



SOLACI '12

MEXICO DF

In partnership with **TCT**

August 8 - 10 2012

CLINICAL FORUM INTERVENTIONAL THERAPIES IN THE DIABETIC POP

Best DES for the Patient with Diabetes: Tough Call or Clear-Cut Decision? *An Answer Based on Recent Randomized Trials Results*

Marcelo Halac, MD - Day 3



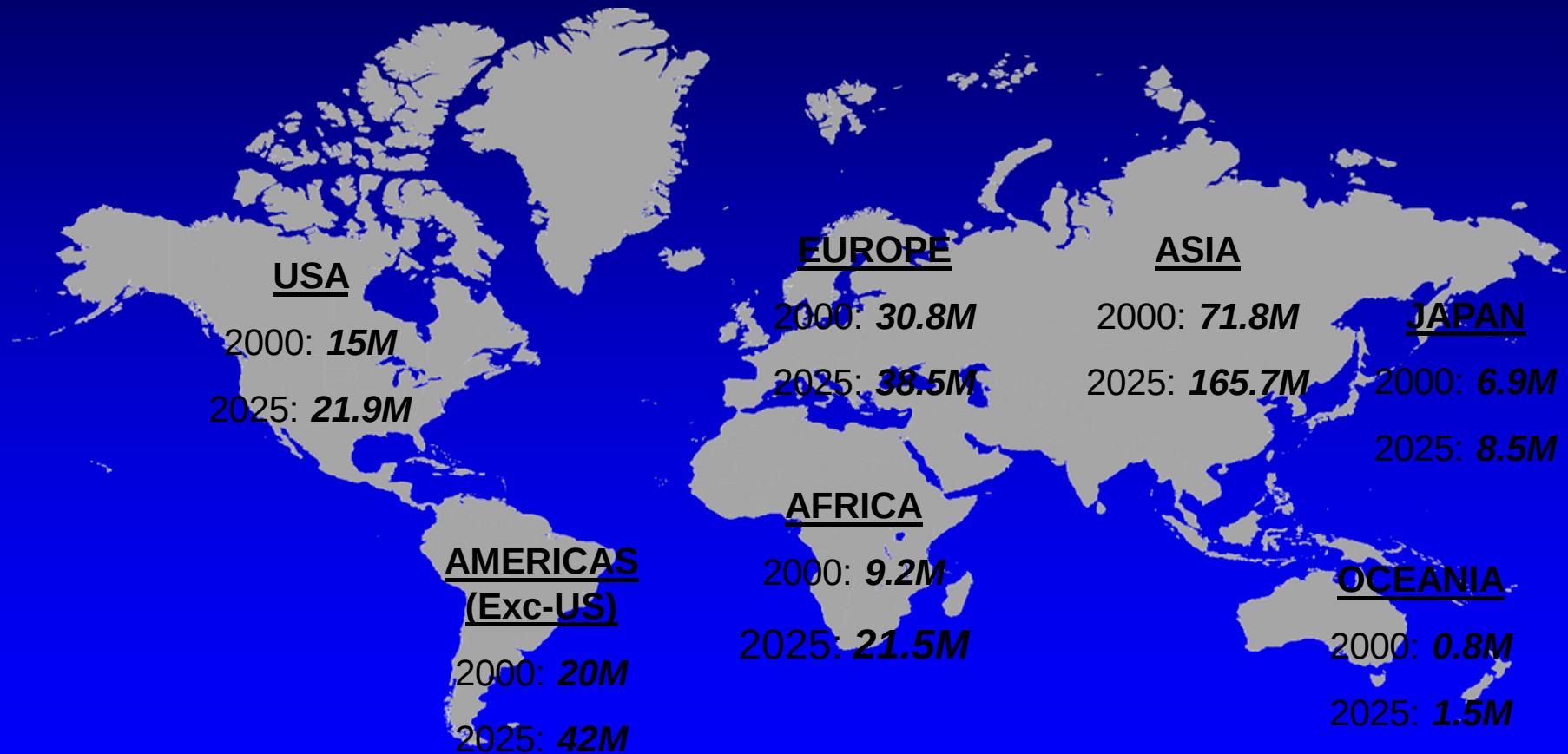
DISCLOSURE

I, Dr. Marcelo Halac, have the following potential conflicts of interest with this presentation to report:

- ☐ Consulting
- ☐ Grant Research
- ☐ Employment in industry
- ☐ Stockholder of a healthcare company
- ☐ Owner of a healthcare company
- ☐ Other(s)
- ☒ I do not have any potential conflict of interest

Diabetes Type II

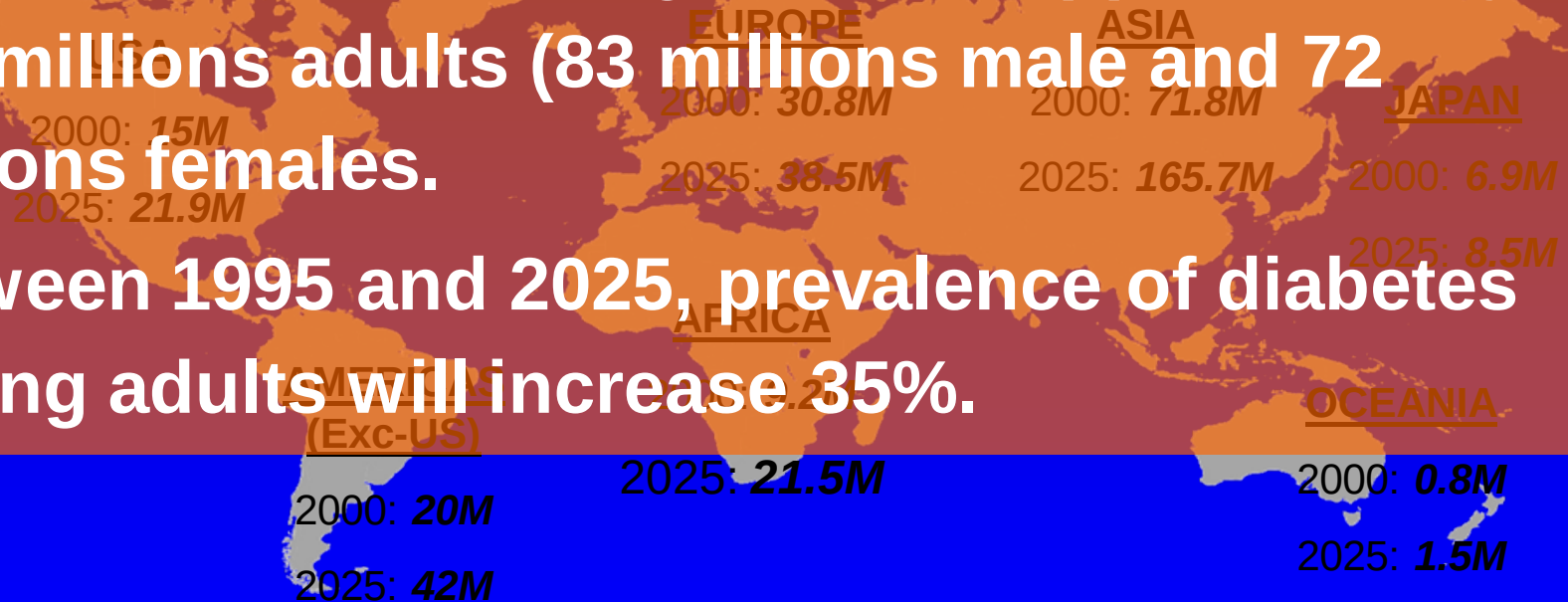
A prevalence around 300 millions is expected in 2025



Diabetes Type II

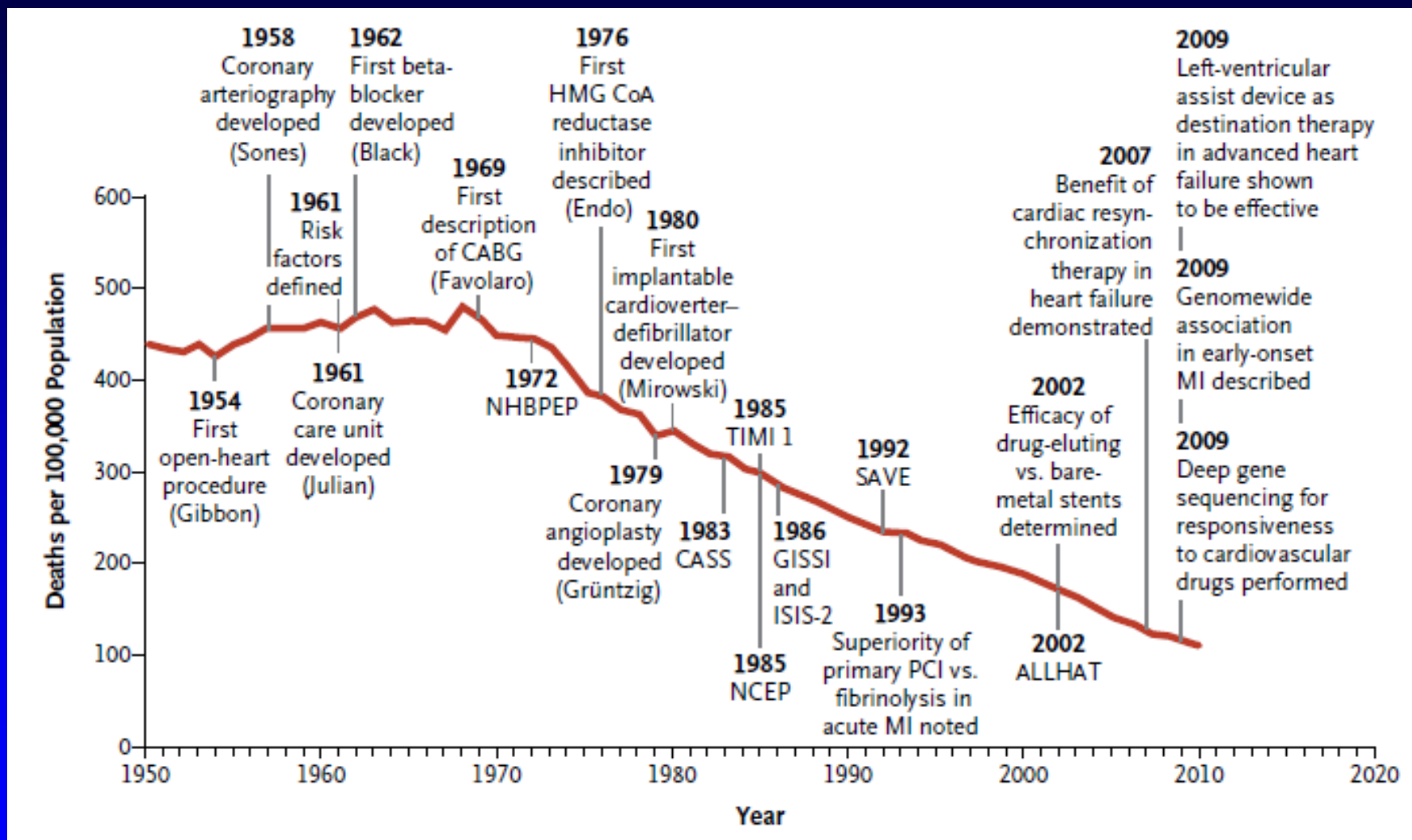
A prevalence around 300 millions is expected in 2025

- In 2K Diabetes was diagnosed in approximately 155 millions adults (83 millions male and 72 millions females).
- Between 1995 and 2025, prevalence of diabetes among adults will increase 35%.

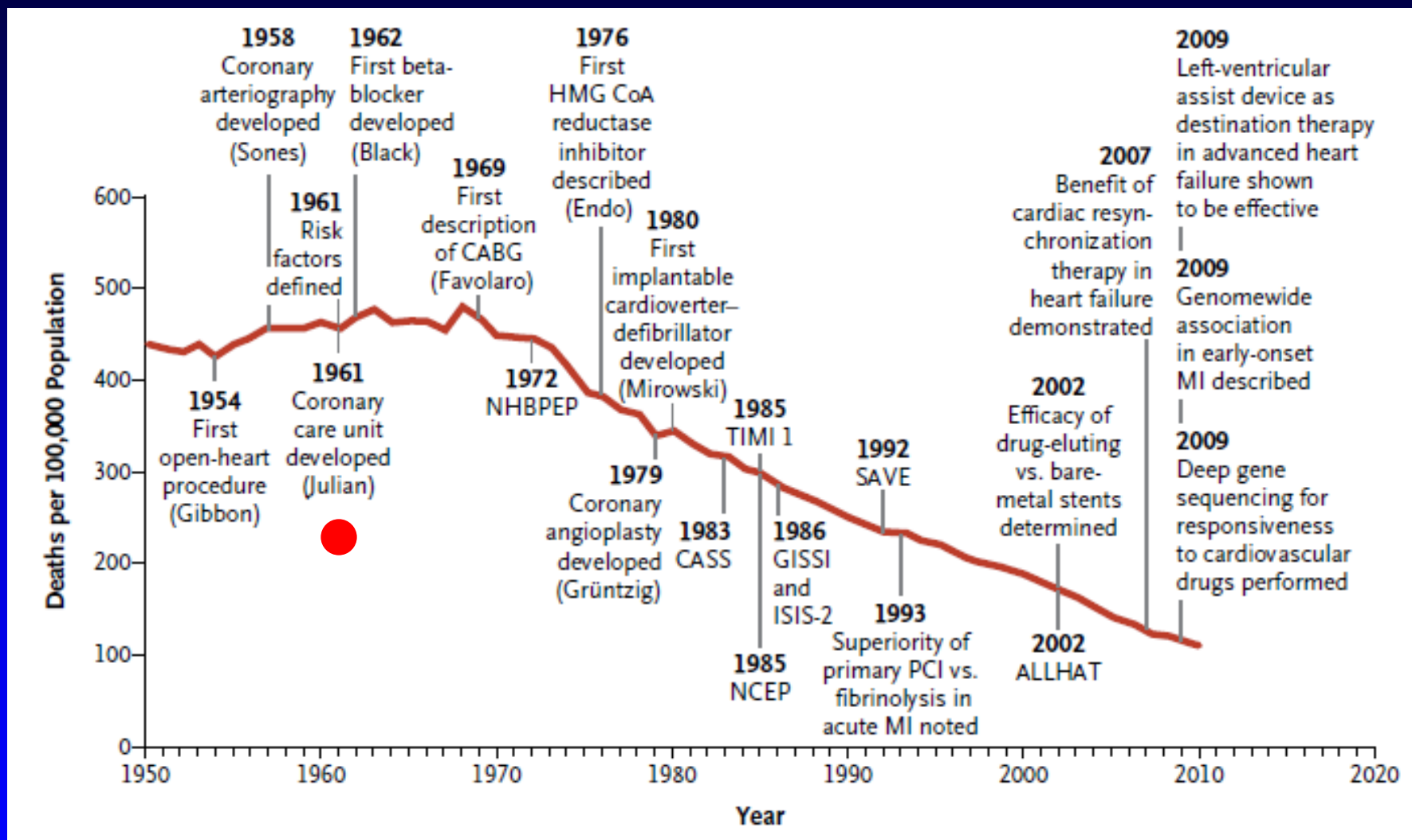


Death curves along time...

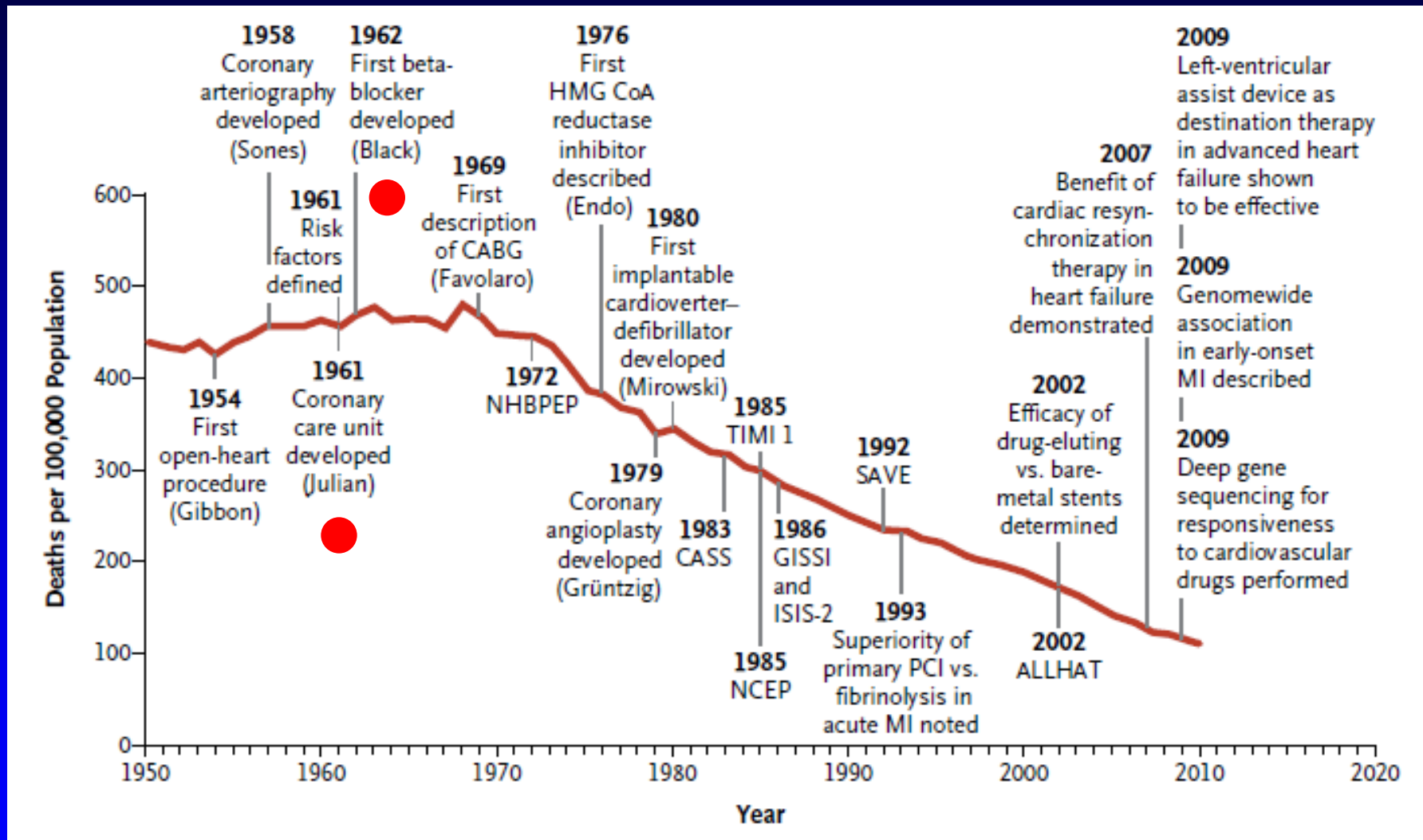
Historical overview of Cardiovascular Deaths



