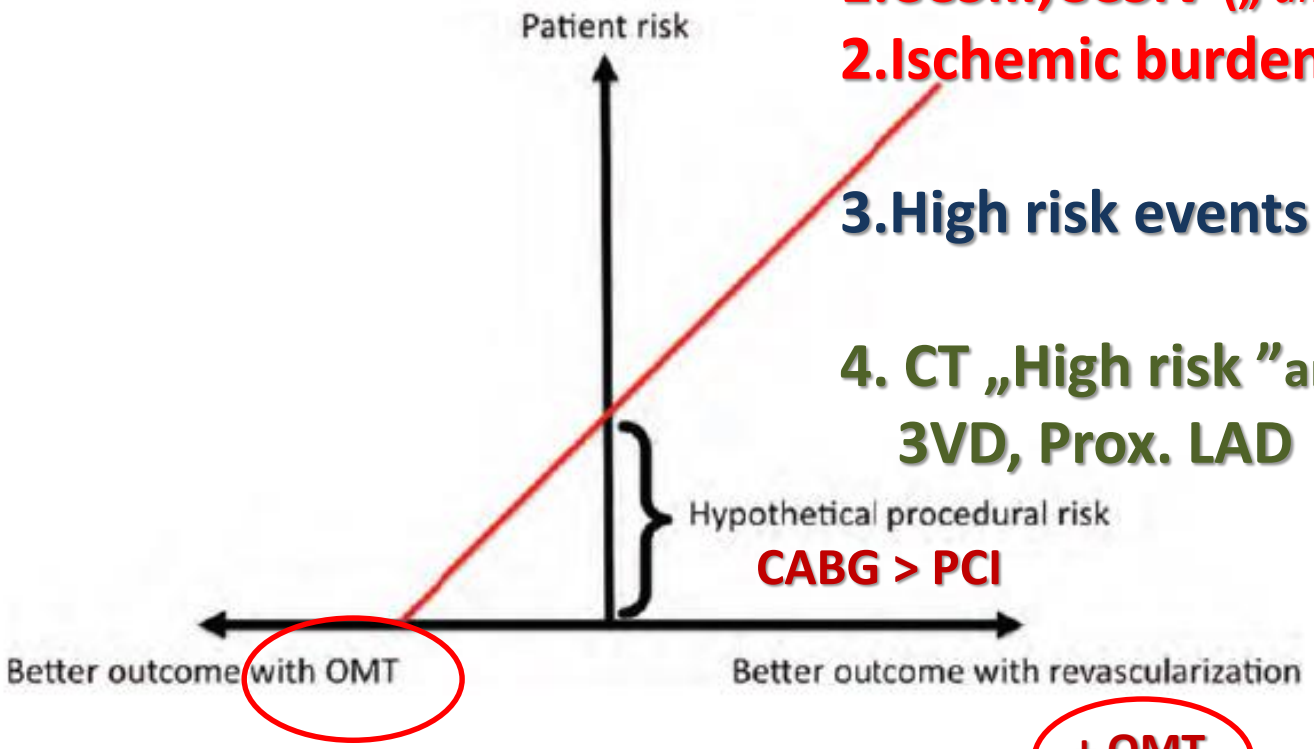
Optymalne leczenie stabilnej choroby wieńcowej w 2016 roku

Stefan Grajek

Benefit of revascularization for stable ischaemic heart disease: the jury is still out

Amir-Ali Fassa[1], William Wijns[2], Philippe Kolh[3], and Philippe Gabriel Steg[1,4,5]*



1.CCSIII,CCSIV („ *angina crescendo*”)

2.Ischemic burden > 10-15%

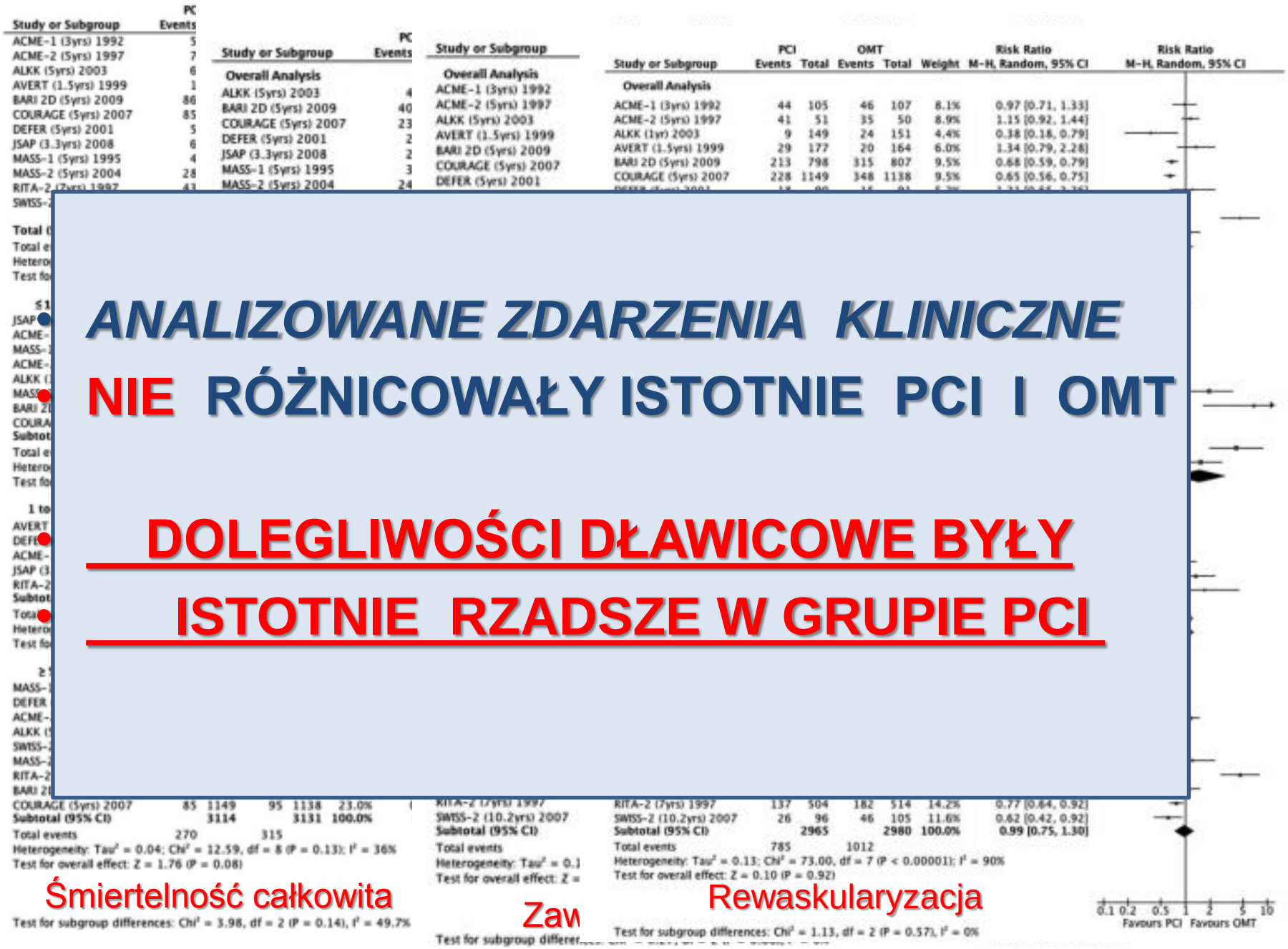
3.High risk events >3%;EF<45- 50%

4. CT „High risk ”anatomy; LM, 3VD, Prox. LAD

+ OMT

Koronarografia

Eur Heart J 2013



ANALIZOWANE ZDARZENIA KLINICZNE

NIE RÓŻNICOWAŁY ISTOTNIE PCI I OMT

DOLEGLIWOŚCI DŁAWICOWE BYŁY ISTOTNIE RZADSZE W GRUPIE PCI

Pursanani et al. Circulation 2012

LESS IS MORE

Initial Coronary Stent Implantation With Medical Therapy vs Medical Therapy Alone for Stable Coronary Artery Disease

Meta-analysis of Randomized Controlled Trials

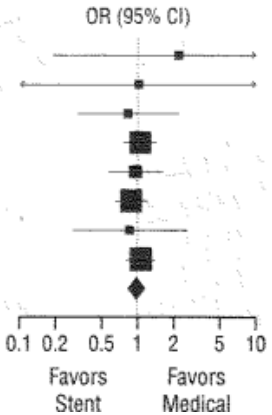
Kathleen Stergiopoulos, MD, PhD; David L. Brown, MD

Arch Inter Med. 2012

B

Source	OR (95% CI)		P Value
TOAT[16]	2.20	(0.19-25.52)	.53
Hambrect et al[17]	1.02	(0.02-52.43)	.99
DECOPI[18]	0.83	(0.31-2.23)	.71
OAT[5]	1.04	(0.76-1.42)	.80
MASS II[14]	0.95	(0.56-1.62)	.86
COURAGE[6]	0.88	(0.65-1.19)	.40
JSAP[21]	0.85	(0.28-2.58)	.78
BARI 2D[7]	1.06	(0.79-1.43)	.70
	0.98	(0.83-1.15)	.83

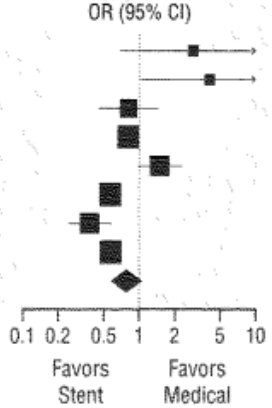
Heterogeneity Q=1.52 (P=.98); I^2=0.00



Mortality

Source	OR (95% CI)		P Value
TOAT[16]	2.89	(0.68-12.35)	.15
Hambrect et al[17]	4.00	(1.03-15.53)	.05
DECOPI[18]	0.81	(0.45-1.45)	.47
OAT[5]	0.80	(0.64-1.00)	.05
MASS II[14]	1.49	(0.97-2.31)	.07
COURAGE[6]	0.56	(0.46-0.68)	<.001
JSAP[21]	0.37	(0.24-0.58)	<.001
BARI 2D[7]	0.57	(0.46-0.70)	<.001
	0.78	(0.57-1.06)	.11

Heterogeneity Q=38.8 (P<.001); I^2=81.9

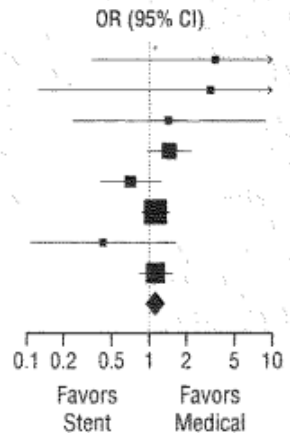


Revascularization

NS

Source	OR (95% CI)		P Value
TOAT[16]	3.41	(0.34-34.65)	.30
Hambrect et al[17]	3.12	(0.12-78.45)	.49
DECOPI[18]	1.43	(0.23-8.73)	.70
OAT[5]	1.45	(0.96-2.19)	.08
MASS II[14]	0.70	(0.39-1.25)	.23
COURAGE[6]	1.12	(0.87-1.45)	.38
JSAP[21]	0.42	(0.11-1.65)	.21
BARI 2D[7]	1.12	(0.82-1.54)	.47
	1.12	(0.93-1.34)	.22

Heterogeneity Q=7.36 (P=.39); I^2=4.86

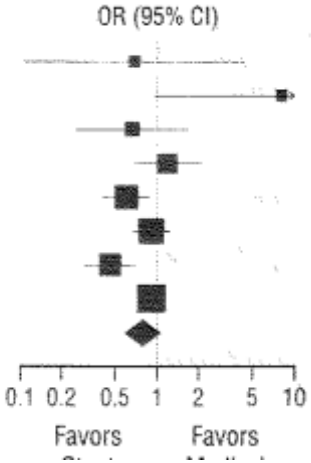


Non fatal MI

NS

Source	OR (95% CI)		P Value
TOAT[16]	0.69	(0.11-4.42)	.69
Hambrect et al[17]	8.14	(0.96-68.81)	.05
DECOPI[18]	0.66	(0.26-1.72)	.40
OAT[5]	1.20	(0.68-2.13)	.53
MASS II[14]	0.60	(0.40-0.89)	.01
COURAGE[6]	0.91	(0.67-1.24)	.56
JSAP[21]	0.46	(0.29-0.72)	<.001
BARI 2D[7]	0.92	(0.75-1.12)	.39
	0.79	(0.60-1.05)	.10

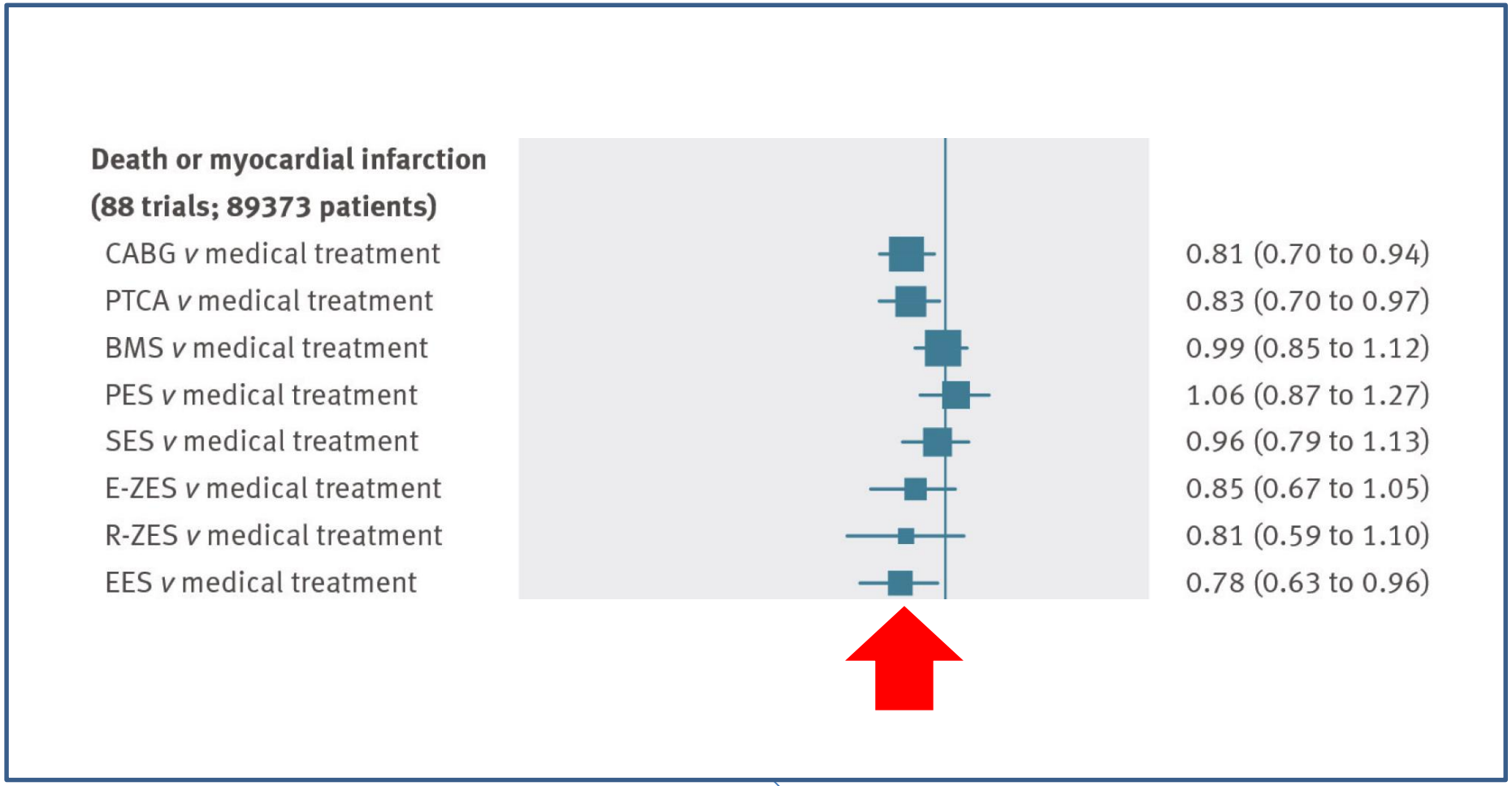
Heterogeneity Q=16.8 (P=.02); I^2=58.2



Persistent angina

Revascularisation versus medical treatment in patients with stable coronary artery disease: network meta-analysis

BMJ 2014



Everolimus

2007 COURAGE n=2287

Optymalne leczenie farmakologiczne vs PCI

	PCI group (n=1149)				Medical therapy group(n=1149)			
Medication	Baseline	1 Yr	3 Yr	5 Yr	Baseline	1 Yr	3 Yr	5 Yr
ACE inhibitor	58%	64%	64%	66%	60%	62%	62%	62%
ARB	4%	9%	12%	11%	5%	10%	13%	16%
Statin	86%	93%	93%	93%	89%	95%	92%	93%
Other antilipid	8%	23%	39%	49%	8%	25%	38%	54%
Aspirin				95%	95%			
Beta - blocker				85%	89%			
Calcium chanel blocker				42%	43%			
Nitrates*				40%	72%			
Angina free**	12%	66%	72%	74%	13%	58%	67%	72%

U 21% chorych wykonano PCI

U 32% chorych wykonano PCI

94% - stent

*Wszystkie różnice istotne **Różnice istotne tylko w 1 i 3 roku

- choroba naczyń (%) :
  - 1- 31 vs 30
  - 2 - 39 vs 39
  - 3 - 30 vs 31.
- cholesterol, RR, BMI - ns

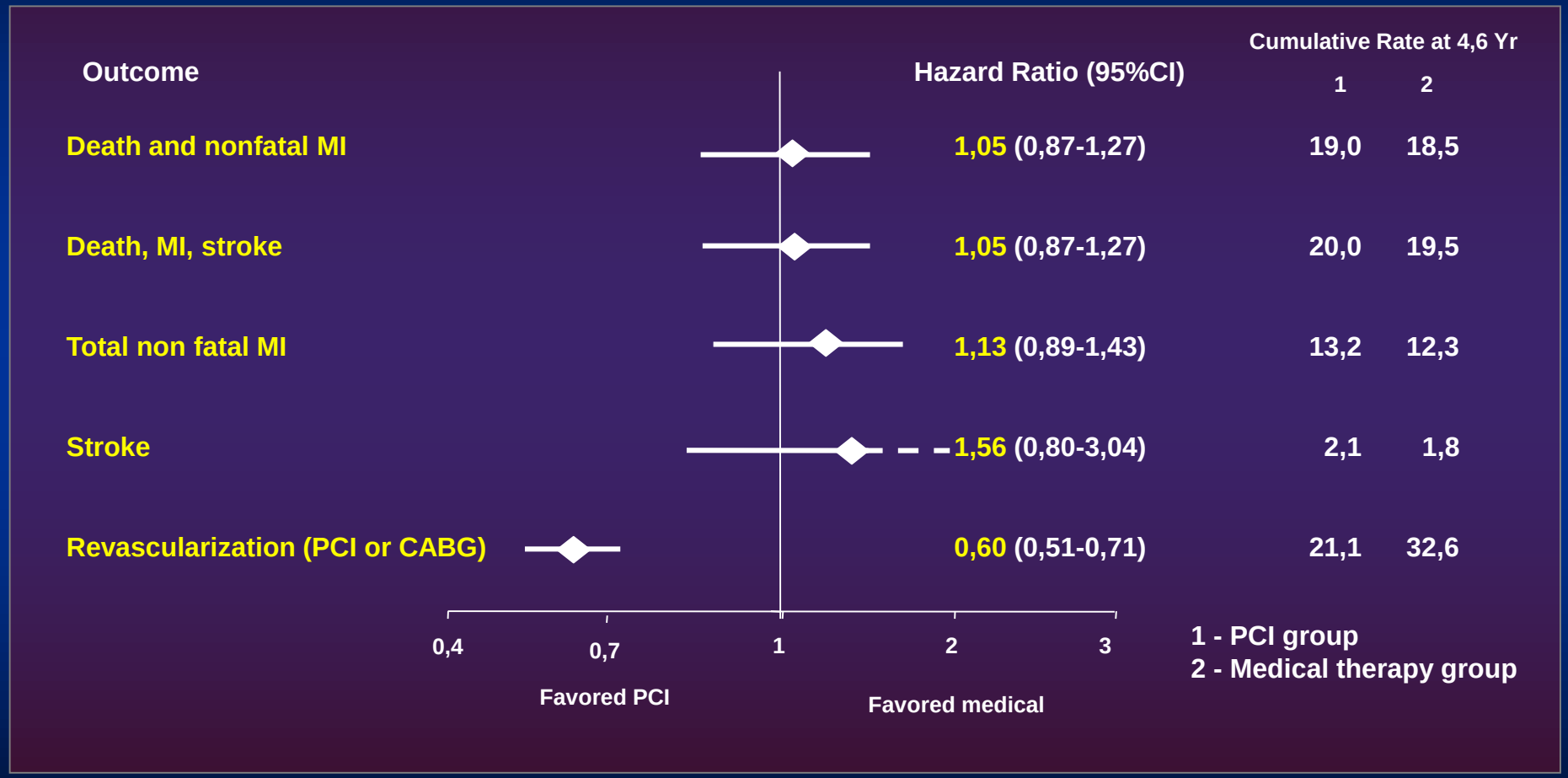
EF 60% vs 60%
CCS I- III

Boden W.E. et all NEJM 2007;356

2007 COURAGE

n=2287

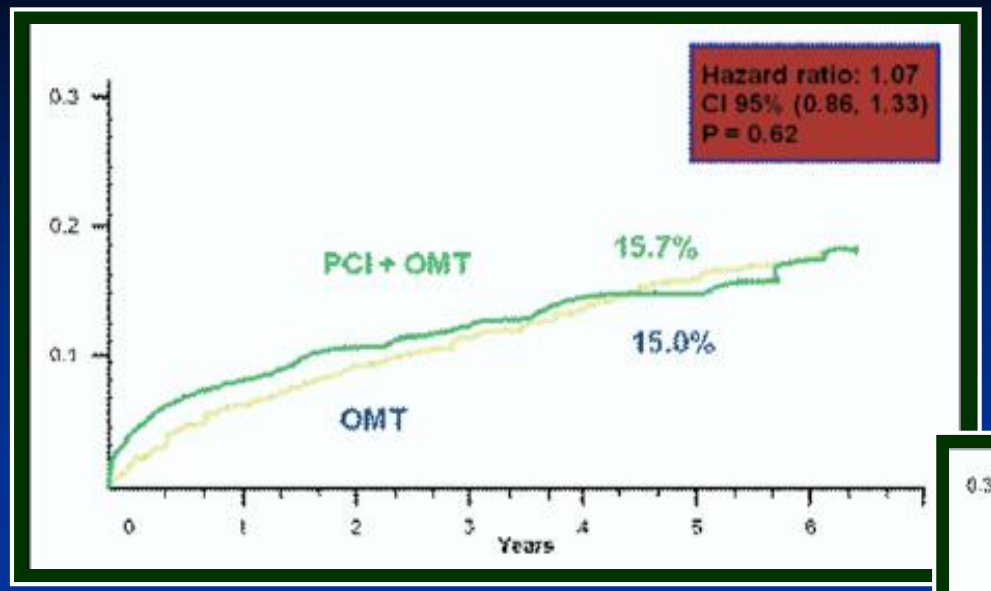
Optymalne leczenie farmakologiczne vs PCI



Złożony punkt końcowy: płeć, wiek, EF, czynniki ryzyka, liczba naczyń, CCS - ns!

