Simposio congiunto ANMCO-AMD

Gestione del paziente diabetico con SCA

Linee Guida ESC 2002

Alto Rischio di progressione verso IMA o morte

Ischemia / Angina ricorrente
Alterazioni transitorie ST
Troponina Elevata

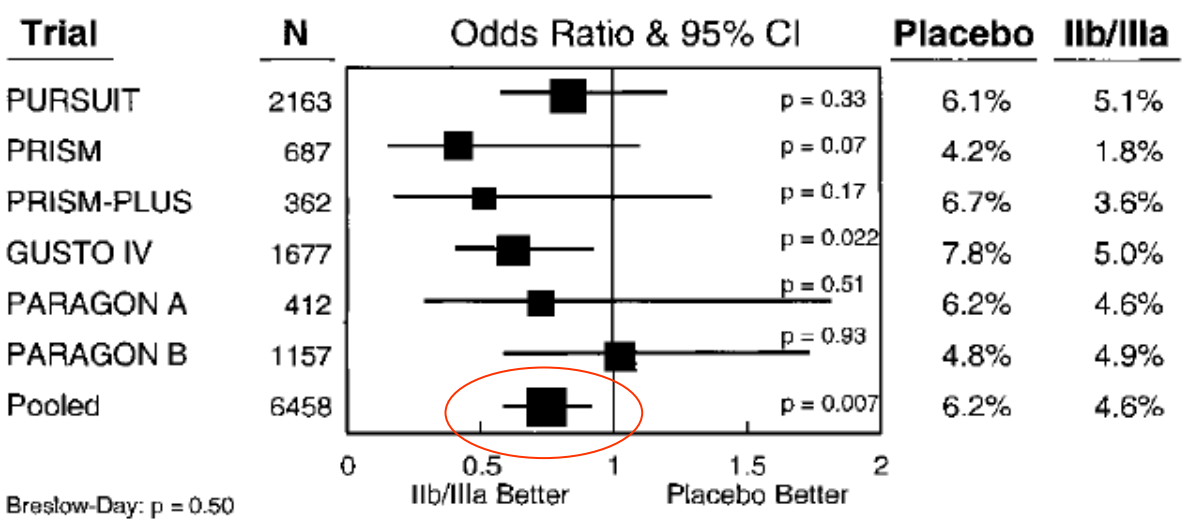
Diabete

Angina instabile post-IMA
Instabilità emodinamica
Aritmie maggiori (FV, TV)

Inibitori 2b/3a
&
Coronarografia

In Emergenza

30-Day Mortality
Diabetic Patients

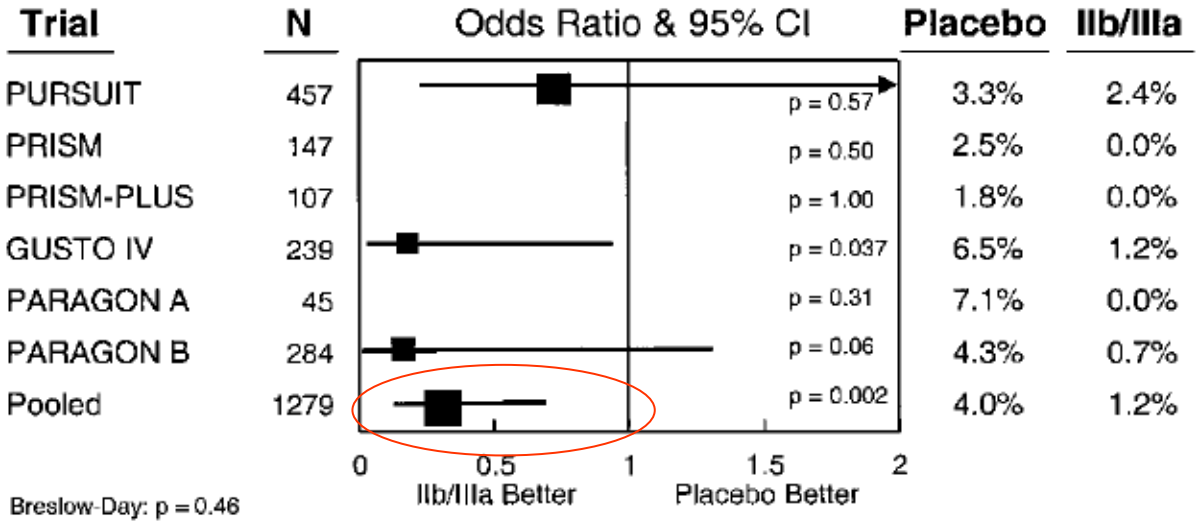


Marco Roffi,

(*Circulation*. 2001;104:2767-2771.)

6458 pts with DM in 6 large ACS trials

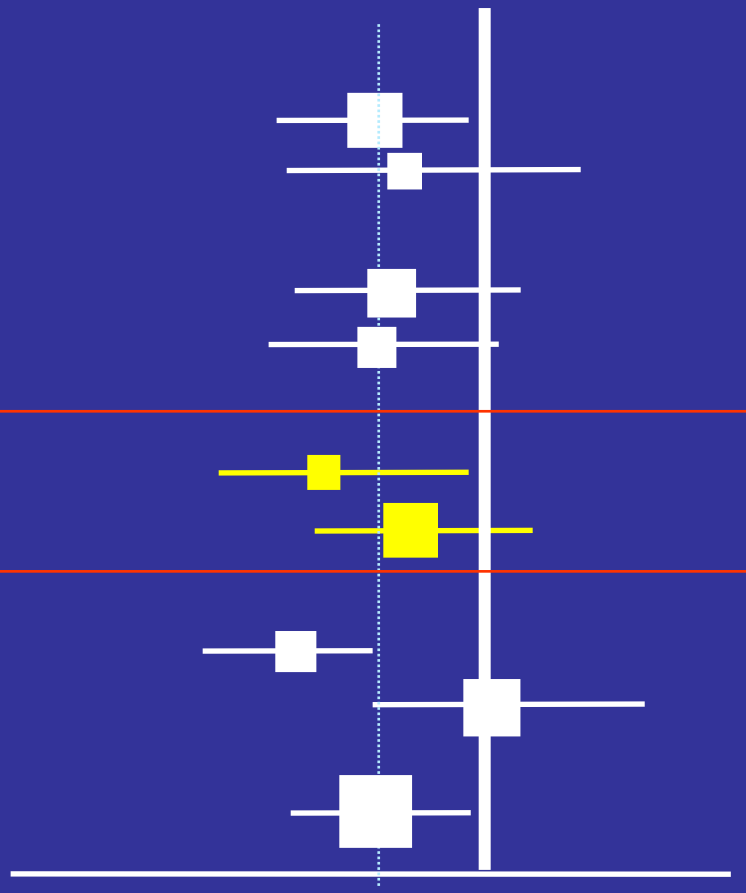
30-Day Mortality
Diabetic Patients
PCI



TACTICS-TIMI 18

Morte, IMA, Ospedalizzazione per SCA a 6 Mesi

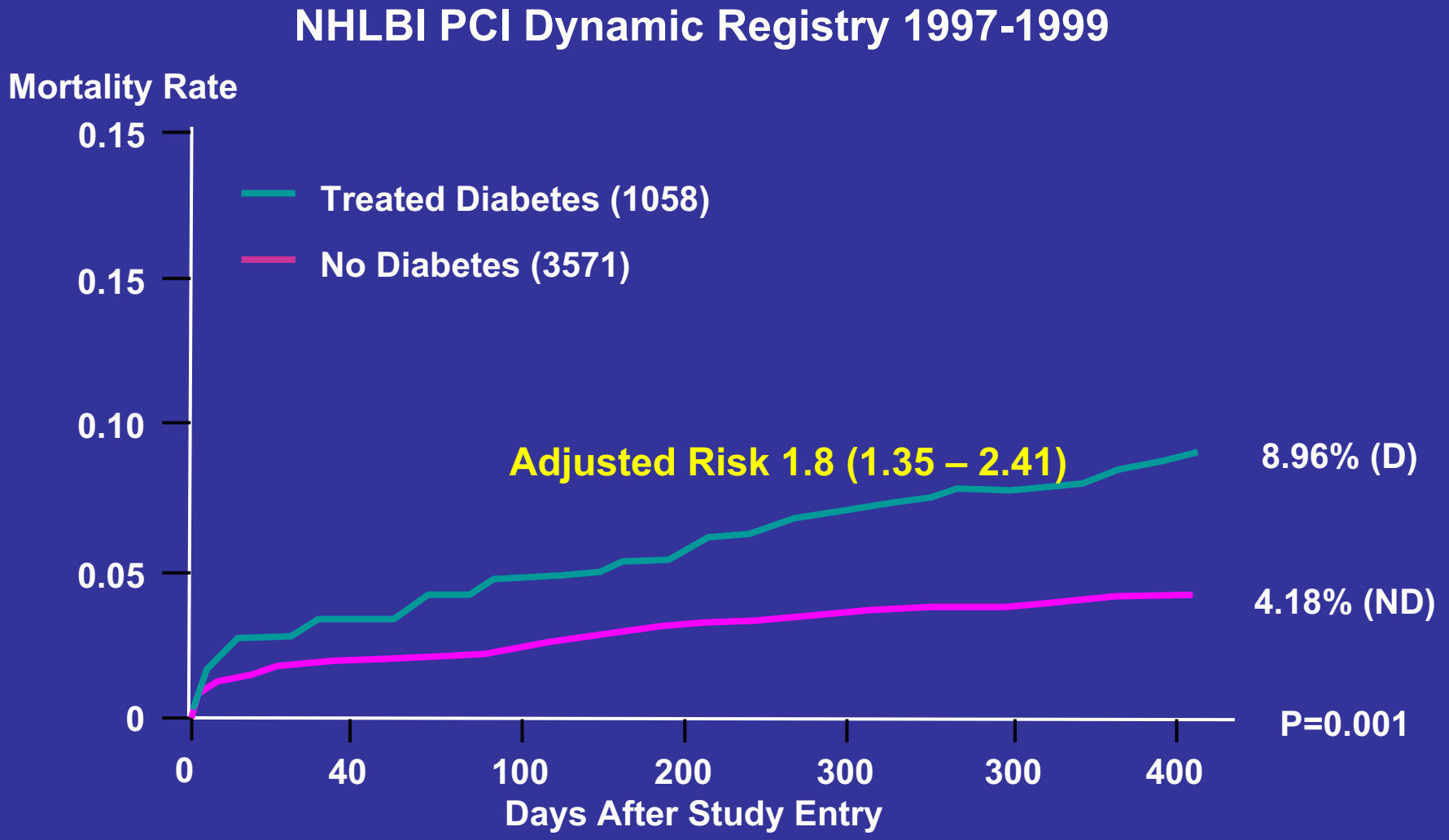
1º Endpoint	%Pts	CONS (%)	INV (%)
Maschi	(66%)	19.4	15.3
Femmine	(34%)	19.6	17.0
Età < 65 aa.	(57%)	17.8	14.9
Età ≥ 65 aa.	(43%)	21.7	17.1
Diabete	**(28%)**	**27.7**	**20.1**
No diabete	**(72%)**	**16.4**	**14.2**
ST Δ *	(38%)	26.3	16.4
No ST Δ	(62%)	15.3	15.6
Popolazione Totale		19.4	15.9



Cannon CP, et al.
N Engl J Med 2001; 344: 1879

PCI or CABG?

Diabetes Doubles Mortality Risk After Successful PCI



Laskey, WK. et al, Am J Cardiol 2002;90:1062-1067

PRESTO Trial *(2000)*

TABLE 4. Major Adverse Events at 9 Months of Patients Undergoing Coronary Stent Intervention According to Diabetes Status

Events	Nondiabetic (n=8798)	Diabetic (n=2684)	*P*
Death	75 (0.9)	57 (2.1)	<0.01
MI	108 (1.2)	50 (1.9)	0.01
MI or death	179 (2.0)	97 (3.6)	<0.01
TVR	1128 (12.8)	480 (17.9)	<0.01

Numbers in parentheses are percentages of the total.

82% 1-Vessel disease
50% vs 57% unstable angina
1.4 les. Treated x pt
34% vs 43% 2b3a inhibitors use
77% vs 75% stent use

Verghese, Circulation 2004

PRESTO Trial (2000)

TABLE 5. Influence of Diabetes on 9-Month Outcomes Adjusted for Baseline Differences

	Nondiabetic (n=8798)	Diabetic (n=2684)	*P*
Death			
Relative risk	1.00	2.50	<0.01
95% CI	. . .	(1.78, 3.53)	
Adjusted relative risk*	1.00	1.87	<0.01
95% CI	. . .	(1.31, 2.68)	

Verghese, Circulation 2004

One-year outcomes of coronary artery bypass graft surgery versus percutaneous coronary intervention with multiple stenting for multisystem disease: A meta-analysis of individual patient data from randomized clinical trials

Nestor Mercado,William Wijns, Patrick Serruys, Ulrich Sigwart, Marcus Flather, Rodney Stables, William O'Neill, Alfredo Rodriguez, Pedro Lemos, Whady Hueb, Bernard Gersh, Jean Booth, and Eric Boersma

J Thorac Cardiovasc Surg 2005;130:512-9

Methods

- 4 Trials included: ARTS-1, SoS, ERACI-2, MASS-2
- Patients enrolled during 1995-2000
- Individual patient level data analysis
- Primary outcome measure: combined rate of death, non-fatal MI or stroke at one year
- Secondary outcomes include repeat revasc

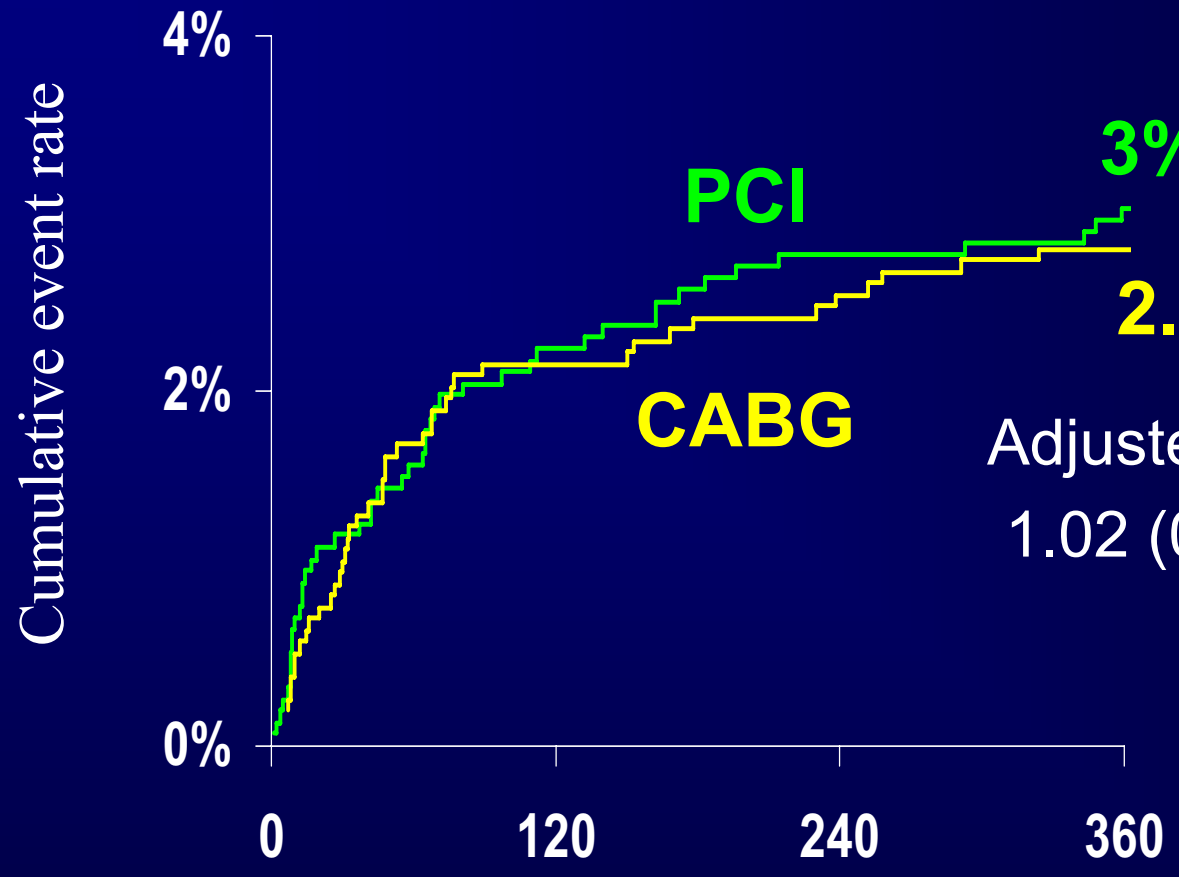
Baseline characteristics/1

	PCI + Stent 1518	Surgery 1533	
Mean Age (yrs±sd)	61 (53, 68)	61 (54, 68)	
Male gender (%)	76.5	76.6	
Prior MI (%)	43	41	
Diabetes (%)	**17.5**	**18.4**	
EF (%)	59±11	59±11	
Unstable angina	**28.5**	**27**	
Lesions >50% sten	2.74±0.98	2.79±0.95	
Length of stay	2 (1, 4)	8 (6, 10)	P<0.001