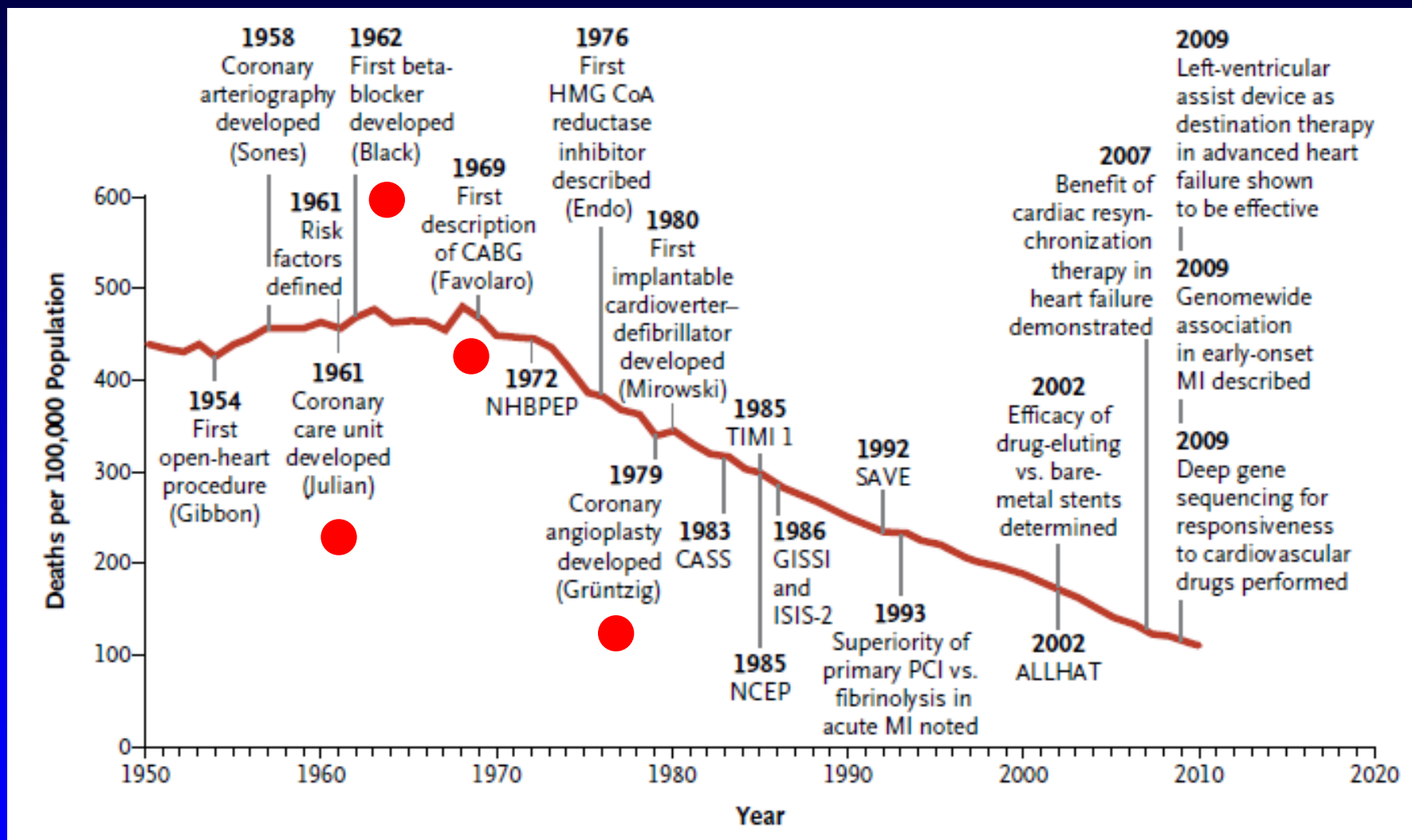
Historical overview of Cardiovascular Deaths



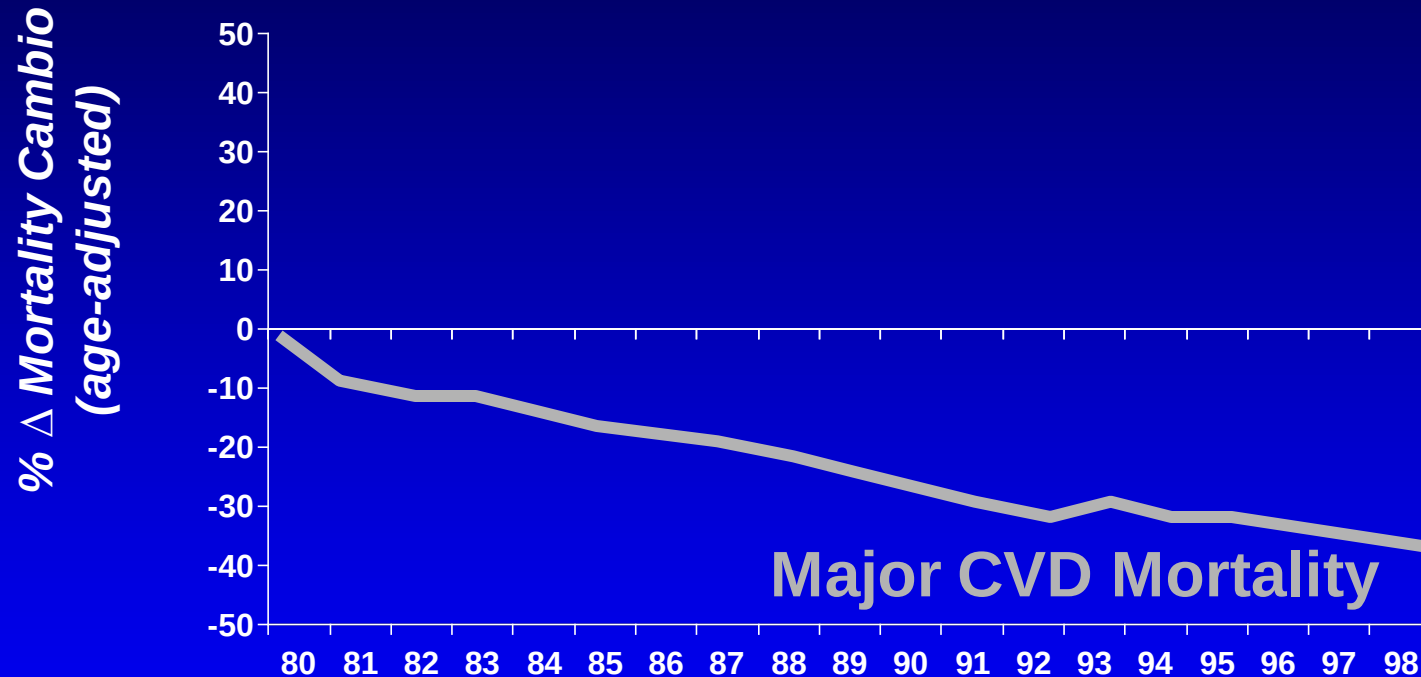
Historical overview of Cardiovascular Deaths



Historical overview of Cardiovascular Deaths

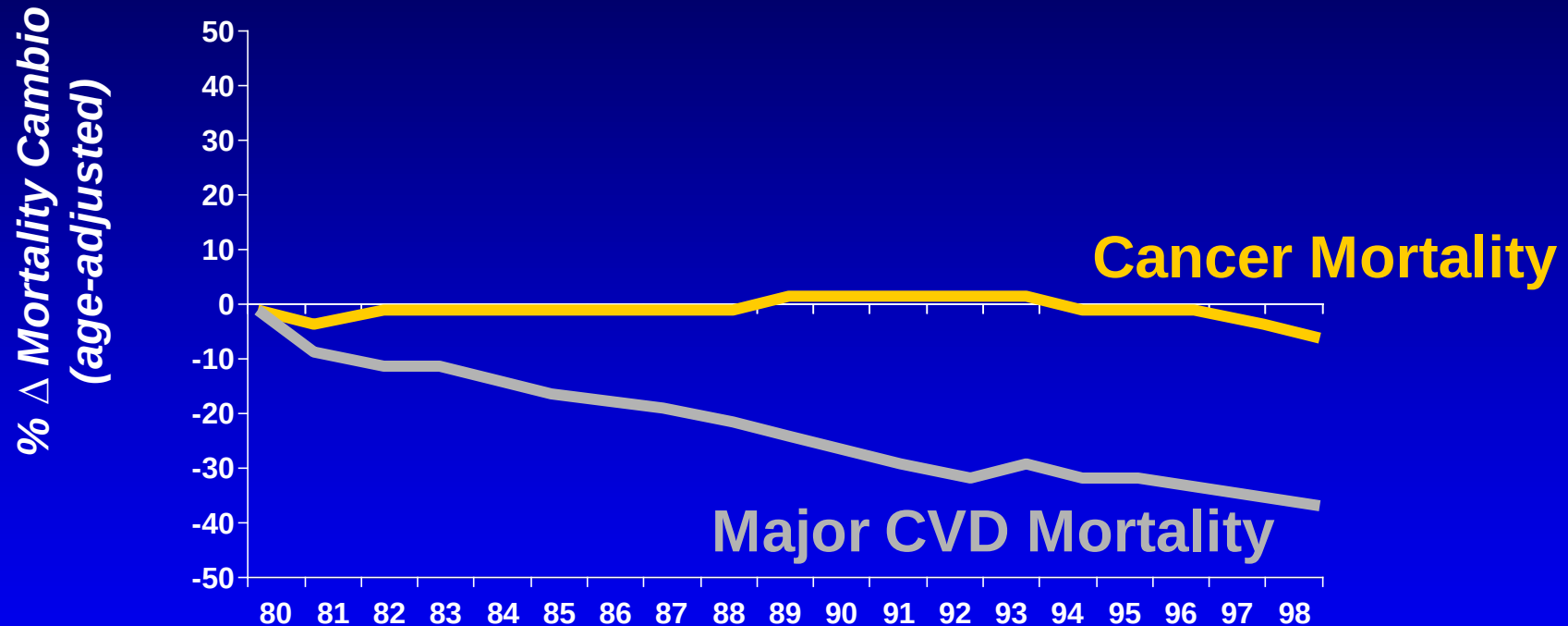


Death curves along time...



Centers for Disease Control and Prevention Mortality Database from
Burgeoning Dilemmas in the Management of Diabetes and Cardiovascular
Disease. BARI 2D Trial. Sobel BE et al. Circ 2003; 107: 636-42

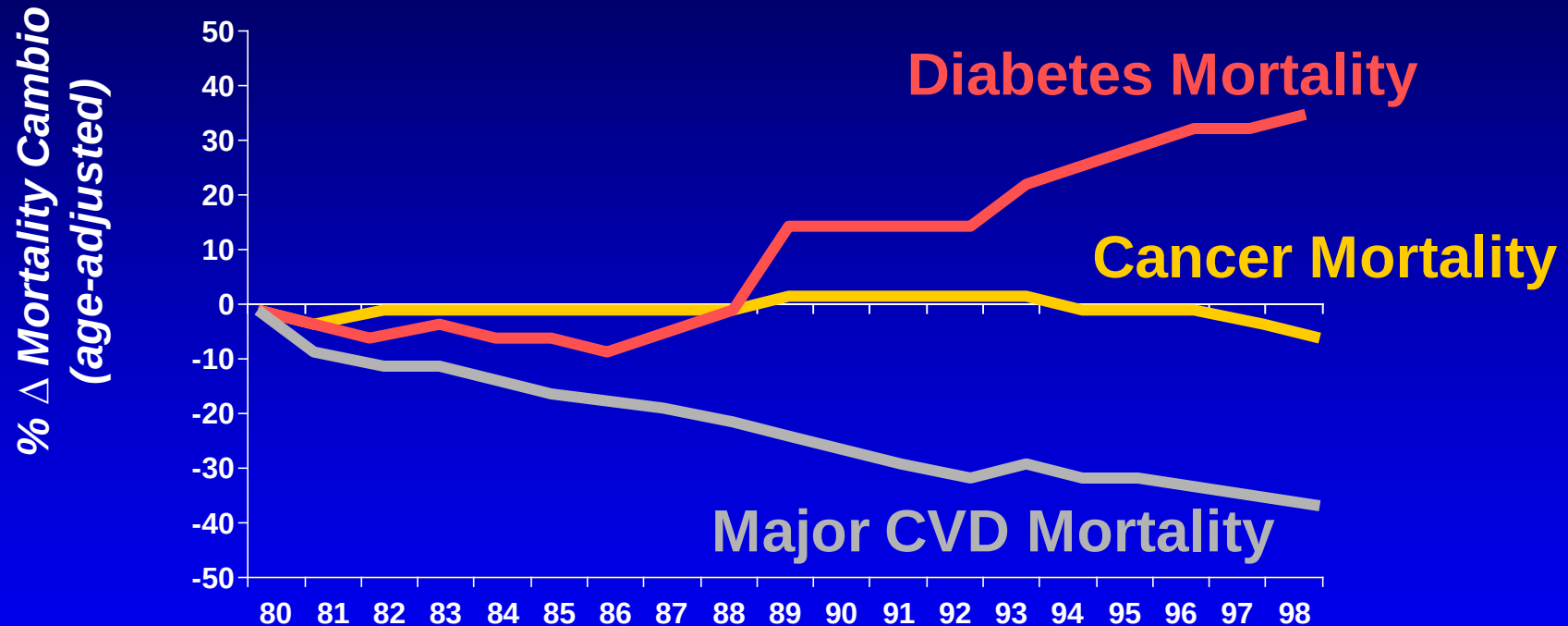
Death curves along time...



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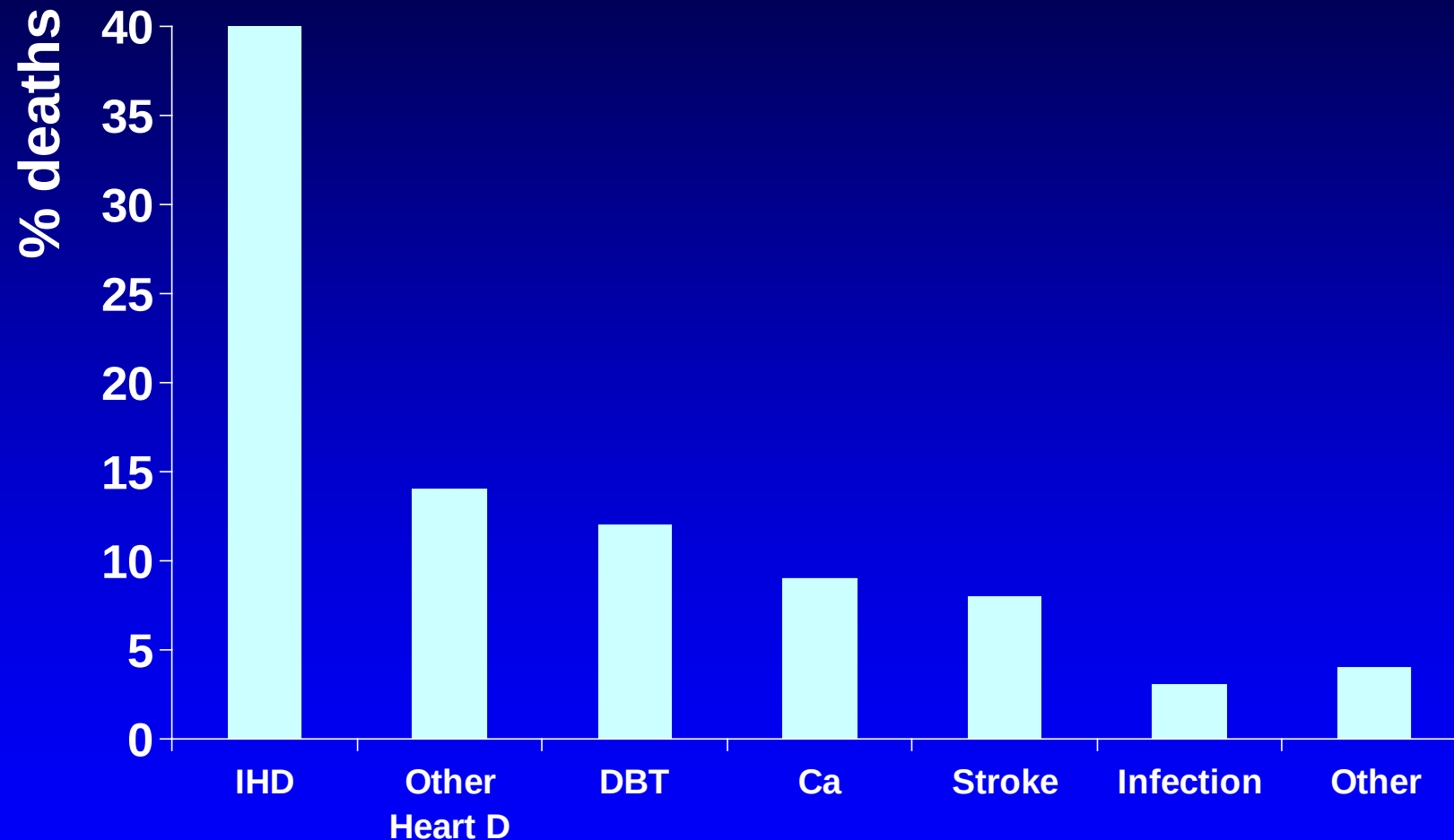
Death curves along time...



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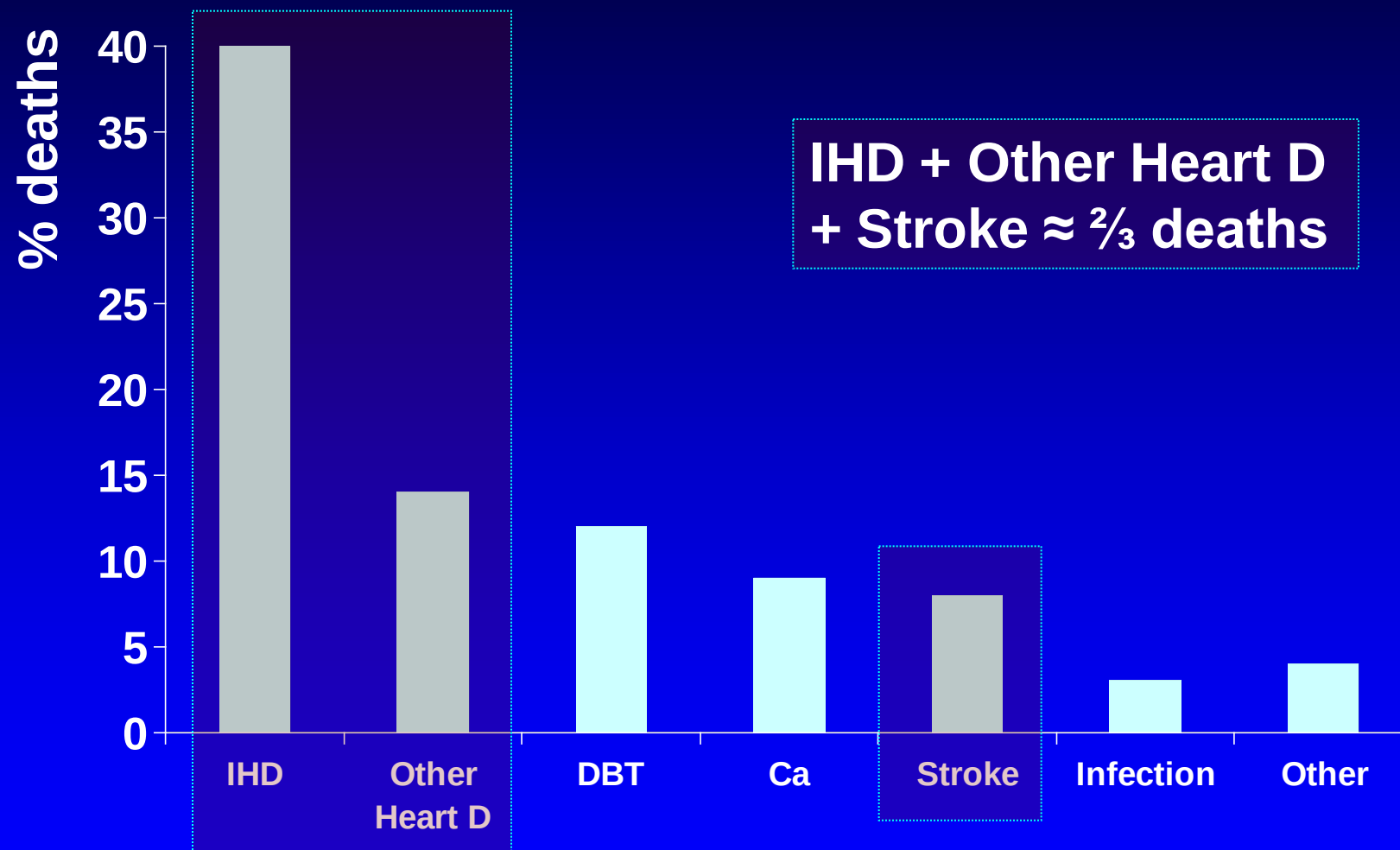
Centers for Disease Control and Prevention Mortality Database from
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Causes of death in diabetics



