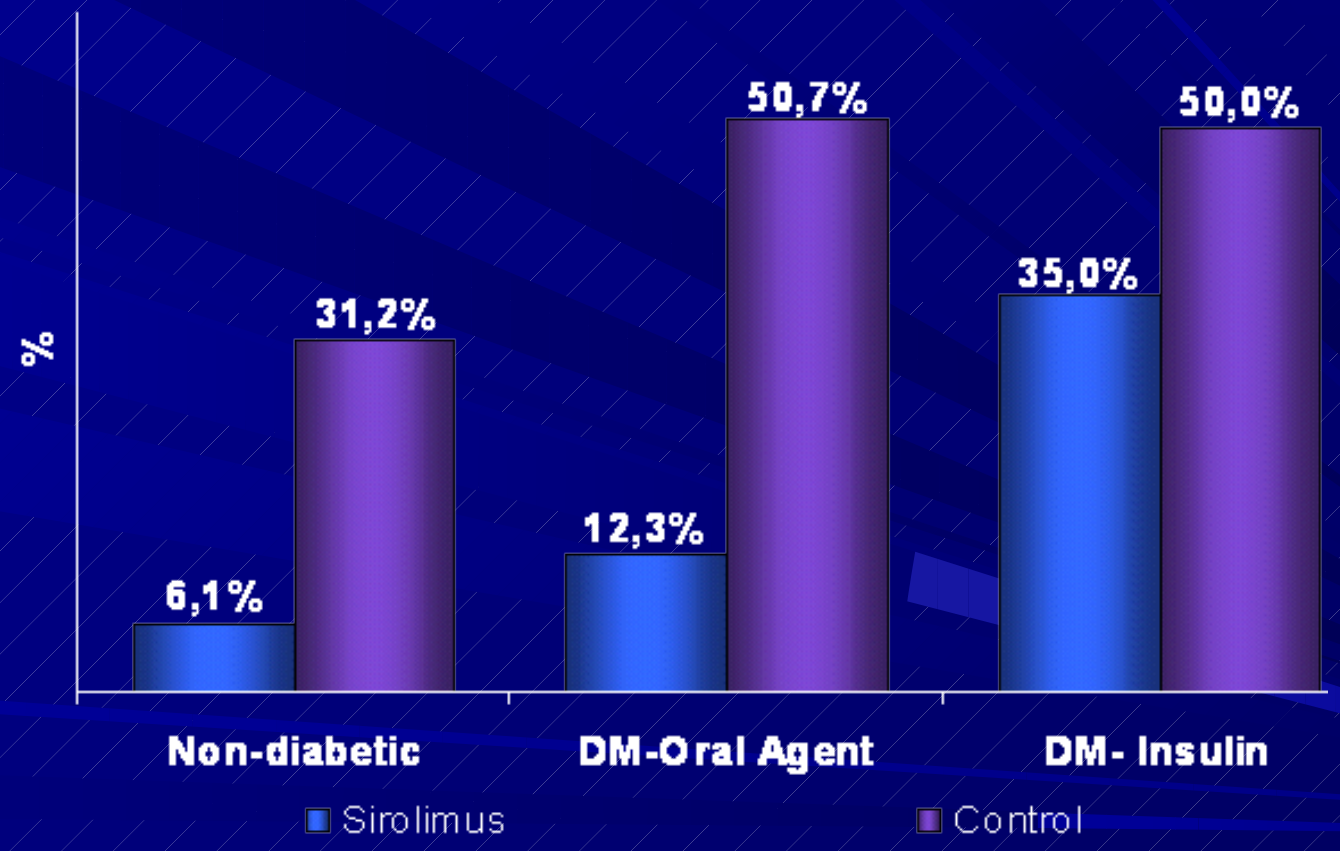


Pooled TAXUS Trials (II, IV, VI)
Overall Diabetic Subset: Angiographic Restenosis



