

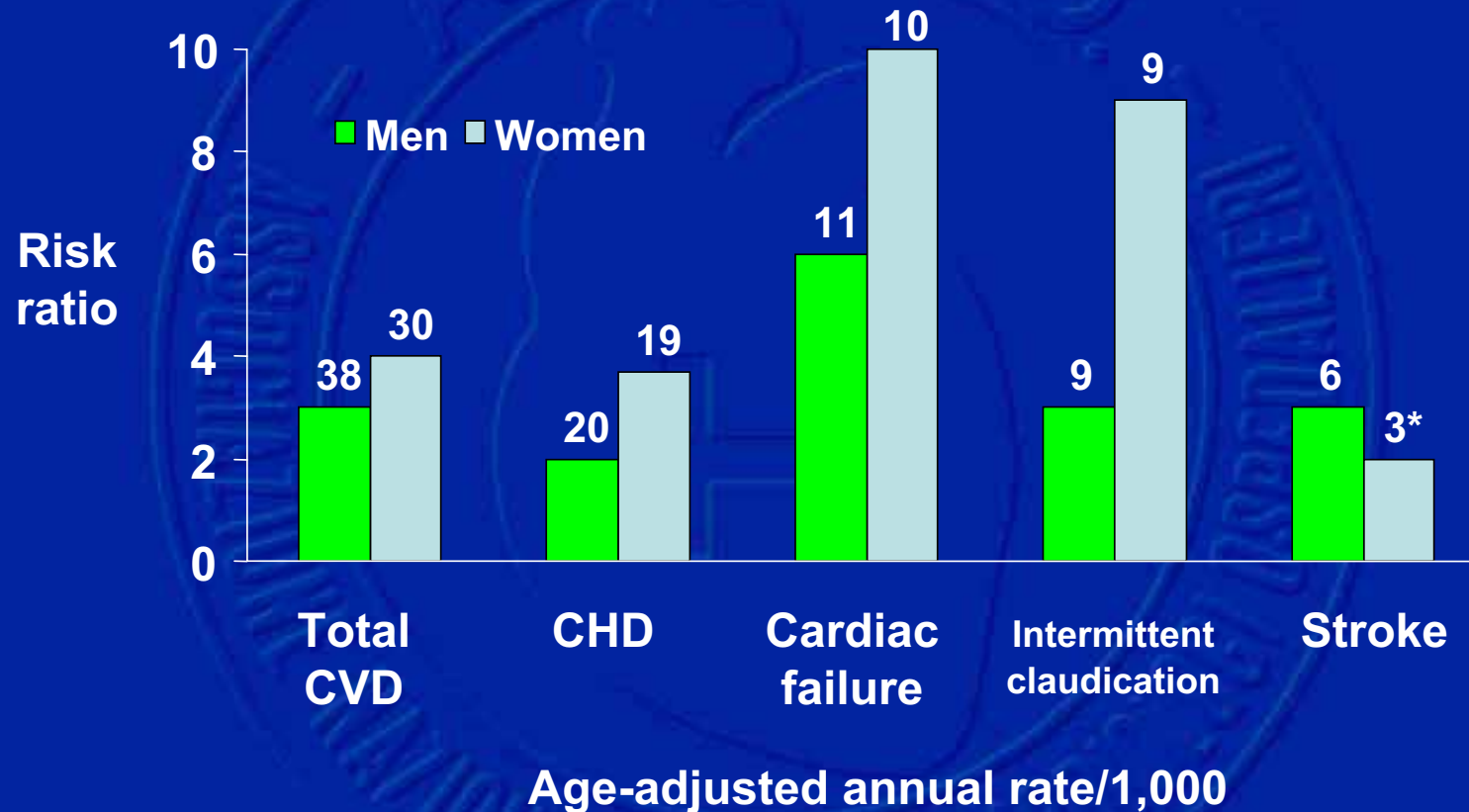
Stratificare il rischio CV nel paziente diabetico:
dalle carte del rischio alla diagnostica
strumentale

La gestione clinica dell'ischemia
silente è una questione di evidenza
o di coscienza?

Massimo Uguccioni

Firenze 1. 06. 2006

Framingham Heart Study 30-Year Follow-Up: CVD Events in Patients With DM (Ages 35-64)



$P < 0.001$ for all values except * $P < 0.05$.

Wilson PWF, Kannel WB. In: *Hyperglycemia, Diabetes and Vascular Disease*.
Ruderman N et al, eds. Oxford; 1992.

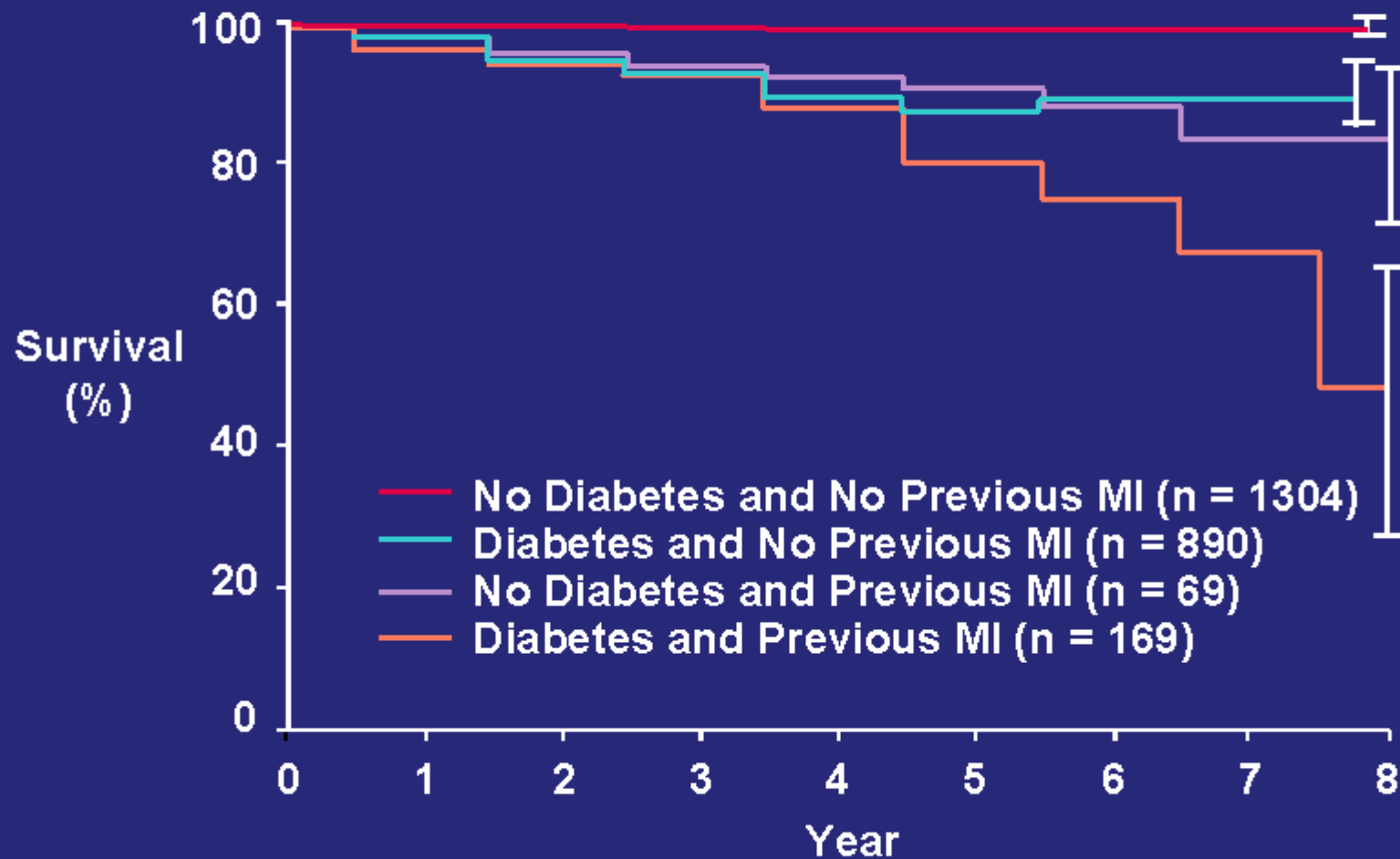
DM and CVD: the Framingham Study

Sub-study based on 20 years of surveillance

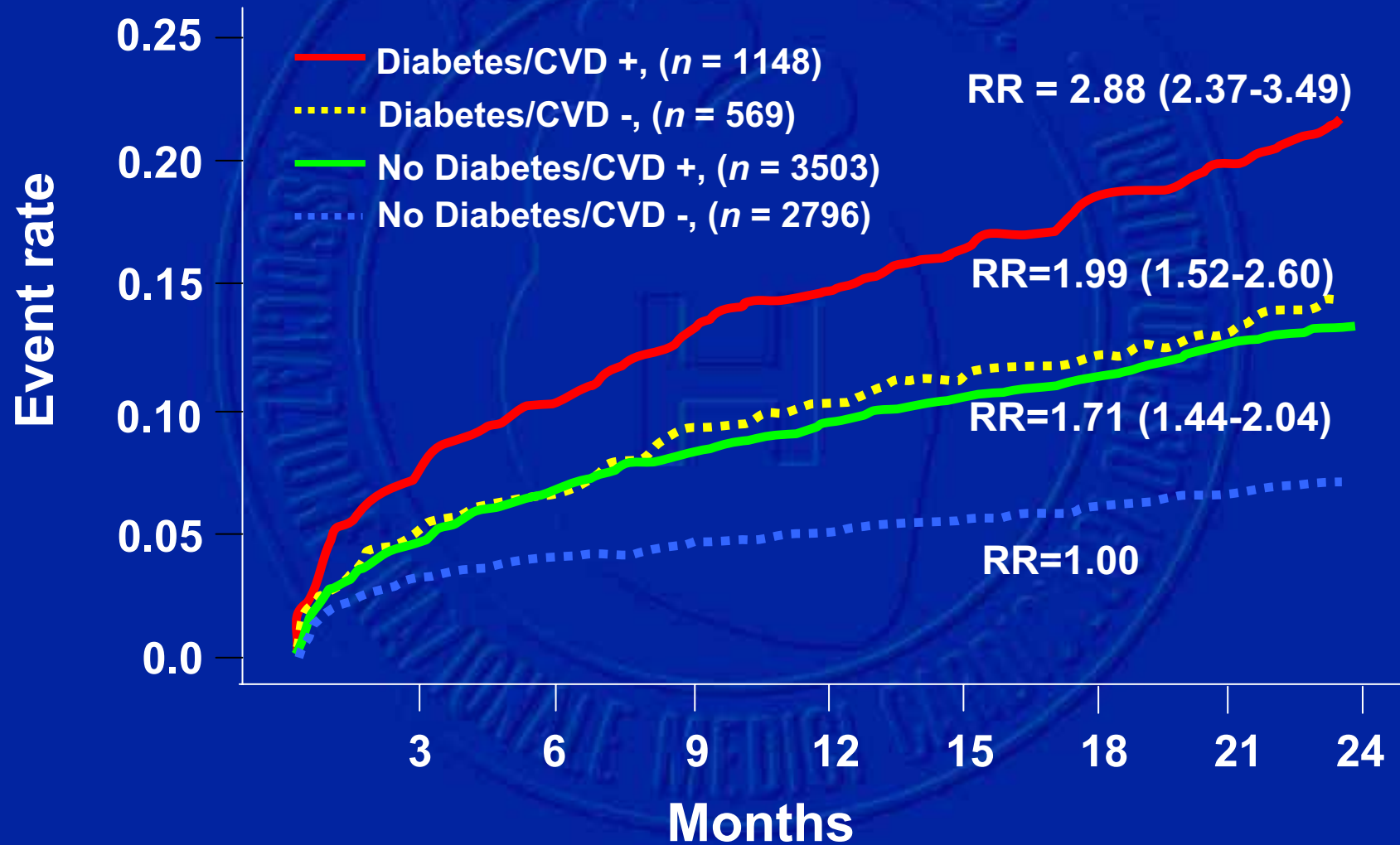
- **DM associated with 2-3x** increased risk for clinical atherosclerosis and associated conditions compared with non diabetic subjects
 - Intermittent claudication
 - CAD
 - Congestive heart failure
- Cardiovascular mortality was equally high in women and men with DM, reflecting a greater increase for women

Kannel WB, McGee DL, *JAMA*. 1979;241:2035-2038.