Baseline characteristics/2

	PCI + Stent	Surgery	
Time from rand to treatment (mean ± SD)	15 ± 22 days	20 ± 29 days	P<0.01
Received assigned treatment	98%	96%	
Mean no. of lesions revasc (± SD)	**2.4±1.1**	**2.7±0.8**	**P<0.01**
"Complete" Revascularization	**54%**	**82%**	**P<0.001**

All cause mortality at one year

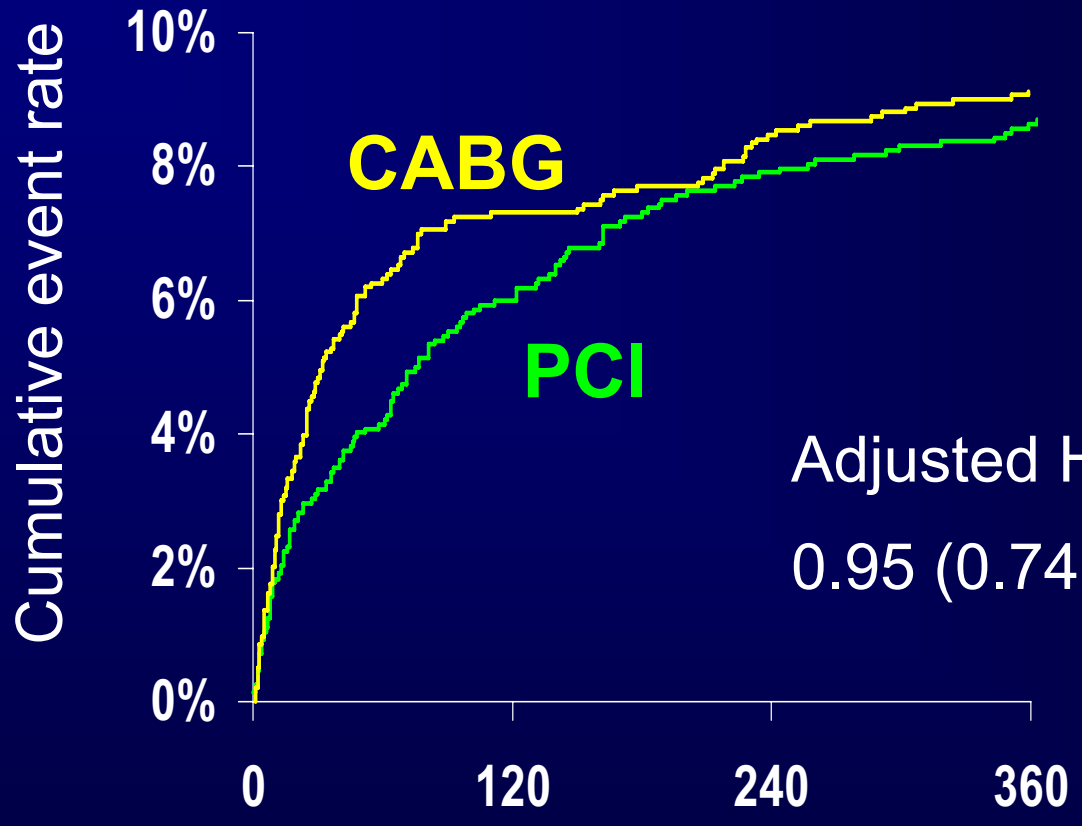


N=3051

Adjusted HR* (95% CI) = 1.02 (0.64 – 1.60)

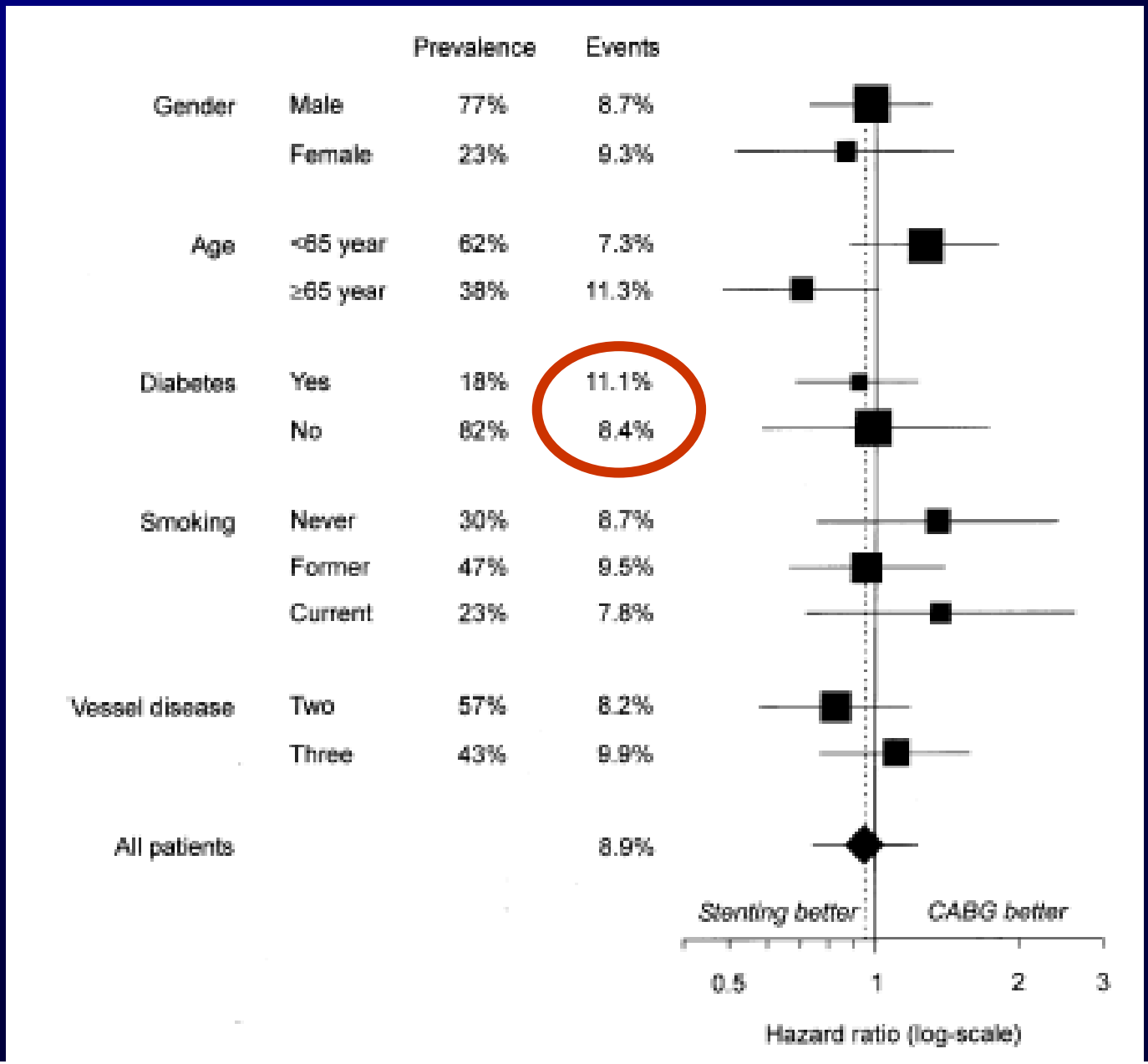
- Diabetics: PCI mortality 5.6% versus CABG 3.5% (HR=1.61 [95%CI 0.72-3.61], p=0.245)

Death, non-fatal myocardial infarction and stroke at one year (n= 3051)

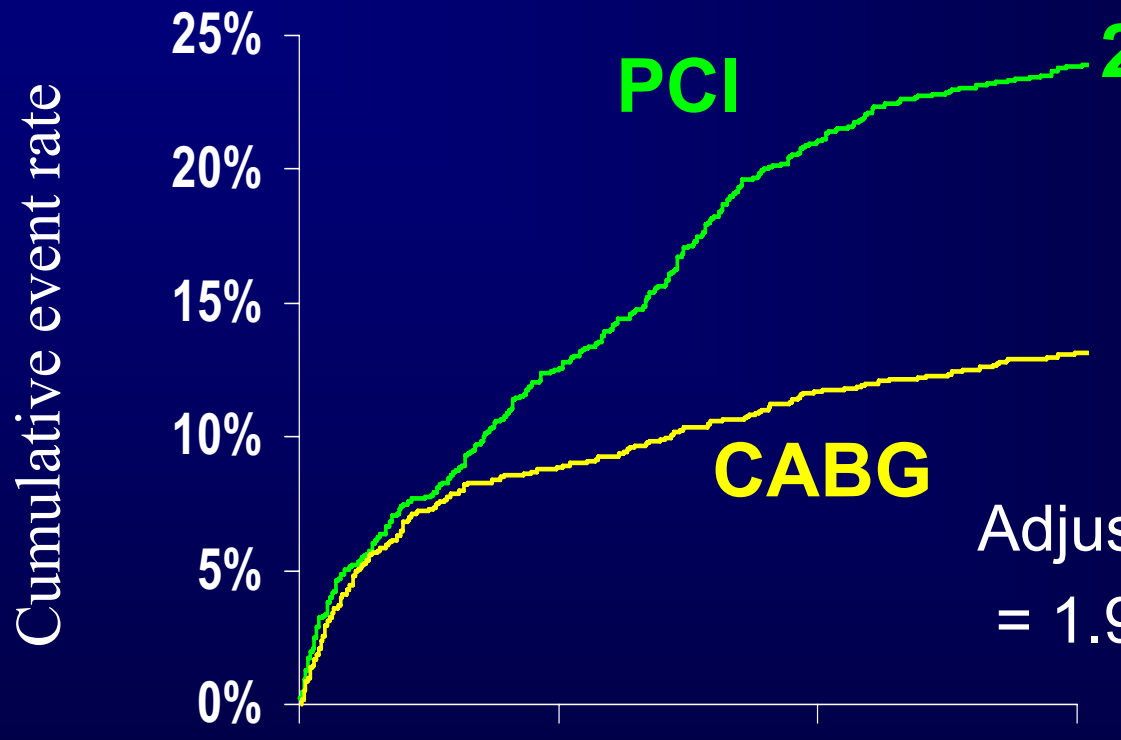


1-year death, MI and stroke

Diabetes
549 pts



Composite MACCE: Death, non-fatal MI, stroke and repeat revascularization procedures



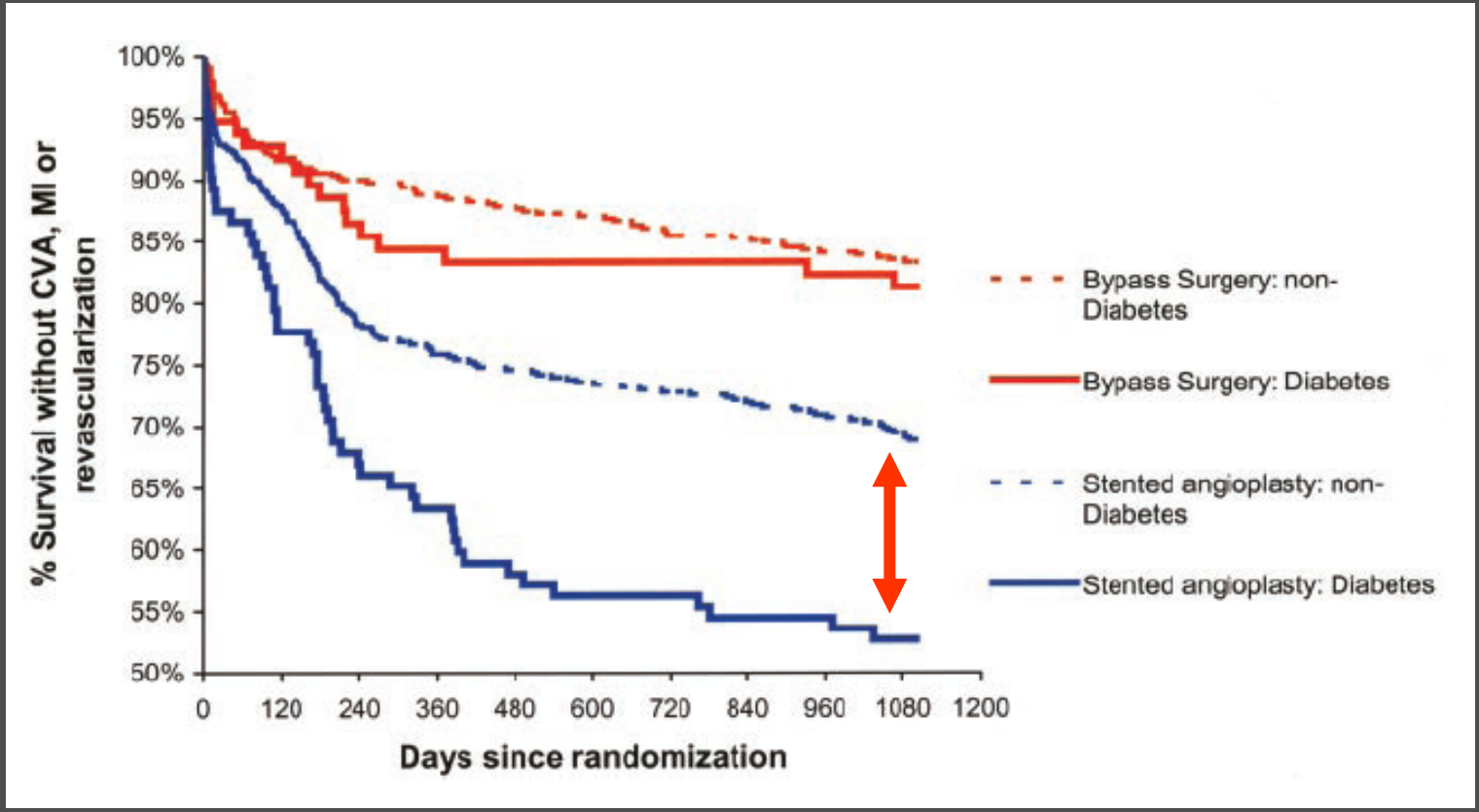
N=3051

Adjusted HR* (95% CI)
= 1.94 (1.61 – 2.34)

Numbers at risk

PCI	1518	1327	1198	1156
CABG	1533	1397	1354	1332

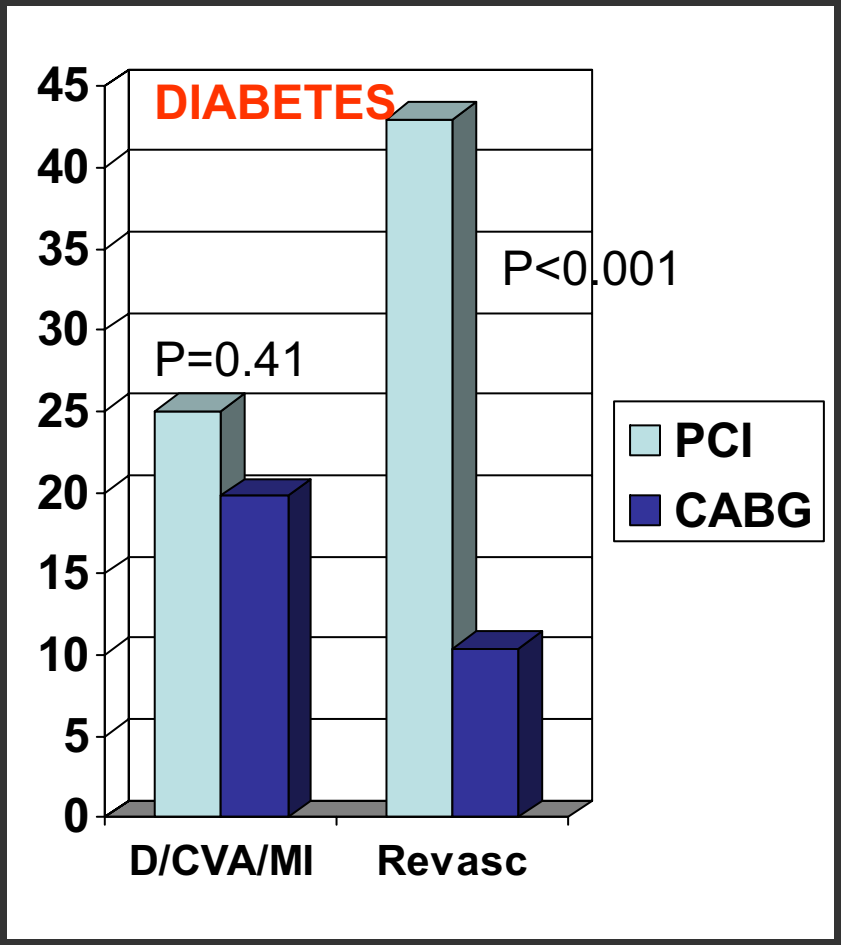
ARTS: 3-year follow-up
(208 diabetic pts 1997-8)