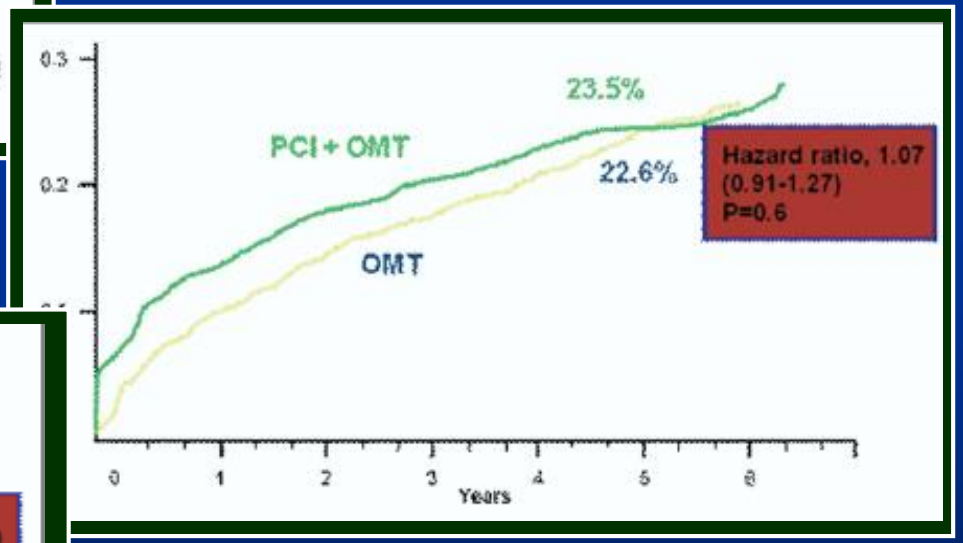
Boden W.E. et all NEJM 2007;356

Zgon sercowy/MI

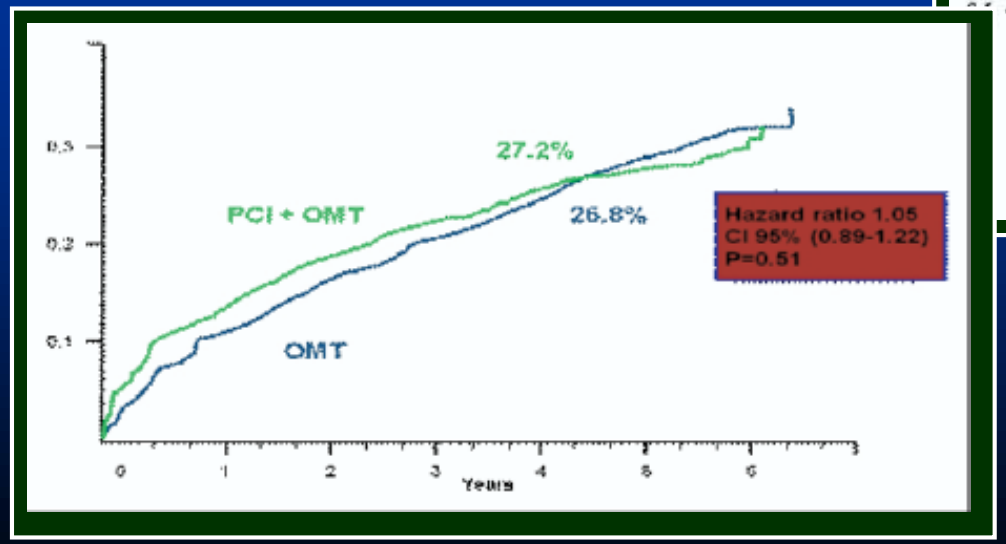


Courage 7 lat

Zgon sercowy/MI/hospitalizacja



Zgon sercowy/MI/udar/hospitalizacja

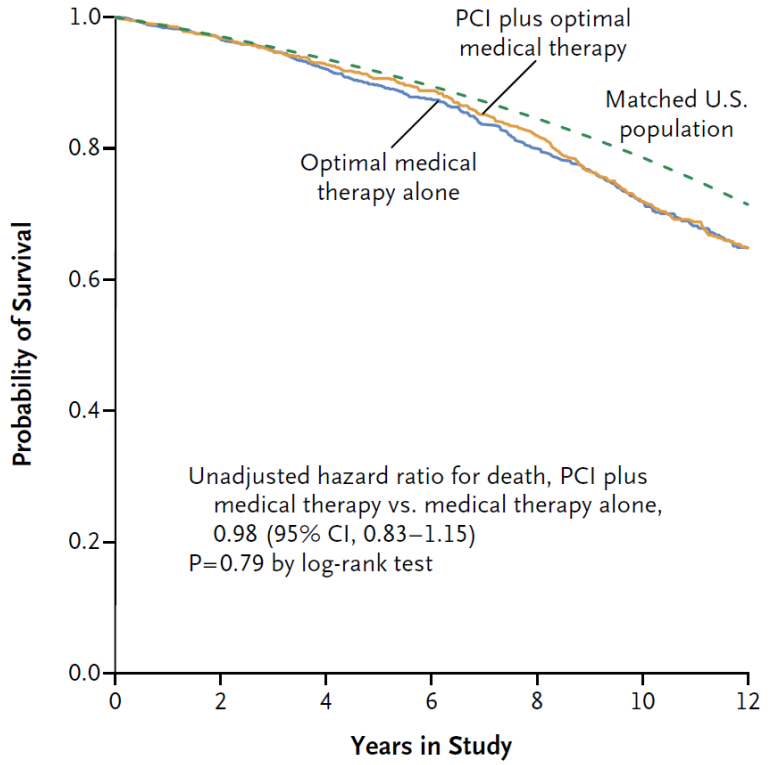


Boden W et al. Am J Cardiol 2010

Effect of PCI on Long-Term Survival in Patients with Stable Ischemic Heart Disease

Steven P. Sedlis, M.D., Pamela M. Hartigan, Ph.D., Koon K. Teo, M.B., B.Ch., Ph.D., David J. Maron, M.D., John A. Spertus, M.D., M.P.H., G.B. John Mancini, M.D., William Kostuk, M.D., Bernard R. Chaitman, M.D., Daniel Berman, M.D., Jeffrey D. Lorin, M.D., Marcin Dada, M.D., William S. Weintraub, M.D., and William E. Boden, M.D., for the COURAGE Trial Investigators*

A Whole Study Cohort

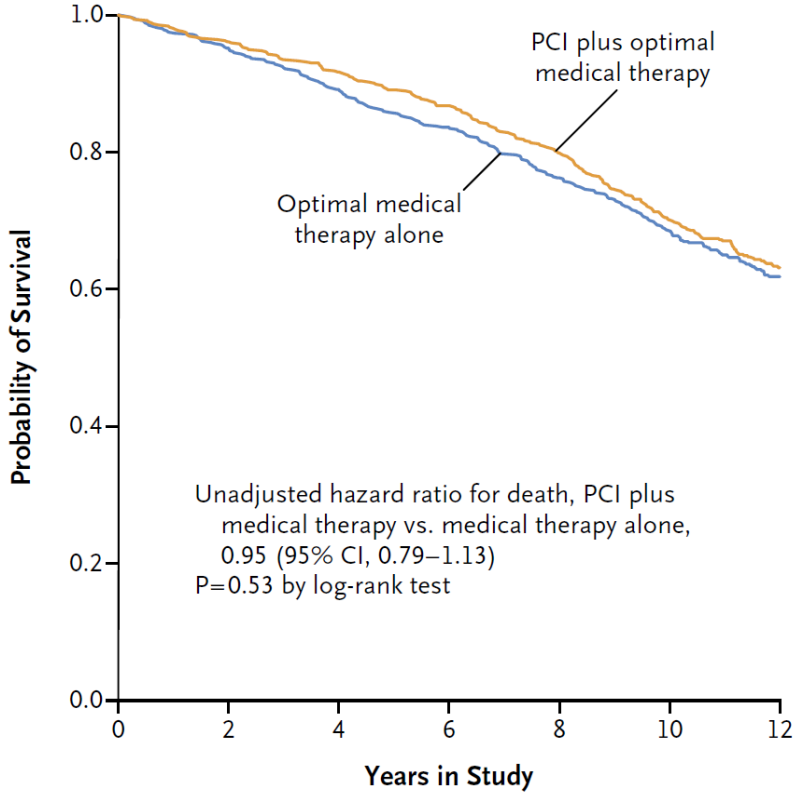


No. at Risk							
Optimal medical therapy	1138	1072	869	590	455	403	280
PCI plus optimal medical therapy	1149	1088	894	620	486	416	302

COURAGE 12-15 lat obserwacji

NEJM 2016

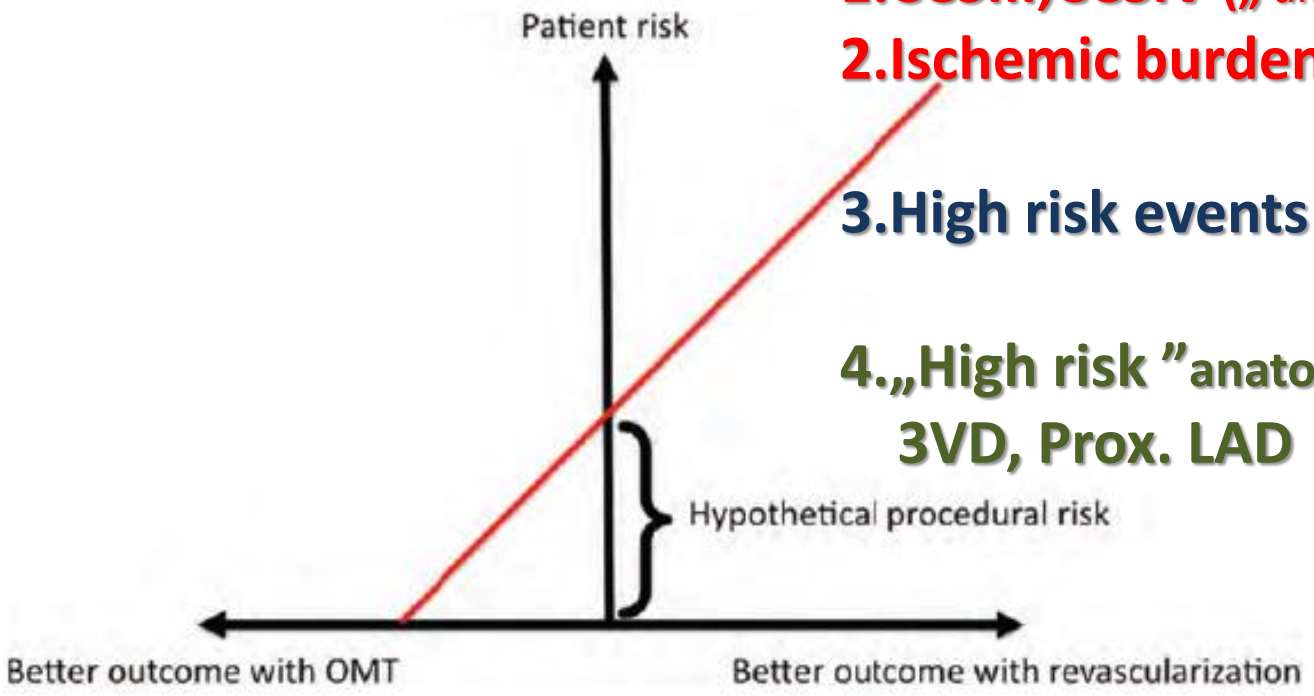
B Extended Follow-up Study Cohort



No. at Risk							
Optimal medical therapy	598	569	533	500	455	403	280
PCI plus optimal medical therapy	613	589	561	529	486	416	302

Benefit of revascularization for stable ischaemic heart disease: the jury is still out

Amir-Ali Fassa[1], William Wijns[2], Philippe Kolh[3], and Philippe Gabriel Steg[1,4,5]*



1.CCSIII,CCSIV („ *angina crescendo*”)

2.Ischemic burden > 10-15%

3.High risk events >3%;EF<50%

4.„High risk ”anatomy CT; LM, 3VD, Prox. LAD

Eur Heart J 2013

Original Investigation

Prevalence of Anginal Symptoms and Myocardial Ischemia and Their Effect on Clinical Outcomes in Outpatients With Stable Coronary Artery Disease

Data From the International Observational CLARIFY Registry

Philippe Gabriel Steg, MD; Nicola Greenlaw, MSc; Michal Tendera, MD; Jean-Claude Tardif, MD; Roberto Ferrari, MD; Muayed Al-Zaibag, MD; Paul Dorian, MD; Dayi Hu, MD; Svetlana Shalnova, MD; Fernando José Sokn, MD; Ian Ford, PhD; Kim M. Fox, MD; for the Prospective Observational Longitudinal Registry of Patients With Stable Coronary Artery Disease (CLARIFY) Investigators

JAMA 2014

58,2% Death or MI

N = 20291

Figure 2. Clinical Patterns of Stable Coronary Artery Disease

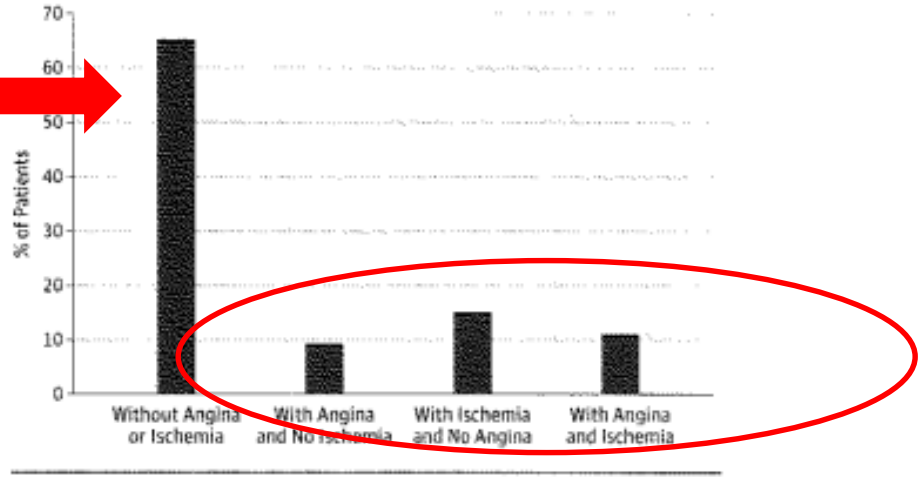
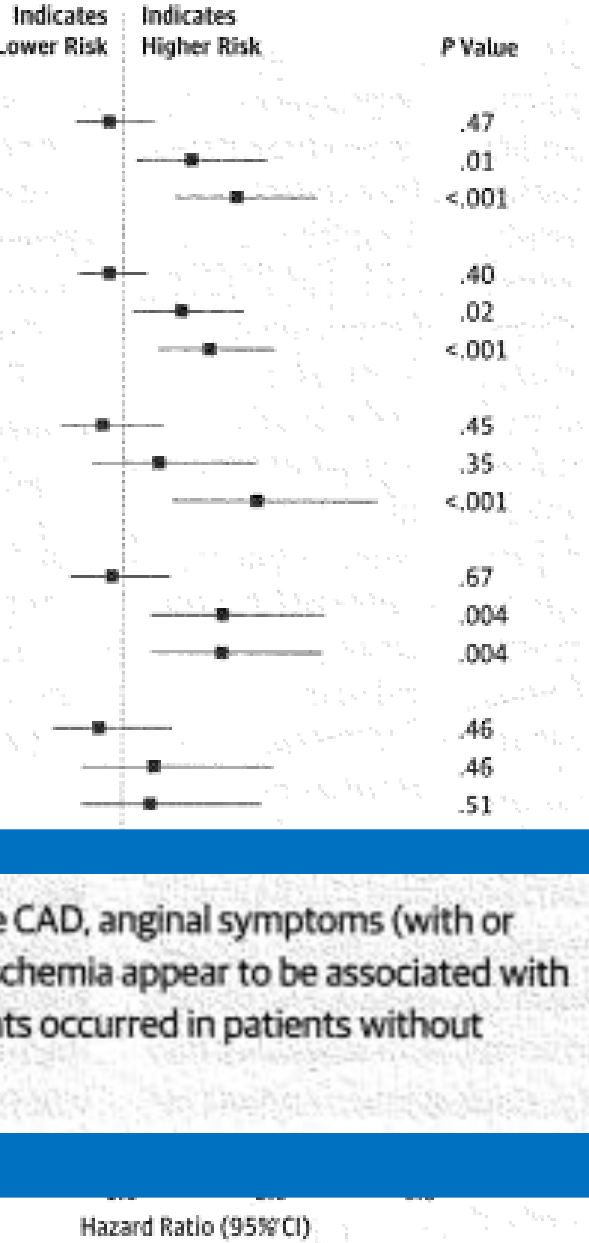


Table 2. Unadjusted 2-Year Event Percentages for the 4 Patient Groups

Outcome	Patient Group, %				
	No Angina or Ischemia (n = 13 207)	Ischemia and No Angina (n = 3028)	Angina and No Ischemia (n = 1842)	Angina and Ischemia (n = 2214)	*P* Value[a]
CV-related death or MI[b]	2.11	1.94	3.13	3.72	<.001
CV death, MI, or stroke	2.75	2.54	3.89	4.41	<.001
CV-related death	1.17	1.03	1.36	2.07	.004
MI[c]	1.35	1.27	2.36	2.34	<.001
Stroke[c]	0.82	0.73	1.04	1.06	.46
All-cause death	2.62	2.84	2.93	3.52	.10
Major bleeding	0.87	0.74	0.67	0.65	.62

Outcome by Patient Group	HR (95% CI)	P Value
CV-related death, nonfatal MI		
Ischemia only	0.90 (0.68-1.20)	.47
Angina only	1.45 (1.08-1.95)	.01
Both	1.75 (1.34-2.29)	<.001
CV-related death, nonfatal MI, or stroke		
Ischemia only	0.90 (0.70-1.15)	.40
Angina only	1.38 (1.06-1.80)	.02
Both	1.57 (1.23-2.01)	<.001
CV-related death		
Ischemia only	0.86 (0.58-1.27)	.45
Angina only	1.23 (0.80-1.89)	.35
Both	1.89 (1.33-2.70)	<.001
MI[a]		
Ischemia only	0.93 (0.65-1.32)	.67
Angina only	1.67 (1.18-2.35)	.004
Both	1.66 (1.18-2.33)	.004
Stroke[a]		
Ischemia only	0.84 (0.53-1.33)	.46
Angina only	1.21 (0.73-2.00)	.46
Both	1.18 (0.72-1.92)	.51



CONCLUSIONS AND RELEVANCE In outpatients with stable CAD, anginal symptoms (with or without ischemia on noninvasive testing) but not silent ischemia appear to be associated with an increased risk for adverse CV outcomes. Most CV events occurred in patients without angina or ischemia.

Percutaneous Coronary Intervention Outcomes in Patients With Stable Obstructive Coronary Artery Disease and Myocardial Ischemia

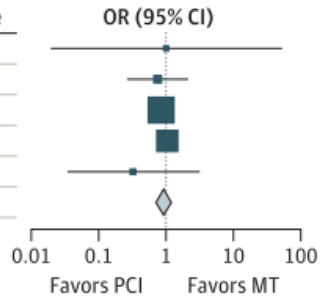
A Collaborative Meta-analysis of Contemporary Randomized Clinical Trials

JAMA 2014

Kathleen Stergiopoulos, MD, PhD; William E. Boden, MD; Pamela Hartigan, PhD; Sven Möbius-Winkler, MD; Rainer Hambrecht, MD; Whady Hueb, MD, PhD; Regina M. Hardison, MS; J. Dawn Abbott, MD; David L. Brown, MD

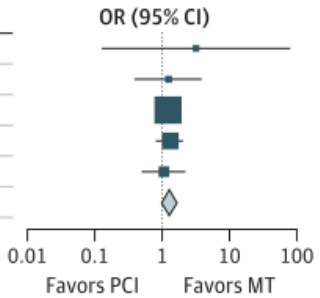
A **Death**

Source	OR (95% CI)	*P* Value
Hambrecht[15]	1.02 (0.02-52.43)	.99
MASS II[13]	0.76 (0.27-2.16)	.60
COURAGE[17]	0.84 (0.61-1.18)	.32
BARI 2D[14]	1.06 (0.71-1.58)	.78
FAME 2[16]	0.33 (0.03-3.16)	.33
Overall	0.90 (0.71-1.16)	.42



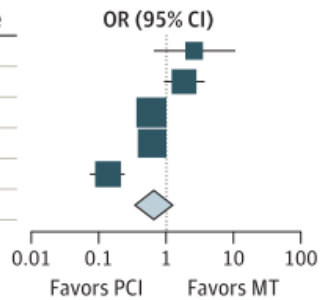
B **Non-fatal MI**

Source	OR (95% CI)	*P* Value
Hambrecht[15]	3.12 (0.12-78.45)	.49
MASS II[13]	1.24 (0.40-3.88)	.71
COURAGE[17]	1.24 (0.94-1.65)	.13
BARI 2D[14]	1.29 (0.82-2.04)	.27
FAME 2[16]	1.06 (0.51-2.22)	.88
Overall	1.24 (0.99-1.55)	.06



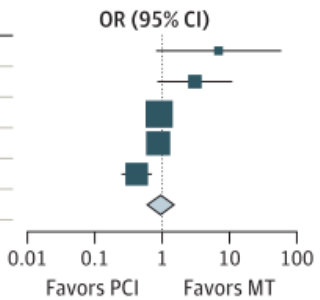
C

Source	OR (95% CI)	*P* Value
Hambrecht[15]	2.60 (0.63-10.71)	.18
MASS II[13]	1.84 (0.91-3.73)	.09
COURAGE[17]	0.60 (0.48-0.74)	<.001
BARI 2D[14]	0.61 (0.46-0.80)	<.001
FAME 2[16]	0.13 (0.07-0.24)	<.001
Overall	0.64 (0.35-1.17)	.14



D

Source	OR (95% CI)	*P* Value
Hambrecht[15]	6.82 (0.79-58.85)	.08
MASS II[13]	3.06 (0.83-11.29)	.09
COURAGE[17]	0.91 (0.74-1.10)	.33
BARI 2D[14]	0.87 (0.59-1.28)	.47
FAME 2[16]	0.42 (0.25-0.72)	<.001
Overall	0.90 (0.57-1.44)	.67



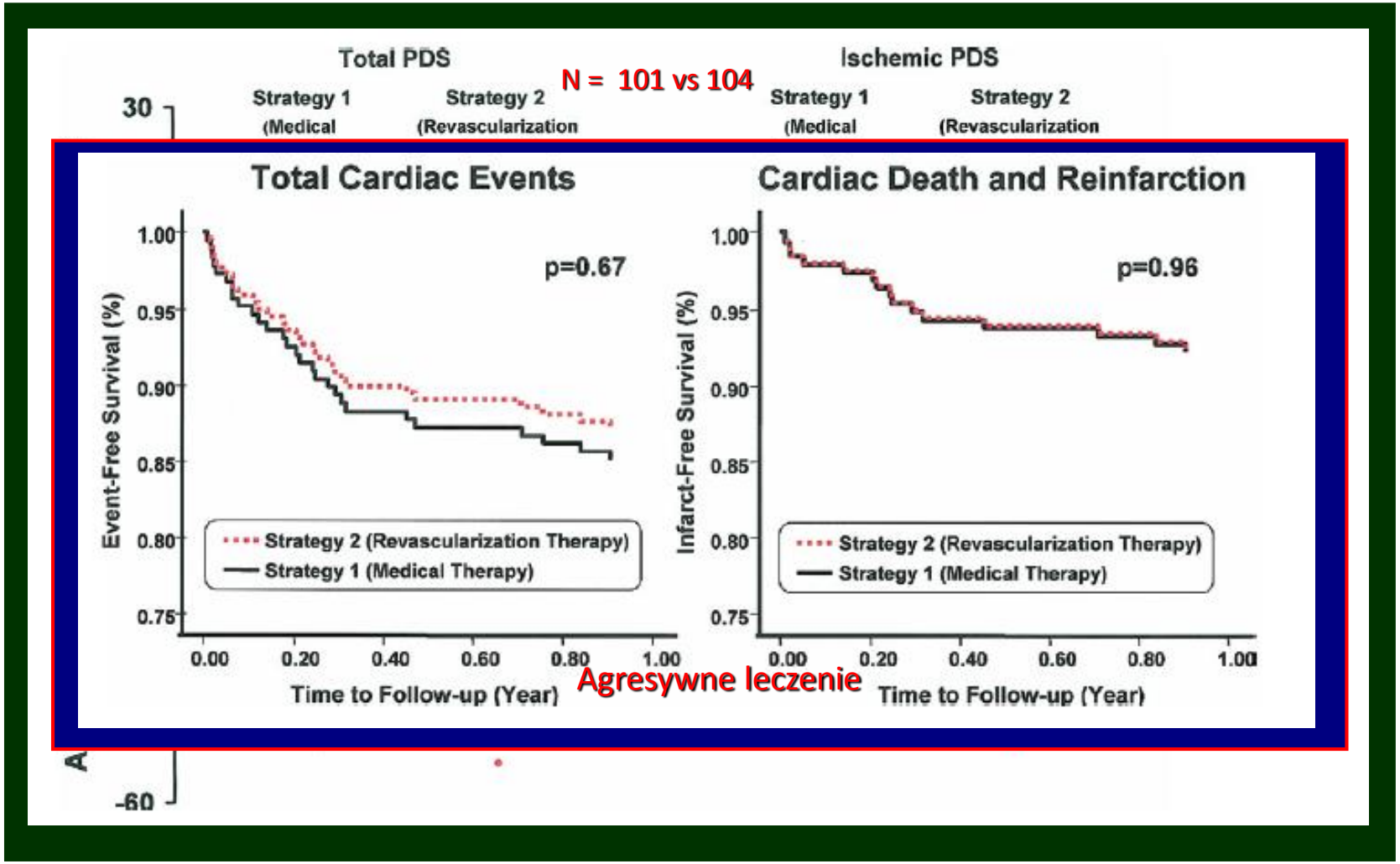
Unplaned revascularisation

Angina during follow-up

Wysokie ryzyko zgonu.