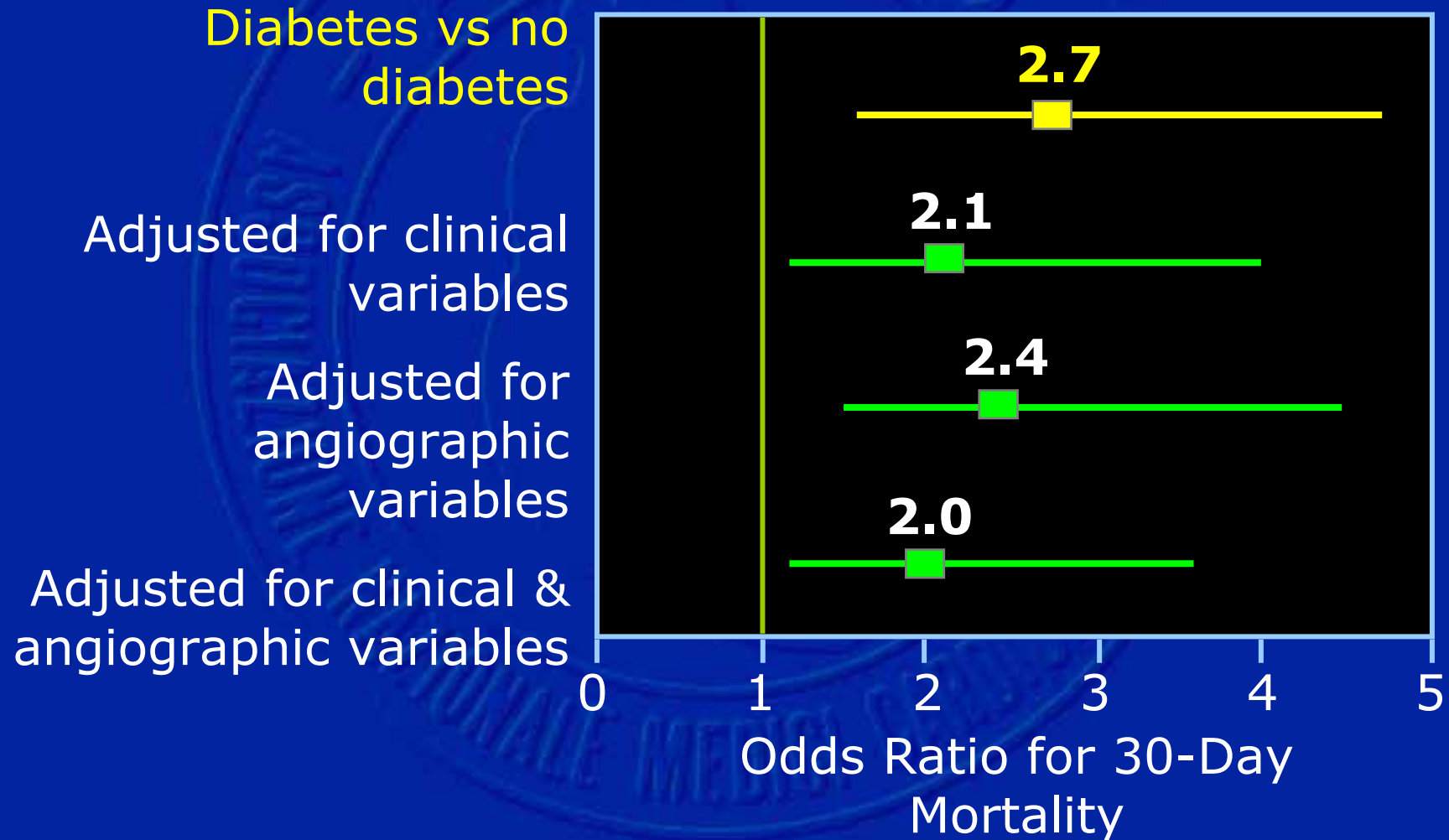
Probability of Death From CHD in Patients With Type 2 Diabetes With or Without Previous MI



OASIS Study: Total Mortality



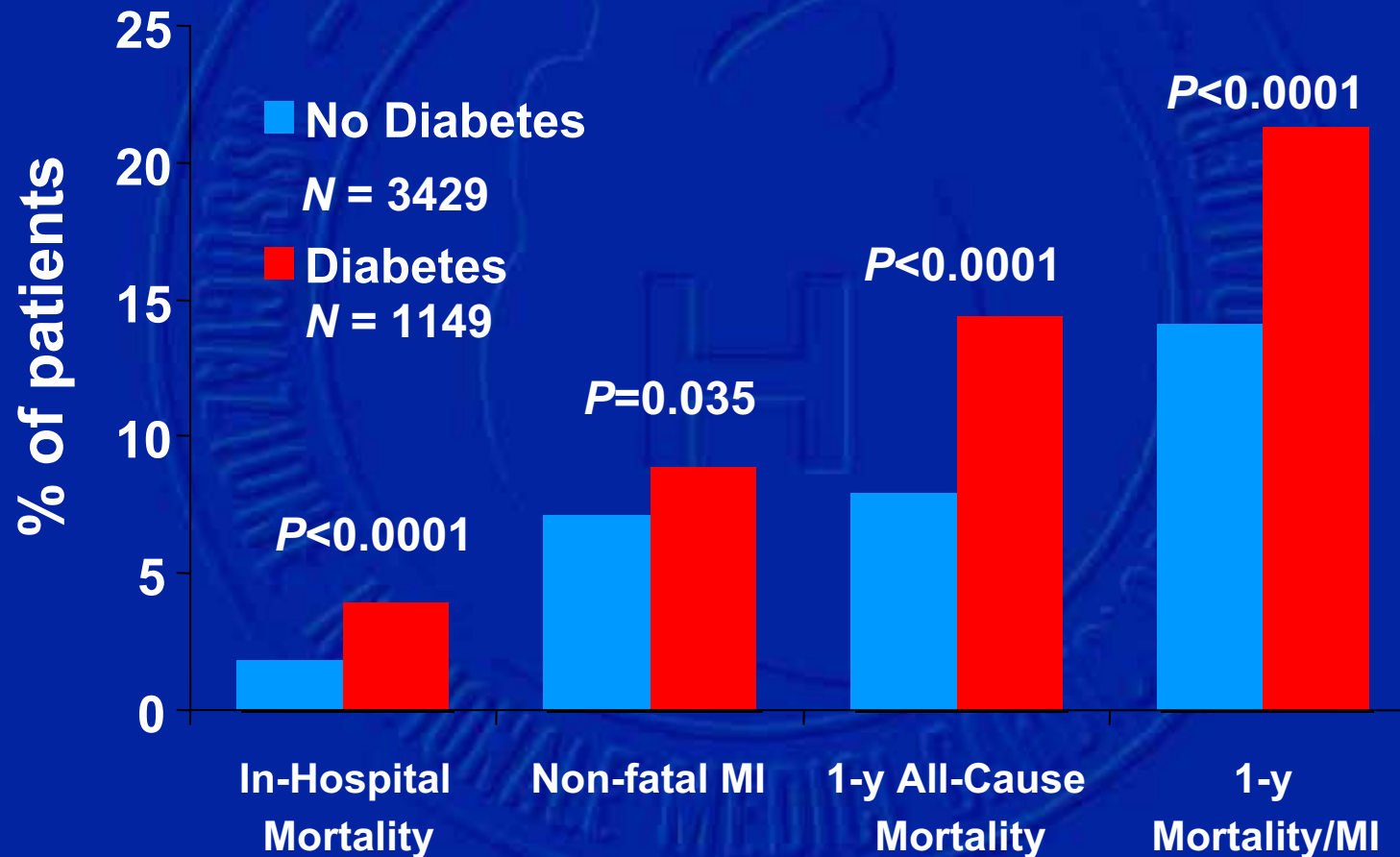
Effect of Diabetes on 30-Day Mortality (GUSTO-I)



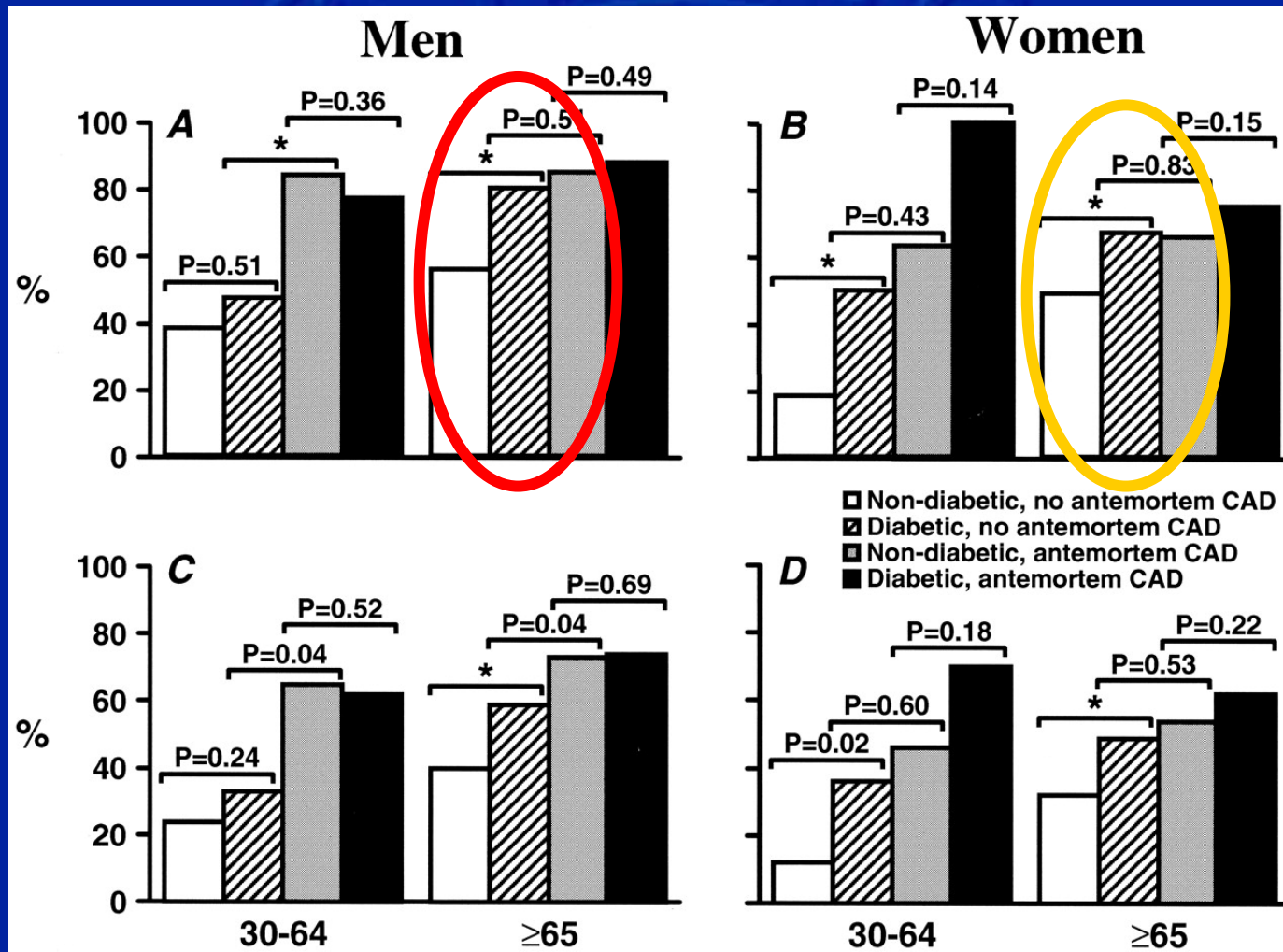
Woodfield SL *J Am Coll Cardiol* 1996;28:1661-1669.

ACS and Diabetes

Clinical Outcomes Up to 1 Year



Prevalence of any high-grade or multivessel coronary atherosclerosis by DM and CAD



Goraya, T. Y. et al. J Am Coll Cardiol 2002;40:946-953

Come identificare i soggetti diabetici a rischio più elevato?

- Quali diabetici **asintomatici** dovrebbero essere sottoposti a screening?
- Quali sono i test più appropriati per identificare l'ischemia silente nel diabetico?
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

Carta del rischio cardiovascolare

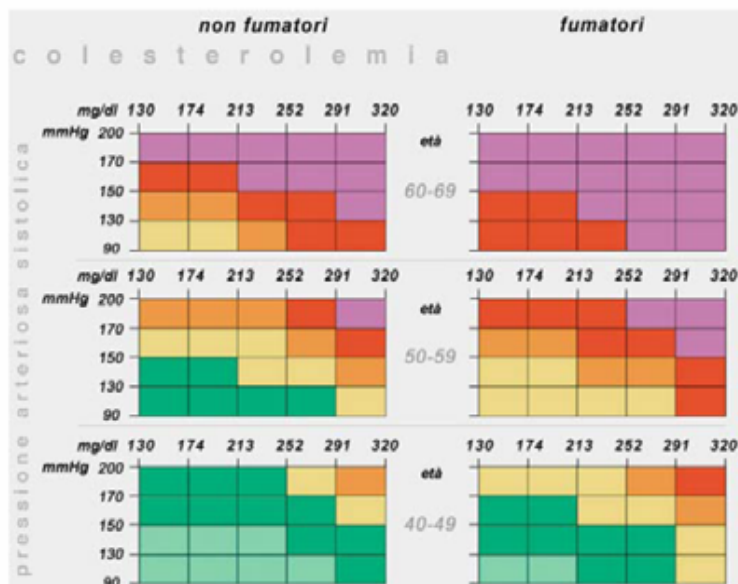
uomini diabetici

rischio cardiovascolare a 10 anni

Come utilizzare la carta

- Posizionarsi nella zona fumatore / non fumatore.
- Identificare il decennio di età.
- Collocarsi sul livello corrispondente a pressione arteriosa sistolica e colesterolemia.
- Identificato il colore, leggere nella legenda a fianco il livello di rischio.

livello di rischio a 10 anni		
rischio MCV VI		oltre 30%
rischio MCV V		20% - 30%
rischio MCV IV		15% - 20%
rischio MCV III		10% - 15%
rischio MCV II		5% - 10%
rischio MCV I		meno 5%



