SHOULD BETA BLOCKERS BE USED ROUTINELY IN POST MI PATIENTS WITH PRESERVED LV FUNCTION?

Doron Zahger, MD

Department of Cardiology, Soroka University Medical Center, Faculty of Health Sciences, Ben Gurion University of the Negev, Beer Sheva , Israel

Conflicts of Interest:

Company Name	Relationship
AstraZeneca	honoraria, consultant
Eli Lilly	honoraria, consultant
Iroko	Honorarium
Bayer	consultant
Sanofi Aventis	consultant
Rafa Laboratories	consultant

A QUIZ TO THE AUDIENCE:

- A 52 y.o. male is admitted for a first inferior STEMI.
- Emergency coronary angiography reveals a totally occluded 1st marginal branch. There are no other lesions.
- Primary PCI is performed with a good result. Pain to balloon time is 150 min.

A QUIZ TO THE AUDIENCE:

- Follow up EKG shows complete ST resolution
- LV function is preserved with posterior hypokinesis.
- The patient is given aspirin, prasugrel and a statin.
- Will his short or long term prognosis be improved by beta blockade?

HOW DO BETA BLOCKERS IMPROVE OUTCOME IN CAD?

- Attenuation of ischemia through reduced demand
- Attenuation of ventricular remodeling
- Prevention of lethal arrhythmias and sudden death

DO BETA BLOCKERS IMPROVE OUTCOME POST MI?

- In patients with residual ischemia – possibly
  - Most patients currently discharged w/o significant residual ischemia
- In patients with LV dysfunction – definitely
- In patients with preserved EF?
  - Remodeling and heart failure not an issue
  - Risk of lethal arrhythmias extremely small.

SUBGROUPS OF AMI PATIENTS

- **NSTEMI**
- **MI with LV dysfunction**
- **STEMI – routine, in hospital phase**
- **STEMI – routine, long term**

Efficacy of Nifedipine and Metoprolol in the Early Treatment of Unstable Angina in the Coronary Care Unit: Findings from the Holland Interuniversity Nifedipine/Metoprolol Trial (HINT)*

- Study conducted 1981-1984
- 338 patients with USAP randomized to metoprolol 100 mg*2/d, nifedipine 10 mg*6/d, both or neither.
- Primary outcome – recurr. ischemia/MI @ 48 h
- 25% had MI within a week.

Lubsen et al, Am J Cardiol 1987;60:18A

Efficacy of Nifedipine and Metoprolol in the Early Treatment of Unstable Angina in the Coronary Care Unit: Findings from the Holland Interuniversity Nifedipine/Metoprolol Trial (HINT)*

- Other medications: antiplatelet: 3%, heparin/coumadin: 67%, nitrates: 67%
- Nifedipine – worse outcome than placebo
- Metoprolol - better outcome than placebo
- Nothing significant!
- Conclusion: Nifedipine monotherapy "probably harmful", metoprolol "probably useful"

Lubsen et al, Am J Cardiol 1987;60:18A

TRIAL OF HEPARIN VERSUS ATENOLOL IN PREVENTION OF MYOCARDIAL INFARCTION IN INTERMEDIATE CORONARY SYNDROME

ANNE M. TELFORD CHARLES WILSON

Cardiac Unit, Waveney Hospital, Ballymena, Co. Antrim, Northern Ireland

- **Study conducted 1977-1980**
- **214 patients with USAP/subendocardial MI randomized to heparin/placebo and atenolol/placebo.**
-

The results of this study suggest that intravenous heparin therapy was highly beneficial in the prevention of myocardial infarction among patients presenting with symptoms consistent with the intermediate coronary syndrome. The beta-adrenergic blocking drug, atenolol, on the other hand, had no demonstrable effect. The benefit conferred by heparin was maintained on follow-up.

Teford et al. Lancet June 6, 1981

The American Journal of Medicine (2007) 120, 685-692

ELSEVIER

THE AMERICAN JOURNAL of MEDICINE®

CLINICAL RESEARCH STUDY

Impact of Acute Beta-Blocker Therapy for Patients with Non–ST-Segment Elevation Myocardial Infarction

Chadwick D. Miller, MD,[a] Matthew T. Roe, MD, MHS,[b] Jyotsna Mulgund, MS,[b] James W. Hoekstra, MD,[a] Renato Santos, MD,[a] Charles V. Pollack, Jr., MD, MA,[c] E. Magnus Ohman, MD,[b] W. Brian Gibler, MD,[d] Eric D. Peterson, MD, MPH[b]

- CRUSADE registry: 72,000 NSTEMI patients
- 509 hospitals, 2001-2004
- Value of acute (<24h) beta blockers examined
- Adjusted risk of mortality with beta blockers – 0.66 (0.60-0.72).

Table 1 Patient and Hospital Characteristics by Acute Beta-Blocker Use

Patient Characteristics	No Acute Beta-Blockers (n = 12,612)	Acute Beta-Blockers (n = 59,442)	*P* Value
Demographics			
Age (years)*	71 (58, 80)	69 (57, 79)	<.001
Women (%)	42.5	40.1	<.001
White (%)	79.1	78.9	.12
Body mass index*	27.3 (23.7, 31.5)	27.6 (24.3, 31.9)	<.001
Medical history			
Hypertension (%)	66.5	71.5	<.001
Diabetes mellitus (%)	33.8	33.7	.95
Current smoking (%)	24.7	25.5	.10
Hyperlipidemia (%)	41.0	48.8	<.001
Family history of coronary artery disease (%)	32.4	34.4	<.001
Renal insufficiency (%)†	14.6	15.1	.022
Prior stroke (%)	12.0	11.3	.024
Prior myocardial infarction (%)	27.8	31.8	<.001
Prior congestive heart failure (%)	22.3	19.4	<.001
Prior percutaneous coronary intervention (%)	19.3	21.3	<.001
Prior coronary artery bypass grafting (%)	18.8	21.1	<.001
Presenting characteristics			
ST depression (%)	28.7	32.3	<.001
Transient ST-elevation (%)	6.5	5.9	<.001
Signs of CHF (%)	28.3	24.0	<.001
Systolic blood pressure (mm Hg)*	141 (120, 161)	147 (128, 168)	<.001
Heart rate (beats per minute)*	84 (70, 100)	84 (72, 100)	.003
Other features			
Cardiology service (%)‡	48.4	53.7	<.001
Academic hospital (%)§	25.7	30.5	<.001
Prior beta-blocker use (%)	21.0	44.6	<.001
Insurance status (%)			<.001
HMO/Private	41.3	44.7	

SUBGROUPS OF AMI PATIENTS

- NSTEMI –
  - Beta blockers never shown to be superior to placebo in a randomized trial
- MI with LV dysfunction
- STEMI – routine, in hospital phase
- STEMI – routine, long term

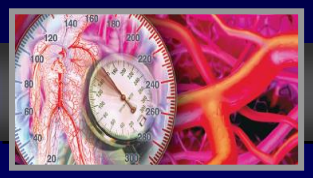
Recommendations for antiischemic agents

Recommendations for anti-ischaemic drugs

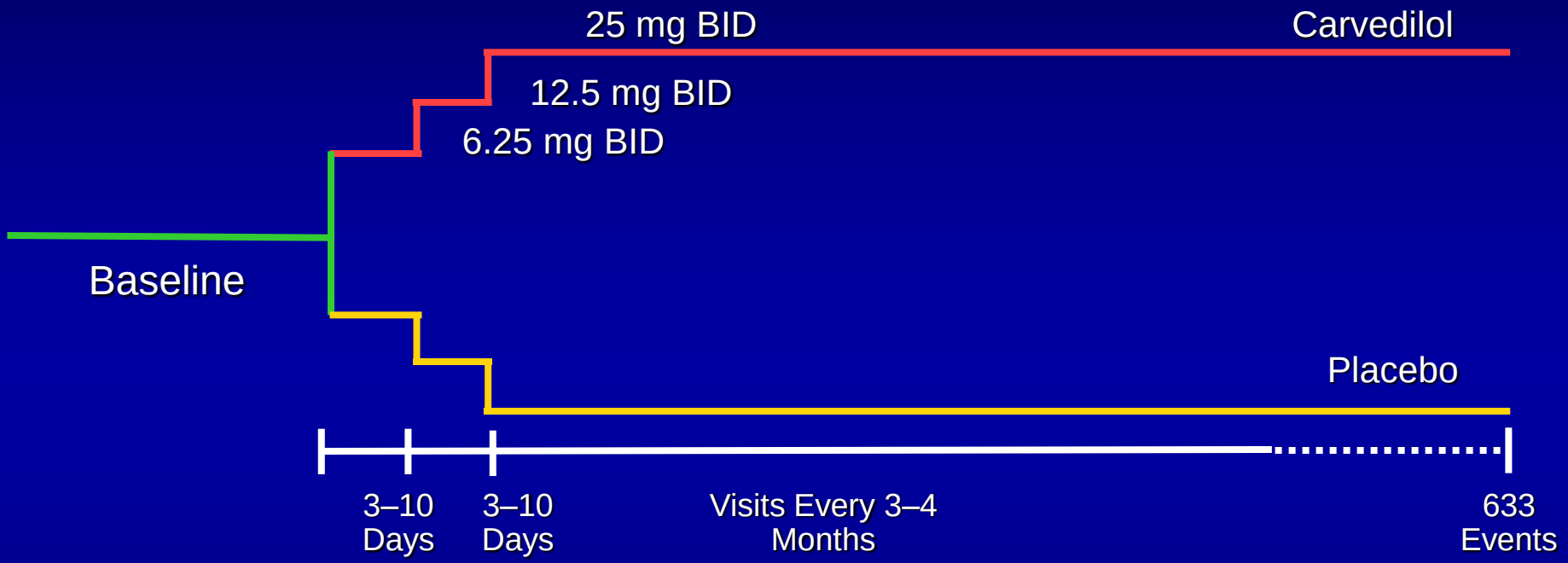
Recommendations	Class [a]	Level [b]	Ref [c]
Oral or intravenous nitrate treatment is indicated to relieve angina; intravenous nitrate treatment is recommended in patients with recurrent angina and/or signs of heart failure.	I	C	-
Patients on chronic β-blocker therapy admitted with ACS should be continued on ß-blocker therapy if not in Killip class ≥III.	I	B	91
Oral β-blocker treatment is indicated in all patients with LV dysfunction (see Section 5.5.5) without contraindications.	I	B	86, 90, 91
Calcium channel blockers are recommended for symptom relief in patients already receiving nitrates and β-blockers (dihydropyridines type), and in patients with contraindications to β-blockade (benzothiazepine or phenylethylamine type).	I	B	88
Calcium channel blockers are recommended in patients with vasospastic angina.	I	C	-
Intravenous β-blocker treatment at the time of admission should be considered for patients in a stable haemodynamic condition (Killip class <III) with hypertension and/or tachycardia.	IIa	C	93
Nifedipine, or other dihydropyridines, are not recommended unless combined with β-blockers.	III	B	88