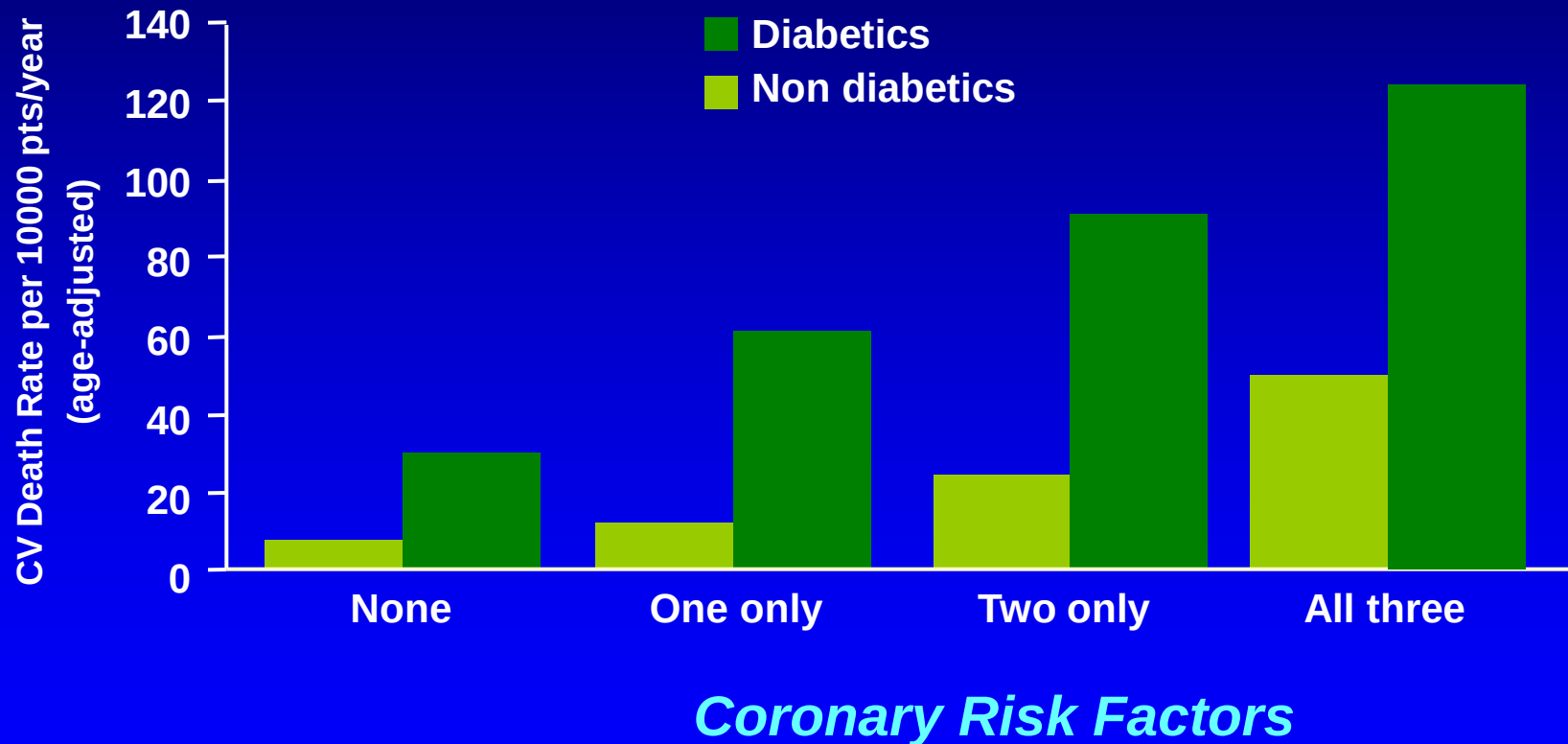
www.solacci.org

Causes of death in diabetics



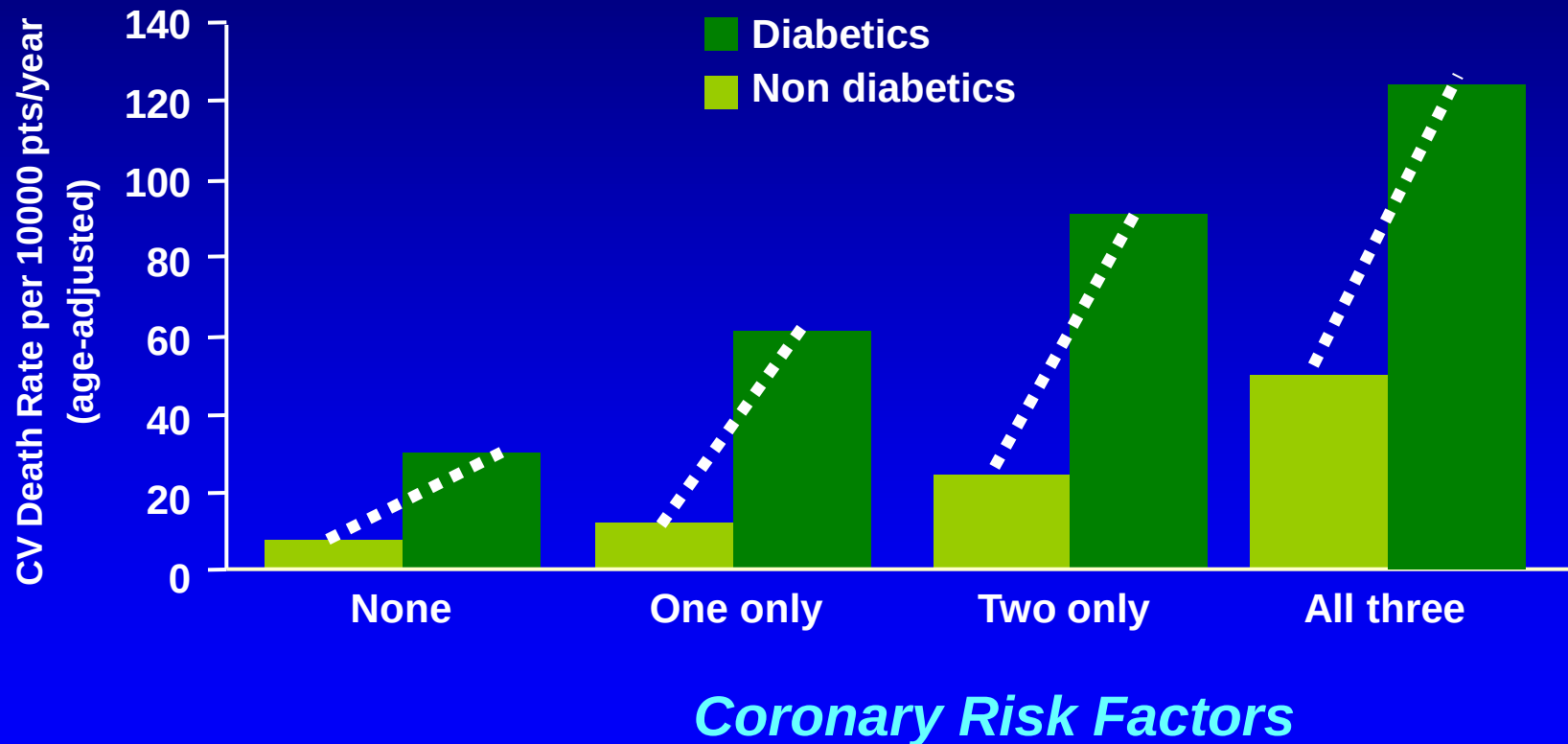
Cardiac Death risk: Diabetes vs All other Risk

Factors (Total Serum Cholesterol >200 mg/dl, Smoking, Systolic Hypertension >120 mmHg)



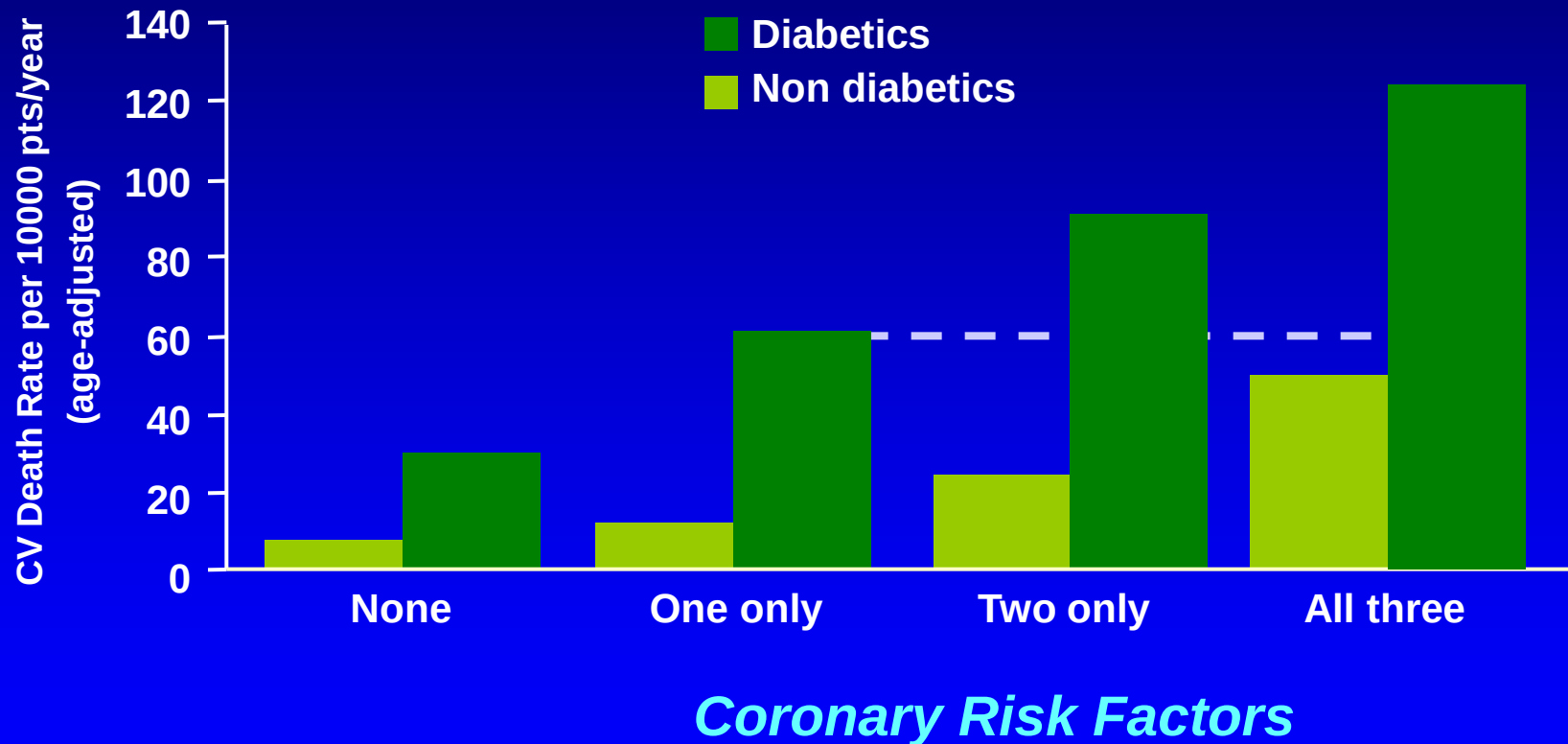
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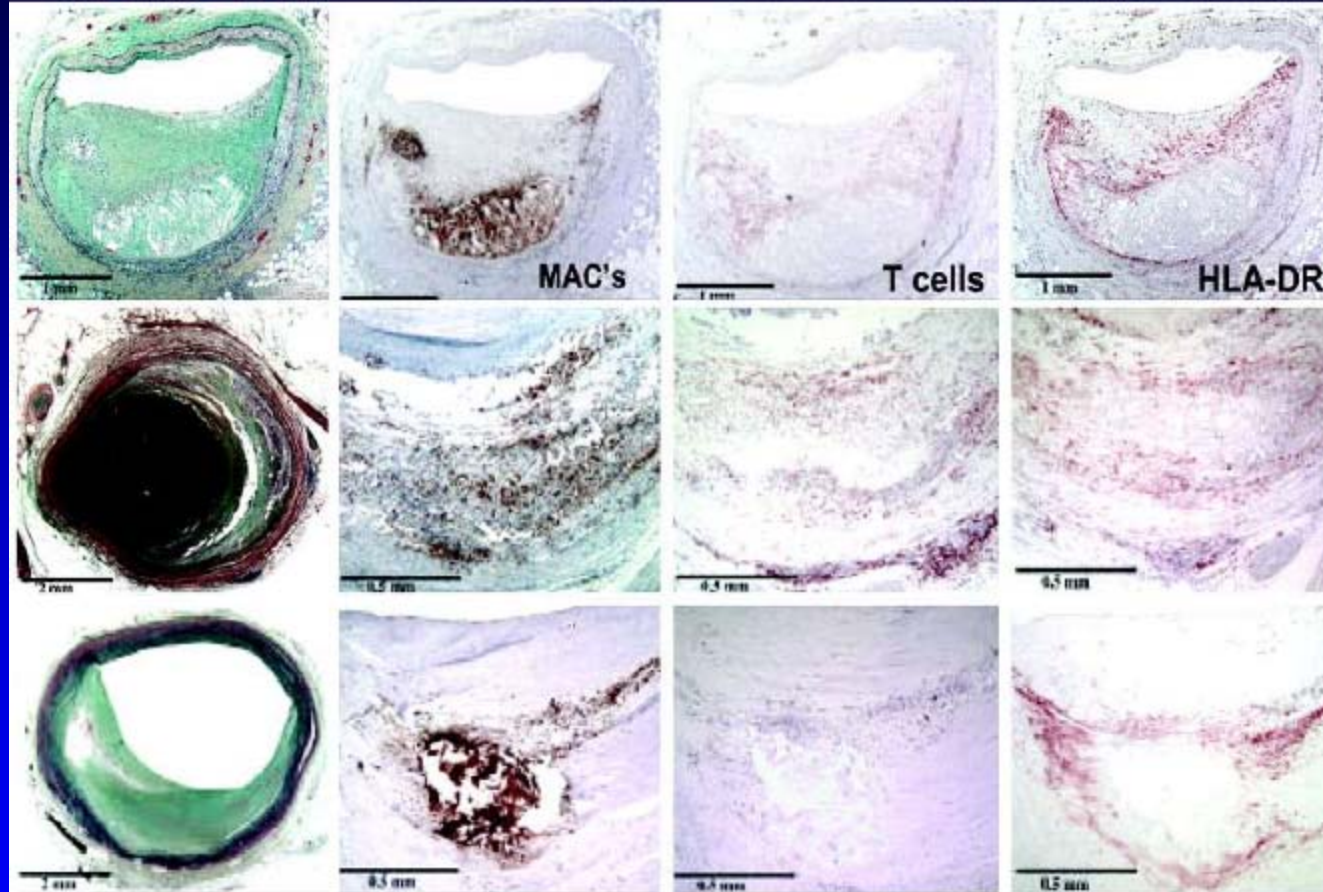


Cardiac Death risk: Diabetes vs All other Risk

Factors (Total Serum Cholesterol >200 mg/dl, Smoking, Systolic Hypertension >120 mmHg)



Diabetic Coronary Arteries



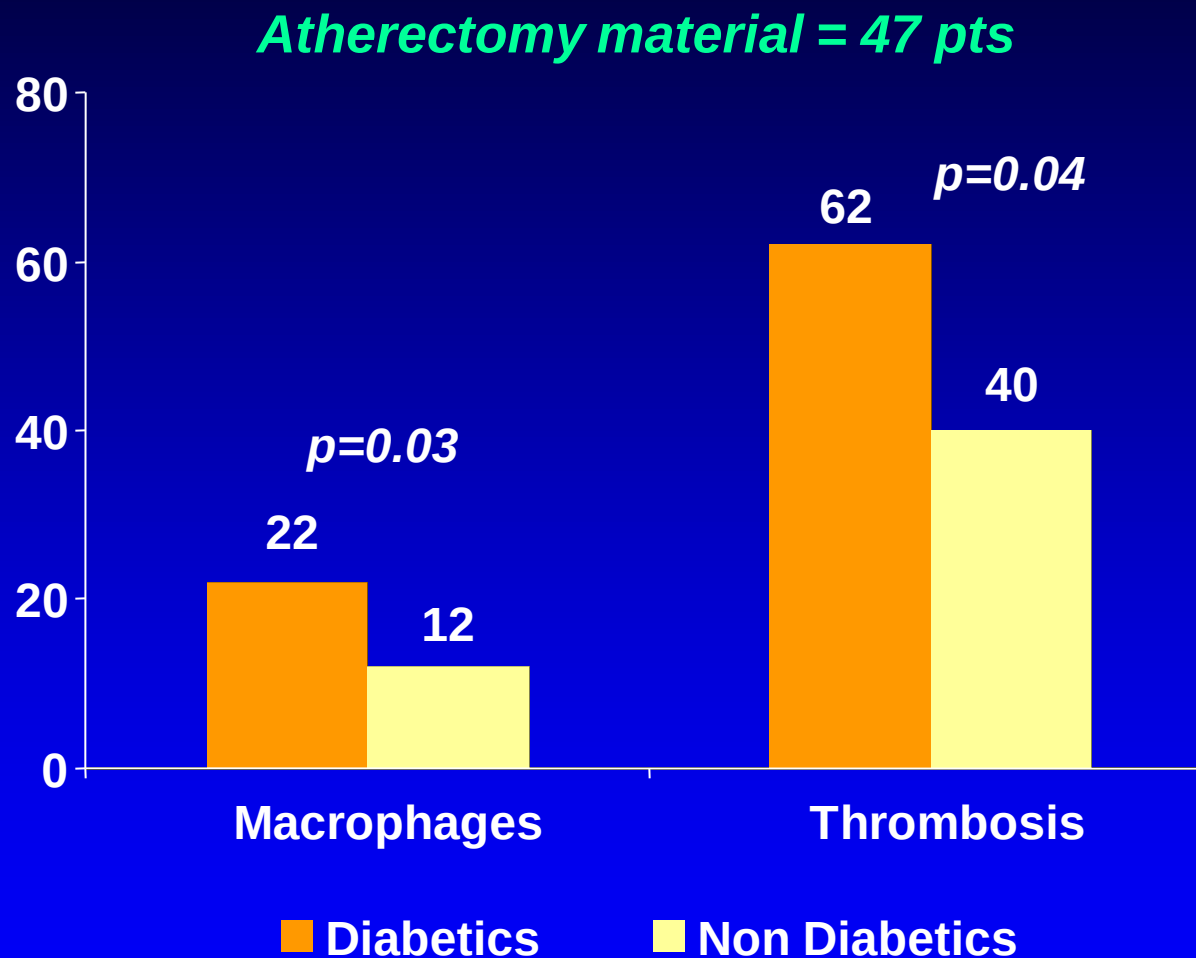
Type II-DM

Type I-DM

Non DM

Burke AP et al. Morphologic findings of coronary atherosclerotic plaques in diabetics: a postmortem study. *Arterioscler Thromb Vasc Biol.* 2004 Jul;24(7):1266-71. Epub 2004 May 13