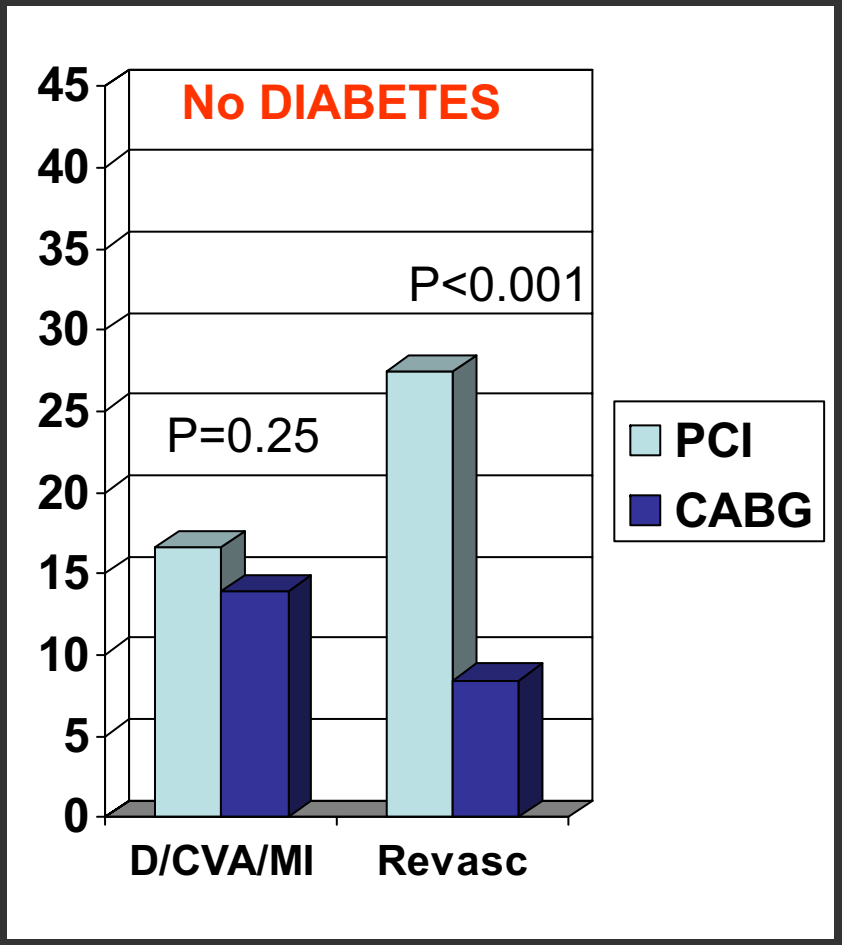


Legrand V, Circulation 2004

ARTS: 5-year follow-up

(208 diabetic pts 1997-8)

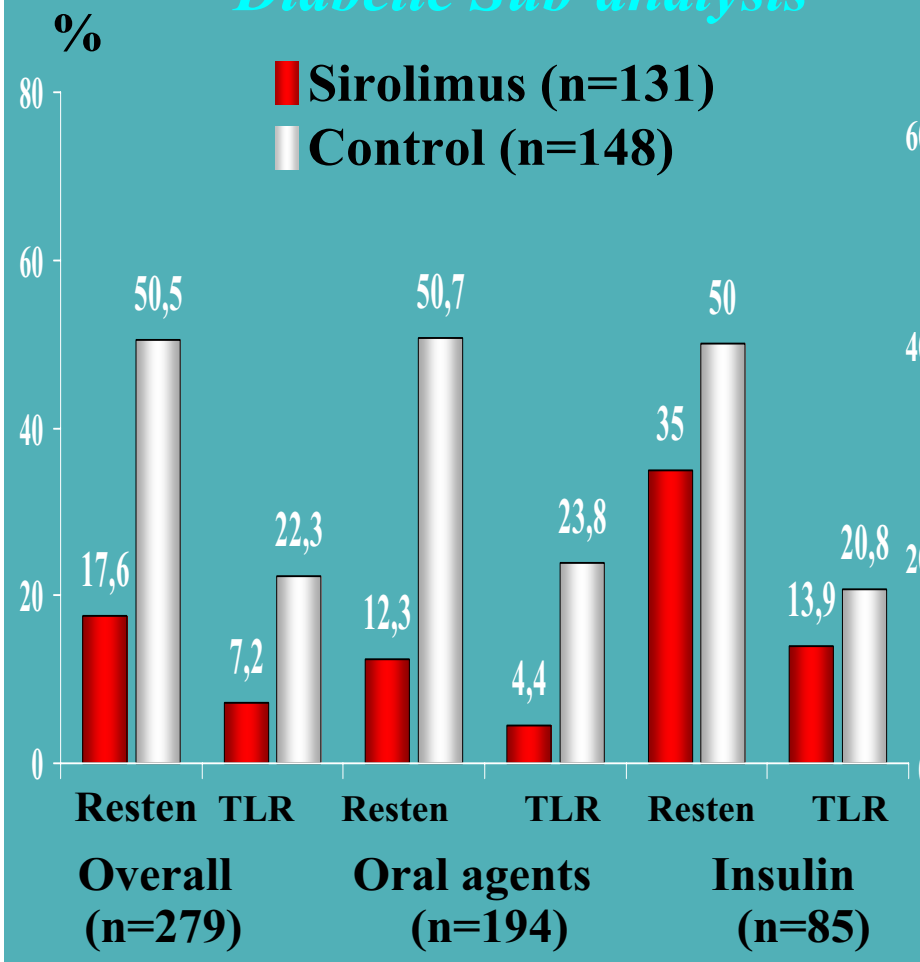




Serruys, JACC 2005

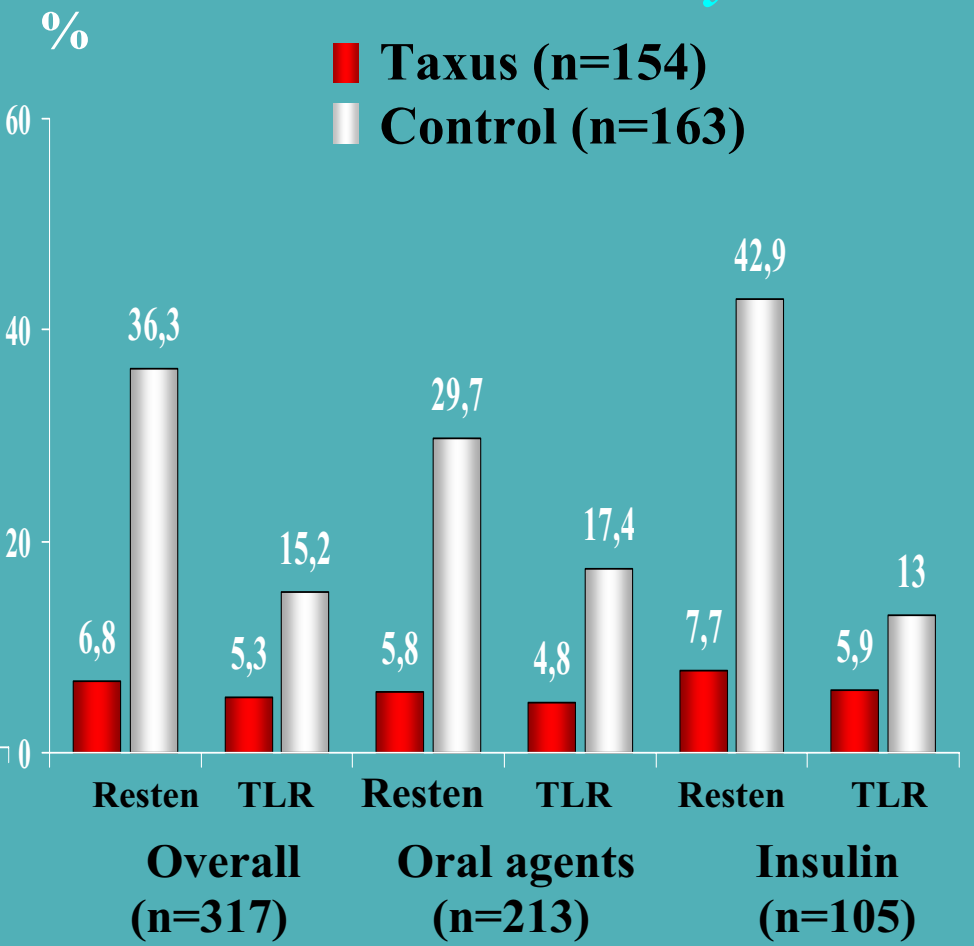
SIRIUS Trial

Diabetic Sub-analysis



TAXUS-IV Trial

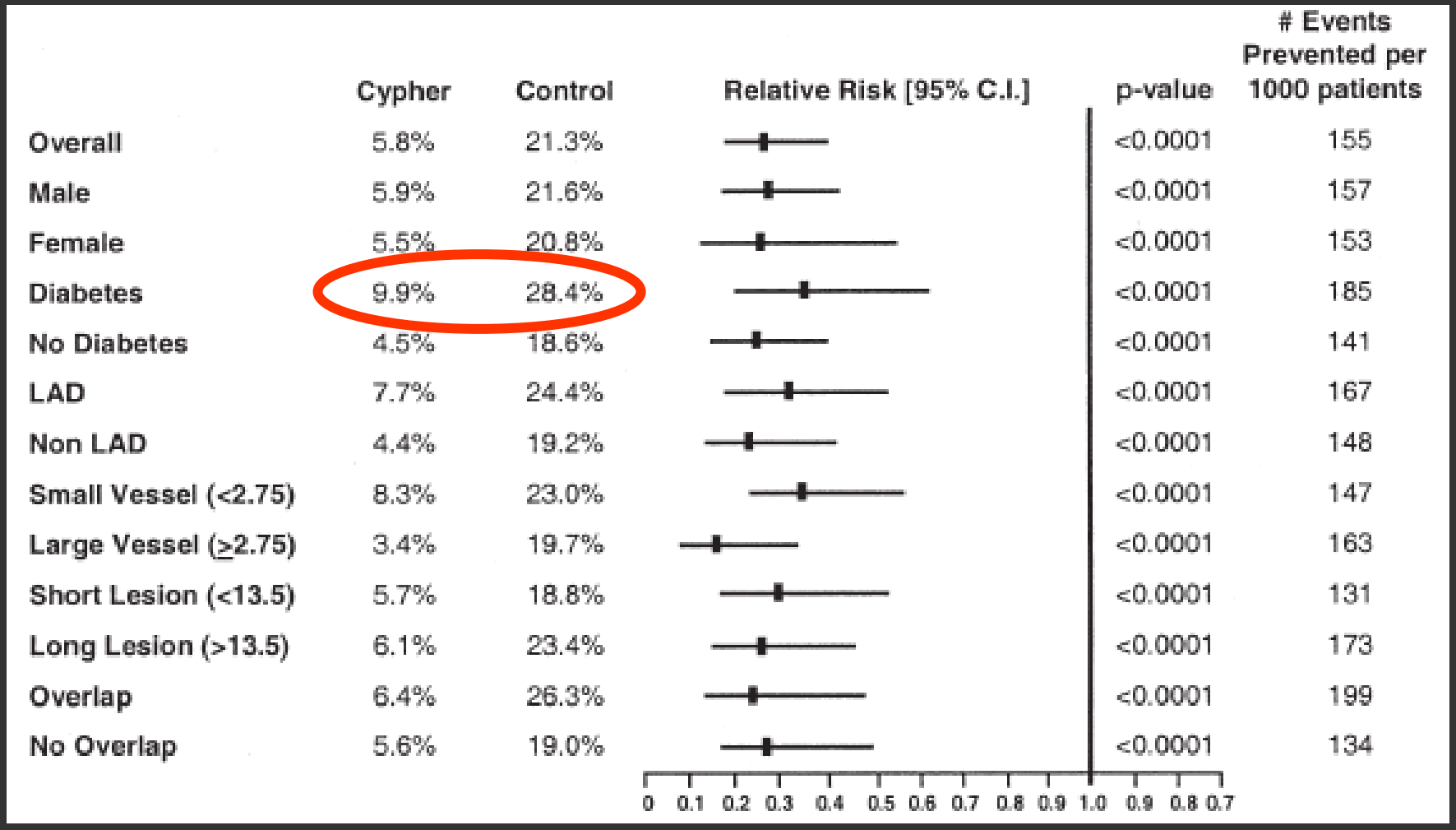
Diabetic Sub-analysis



Stone et al. NEJM 2004;350:221.
Moses et al. NEJM 2003;349:1315.

SIRIUS Trial 2-year follow-up

OR for TLR at 720 days



(Weisz, JACC 2006)

e-Cypher Registry,(15.157 pts): 1-year MACE

TABLE 4. Predictors at 12 Months of Overall MACEs and Stent Thrombosis by Multiple Variable Regression Analysis

Variable	OR (95% CI)	*P*
MACE		
Clinical		
Insulin-dependent diabetes	2.25 (1.60, 3.13)	<0.0001
History of prior coronary artery bypass surgery	2.01 (1.47, 2.71)	<0.0001
Age (10-year increment)	1.22 (1.09, 1.37)	0.0007
History of hypertension	1.57 (1.20, 2.08)	0.0012
Non-insulin-dependent diabetes	1.43 (1.06, 1.90)	0.0158

Urban, Circulation 2006)

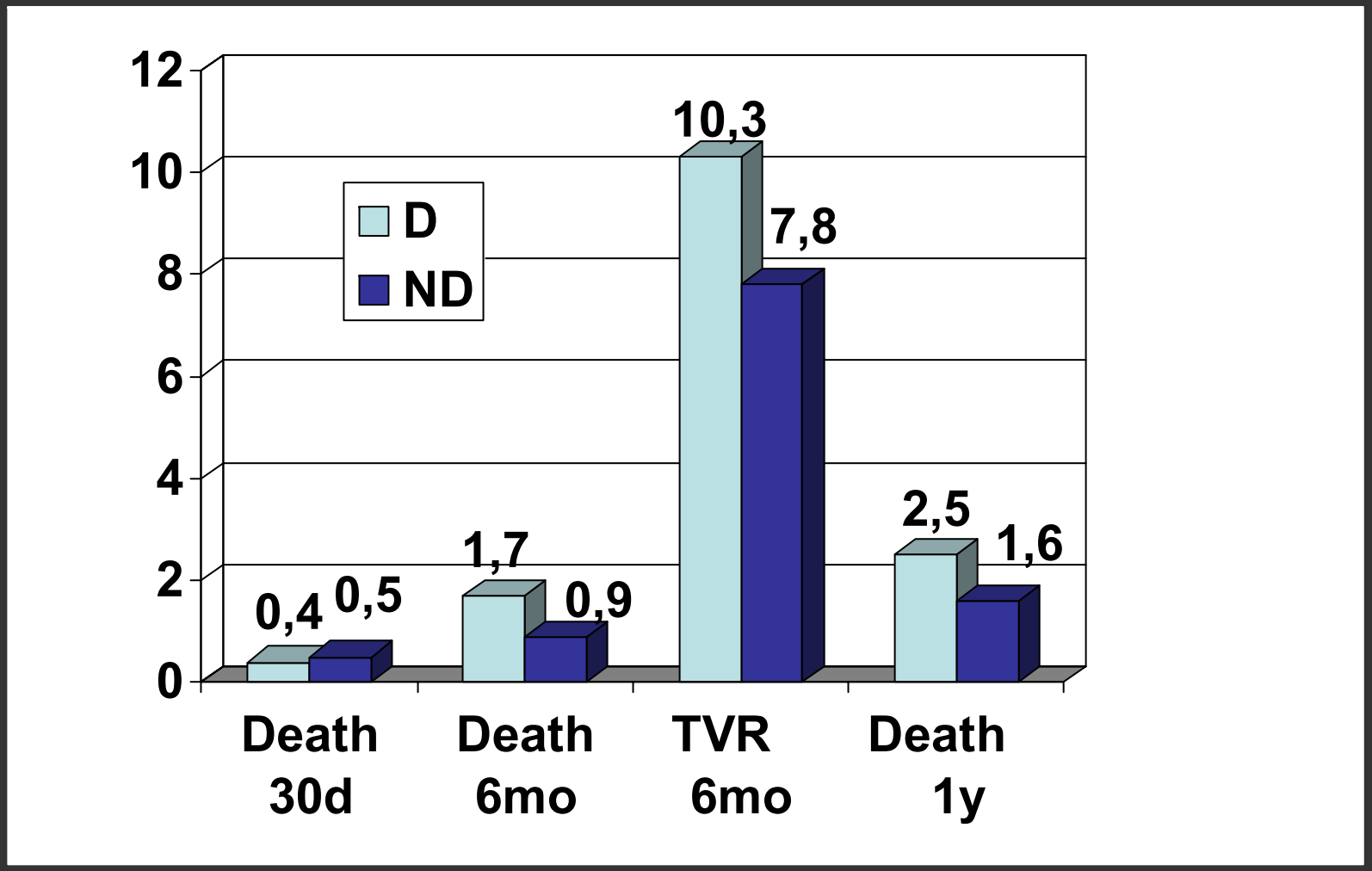
RESEARCH Registry (508 pts): MACE and TVR at 2 years