SUBGROUPS OF AMI PATIENTS

- NSTEMI
- MI with LV dysfunction
- STEMI – in hospital phase
- STEMI – long term

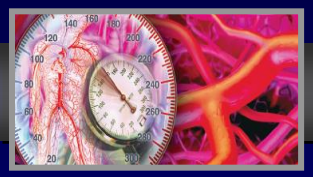


CAPRICORN
Study Design



- Encouraged adjunctive therapy
- Receiving ACE inhibitor ≥ 48 hrs
- Clinically stable, but may have had pulmonary edema or cardiogenic shock during index infarction

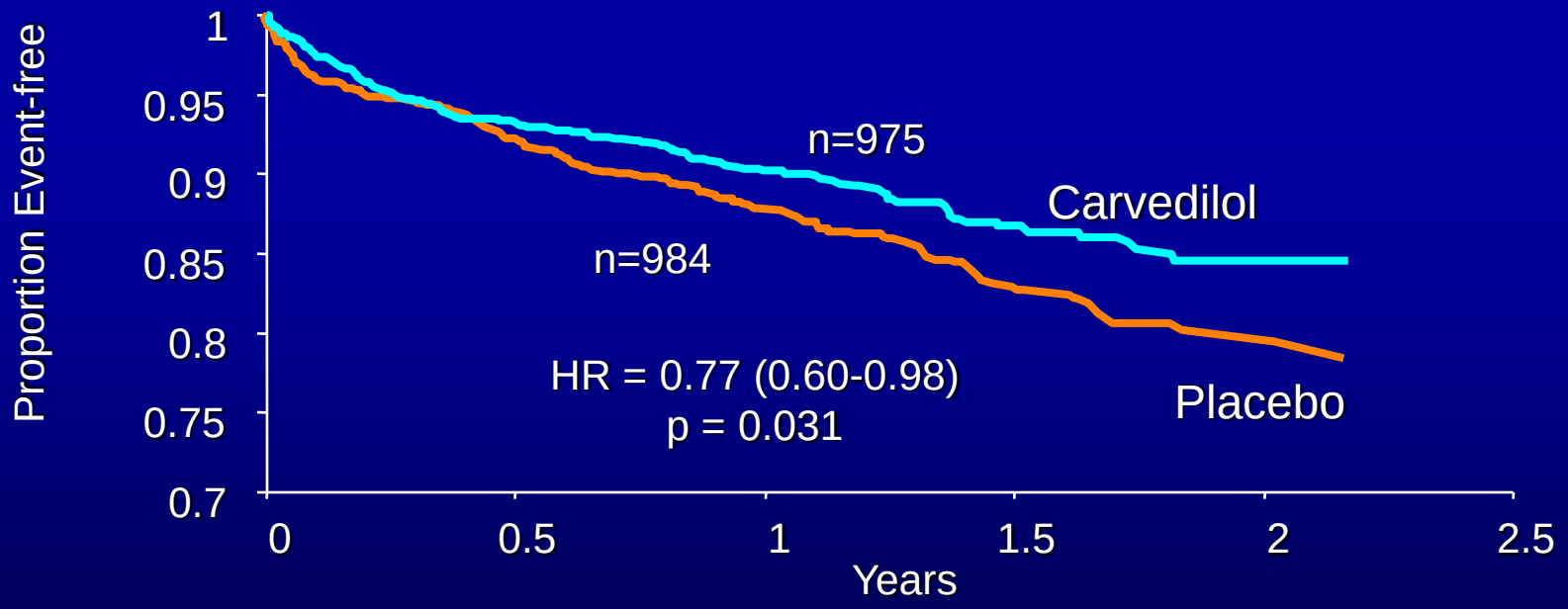
Dargie HJ, et al. *Eur J Heart Fail* 2000;2:325-332.



CAPRICORN:
All-Cause Mortality

Carvedilol Post-Infarct Survival Control in LV Dysfunction (CAPRICORN)

- 6,644 patients with LVEF<40% after a MI with or without HF randomized to carvedilol or placebo for 24 months



The CAPRICORN Investigators. *Lancet* 2001;357:1385-1390.

SUBGROUPS OF AMI PATIENTS

- NSTEMI
- MI with LV dysfunction
- STEMI – routine, in hospital phase
- STEMI – routine, long term

Does the Early Administration of Beta-blockers Improve the In-hospital Mortality Rate of Patients Admitted with Acute Coronary Syndrome?

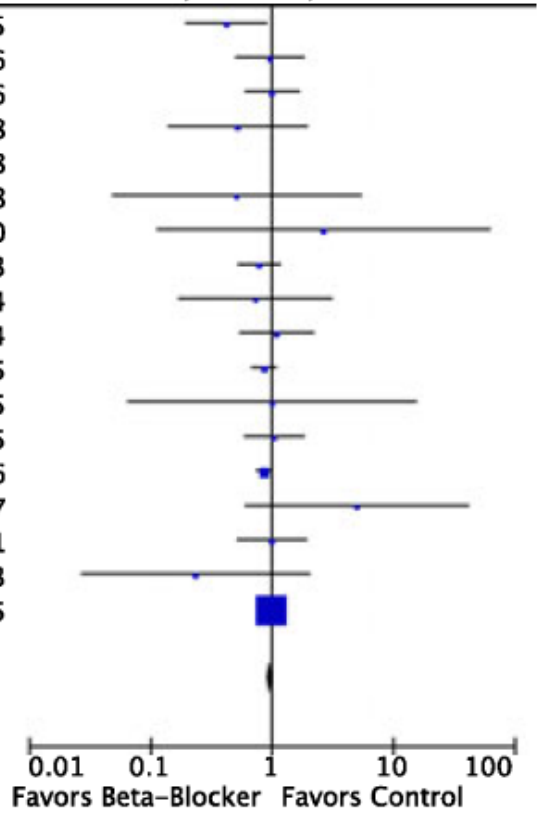
Ethan Brandler, MD, MPH, Lorenzo Paladino, MD, and Richard Sinert, DO

Study or Subgroup	Beta-Blocker Events	Beta-Blocker Total	no Beta-Blocker Events	no Beta-Blocker Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
Snow 1965	7	45	17	46	0.5%	0.42 [0.19, 0.92]	1965
Balcon 1966	13	56	14	58	0.7%	0.96 [0.50, 1.86]	1966
Clausen 1966	18	53	19	56	1.1%	1.00 [0.59, 1.69]	1966
Evenmy 1978	3	46	6	48	0.2%	0.52 [0.14, 1.96]	1978
Norris 1978	0	20	0	23		Not estimable	1978
Peter 1978	1	47	2	48	0.1%	0.51 [0.05, 5.44]	1978
Norris 1980	1	33	0	29	0.0%	2.65 [0.11, 62.56]	1980
Yusuf 1983	36	244	44	233	1.8%	0.78 [0.52, 1.17]	1983
ICSG 1984	3	73	4	71	0.1%	0.73 [0.17, 3.14]	1984
Norris 1984	15	364	14	371	0.6%	1.09 [0.53, 2.23]	1984
MIAMI 1985	118	2877	138	2901	5.1%	0.86 [0.68, 1.10]	1985
Owensby 1985	1	50	1	50	0.0%	1.00 [0.06, 15.55]	1985
Salathia 1985 (1)	25	416	20	348	0.9%	1.05 [0.59, 1.85]	1985
ISIS-1 1986	317	8017	367	7980	13.7%	0.86 [0.74, 1.00]	1986
Heber 1987	5	83	1	83	0.1%	5.00 [0.60, 41.88]	1987
Roberts TIMI II-B 1991	17	720	17	714	0.7%	0.99 [0.51, 1.93]	1991
Van de Werf 1993	1	100	4	94	0.1%	0.23 [0.03, 2.06]	1993
COMMIT 2005	1774	22929	1797	22923	74.4%	0.99 [0.93, 1.05]	2005
Total (95% CI)		**36173**		**36076**	**100.0%**	**0.95 [0.90, 1.01]**	
Total events	2355		2465				

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 14.72$, df = 16 (P = 0.55); $I^2 = 0\%$

Test for overall effect: Z = 1.72 (P = 0.09)

(1) M-H = Mantel-Haenszel

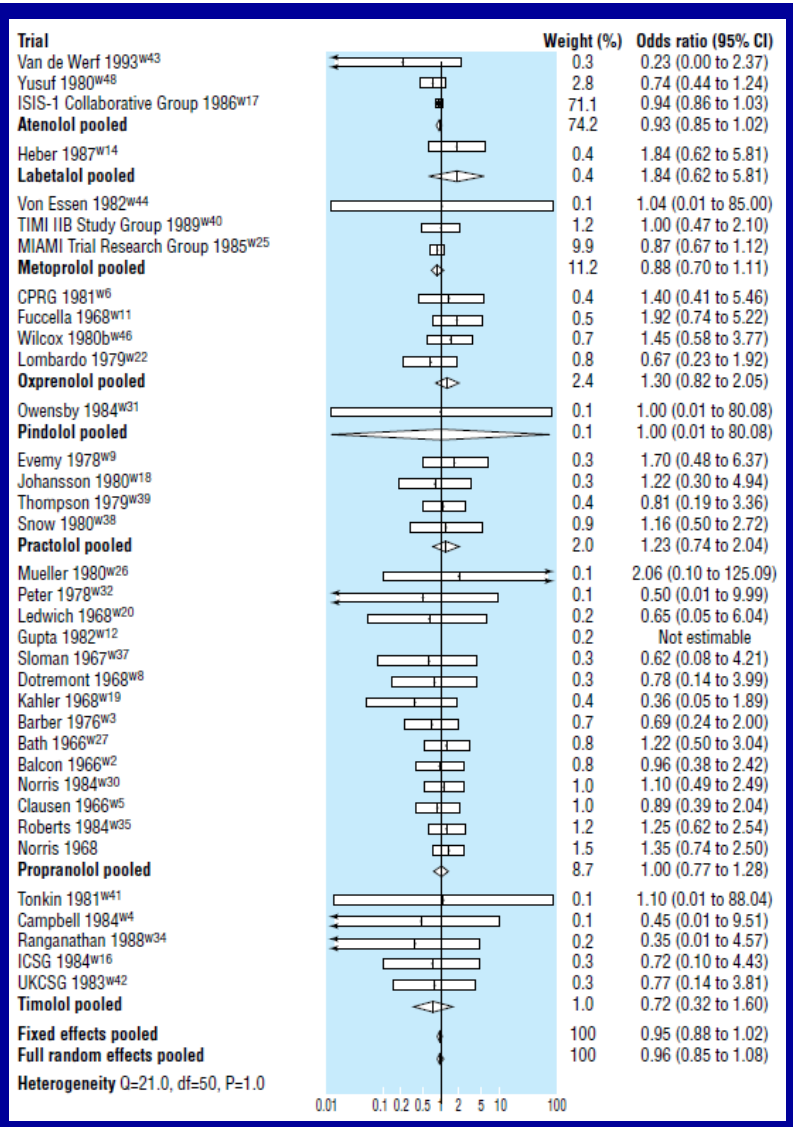


Academic Emergency Med 2010;17:1-10

β Blockade after myocardial infarction: systematic review and meta regression analysis