INSPIRE

Chorzy po zawale serca, stabilna dławica prawidłowa EF
Adenosine induced total Perfusion Defect Size > 20%,
ischemic PDS > 10%



EF 47 % vs 49% Ponowne badanie SPECT po 2 miesiacach

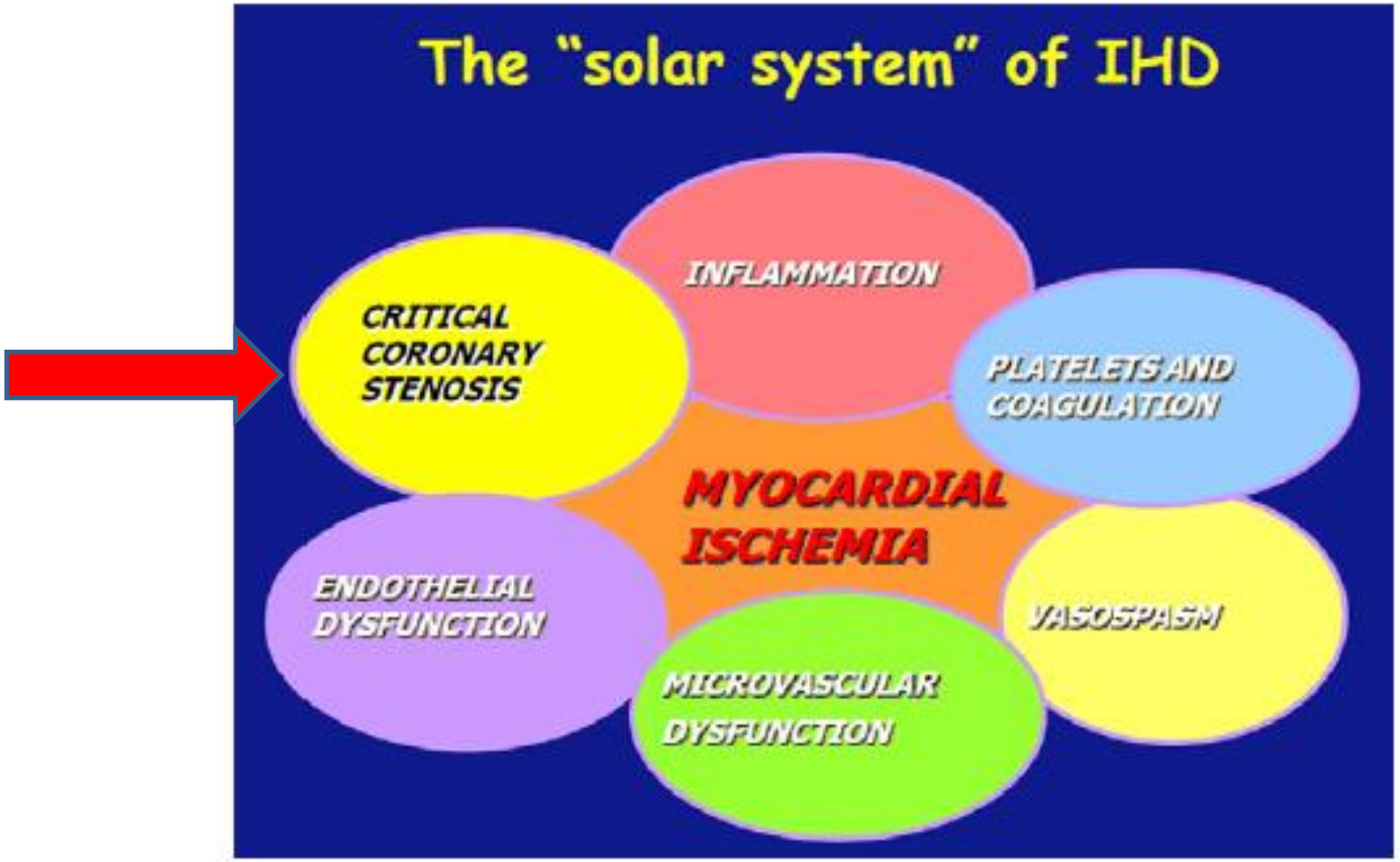
Mahmarian J et al. JACC 2006

2013 ESC guidelines on the management of stable coronary artery disease—addenda

Table W3 Decision making according to severity of symptoms/ischaemia

Severe: Angina CCS III–IV or ischaemia >10% ➡ catheterization laboratory.
Moderate-to-severe: Angina CCS II or ischaemia 5–10% ➡ OMT[a] only or catheterization laboratory.
Mild-to-moderate: Angina CCS I or ischaemia <5% ➡ OMT[a] first and defer catheterization laboratory.

Coronary Heart Disease vs Ischemic Heart disease



Marzilli M et al. JACC 2012

European Heart Journal Advance Access published August 30, 2013

European Heart Journal
doi:10.1093/eurheartj/eht296

ESC GUIDELINES

2013 ESC guidelines on the management of stable coronary artery disease

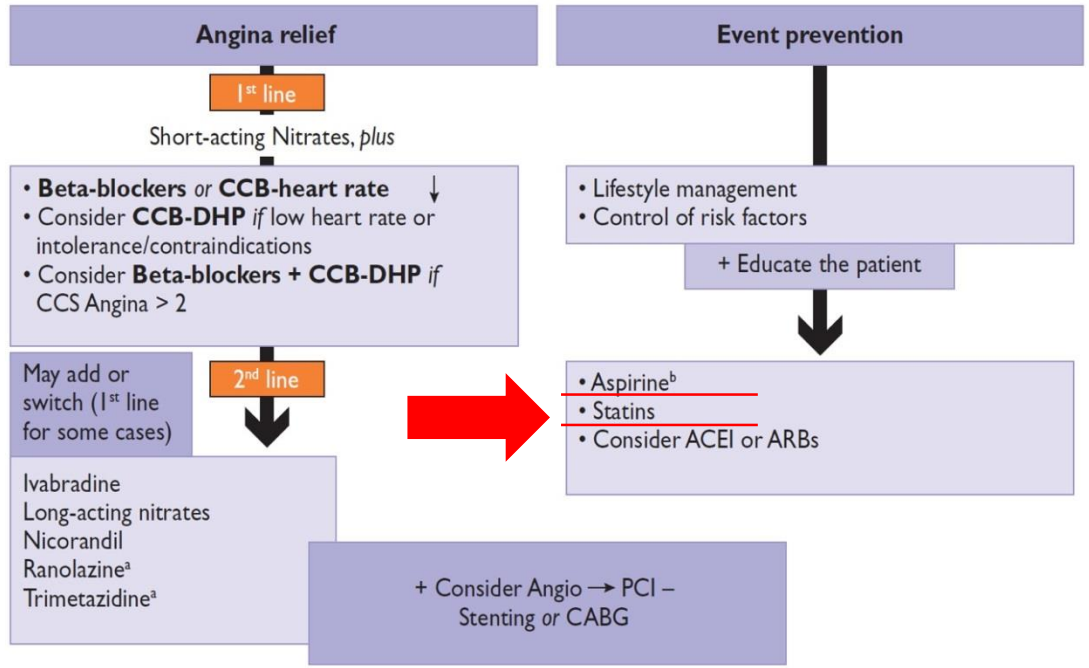


Figure 4 Medical management of patients with stable coronary artery disease. ACEI = angiotensin converting enzyme inhibitor; CABG = coronary artery bypass graft; CCB = calcium channel blockers; CCS = Canadian Cardiovascular Society; DHP = dihydropyridine; PCI = percutaneous coronary intervention.

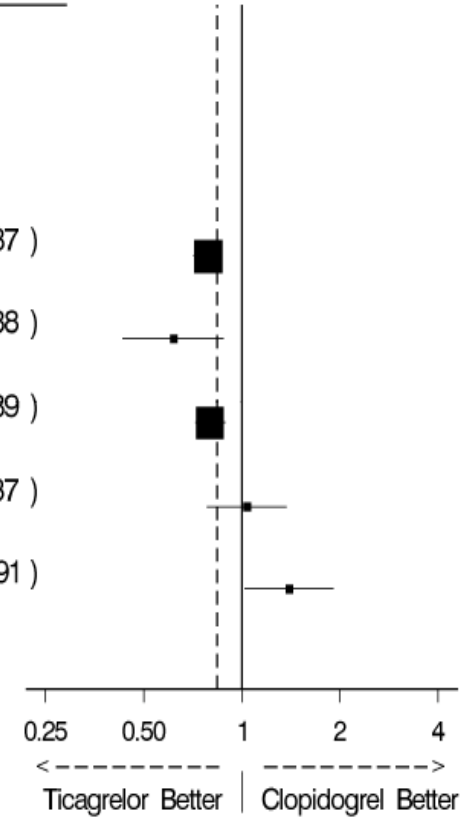
[a]Data for diabetics.

[b]if intolerance, consider clopidogrel

1.

Aspiryna osłabia kliniczną skuteczność Tikagreloru .

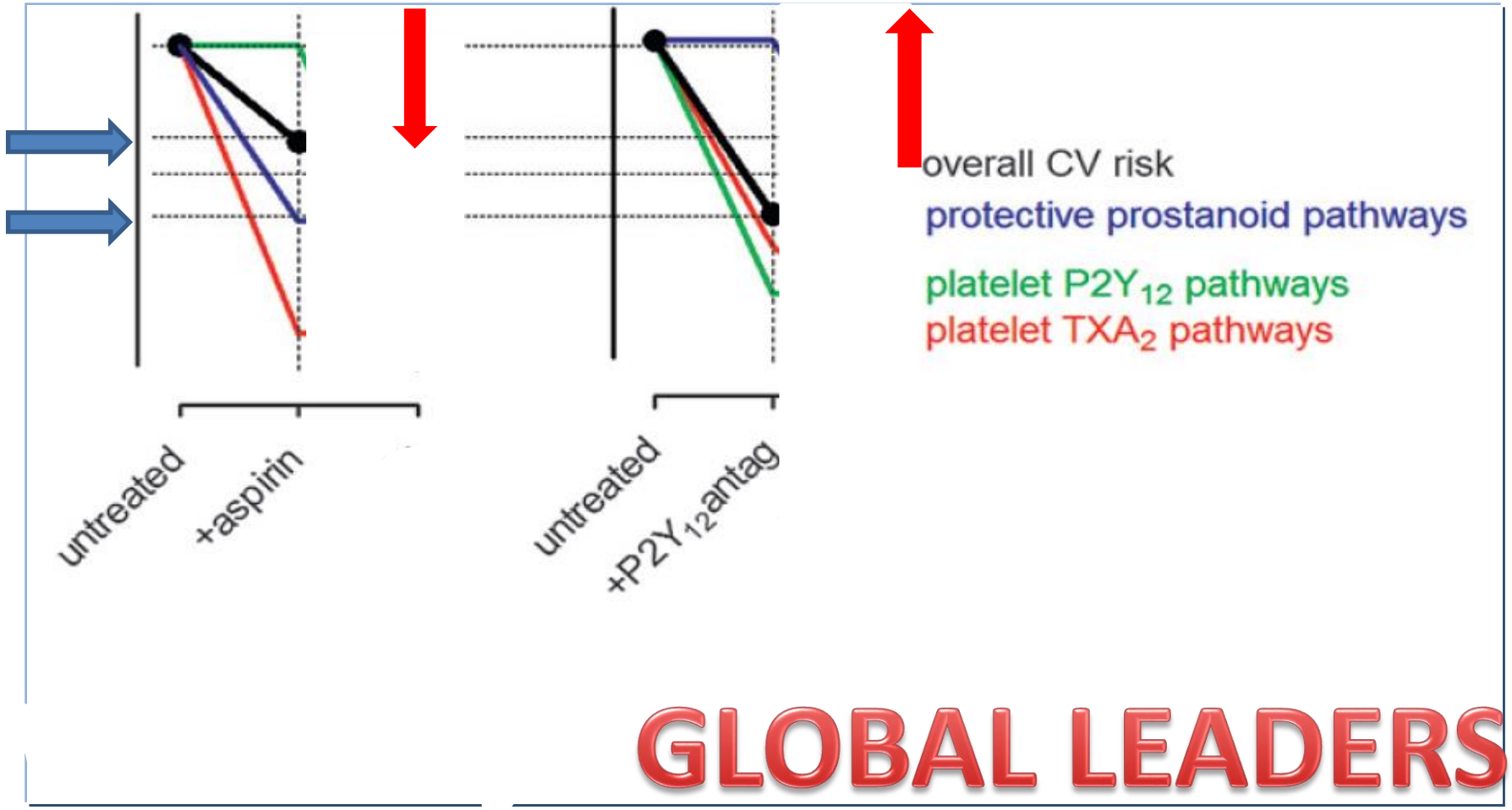
ASA Dose	Ticagrelor N	Ticagrelor E	Clopidogrel N	Clopidogrel E	HR (95% CI)
A6: Med. 30d prior to PE/Censor					
< = 100mg	8362	677	8275	845	0.79 (0.71, 0.87)
0mg	460	50	456	78	0.62 (0.43, 0.88)
> 0 – < = 100mg	7902	627	7819	767	0.80 (0.72, 0.89)
> 100 – < 300mg	535	98	562	101	1.04 (0.78, 1.37)
> = 300mg	436	89	454	68	1.40 (1.02, 1.91)



Zgon CV, zawał, udar vs dawka ASA

PLATO L. Wallentin 2010

Hipoteza niekorzystnego działania aspiryny z silnym inhibitorem receptora P2Y12



Warner TD, Armstrong P, Curzen NP. Heart 2010;96:1693-4

mes after coronary

stents (ADAPT-DES):

	Event	No event	Unadjusted HR (95% CI)	p value
Definite ST				
Number of events	53	8530		
Deaths	5 (9·6%)	156 (1·9%)	5·47 (2·25–13·31)	<0·0001
MI without ST				
Number of events	224	8359		
Deaths	21 (9·7%)	140 (1·7%)	5·78 (3·65–9·14)	<0·0001
Bleeding				
Number of events	531	8052		
Deaths	45 (8·6%)	116 (1·5%)	5·97 (4·23–8·42)	<0·0001

HR=hazard ratio. MI=myocardial infarction. ST=stent thrombosis.

Table 6: Relationship between adverse events and death though 1 year follow-up

Aspiryna nie redukuje

umani… D Christopher Metzger, Timothy D Henry,

…Mehran,

Aspiryna nie redukuje

Aspiryna zwiększa

					ar (unadjusted)		Adjusted HR (95% CI)	p value
porność					ARU >550 (n=478)	ARU ≤550 (n=8049)		
Definite or probable	1·3% (45)	0·5% (24)	2·49 (1·43–4·31)	0·001	1·1% (5)	0·8% (64)	1·46 (0·58–3·64)	0·42
Definite	1·0% (35)	0·4% (18)	3·05 (1·62–5·75)	0·0006	0·9% (4)	0·6% (48)	1·60 (0·57–4·48)	0·37
Myocardial infarction	3·9% (137)	2·7% (126)	1·42 (1·09–1·86)	0·01	2·8% (13)	3·2% (253)	0·81 (0·46–1·42)	0·46
Clinically relevant bleeding	5·6% (198)	6·7% (320)	0·73 (0·61–0·89)	0·002	5·4% (26)	6·2% (501)	0·65 (0·43–0·99)	0·04
Death, all-cause*	2·4% (85)	1·5% (71)	1·20 (0·85–1·70)	0·30	3·7% (17)	1·8% (143)	1·42 (0·83–2·43)	0·20

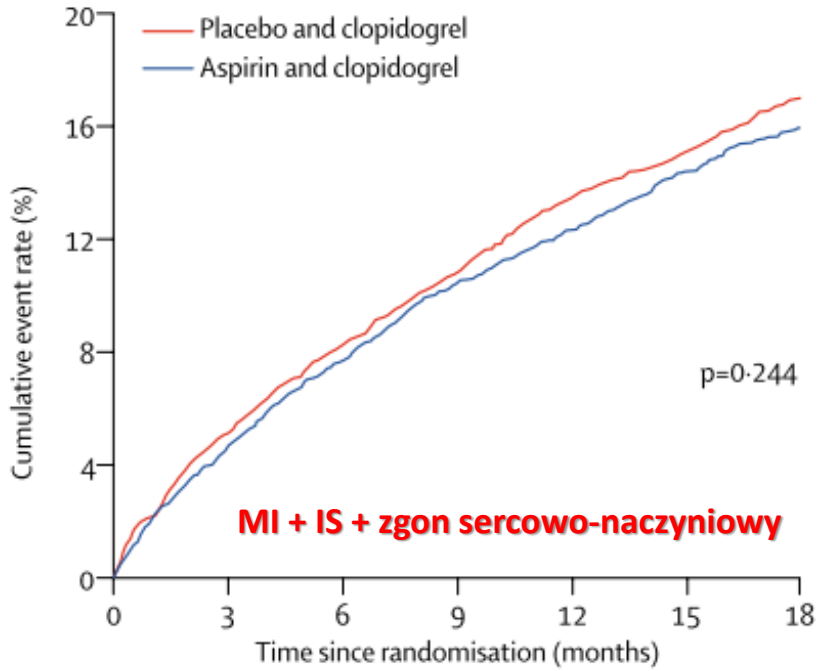
72,5% miało wszczepiony everolimus lub zotarolimus.

Table 4: Propensity-adjusted multivariable risk of high platelet reactivity for subsequent 1-year adverse events

Skuteczne blokada aktywności płytek przez aspirynę nie przyniosła korzystnych efektów a zwiększyła istotnie powikłania krwotoczne.

Aspirin and clopidogrel compared with clopidogrel alone after recent ischaemic stroke or transient ischaemic attack in high-risk patients (MATCH): randomised, double-blind, placebo-controlled trial

Lancet 2004



MI + IS + zgon sercowo-naczyniowy

	Number (%) with event		Difference (%) between aspirin and placebo (95% CI)	p*
	Aspirin and clopidogrel (n=3759)	Placebo and clopidogrel (n=3781)		
Life-threatening bleeding	96 (3%)	49 (1%)	1·26 (0·64 to 1·88)	<0·0001
Fatal bleeding	16 (<1%)	11 (<1%)	0·13 (−0·14 to 0·40)	
Non-fatal bleeding	81 (2%)	38 (1%)	1·15 (0·59 to 1·71)	
Symptomatic intracranial haemorrhage†	40 (1%)	25 (1%)	0·40 (−0·01 to 0·82)	
Primary intracranial haemorrhage	32 (1%)	17 (<1%)	0·40 (0·04 to 0·76)	
Major bleeding	73 (2%)	22 (1%)	1·36 (0·86 to 1·86)	<0·0001
Minor bleeding	120 (3%)	39 (1%)	2·16 (1·51 to 2·81)	<0·0001

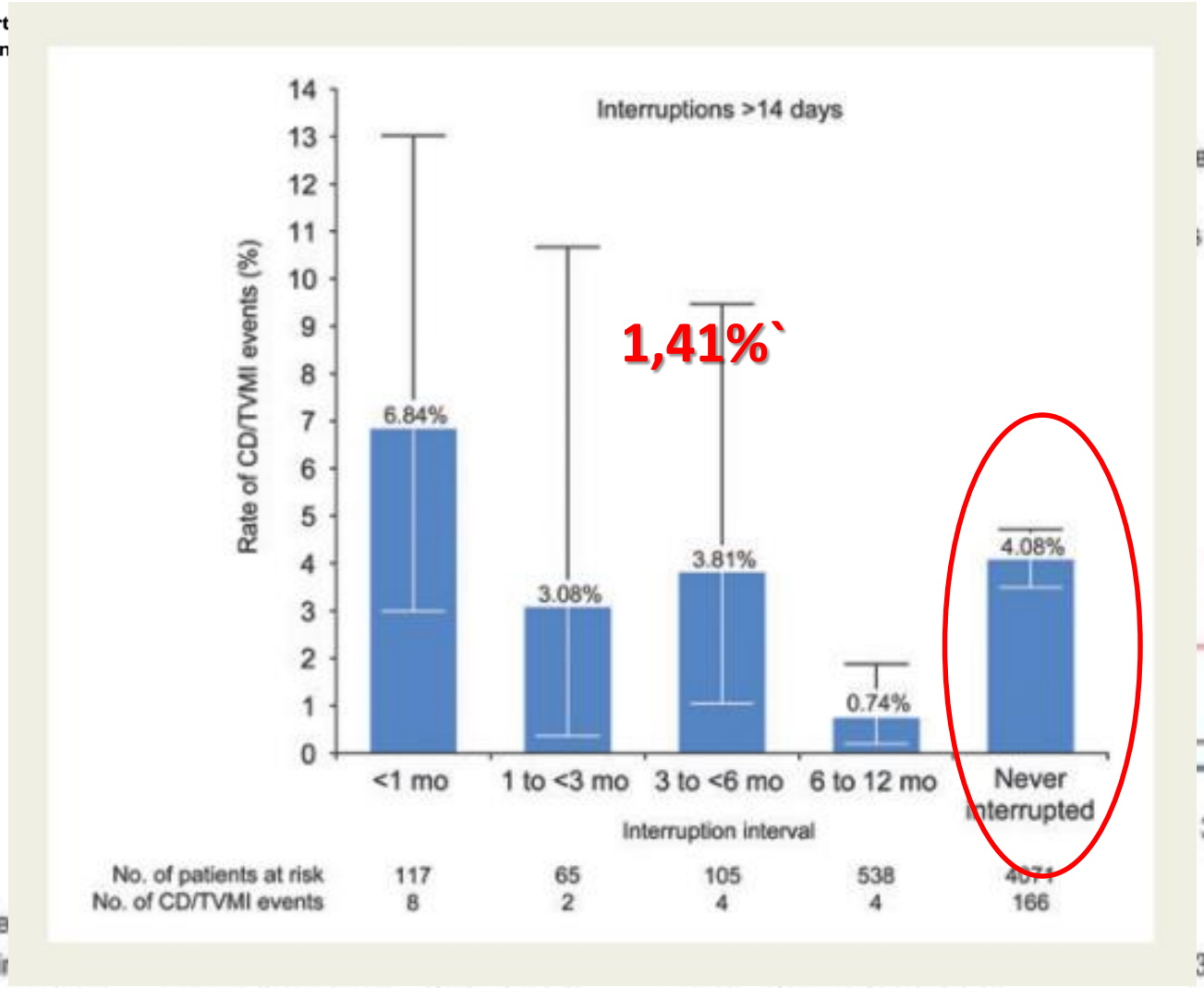
*Pearson's χ^2 test. †All symptomatic (and thus primary) intracranial haemorrhages were life-threatening bleeds.