Table 4. Separate Cox Regression Analyses Performed to Determine Independent Predictors of MACE and TVR at Two-Year Follow-Up

	HR	95% CI	p Value
MACE*			
Use of SES	0.58	0.43–0.80	0.001
Total stented length (per 10-mm increment)	1.12	1.06–1.18	<0.001
Previous PCI	1.71	1.20–2.43	0.003
Diabetes mellitus	2.00	1.42–2.80	<0.001
Left main stenting	2.23	1.19–4.16	0.01
Cardiogenic shock at entry	4.19	2.04–8.59	<0.001
TVR†			
Use of SES	0.45	0.37–0.68	<0.001
Acute coronary syndrome at entry	0.56	0.37–0.83	0.004
Total stented length (per 10-mm increment)	1.14	1.07–1.22	<0.001
Previous PCI	1.73	1.11–2.69	0.016
Diabetes mellitus	2.05	1.33–3.17	0.001

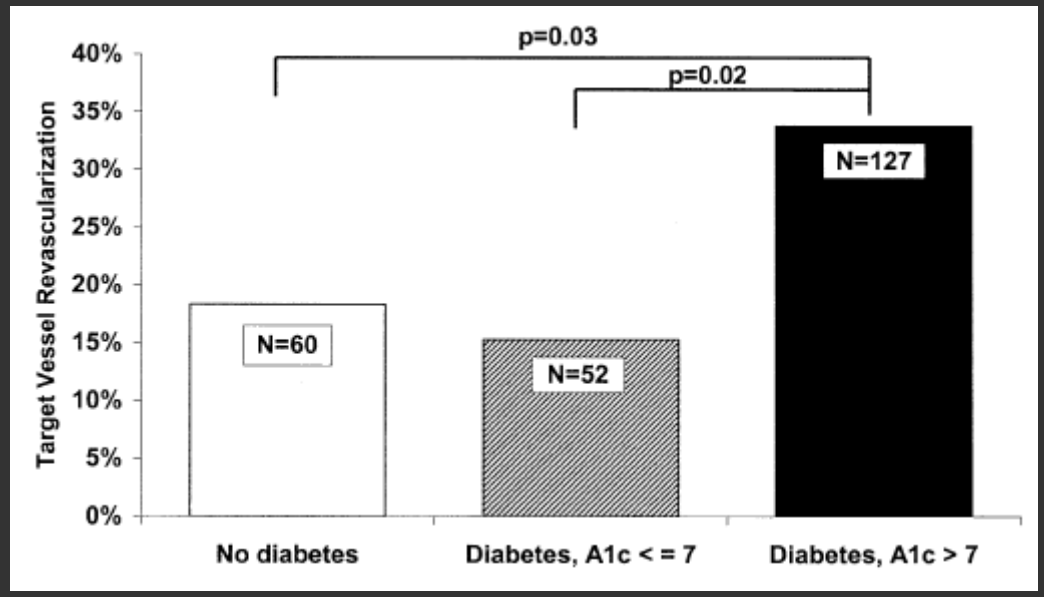
(Ong, JACC 2006)

TARGET Trial (PCI in 1117 diabetics / 3692 nd), trx tirofiban vs abciximab + double anti-plts, 65% ACS,

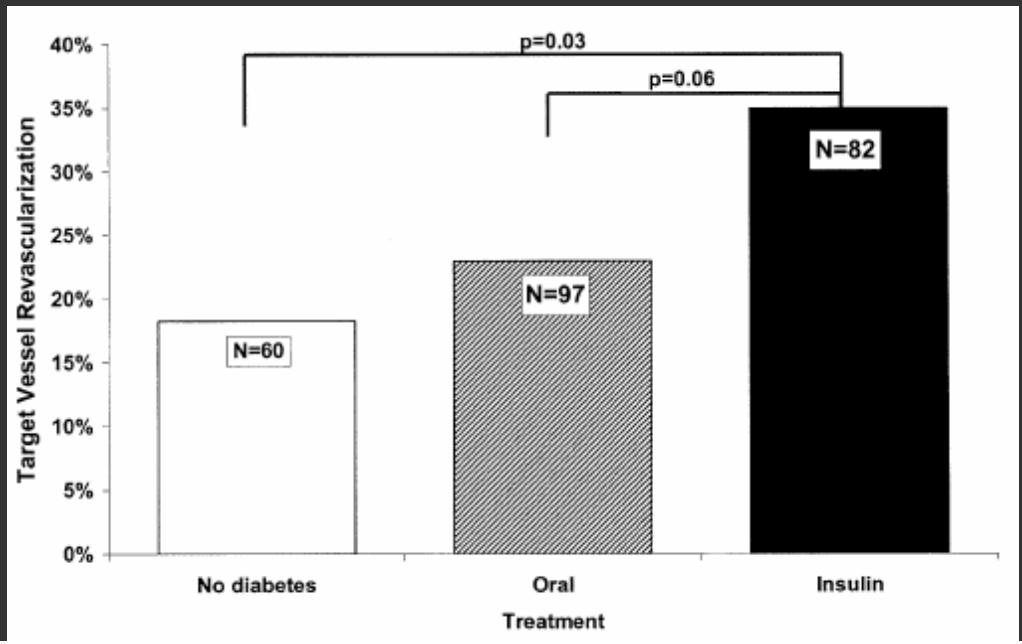


Roffi, Circulation 2002

Glycemic control and 1-yTVR in type II diabetics

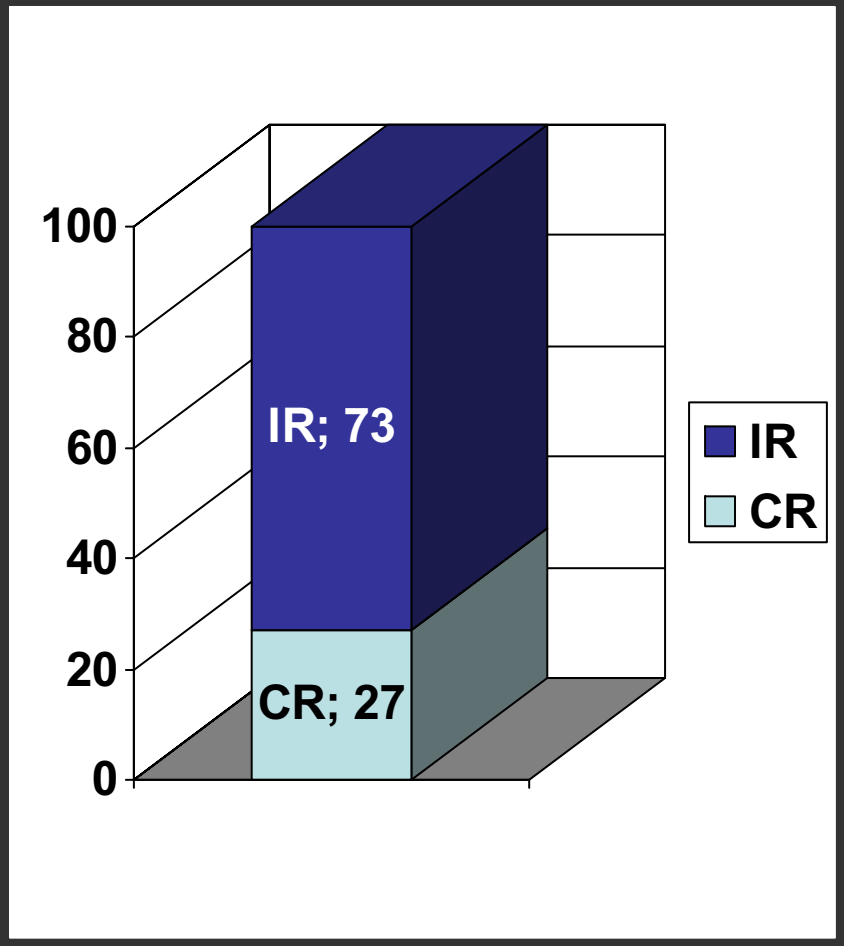


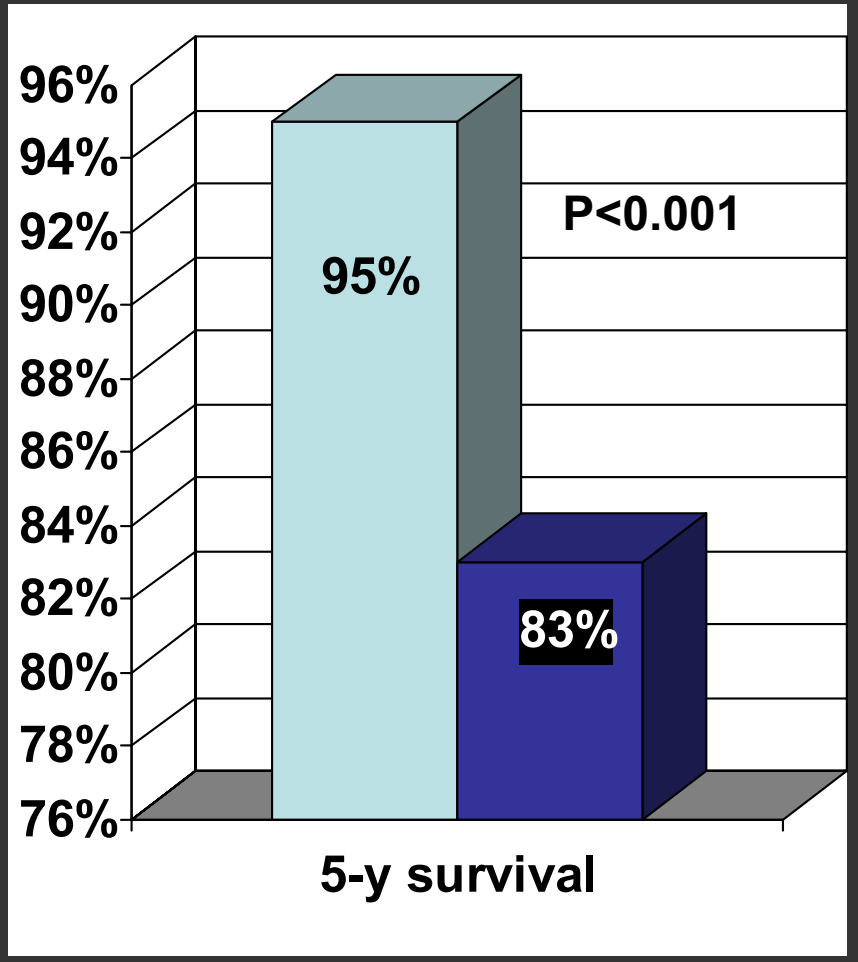
1998-99
Elective PCI, stable pts
68% stents
De novo lesions
Native vessels
Mostly 1-lesion PCI



Corpus, JACC 2004

PCI: complete / incomplete revascularization in 352 diabetics with MV CAD: 5-y survival

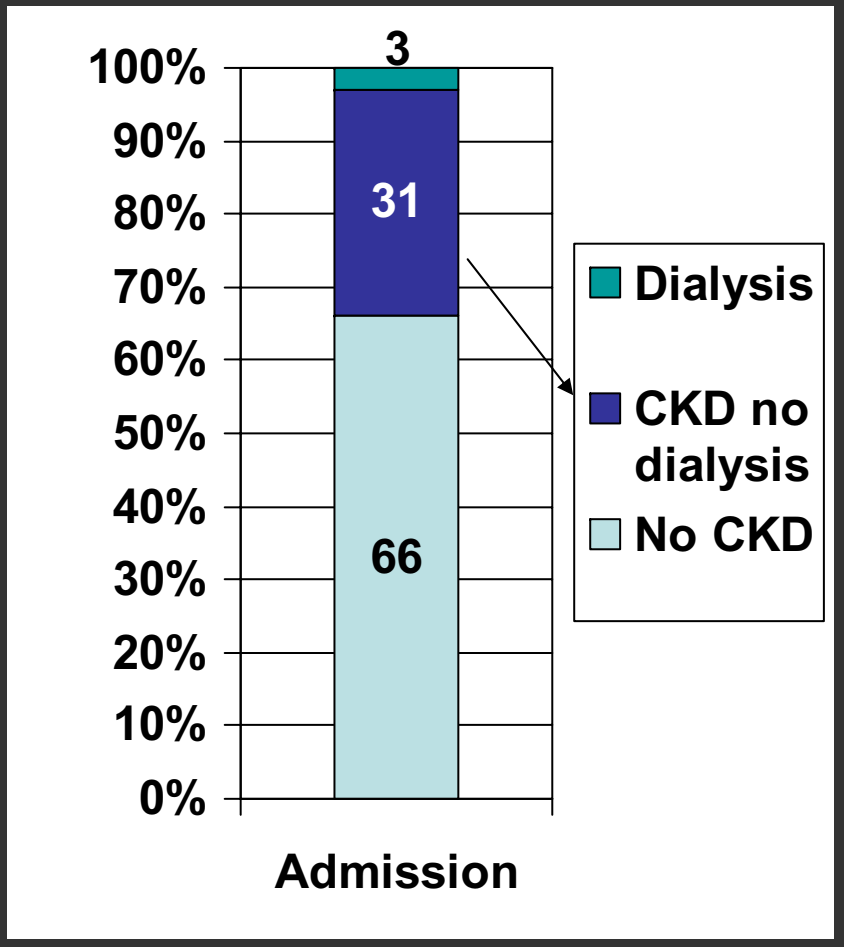


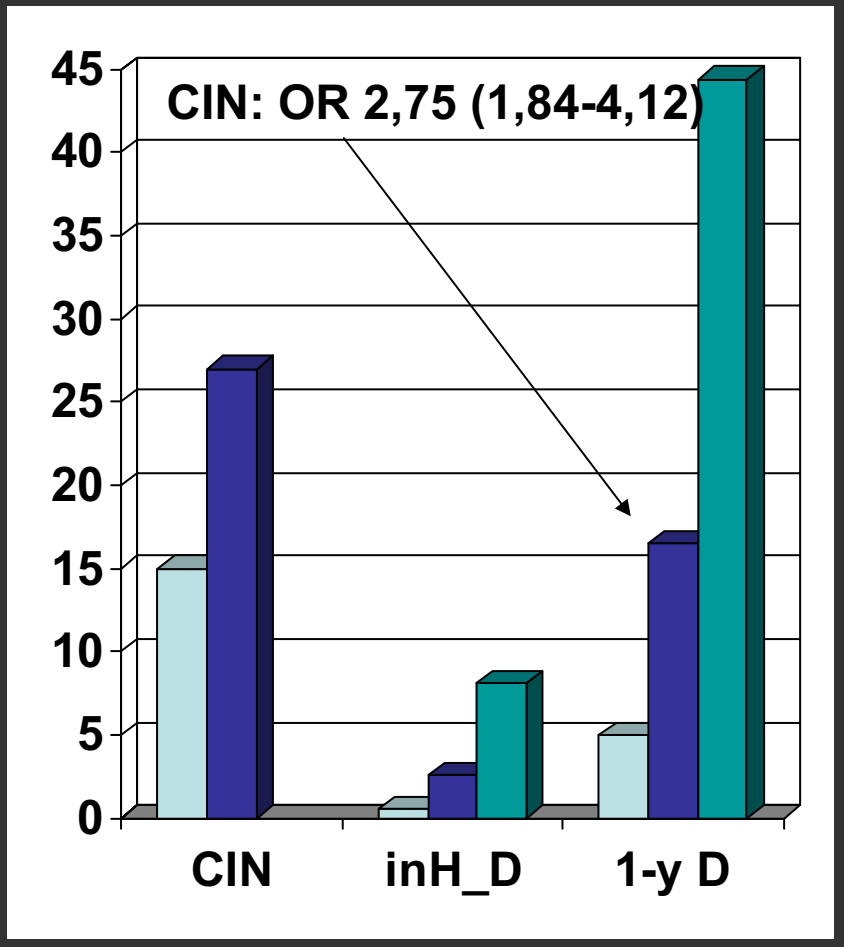


Nikolsky, J Invasive Cardiol 2004

RR = 3 (1.54-7,69)