Nick Freemantle, John Cleland, Philip Young, James Mason, Jane Harrison

Acute trials



BMJ 1999;318:1730

SUBGROUPS OF AMI PATIENTS

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- MI with LV dysfunction
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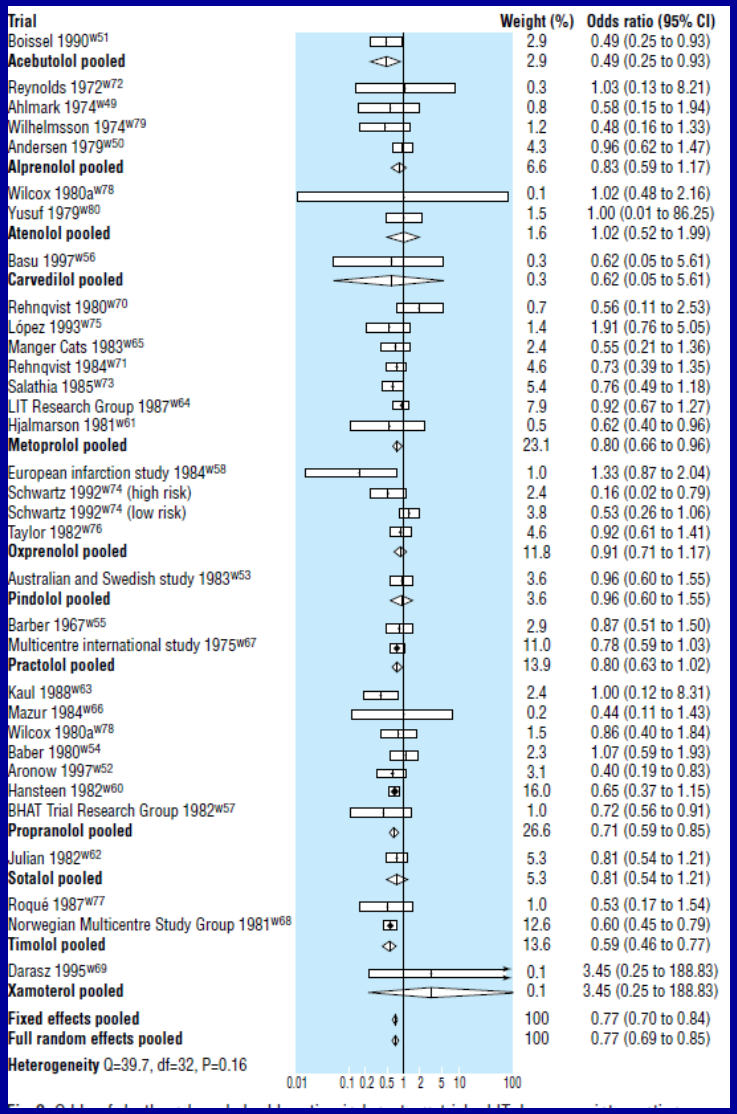
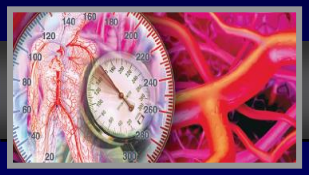
Nick Freemantle, John Cleland, Philip Young, James Mason, Jane Harrison

Long term trials

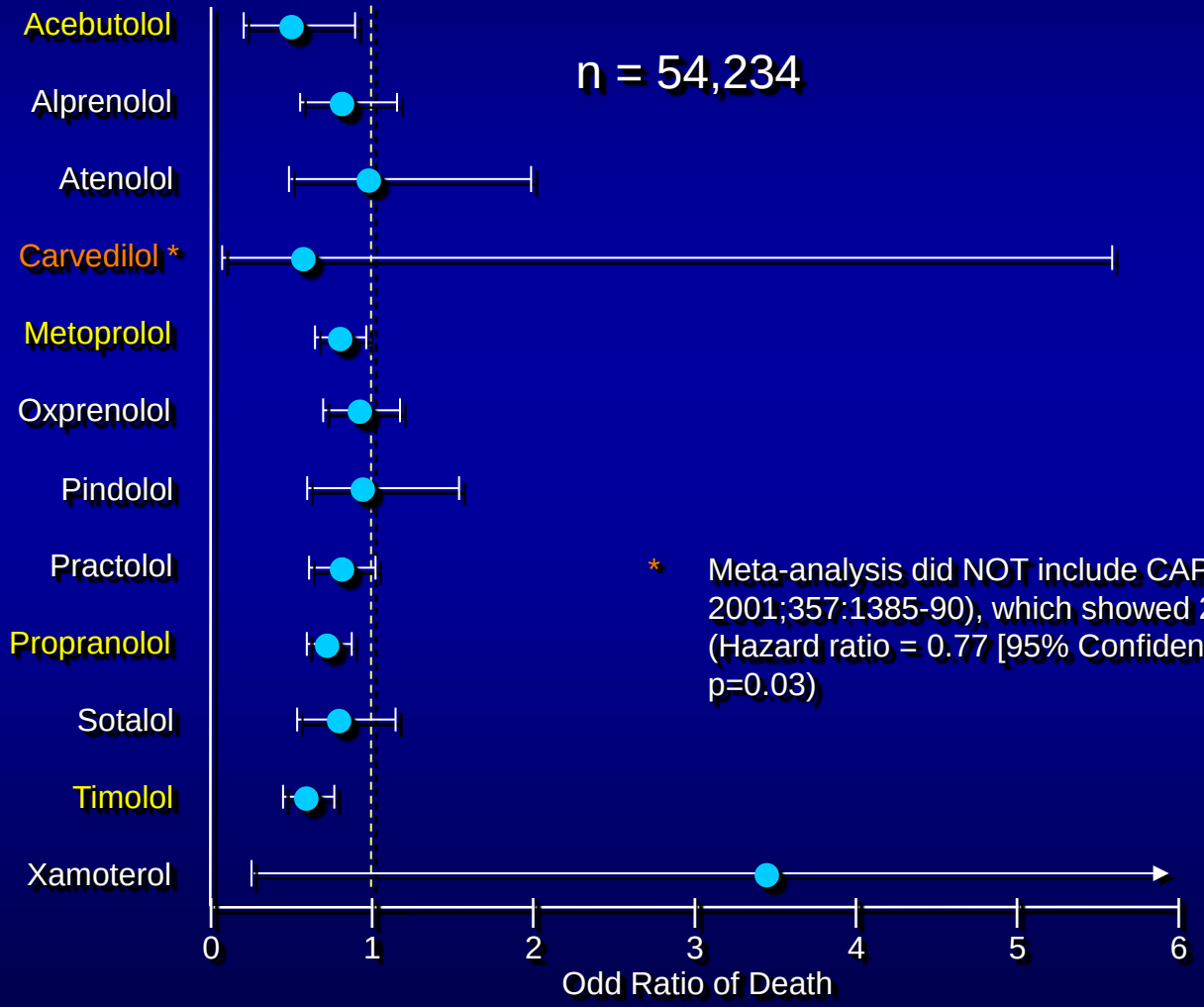


BMJ 1999;318:1730



Myocardial Infarction: Is there a Class Effect for β-blockers?

Total Mortality Reduction after Myocardial Infarction



* Meta-analysis did NOT include CAPRICORN Trial (Lancet 2001;357:1385-90), which showed 23%↓ in all-cause mortality (Hazard ratio = 0.77 [95% Confidence interval = 0.60-0.98], p=0.03)

Freemantle N, et al. *BMJ* 1999;318:1730-7.

STUDIES SHOWING BENEFIT POST STEMI

- Mostly from the 70's and 80's.
- Before:
  - Reperfusion therapy
  - Aspirin
  - ADP receptor antagonists
  - Statins
  - ICD's
  - PCI
- In the absence of reperfusion the prevalence of LV dysfunction was much higher

REDUCTION OF INFARCT SIZE WITH THE EARLY USE OF TIMOLOL IN ACUTE MYOCARDIAL INFARCTION

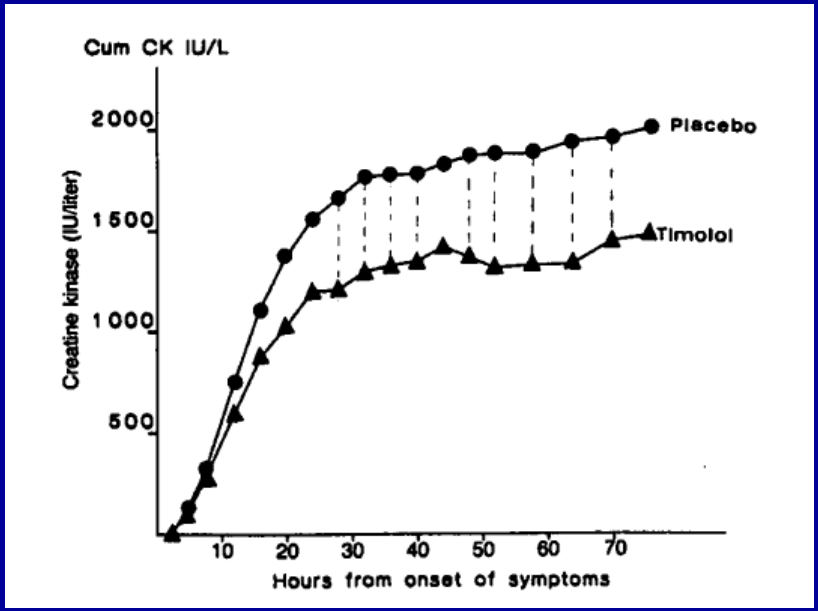
THE INTERNATIONAL COLLABORATIVE STUDY GROUP

Abstract One hundred forty-four patients admitted to the hospital within four hours after onset of symptoms of myocardial infarction were randomly assigned to either intravenous timolol treatment or to placebo. Timolol was given intravenously for the first 24 hours and orally thereafter for the duration of hospitalization. Infarct evolution was assessed by continuous vectorcardiography and creatine kinase release. The timolol group had reduced myocardial ischemia and infarct size as measured by an accelerated reduction of ST-vector magnitude, a significant reduction of maximal cumulative creatine kinase release (29.5 per cent), and significantly smaller changes in QRS-vector variables (20 to 25 per cent). Furthermore, the predicted creatine kinase release and maximal QRS-vector change for a given initial ST-vector magnitude was significantly reduced in the timolol group. Timolol was also associated with significant reductions in pain and need for analgesics and was well tolerated overall.

This study supports the use of intravenous timolol in the early phase of suspected myocardial infarction to limit infarct size. (N Engl J Med 1984; 310:9-15.)

Table 1. Concomitant Drug Therapy in the Timolol and Placebo Groups.