Table 4: **Number (%) of patients with bleeding events**

Lack of association between dual antiplatelet therapy use and stent thrombosis between 1 and 12 months following resolute zotarolimus-eluting stent implantation

Eur Heart J 2014 *on-line*

Sigmund Silber[1]*, Ajay J. Kirt
Sandeep Brar[4], Martin Rothn



Numbe										
No interruption within										3780
Interrupted 0–1 month	166	164	149	147	144	142	141	139	138	137
Interrupted >1–12 months	903	903	902	892	883	877	855	844	841	837

Lack of association between dual antiplatelet therapy use and stent thrombosis between 1 and 12 months following resolute zotarolimus-eluting stent implantation

Sigmund Silber[1]*, Ajay J. Kirtane[2], Jorge A. Belardi[3], Minglei Liu[4], Sandeep Brar[4], Martin Rothman[4], and Stephan Windecker[5]

Eur Heart J 2014

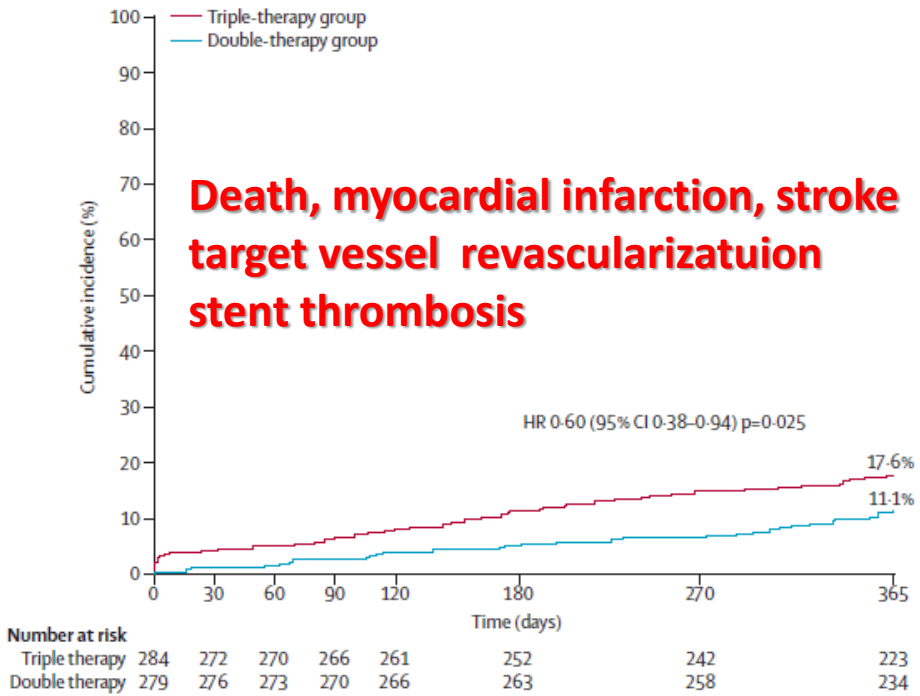
Acetylsalicylate interruption

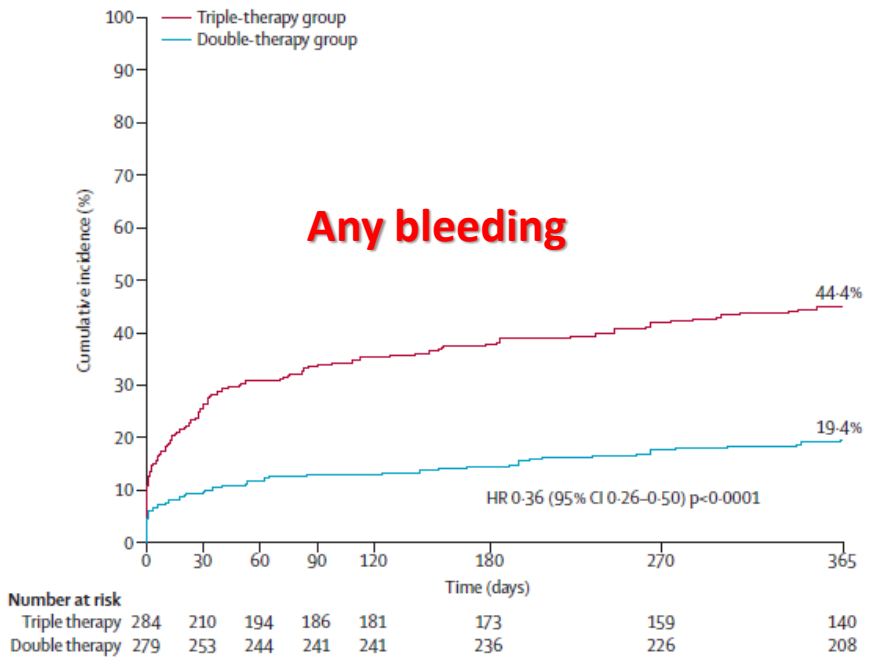
In patients with a DAPT interruption, the ASA alone was interrupted in 196 (18.3%) patients; there were four total ST events in this group. Among patients interrupting ASA only, 78 patients interrupted ASA within 1 month [with four ST events (5.1%)], and 118 patients interrupted ASA between 1 and 12 months (no ST events).

Use of clopidogrel with or without aspirin in patients taking oral anticoagulant therapy and undergoing percutaneous coronary intervention: an open-label, randomised, controlled trial

Lancet 2013

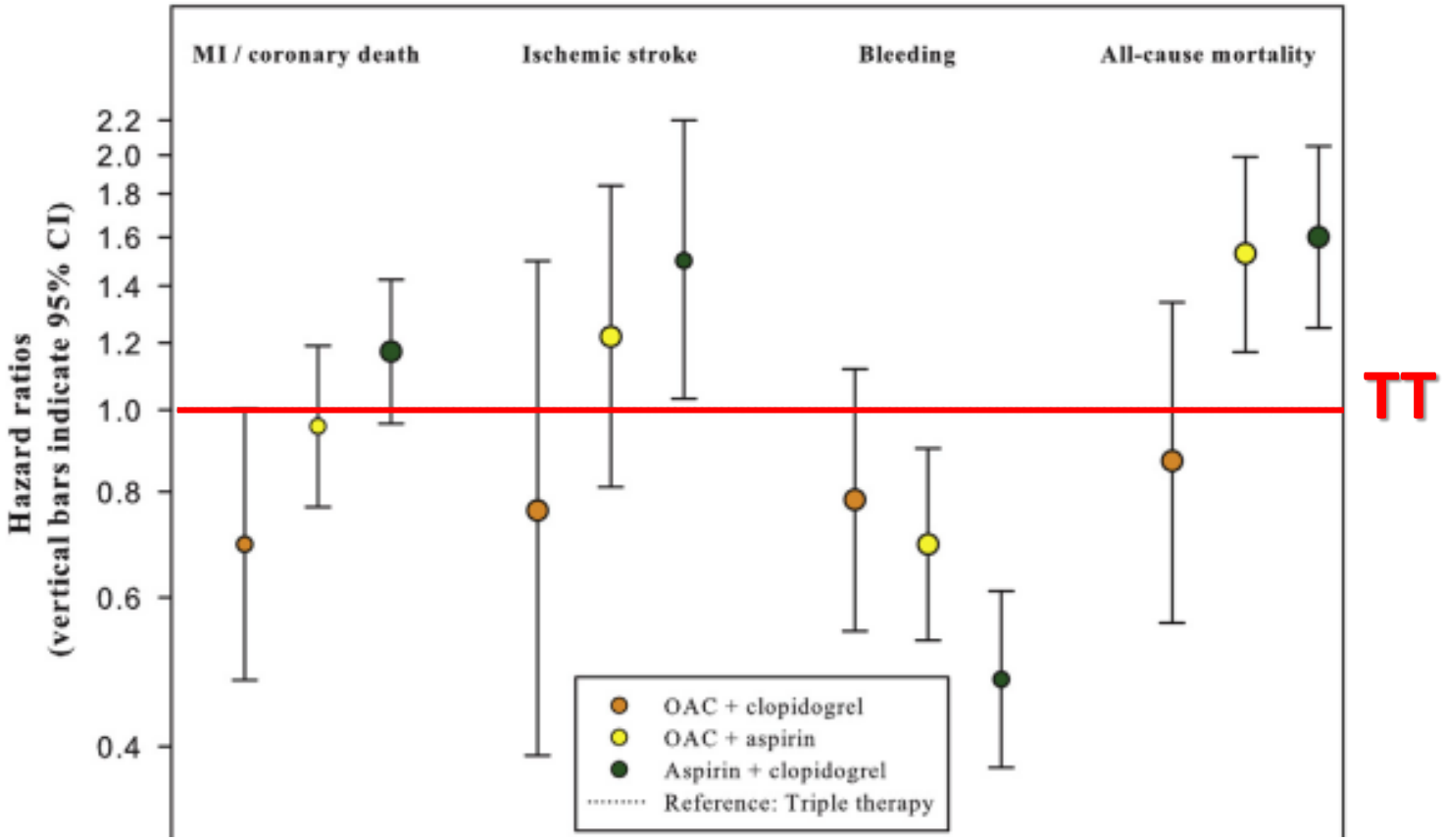
Willem J M Dewilde, Tom Oirbans, Freek W A Verheugt, Johannes C Kelder, Bart J G L De Smet, Jean-Paul Herrman, Tom Adriaenssens, Mathias Vrolix, Antonius A C M Heestermans, Marije M Vis, Jan G P Tijsen, Arnoud W van 't Hof, Jurriën M ten Berg, for the WOEST study investigators





Oral Anticoagulation and Antiplatelets in Atrial Fibrillation Patients After Myocardial Infarction and Coronary Intervention

Lamberts M et al. JACC 2013



Conclusions In real-life AF patients with indication for multiple antithrombotic drugs after MI/PCI, OAC and clopidogrel was equal or better on both benefit and safety outcomes compared to triple therapy. (J Am Coll Cardiol 2013;62:981–9)

Articles

A randomised, blinded, trial of clopidogrel versus aspirin in patients at risk of ischaemic events (CAPRIE)

Klopidogrel 75mg vs aspiryna 375mg
Obserwacja od roku do 3 lat (1,9)

*CAPRIE Steering Committee**

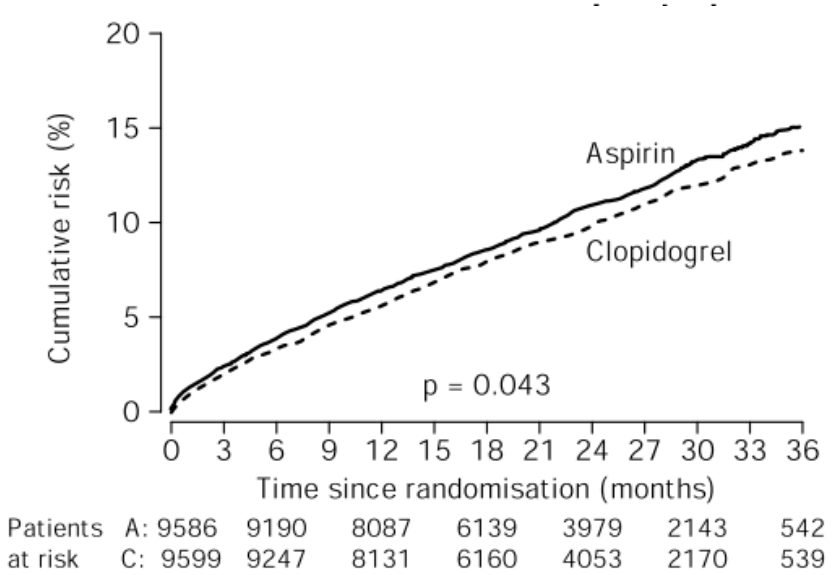
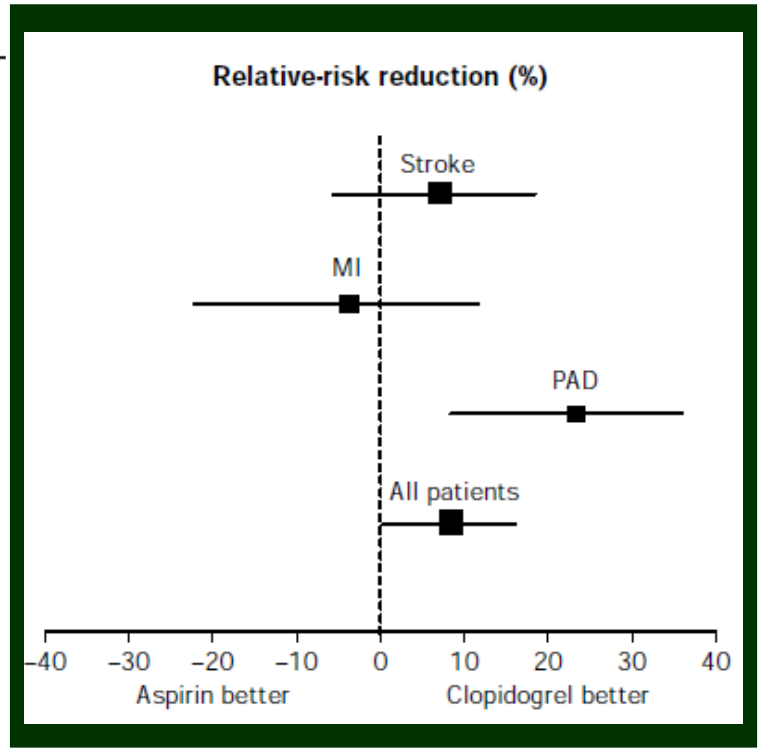


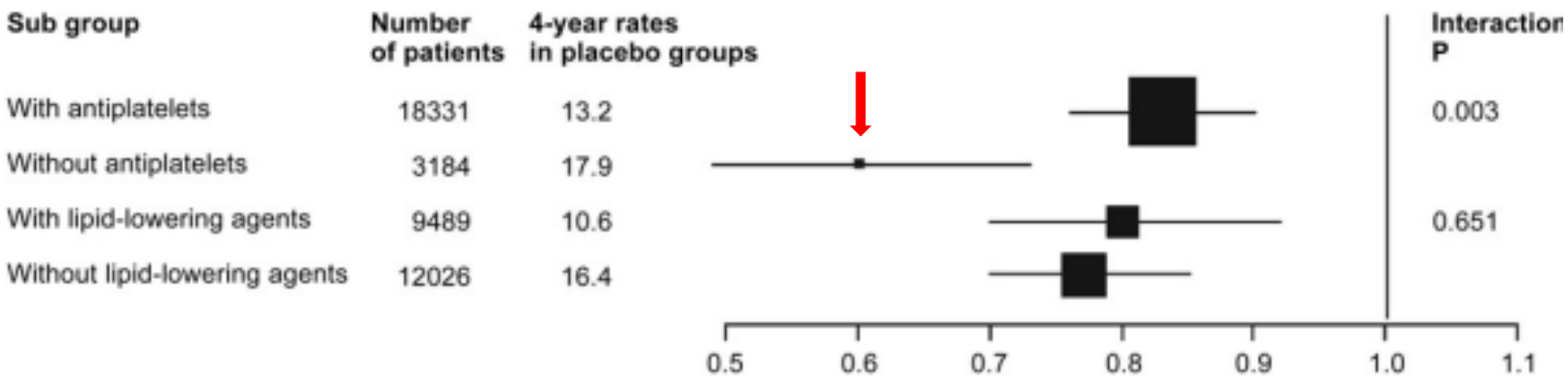
Figure 3: **Cumulative risk of Ischaemic stroke, myocardial infarction, or vascular death**



Adverse experience	Patients ever reporting		Severe	
	Clopidogrel	Aspirin	Clopidogrel	Aspirin
Rash	578 (6·02%)	442 (4·61%)*	25 (0·26%)	10 (0·10%)*
Diarrhoea	428 (4·46%)	322 (3·36%)*	22 (0·23%)	11 (0·11%)
Indigestion/nausea/vomiting	1441 (15·01%)	1686 (17·59%)*	93 (0·97%)	118 (1·23%)
Any bleeding disorder	890 (9·27%)	890 (9·28%)	132 (1·38%)	149 (1·55%)
Intracranial haemorrhage	34 (0·35%)	47 (0·49%)	30 (0·31%)	41 (0·43%)
Gastrointestinal haemorrhage	191 (1·99%)	255 (2·66%)*	47 (0·49%)	68 (0·71%)*
Abnormal liver function	285 (2·97%)	302 (3·15%)*	11 (0·11%)	9 (0·09%)

Lancet 1996

Perindopryl, Ramipryl Trandolapryl



Zgon, Mi – nie zakończony zgonem, Udar.

Cleland J G Eur Heart J 2013;34:3412-3418

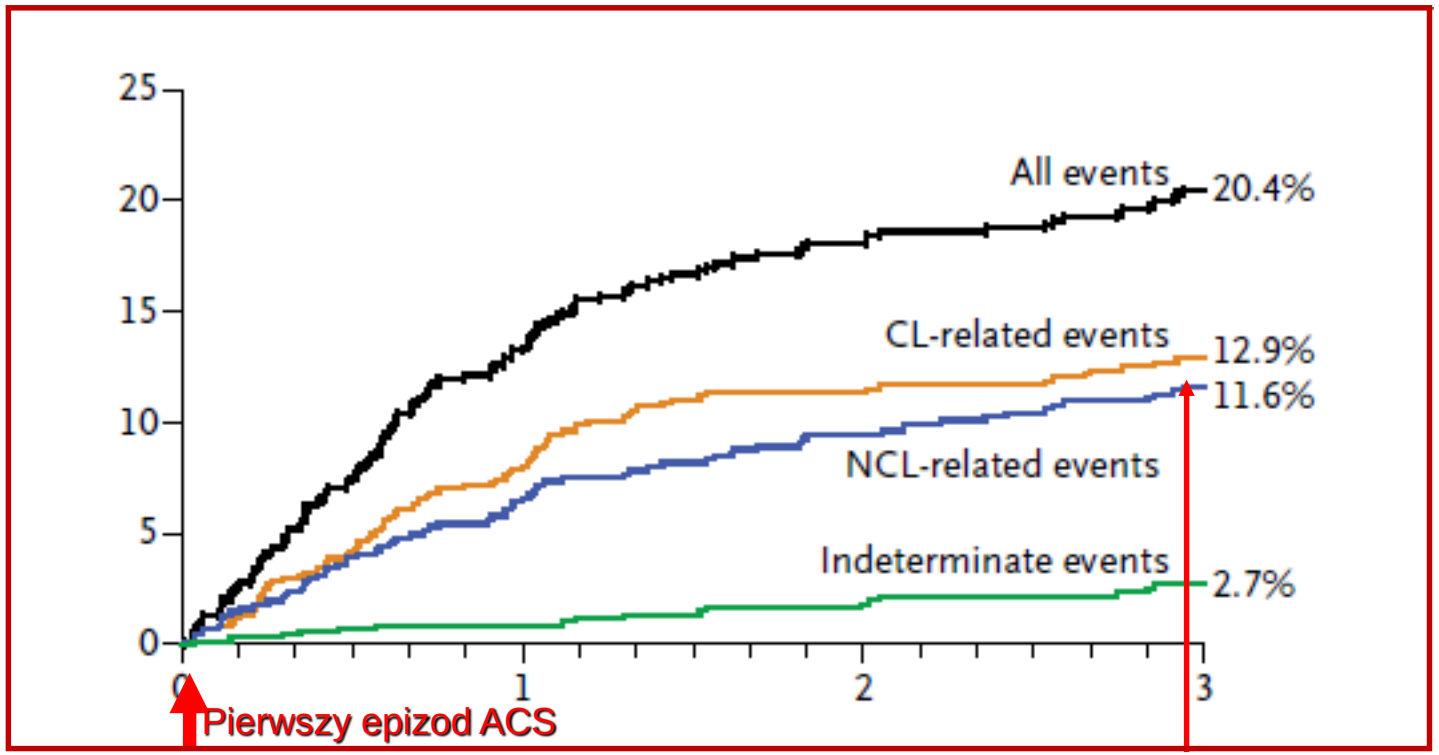
2.

A Prospective Natural-History Study of Coronary Atherosclerosis

Gregg W. Stone, M.D., Akiko Maehara, M.D., Alexandra J. Lansky, M.D., Bernard de Bruyne, M.D., Ecaterina Cristea, M.D., Gary S. Mintz, M.D., Roxana Mehran, M.D., John McPherson, M.D., Naim Farhat, M.D., Steven P. Marso, M.D., Helen Parise, Sc.D., Barry Templin, M.B.A., Roseann White, M.A., Zhen Zhang, Ph.D., and Patrick W. Serruys, M.D., Ph.D., for the PROSPECT Investigators*

NEJM 2011

MACE



IVUS
Virtual Histology

Angio stenosis diameter 32,3% +/-20,6% → 65,4%+/-16,3%

Leczenie: lokalne standardy

Stone G et al. NEJM 2011

Original Investigation

Nonobstructive Coronary Artery Disease and Risk of Myocardial Infarction

Thomas M. Maddox, MD, MSc; Maggie A. Stanislawski; Gary K. Grunwald, PhD; Steven M. Bradley, MD, MPH; P. Michael Ho, MD, PhD; Thomas T. Tsai, MD, MSc; Manesh R. Patel, MD; Amneet Sandhu, MD; Javier Valle, MD; David J. Magid, MD, MPH; Benjamin Leon, BS; Deepak L. Bhatt, MD; Stephan D. Fihn, MD, MPH; John S. Rumsfeld, MD, PhD

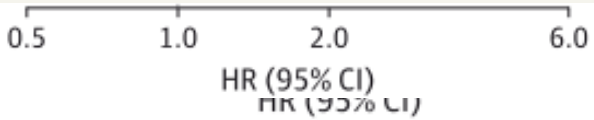
JAMA 2014

Nonobstructive 20%– 70%
No apperent 20%<
Obstructive > 70%

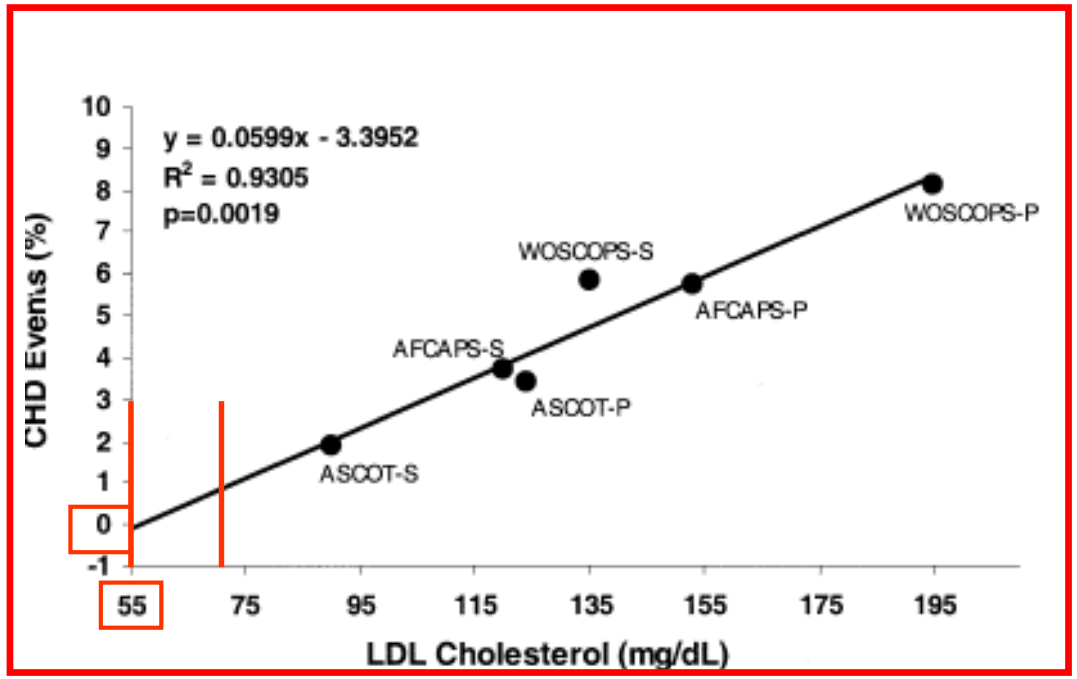
1-Year combined myocardial infarction and mortality

	No. of Events	No. of Patients	HR (95% CI)
Obstructive CAD			
3-Vessel or left main	358	6036	4.5 (3.5-5.7)

CONCLUSIONS AND RELEVANCE In this cohort of patients undergoing elective coronary angiography, nonobstructive CAD, compared with no apparent CAD, was associated with a significantly greater 1-year risk of MI and all-cause mortality. These findings suggest clinical importance of nonobstructive CAD and warrant further investigation of interventions to improve outcomes among these patients.