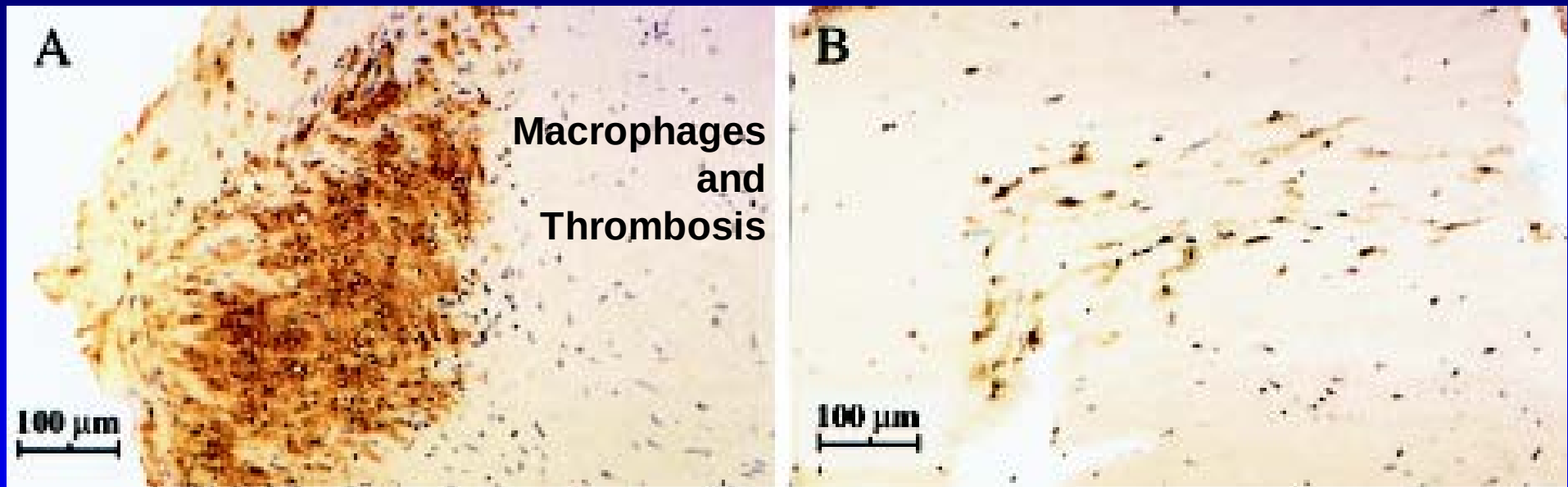
Plaque burden in Diabetics



Coronary composition and macrophage infiltration in atherectomy specimens from patients with diabetes mellitus. Moreno PR et al. Circ 2000; 102: 2180-4

Atherosclerotic Plaque composition in Diabetics

Endarterectomy rescued material = 47 pts.



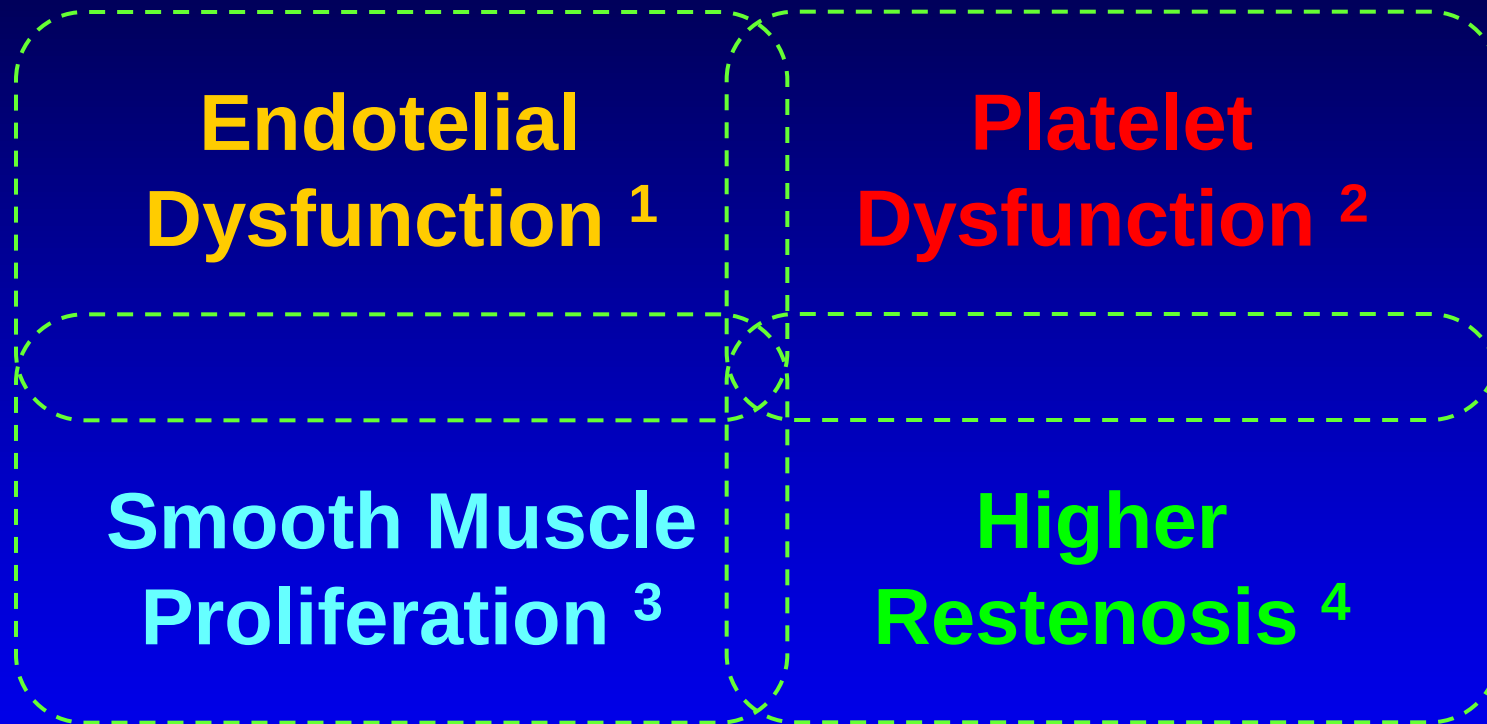
A. Diabetics

B. Non Diabetics

Coronary composition and macrophage infiltration in atherectomy specimens from patients with diabetes mellitus. Moreno PR et al. Circ 2000; 102: 2180-4

MH – D # 20 - 10-aug-12

DBT leads to a Prothrombotic State



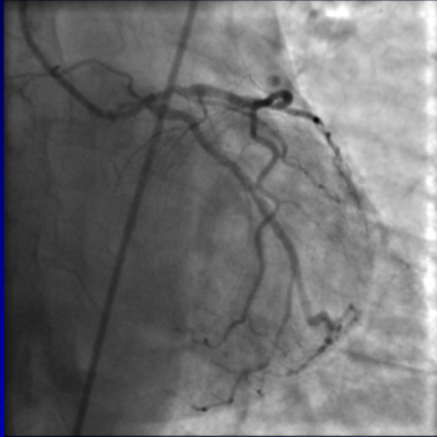
¹ De Vriese AS et al. *Br J pharmacol* 2000; 130; 963-74

² Angiolillo D et al. *Diabetes* 2005; 54: 2430-5

³ Suzuki LA et al. *Diabetes* 2001; 50: 851-60

⁴ Elezi S et al. *J Am Coll Cardiol* 1998; 32: 1866-73

Diabetics are pts with a more complex disease



- ❑ Smaller vessels
- ❑ More MVD
- ❑ Higher rate of calcified lesions
- ❑ Higher incidence of Type C lesions
- ❑ In-stent restenosis increased
- ❑ More comorbidities
(Hypertension,
Hyperlipidemias, CKD)

What we know about Diabetes...

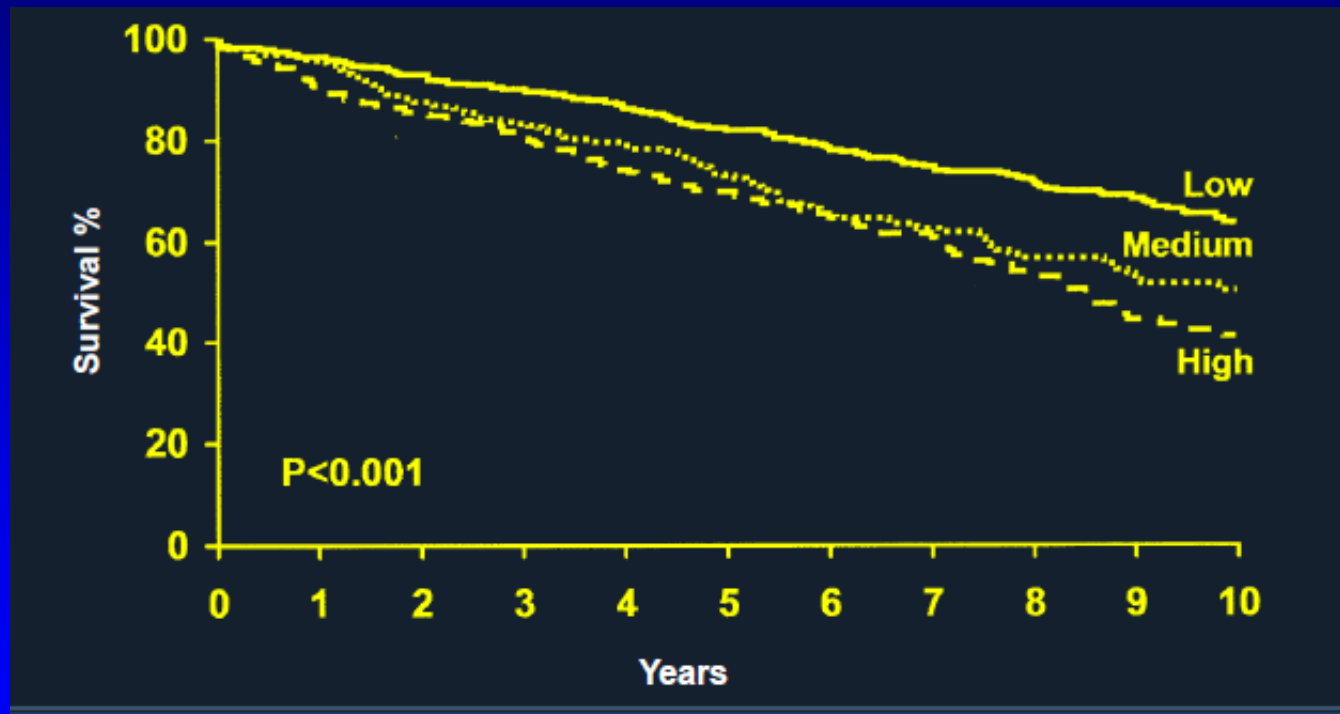
- **DBT $\equiv$ CAD (CAD = $\frac{2}{3}$ of DBT Deaths)**
- **Almost $\frac{1}{8}$ of adult pop has DBT or Impaired Fasting Glucose ($\approx \frac{1}{3}$ >60yrs)**
- **CAD in DBT is more severe and diffuse than in non-DBT**
- **49% of DBT has CAD in autopsy**
- **Case Fatality Rate higher in DBT**

**But a vast majority of this
patients are asymptomatic.**

Asymptomatic Pts: Mayo Observational Studies

SPECT Scanning

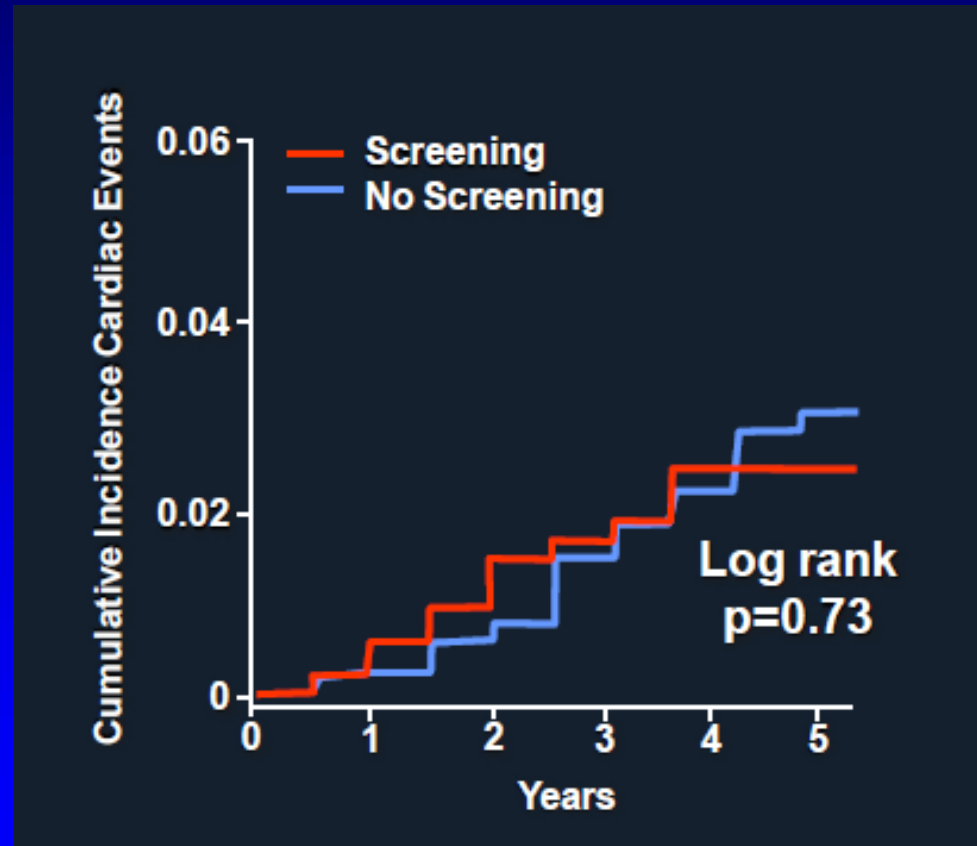
- 58% of the pts had an abnormal SPECT scan (826 of 1427)
- 18% High Risk Scan (*those with angiography 61% high risk CAD*)



Rajagopalan N et al. Identifying high-risk asymptomatic diabetic patients who are candidates for screening stress single-photon emission computed tomography imaging. J Am Coll Cardiol 2005 Jan 4; 45(1): 43-9.

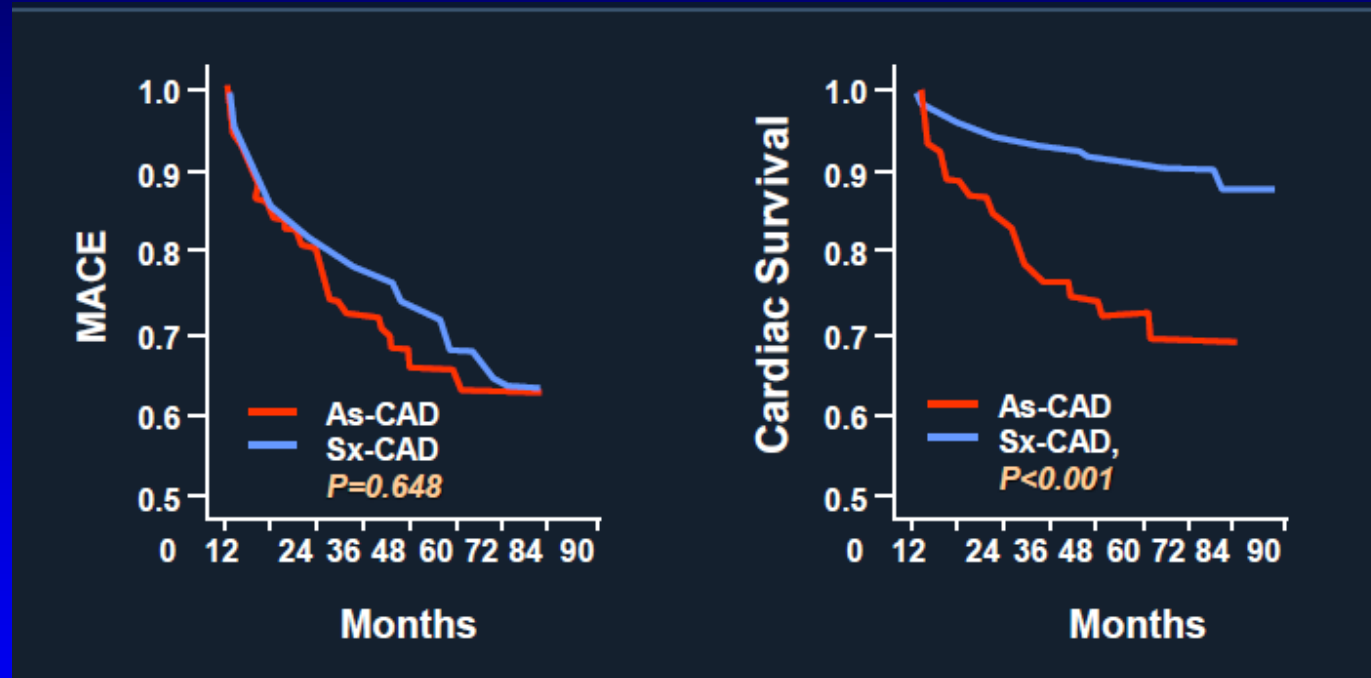
Asymptomatic Diabetic Pts: Routine Screening should be a “must”?