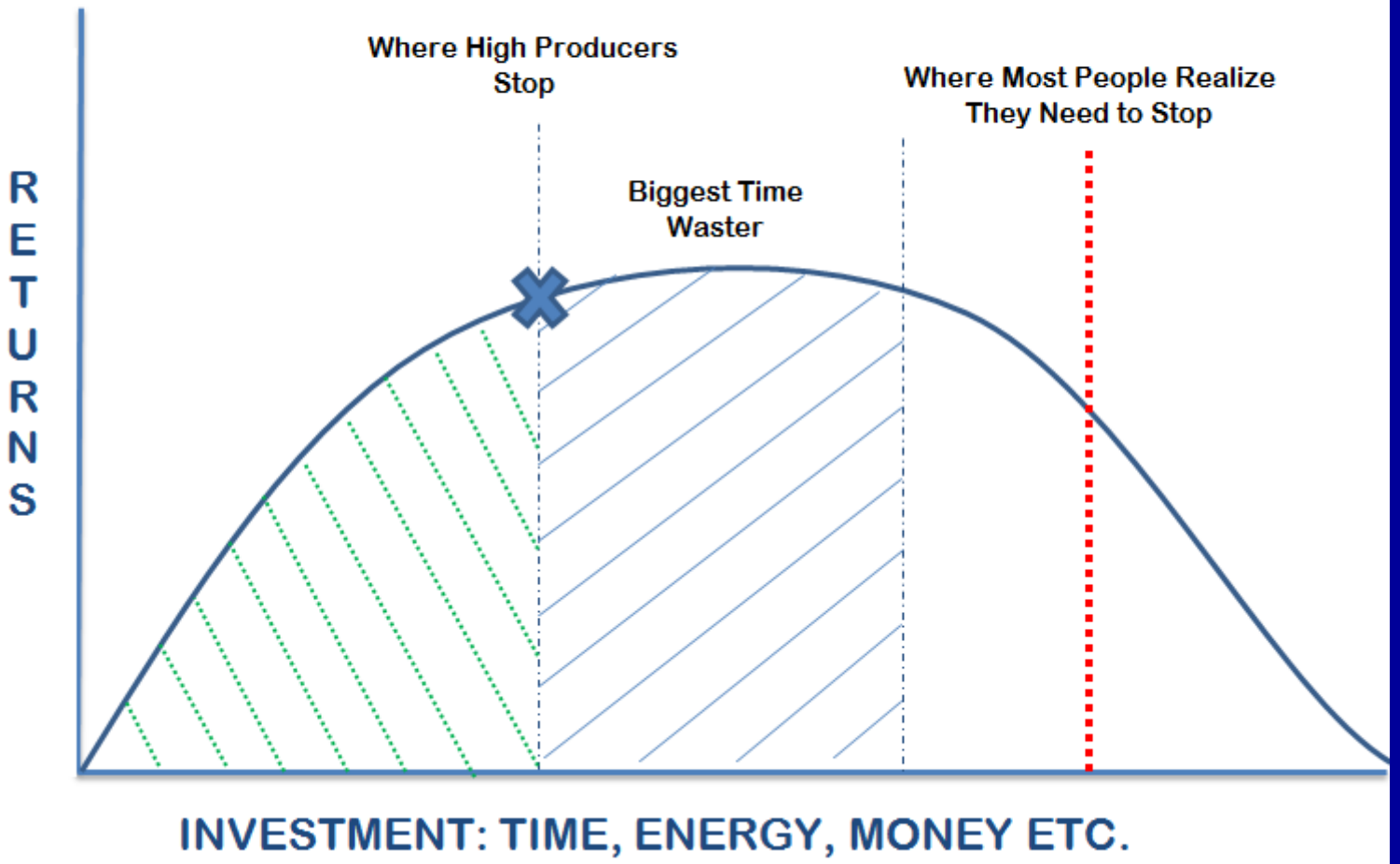
	TIMOLOL GROUP (n = 73)	PLACEBO GROUP (n = 71)	P VALUE *
	milligrams of drug		
During test-drug administration — 1st 24 hr			
Morphine or equivalent analgesics	630	838	<0.05
Furosemide	1280	1260	NS
More than 24 hr after test-drug administration			
Heart-failure therapy			
Digitalis	6	6	NS
Diuretics	33	37	NS
Ischemia therapy			
Beta-blockers	3	8	NS
Nitrates	7	11	NS
Pain therapy			
Analgesics	21	33	<0.05



Law of diminishing returns

Law of diminishing returns: output will ultimately increase by progressively smaller amounts when the use of a variable input increases while other inputs are held constant.

Law of Diminishing Returns



THE LAW OF DIMINISHING RETURNS

- The absolute benefit of a medical intervention, and therefore the NNT and the ability to demonstrate benefit, vary directly with baseline risk, which in a randomized trial can be assessed by event rate in the placebo group.
- Each successive intervention that reduces RELATIVE risk will progressively reduce the ABSOLUTE benefit of further interventions
- As the baseline risk of a population decreases, interventions that do not explain this decline (at least not largely) should be re-examined.

The Law of Diminishing Returns in Clinical Medicine: How Much Risk Reduction is Enough?

James W. Mold, MD, MPH, Robert M. Hamm, PhD, and Laine H. McCarthy, MLIS

The law of diminishing returns, first described by economists to explain why, beyond a certain point, additional inputs produce smaller and smaller outputs, offers insight into many situations encountered in clinical medicine. For example, when the risk of an adverse event can be reduced in several different ways, the impact of each intervention can generally be shown mathematically to be reduced by the previous ones. The diminishing value of successive interventions is further reduced by adverse consequences (eg, drug-drug, drug-disease, and drug-nutrient interactions), as well as by the total expenditures of time, energy, and resources, which increase with each additional intervention. It is therefore important to try to prioritize interventions based on patient-centered goals and the relative impact and acceptability of the interventions. We believe that this has implications for clinical practice, research, and policy. (J Am Board Fam Med 2010;23: 371–375.)

Saving Mr. Martin

- 65 y.o. African American
- BMI: 30.5
- Type 2 diabetes, HBA1C: 10%
- Blood pressure: 200/100
- LDL: 140 mg/dl, HDL: 40 mg/dl
- Therapeutic targets: weight loss, exercise, lower BP, aspirin, reduce HBA1C, ACE-I, beta blocker?

Table 1. Individual and Cumulative Absolute Risk Reductions of Interventions on 10-Year Risk for Myocardial Infarction for Mr. Martin from the Archimedes Risk Calculator*

Interventions	Individual ARRs (%)	Sequential ARRs (%)	Risk (%)
Aspirin	13.5	13.5	22.9
Lower SBP to 130	7	4.1	18.8
Moderate exercise	6.8	5.4	13.4
β-blocker	4.5	0.4	13.0
ACE inhibitor	2.9	1.1	11.9
Lower LDL to 100	2.6	0.2	11.7

*Base risk, 36.4%.