Chronic kidney disease and outcomes in 1571 diabetics with PCI



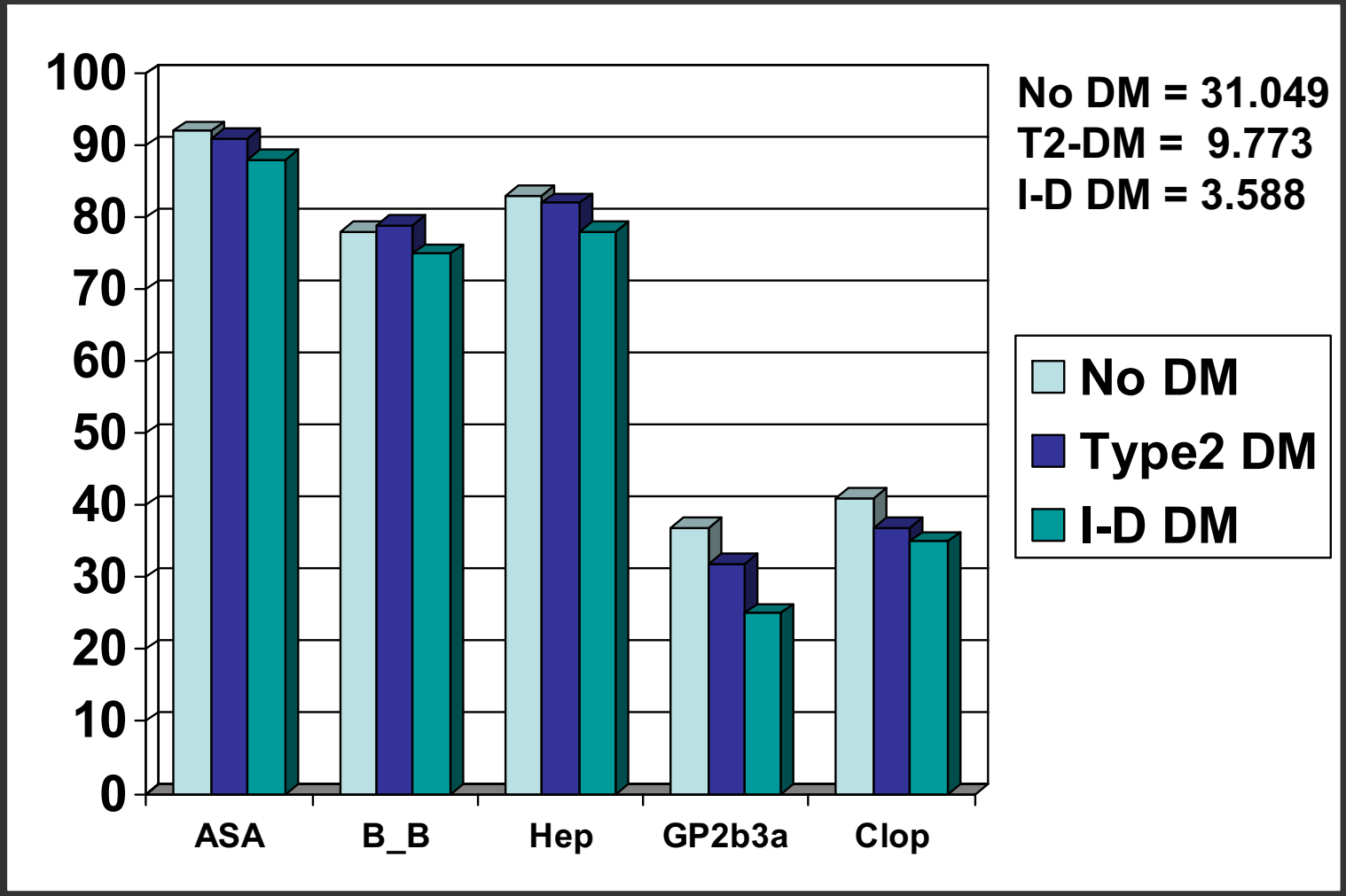


CKD= cr >1,5 or GFR <60ml/m/1.73m2

Nikolsky, Am J Cardiol 2004

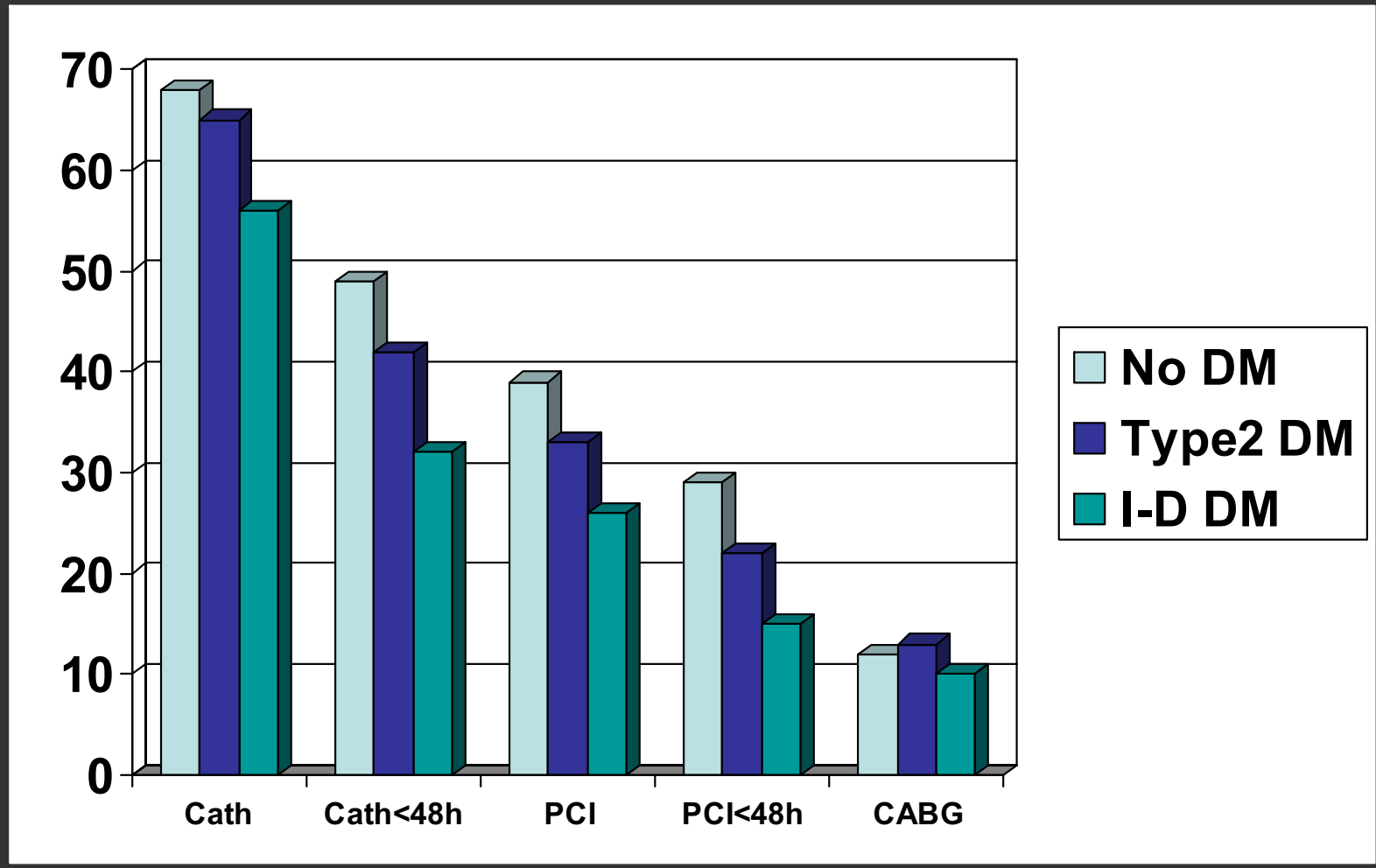
CRUSADE: *care of 46.410 pts with NSTE-ACS*

acute (<24h) medications



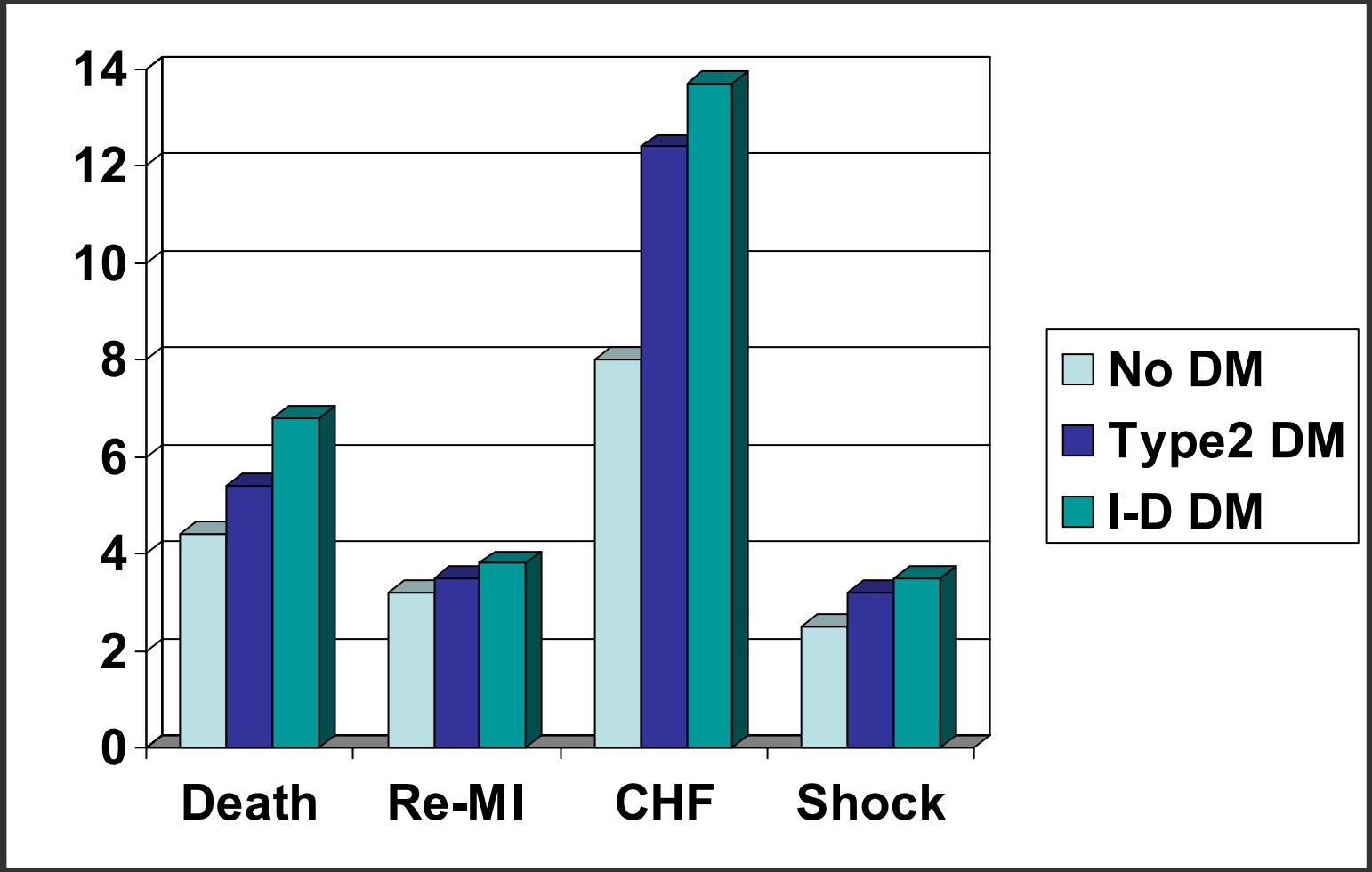
Brogan, Diabetes Care 2006

CRUSADE: *care of 46.410 pts with NSTE-ACS*
invasive cardiac procedures



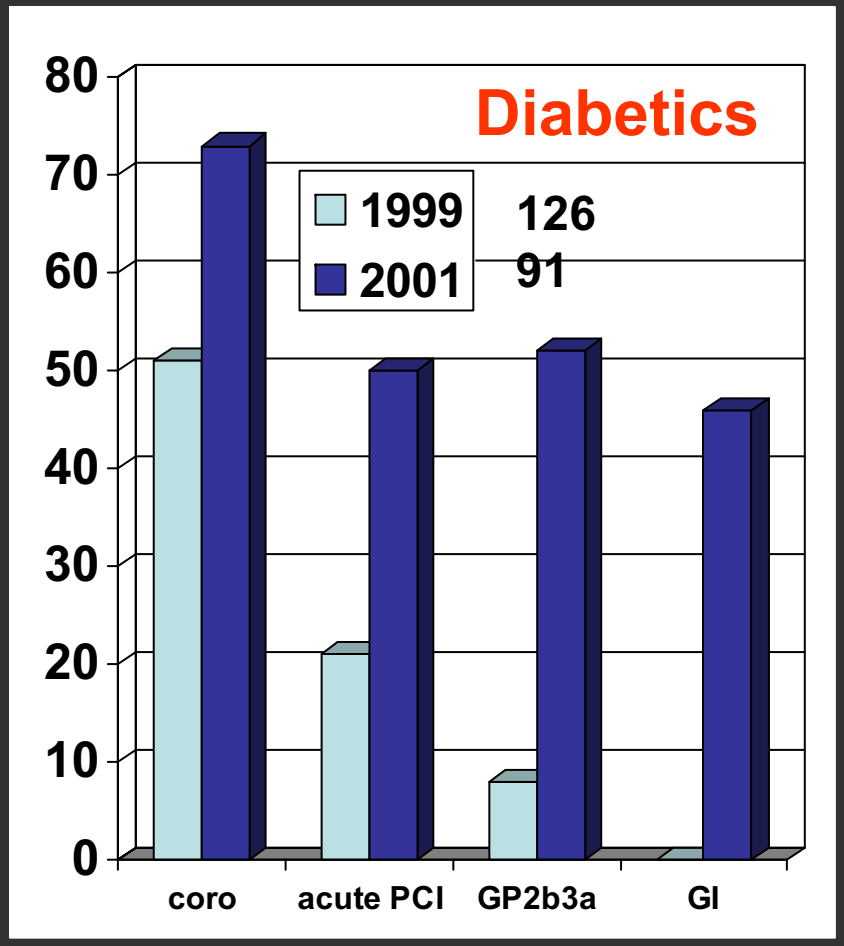
Brogan, Diabetes Care 2006

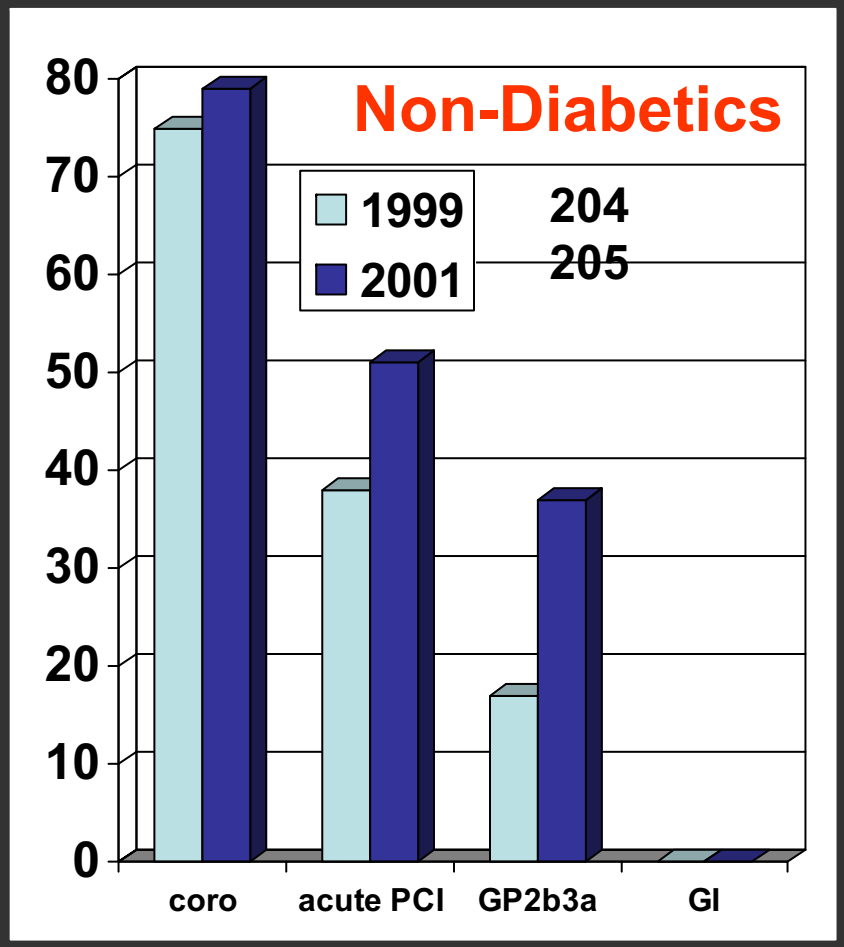
CRUSADE: *care of 46.410 pts with NSTE-ACS*
in-hospital outcomes