2004 O'Keefe

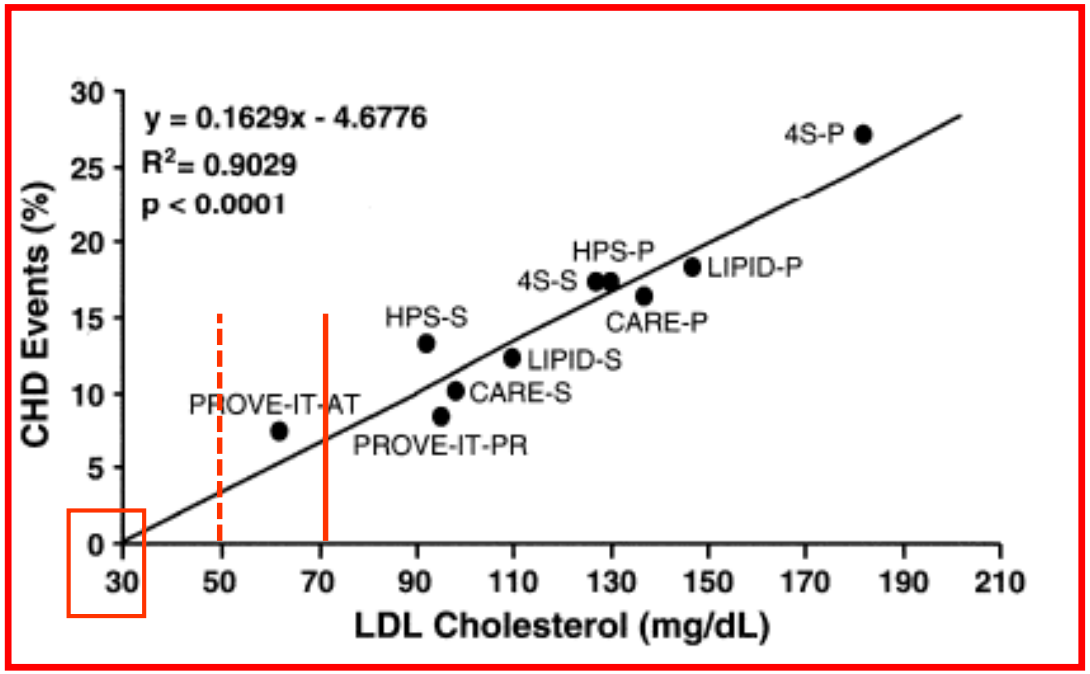


Prewencja pierwotna"

50 – 70 mg%

„Prewencja wtórna"

50 – 70 mg%

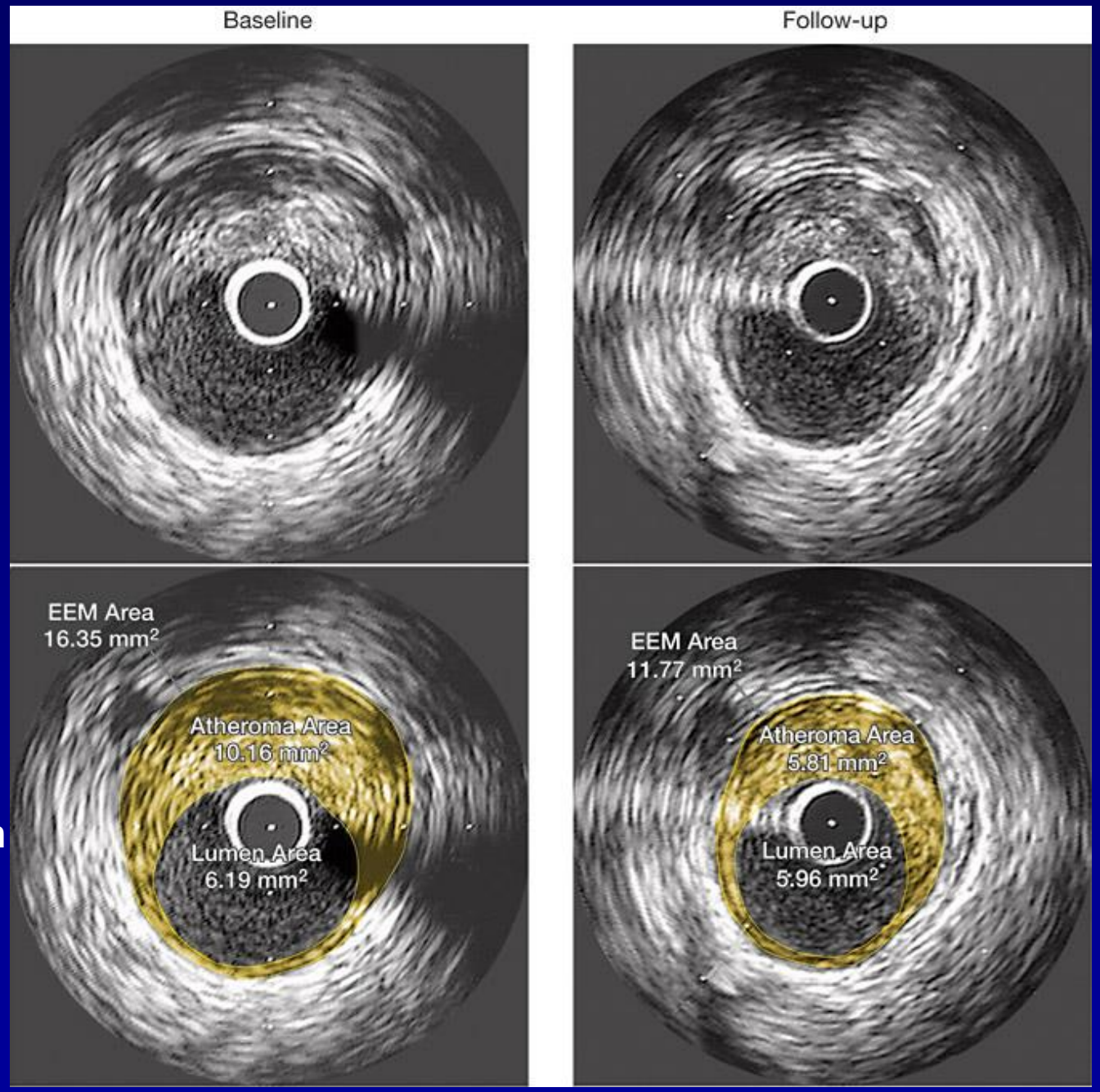


ASTEROID

24 m follow-up,n= 346
Rosuvastatyna 40mg

LDL -130,4 mg%
60,8 mg%
53,2 %

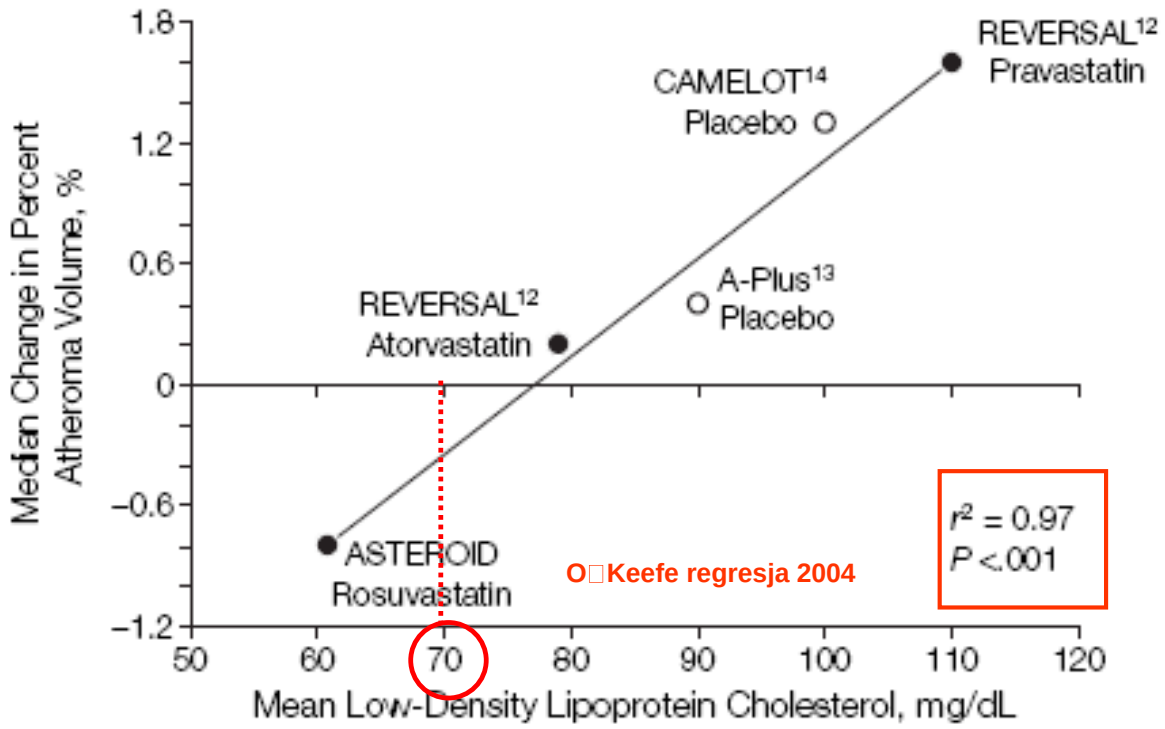
Po raz pierwszy wykazano remisję zmian miażdżycowych



Nissen S et al. JAMA 2006;295:1556

ASTEROID

Figure 3. Relationship Between Mean Low-Density Lipoprotein Cholesterol Levels and Median Change in Percent Atheroma Volume for Several Intravascular Ultrasound Trials



Nissen S et al. JAMA 2006;295:1556

SATURN

Rosuwastatyna; 119 mg% – 62mg%
Atorwastatyna; 120mg% - 70 mg%

104 tygodnie leczenia
1039 chorych
40 mg rosuwastatyny
80 mg atorwastatyny

Objętość blaszki. Ocena IVUS

Characteristic	No.	Median (95% CI)	P Value for Treatment	P Value for Interaction
		Remisja / Progresja		
Age				0.22
<Median			0.95	
Atorvastatin	252	−1.06 (−1.43 to −0.46)		
Rosuvastatin	253	−1.12 (−1.60 to −0.73)		
≥Median			0.07	
Atorvastatin	267	−0.84 (−1.28 to −0.46)		
Rosuvastatin	267	−1.35 (−1.68 to −0.90)		
Sex				0.03
Male			1.00	
Atorvastatin	386	−1.03 (−1.32 to −0.70)		
Rosuvastatin	379	−1.09 (−1.44 to −0.72)		
Female			0.01	
Atorvastatin	133	−0.71 (−1.38 to −0.25)		
Rosuvastatin	141	−1.76 (−2.39 to −1.02)		
Diabetes				0.63
Yes			0.95	
Atorvastatin	87	−0.50 (−1.30 to 0.01)		
Rosuvastatin	72	−0.86 (−1.86 to −0.31)		
No			0.16	
Atorvastatin	432	−1.04 (−1.35 to −0.70)		
Rosuvastatin	448	−1.31 (−1.53 to −0.91)		

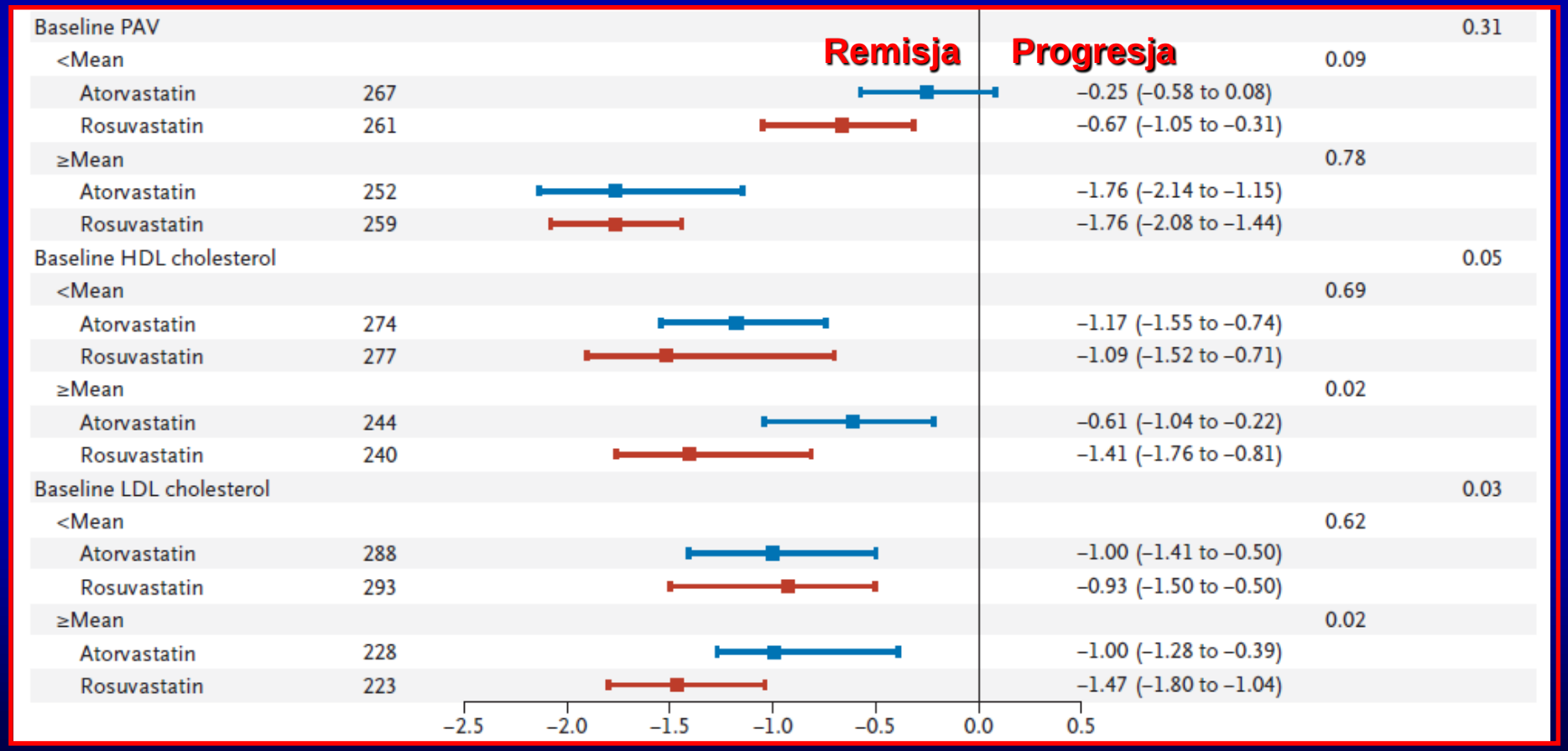
Nicholls S et al. NEJM 2011

SATURN

Rosuwastatyna; 119 mg% – 62mg%
Atorwastatyna; 120mg% - 70 mg%

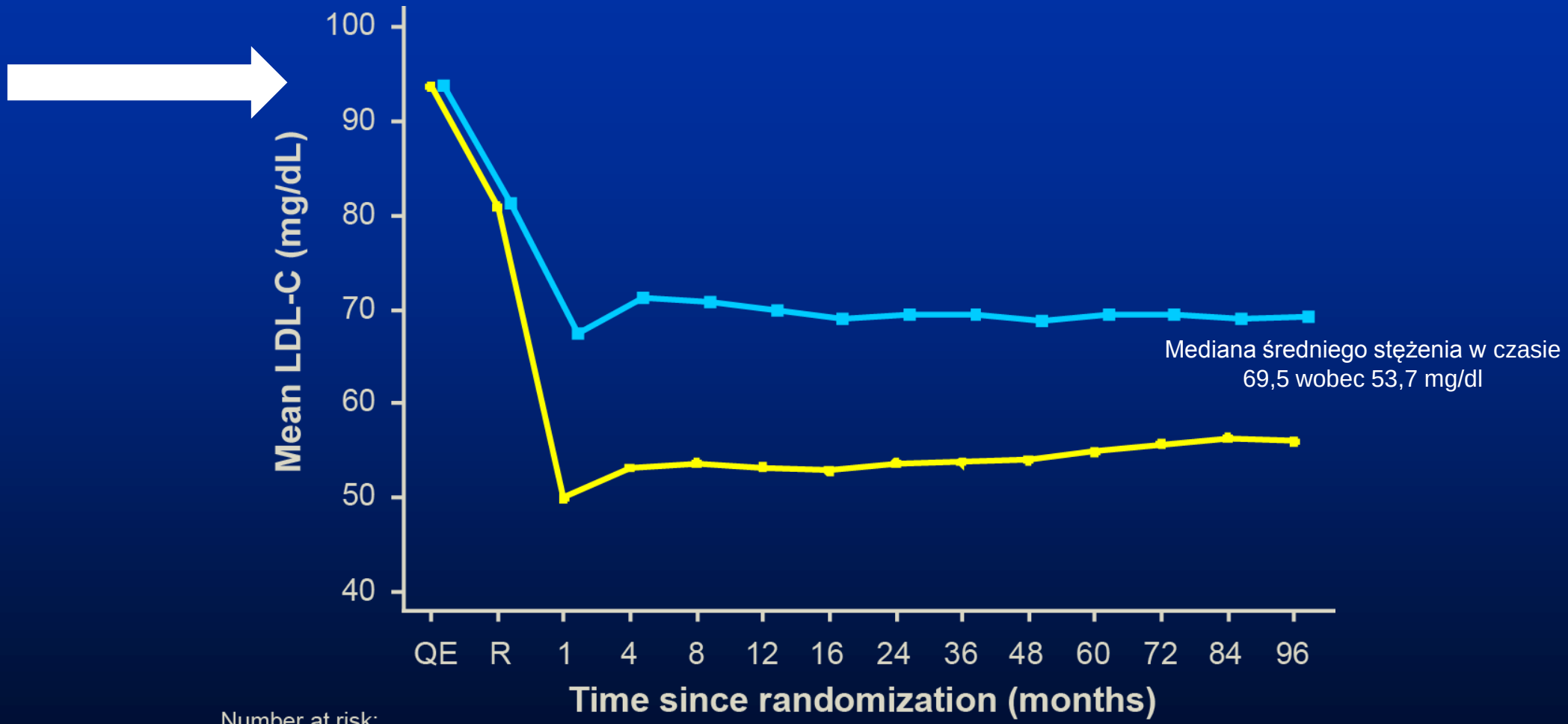
104 tygodnie leczenia
1039 chorych
40 mg rosuwastatyny
80 mg atorwastatyny

Objętość blaszki. Ocena IVUS



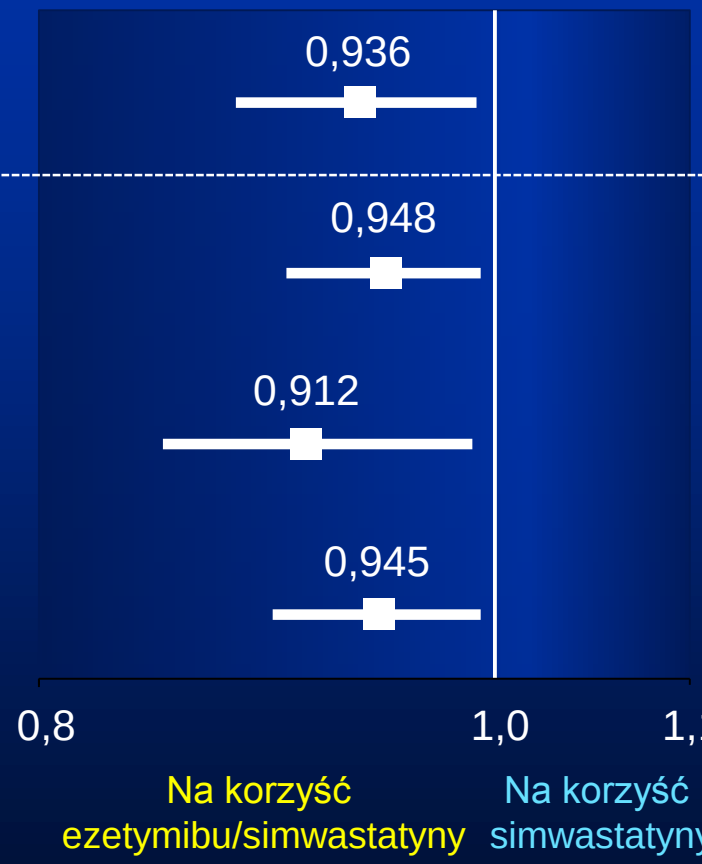
Nicholls S et al. NEJM 2011

Zmiany stężeń LDL-C i lipidów



Mediana średniego stężenia w czasie
69,5 wobec 53,7 mg/dl

Analiza ITT dla pierwszorzędowego i 3 określonych z góry punktów końcowych

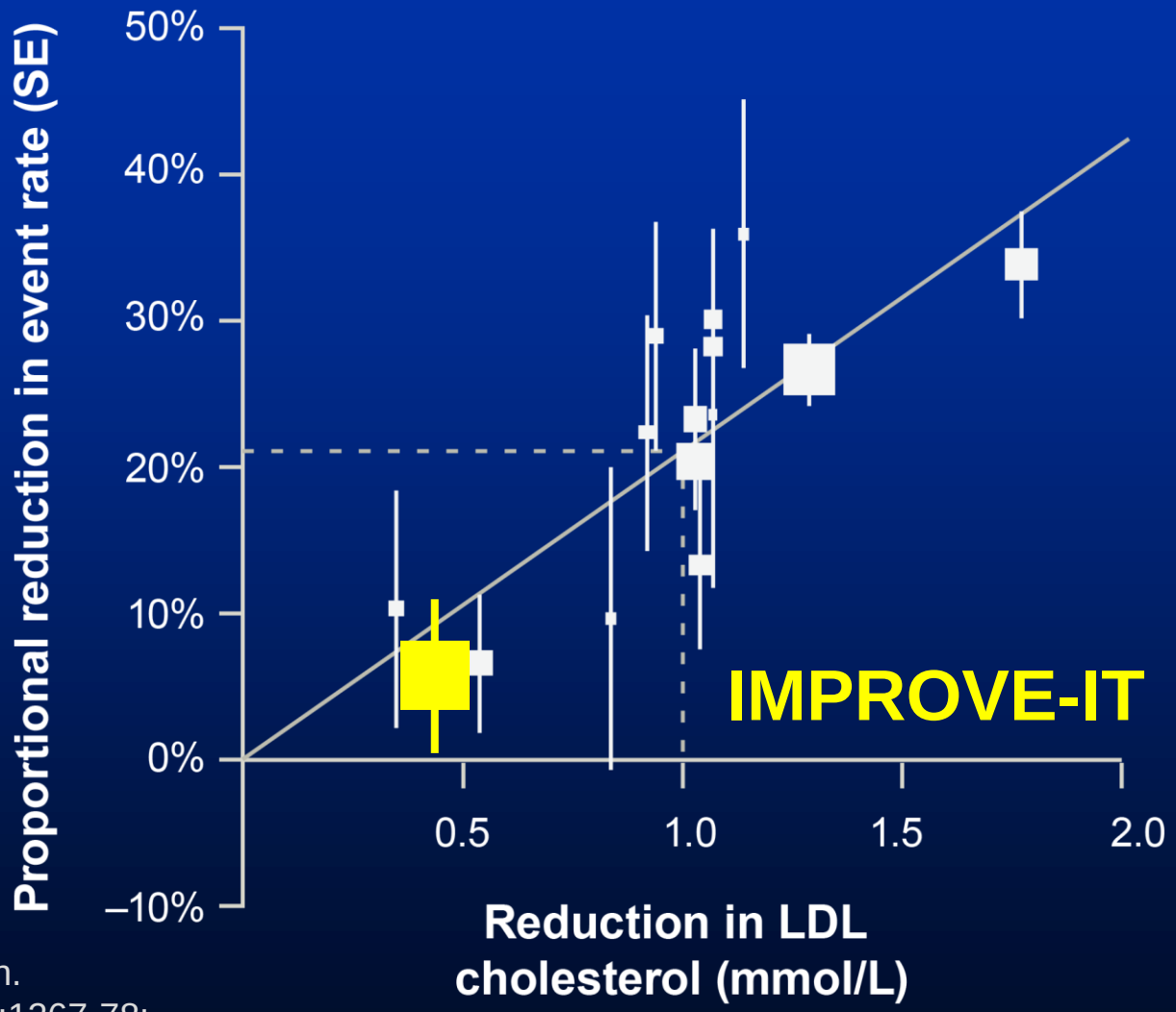


	Simwastatyna*	EZ/Simwastatyna*	Wartość p
Pierwszorzędowy CVD/MI/UA/rewask. w./CVA	34,7	32,7	0,016
Drugorzędowy Nr 1 Zgony/MI/UA/rewask. w./CVA	40,3	38,7	0,034
Drugorzędowy Nr 2 CHD/MI/pilna rewask. w.	18,9	17,5	0,016
Drugorzędowy Nr 3 CVD/MI/UA/rewask. ogółem/CVA	36,2	34,5	0,035

**Częstość występowania zdarzeń w ciągu 7 lat (%)*

UA — udokumentowana niestabilna dławica piersiowa wymagająca hospitalizacji; rewask. w. — rewaskularyzacja wieńcowa (≥ 30 dni po randomizacji); zgony — niezależnie od przyczyny; CHD — zgon z powodu choroby wieńcowej; rewask. ogółem — wieńcowa i pozawieńcowa (≥ 30 dni)

Badanie IMPROVE-IT a badanie CTT: porównanie korzyści ze stosowania ezetymibu i statyny



CTT Collaboration.
Lancet 2005; 366:1267-78;
Lancet 2010;376:1670-81.