Landmark Practice Advances in Acute Coronary Syndromes

ESC Congress 2008 MUNICH

STEMI

SK

SK+ ASPIRIN

PRIMARY PCI

r-tPA

TNK

Pre-H lysis Morrison

VIENNA REGISTRY

ABCIXIMAB

BIVALIRUDIN

CLOPIDOGREL

REACT

CARESS

1986 1988 1990 1992 1994 1996 1998 2000 2002 2004 2006 2008

NSTE-ACS

ASPIRIN + HEPARIN 1983-'88

TROPONIN

EARLY INVASIVE

ENOXAPARIN

UPSTREAM GP IIb/IIIa

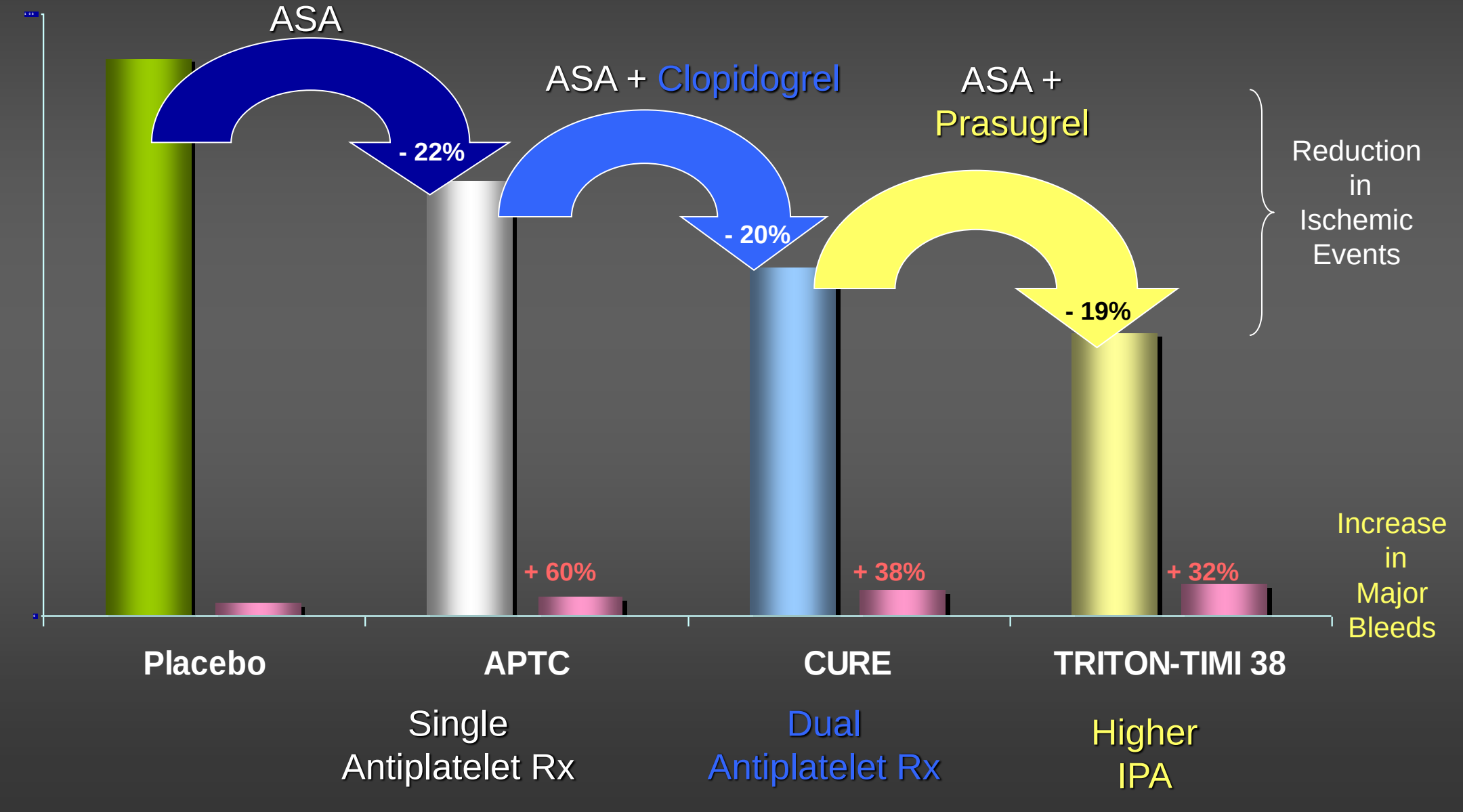
CLOPIDOGREL

ABCIXIMAB IN CATH LAB

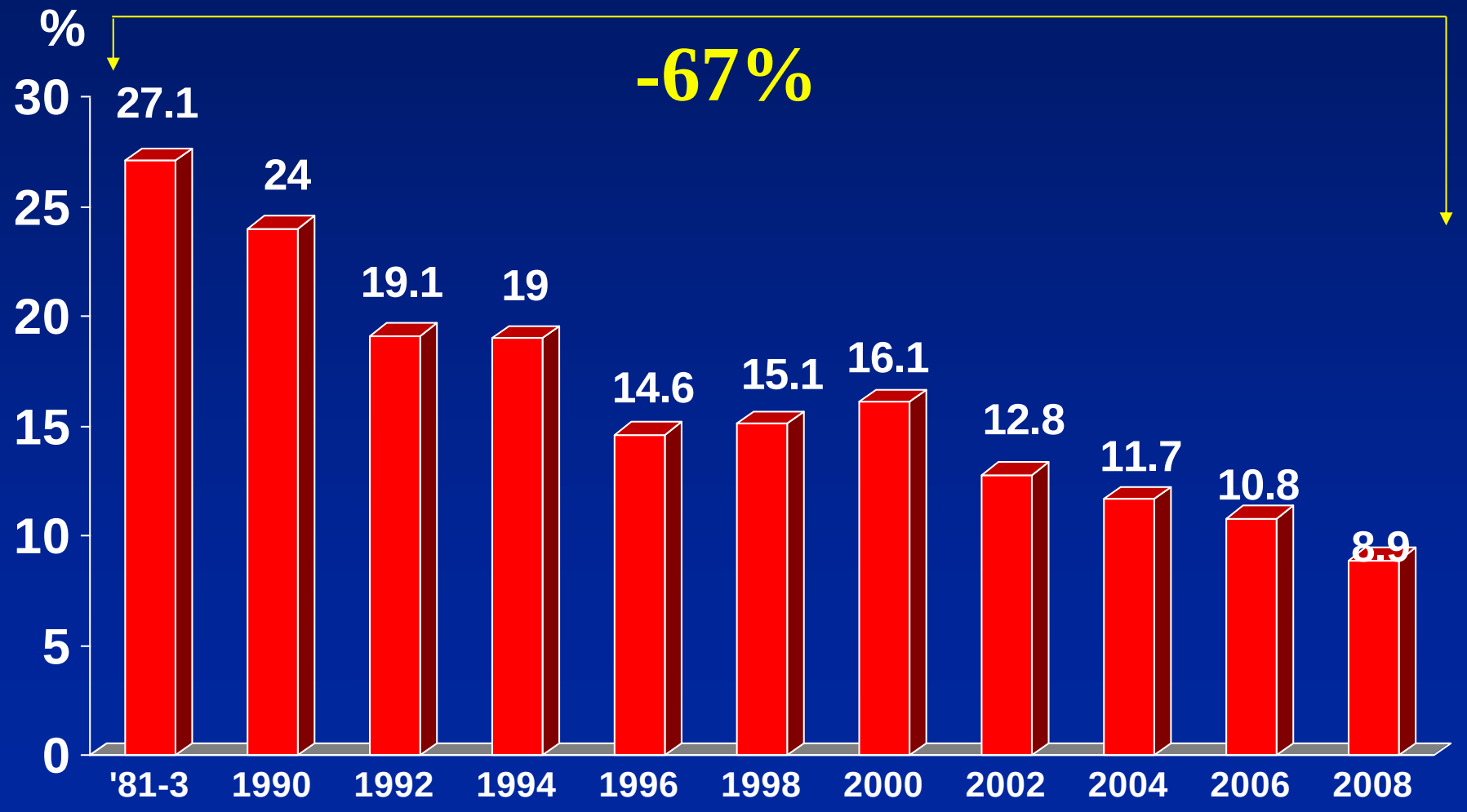
FONDAPARINUX

BIVALIRUDIN

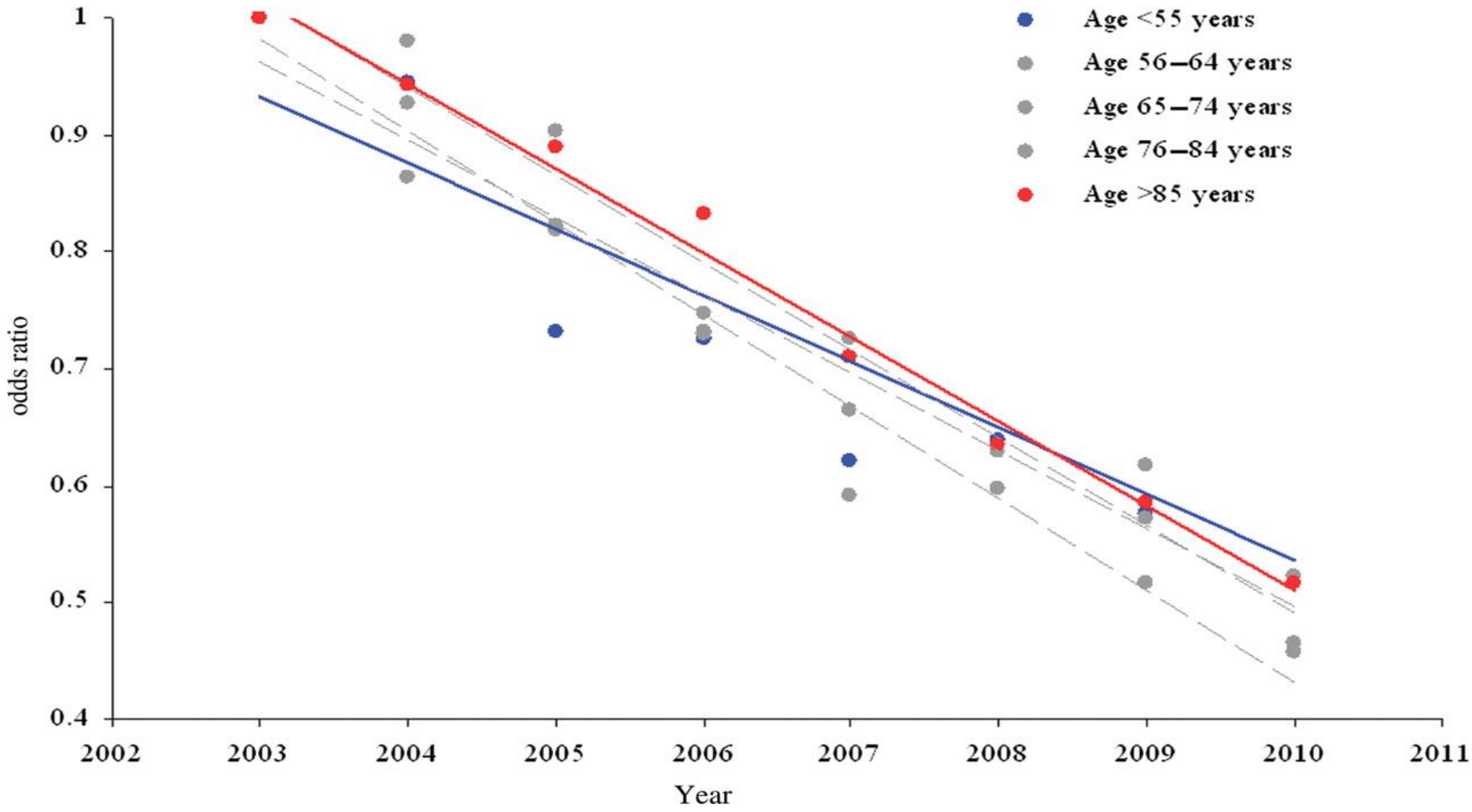
Antiplatelet Therapy in ACS



1-Year Mortality
AMI Israel, 1981 to 2010



Odds ratios by year for in-hospital all-cause mortality, stratified by age category. 2003 = base, adjustment for final diagnosis and hospital-level random effects.



Gale C P et al. Eur Heart J 2012;33:630-639

European Heart Journal

Circulation

JOURNAL OF THE AMERICAN HEART ASSOCIATION

American Heart Association®

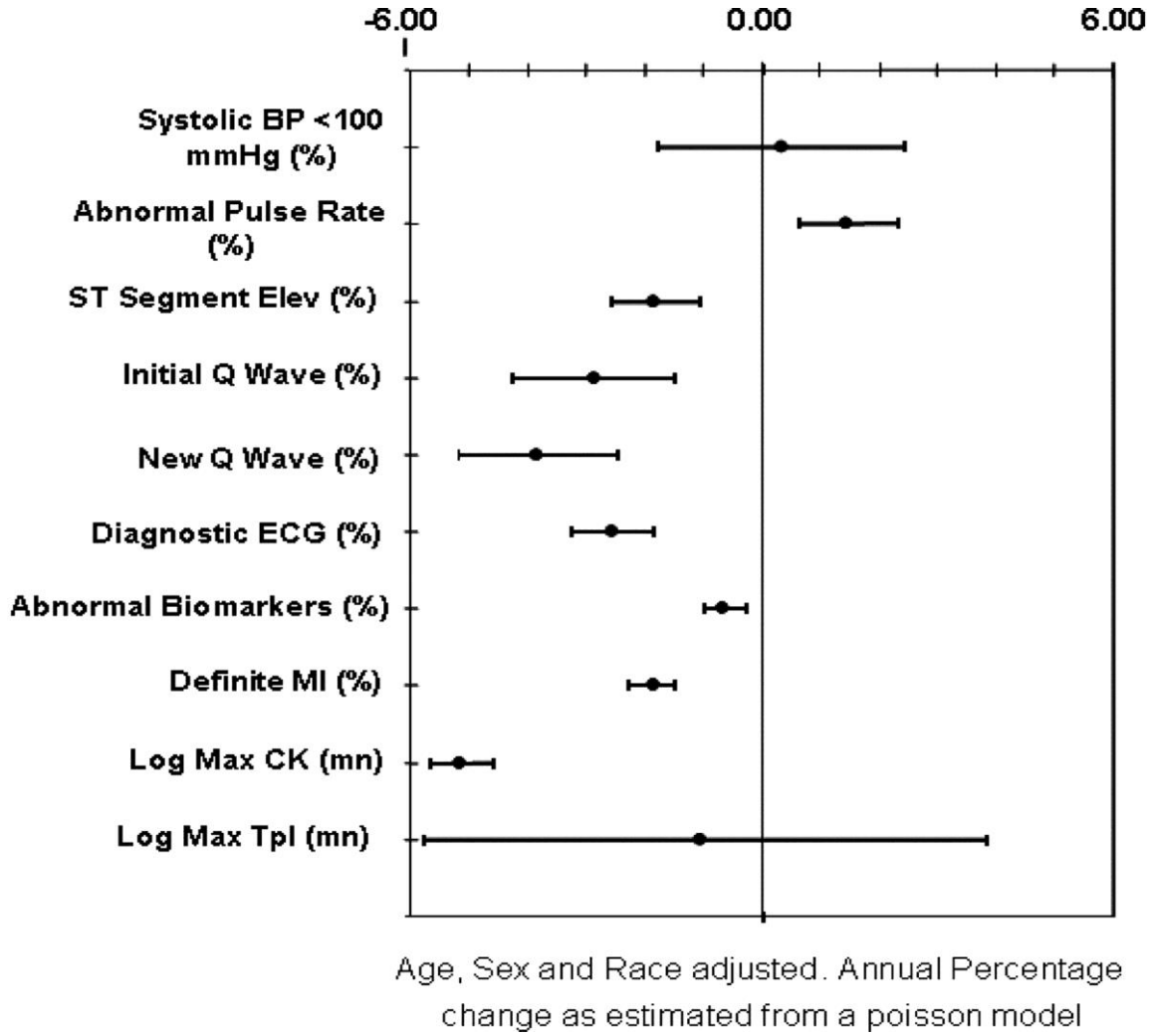
Learn and Live℠

Declining Severity of Myocardial Infarction From 1987 to 2002 : The Atherosclerosis Risk in Communities (ARIC) Study