Carta del rischio cardiovascolare

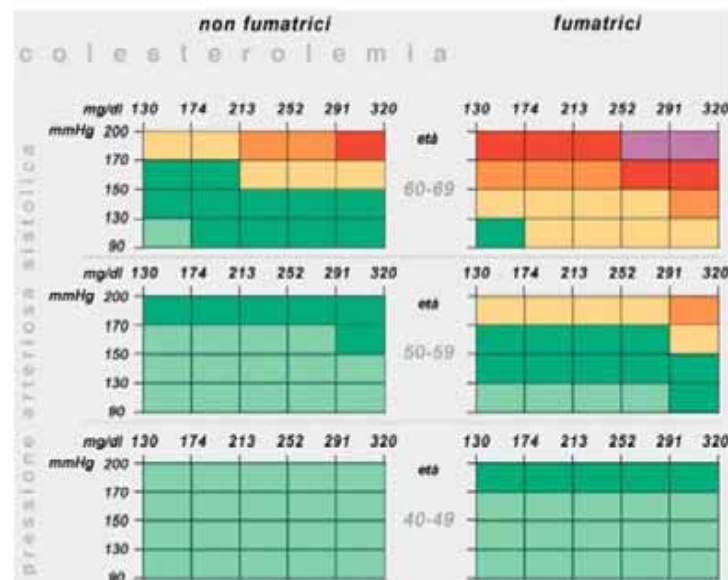
donne diabetiche

rischio cardiovascolare a 10 anni

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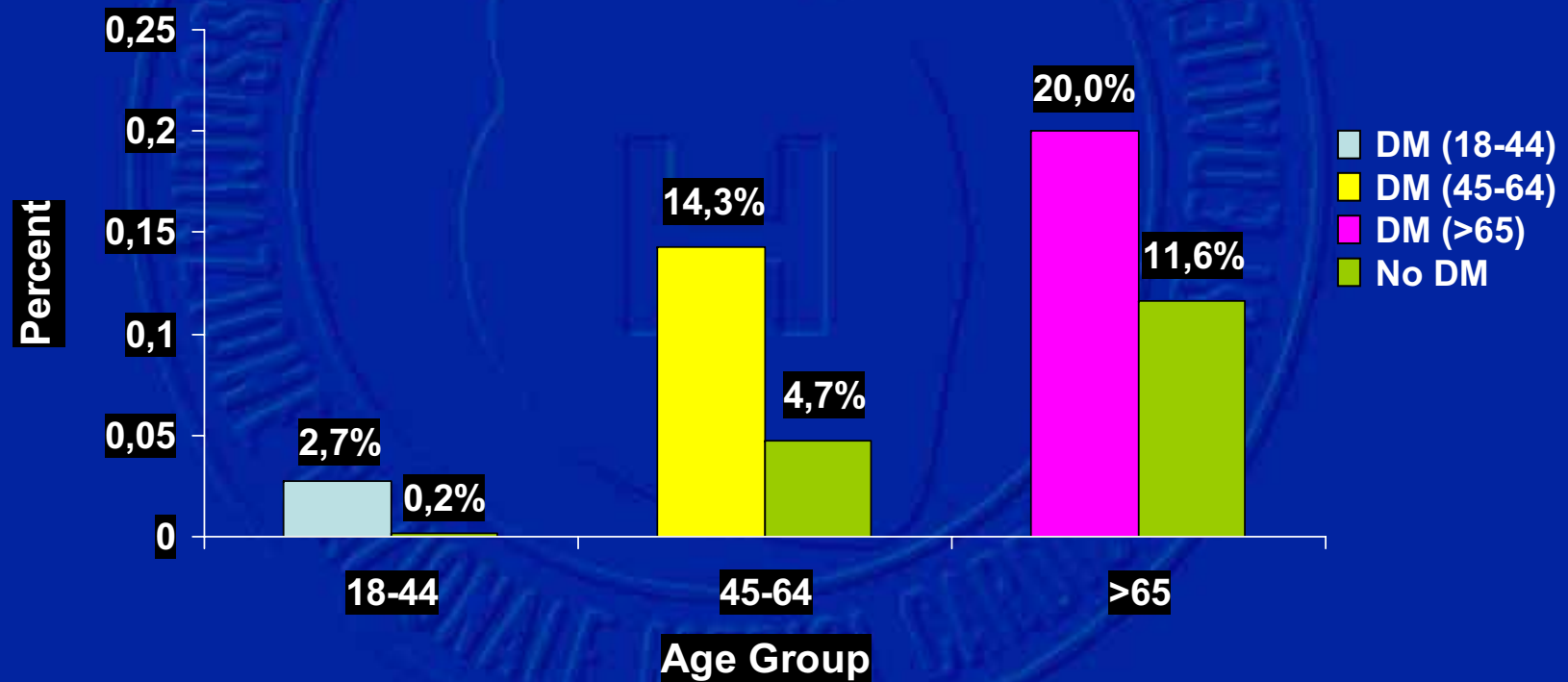
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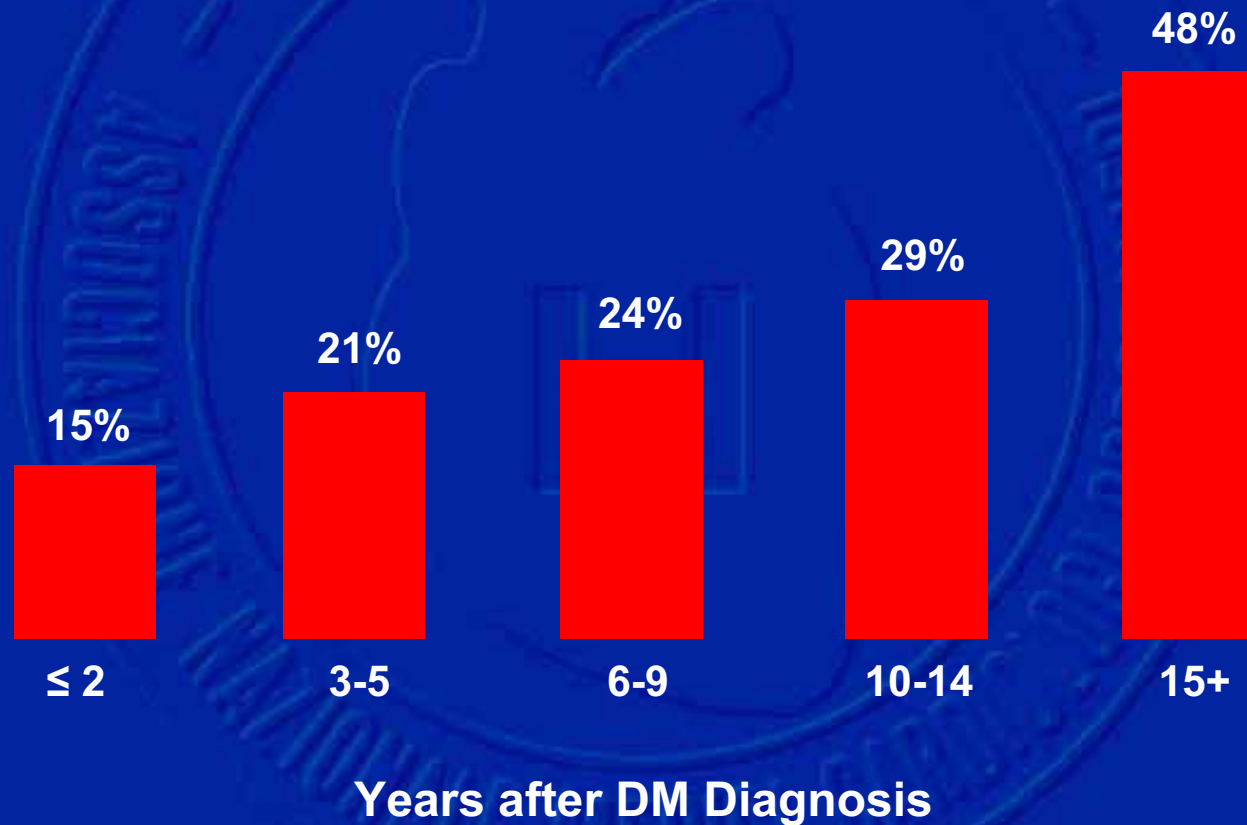
Le carte del rischio sono on-line sul sito del Progetto Cuore 'www.cuore.iss.it'

DM and Risk for Ischemic Heart Disease by Age

Percentage of adults reporting ischemic heart disease by DM status and age, United States, 1989



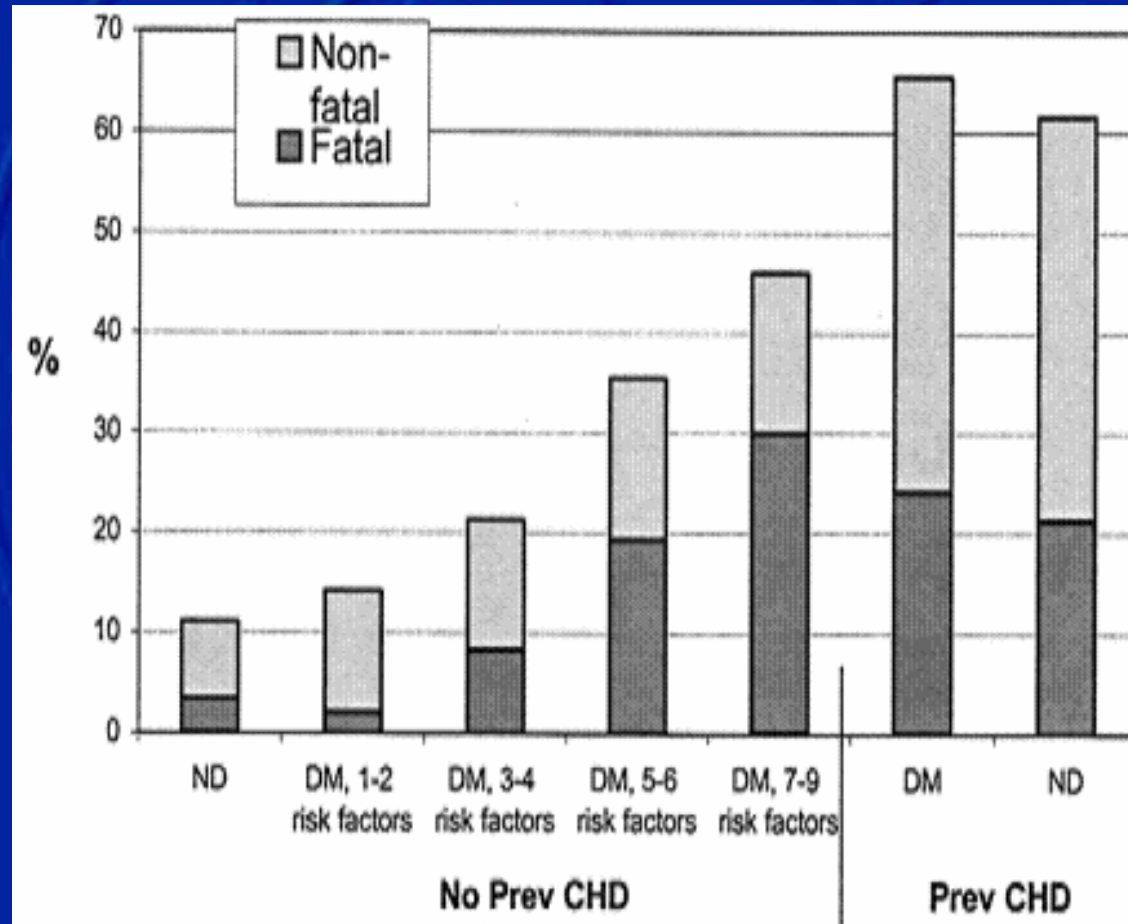
Proportion of Patients with Cardiovascular Disease Increases with Duration of type 2 Diabetes



Harris, S *et al.*; Type 2 Diabetes and Associated Complications in Primary Care in Canada: The Impact of Duration of Disease on Morbidity Load. CDA 2003.

10-year cumulative incidence of CHD by number of risk factors

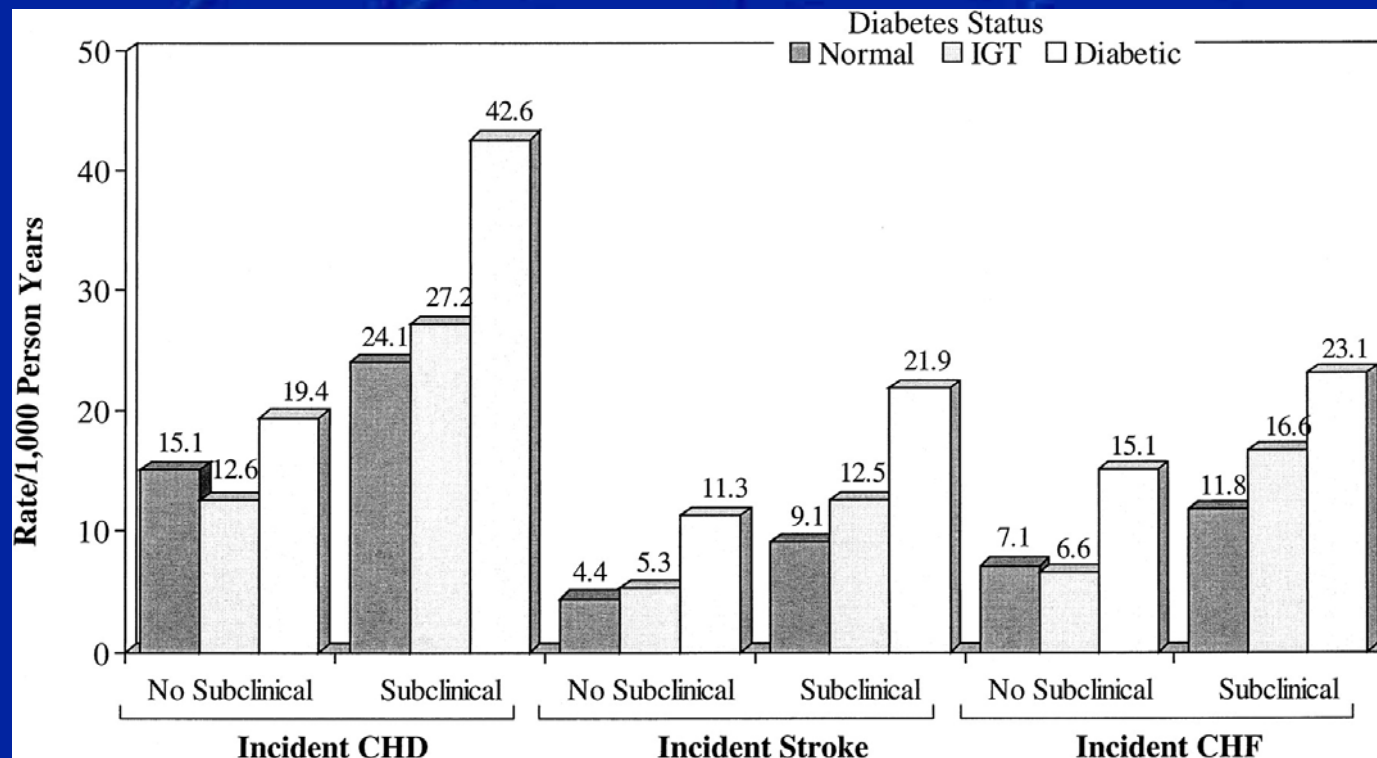
Strong Heart Study – n. 4549



Diabetes Care 2006; 29: 391 - 7

DM - presence of subclinical CVD and incidence of events

Cardiovascular Health Study – n. 5197



Kuller, L. H. 2000; 20: 823-829

Arteriosclerosis, Thrombosis,
and Vascular Biology

Incidence of CAD by History of HTN or DM and Presence of Subclinical Disease

Cardiovascular Health Study - n. 5888

Table 6. Incidence of Coronary Heart Disease by History of Hypertension or Diabetes Mellitus and Presence of Subclinical Disease at Baseline