DIAD Study (1123 pts, 4.8 yrs Follow Up)



CV Risks in Symptomatic vs Asymptomatic diabetic pts

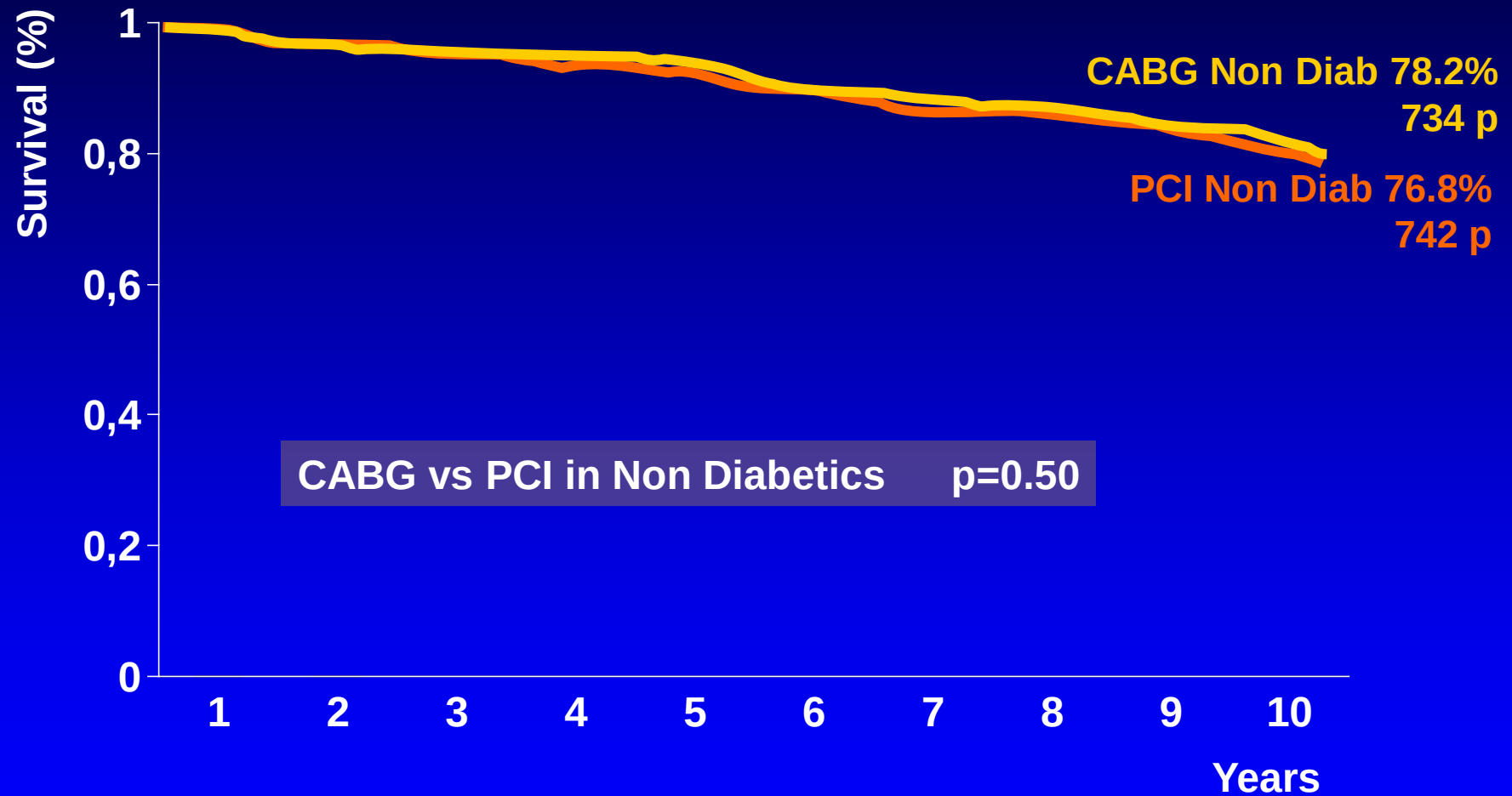
MACE and Cardiac Risks in Symp vs Asymp patients
300 pts undergoing angiography; symptoms assessed at Cath Lab



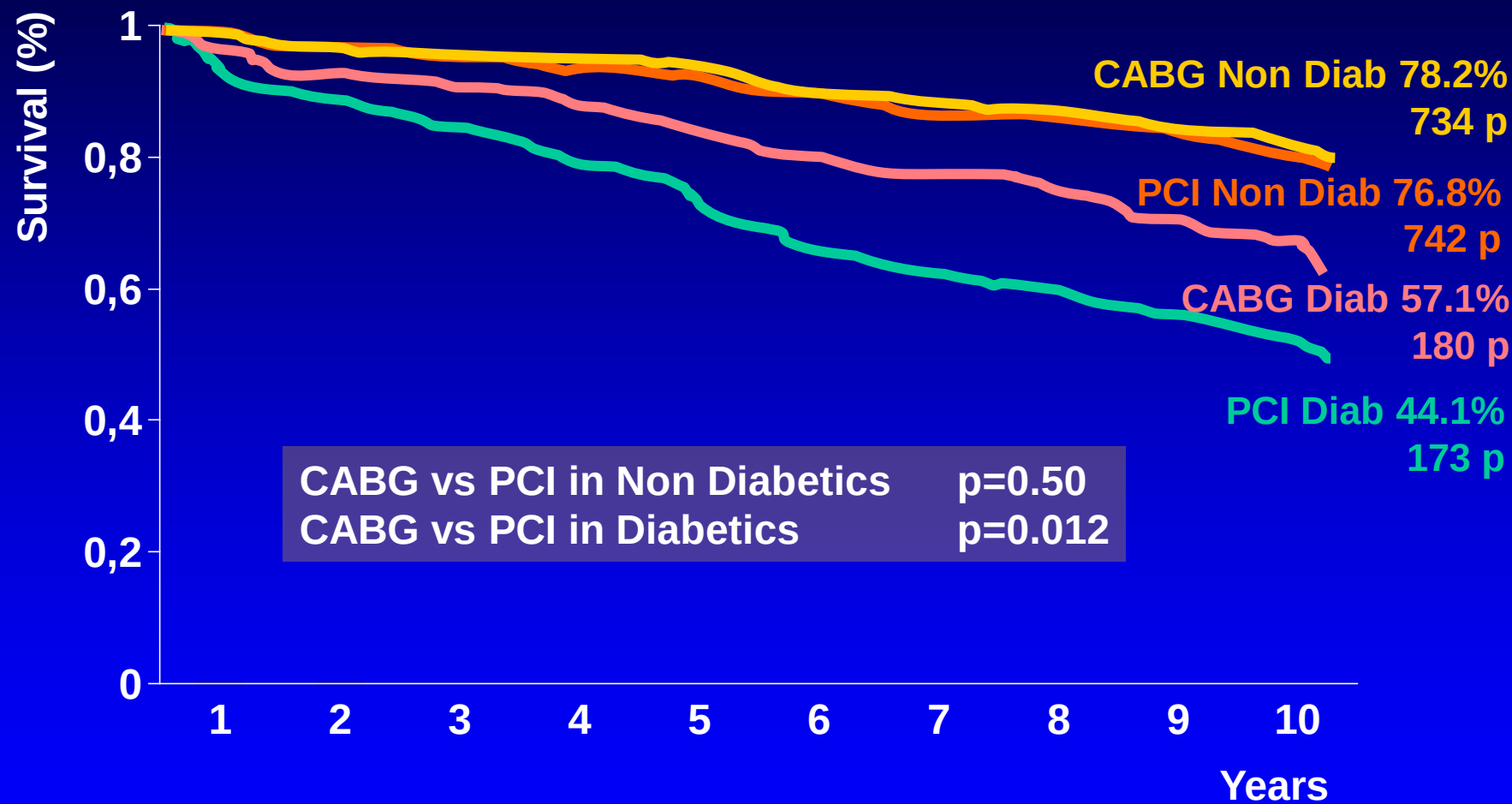
3-fold higher rate of revascularization among symptomatic pts

**Our first approach was
shakespearean: to revascularize or
not to revascularize**

BARI Diabetics vs Non-Diabetics: 10-yr Survival

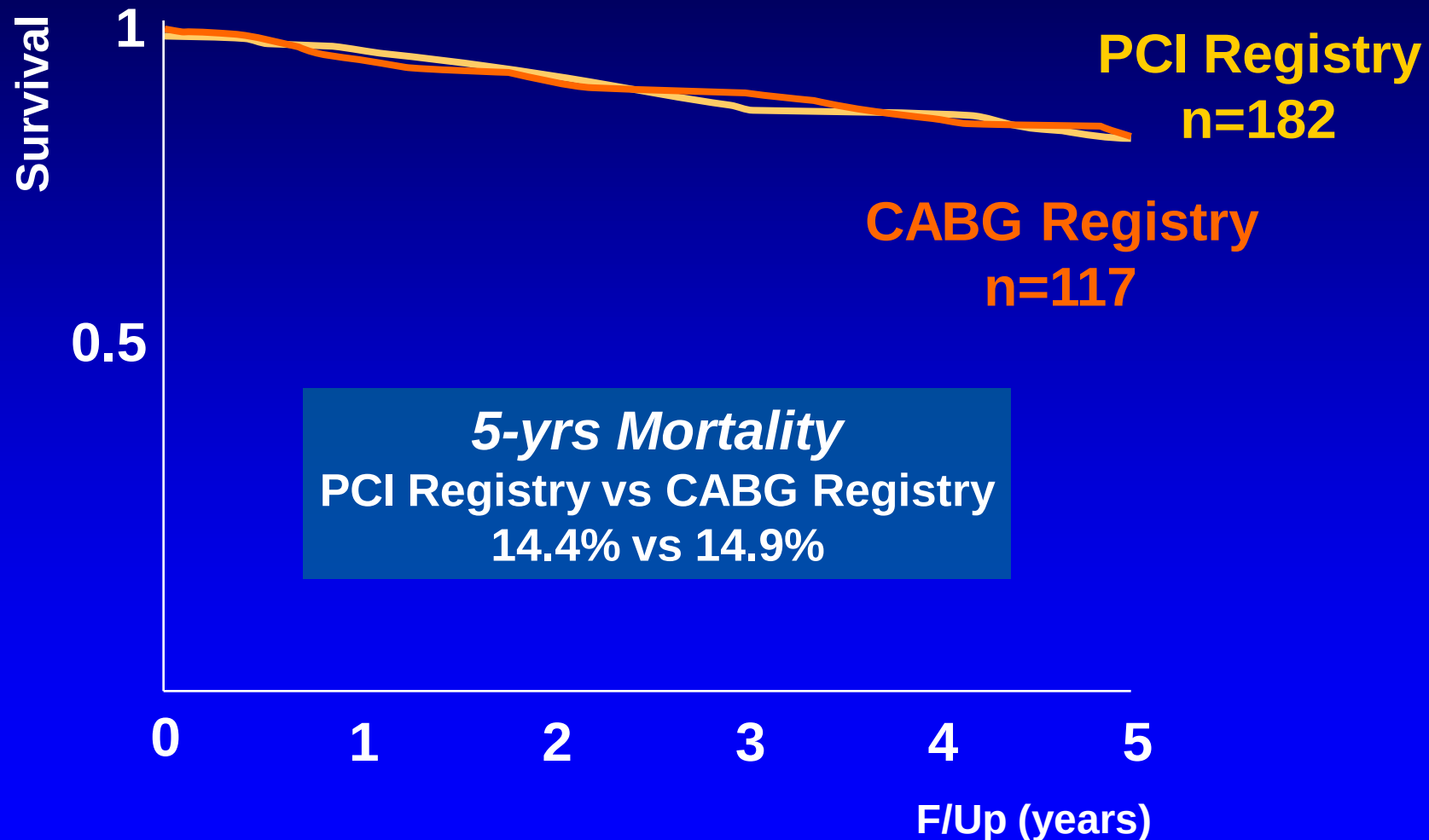


BARI Diabetics vs Non-Diabetics: 10-yr Survival



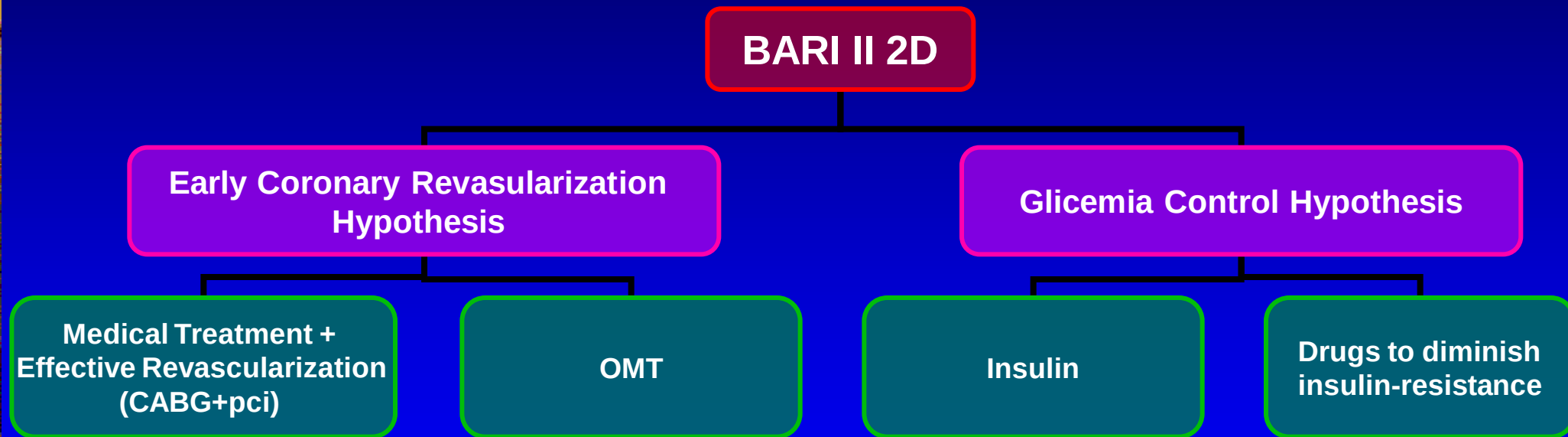
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BARI Registry Diabetics vs Non-Diabetics: 5-yrs Survival



2800 pts

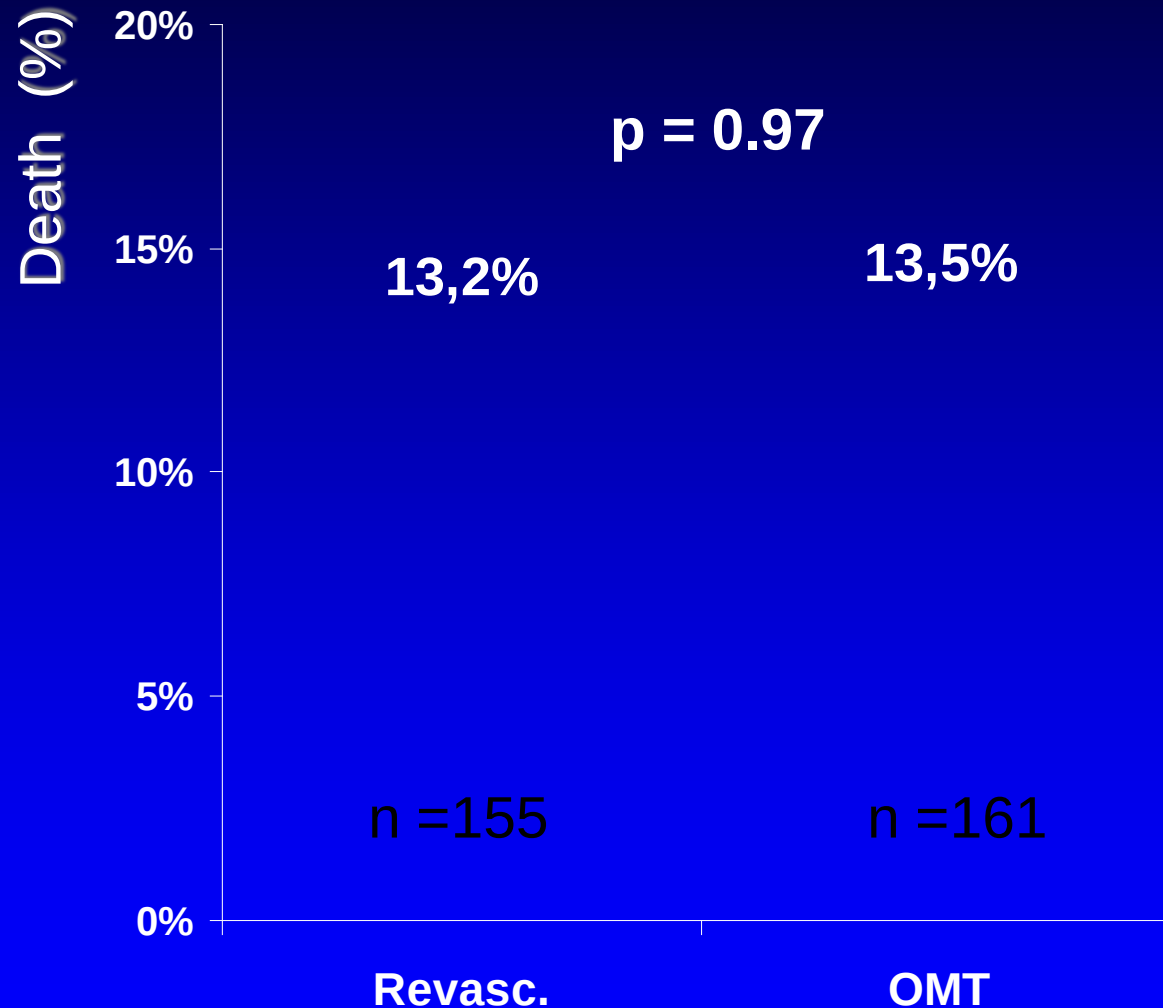
Stable CAD candidates for revasc + Type II DBT



Composite Endpoint = 5-yr Mortality

Burgeoning Dilemmas in the Management of Diabetes and Cardiovascular Disease. BARI 2D Trial. Sobel BE et al. Circ 2003; 107: 636-42

BARI 2D Trial: Primary Endpoint

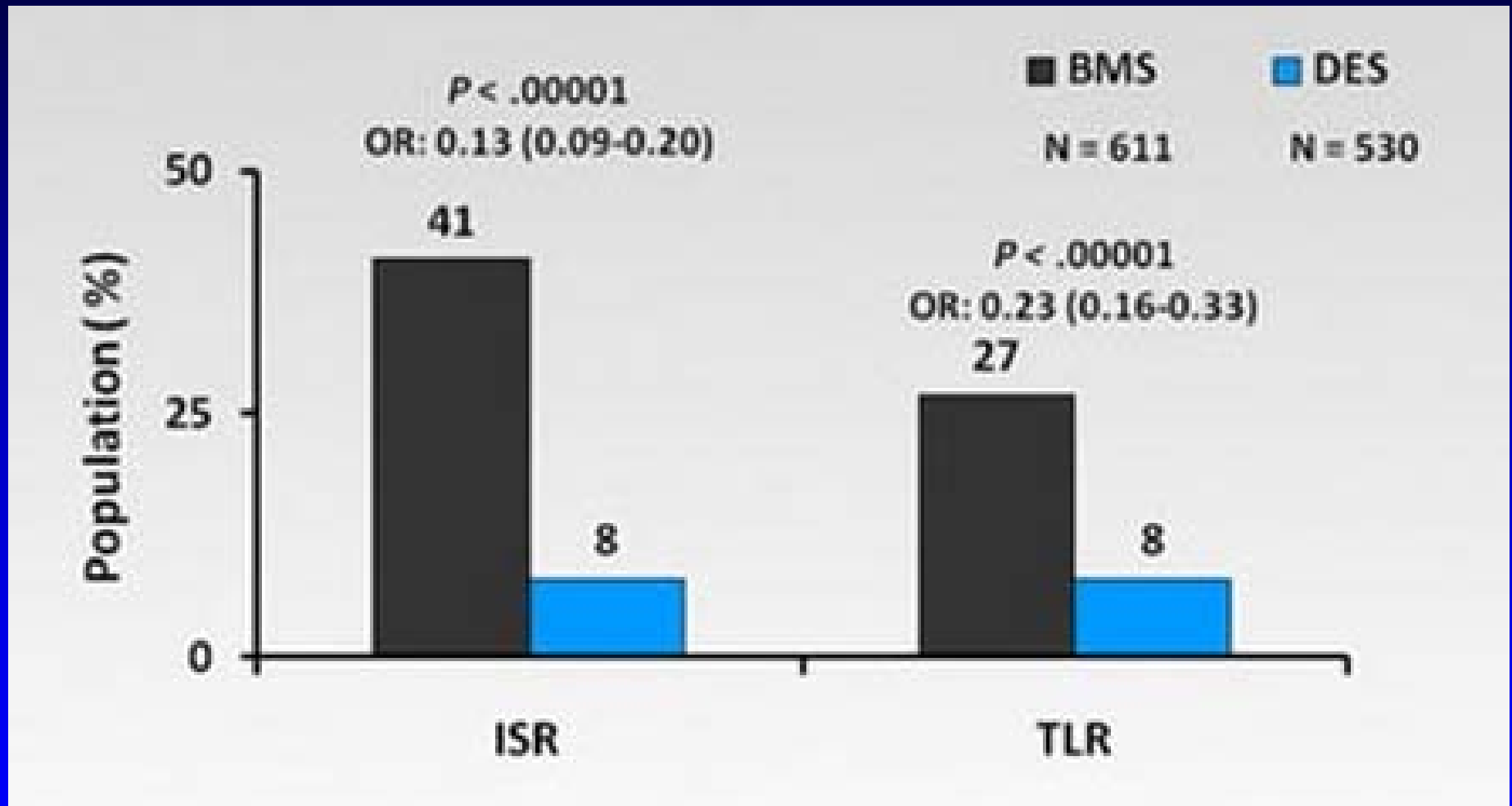


- The 5-year death rate for the group receiving revascularization plus optimal medical therapy was 13.2% vs. 13.5% in the group receiving optimal medical therapy alone.
- The difference between the two treatment groups did not reach statistical significance.