European Heart Journal Advance Access published August 30, 2013

European Heart Journal
doi:10.1093/eurheartj/eht296

2013 ESC guidelines on the management of stable coronary artery disease

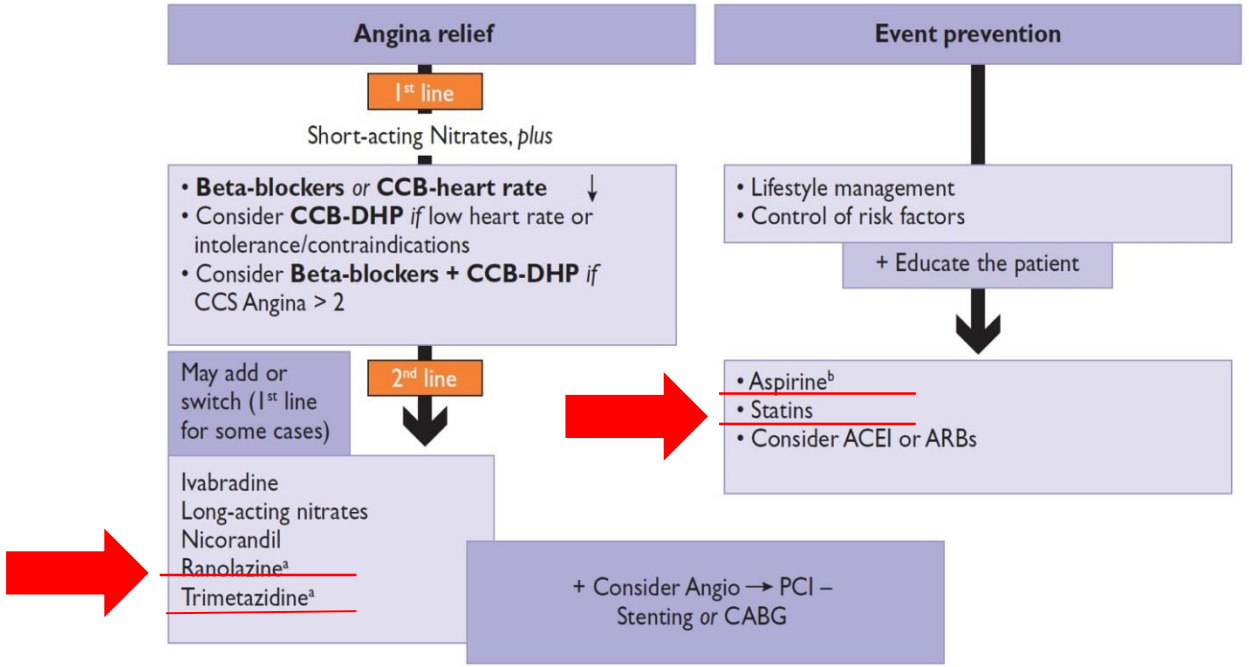


Figure 4 Medical management of patients with stable coronary artery disease. ACEI = angiotensin converting enzyme inhibitor; CABG = coronary artery bypass graft; CCB = calcium channel blockers; CCS = Canadian Cardiovascular Society; DHP = dihydropyridine; PCI = percutaneous coronary intervention.

[a]Data for diabetics.

[b]if intolerance, consider clopidogrel

Stabilna choroba wieńcowa..

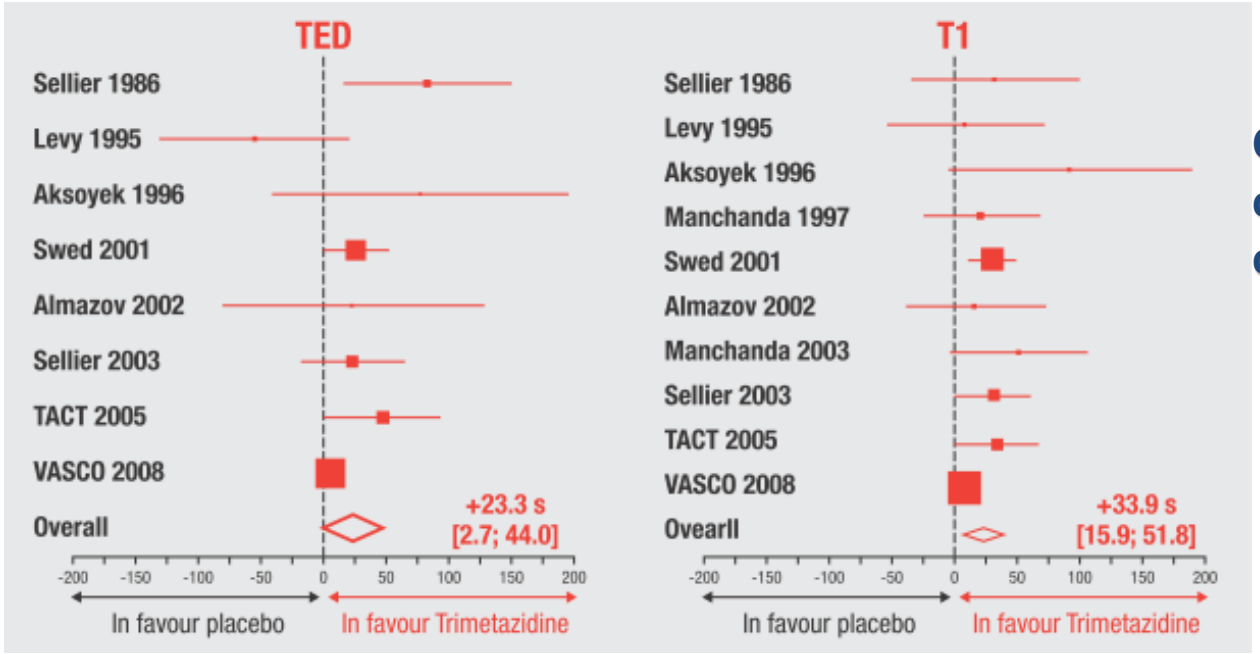
Trimetazidine in the treatment of stable angina pectoris: a meta-analysis of randomized, controlled clinical trials

3.

DANCHIN N[1], MARZILLI M[2], PARKHOMENKO A[3], RIBEIRO J[4]

		TED	T1	AA	SAN
N_t (n_{TMZ}/n_{Pbo})		2160 (1092/1068)	2245 (1131/1114)	2461 (1239/1222)	2417 (1216/1201)
Heterogeneity test (p-value)		0.084	0.208	0.0001	0.0009
Treatment effect TMZ vs. placebo	Monotherapy	+84.0 s	+48.0 s	-1.2	-1.7
	Combination therapy	-17.5 s	+34.6 s	-1.6	-1.1
	Total	**+23.3 s**	**+33.9 s**	**-1.4**	**-1.3**
	CI95%	[2.7; 44.0]	[15.9; 51,8]	[-2.1; -0.8]	[-1.9; -0.7]

Całkowity czas testu wysiłkowego.

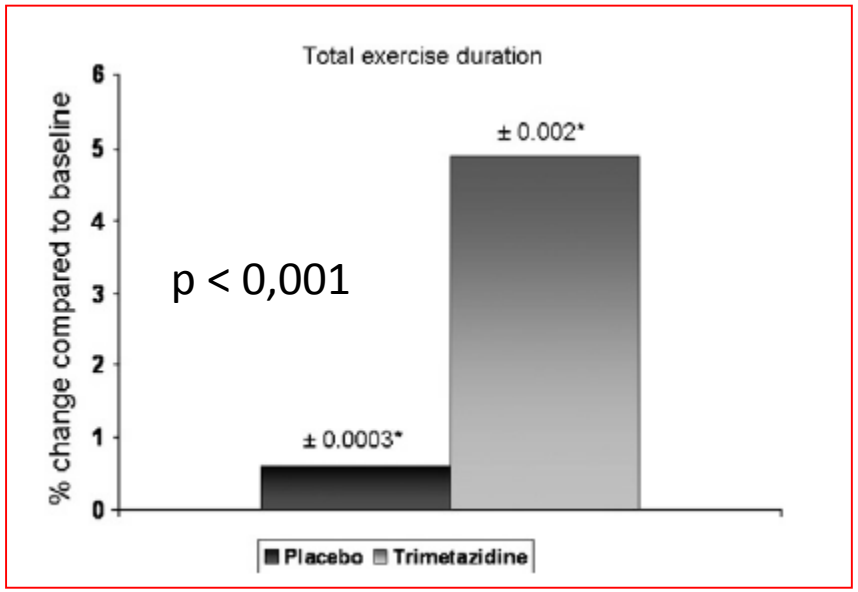


Czas do obniżenia odcinka ST 1 mm

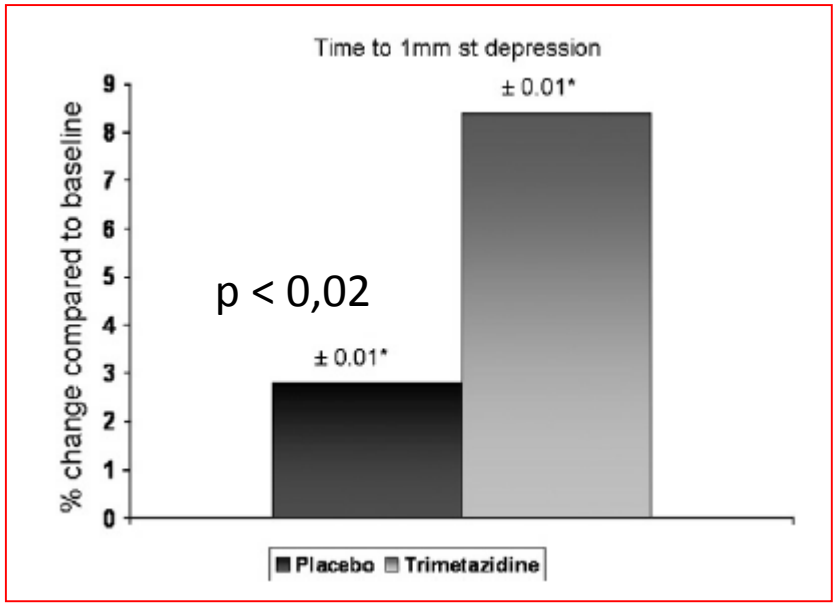
Stabilna choroba wieńcowa..

VASCO – angina study.

Dusznica bolesna wysiłkowa pomimo leczenia β-blokerami, n=645.
Dawki Trimetazydynay 70mg/d i 140mg/d



Obie dawki łącznie



Obie dawki łącznie.

Obie dawki istotnie lepsze od placebo jakkolwiek dawka 140 mg > lepsza od 70 mg

Viatle C et al. Int Journal Cardioloigy 2012

Chronic treatment with trimetazidine after discharge reduces the incidence of restenosis in patients who received coronary stent implantation: A 1-year prospective follow-up study

Jinsong Chen [1], Shanshan Zhou [1], Jing Jin, Feng Tian, Yunfeng Han, Jing Wang, Jie Liu, Yundai Chen *

Division of Cardiology, Chinese PLA General Hospital, Beijing 100853, China

International Journal of Cardiology 2014

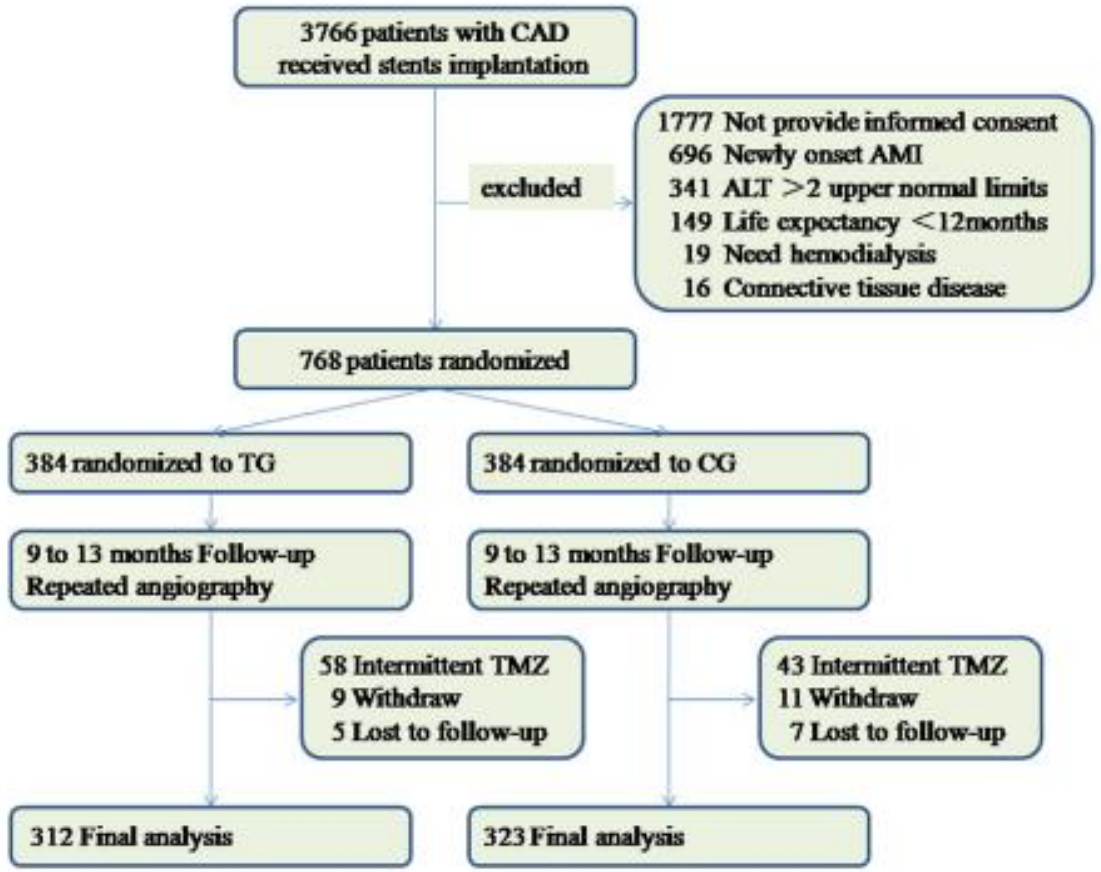


Fig. 1. Flow chart of the protocol used in this study.

Chronic treatment with trimetazidine after discharge reduces the incidence of restenosis in patients who received coronary stent implantation: A 1-year prospective follow-up study

International Journal of Cardiology 2014

Table 1
Baseline patient characteristics in the treatment and control groups.

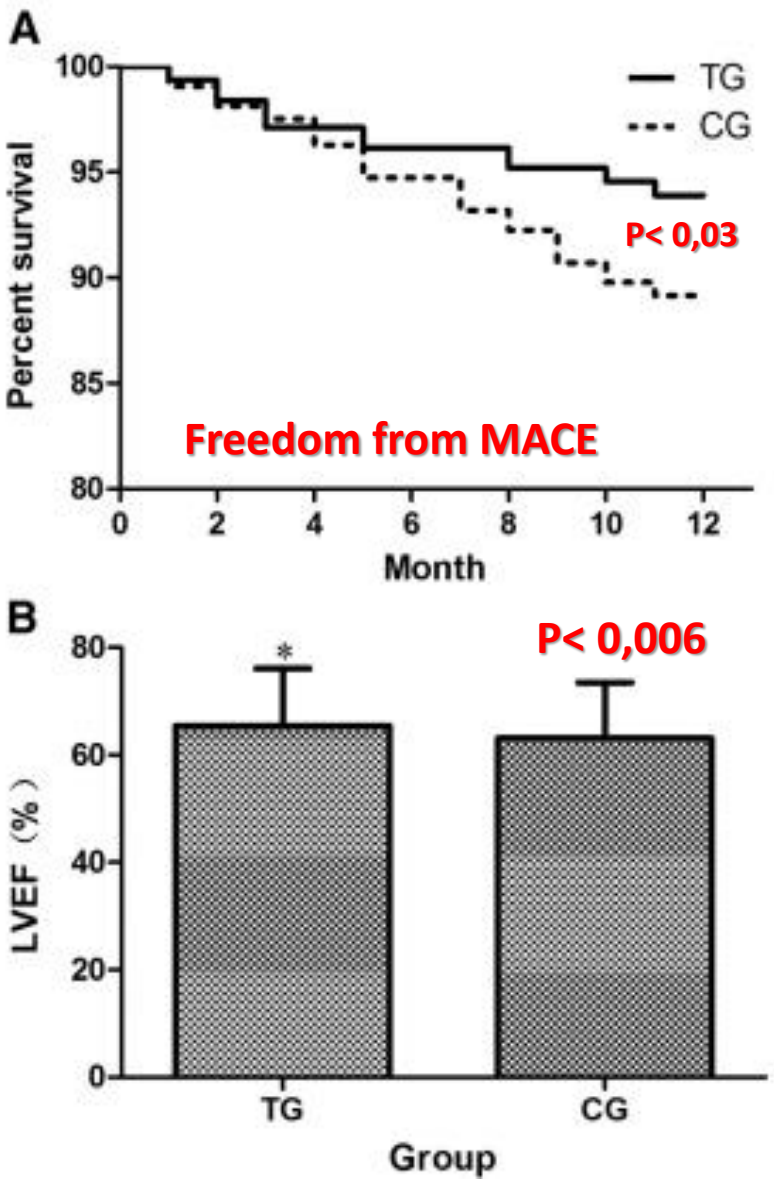
Characteristics	TG (n = 312)	CG (n = 323)	*p*-Value
Age (years)	61.6 ± 11.9	60.9 ± 11.6	0.442
Male, n (%)	253 (81.1%)	247 (76.5%)	0.155
BMI (kg/m^2)	26.26 ± 4.07	25.83 ± 3.98	0.179
Diabetes mellitus, n (%)	78 (25.0%)	93 (28.8%)	0.282
Hypertension, n (%)	214 (68.6%)	203 (62.8%)	0.128
Current smoker, n (%)	116 (37.2%)	107 (33.1%)	0.285
Alcohol, n (%)	56 (17.9%)	75 (23.2%)	0.101
Previous MI, n (%)	38 (12.2%)	46 (14.2%)	0.443
SAP, n (%)	137 (43.9%)	131 (40.6%)	0.392
UAP, n (%)	175 (56.1%)	192 (59.3%)	
On admission			
LDL-C (mmol/L)	2.05 ± 0.67	1.98 ± 0.63	0.182
HDL-C (mmol/L)	1.01 ± 0.22	1.00 ± 0.22	0.348
TrG (mmol/L)	1.75 ± 1.42	1.60 ± 1.01	0.118
Glucose (mmol/L)	6.82 ± 1.97	6.65 ± 2.03	0.291
Medication			
ACEI, n (%)	83 (26.6%)	104 (32.2%)	0.122
ARB, n (%)	76 (24.4%)	89 (27.6%)	0.359
CCB, n (%)	105 (33.7%)	121 (37.5%)	0.316
BB, n (%)	57 (18.3%)	51 (15.8%)	0.406
Statins, n (%)	239 (76.6%)	227 (71.5%)	0.144
LVEF (%)	62.6 ± 9.8	63.3 ± 9.3	0.356

Table 2
Baseline PCI characteristics of patients in the treatment and control groups.

Characteristics	TG (n = 312)	CG (n = 323)	*p*-Value
Target artery (%)			0.485
RCA, n (%)	87 (27.9%)	96 (29.7%)	
LAD, n (%)	143 (45.8%)	137 (42.4%)	
LCX, n (%)	19 (6.1%)	31 (9.6%)	
LMA, n (%)	5 (1.6%)	4 (1.2%)	
Multiple, n (%)	58 (18.6%)	55 (17.0%)	
Lesions			
Bifurcation, n (%)	36 (11.5%)	49 (15.2%)	0.179
CTO, n (%)	7 (2.2%)	11 (3.4%)	0.378
Stents			
Number of stents	1.71 ± 0.97	1.70 ± 0.99	0.899
Mean stent length	23.6 ± 7.9	23.4 ± 6.6	0.767
Mean stent diameter	3.13 ± 0.73	3.13 ± 0.84	0.998
Sirolimus	407 (76.5%)	454 (74.3%)	0.350
Paclitaxel	125 (23.5%)	157 (25.7%)	0.727
Initial TIMI Flow			
1, n (%)	121 (22.8%)	151 (24.7%)	
2, n (%)	147 (27.6%)	162 (26.5%)	
3, n (%)	264 (49.6%)	298 (48.8%)	
Stenting			
Predilation, n (%)	514 (96.4%)	596 (97.5%)	0.270
Direct stenting, n (%)	19 (3.6%)	15 (2.5%)	
Postdilation, n (%)	180 (33.7%)	188 (30.8%)	0.278

Brak istotnych różnic w charakterystyce klinicznej i proceduralnej (PCI) między porównywalnymi grupami.