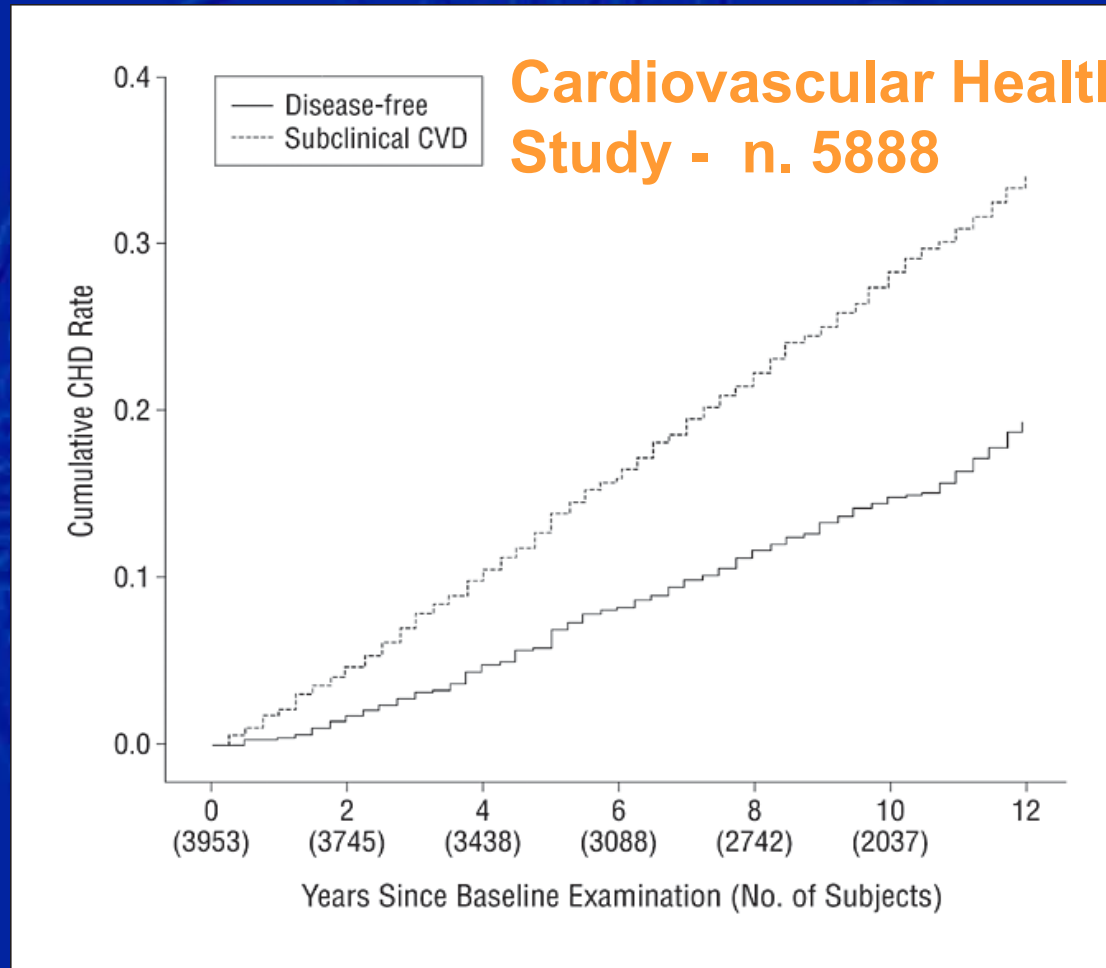
Disease	Subclinical Disease	Women			Men		
		No. of Events/ No. at Risk	Incidence per 1000 Person-Years	HR*	No. of Events/ No. at Risk	Incidence per 1000 Person-Years	HR*
Hypertension							
No	No	57/530	10.6 (8.2-13.8)	1.00	58/298	21.0 (16.2-27.1)	1.00
Yes	No	77/464	17.3 (13.8-21.6)	1.57	48/205	24.6 (18.5-32.7)	1.15
No	Yes	91/525	18.5 (15.1-22.8)	1.64	13/412	33.7 (28.1-40.6)	1.53
Yes	Yes	226/888	29.8 (26.0-33.8)	2.54	234/627	52.6 (46.2-59.8)	2.30
Diabetes Mellitus							
No	No	120/911	13.3 (11.1-15.9)	1.0	96/451	22.6 (18.5-27.6)	1.00
Yes	No	13/75	19.1 (11.1-32.9)	1.45	10/52	21.6 (11.6-40.2)	0.97
No	Yes	247/1187	22.9 (20.1-25.9)	1.60	261/839	39.9 (35.3-45.0)	1.68
Yes	Yes	68/212	42.6 (33.6-54.1)	3.11	84/190	68.7 (55.4-85.0)	3.00

*Age-adjusted hazard ratio.

Kuller, L. H. et al. Arch Intern Med 2006; 166: 71-78

ARCHIVES OF
INTERNAL MEDICINE

Incidence of CHD by presence or absence of subclinical disease at baseline

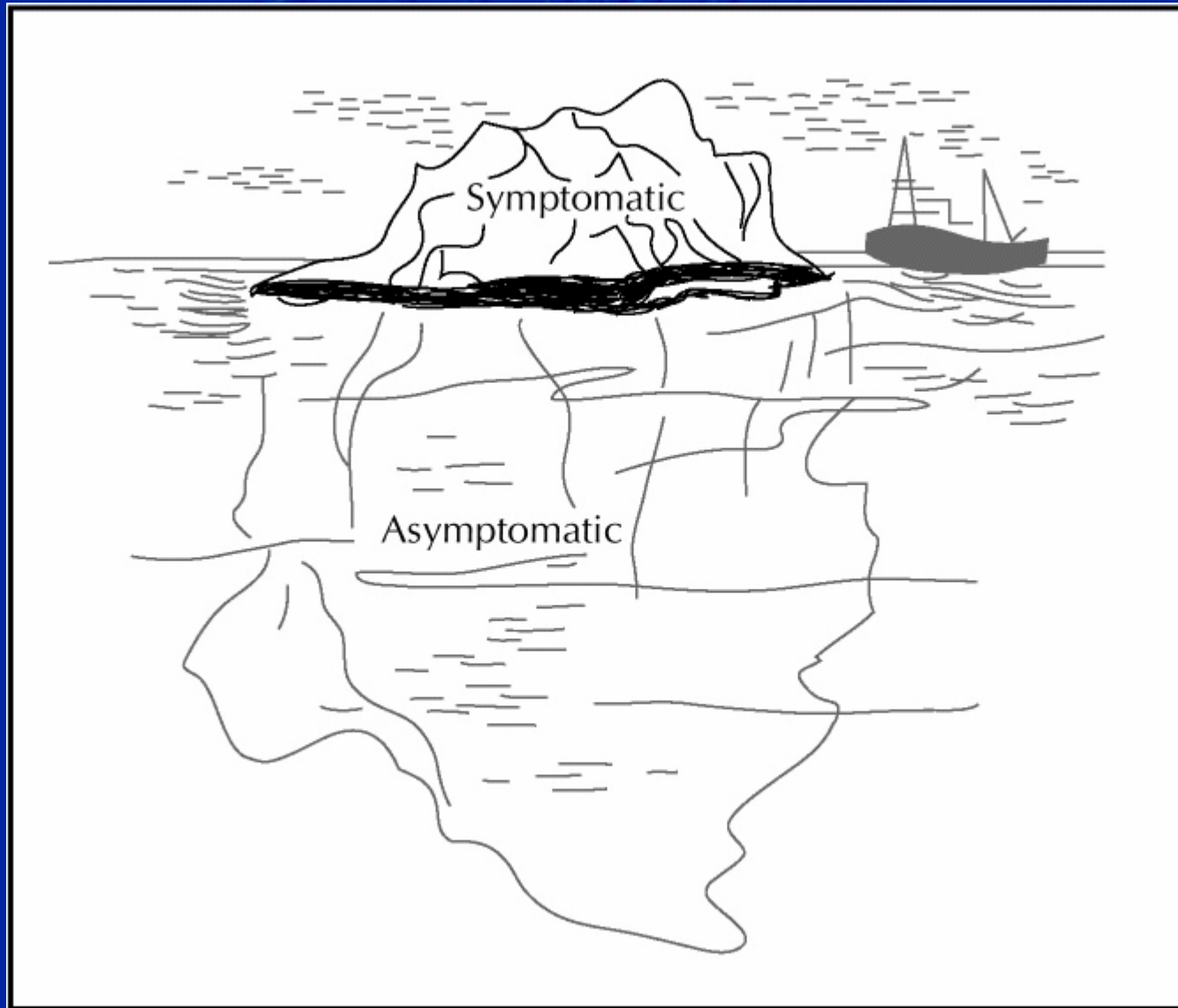


Kuller, L. H. et al. 2006; 166: 71-78

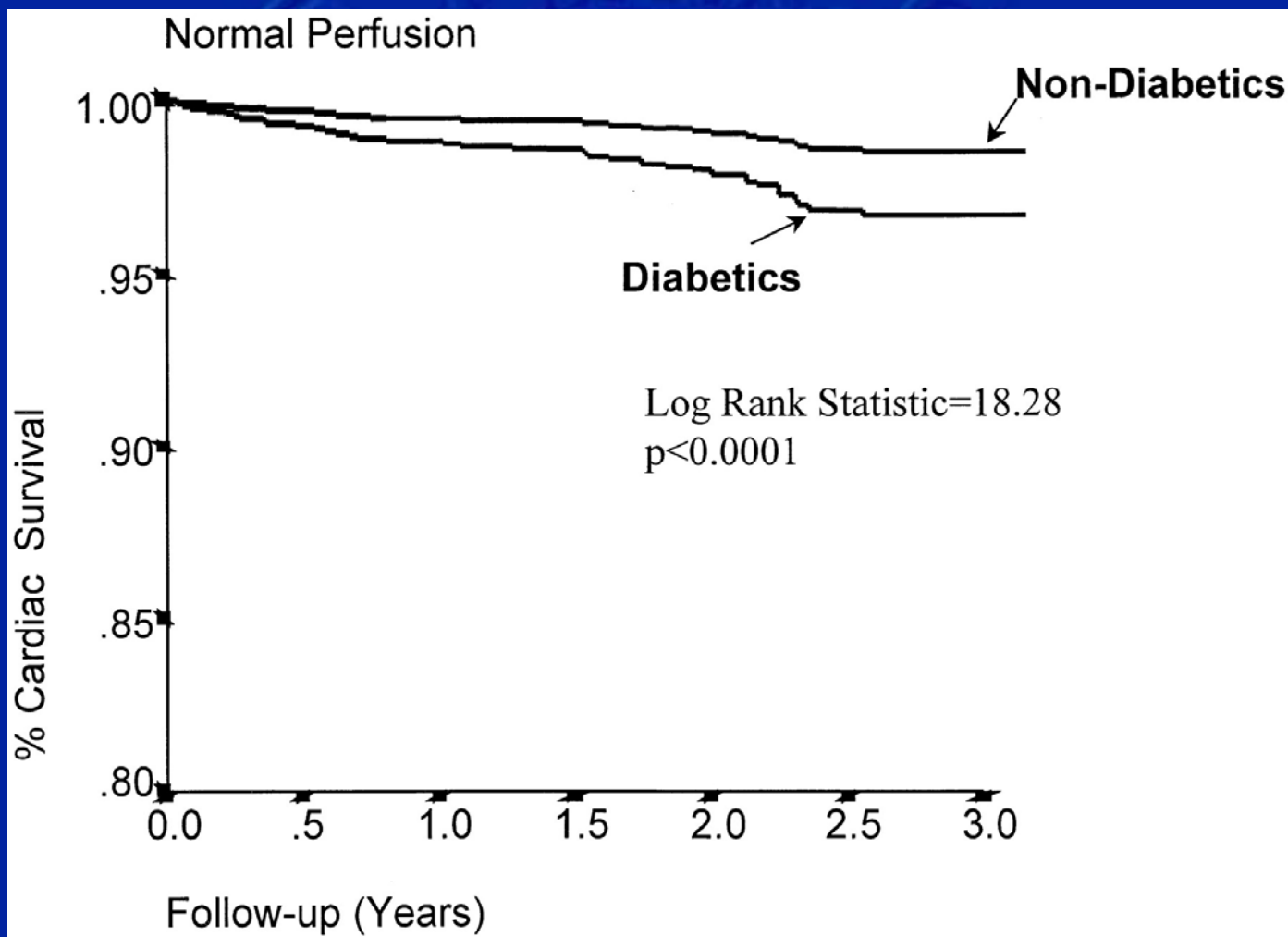
Come identificare i soggetti diabetici a rischio più elevato?