Brogan, Diabetes Care 2006

The Munich Registry: intensification of therapeutic approaches in STE-MI pts with DM*



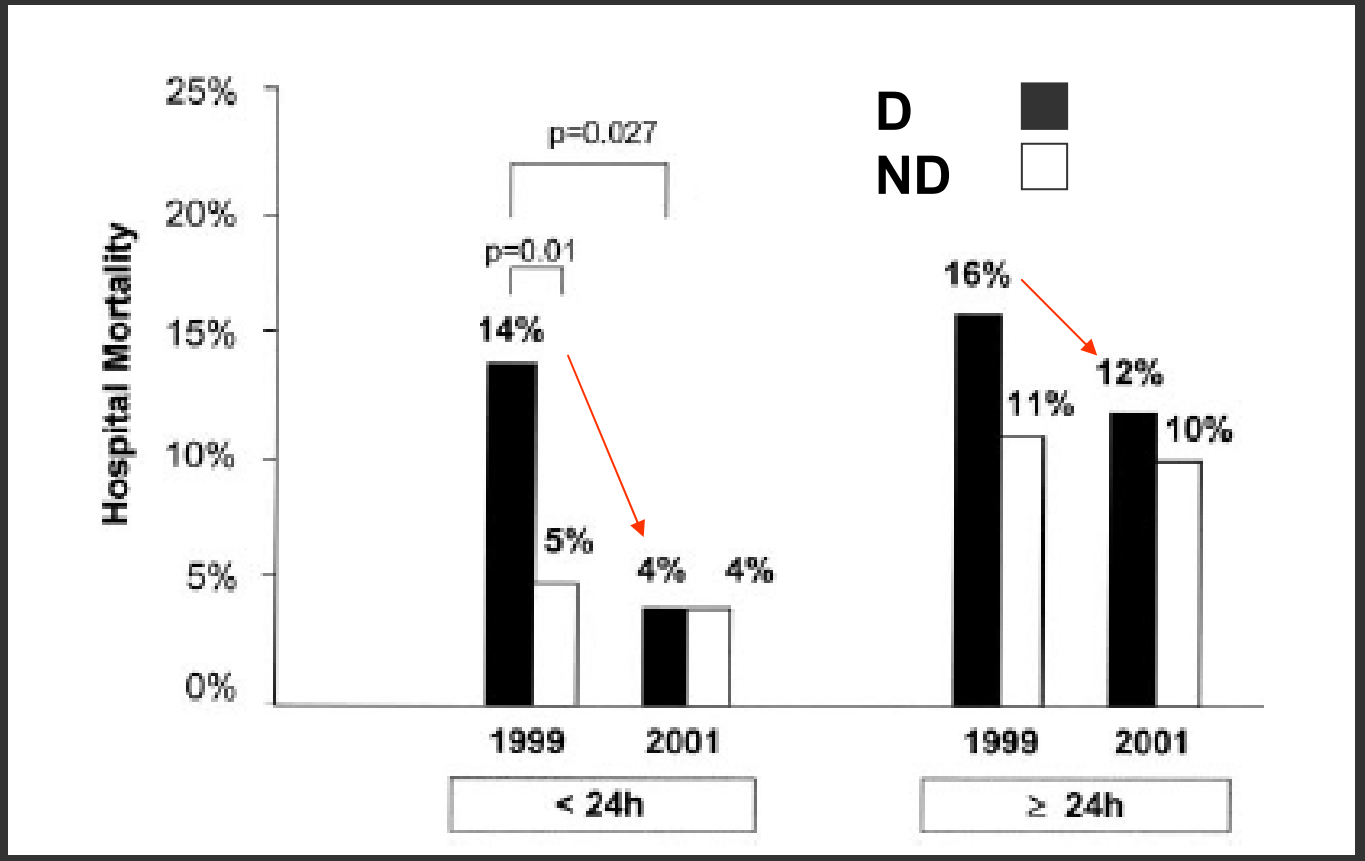


Schnell, Diabetes Care 2004

*Known DM or blood glucose o.a. >200 mg/dl

*

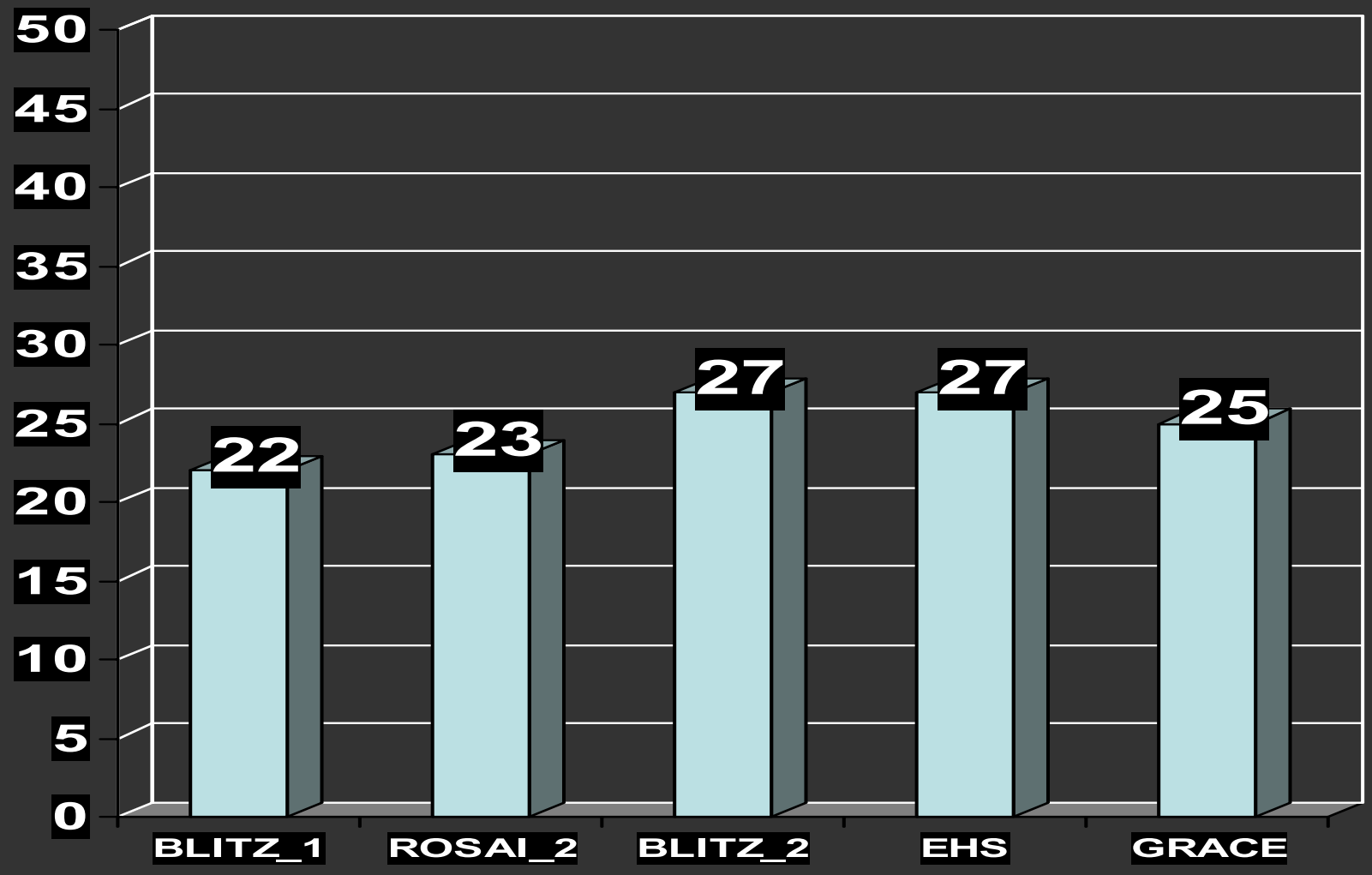
The Munich Registry: intensification of therapeutic approaches in STE-MI pts with DM*



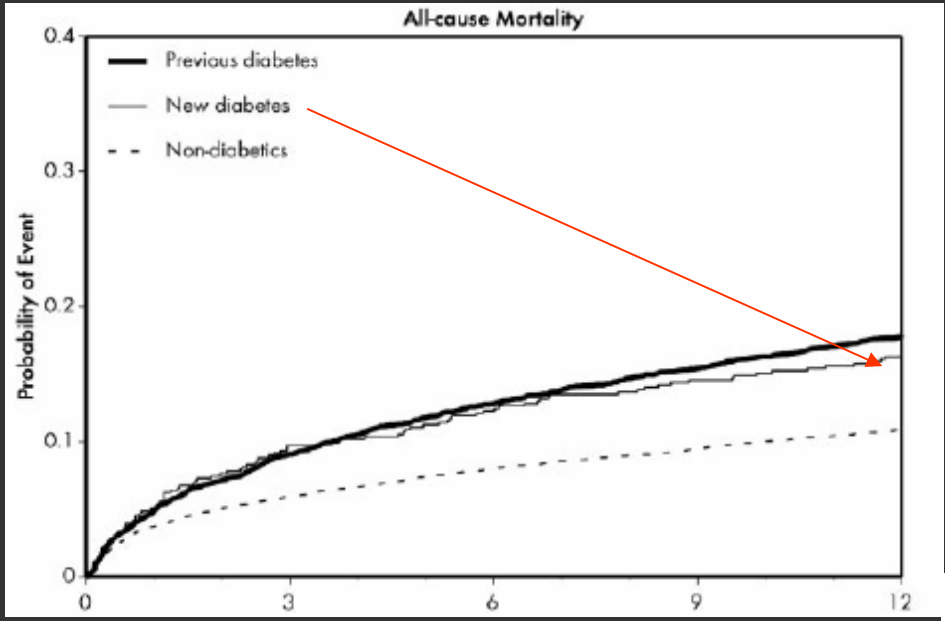
Schnell, Diabetes Care 2004

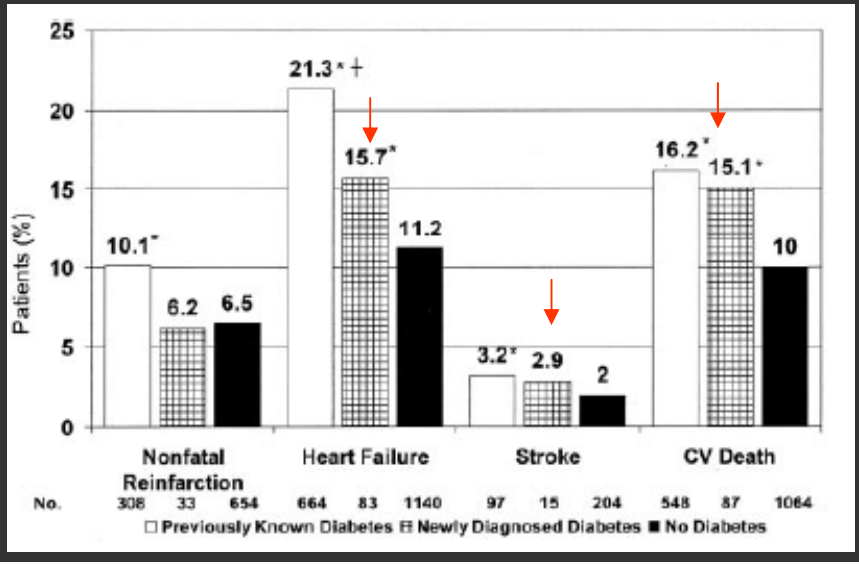
*Known DM or blood glucose o.a. >200 mg/dl

Prevalenza del diabete nelle SCA: registri
(pazienti con storia di DM)



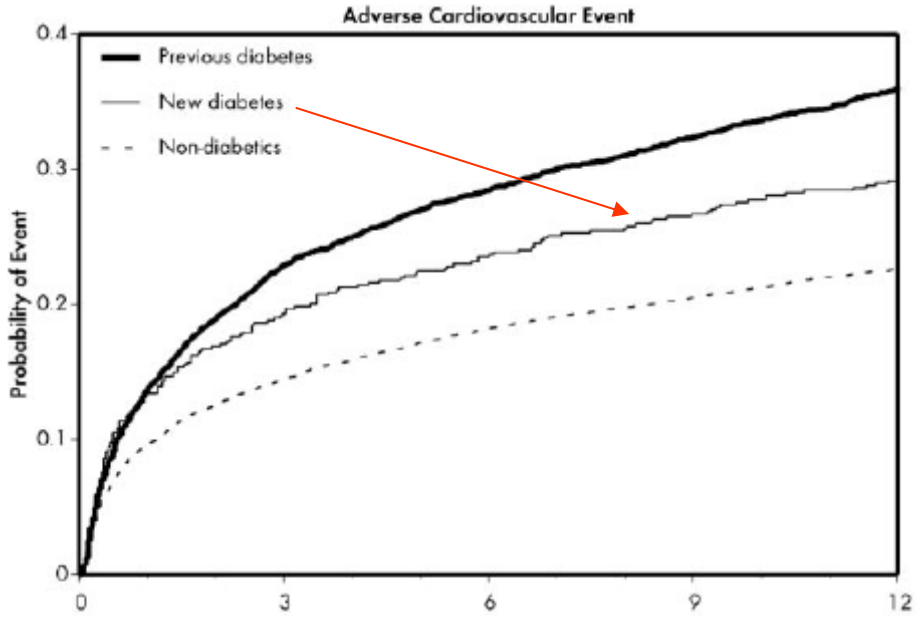
Known and Newly Diagnosed DM and 1-y outcomes of AMI (*VALIANT trial*, pts with LV disfunction)





Previous DM (3400) **HR 1.43 (1.29-1.59)**
New DM (580) **HR 1.50 (1.21-1.85)**
No DM (10719)