Merle Myerson, Sean Coady, Herman Taylor, Wayne D. Rosamond and David C. Goff, Jr

Circulation 2009, 119:503-514: originally published online January 19, 2009
doi: 10.1161/CIRCULATIONAHA.107.693879

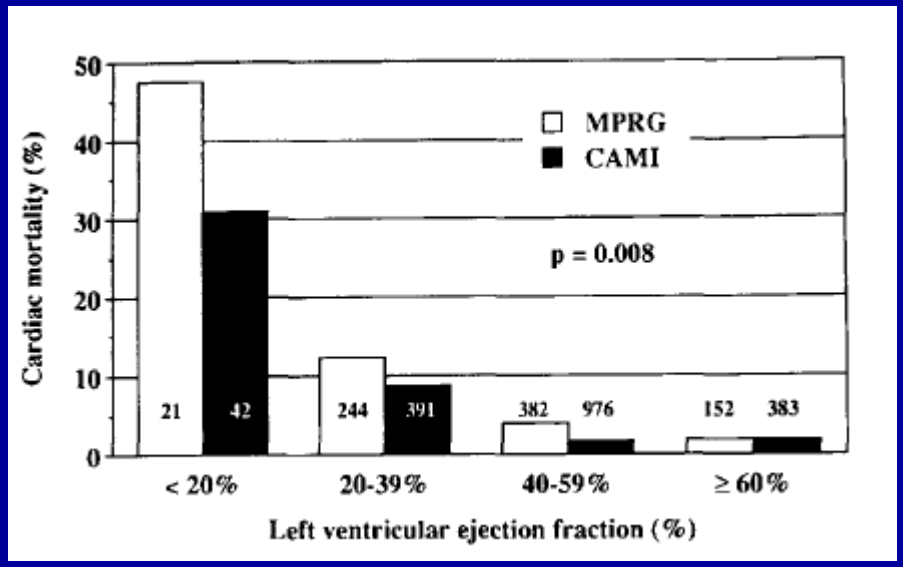
Figure 2. Annual percentage change and 95% CIs for selected indicators of MI severity: ARIC Community Surveillance, 1987 to 2002.

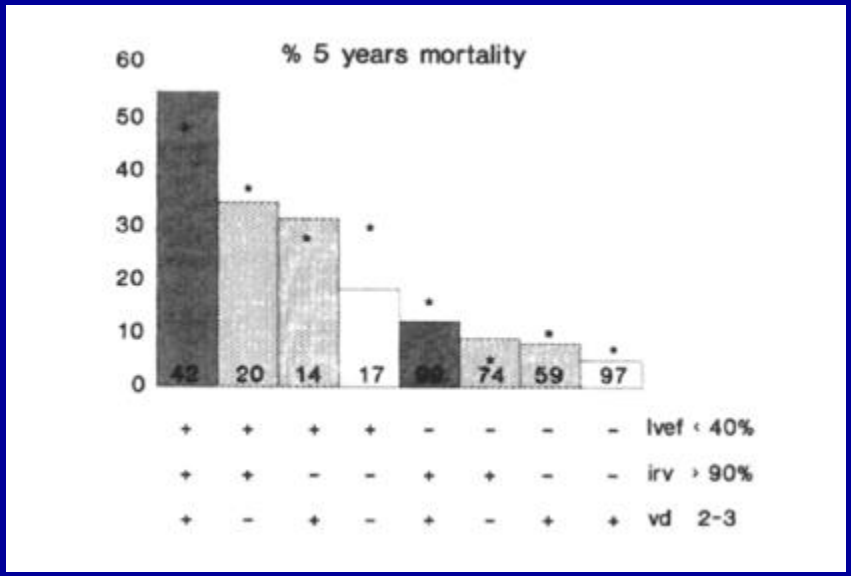


Myerson M et al. Circulation 2009;119:503-514

American Heart Association
Learn and Live

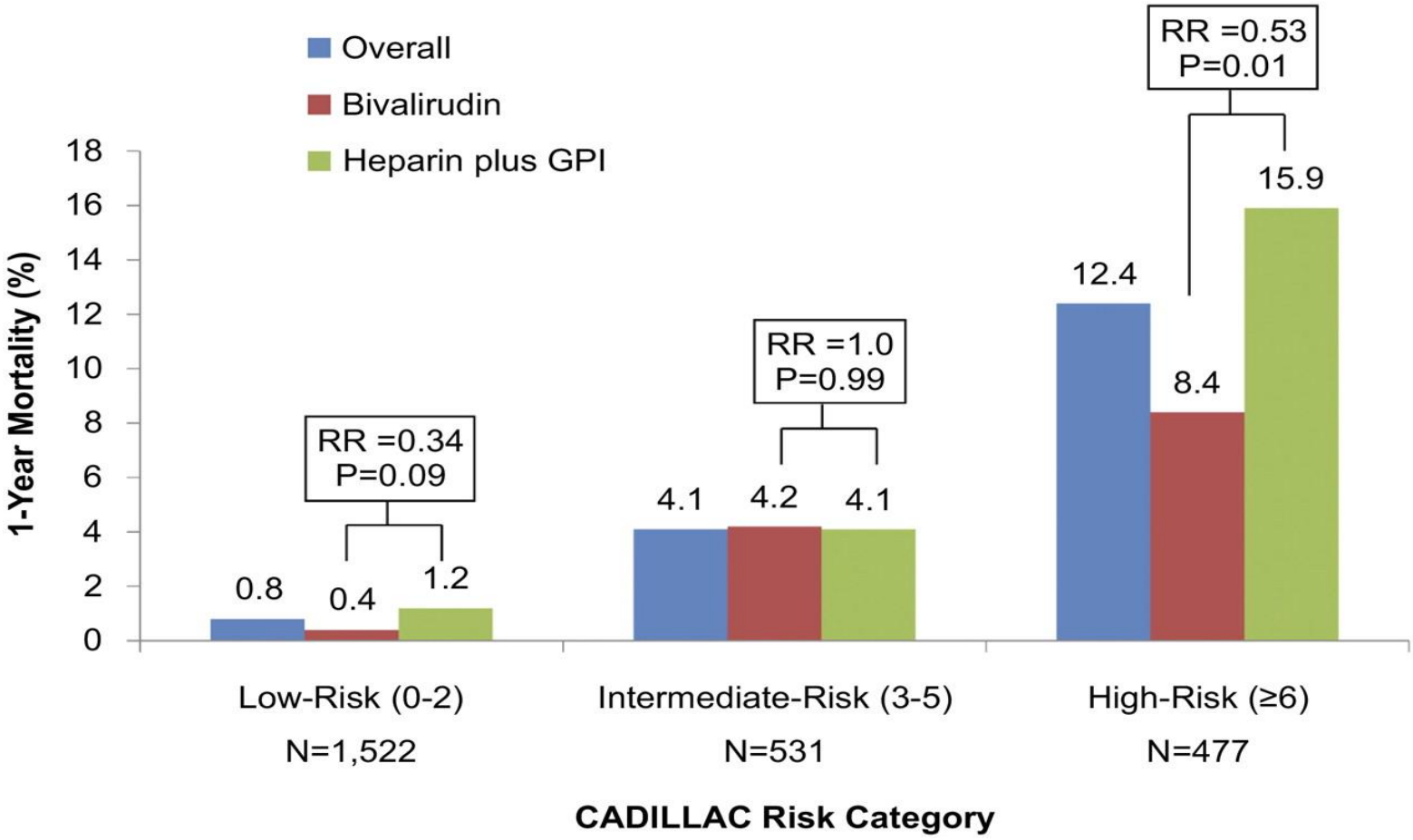
LONG TERM PROGNOSIS OF POST MI PATIENTS WITH PRESERVED LV IS EXTREMELY GOOD





Simoons et al. JACC 1989;14:1609
Rouleau et al. JACC 1996;27:1119

Mortality Rates According to Risk Category and Treatment



Parodi, G. et al. J Am Coll Cardiol Intv 2010;3:796-802

JACC cardiovascular Interventions

Can the risk of low risk patients be further reduced?

- 1 year mortality among low risk patients in HORIZONS : 0.8%.
- If beta blockers reduce mortality by 15% in these patients (questionable!) the mortality would be 0.68%.
- Absolute risk reduction: 0.12%
- NNT: 833

β-Blocker Use and Clinical Outcomes in Stable Outpatients With and Without Coronary Artery Disease

Sripal Bangalore, MD, MHA
Ph. Gabriel Steg, MD
Prakash Deedwania, MD
Kevin Crowley, MS
Kim A. Eagle, MD
Shinya Goto, MD, PhD
E. Magnus Ohman, MD
Christopher P. Cannon, MD
Sidney C. Smith Jr, MD
Uwe Zeymer, MD
Elaine B. Hoffman, PhD
Franz H. Messerli, MD
Deepak L. Bhatt, MD, MPH
for the REACH Registry Investigators

Context β-Blockers remain the standard of care after a myocardial infarction (MI). However, the benefit of β-blocker use in patients with coronary artery disease (CAD) but no history of MI, those with a remote history of MI, and those with only risk factors for CAD is unclear.

Objective To assess the association of β-blocker use with cardiovascular events in stable patients with a prior history of MI, in those with CAD but no history of MI, and in those with only risk factors for CAD.

Design, Setting, and Patients Longitudinal, observational study of patients in the Reduction of Atherothrombosis for Continued Health (REACH) registry who were divided into 3 cohorts: known prior MI (n=14 043), known CAD without MI (n=12 012), or those with CAD risk factors only (n=18 653). Propensity score matching was used for the primary analyses. The last follow-up data collection was April 2009.

Main Outcome Measures The primary outcome was a composite of cardiovascular death, nonfatal MI, or nonfatal stroke. The secondary outcome was the primary outcome plus hospitalization for atherothrombotic events or a revascularization procedure.