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- Qual è il valore prognostico di un test positivo nel diabetico asintomatico?
- Quali sono i benefici terapeutici di una diagnosi precoce di ischemia silente?

Silent myocardial ischemia



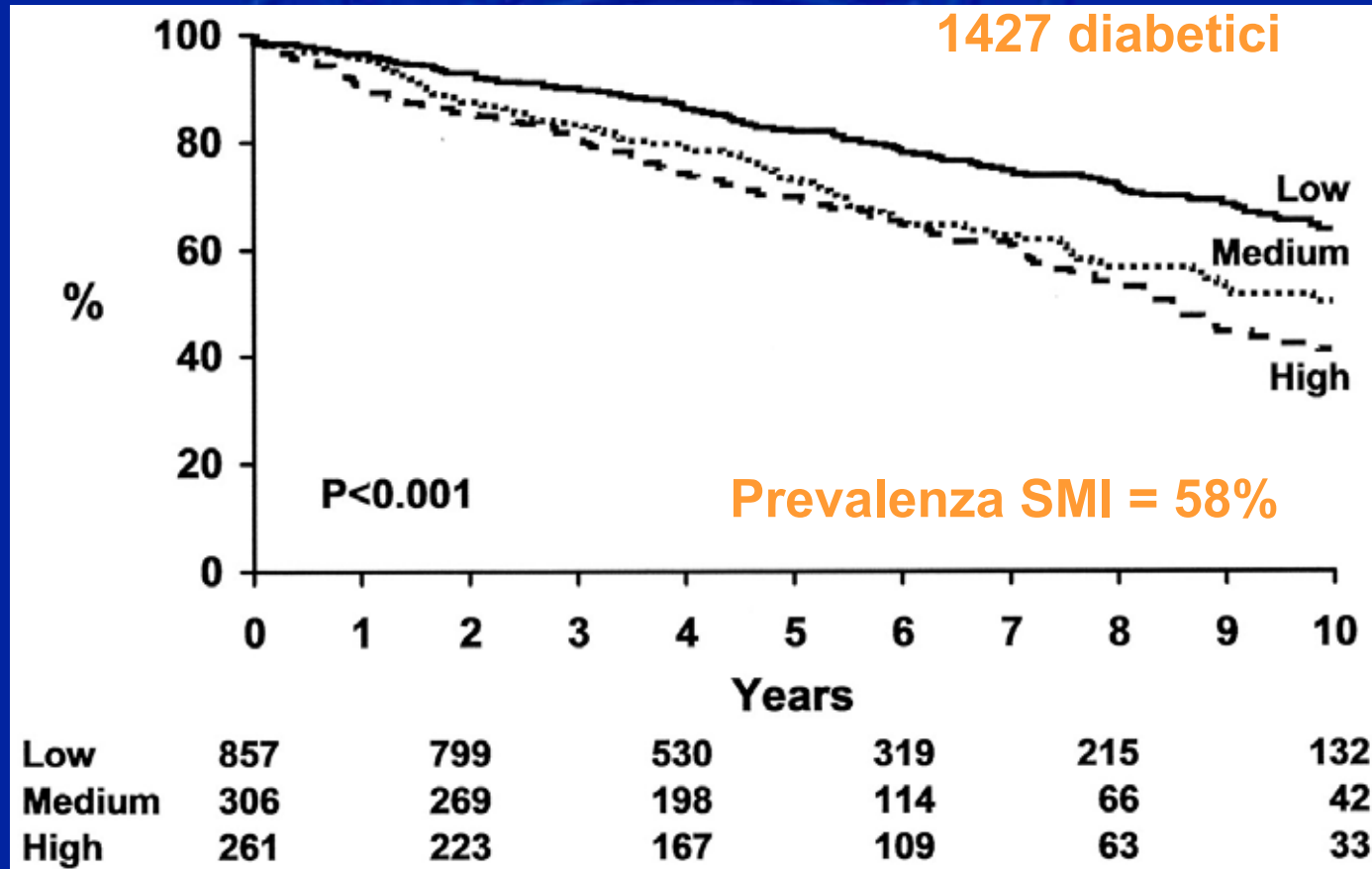
Kaplan-Meier curves comparing DM and non-DM patients with normal stress MPI



Giri, S. et al. *Circulation* 2002;105:32-40

Circulation

Survival of patients categorized by high intermediate and low-risk CT scans



Rajagopalan, N. et al. J Am Coll Cardiol 2005;45:43-49

Prevalence of Asymptomatic CAD in DM

		<u>Positive ETT</u>	<u>Positive Angiography</u>
Koistinen MJ. <i>BMJ</i> 1990;301:92-95.			
Type 2	n = 64	36%	9%
Type 1	n = 72	24%	11%
Controls	n = 80	9%	9%
Naka M et al. <i>Am Heart J</i> 1992;123:46-53.			
Type 2	n = 142	31%	12.1%
Controls	n = 149	30%	5.3%
MiSAD Group. <i>Am J Cardiol</i> 1997;79:134-139.			
Type 2	n = 925	12.1%	6.4% (thal ²⁰¹)
Rutter MK et al. <i>Am J Cardiol</i> 1999;83:27-31.			
Type 2 w microalb	n = 43	65%	—
Type 2 w/o microalb	n = 43	40%	—
Le A et al. <i>Am J Kidney Dis</i> 1994;24:65-71.			
Type 1 Renal Transplant		58%	35%

Factors Limiting Accuracy of Noninvasive "Stress" Tests for CAD

- Hypertensive Cardiomyopathy
- Diabetic Cardiomyopathy
- **Autonomic Cardiomyopathy**
- Renal Insufficiency
- **Microvascular Dysfunction**

Table III

Predictive factors for coronary stenoses in the diabetic patients with silent myocardial ischemia.

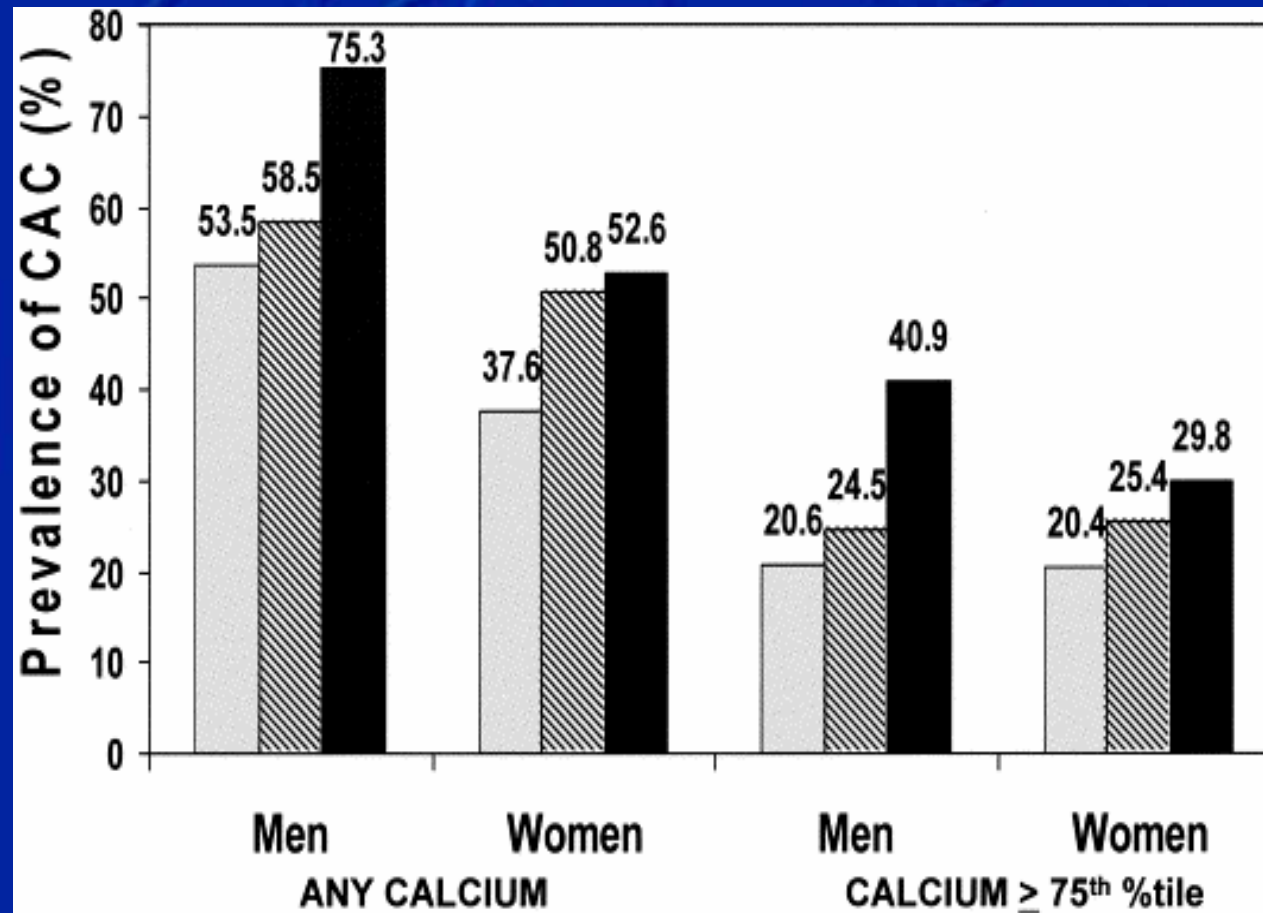
In these studies, only the patients who had silent myocardial ischemia and underwent consequently a coronary angiography are considered. The patients with both silent myocardial ischemia and silent coronary stenoses are compared with the patients with silent myocardial ischemia but no coronary stenosis.

CV: cardiovascular, ECG: electrocardiogram, chol: cholesterol.

Reference	Coronary angiographies (n)	Selection criteria	Cardiac testing for silent myocardial ischemia	Predictors of silent coronary stenoses in the patients with silent myocardial ischemia	
				Univariate analysis	Multivariate analysis
Naka 1992 [8]	36	hypertension	ECG stress test	gender, insulin treatment, retinopathy	none
Valensi 1997 [18]	24	≥ 2 CV risk factors	ECG stress test or myocardial scintigraphy or continuous ECG monitoring	age, systolic blood pressure, postprandial glycemia, total chol, LDL chol, triglycerides, apoB	
Cosson 2001 [68]	93	≥ 2 CV risk factors	ECG stress test or myocardial scintigraphy or both	age	none
Piot 2003 [64]	85	≥ 1 CV risk factors	ECG stress test or myocardial scintigraphy or both	microalbuminuria, hypertension, C reactive protein, fibrinogen, leukocytes counts	C reactive protein, fibrinogen, leukocytes counts