International Journal of Cardiology 2014



	C.G. (n = 323)	p-Value
	35 (10.8%)	0.032
	6	
	10	
	5	
	7	
	8	
	63.1 ± 10.4	0.006
	112.6 ± 21.8	0.009
	48.4 ± 16.7	0.004
	36 (11.1%)	0.001
	102 (31.6%)	0.309
	57 (17.6%)	0.021

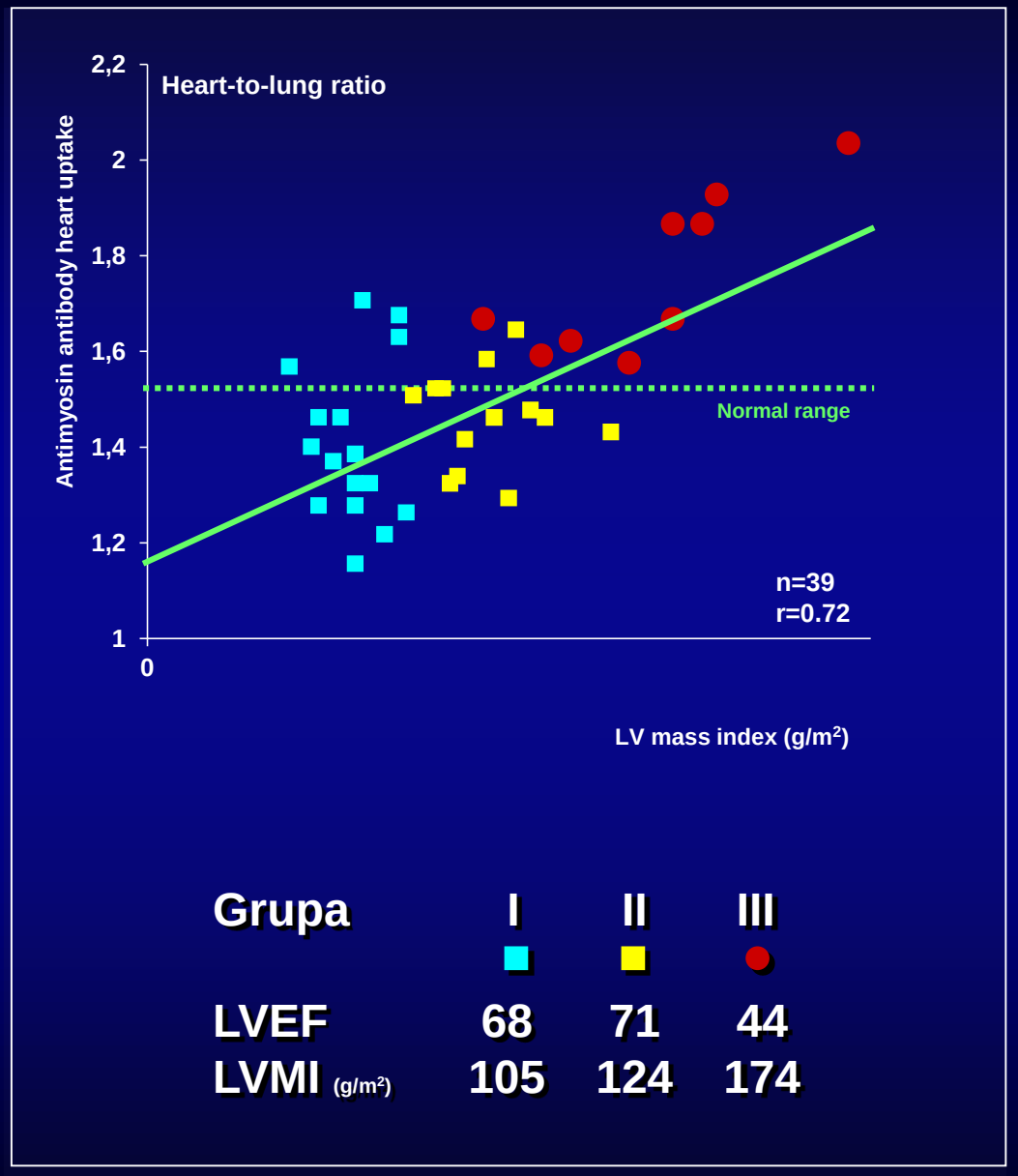
Chronic treatment with trimetazidine after discharge reduces the incidence of restenosis in patients who received coronary stent implantation: A 1-year prospective follow-up study

International Journal of Cardiology 2014

Table 5
Pre-PCI predictors for ISR at approximately 1 year after PCI.

Factors	OR value	95% CI	*p*-Value
Age	0.940	0.914–0.968	<0.001
Diabetes	3.221	1.609–6.446	0.001
Hypertension	2.085	0.915–4.751	0.080
Current smoking	2.625	1.378–5.000	0.003
SBP	1.013	0.999–1.027	0.076
Mean stent length	1.046	1.008–1.085	0.017
Mean stent diameter	1.531	1.114–2.104	0.009
TMZ treatment	0.376	0.196–0.721	0.003

PCI, percutaneous coronary intervention; ISR, in-stent restenosis; SBP, systolic blood pressure; TMZ, trimetazidine.



Spadek liczby miocytów towarzyszy nam przez całe życie.

Mechanizmy:

- necrosis (miocytoliza)
- apopptosis
- przedwczesne starzenie (krótsze telomery)
- oncosis

Pons-Ilado G. et al. JACC 2000.36.2198

A Sensitive Cardiac Troponin T Assay in Stable Coronary Artery Disease

Torbjørn Omland, M.D., Ph.D., M.P.H., James A. de Lemos, M.D., Marc S. Sabatine, M.D., M.P.H., Costas A. Christophi, Ph.D., Madeline Murguia Rice, Ph.D., Kathleen A. Jablonski, Ph.D., Solve Tjora, M.D., Michael J. Domanski, M.D., Bernard J. Gersh, M.B., Ch.B., D.Phil., Jean L. Rouleau, M.D., Marc A. Pfeffer, M.D., Ph.D., and Eugene Braunwald, M.D., for the Prevention of Events with Angiotensin Converting Enzyme Inhibition (PEACE) Trial Investigators

NEJM 2009

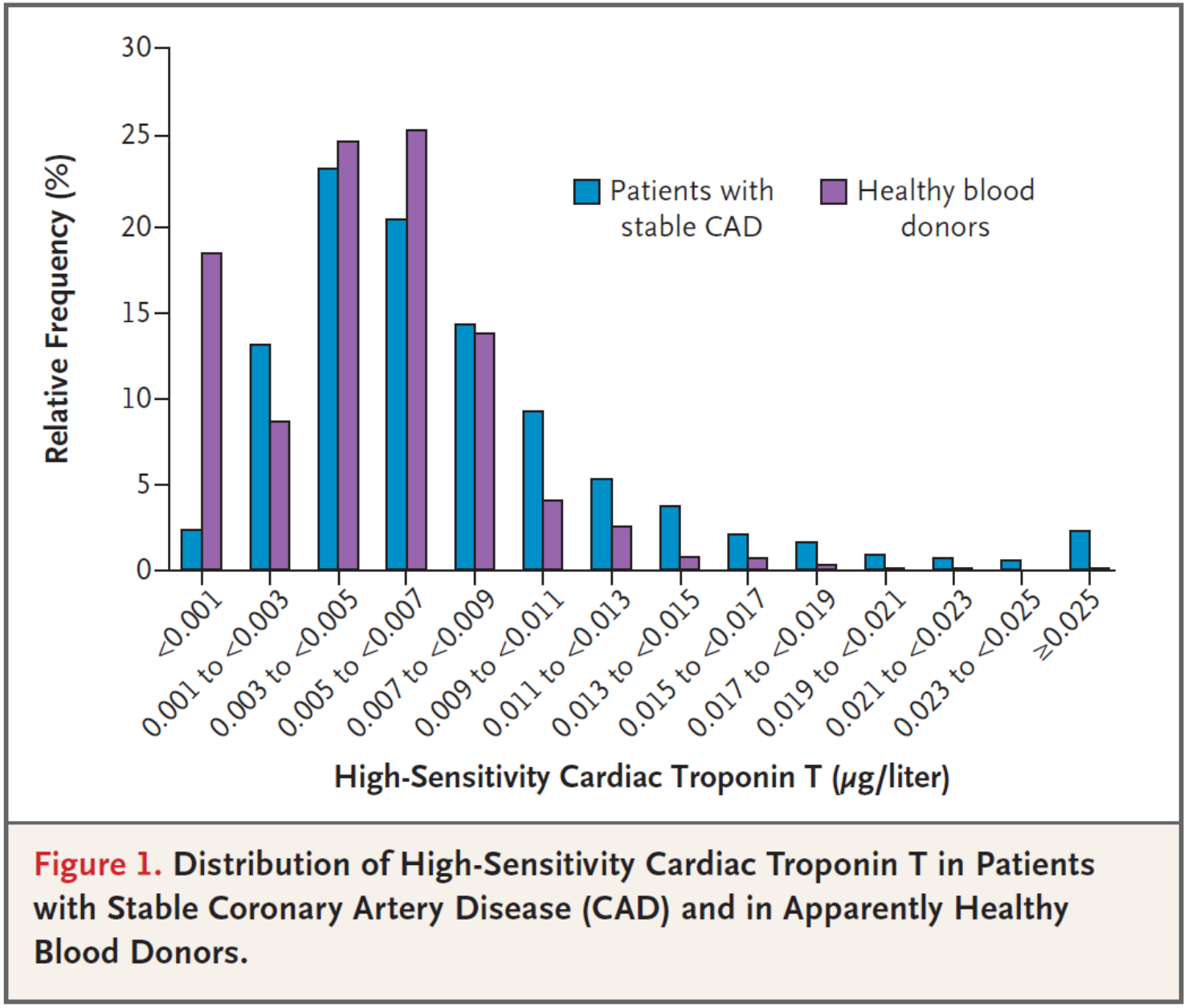


Figure 1. Distribution of High-Sensitivity Cardiac Troponin T in Patients with Stable Coronary Artery Disease (CAD) and in Apparently Healthy Blood Donors.

A Sensitive Cardiac Troponin T Assay in Stable Coronary Artery Disease

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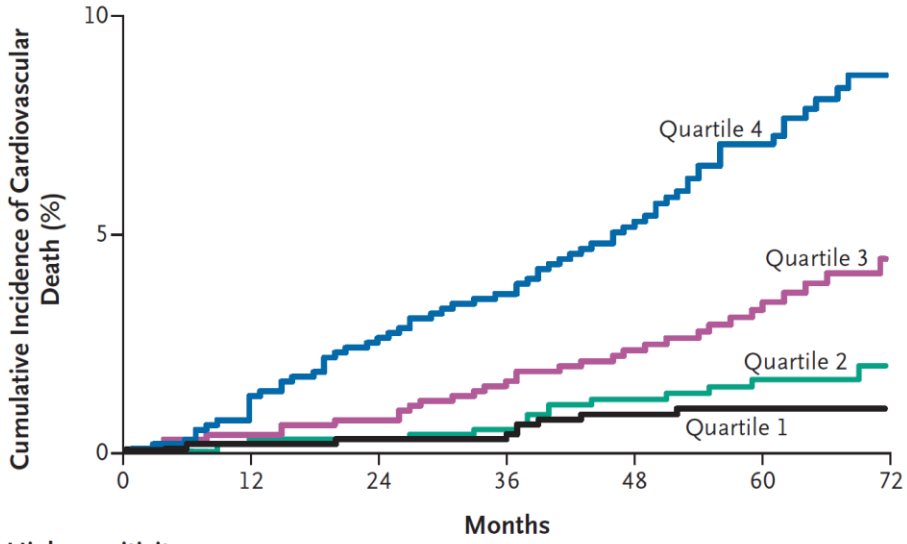
NEJM 2009



High-sensitivity cardiac troponin T levels (μg/liter)	Q1	Q2	Q3	Q4
Men	≤0.0042	0.0043–0.0062	0.0063–0.0095	≥0.0096
Women	≤0.0027	0.0028–0.0045	0.0046–0.0073	≥0.0074

Figure 2. Incidence of Cardiovascular Death According to Quartile of High-Sensitivity Cardiac Troponin T Level.

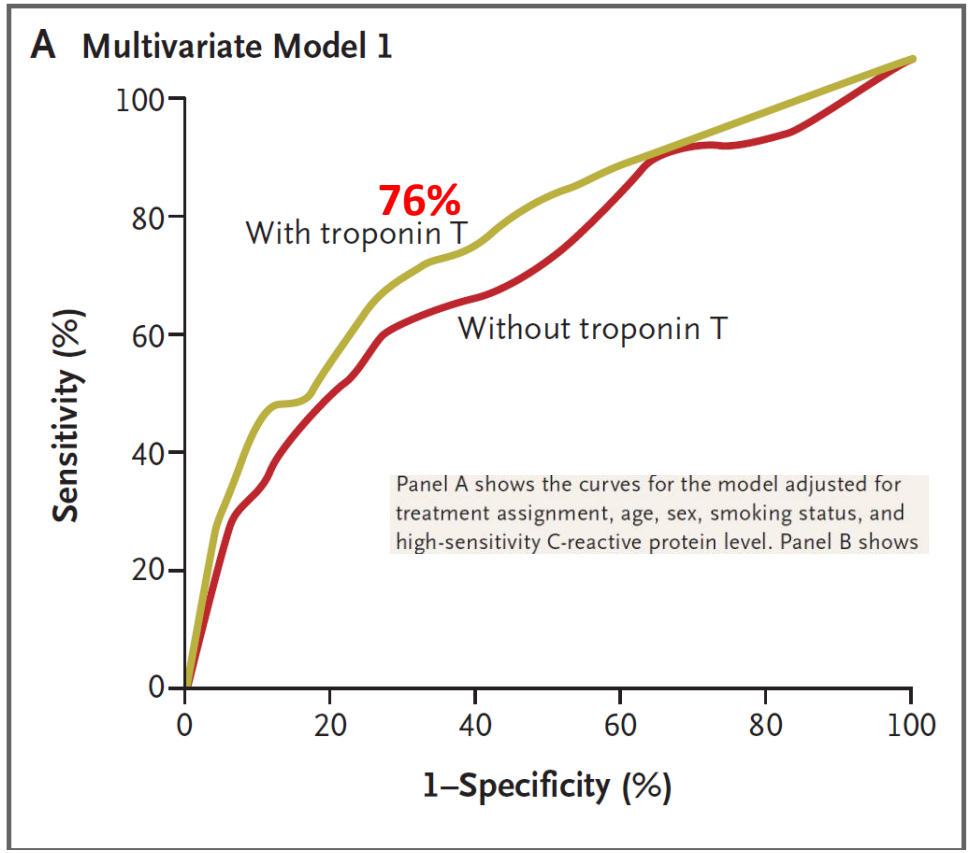


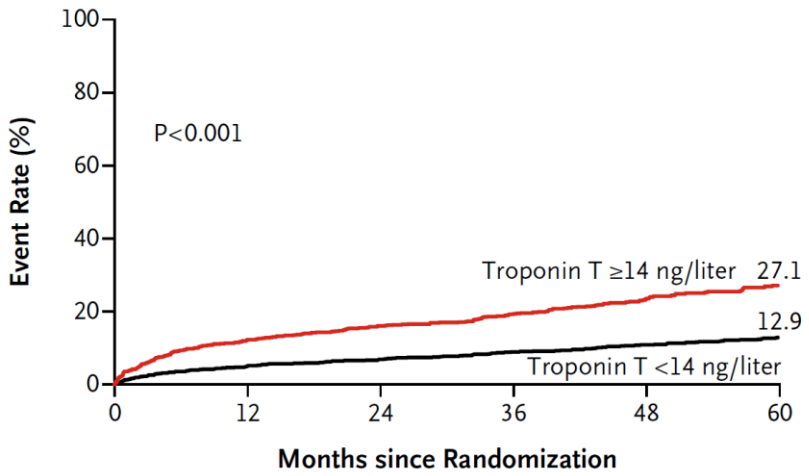
Figure 3. Covariate-Adjusted Receiver-Operating-Characteristic Plots for the Use of High-Sensitivity Cardiac Troponin T to Predict the Risk of Cardiovascular Death.

Troponin and Cardiac Events in Stable Ischemic Heart Disease and Diabetes

Brendan M. Everett, M.D., M.P.H., Maria Mori Brooks, Ph.D., Helen E.A. Vlachos, M.S., Bernard R. Chaitman, M.D., Robert L. Frye, M.D., and Deepak L. Bhatt, M.D., M.P.H., for the BARI 2D Study Group*

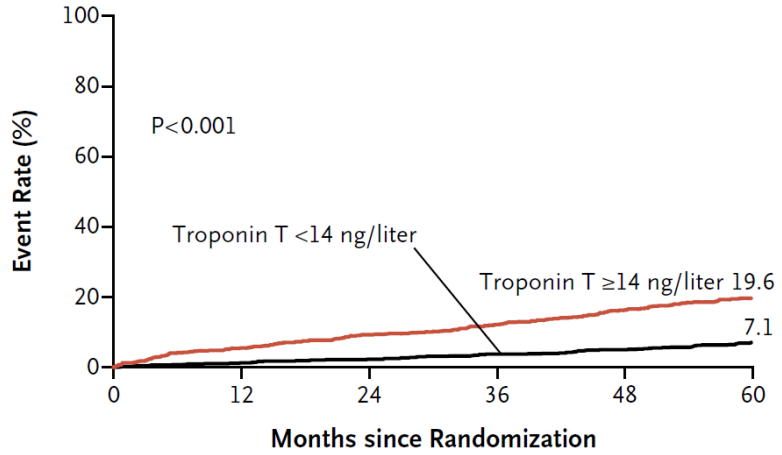
NEJM 2015

A 5-Yr Rate of Primary Composite End Point



No. at Risk						
Troponin T ≥14 ng/liter	897	737	684	620	455	255
Troponin T <14 ng/liter	1388	1281	1229	1124	892	529

B 5-Yr Rate of Death from Any Cause



No. at Risk						
Troponin T ≥14 ng/liter	897	847	813	787	665	406
Troponin T <14 ng/liter	1388	1370	1355	1334	1160	739

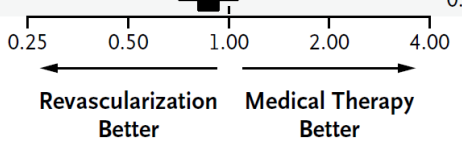
Troponin and Cardiac Events in Stable Ischemic Heart Disease and Diabetes

Brendan M. Everett, M.D., M.P.H., Maria Mori Brooks, Ph.D., Helen E.A. Vlachos, M.S., Bernard R. Chaitman, M.D., Robert L. Frye, M.D., and Deepak L. Bhatt, M.D., M.P.H., for the BARI 2D Study Group*

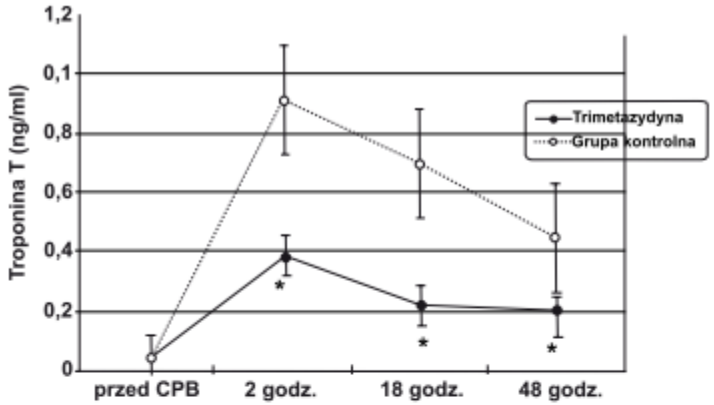
NEJM 2015

NEJM 2015

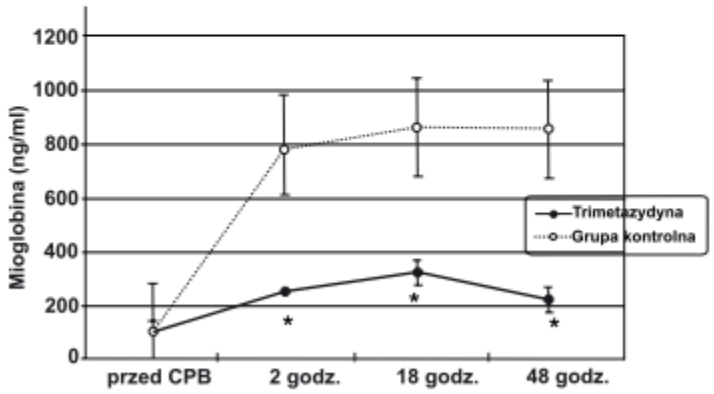
Subgroup	Revascularization Group	Medical-Therapy Group	Hazard Ratio (95% CI)	P Value for Heterogeneity
	5-yr event rate (%)			
Death from cardiovascular causes, myocardial infarction, or stroke				0.99
Troponin T <14 ng/liter	11.8	14.0	0.96 (0.71–1.30)	
Troponin T ≥14 ng/liter	26.5	27.6	0.96 (0.74–1.25)	
Death from cardiovascular causes				0.05
Troponin T <14 ng/liter	2.6	4.4	0.63 (0.34–1.14)	
Troponin T ≥14 ng/liter	11.7	10.1	1.27 (0.85–1.91)	
Myocardial infarction				0.28
Troponin T <14 ng/liter	8.2	10.1	0.94 (0.66–1.35)	
Troponin T ≥14 ng/liter	15.6	21.7	0.72 (0.52–1.00)	
Stroke				0.75
Troponin T <14 ng/liter	2.1	2.5	0.87 (0.43–1.77)	
Troponin T ≥14 ng/liter	4.6	4.2	1.03 (0.51–2.05)	
Death from any cause				0.20
Troponin T <14 ng/liter	6.4	7.7	0.77 (0.53–1.14)	
Troponin T ≥14 ng/liter	19.4	19.8	1.06 (0.80–1.39)	
Heart failure				0.32
Troponin T <14 ng/liter	11.5	10.7	1.07 (0.78–1.47)	
Troponin T ≥14 ng/liter	23.8	27.6	0.87 (0.67–1.13)	
Death from any cause, myocardial infarction, stroke, or heart failure				0.24
Troponin T <14 ng/liter	22.3	22.2	1.03 (0.83–1.29)	
Troponin T ≥14 ng/liter	42.2	47.8	0.87 (0.71–1.05)	



Cytoprotekcja; CABG w stabilnej chorobie wieńcowej.



Rycina 1. Osoczowe stężenie troponiny T w grupie leczonej trimetazydyną i w grupie kontrolnej. CPB – krążenie pozaustrojowe. *P <0,05.



Rycina 2. Osoczowe stężenie mioglobiny w grupie leczonej trimetazydyną i w grupie kontrolnej. CPB – krążenie pozaustrojowe. *P <0,05.

Trimetazydyna w dawce 3 x 20 mg 14 dni przed zabiegiem pomostowania zmniejsza okołooperacyjny wzrost markerów martwicy

Przed- i pooperacyjne wartości parametrów w obu grupach*

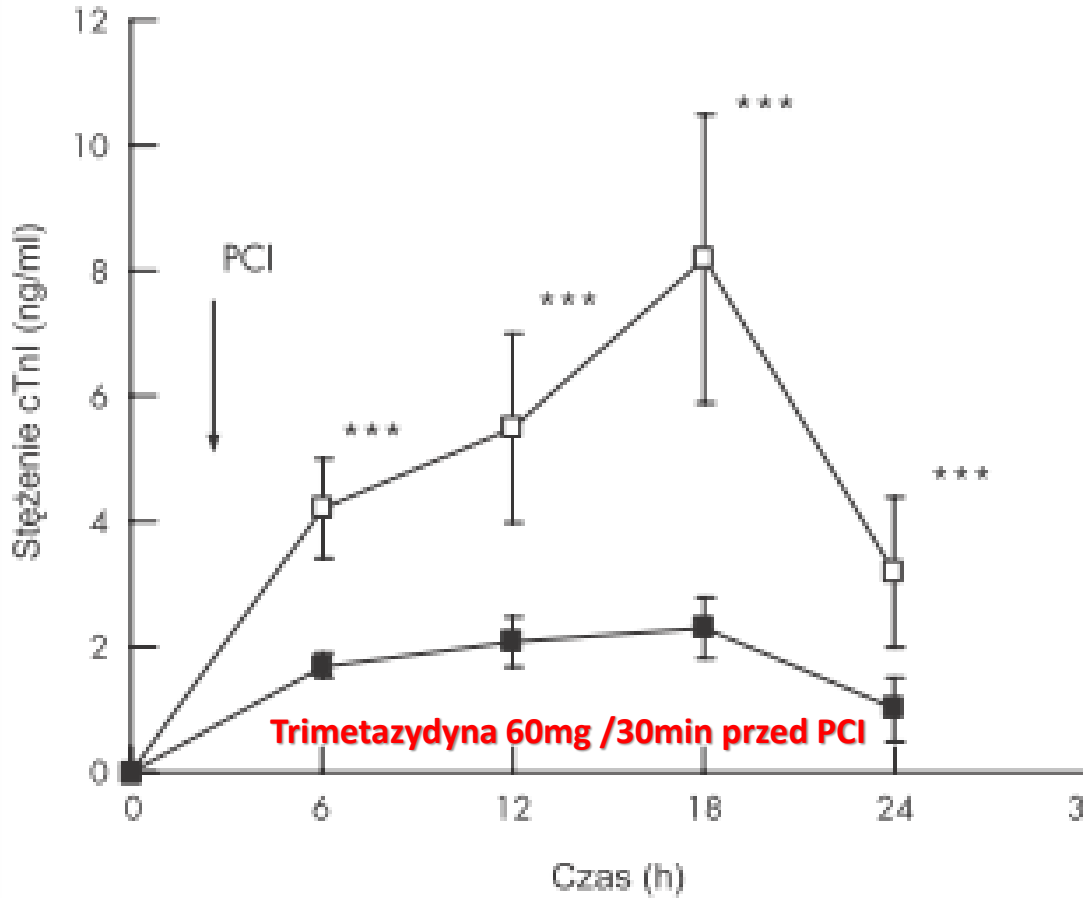
Parametr	Grupa leczona trimetazydyną (n = 15)	Grupa kontrolna (n = 15)
		60,2 ± 2,1
Średni wiek (lata)	57,5 ± 2,6	(P=0,15)
Mężczyźni/Kobiety (n)	12/3	11/4
Choroba pojedynczego naczynia (n)	2	1
Choroba dwóch naczyń (n)	3	6
Choroba trzech naczyń (n)	10	8
Średnia liczba pomostów/ pacjenta (n)	2,53	2,06
Przedoperacyjna EF (%)	43,3 ± 3,1	42,1 ± 2,6
Czas zacisku (min)	37 ± 9,2	35 ± 6,4
Zawał okołooperacyjny (n)	0	0
Okołooperacyjny CI (l/min/m^2)	2,23 ± 0,5	248 ± 0,1

* Określone dane przedstawiono w postaci średnich ± standardow błąd pomiaru. Grupa leczona trimetazydyną i grupa kontrolna nie różnił się w sposób znamienny statystycznie pod względem parametrów klinicznych. EF – frakcja wyrzutowa; CI – wskaźnik sercowy.