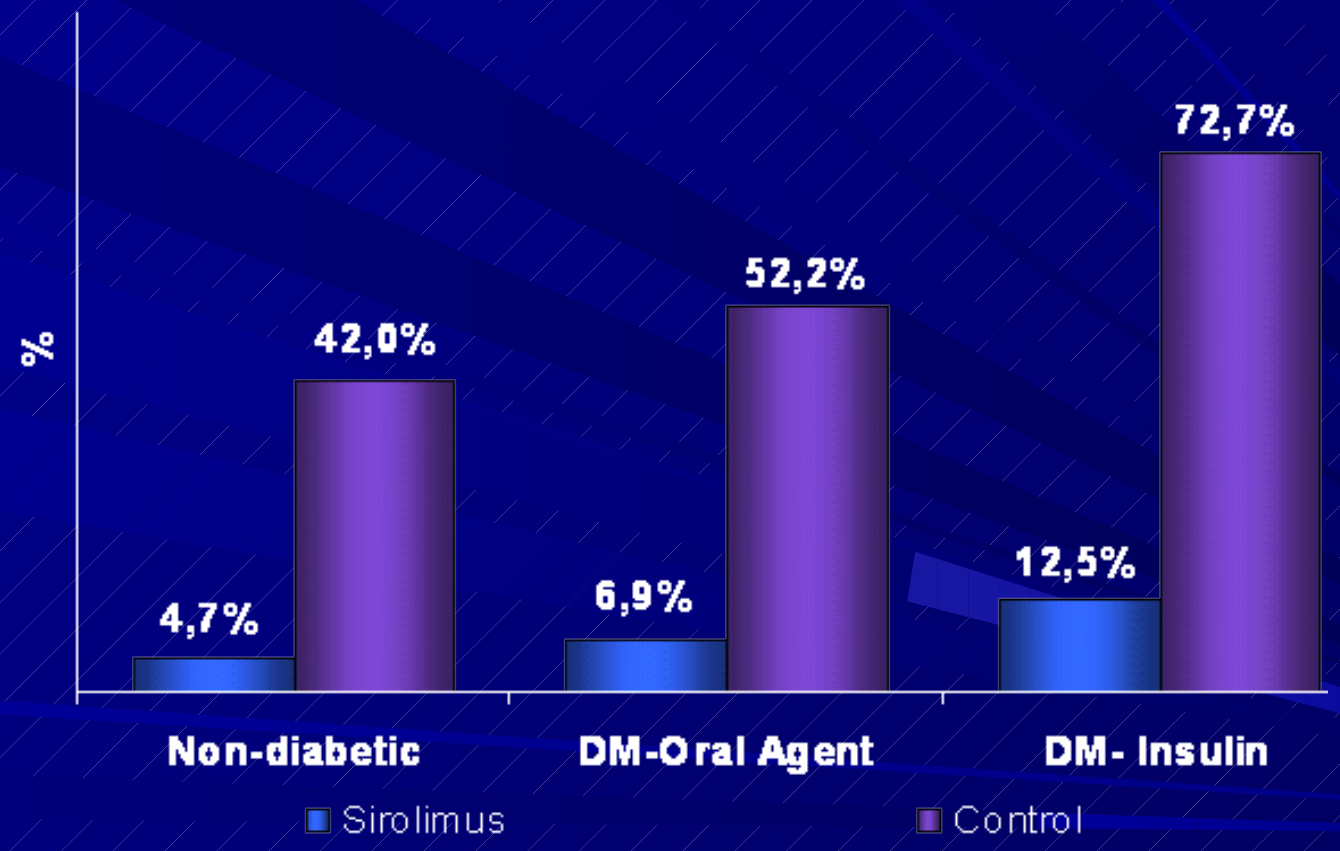
SIRIUS - Reduced Efficacy in IDDM

In-Segment Restenosis



CYPHER Trials-- Excluding SIRIUS

In-Segment Restenosis



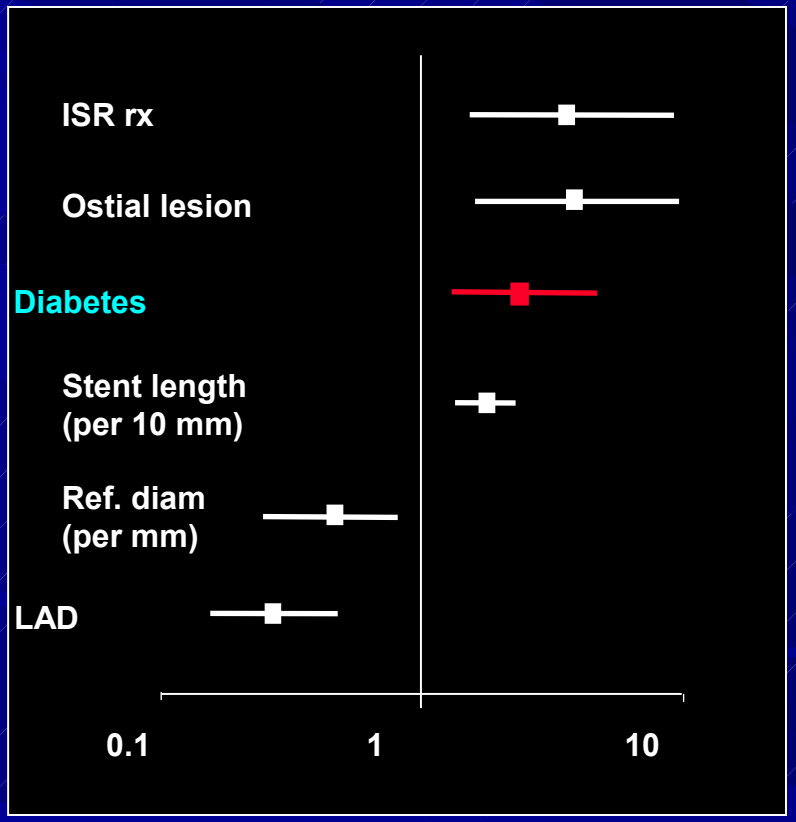
Оптимизиране на PCI резултатите при диабетици

Drug-Eluting Stents

- Работят ли при пациенти с диабет?
  - Различни ефекти при ИЗТ vs. НИЗТ?
- Диабетът все още ли е рисков фактор за рестеноза в DES ера?
- Селекция
  - Има ли предпочитан DES за диабетични пациенти?
  - Поглед към регистрите и сравнителните проучвания

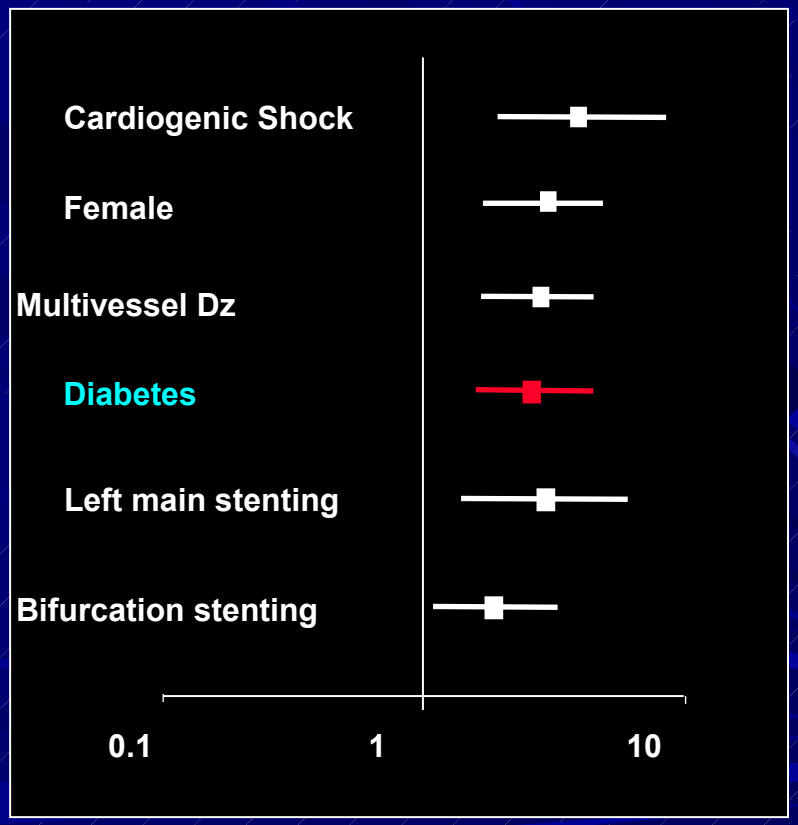
Independent Predictors of TVR after DES: RESEARCH and T-SEARCH Results

Angio. Restenosis (n=238)



Lemos PA et al. Circulation 2004;109:1366-70

1-year MACE (n=1084)



Ong ATL, et al. JACC 2005;45:1135-41

Оптимизиране на PCI резултатите при диабетици

Drug-Eluting Stents

- Работят ли при пациенти с диабет?
  - Различни ефекти при ИЗТ vs. НИЗТ?
- Диабетът все още ли е рисков фактор за рестеноза в DES ера?
- Селекция
  - Има ли предпочитан DES за диабетични пациенти?
  - Поглед към регистрите и сравнителните проучвания

Study Protocol

Patients with Diabetes Mellitus
(n = 250)

CYPHER®
(n = 125)

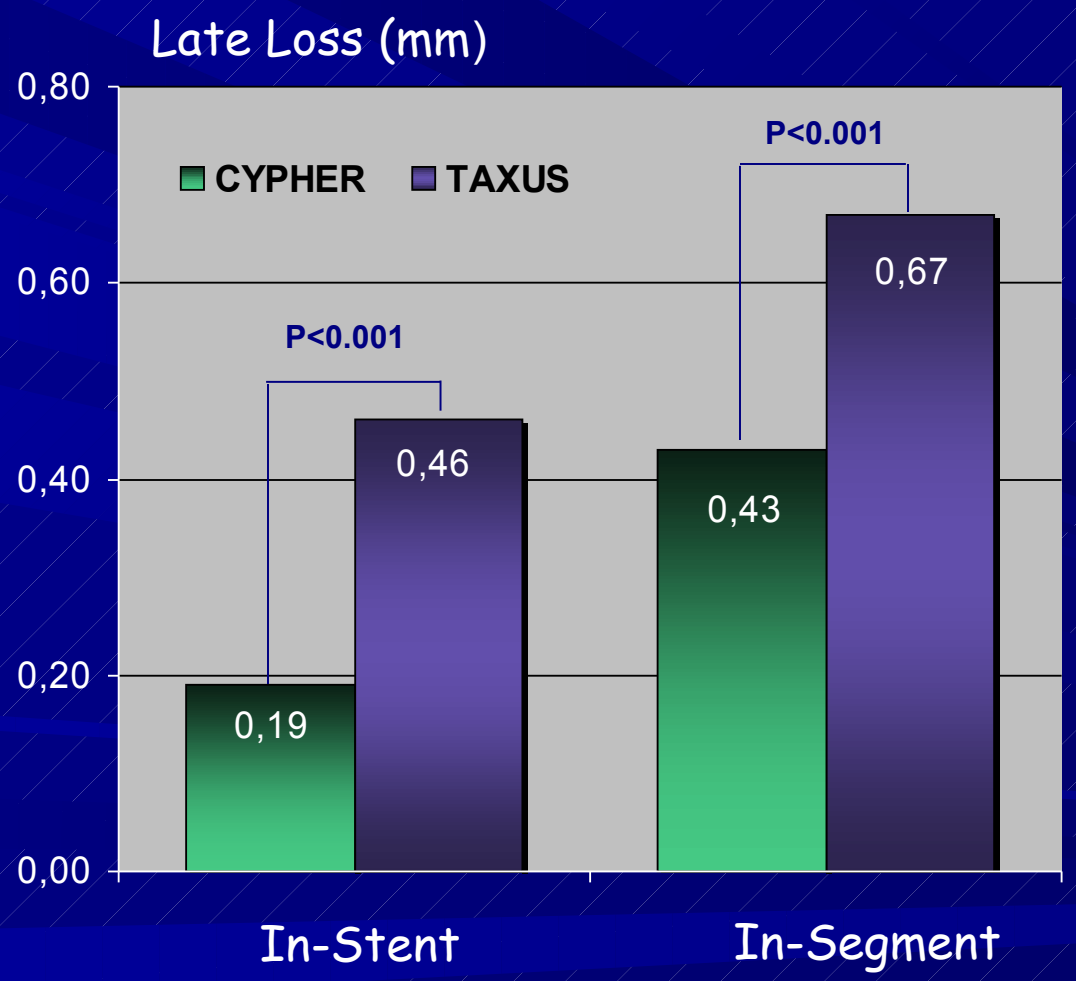
TAXUS™
(n = 125)