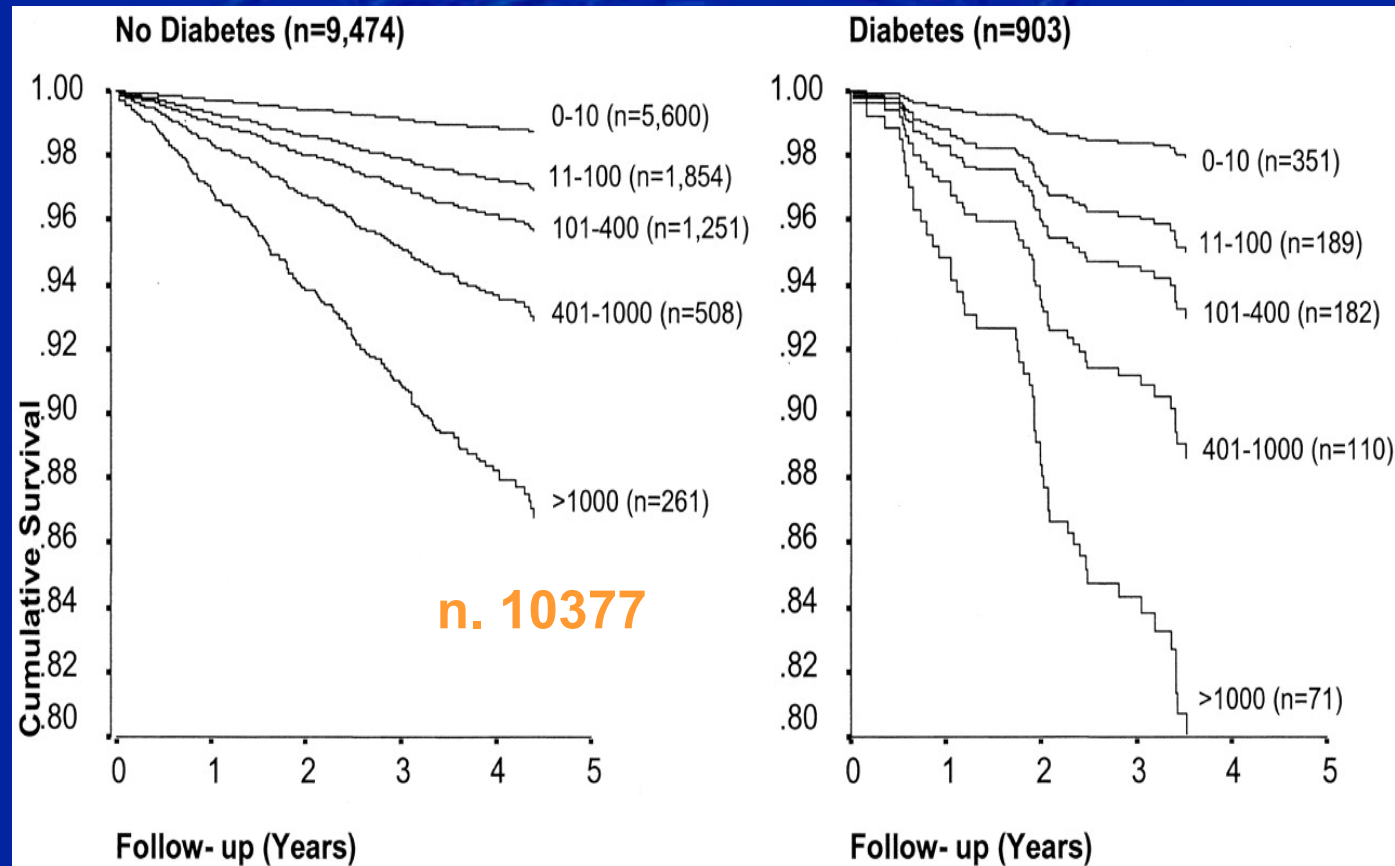
Diabetes Metab 2005; 31: 205-13

Prevalence of coronary artery calcium by disease category and gender



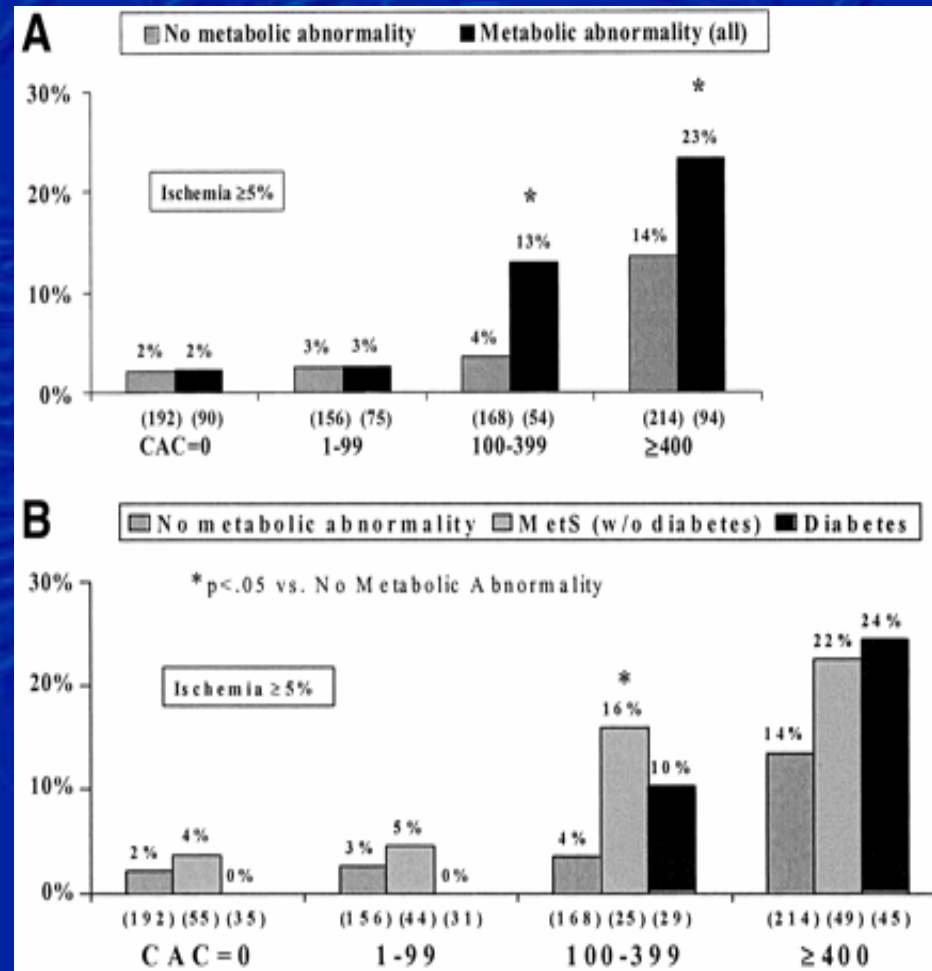
JACC 2003; 41: 1547- 53

Survival by EBCT coronary calcium in subjects with and without DM



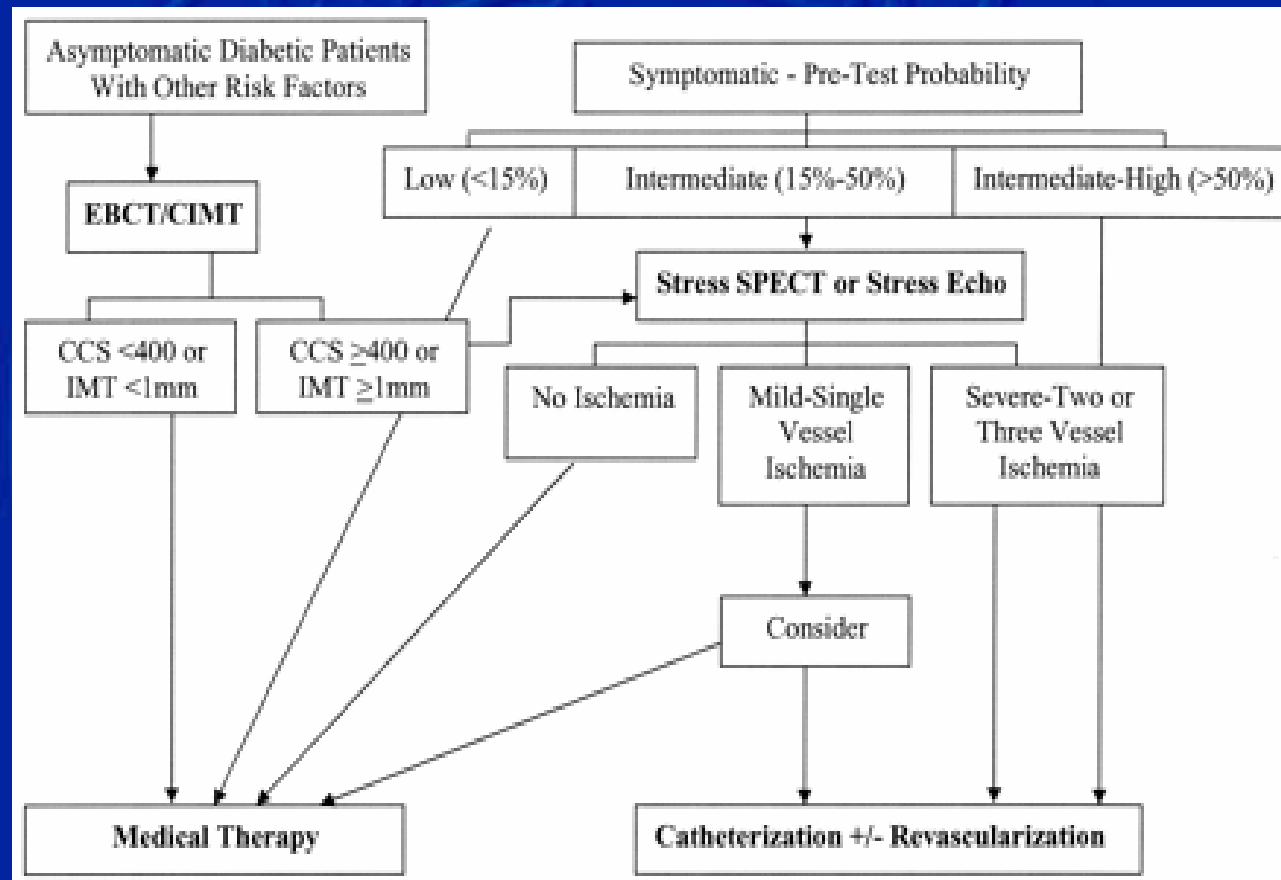
Raggi, P. et al. J Am Coll Cardiol 2004;43:1663-1669

Frequency of ischemia during MPS and coronary calcium categories



Diabetes Care 2005; 28: 1445-50

EBCT Echocardiography and SPECT

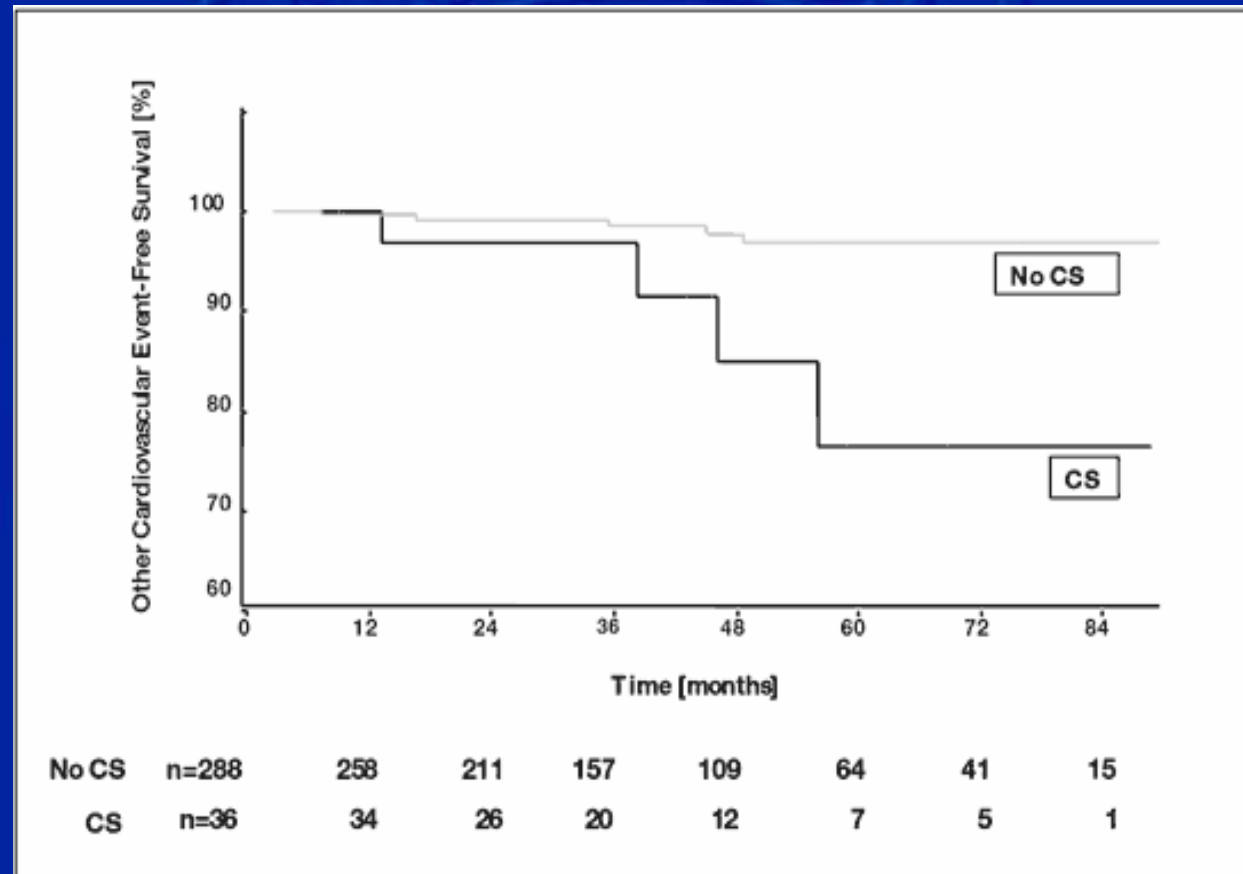


Raggi P. Diabetes Care 2005; 28: 2787- 94

Come identificare i soggetti diabetici a rischio più elevato?