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**Then we tried to answer whether DES
were more convenient than BMS for
this patients subgroup.**

Meta-analysis BMS vs 1st Generation DES in Diabetics



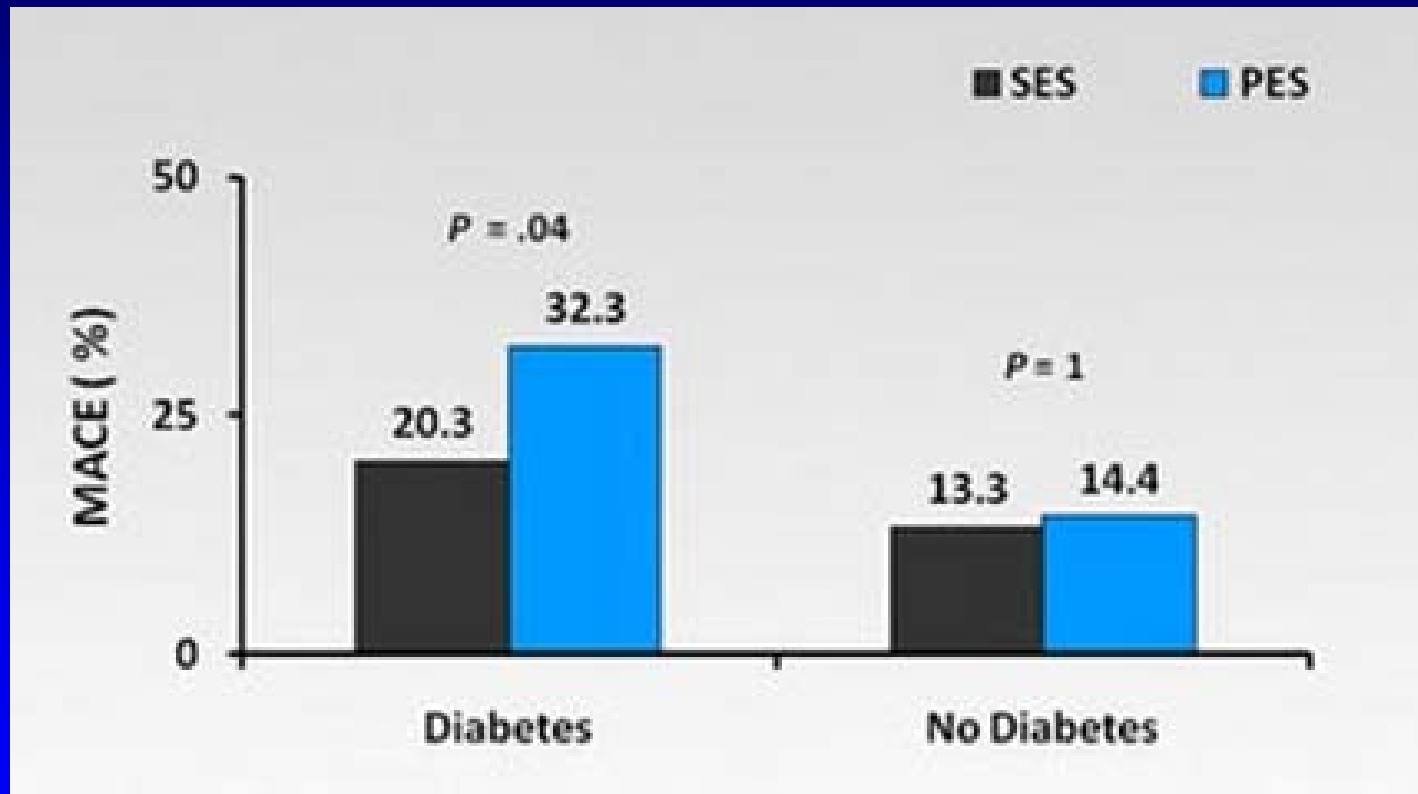
Patti G et al. Meta-Analysis Comparison (Nine Trials) of Outcomes With Drug-Eluting Stents Versus Bare Metal Stents in Patients With Diabetes Mellitus. *Am J Cardiol* 2008;102:1328 –1334

**But... all the DES can reach the
same goals?**

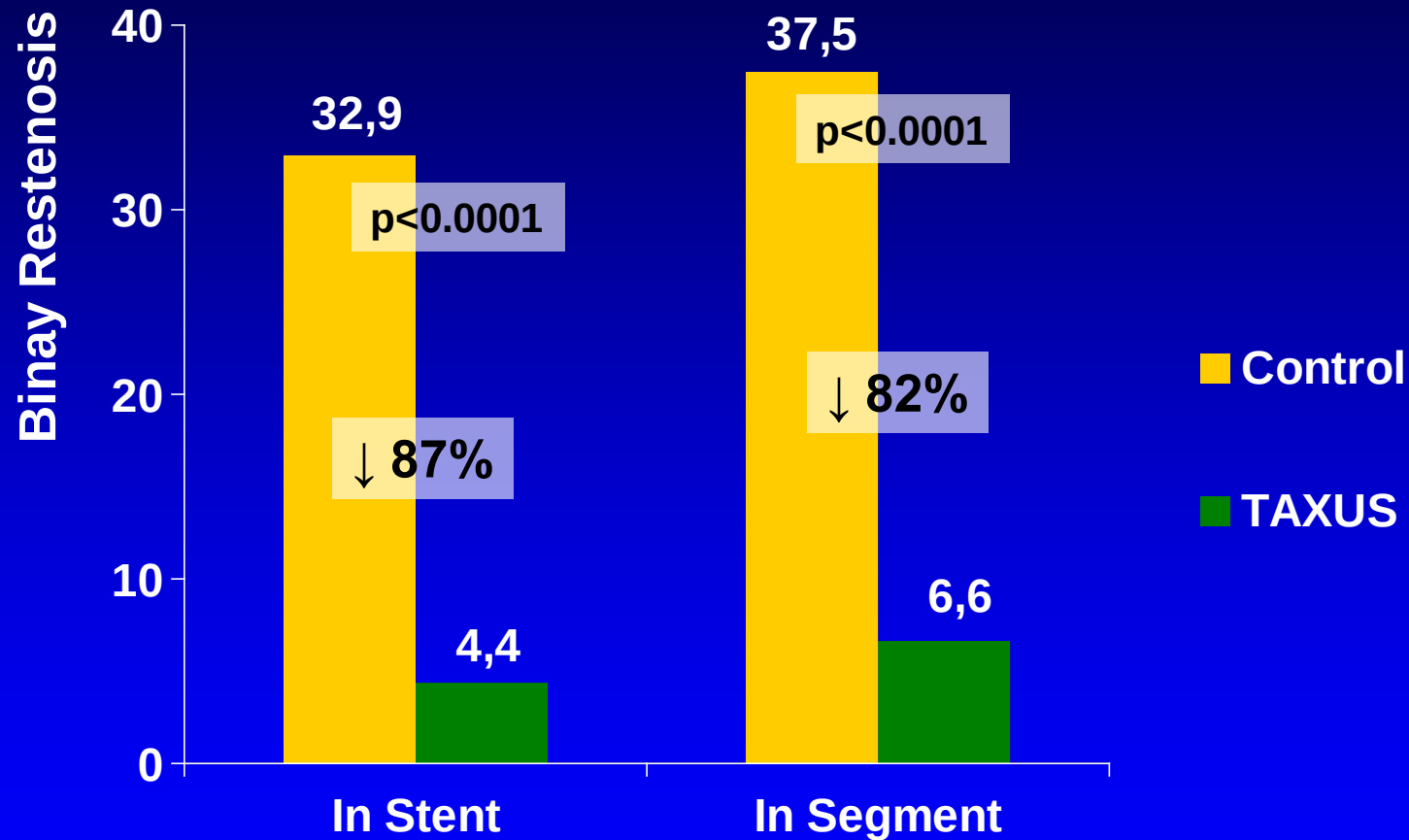
Diabetics have a higher global risk

SIRTAX LATE: MACE at 5 yrs

PCI w/DES: 201 pts w/DBT and 811 without DBT

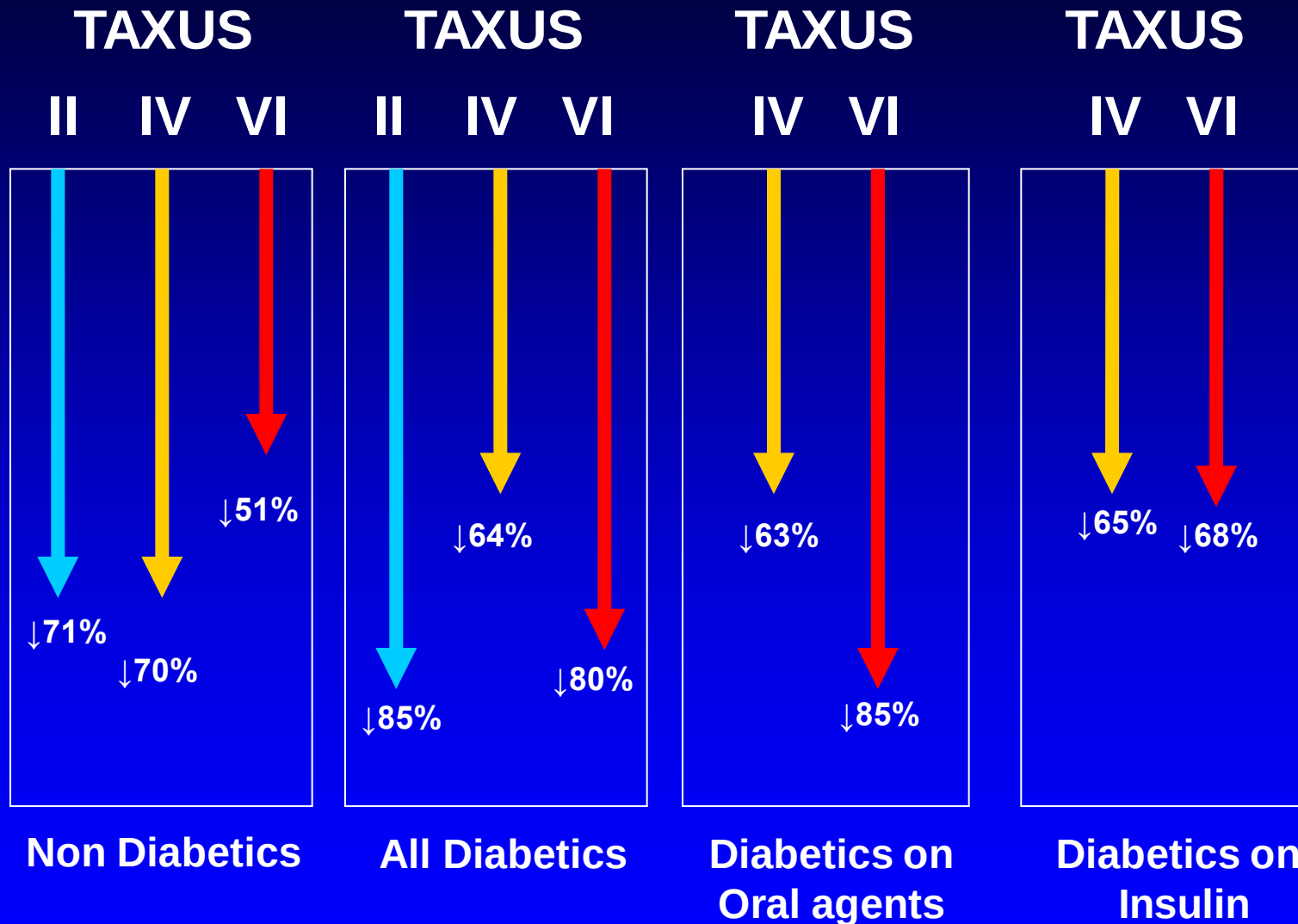


TAXUS Trials- Restenosis in NIDDM



TLR Reduction across TAXUS Trials

TCT2011



www.solacii.org

Reality Trial

Clinical events at 8 mo

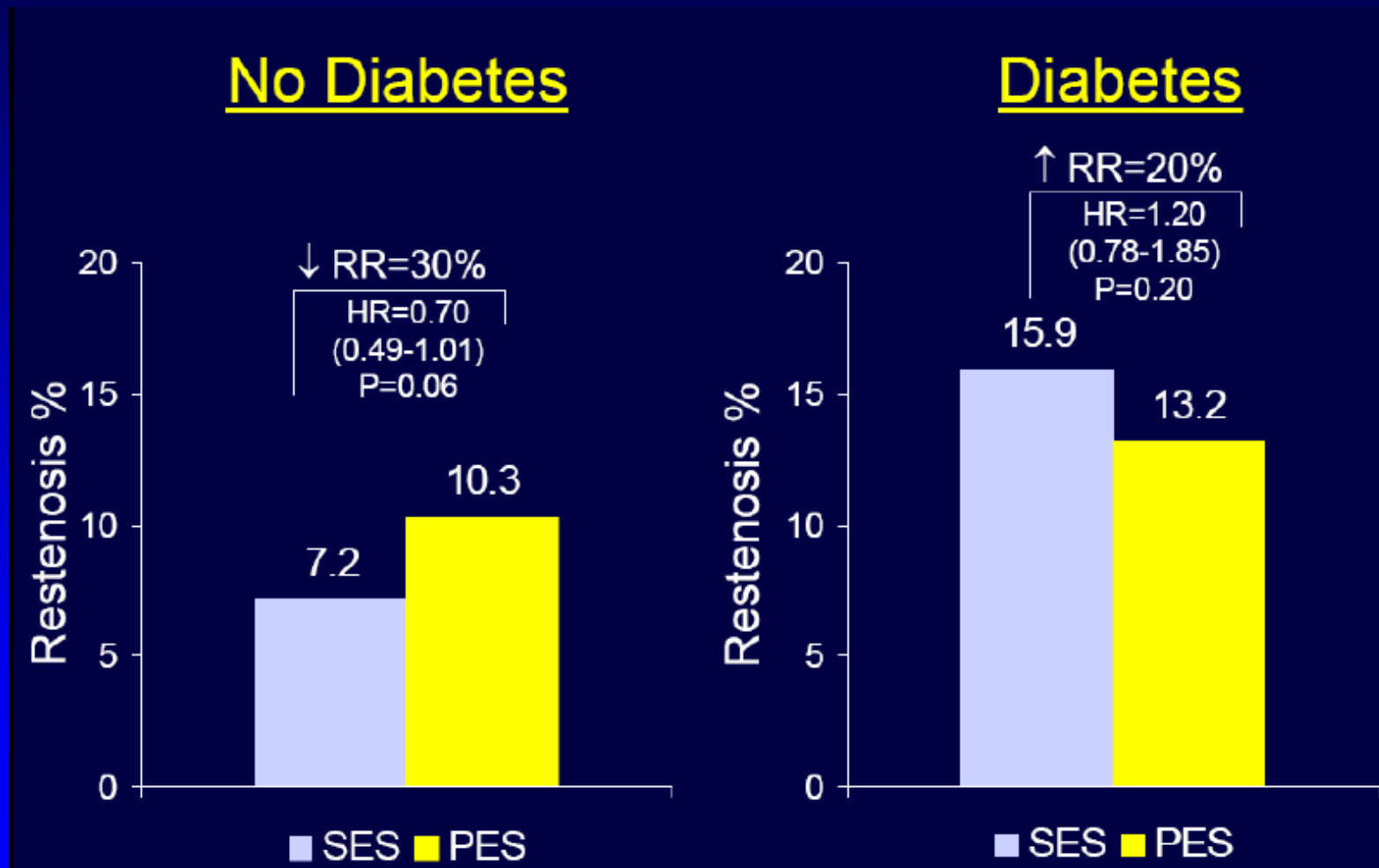
REALITY

	CYPHER® (684 patients; 970 lesions)	TAXUS™ (669 patients; 941 lesions)	P-Value
MACE (%) (n)	9.2% (63)	10.6% (71)	0.41
Death (%) (n)	1.8% (12)	1.2% (8)	0.50
Cardiac Death	1.0% (7)	0.9% (6)	0.99
MI (all) (%) (n)	4.8% (33)	5.5% (37)	0.62
Q-Wave	0.15% (1)	0.90% (6)	0.067
Non Q-Wave	4.7% (32)	4.6% (31)	0.99
TLR (all) (%) (n)	5.0% (34)	5.4% (36)	0.81
TVR (non-TL)	1.6% (11)	1.2% (8)	0.65
TVF (%) (n)	10.4% (71)	11.5% (77)	0.54

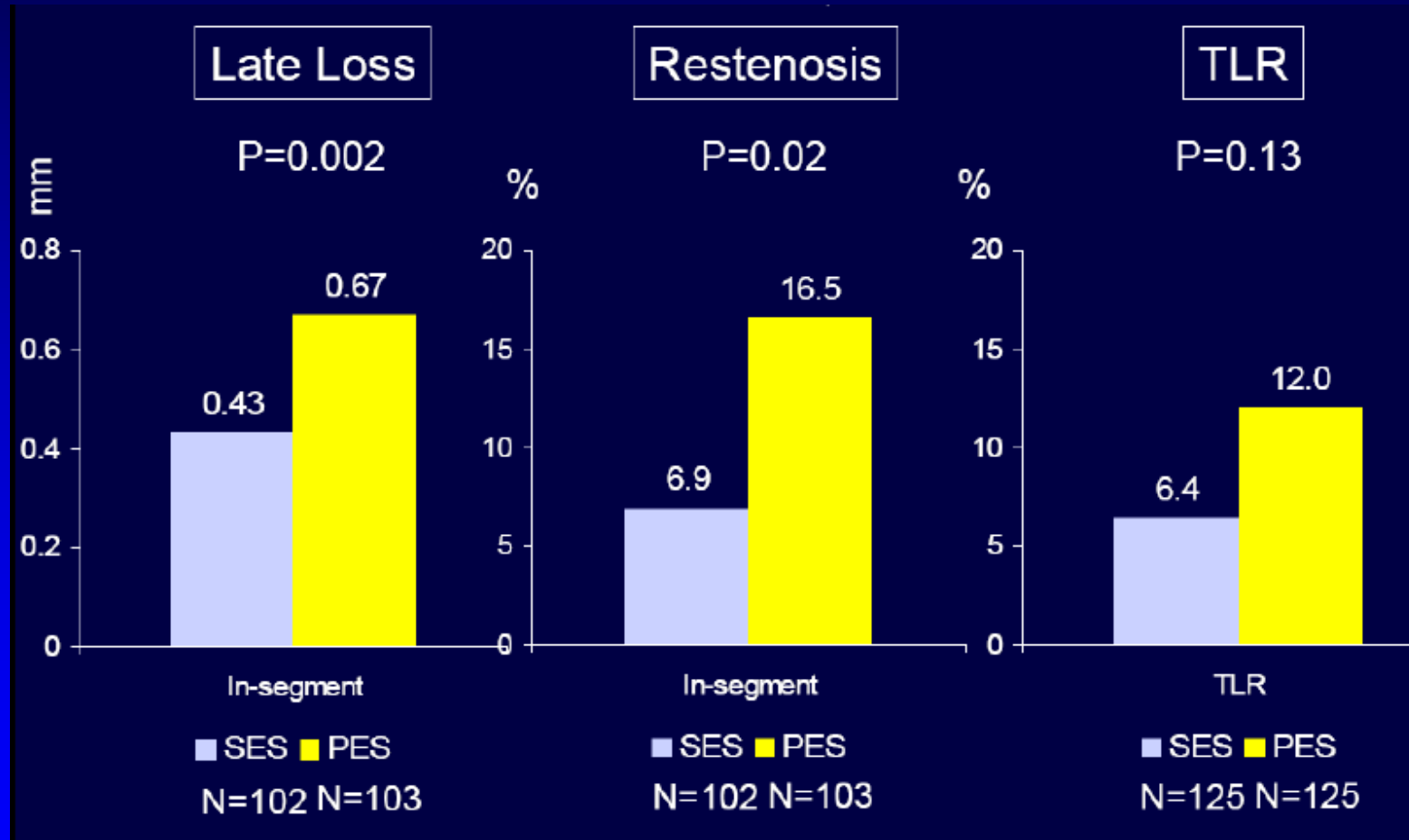
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Reality Trial: Diabetics Subgroup