Aguilar, Circulation 2004

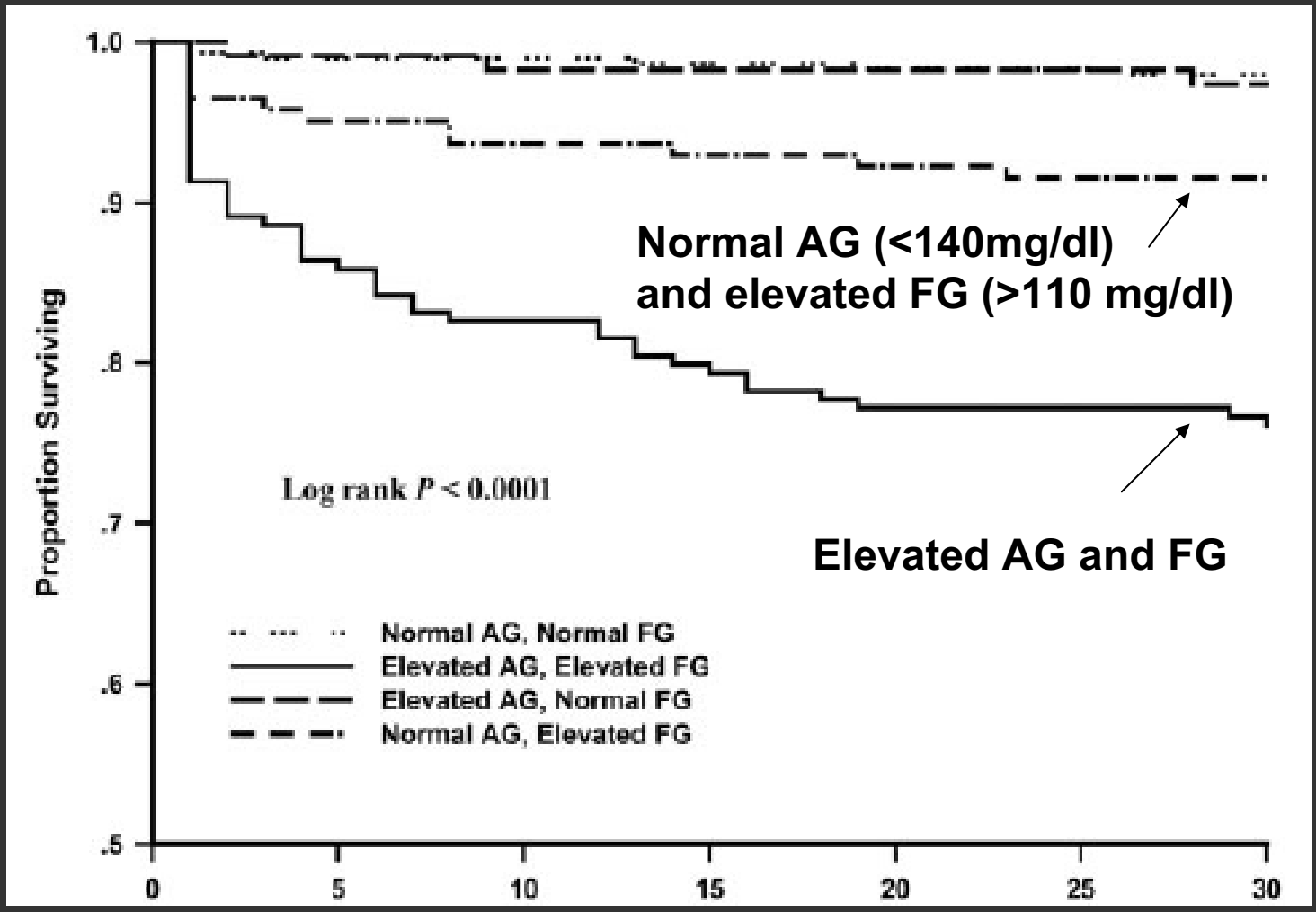


FG and 30-d mortality in 735 non-diabetic and 310 known diabetics pts with AMI

End Point	n	Events (%)	Adjusted OR (95% CI)	*P*
Death				
Normal FG (<110 mg/dL)†	409	9 (2.2)	1.0	
Impaired FG (110–125 mg/dL)	145	14 (9.7)	4.0 (1.5–10.5)	0.004
FG in the diabetes range (≥126 mg/dL)	181	42 (23.2)	10.2 (4.4–23.7)	<0.0001
Previously known diabetes	310	35 (11.3)	2.4 (1.03–5.5)	0.04
Death and heart failure				
Normal FG (<110 mg/dL)	409	24 (5.9)	1.0	
Impaired FG (110–125 mg/dL)	145	22 (15.2)	2.6 (1.3–5.0)	0.004
FG in the diabetes range (≥126 mg/dL)	181	56 (30.9)	5.8 (3.3–10.3)	<0.0001
Previously known diabetes	310	48 (15.5)	1.6 (0.9–2.9)	0.08

Suleiman, Circulation 2005

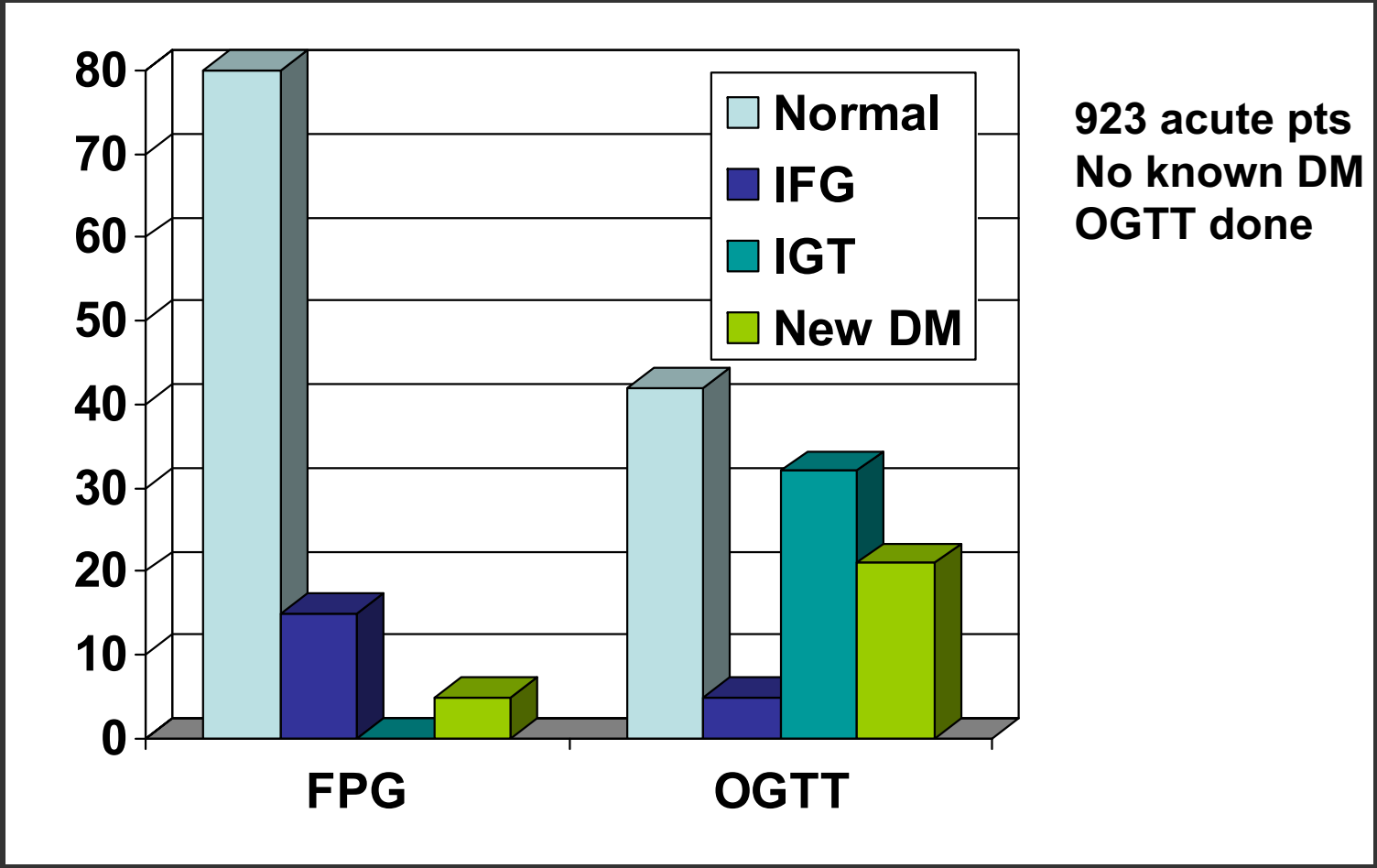
AG/FG and 30-d mortality in 735 non-diabetic pts with AMI



Suleiman, Circulation 2005

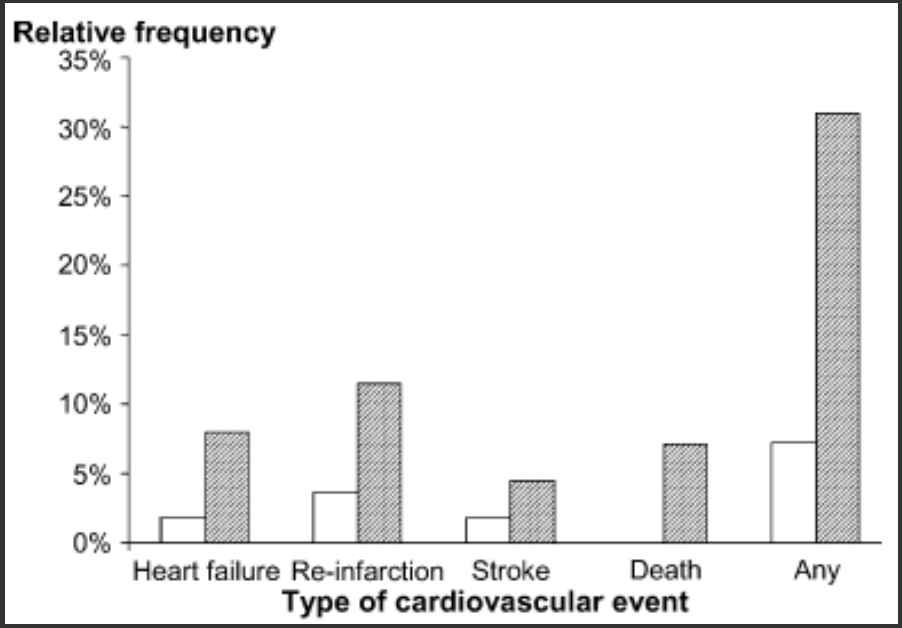
Abnormal glucose regulation in pts with acute CAD

Euro Heart Survey (Bartnik EHJ 2004)



32% of acute pts had known DM

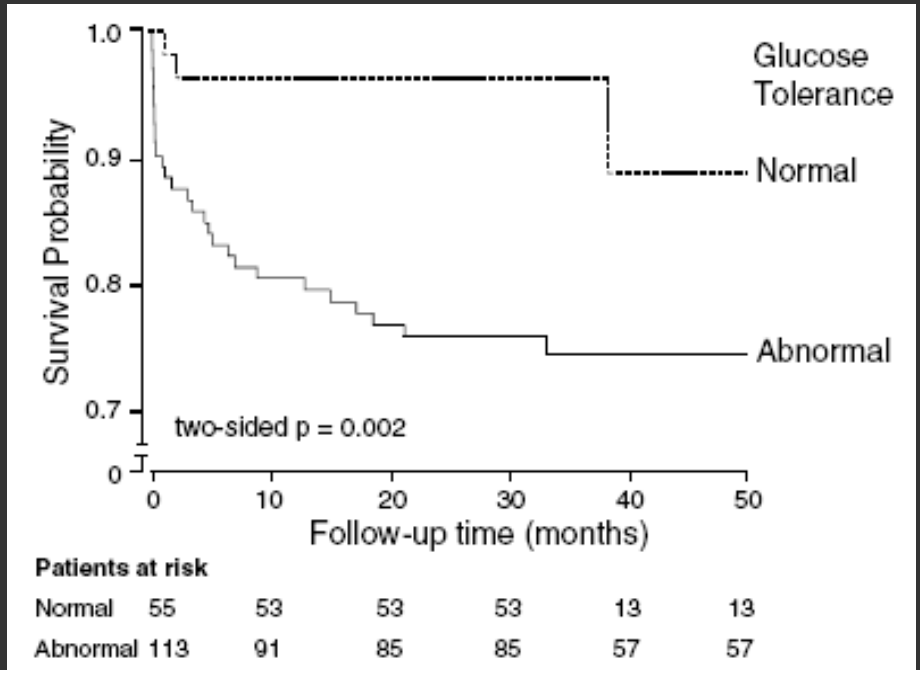
Newly detected abnormal glucose tolerance (OGTT) and prognosis after AMI (113pts)



No known DM and
admission blood glucose <200 mg/dl:

OGTT before H discharge
And major CV events at 34m

Bartnik, EHJ 2004

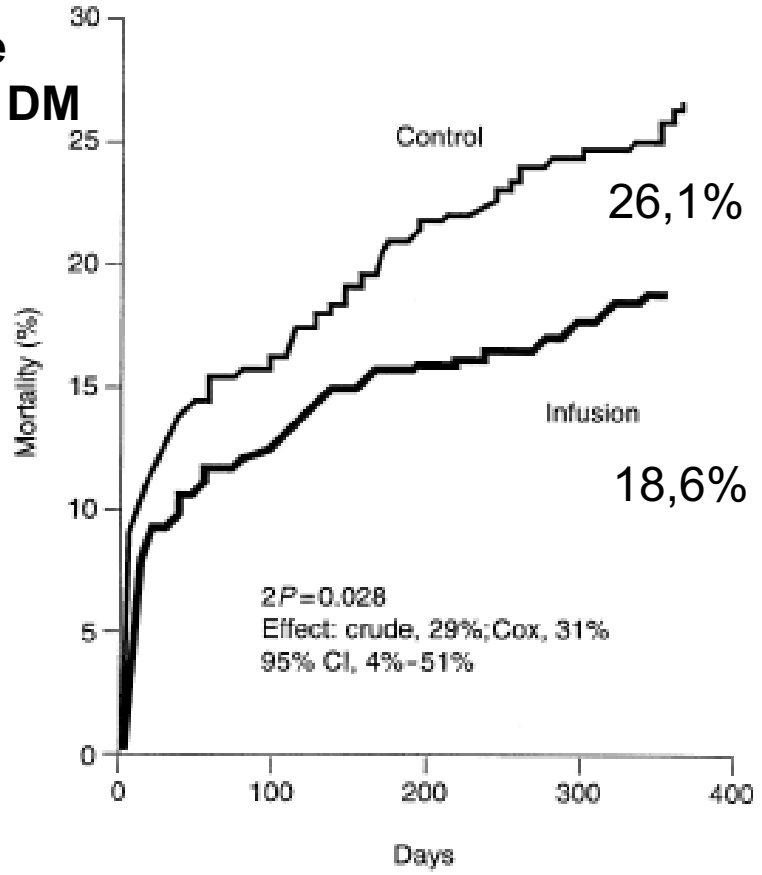


DIGAMI (Malmberg, JACC 1995)

AMI + blood glucose >200 mg/dl ± known DM

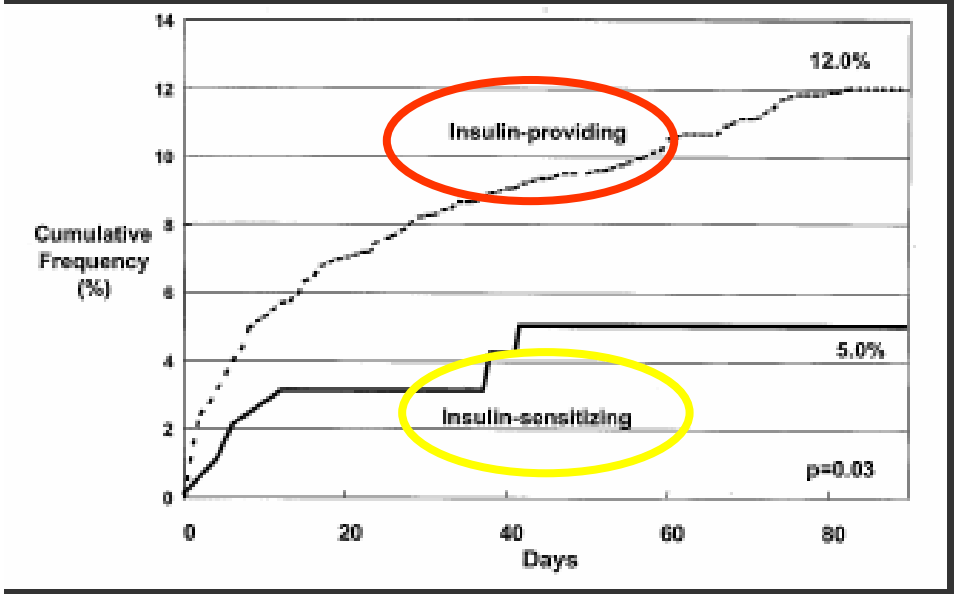
620 Patients

Insulin	Control
• Glucose-insulin infusion • Multidose subcutaneous insulin for ≥3 months	• Standard therapy • Insulin if needed



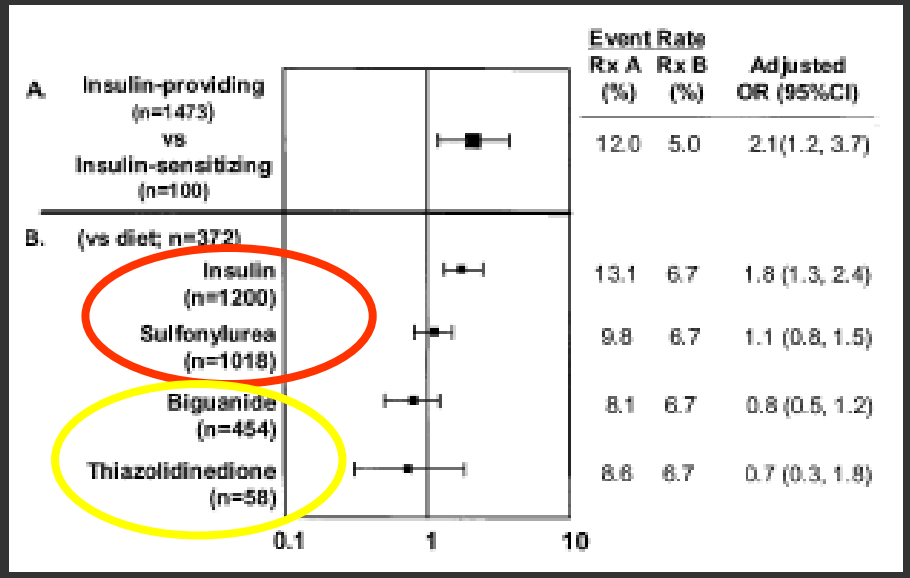
Nei 272 pz "NO PREVIOUS INSULIN, LOW CV RISK (strato 1), la riduzione di mortalità era 52% a 3 mesi e a 1 anno

Association of DM and glycemic ctrl strategies with outcomes after ACS (1997-99; 15.800 pts in sibrafiban trials)



90-days
death / MI / recurrent isch.