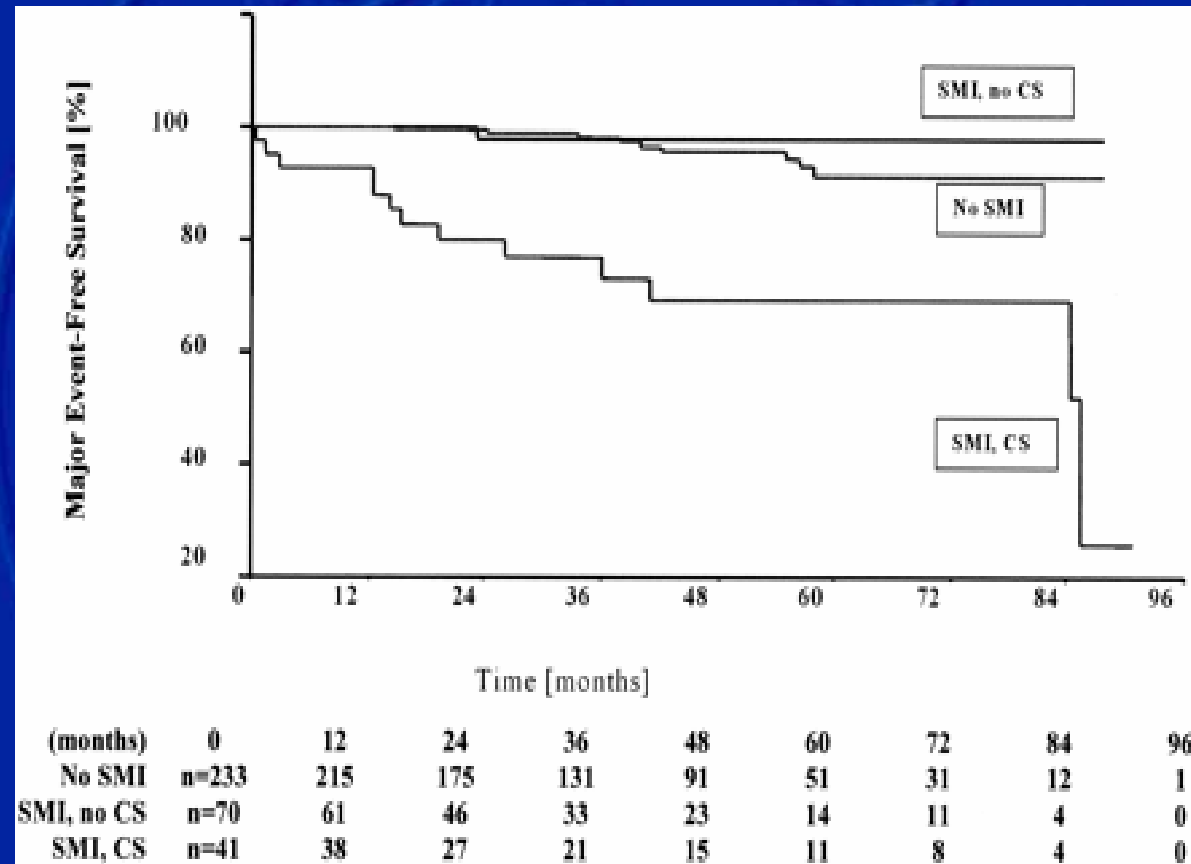
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Survival CV events-free according to silent coronary stenoses



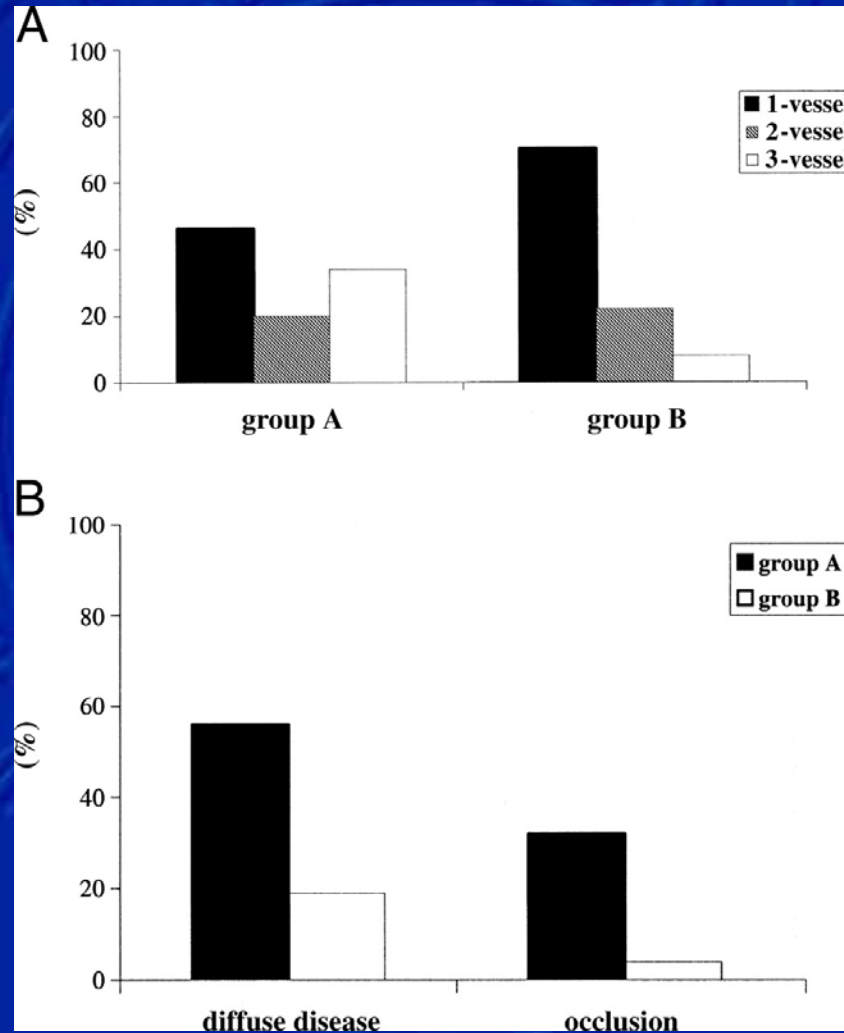
Diabetes Metab 2003; 29: 470-6.

Survival for major CV events according to SMI or silent coronary stenoses



Cosson E. Diabetes Care 2003; 26: 1313

Prevalence of CAD in DM2 patients with perfusion abnormalities at stress contrast echocardiography

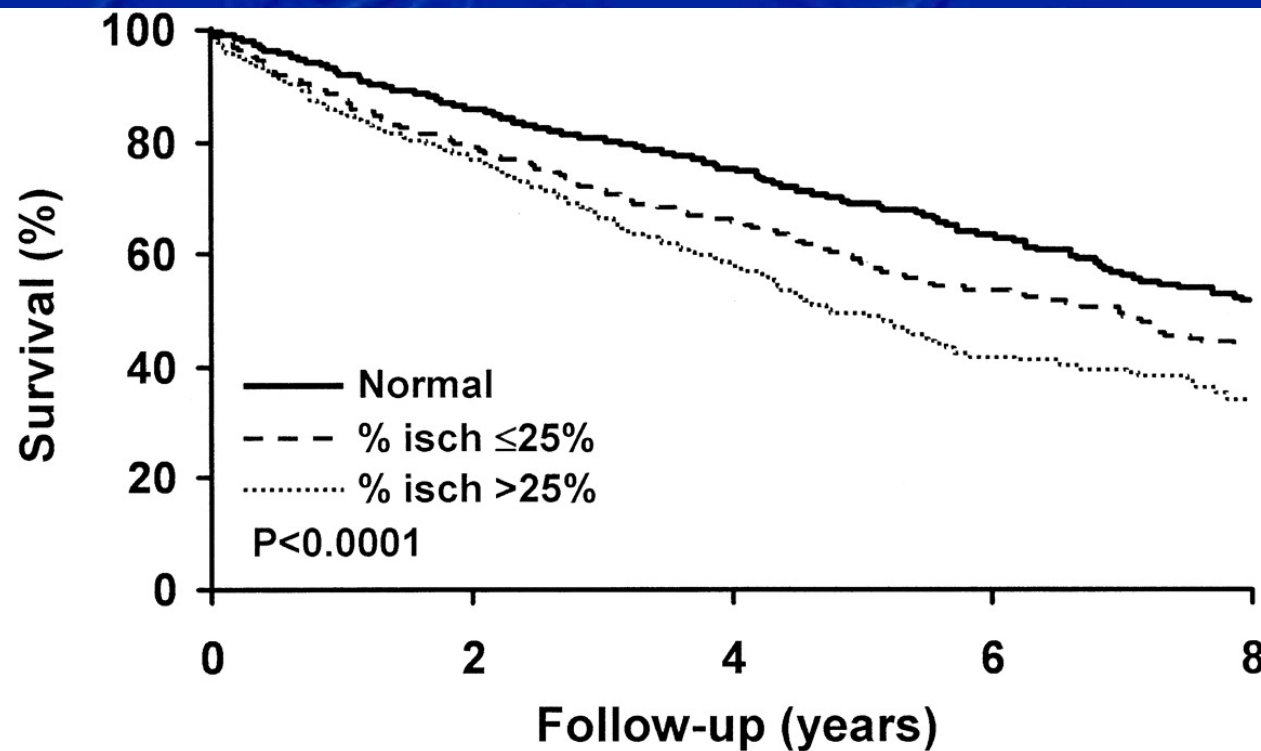


Group A \geq 2 RF

Group B 0-1 RF

Scognamiglio, R. et al 2006;47:65-71

Survival curves for patients with DM according to test result and extent of ischemia



No. at risk					
Normal	844	723	421	184	83
% isch $\leq 25\%$	596	469	307	153	71
% isch $> 25\%$	411	317	187	83	31

Chaowalit, N. et al. J Am Coll Cardiol 2006;47:1029-1036

Detection of Silent Myocardial Ischemia in Asymptomatic Diabetic Subjects

The DIAD study

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LAWRENCE H. YOUNG, MD¹
SILVIO E. INZUCCHI, MD²
DEBORAH A. CHYUN, PHD³
JANICE A. DAVEY, MSN¹
EUGENE J. BARRETT, MD⁴
RAYMOND TAILLEFER, MD⁵
STEVEN D. WITTLIN, MD⁶

GARY V. HELLER, MD⁷
NEIL FILIPCHUK, MD⁸
SAMUEL ENGEL, MD⁹
ROBERT E. RATNER, MD¹⁰
AMI E. ISKANDRIAN, MD¹¹
FOR THE DETECTION OF ISCHEMIA IN
ASYMPTOMATIC DIABETICS (DIAD)
INVESTIGATORS*

Prevalenza SMI = 22%

OBJECTIVE — To assess the prevalence and clinical predictors of silent myocardial ischemia in asymptomatic patients with type 2 diabetes and to test the effectiveness of current American Diabetes Association screening guidelines.

RESEARCH DESIGN AND METHODS — In the Detection of Ischemia in Asymptomatic Diabetics (DIAD) study, 1,123 patients with type 2 diabetes, aged 50–75 years, with no known or suspected coronary artery disease, were randomly assigned to either stress testing and 5-year clinical follow-up or to follow-up only. The prevalence of ischemia in 522 patients randomized to stress testing was assessed by adenosine technetium-99m sestamibi single-photon emission-computed tomography myocardial perfusion imaging.

RESULTS — A total of 113 patients (22%) had silent ischemia, including 83 with regional myocardial perfusion abnormalities and 30 with normal perfusion but other abnormalities (i.e., adenosine-induced ST-segment depression, ventricular dilation, or rest ventricular dysfunction). Moderate or large perfusion defects were present in 33 patients. The strongest predictors

for abnormal tests were abnormal Valsalva (odds ratio [OR] 5.6), male sex (2.5), and diabetes duration (5.2). Other traditional cardiac risk factors or inflammatory and prothrombotic markers were not predictive. Ischemic adenosine-induced ST-segment depression with normal perfusion ($n = 21$) was associated with women (OR 3.4). Selecting only patients who met American Diabetes Association guidelines would have failed to identify 41% of patients with silent ischemia.

CONCLUSIONS — Silent myocardial ischemia occurs in greater than one in five asymptomatic patients with type 2 diabetes. Traditional and emerging cardiac risk factors were not associated with abnormal stress tests, although cardiac autonomic dysfunction was a strong predictor of ischemia.

Diabetes Care 27:1954–1961, 2004

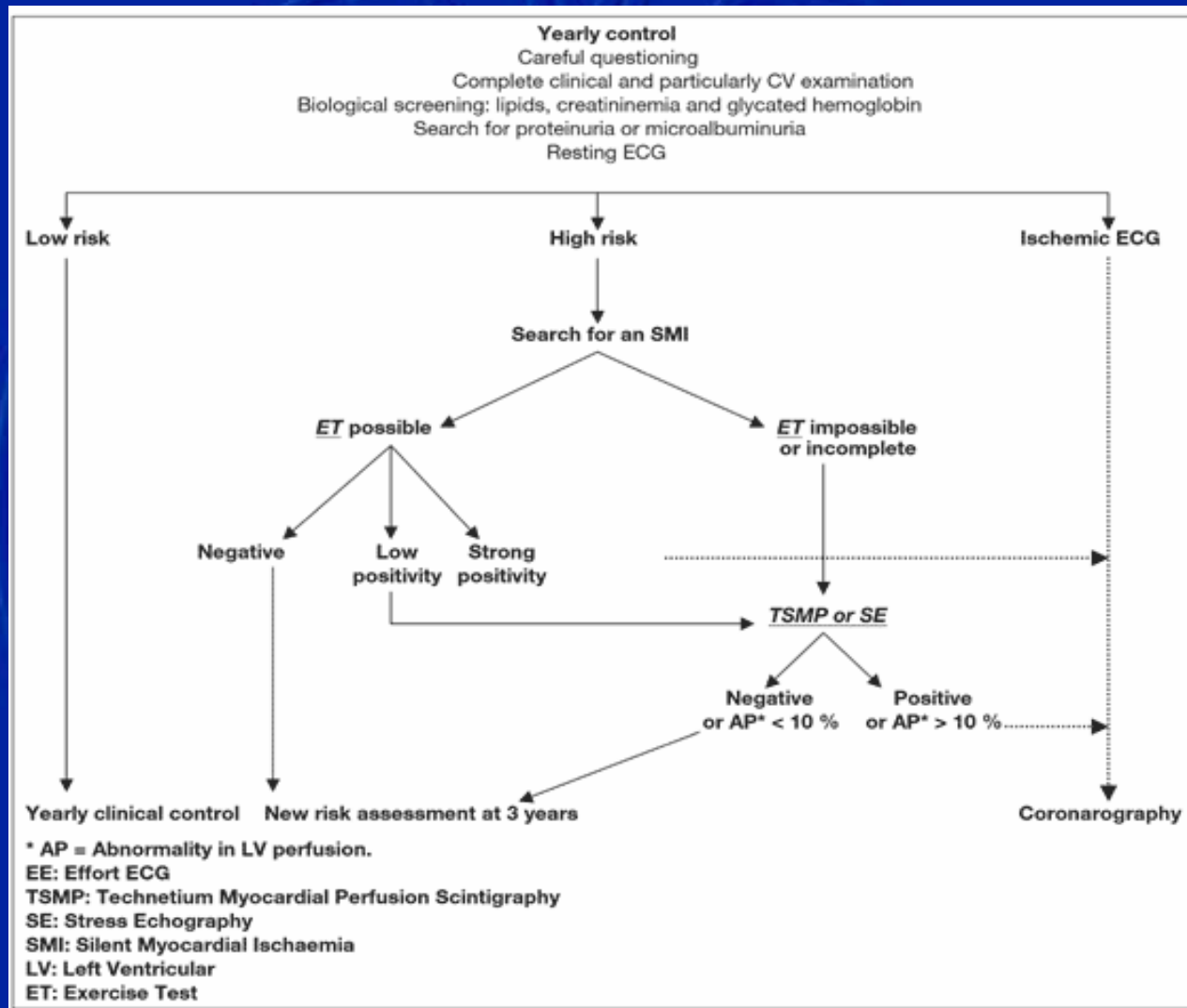
Coronary artery disease (CAD) is the leading cause of death in patients with diabetes (1). Myocardial ischemia in patients with diabetes is often