Clinical events at 8 mo



ISAR-DIABETES: Randomized Comparison of CYPHER vs TAXUS in Diabetics



**Nowadays we need to answer if ,
regarding diabetics, second or new-
generation DES are an advance
over first-generation stents**

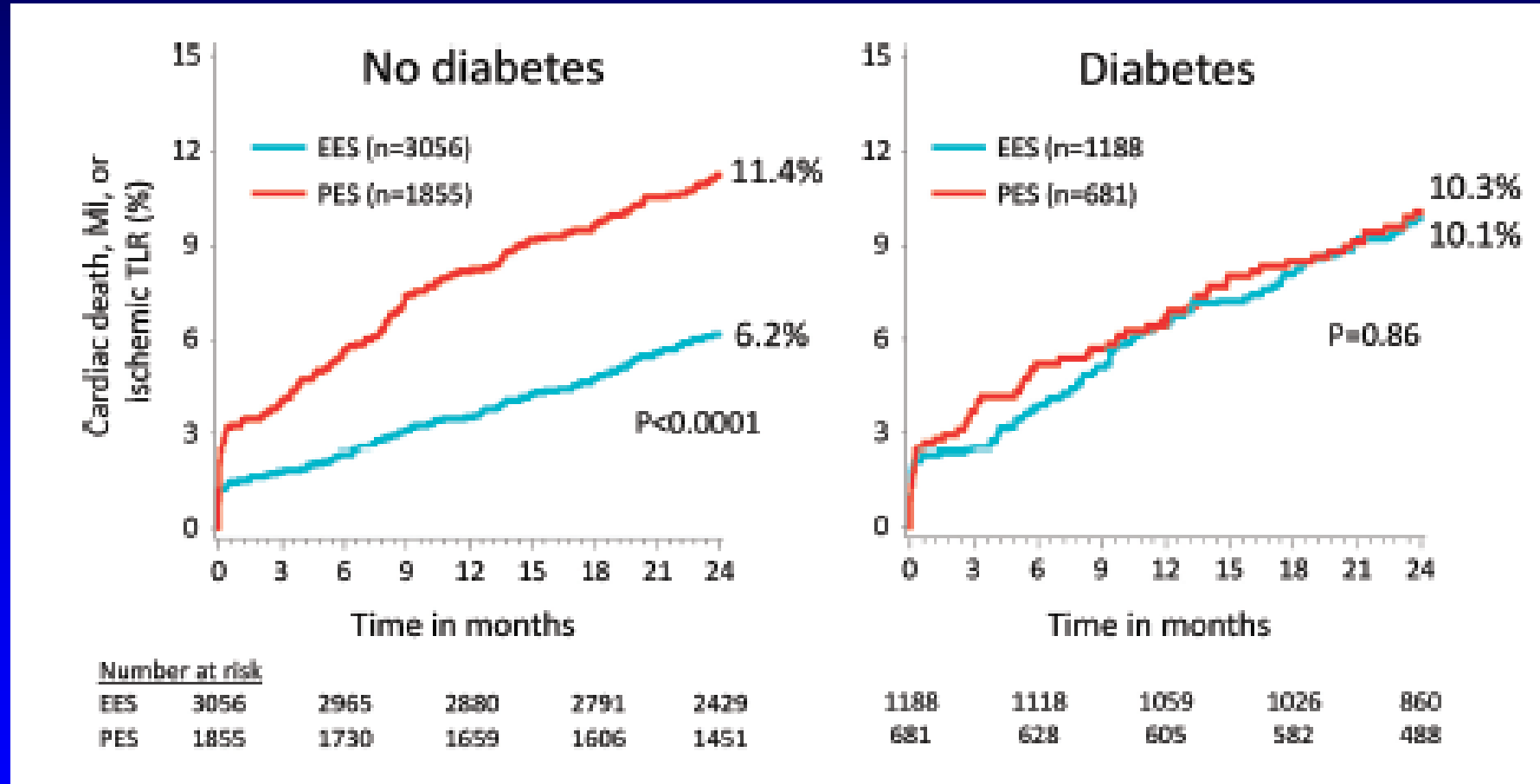
EES vs PES in Diabetics

Prospective, Randomized Clinical Evaluation of the Xience V Everolimus Eluting Coronary Stent System in the Treatment of Patients With De Novo Native Coronary Artery Lesions (**SPRIT**) Trial and a Trial of Everolimus-Eluting Stents and Paclitaxel-Eluting Stents for Coronary Revascularization in Daily Practice (**COMPARE**)

	SPRIT II	SPRIT III	SPRIT IV	COMPARE
Geography	Europe, India, and New Zealand	US	US	Netherlands
Sites, n	28	65	66	1
ITT patients, n	300	1002	3687	1800
Patients with diabetes mellitus, n (%)*	69/299 (23.1)	290/999 (29.0)	1195/3683 (32.4)	325/1799 (18.1)
Randomization, EES:PES	3:1	2:1	2:1	1:1
PES platform	Express	Express	Express	Liberté
Primary end point(s)	In-stent LL at 6 mo	In-segment LL at 8 mo and TVF at 9 mo	TLF at 12 mo	MACE at 12 mo
Recruitment period	July 2005–November 2005	June 2005–March 2006	August 2006–July 2008	February 2007–September 2008
RVD, mm	2.5–4.25	2.5–3.75	2.5–3.75	No prespecified criteria
Lesion length, mm	≤28	≤28	≤28	No limit
Maximum lesions/patient, n	2	2	3	No limit
Major patient and lesion exclusion criteria†	Complex or high risk‡	Complex or high risk‡	Complex or high risk‡	None
Routine angiographic follow-up				
Timing, mo	6 and 24	8	None	None
Intended, n	300 and 152	564	0	0
Completed, n	275 and 115	436	0	0

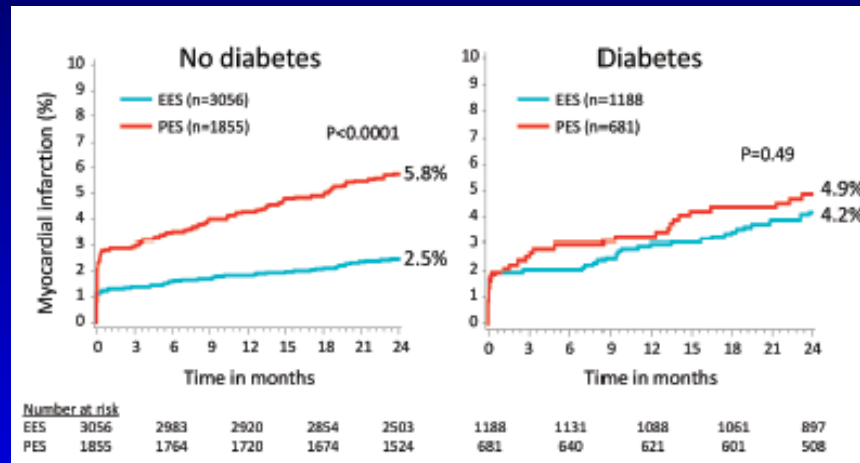
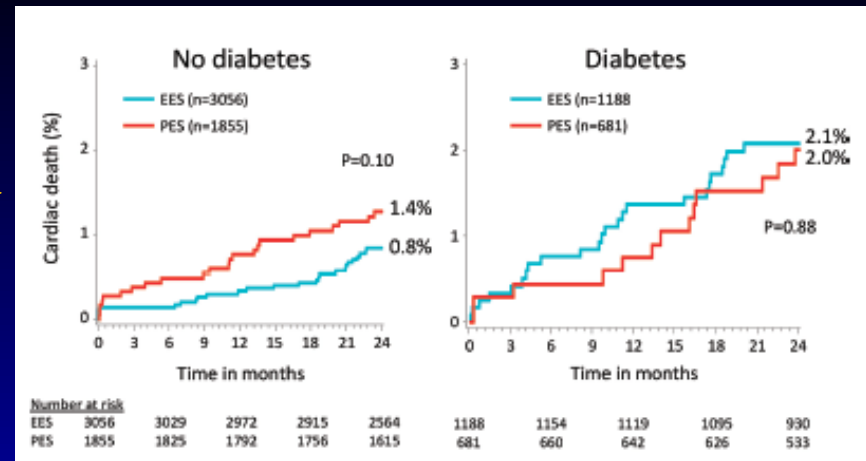
Stone G et al. Differential Clinical Responses to Everolimus-Eluting and Paclitaxel-Eluting Coronary Stents in Patients With and Without Diabetes Mellitus. *Circulation*. 2011; 124: 893-900

Time-to-event curves for major adverse cardiac events (cardiac death, myocardial infarction or ischemia-driven target lesion revascularization)



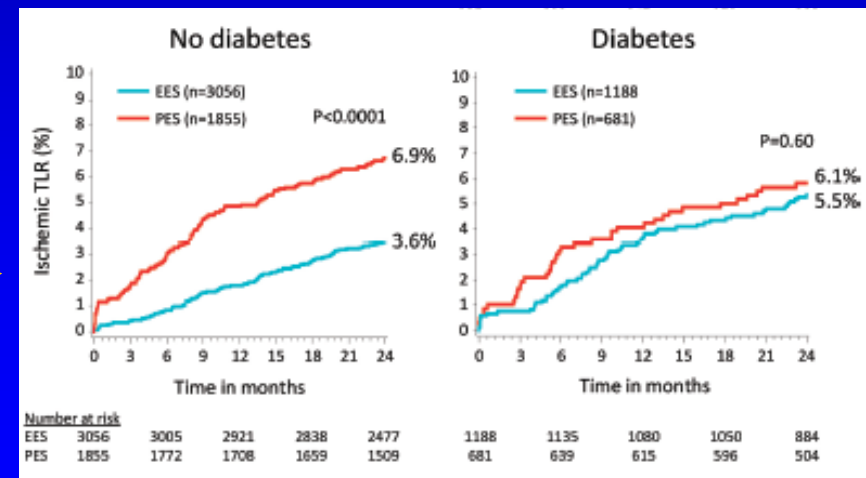
Stone G et al. Differential Clinical Responses to Everolimus-Eluting and Paclitaxel-Eluting Coronary Stents in Patients With and Without Diabetes Mellitus. *Circulation*. 2011; 124: 893-900

Cardiac Death ►



◄ Myocardial Infarction

TLR ►

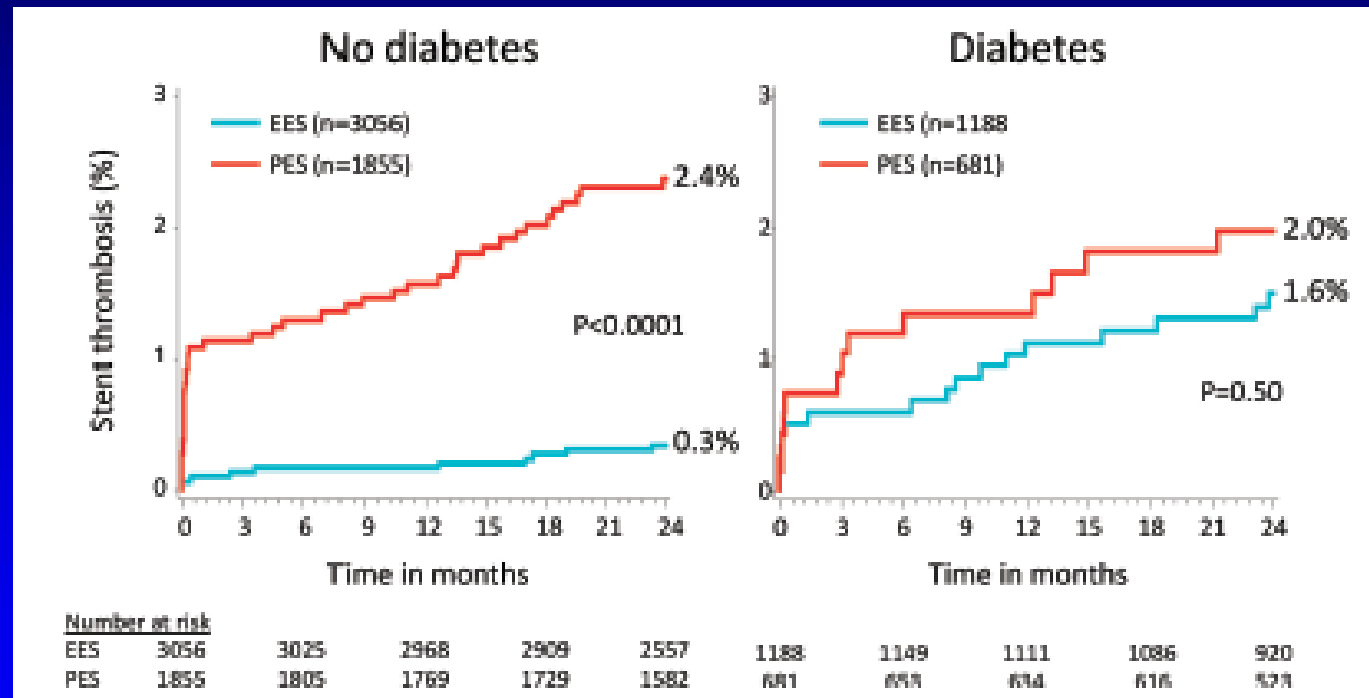


Stone G et al. Circulation. 2011; 124: 893-900

MH – D # 53 - 10-aug-12

Stent Thrombosis

according to the Academic Research Consortium definition of definite or probable

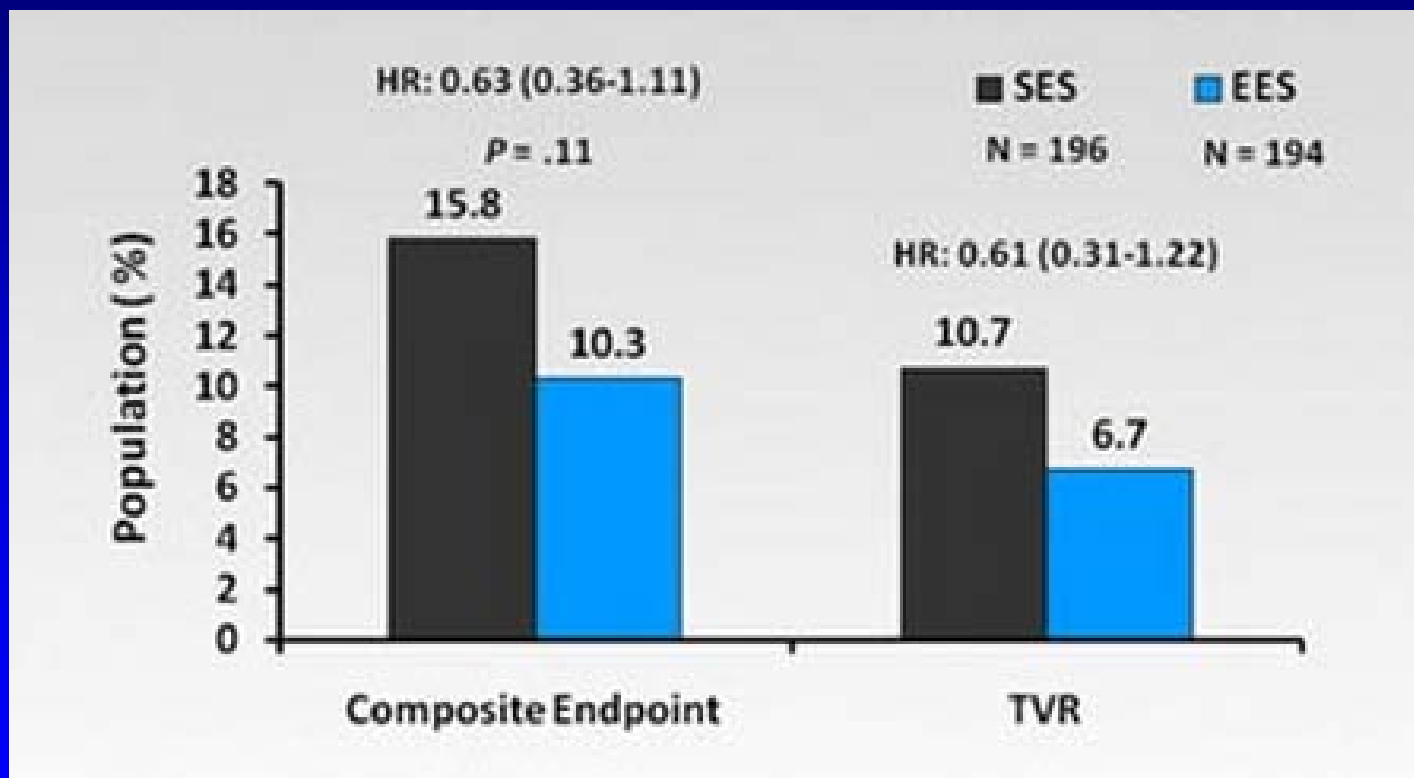


Stone G et al. Differential Clinical Responses to Everolimus-Eluting and Paclitaxel-Eluting Coronary Stents in Patients With and Without Diabetes Mellitus. *Circulation*. 2011; 124: 893-900

EES vs SES in Diabetics

SORT OUT IV: Diabetes Subgroup Analysis

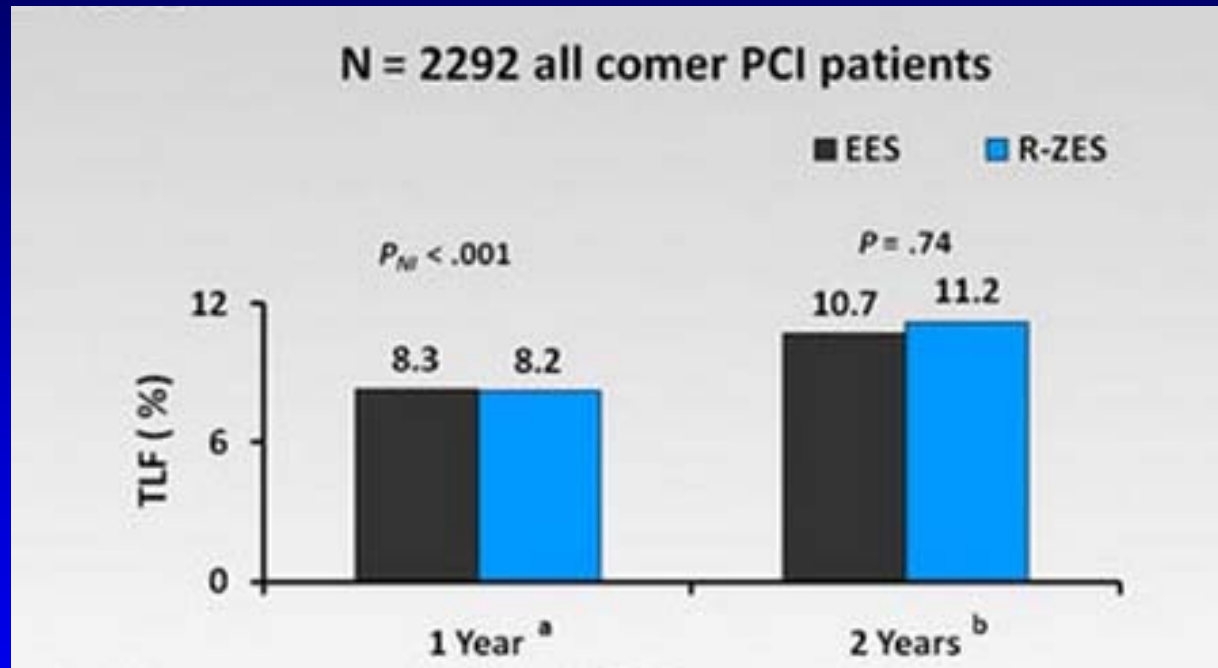
Randomized trial of DES in all-comer PCI pts