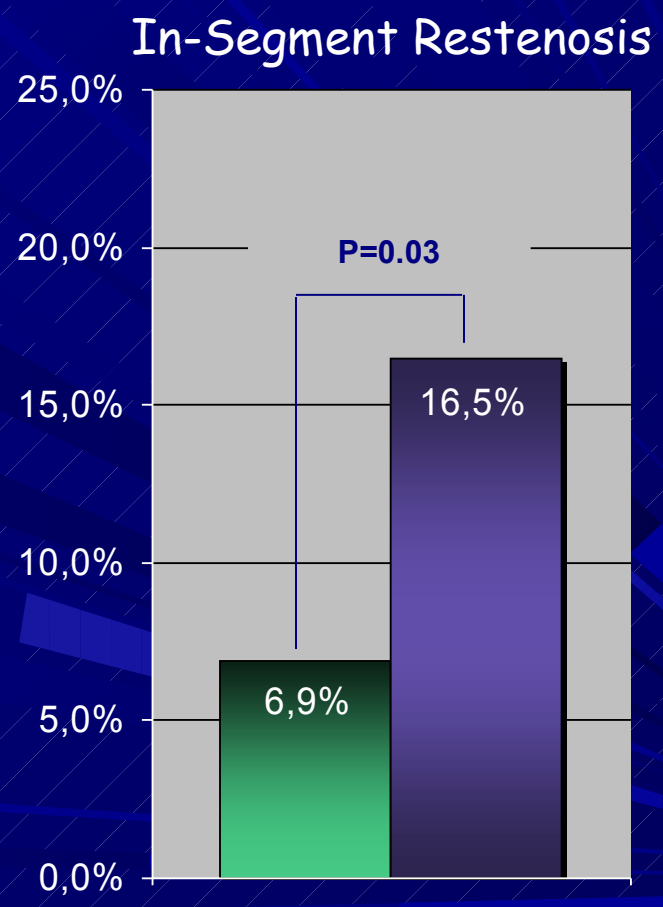
1° EP: Late lumen loss at 6 months (in-segment analysis)

2° EP: Angiographic restenosis at 6 months ≥ 50% diameter stenosis (in-segment analysis)

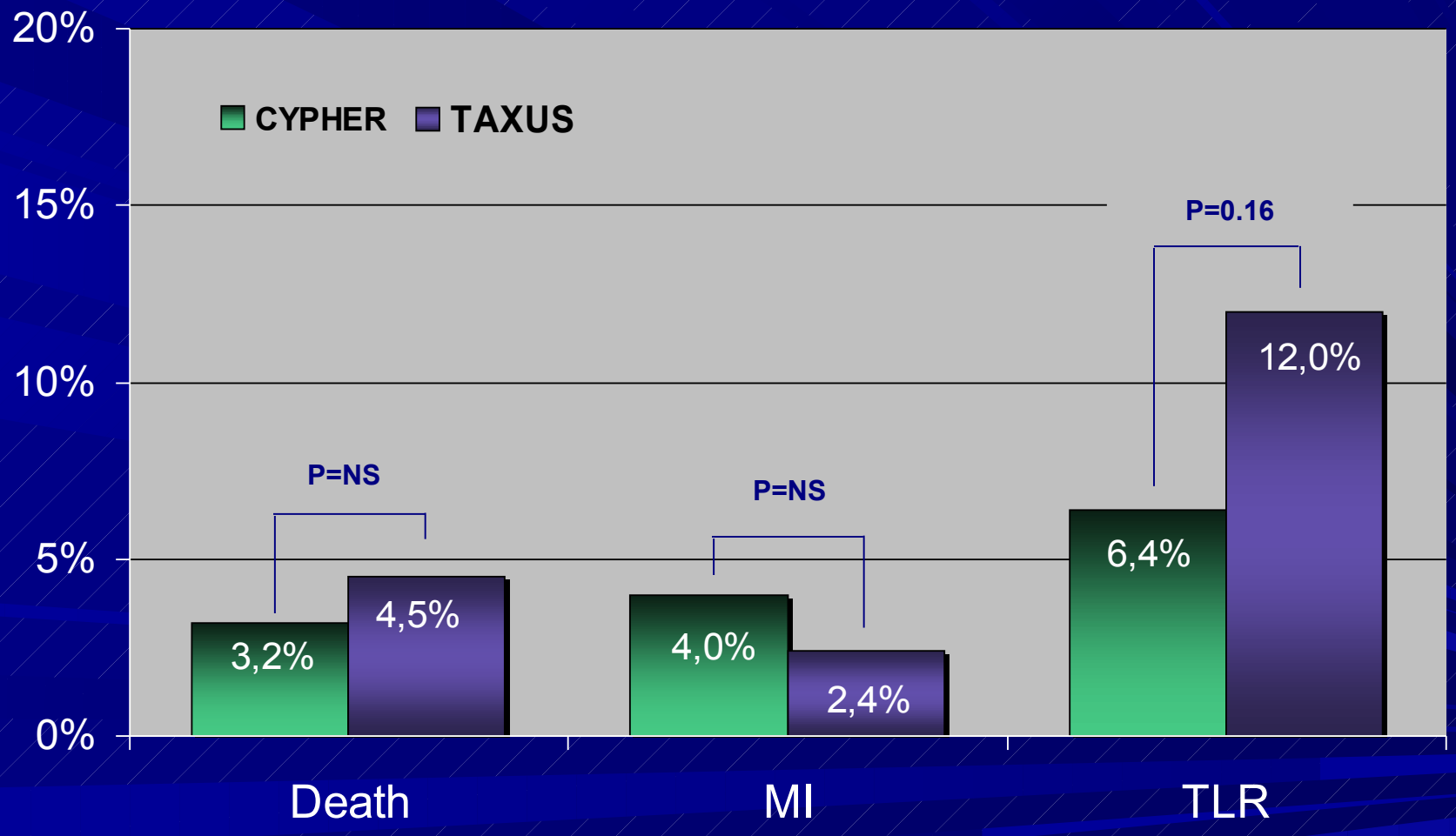
Target lesion revascularization at 6 months