Indications for Cardiac Testing in Diabetic Patients

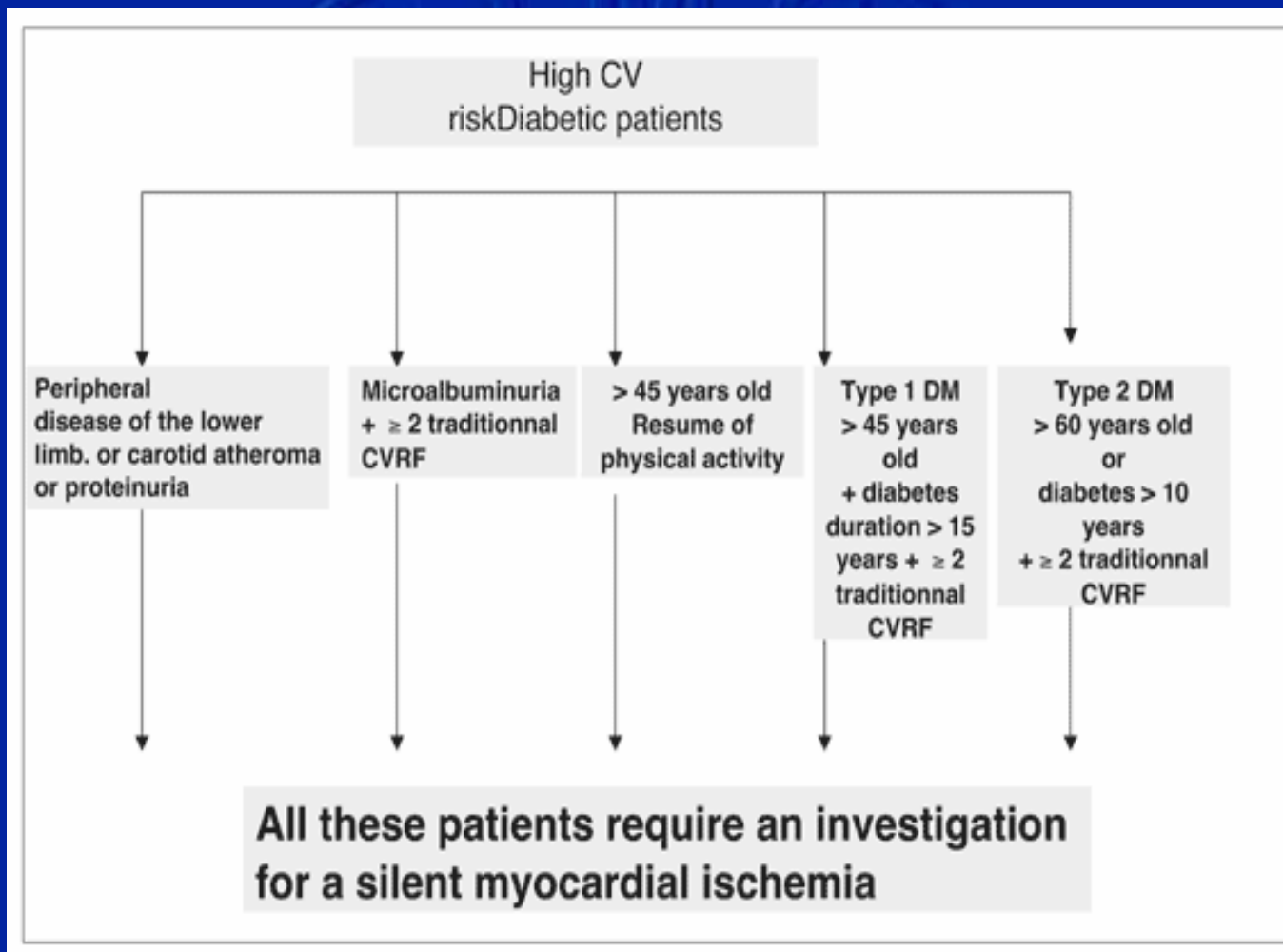
- Typical or atypical cardiac symptoms
- Resting ECG suggestive of ischemia or infarction
- Peripheral or carotid occlusive arterial disease
- Sedentary lifestyle or plan to begin a vigorous exercise program
- Two or more of the risk factors listed below
 - Total cholesterol ≥ 240 mg/dL, LDL cholesterol ≥ 160 mg/dL, or HDL cholesterol < 35 mg/dL
 - Blood pressure $> 140/90$ mmHg
 - Smoking
 - Family history of premature CAD
 - Positive micro/macro-albuminuria

ADA. Diabetes Care 2006; 29: S4 - S42

ALFEDIAM - SFC



Diabetes Metab 2004; 30: S3-S18



Diabetes Metab 2004; 30: S3-S18

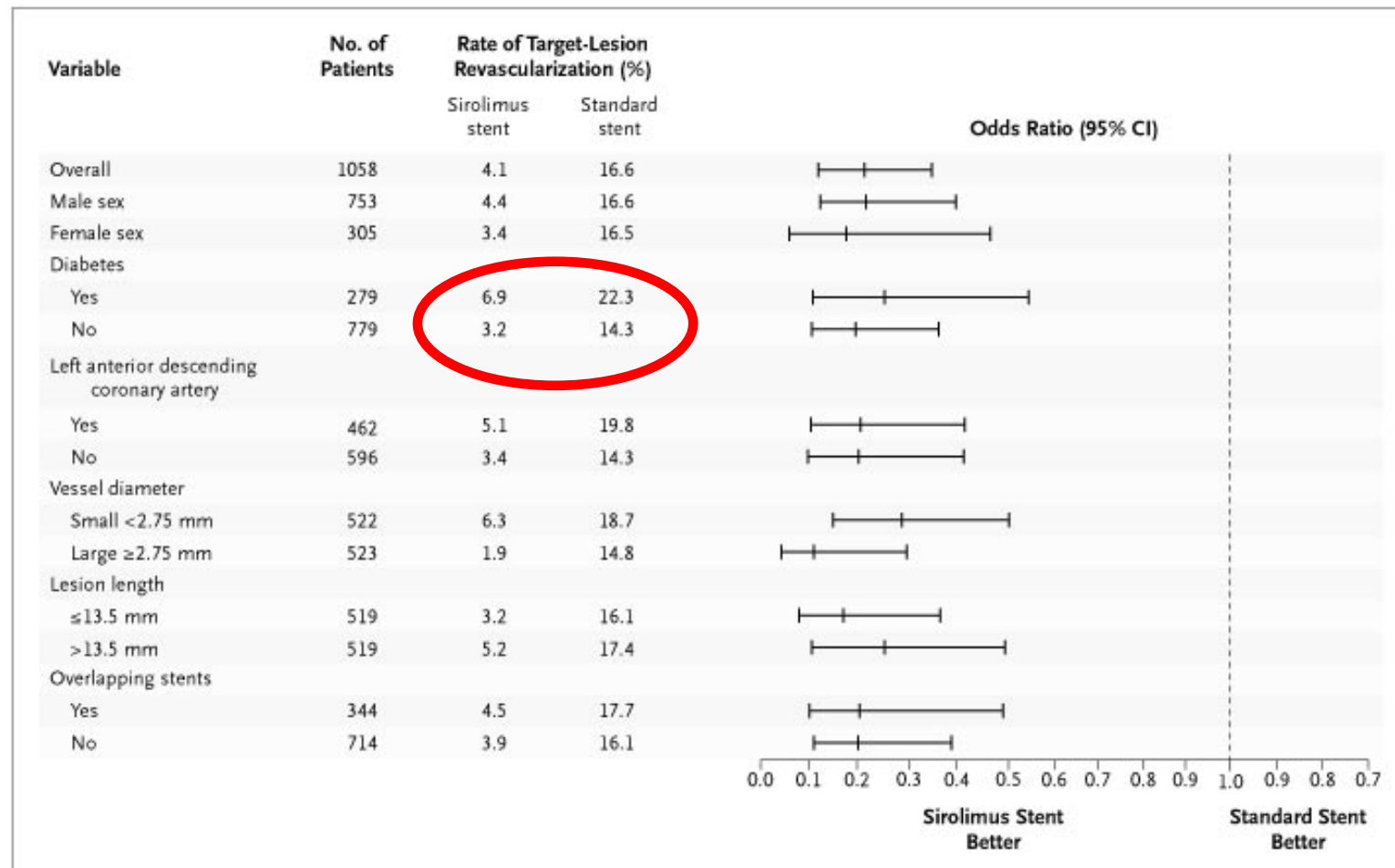
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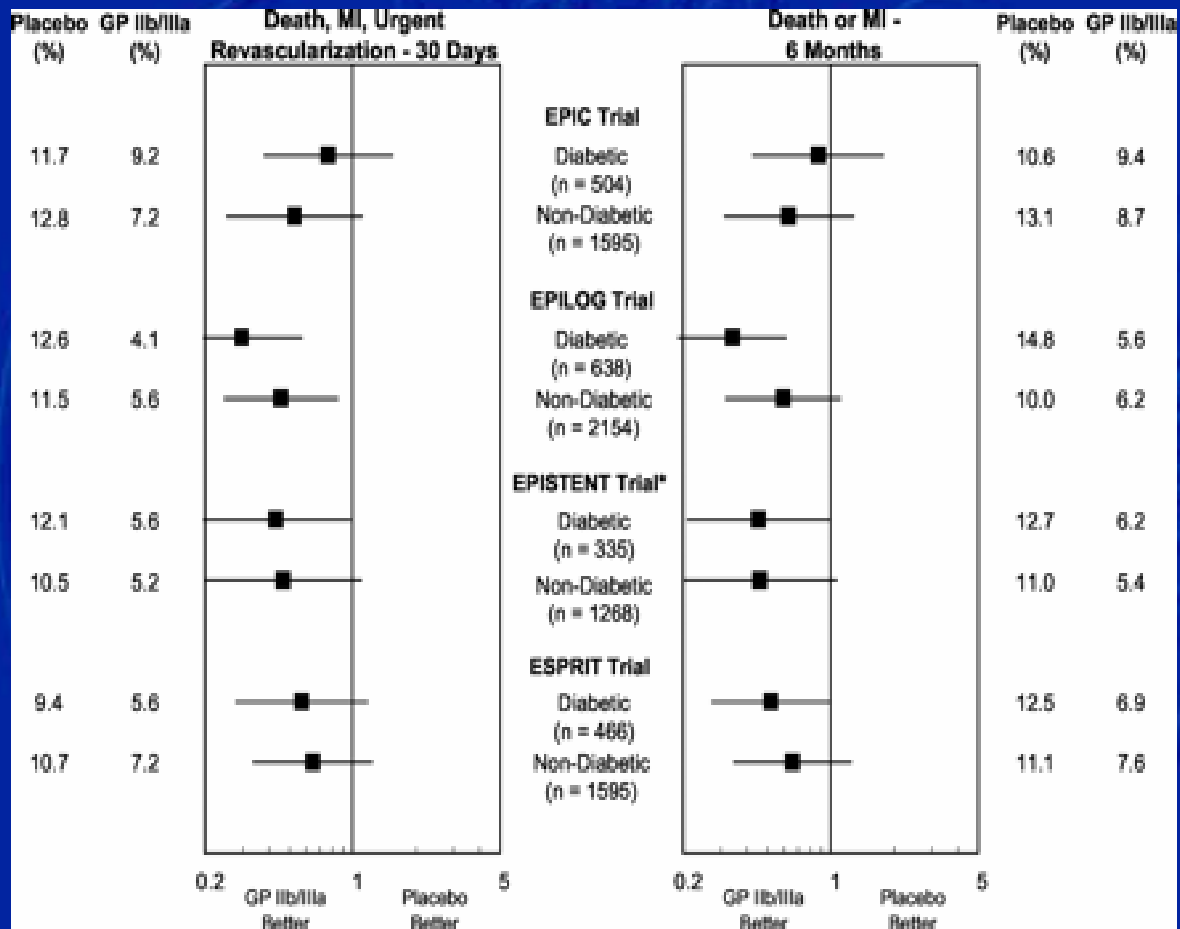
Benefits of Early Detection of CAD

- Implement more aggressive CHD prevention regimen
- Initiate anti-ischemic medications
- Identify patients who would benefit from revascularization
- Educate patients to recognize coronary symptoms

Rates of Target-Lesion Revascularization (Either Percutaneous Transluminal Coronary Angiography or Coronary-Artery Bypass Grafting) and Odds Ratios at 270 Days for Various Subgroups of Patients



Moses, J. et al. N Engl J Med 2003;349:1315-1323



CDA Guidelines

Cardiorenal Prioritization

1. Vascular Protection



In all patients

2. Hypertension Control

3. Control of Nephropathy

1. ASA
2. Lipid Control (statin)
3. ACE inhibitor
4. BP Control
5. Also as required:
 - Glycaemic control
 - Lifestyle
 - Smoking cessation

Steno 2: Event Reduction