Results Among the 44 708 patients, 21 860 were included in the propensity score–matched analysis. With a median follow-up of 44 months (interquartile range, 35-45 months), event rates were not significantly different in patients with β-blocker use compared with those without β-blocker use for any of the outcomes tested, even in the prior MI cohort (489 [16.93%] vs 532 [18.60%], respectively; hazard ratio [HR], 0.90 [95% CI, 0.79-1.03]; *P*=.14). In the CAD without MI cohort, the associated event rates were not significantly different in those with β-blocker use for the primary outcome (391 [12.94%]) vs without β-blocker use (405 [13.55%]) (HR, 0.92 [95% CI, 0.79-1.08]; *P*=.31), with higher rates for the secondary outcome (1101 [30.59%] vs 1002 [27.84%]; odds ratio [OR], 1.14 [95% CI, 1.03-1.27]; *P*=.01) and for the tertiary outcome of hospitalization (870 [24.17%] vs 773 [21.48%]; OR, 1.17 [95% CI, 1.04-1.30]; *P*=.01). In the cohort with CAD risk factors only, the event rates were higher for the primary outcome with β-blocker use (467 [14.22%]) vs without β-blocker use (403 [12.11%]) (HR, 1.18 [95% CI, 1.02-1.36]; *P*=.02), for the secondary outcome (870 [22.01%] vs 797 [20.17%]; OR, 1.12 [95% CI, 1.00-1.24]; *P*=.04) but not for the tertiary outcomes of MI (89 [2.82%] vs 68 [2.00%]; HR, 1.36 [95% CI, 0.97-1.90]; *P*=.08) and stroke (210 [6.55%] vs 168 [5.12%]; HR, 1.22 [95% CI, 0.99-1.52]; *P*=.06). However, in those with recent MI (≤1 year), β-blocker use was associated with a lower incidence of the secondary outcome (OR, 0.77 [95% CI, 0.64-0.92]).

Conclusion In this observational study of patients with either CAD risk factors only, known prior MI, or known CAD without MI, the use of β-blockers was not associated with a lower risk of composite cardiovascular events.

TREATMENT WITH β-BLOCKERS remains the standard of care for patients with coronary artery disease (CAD), especially when they have had a myocardial infarction (MI).[1,2] The evidence is derived from relatively old post-MI studies, most of which antedate modern reperfusion or medical therapy, and from heart failure trials, but has been widely extrapolated to patients with CAD and even to patients at high risk for but without established CAD. It is not known if these extrapolations are justified. Moreover, the long-term efficacy of these agents in patients treated with contemporary medical therapies is not known, even in patients with prior MI.

β-Blockers are not without adverse

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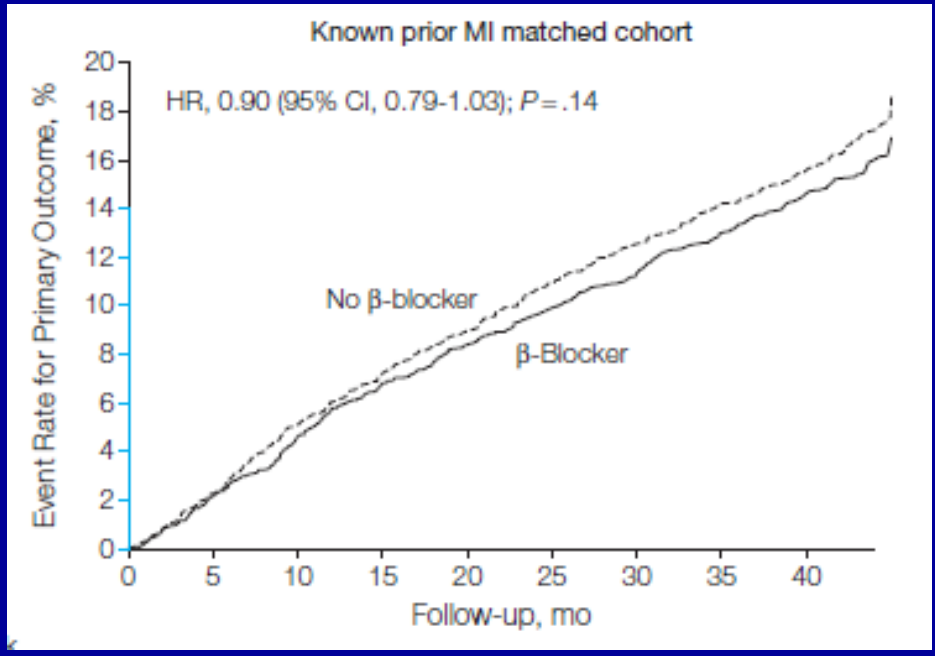
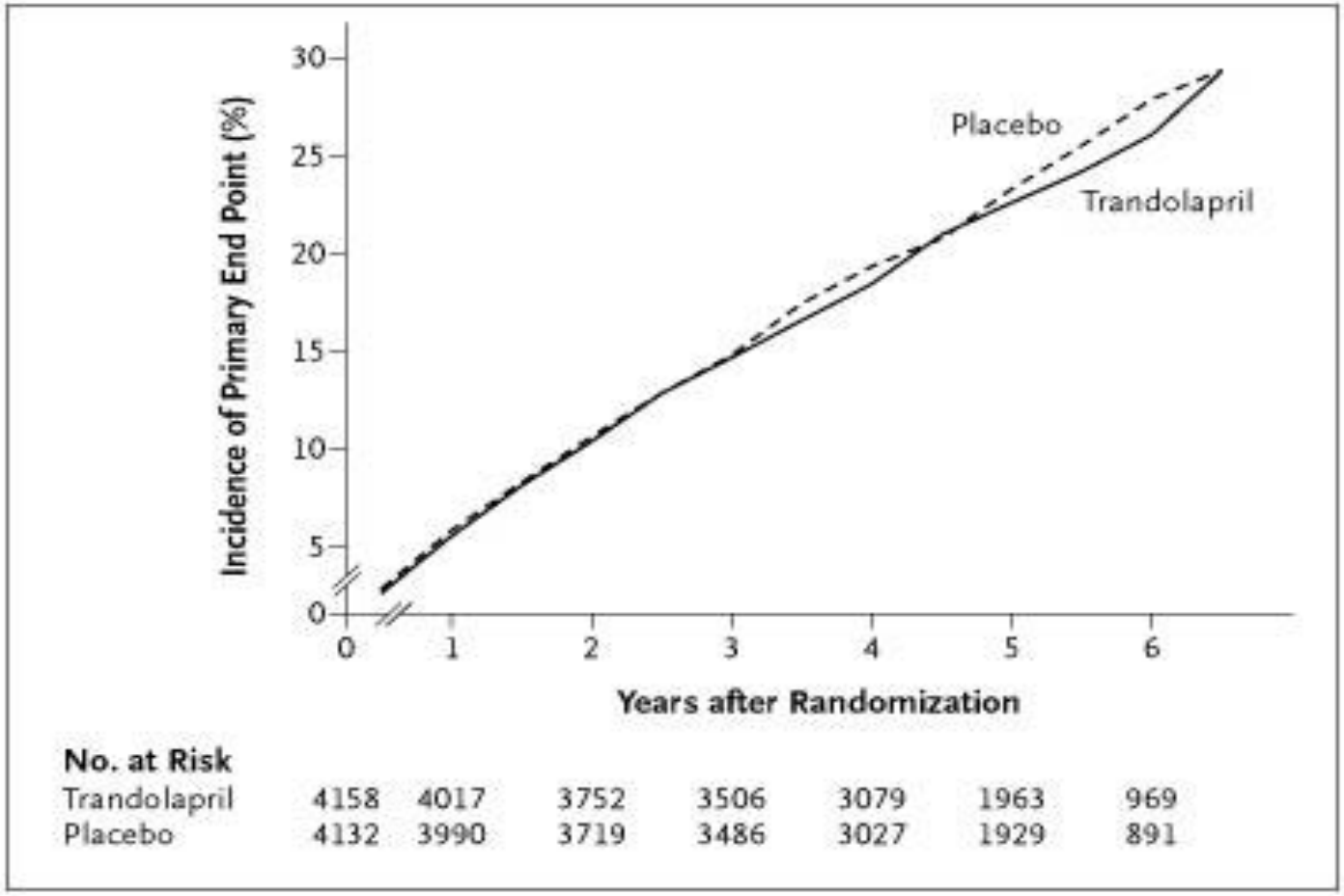


EXAMPLE 1: ACE-I IN PATIENTS WITH PRESERVED LV FUNCTION

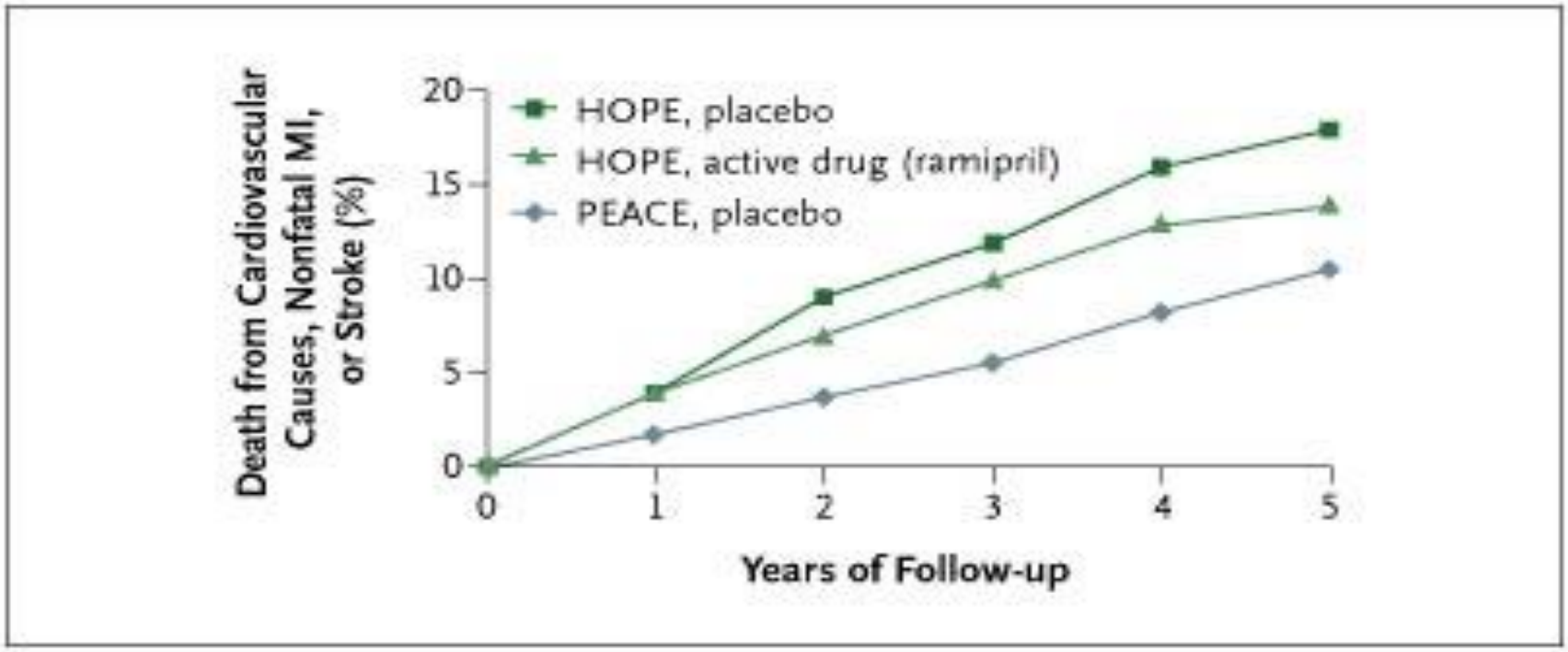
- The HOPE and EUROPA trials showed significant benefit of ACE inhibitors in patients at risk who did not have significant LV dysfunction.
- The PEACE trial could not confirm these findings.
- All 3 trials had similar designs