Iskesen I et al. Heart Surg Forum 2009

II. Cytoprotekcja; PCI w stabilnej chorobie wieńcowej.

Trimetazydyna zmniejsza ryzyko martwicy okołozabiegowej.



130 chorych

136 chorych

Bonello et al. Heart 2007

Beneficial effects of trimetazidine treatment on exercise tolerance and B-type natriuretic peptide and troponin T plasma levels in patients with stable ischemic cardiomyopathy

Am Heart J 2007

Pericle Di Napoli, MD,[a] Paolo Di Giovanni, MD,[a] Marta Assunta Gaeta, MD,[a] Giuseppina D'Apolito, MD, and Antonio Barsotti, MD[b] *Chieti and Genoa, Italy*

A Sensitive Cardiac Troponin T Assay in Stable Coronary Artery Disease

NEJM 2009

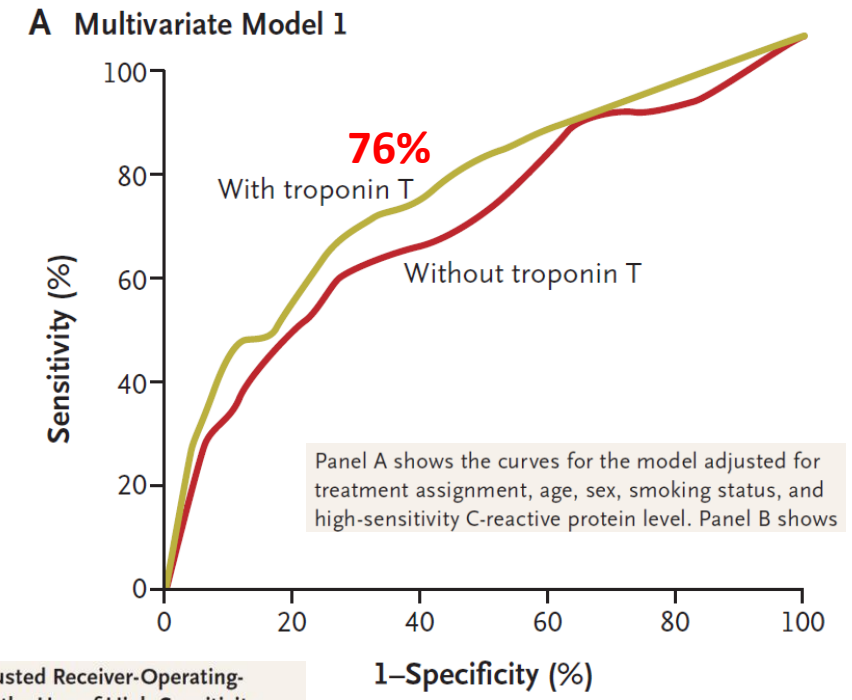


Figure 3. Covariate-Adjusted Receiver-Operating-Characteristic Plots for the Use of High-Sensitivity Cardiac Troponin T to Predict the Risk of Cardiovascular Death.

Long term cardioprotective action of trimetazidine and potential effect on the inflammatory process in patients with ischaemic dilated cardiomyopathy

P Di Napoli, A A Taccardi, A Barsotti

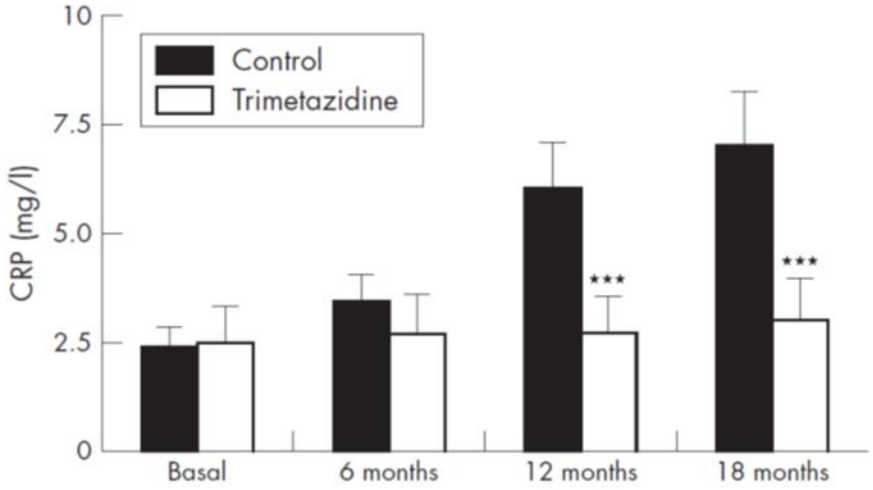


Figure 3 Changes in C reactive protein (CRP) plasma concentrations. Data are mean (SD). ***p<0.001 *v* control.

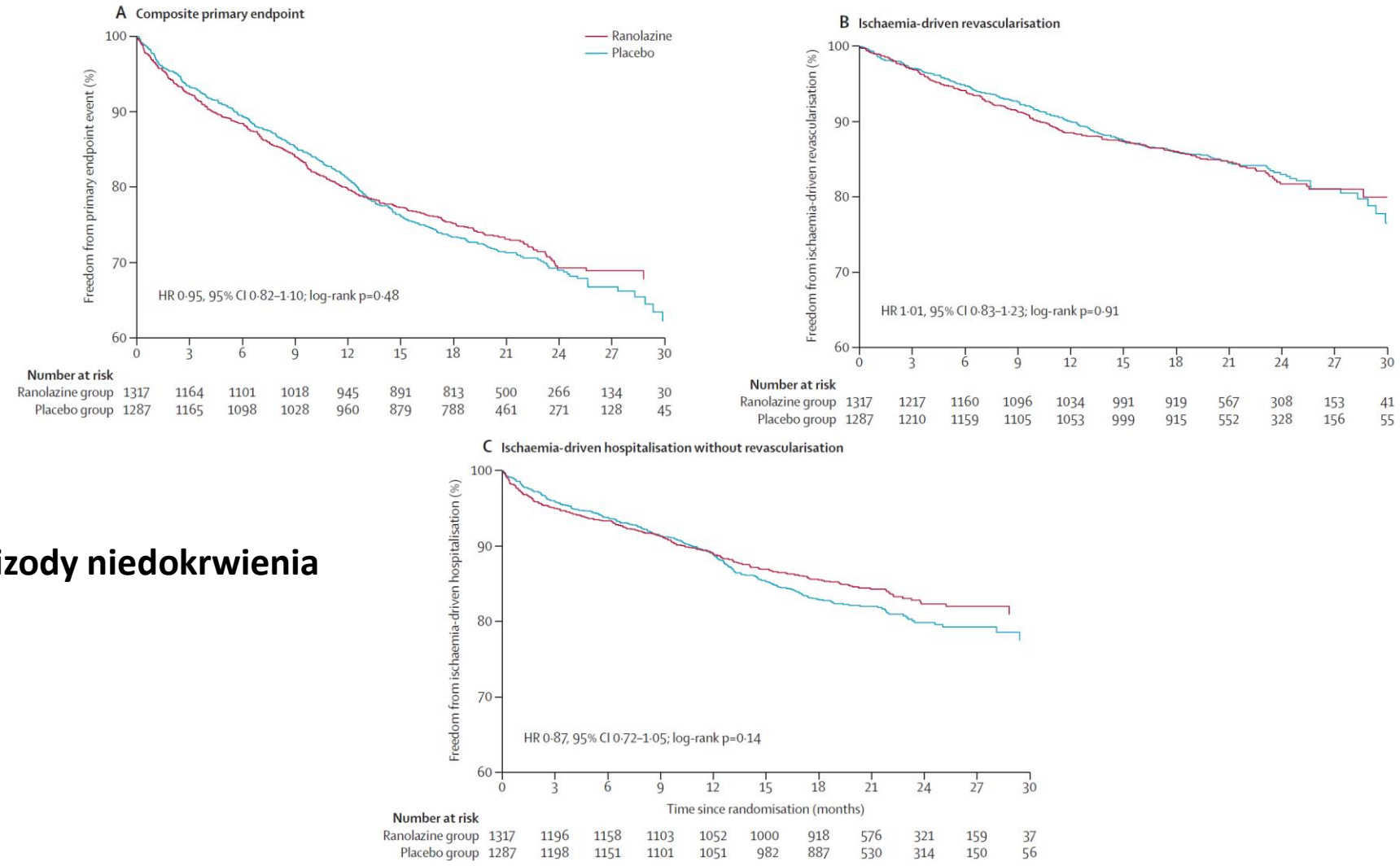
4.

Ranolazine in patients with incomplete revascularisation after percutaneous coronary intervention (RIVER-PCI): a multicentre, randomised, double-blind, placebo-controlled trial

Lancet 2015

Giora Weisz, Philippe Généreux, Andres Iñiguez, Aleksander Zurakowski, Michael Shechter, Karen P Alexander, Ovidiu Dressler, Anna Osmukhina,

Wpływ na epizody niedokrwienia



Uwagi do leczenia SCAD w 2016 roku.

1. **OMT i rewaskularyzacja są metodami komplementarnymi a nie alternatywnymi.**
2. **Rewaskularyzacja jest rekomendowana chorym wysokiego ryzyka: CCS III-IV, niedokrwienie > 12-15%, roczne ryzyko zgonu > 3%, EF < 50%, zmiany w tt. wieńcowych : LM, 3VD, prox. LAD .**
3. **Podstawą OMT- jest indywidualizacja leczenia.**
4. **Standardowe leczenie oparte jest na normalizacji czynników ryzyka, stosowania leków blokujących receptory beta, blokerów kanału wapniowego, nitratów , inhibitorów enzymu konwertującego,**

Uwagi do leczenia SCAD w 2016 roku.

5.Leczenie przeciwpłytkowe w monoterapii zmierza w kierunku zastąpienia aspiryny silniejszymi lekami: aspiryna < klopidogrel < tikagrelor.

DAPT po wszczepieniu stentu (DES II generacja) u chorych podwyższonego ryzyka powikłań krwotocznych aspiryna może być odstawiona po miesiącu i kontynuacja klopidogrelem (tikagrelor) do 6 miesięcy.

U chorych z FA i wszczepionym stencie (DES II generacja) na potrójnym leczeniu (TT) przy podwyższonym ryzyku powikłań krwotocznych można zrezygnować z aspiryny.

Uwagi do leczenia SCAD w 2016 roku.

6. LDL cholesterol. Chory z rozpoznaną chorobą niedokrwienną obligatoryjnie winien mieć poziom cholesterolu LDL poniżej 70mg%.

7. Cytoprotekcja ma coraz większe znaczenie - Trimetazydyna.
Lek zmniejsza uwalnianie wysokoczułej troponiny T będącej istotnym wskaźnikiem śmiertelności, *(szczególnie u chorych z cukrzycą i SCAD)*
niezależnym od zastosowanego leczenia *(OMT i/lub Rewaskularyzacja)*

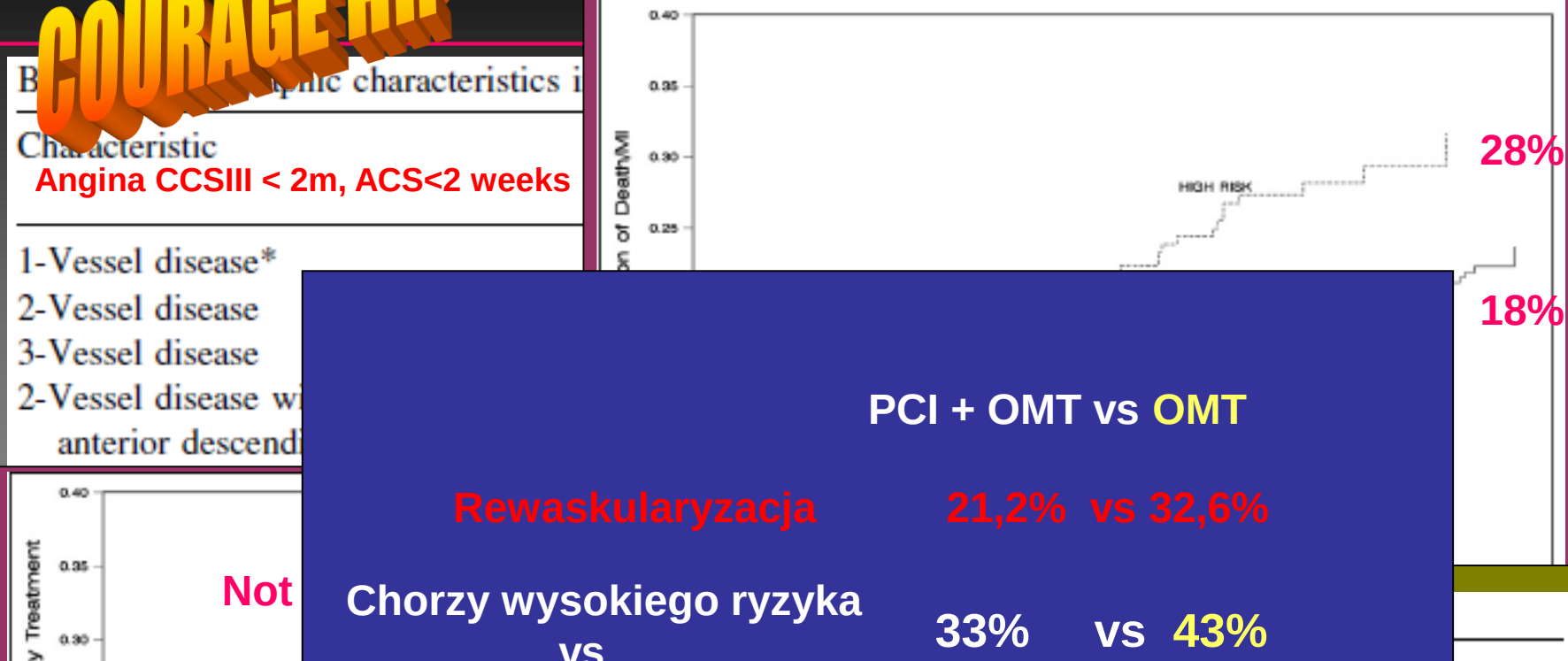
COURAGE HR

B… characteristics i…

Characteristic

Angina CCSIII < 2m, ACS<2 weeks

1-Vessel disease*
2-Vessel disease
3-Vessel disease
2-Vessel disease wi…
anterior descendi…



PCI + OMT vs OMT

Rewaskularyzacja	21,2% vs 32,6%
Chorzy wysokiego ryzyka vs Chorzy niskiego ryzyka	33% vs 43% 20% vs 31%

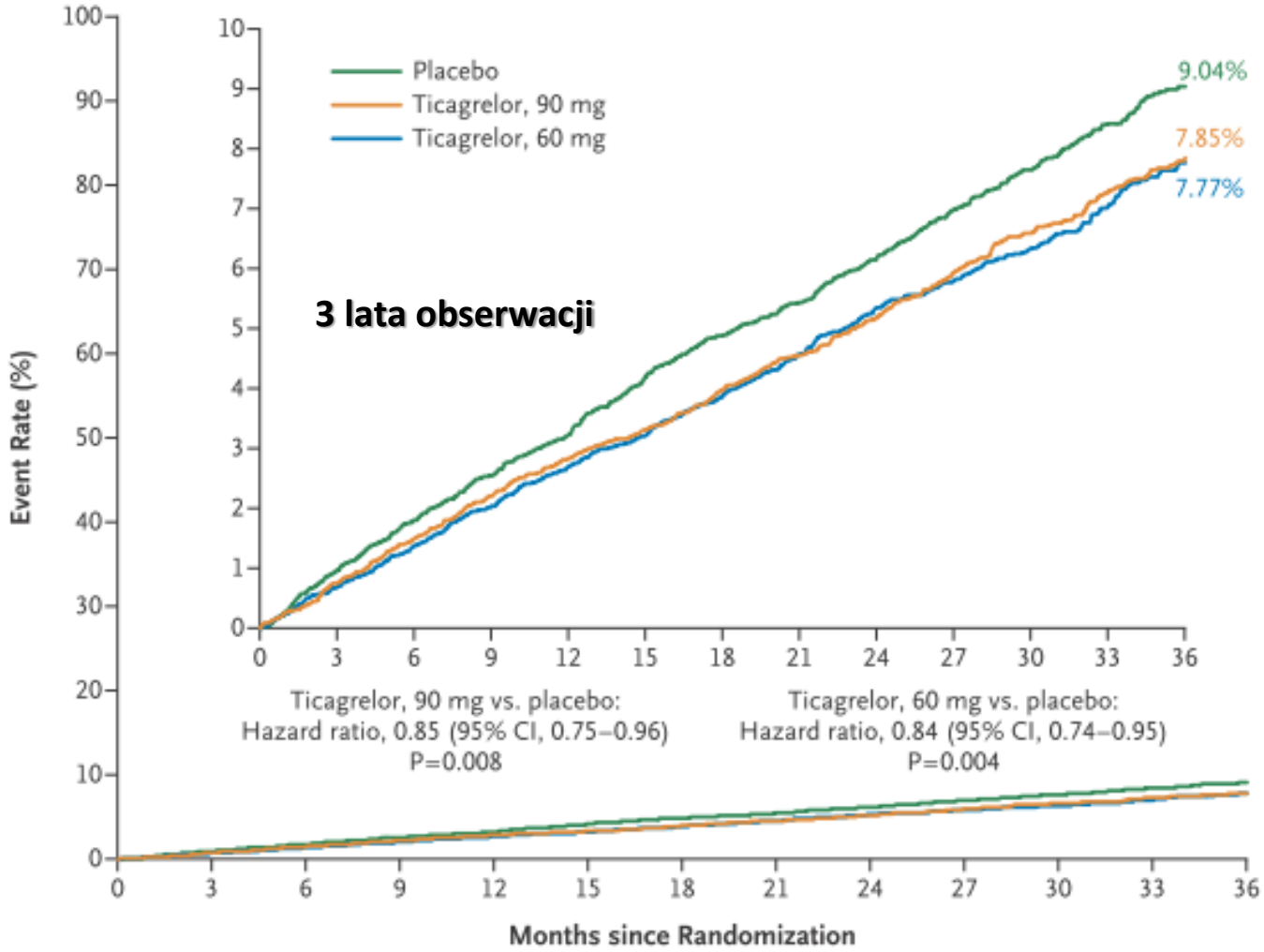
Not …

				p Value
…9)				0.68
…5)				0.98
Myocardial infarction*	25 (19%)	22 (17%)	1.14 (0.64.2.02)	0.66
Acute coronary syndrome	22 (17%)	27 (20%)	0.78 (0.45.1.37)	0.39

Maron J et al. Am J Cardiol 2010

PEGASUS – TIMI 54

Wszyscy chorzy 1 do 3 lat po przebyciu zawału serca, 32% cukrzyca, 77% nadciśnienie tętnicze 16% > 1 zawał serca.

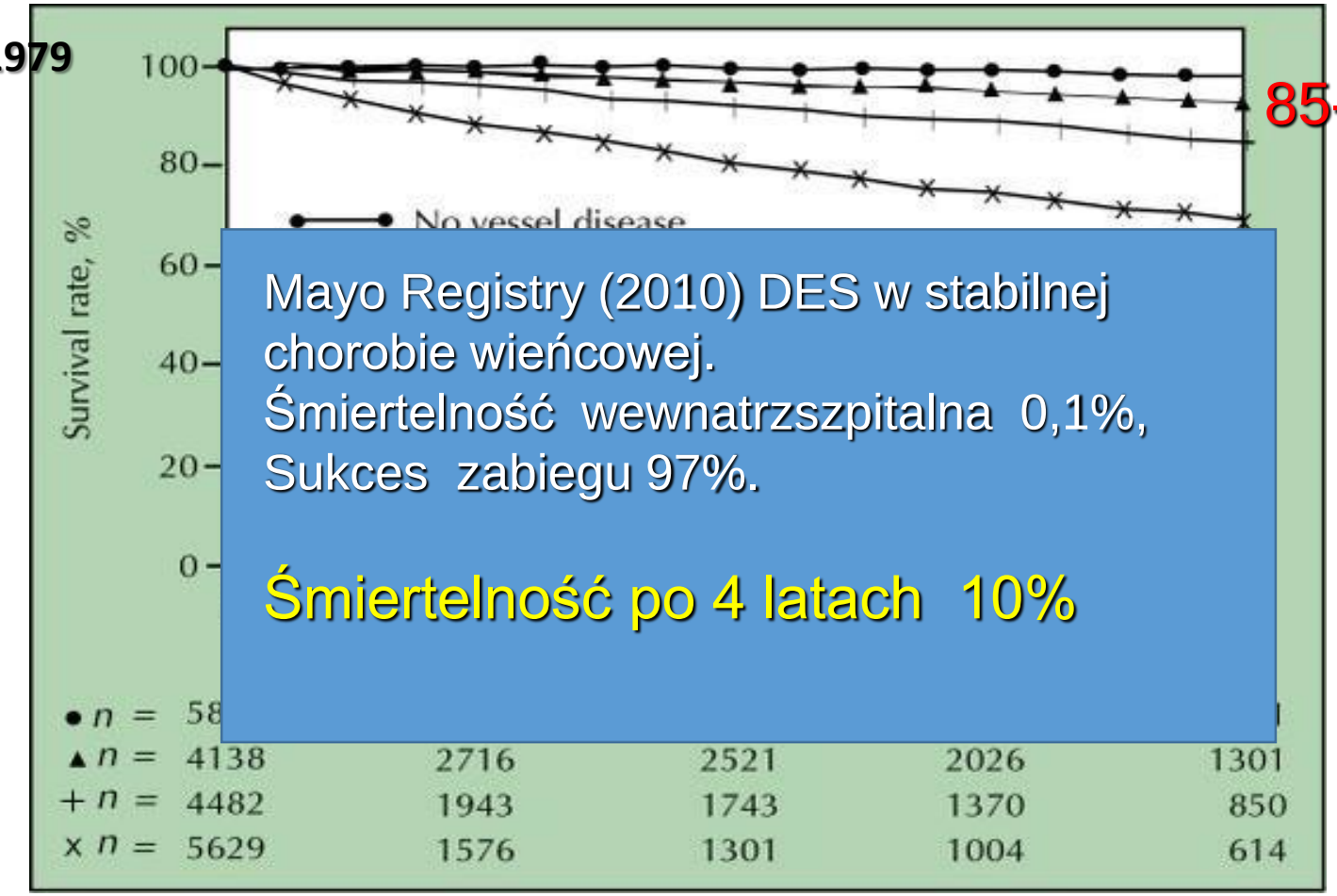


Bonaca M et al. NEJM 2015

Przeżycie w grupie leczonej zachowawczo (CASS)

Nie stosowano OMT, u 75% chorych EF powyżej 50%

Populacja 1975 -1979



85-90%

Mayo Registry (2010) DES w stabilnej chorobie wieńcowej.
Śmiertelność wewnatrzszpitalna 0,1%,
Sukces zabiegu 97%.

Śmiertelność po 4 latach 10%

Przeżywalność w obu grupach (CABG vs MT) niemal identyczna

Wniosek ; CABG w grupie MT tylko w przypadku zaostrzenia obj. klinicznych