Angiographic Outcomes





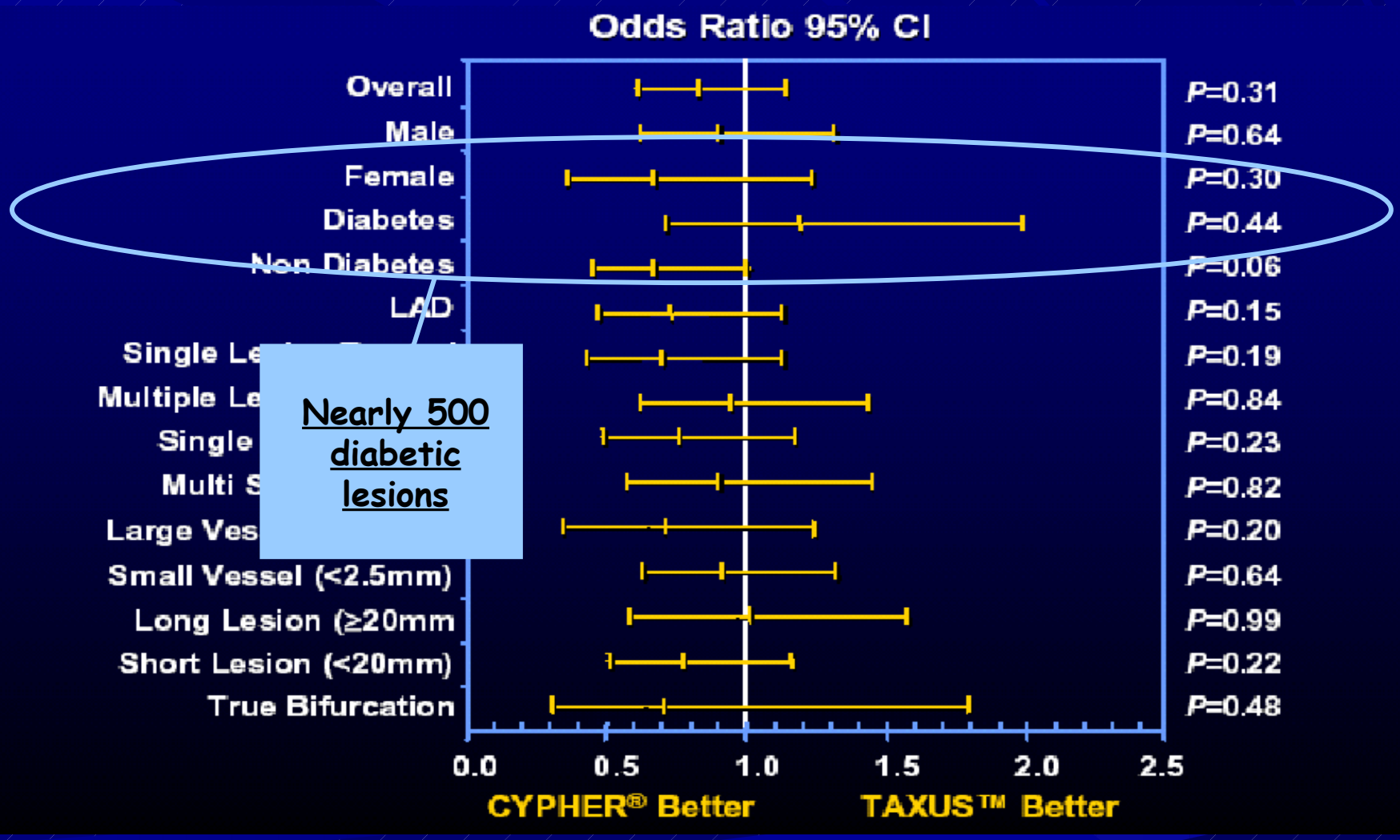
9-Month Clinical Outcomes



Are the ISAR-Diabetes Findings Real?
Comparison with SIRIUS and TAXUS

	Placebo-Control Trials		ISAR-Diabetes	
	CYPHER	TAXUS	CYPHER	TAXUS
In-stent LL (mm)	0.26	0.36	0.19	0.46
In-segment LL (mm)	0.32	0.22	**0.43**	**0.67**
In-stent restenosis	5.7%	5.2%	N/A	N/A
In-segment restenosis	8.3%*	7.4%	6.9%	**16.5%**
TLR	5.8%	6.0%	6.4%	**12.0%**

Are the ISAR-Diabetes Findings Real?
Comparison with REALITY



Обобщение : DES при ЗД

- Sirolimus- и Paclitaxel-eluting stents значимо редуцират ангиографската и клинична рестеноза в сравнение с BMS.
- Независимо от това , DES не елиминират повишеният риск от рестеноза при диабетици с/у не-диабетици.
- Head to head trials не съответстват напълно → 2 - 3 trials предполагат предимство на рестенозата със Cypher, но истинският размер на клиничната полза вероятно се надценява.

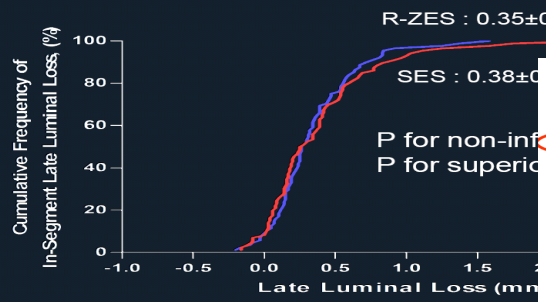
Randomized Comparison of Zotarolimus-*E*luting *S*tent versus *S*irolimus-*E*luting Stent Implantation for De *N*ovo *C*oronary Artery Dis*E*ase in Patients with *DIABETES* Mellitus

ESSENCE-DIABETES

Gyung-Min Park, Seung–Whan Lee, Seong–Wook P
Jung-Min Ahn, Jong-Young Lee, Won-Jang Kim
Soo-Jin Kang, Young–Hak Kim, Cheol Whan Lee
on behalf of the ESSENCE-DIABETES II stu
Asan Medical Center,
University of Ulsan College of Medicine, S

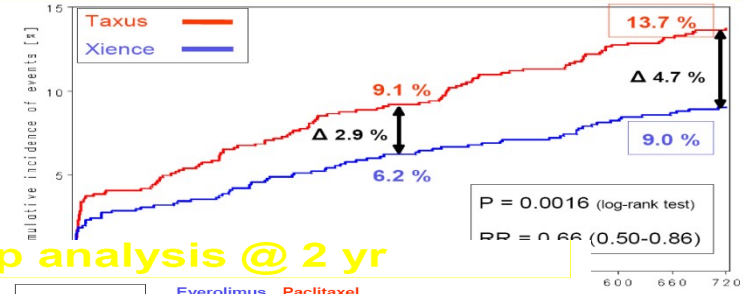
Primary Endpoint: In-Segment Late Loss at 9 month

Late loss was calculated using maximal regional late loss

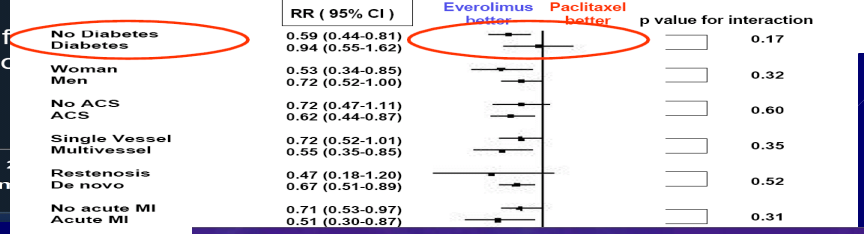


Primary Endpoint Result @ 2 yr

MACE (all death, non-fatal MI and TVR)



Subgroup analysis @ 2 yr



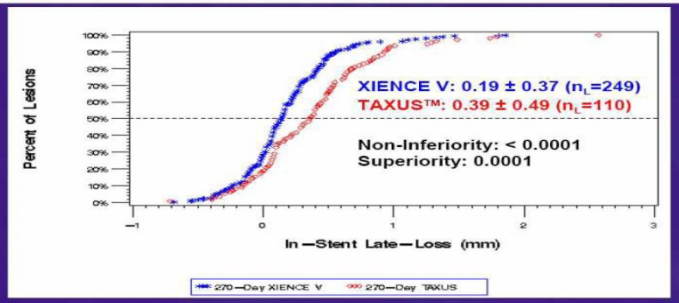
euro PCR Baseline Patient Characteristics

Variable, %	R-Zotarolimus stent N = 1140 pts	Everolimus stent N = 1152 pts
Age, years (mean ± SD)	64.4 ± 10.9	64.2 ± 10.8
Men	76.7%	77.2%
Diabetes mellitus	23.5%	23.4%
Insulin treated	8.4%	7.1%
Arterial hypertension	71.1%	71.3%
Hyperlipidemia	63.9%	67.7%
Current smoker	26.5%	26.5%
Premature CAD in first degree relative	34.1%	36.7%
Prior myocardial infarction	28.9%	30.4%
Prior percutaneous coronary intervention	31.8%	32.1%
Prior coronary artery bypass grafting	10.0%	9.5%
Stable angina	33.5%	36.1%
Unstable angina	19.4%	18.9%
Acute Myocardial infarction ≤72 hours	28.9%	28.8%

Serruys P, et al. PCR 2010 Serruys P, et al. PCR 2010

SPIRIT V Diabetic RCT: Primary Endpoint:

XIENCE V is Superior to TAXUS Liberté in In-stent Late Loss



Angiographic follow-up at 270-days: XIENCE V: 88% TAXUS: 86%

SPIRIT V Diabetic RCT: Design

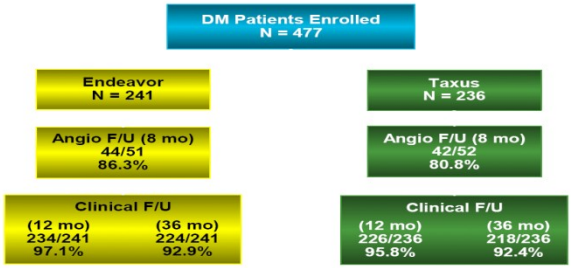
Primary endpoint:
In-stent late loss at 270 days

- **PI:** Prof Eberhard Grube, Siegburg, Germany
- **Co-PI:** Dr Upendra Kaul, New Delhi, India
- **Steering Committee**: Dr G Guagliumi, Bergamo, Italy, Dr B Chevalier, Massy, France, Dr V Dzavik, Toronto, Canada, Dr P Smits, Rotterdam, The Netherlands
- **Angiographic Core Lab: BioClinica, Leiden, The Netherlands**
- **All Events adjudicated by CEC to Academic Research Consortium (ARC) Definitions**
- **Diabetic RCT Enrollment Complete:** 06 October 2008
- **SAS Enrollment Complete:** 21 November 2007 (1 Year clinical data presented at EURO PCR 2009)

* TAXUS Liberté Coronary Stent System is a registered trademark of Boston Scientific or its affiliates

ENDEAVOR IV Diabetes

Diabetic Patient Flowchart



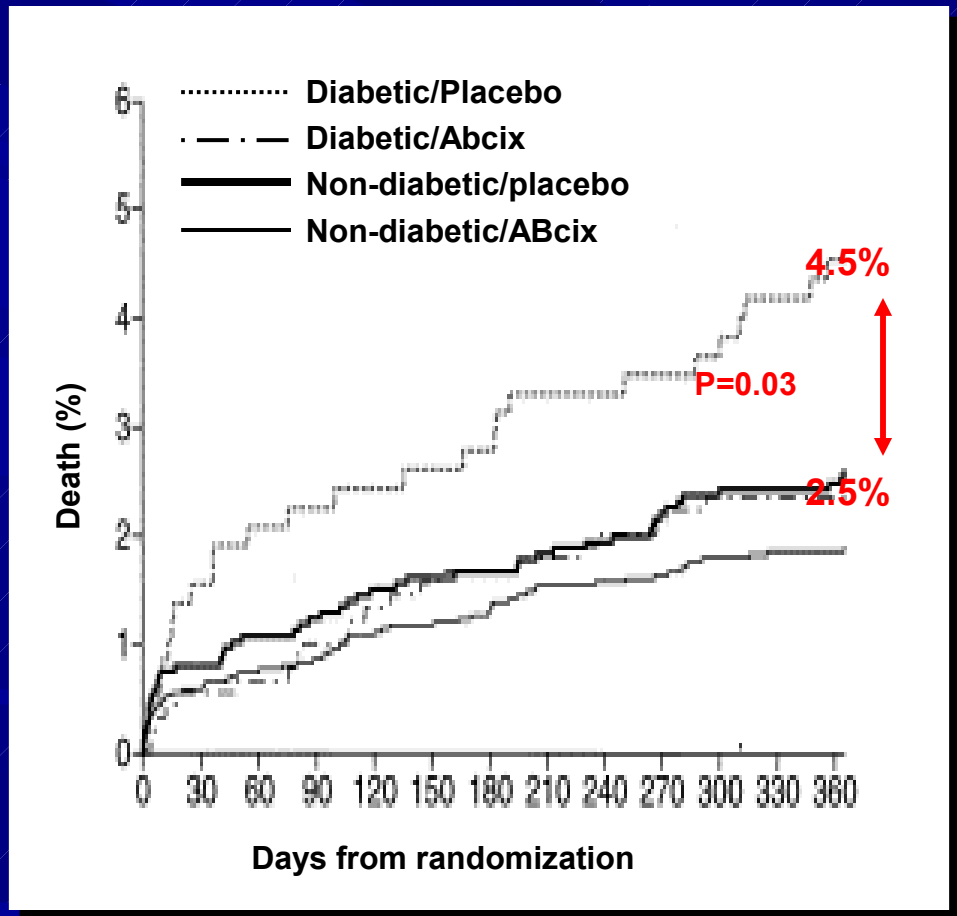
Оптимизиране на PCI резултатите при диабетици

- Drug-eluting stents– кой стент за кой пациент?
- Какъв е оптималния антитромботичен режим?
- Селекция на пациентите : PCI vs. CABG
- Болнично лечение и вторична профилактика

Хематологични нарушения при диабет

- Повишена тромбоцитна адхезия и активация в отговор на shear stress (↑P-selectin, ↑Fibrinogen binding capacity)
- Up-regulation of GpIIb/IIIa receptors свързана с хипергликемията, водеща до засилена тромбоцитна агрегация
- Намален капацитет на ендогенната тромболиза
- Наличие на ендотелна дисфункция → намален толеранс към in-situ тромбози и дистална емболизация

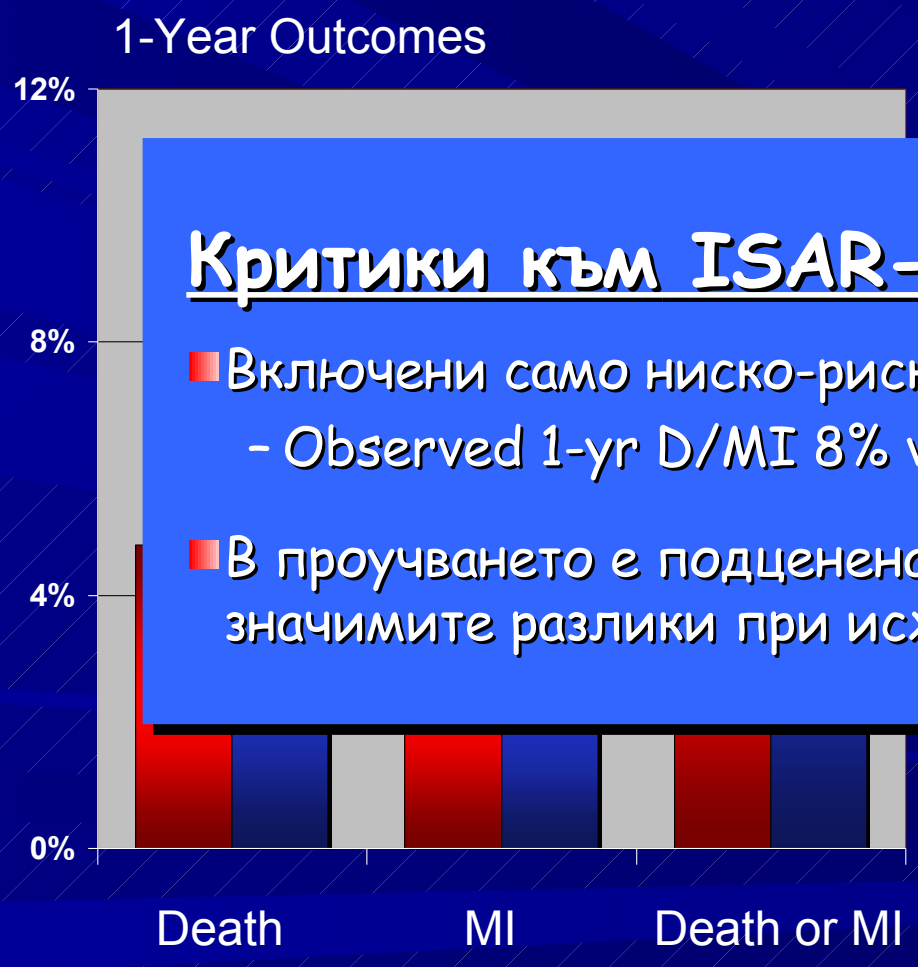
Mortality Benefit of Abciximab in Diabetic Pts



- Pooled analysis of 1-year mortality from EPIC, EPILOG, and EPISTENT databases
- Among patients with diabetes (n=1420), abciximab reduced 1-year mortality by 45% (20 lives saved per 1000 pts; p=0.03)
- Mortality benefits particularly striking among diabetic patients with:
  - IDDM (4.2% vs. 8.1%, p=0.07)
  - Multivessel PCI (0.9% vs. 7.7%; p=0.02)

Bhatt DL et al. JaCC 2000;35:922-8

Има ли все още полза от Gp2b/3a Inhibitors в ерата на високата доза Clopidogrel ?