Cumulative Incidence of the Primary End Point, According to Treatment Group



The PEACE Trial Investigators, . N Engl J Med 2004;351:2058-2068

Comparison of Outcomes in the PEACE Trial and HOPE



The PEACE Trial Investigators, . N Engl J Med 2004;351:2058-2068

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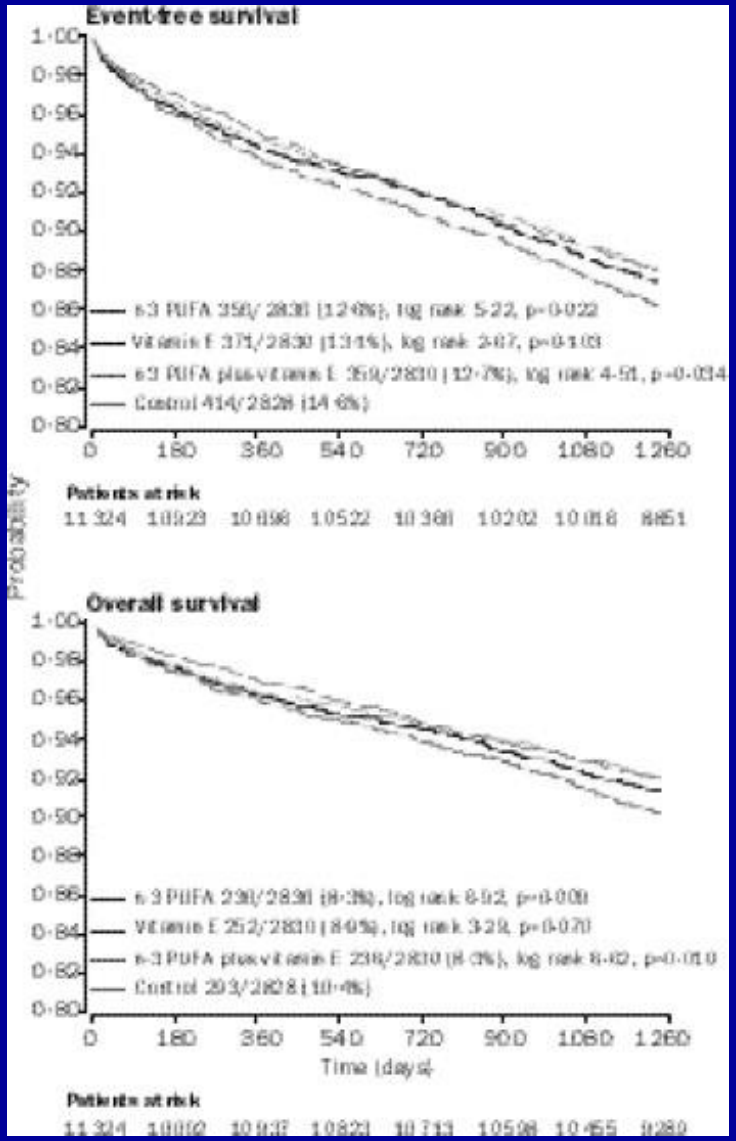
EXAMPLE 2: FISH OIL TO PREVENT CV EVENTS

Articles

Dietary supplementation with n-3 polyunsaturated fatty acids and vitamin E after myocardial infarction: results of the GISSI-Prevenzione trial

*GISSI-Prevenzione Investigators** (Gruppo Italiano per lo Studio della Sopravvivenza nell'Infarto miocardico)

GISSI PREVENZIONE



Circulation

JOURNAL OF THE AMERICAN HEART ASSOCIATION

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OMEGA, a Randomized, Placebo-Controlled Trial to Test the Effect of Highly Purified Omega-3 Fatty Acids on Top of Modern Guideline-Adjusted Therapy After Myocardial Infarction

Bernhard Rauch, Rudolf Schiele, Steffen Schneider, Frank Diller, Norbert Victor, Helmut Gohlke, Martin Gottwik, Gerhard Steinbeck, Ulrike Del Castillo, Rudolf Sack, Heinrich Worth, Hugo Katus, Wilhelm Spitzer, Georg Sabin, Jochen Senges and for the OMEGA Study Group

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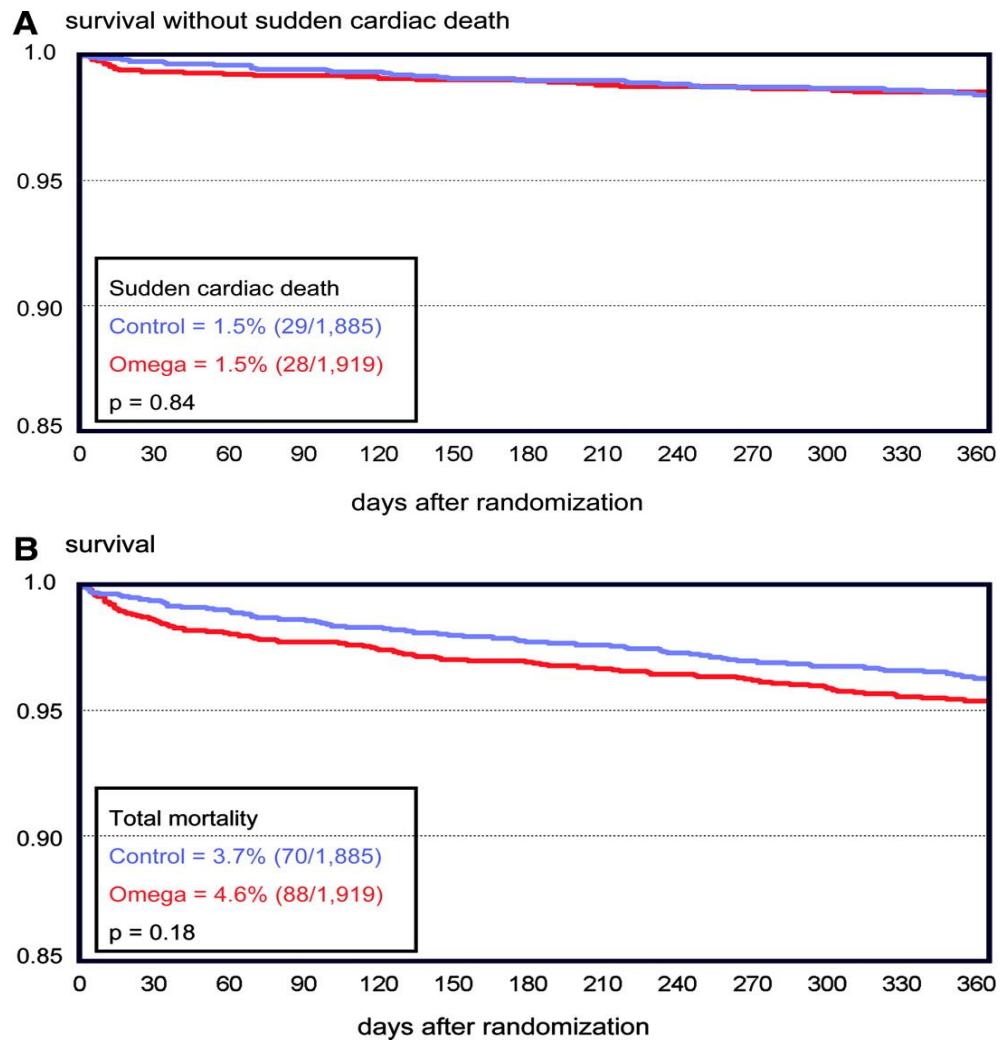
Kaplan–Meier diagrams (P values are those of the univariate analysis; see Table 4).



Rauch B et al. Circulation 2010;122:2152-2159

WHY THE DIFFERENCE?

	GISSI-P	OMEGA
Statins	29%	94%
Control event rate	15.8/1000	8.9/1000
Sudden death	10.4/1000	3.7/1000

CONCLUSIONS

- **NSTEMI: No evidence that beta blockers are superior to placebo, particularly in the absence of LV dysfunction**
- **STEMI with LV dysfunction – beta blockers should be given based on CAPRICORN and older data which include many patients with LV dysfunction.**

CONCLUSIONS

- **STEMI with preserved LV function – beta blockers never shown to be beneficial in such patients. The possible absolute benefit with contemporary management is extremely small, if any.**
- **ACE inhibitors: definitely indicated in the presence of LV dysfunction. With preserved LV: tailor therapy according to individual risk**

Routine therapies in the acute, subacute and long term phase of STEMI

Oral treatment with beta-blockers should be considered during hospital stay and continued thereafter in all STEMI patients without contraindications.	IIa	B
Oral treatment with beta-blockers is indicated in patients with heart failure or LV dysfunction.	I	A
Intravenous beta-blockers must be avoided in patients with hypotension or heart failure.	III	B
Intravenous beta-blockers should be considered at the time of presentation in patients without contraindications, with high blood pressure, tachycardia and no signs of heart failure.	IIa	B
A fasting lipid profile must be obtained in all STEMI patients, as soon as possible after presentation.	I	C
It is recommended to initiate or continue high dose statins early after admission in all STEMI patients without contraindication or history of intolerance, regardless of initial cholesterol values.	I	A
Reassessment of LDL-cholesterol should be considered after 4–6 weeks to ensure that a target value of ≤1.8 mmol/L (70 mg/dL) has been reached.	IIa	C
Verapamil may be considered for secondary prevention in patients with absolute contraindications to beta-blockers and no heart failure.	IIb	B
ACE inhibitors are indicated starting within the first 24 h of STEMI in patients with evidence of heart failure, LV systolic dysfunction, diabetes or an anterior infarct.	I	A
An ARB, preferably valsartan, is an alternative to ACE inhibitors in patients with heart failure or LV systolic dysfunction, particularly those who are intolerant to ACE inhibitors.	I	B
ACE inhibitors should be considered in all patients in the absence of contraindications.	IIa	A
Aldosterone antagonists, e.g. eplerenone, are indicated in patients with an ejection fraction ≤40% and heart failure or diabetes, provided no renal failure or hyperkalaemia.	I	B

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A QUIZ TO THE AUDIENCE:

- 52 y.o. male, inferior STEMI.
- Successful primary PCI, good reperfusion.
- Single vessel disease, preserved LV function.
- Aspirin, prasugrel, statin
- If you think data obtained 30 years ago in the absence of all the above modalities are relevant – you should give a beta blocker

THANK YOU!