In 3101 diabetics
With ACS



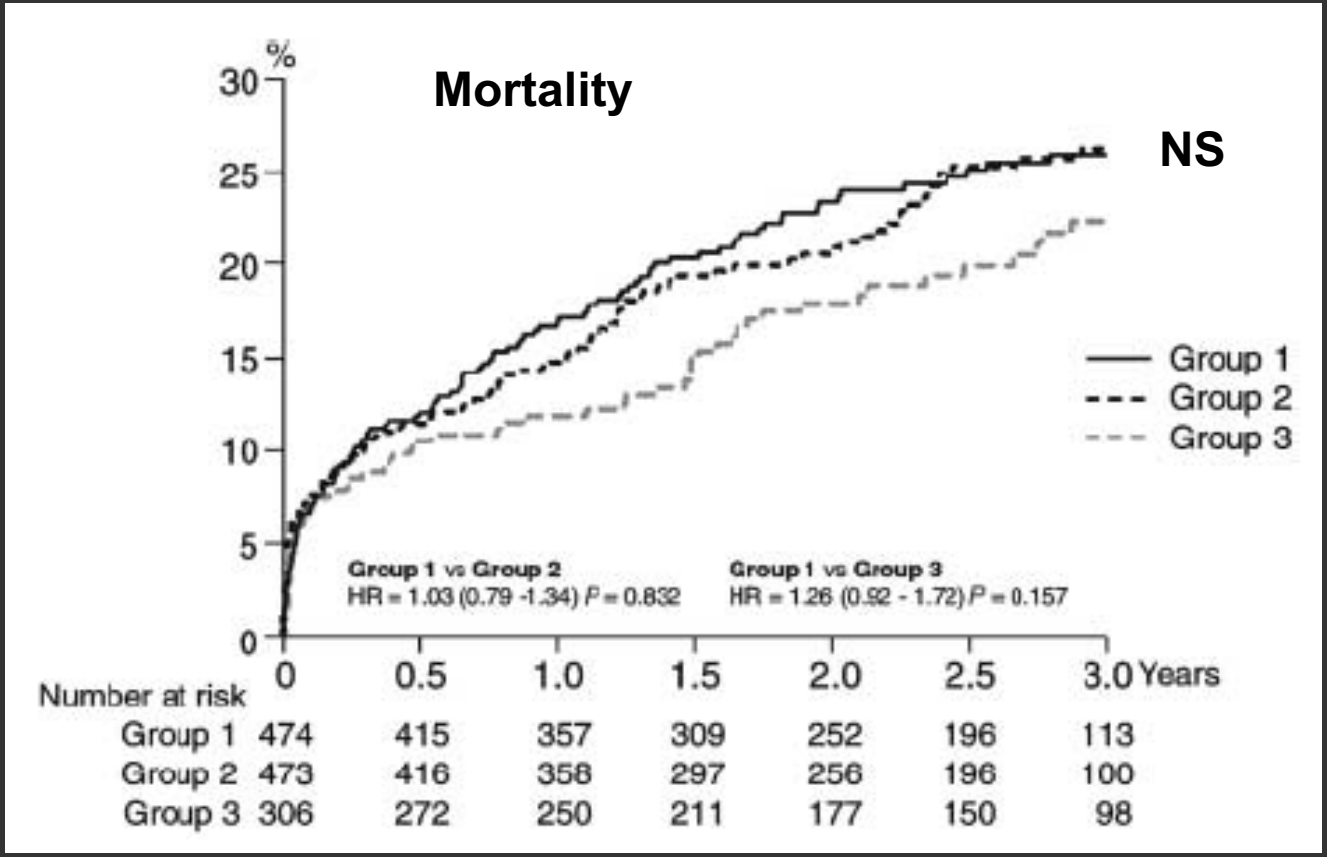
McGuire, AmHeartJ 2004

DIGAMI-2 (Malmberg, EHJ 2005)

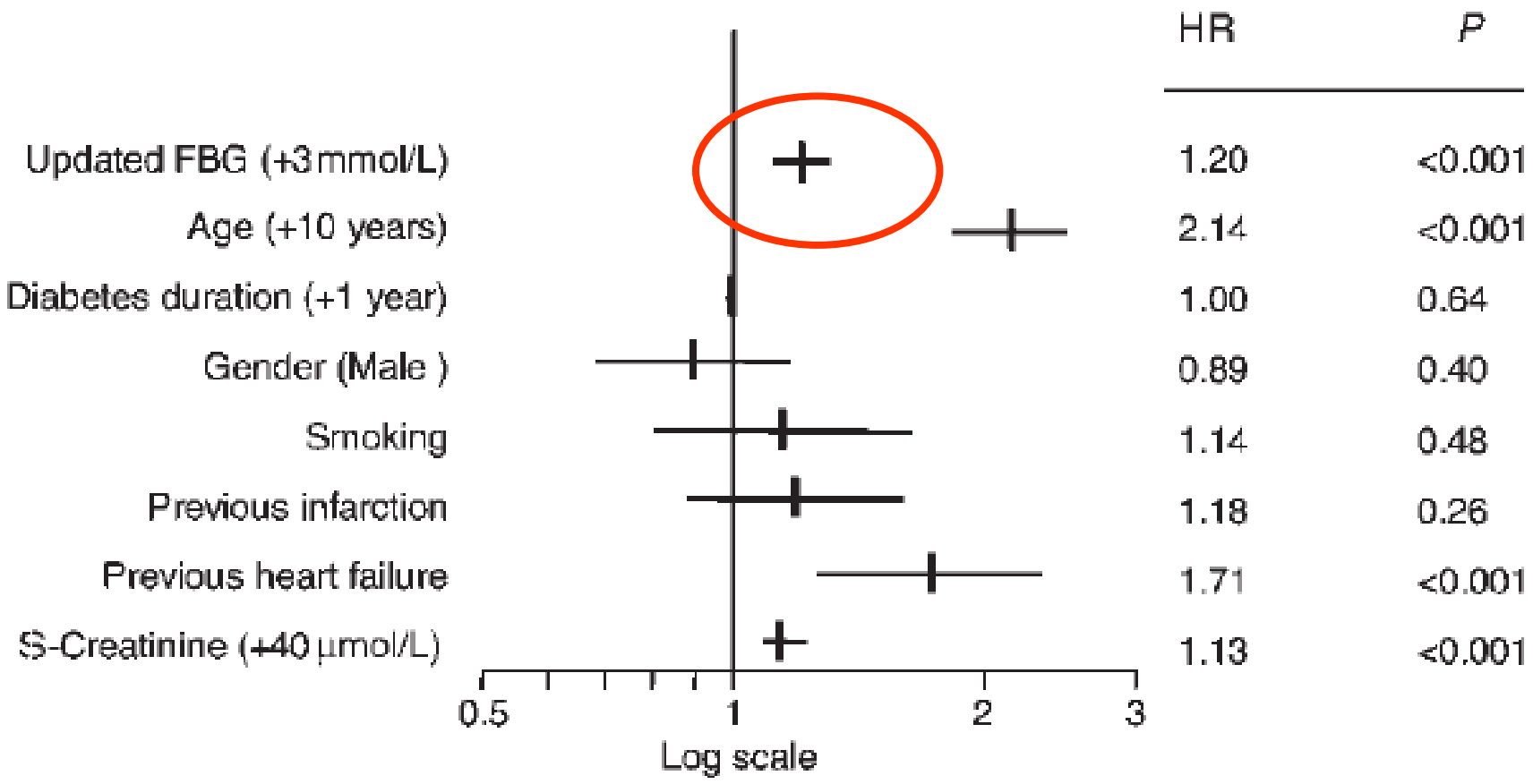
Group 1 — **Acute insulin + long-term insulin**

Group 2 — **Acute insulin + standard control**

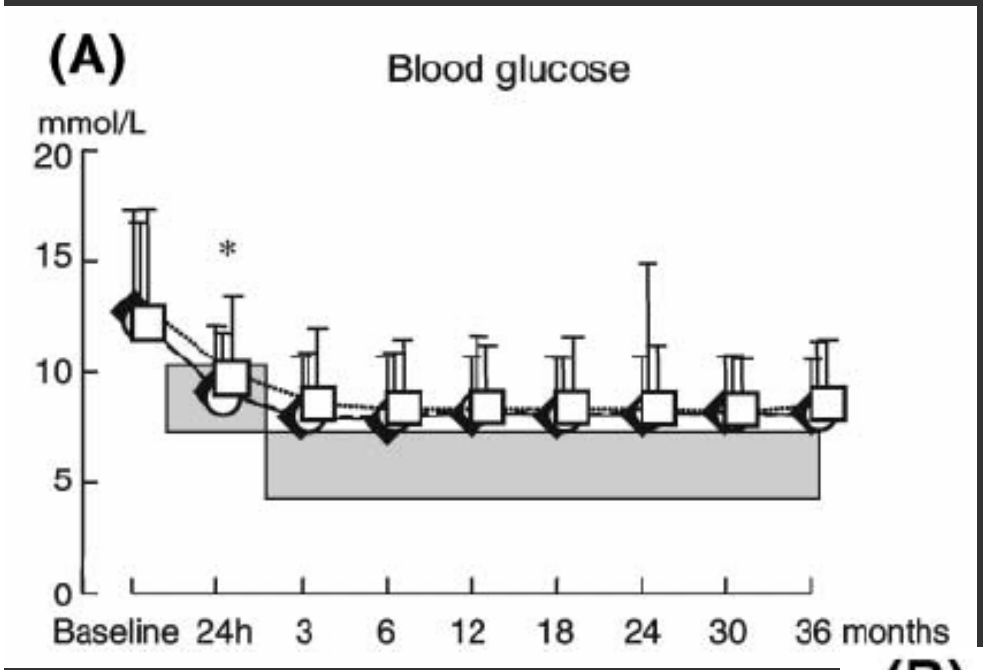
Group 3 — **Routine metabolic management**



Independent predictors for mortality. FBG updated values during follow-up



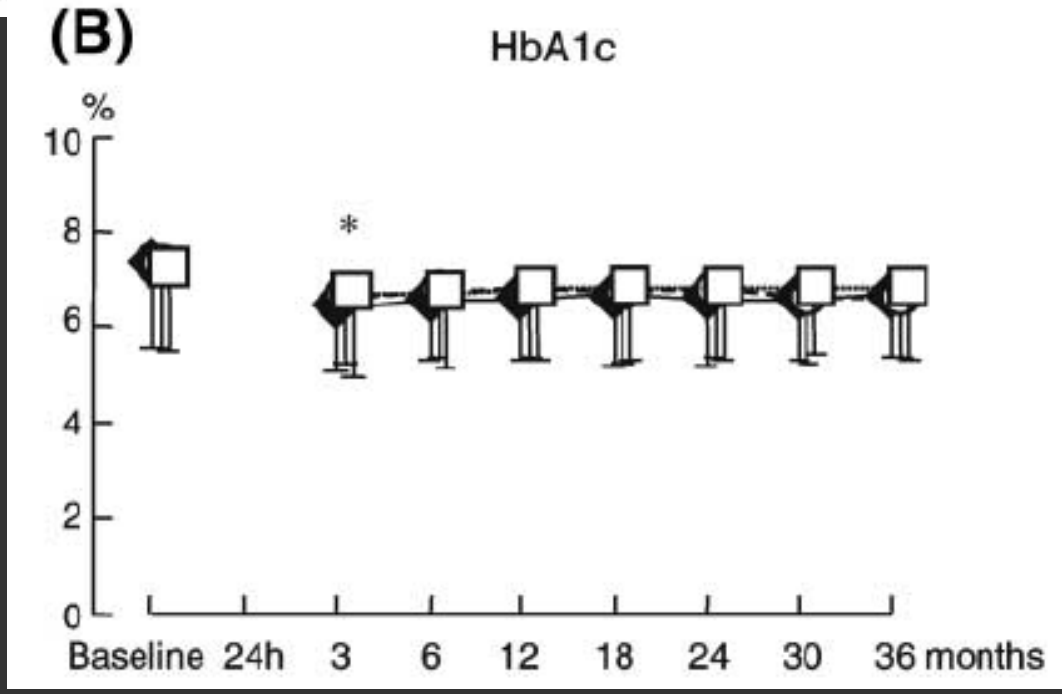
DIGAMI-2 (Malmberg, EHJ 2005)



Long-term glucose control did not differ among strategies and was suboptimal

DIGAMI-2

(Malmberg, EHJ 2005)



Taylor, Diabetologia 2006

Digami 1

Aim

To test the hypotheses that:

- acute improvement of metabolic control decreased initial mortality
- continued good control improved subsequent prognosis

Digami 2

Aim

To explore further the hypotheses that:

- early and continued intense metabolic control using insulin is a key to mortality reduction

Outcomes

600 subjects needed; 620 recruited

24 h blood glucose 9.6 vs.11.7 mmol/l

1 year HbA_{1c} 7.3 vs 7.7%

Mortality decreased by 18% in hospital and 29% at 1 year

Mortality decreased by 52% in stress hyperglycaemia and no-prior-insulin group

Outcomes

3000 subjects needed; 1253 recruited

Study stopped due to recruitment failure

24 h blood glucose 9.1 vs 10.0 mmol/l

1-3 year HbA_{1c}~6.9% both groups

Mortality - no difference in hospital and cardiovascular deaths 18.4 vs 17.3% at 3 years

Overall, Digami 2

- **does not contradict the conclusions of Digami 1**
- **achieved no effective difference in blood glucose levels**
- **demonstrated the weight gain associated with indiscriminate use of long-term insulin despite lack of benefit for achieved glucose control**
- **did not consider door-to-needle time for insulin therapy**

Association between hyper- and hypoglicemia and 2-year mortality in 713 consecutive diabetics with ACS

GÖTEBORG ÖSTRA HOSPITAL REGISTRY 1988-98

	Adjusted HR	95% CI	
Quartile blood glucose ↑ on adm.	1,17	1,02	1,34
Lowest blood glucose in H stay			
<55 vs 56-119 mg/dl	1,93	1,18	3,17
≥120 vs 56-119 mg/dl	1,48	1,09	1,99
Treated hyperlipid.	0,38	0,19	0,76
B_blockers at disch.	0,58	0,43	0,78

Svensson, EHJ 2005

Conclusioni

- Gestione dell' iperglicemico con SCA
- Anti IIb /IIIa e coronarografia precoce
- Rivascolarizzazione (DES / CABG)
- Rivascolarizzazione completa PCI / CKD
- Normalizzazione precoce della glicemia
- Controllo ottimale persistente della glicemia: con quali farmaci?
- Controllo ottimale PA (ACE-i / sartani) e Colesterolemia (statine)
- Impaired Fasting Glucose e OGTT+

ANMCO – Sweet ACS