ISAR-SWEET Trial

IDDM,
g

ACS,
F<30%

grel 600
CI

vs.

- Primary Endpoint: 1-year D/MI

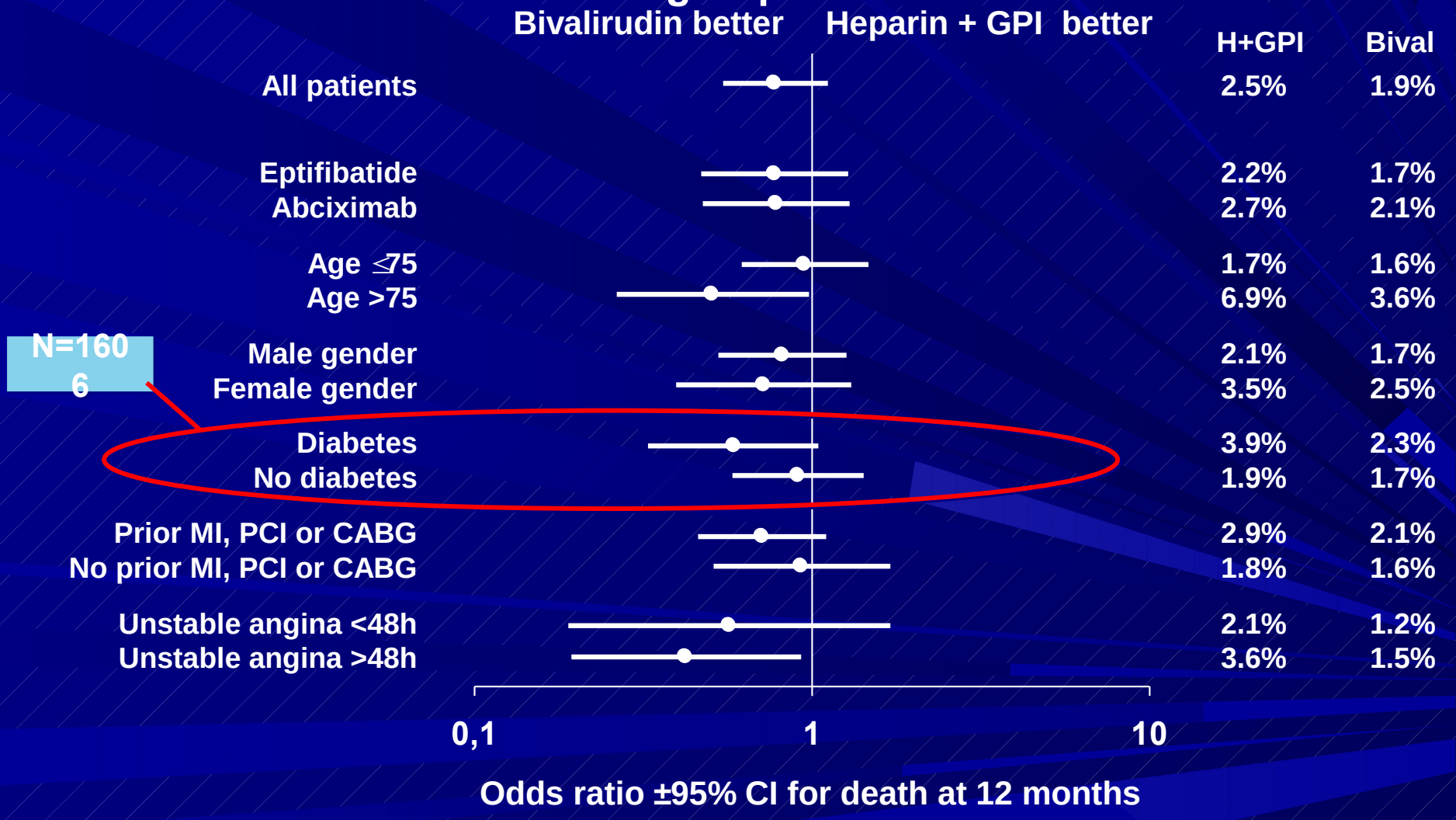
Критики към ISAR-SWEET

- Включени само ниско-рискови пациенти с диабет
  - Observed 1-yr D/MI 8% vs. 14% expected
- В проучването е подценена оценката на клинично значимите разлики при исхемични усложнения