Cypher Select® vs Xience V®

EES vs ZES in Diabetics

RESOLUTE All Comers Trial TLR in Xience V vs Resolute

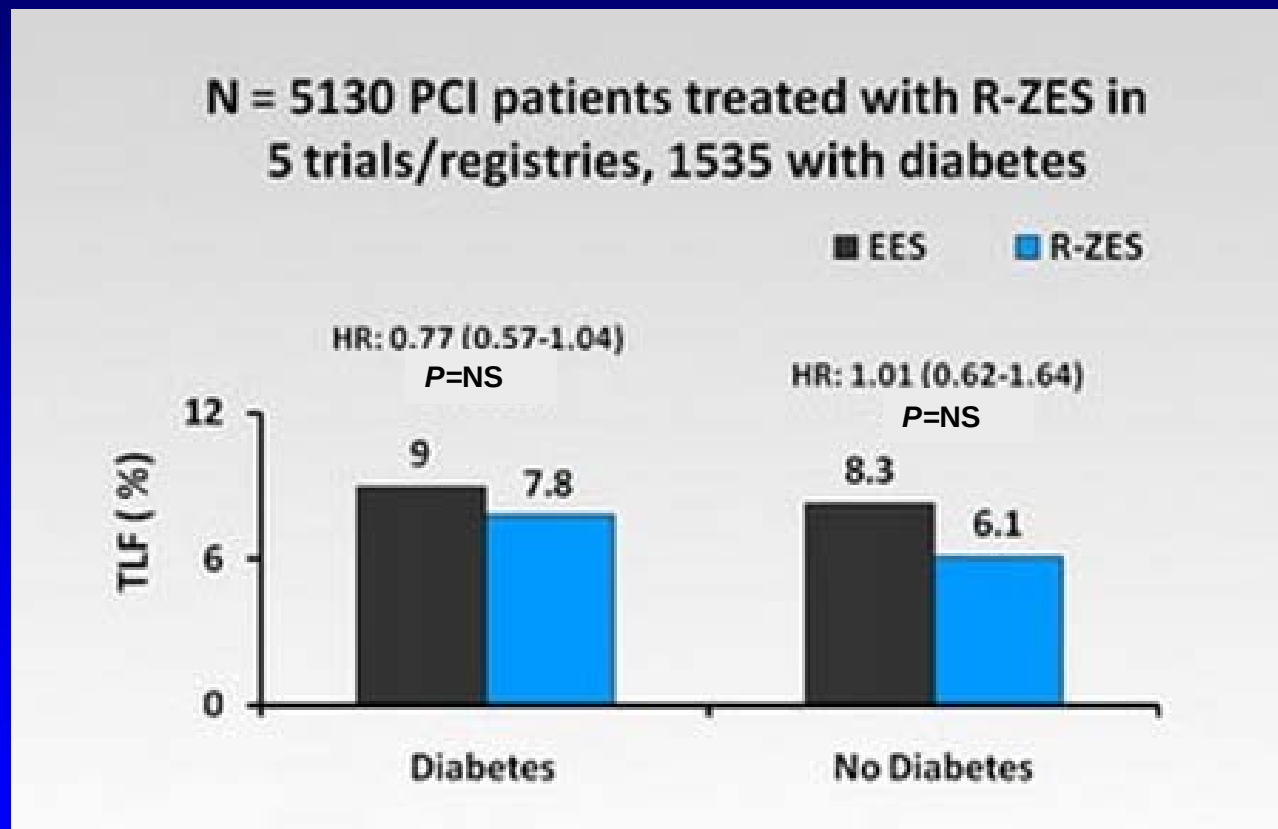


^a Serruys P et al. Comparison of zotarolimus-eluting and everolimus-eluting coronary stents. *N Engl J Med* 2010 Jul 8;363(2):136-46. Epub 2010 Jun 16.

^b Silber S. Unrestricted randomised use of two new generation drug-eluting coronary stents: 2-year patient-related versus stent-related outcomes from the RESOLUTE All Comers trial. *Lancet* 2011 Apr 9;377(9773):1241-7. Epub 2011 Apr 1.

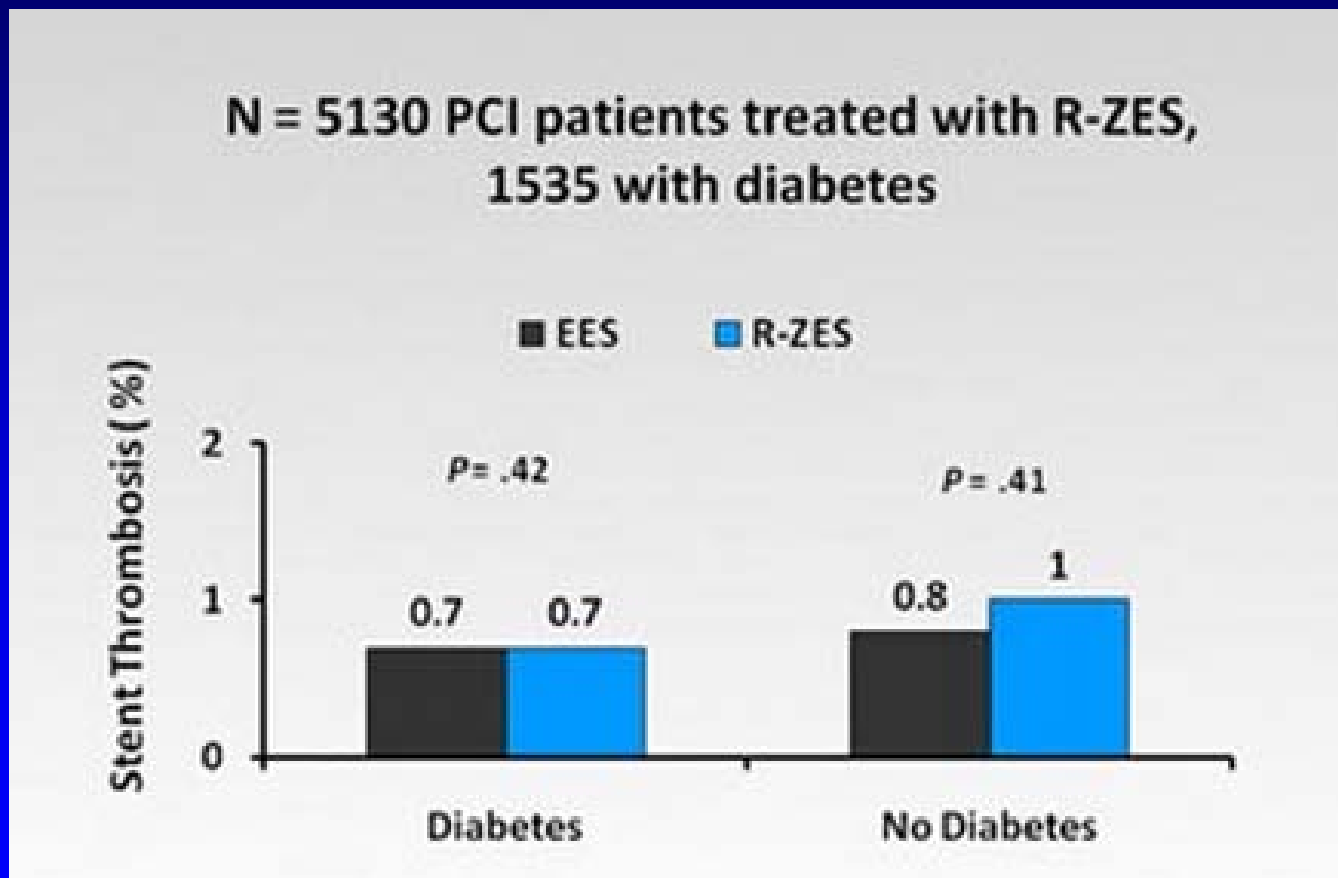
EES vs ZES in Diabetics

Pooled Resolute Trials: TLR @1 year



EES vs ZES in Diabetics

Pooled Resolute Trials:
Definite/Probable Stent Thrombosis @1 year



TUXEDO-India

Diabetic RCT Study Flow

1,830 Diabetic Mellitus patients undergoing PCI
enrolled up to 50 clinical sites in India

TAXUS Element (N=915)

Xience Prime (N=915)

30-Day f/u

180-Day f/u

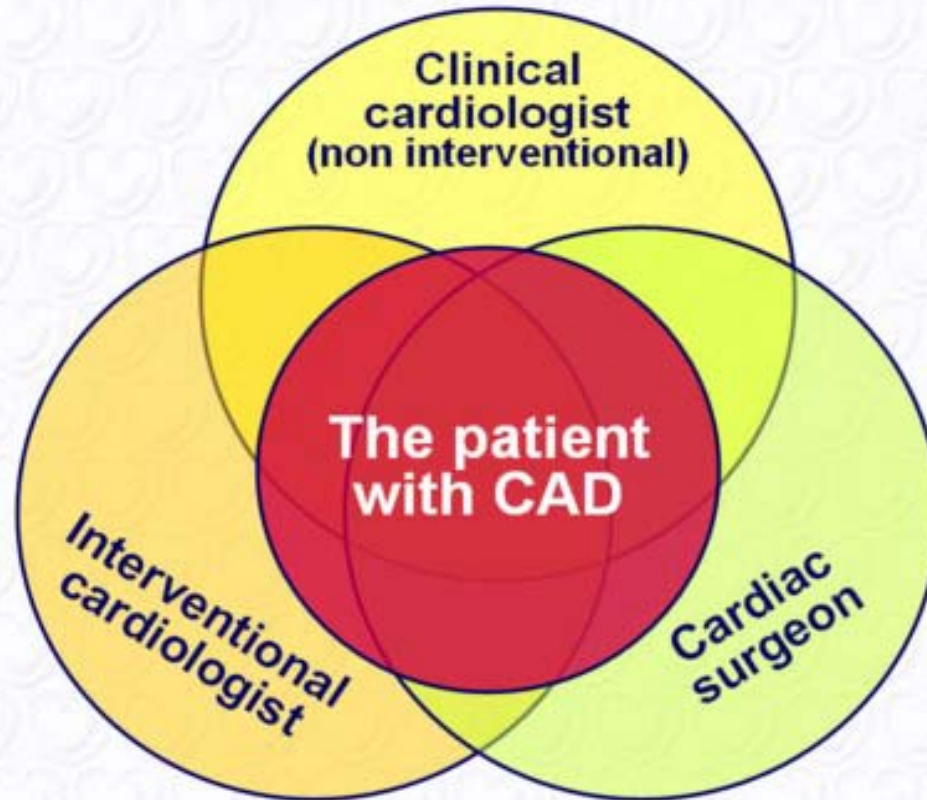
12-Month f/u

24-Month f/u

TUXEDO-India : RCT Design

- ◆ **OBJECTIVE:** Compare the safety and performance of the TAXUS Element™ against the Xience Prime™ in medically treated diabetic patients.
- ◆ **DESIGN:** A Prospective, Single Blind, Multi-center, Randomized Trial
- ◆ **PRIMARY ENDPOINT:** composite efficacy and safety endpoint of target vessel failure (TVF) rate at 12 months post-index procedure:

The Heart Team



**Task Force composition = 8 clinical cardiologists (non interventional)
+ 9 interventional cardiologists + 8 cardiac surgeons**

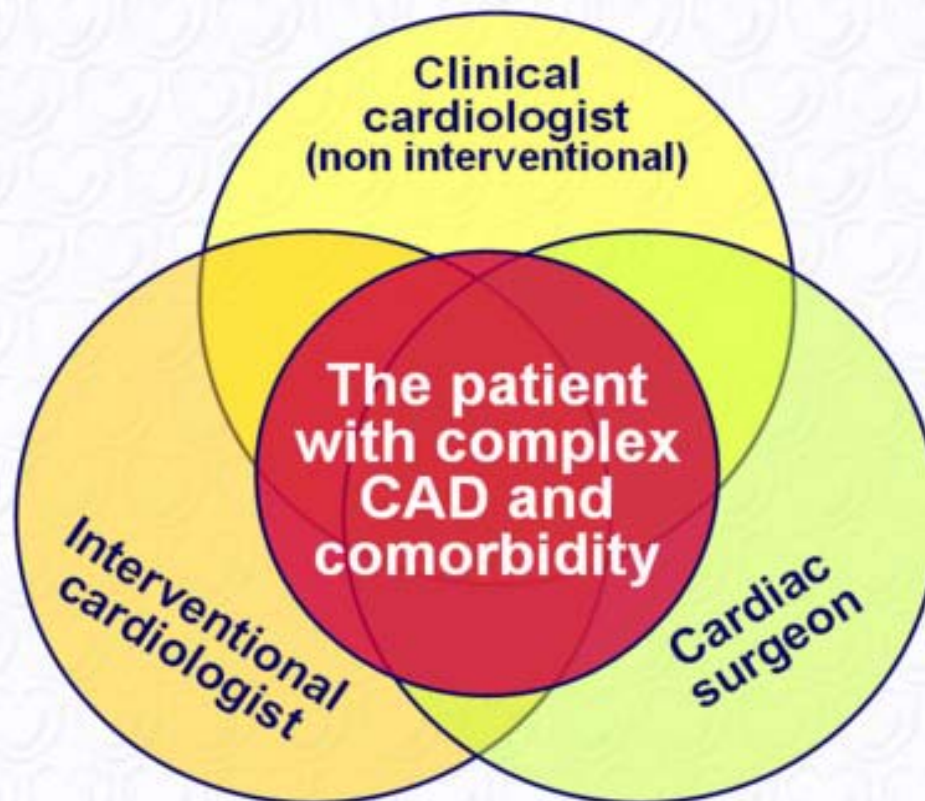
European Heart Journal (2010) 31, 2501-2555
European Journal of Cardio-thoracic Surgery (2010) 38, S1-S52

www.escardio.org/guidelines

Joint 2010 ESC - EACTS Guidelines
on Myocardial Revascularisation



The Expanded Heart Team



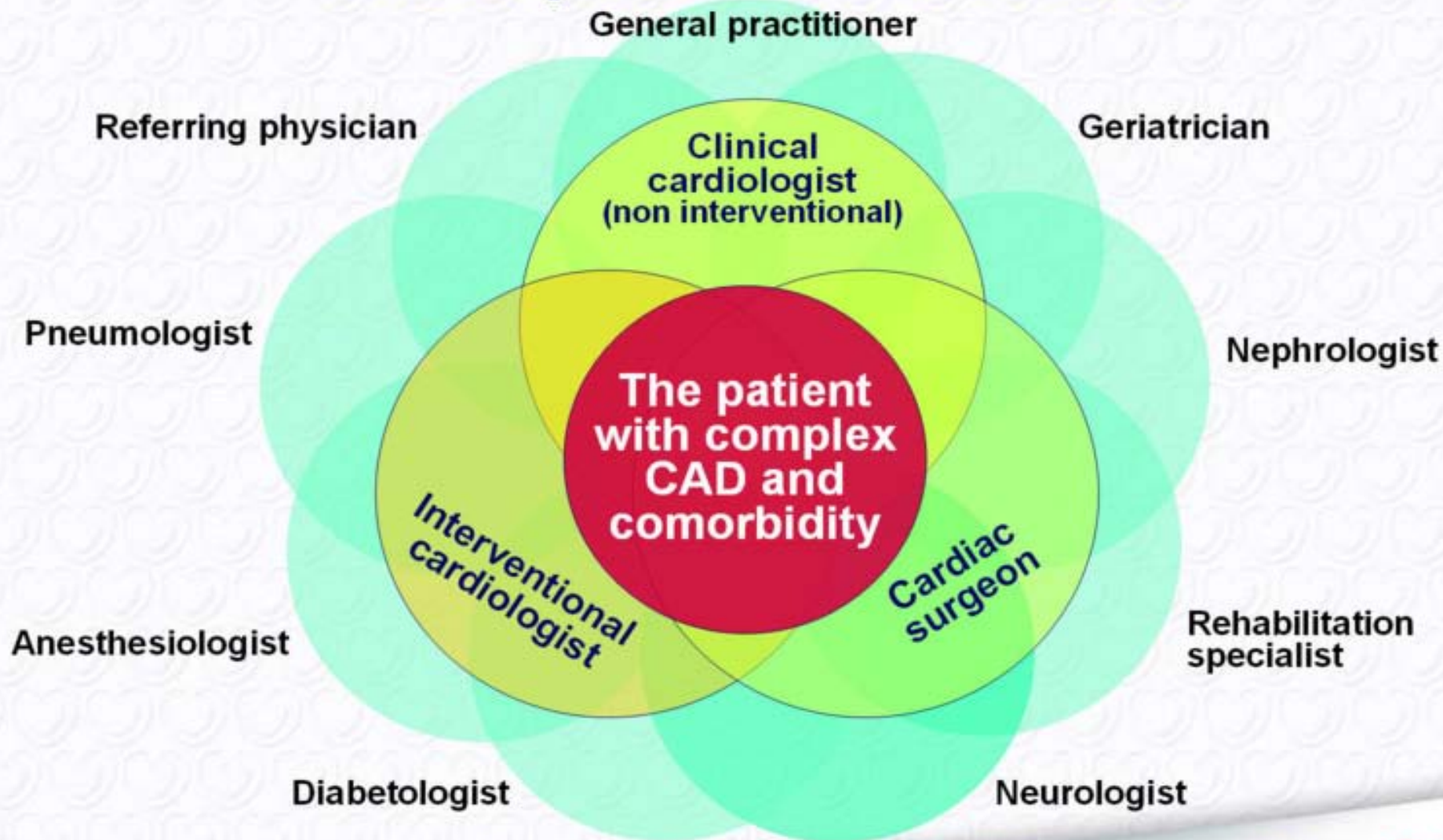
European Heart Journal (2010) 31, 2501-2555
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European Heart Journal (2010) 31, 2501-2555
European Journal of Cardio-thoracic Surgery (2010) 38, S1-S52

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Joint 2010 ESC - EACTS Guidelines
on Myocardial Revascularisation



Conclusions

- Diabetics are a higher-risk group of patients for adverse outcomes after our stent procedures.

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- **We definitely have good evidence that DES are a better option than BMS for diabetics.**

Conclusions

- Diabetics are a higher-risk group of patients for adverse outcomes after our stent procedures.
- We definitely have good evidence that DES are a better option than BMS for diabetics.
- Among the current new-generation DES and according to actual EBM, stents are probably as good as each other in treating this patient subset.

Thanks for your attention!
www.solaci.org