Mehilli J et al. Circulation 2004;110:3627-35

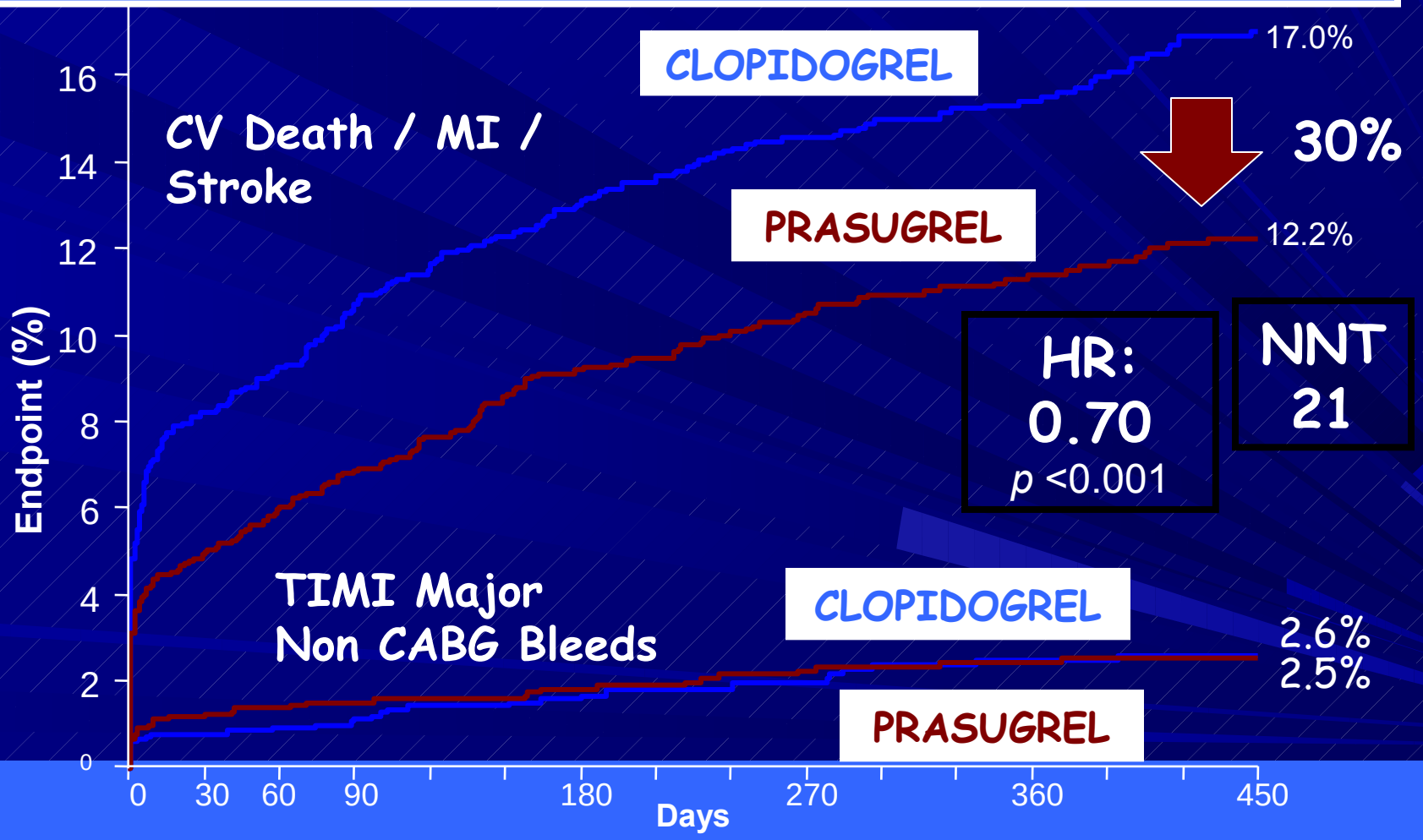
1-year mortality – subgroups

Results consistent across subgroups



TRITON: Diabetes Subgroup - Prasugrel

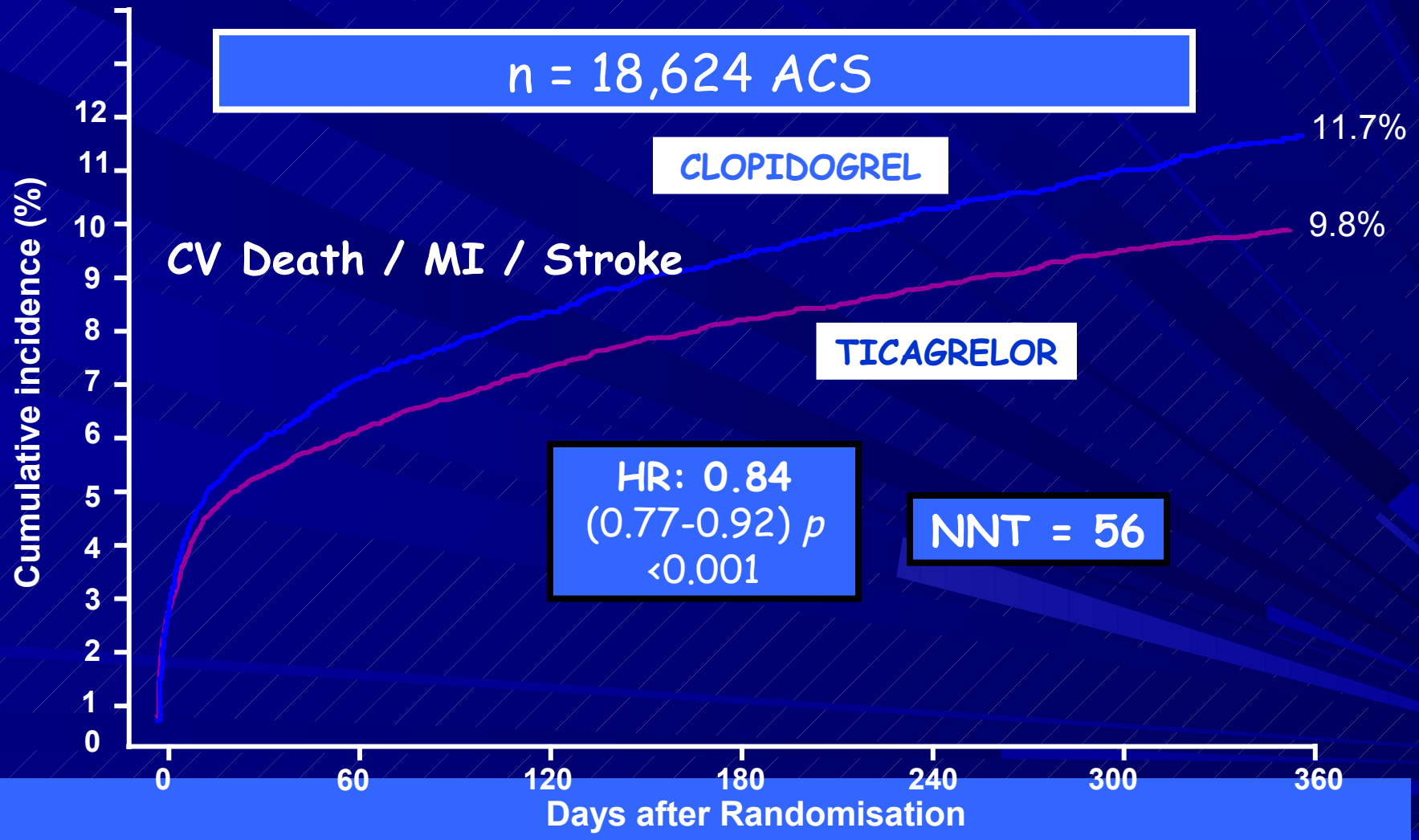
n = 3146 ACS (STEMI or NSTE ACS) & Planned PCI



ACS = Acute Coronary Syndrome; STEMI = ST-elevation Myocardial Infarction; NSTE ACS = Non-ST-elevation Acute coronary Syndrome; PCI = Percutaneous Coronary Intervention; LD = Loading Dose; MD = Maintenance Dose; NNT = Number Needed to Treat; CV = Cardiovascular

Modified from Wiviott SD et al. *Circulation* 10-14-2008;118:1626-1636

PLATO Study: Ticagrelor vs. Clopidogrel



ACS = Acute Coronary Syndrome; PCI = Percutaneous Coronary Intervention; NNT = Number Needed to Treat; CV=Cardiovascular

Modified: Wallentin *et al. New Eng J Med* 2009; 361(11): 1045-1057

Двойна анти-тромбоцитна Th при пациенти със ЗД и ОКС

Подлежаща PCI

Prasugrel

- Възраст под 75 г
- Тегло над 65 кг. Липса на анамнеза за преживян инсулт.

или

Ticagrelor

- Липса на анамнеза за хеморагичен инсулт
- Липса на екстремна брадикардия

Clopidogrel

За редукция на последващи исхемични събития

Оптимизиране на PCI резултатите при диабетици

- Drug-eluting stents– кой стент за кой пациент?
- Какъв е оптималния антитромботичен режим?
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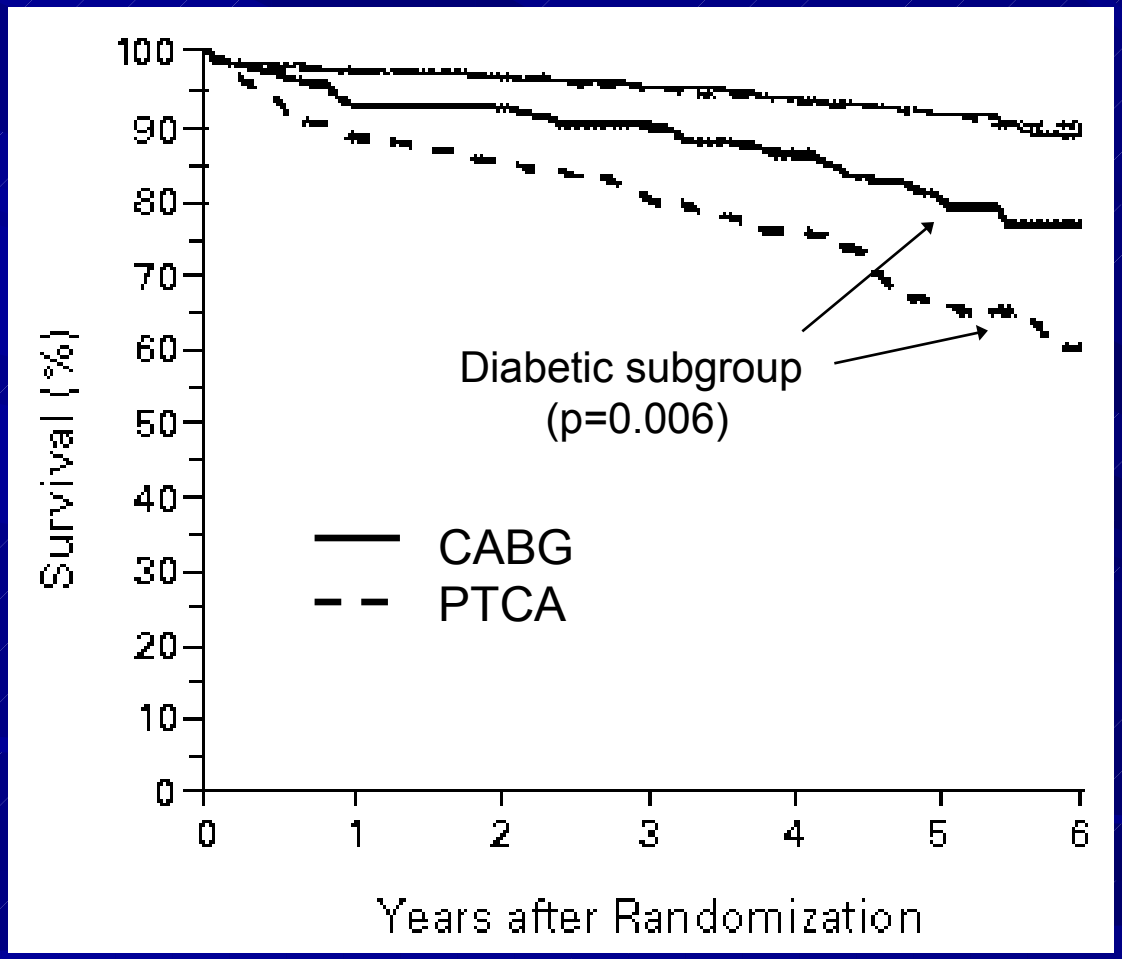
BARI: Impact of Diabetes on Survival



BARI Subgroups

- Treated diabetic pts only subgroup to show significant survival advantage with CABG
- 5 year survival
  - *CABG 81%*
  - *PTCA 65%*

NEJM 1996;335:217-25

По-висока ли е смъртността при диабетици след многоклоново стентиране ?

Study (yrs f/u)	Type of Study	N	Adjusted Hazard Ratio
BARI (8)	RCT	353	1.87 *
E			
B			
D			
Emory databank (6)	Obs	[illegible]	[illegible]
NNE (2)	Obs	2766	1.49*
ARTS (3)	RCT	210	1.70
SOS (1)	RCT	142	>10

Стентовете не дават предимство по показател смъртност при многоклонова ИБС в сравнение с CABG

Yellow = Stent vs. CABG

* P<0.05

PCI и захарен диабет …

2013

- Мисли два пъти (особено при многоклонова болест)
- Използвай DES (drug-eluting stents)
- Използвай Gp 2b/3a inhibitor (при възможност bivalirudin)
- Максимална вторична коронарна превенция, дори и в кратки срокове
  - Оптимален гликемичен контрол
  - Агресивна статинова терапия (? LDL<80)
  - ACE-inhibition

Acute Coronary Syndrome Checklist

2013

- **SCREEN** за ЗД pts с ОКС
- **Използвай анти-тромбоцитна Th , prasugrel или ticagrelor**, вместо clopidogrel при pts със ЗД подлежащи на PCI (percutaneous coronary intervention)
- **Избягвай и двете** hyper- и hypoglycemia при pts със ЗД приети с ОКС

Гликемичен контрол при Pts с ОКС

2013

- Хипергликемия по време на първите 24-48 часа след приемане → ↑ ранна смъртност при pts с ОКС

- Pts с остър МИ, кръвна захар при приема > 11 ммол/л → с вероятна полза при стойности 7.0-10.0 mmol/l

  Изискват лечение с Insulin

  Полза от налични протоколи

Заключение

2013

1. Pts с ОКС трябва да бъдат скенирани за диабет чрез изследване на кр. захар на гладно, A1C или 75 gram OGTT преди дехоспитализацията. [Grade D consensus]
2. Всички pts със диабет и ОКС трябва да получат същото лечение, което се препоръчва за pts с ОКС без диабет поради еднаквите ползи [Grade D, consensus].

Заключение

2013

3. Pts с диабет и ОКС подлежащи на PCI трябва да получат анти-тромбоцитна Th. с Prasugrel (тегло >65 кг и липса на анамнеза за инсулт) [Grade A, Level 1] или Ticagrelor [Grade B, Level 1], вместо Clopidogrel, за редукция на бъдещи исхемични инциденти.

4. Pts с Диабет и non-STE ACS и показатели за висок риск , трябва да получат ранна инвазивна стратегия, а не избирателно инвазивен подход за реваскуларизация, за намаляване на повтарящи се коронарни инциденти, освен ако има противопоказания. [Grade B Level 2].

Заключение

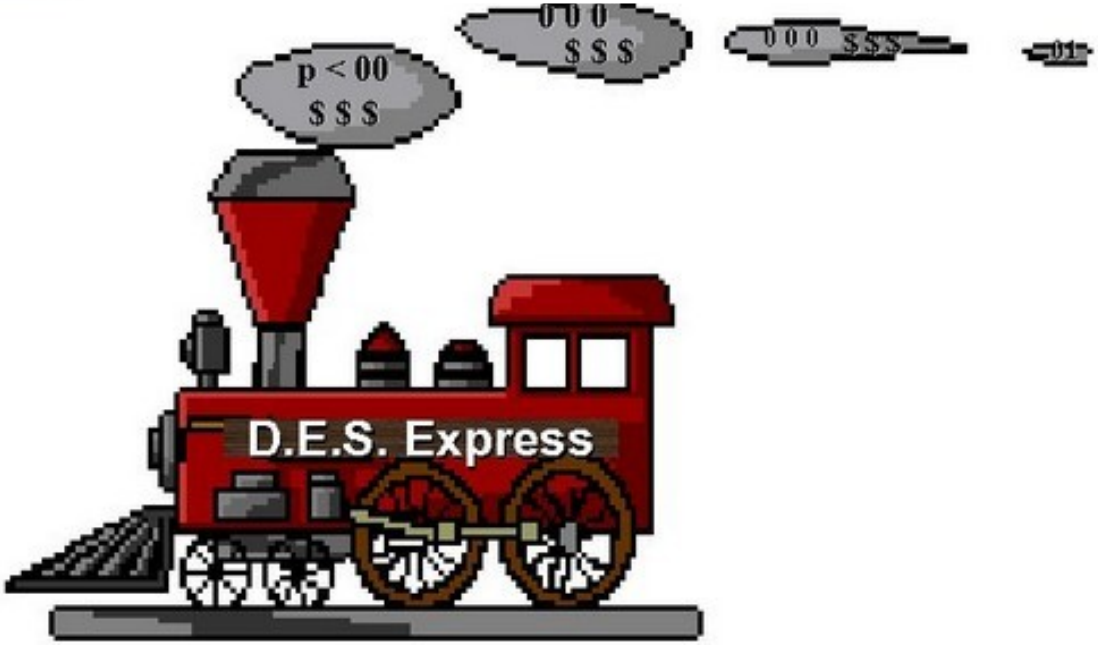
2013

5. Болничното лечение на диабетиците с ОКС трябва да включва стратегия за избягване както на хипер-, така и на хипогликемията:
   - Кр. захар трябва да бъде измервана при приема и мониторирана по време на пролежаването [Grade D, Consensus]
   - Pts с остър MI и кр.захар при приема >11 mmol/L трябва да получават гл. контрол в границите на 7.0 to 10.0 mmol/L последвано от стратегия за достигане на препоръчителните таргетни стойности в дългосрочен период.[Grade C, Level 2]

Вторична профилактика при ЗД

2013

Intervention	Evidence
High-intensity statin	▪ HPS: 27% ↓ in CHD death or MI among DM subgroup (20% ↓ in CHD death, p=0.02)
ACE-Inhibitor	▪ HOPE diabetic substudy: 25% ↓ in CV-death/MI/stroke (p<0.001); 37% ↓ in CV-death over 5 yr follow-up (p=0.001)
Intensive glycemic control	▪ Clearcut benefits on microvascular complications (UKPDS trial) ▪ Observational studies suggest improved CV outcomes and less restenosis associated with lower HbA1c ▪ ? Specific benefit of glitazones

Благодаря за вниманието !

TREATMENT FOR RESTENOSIS