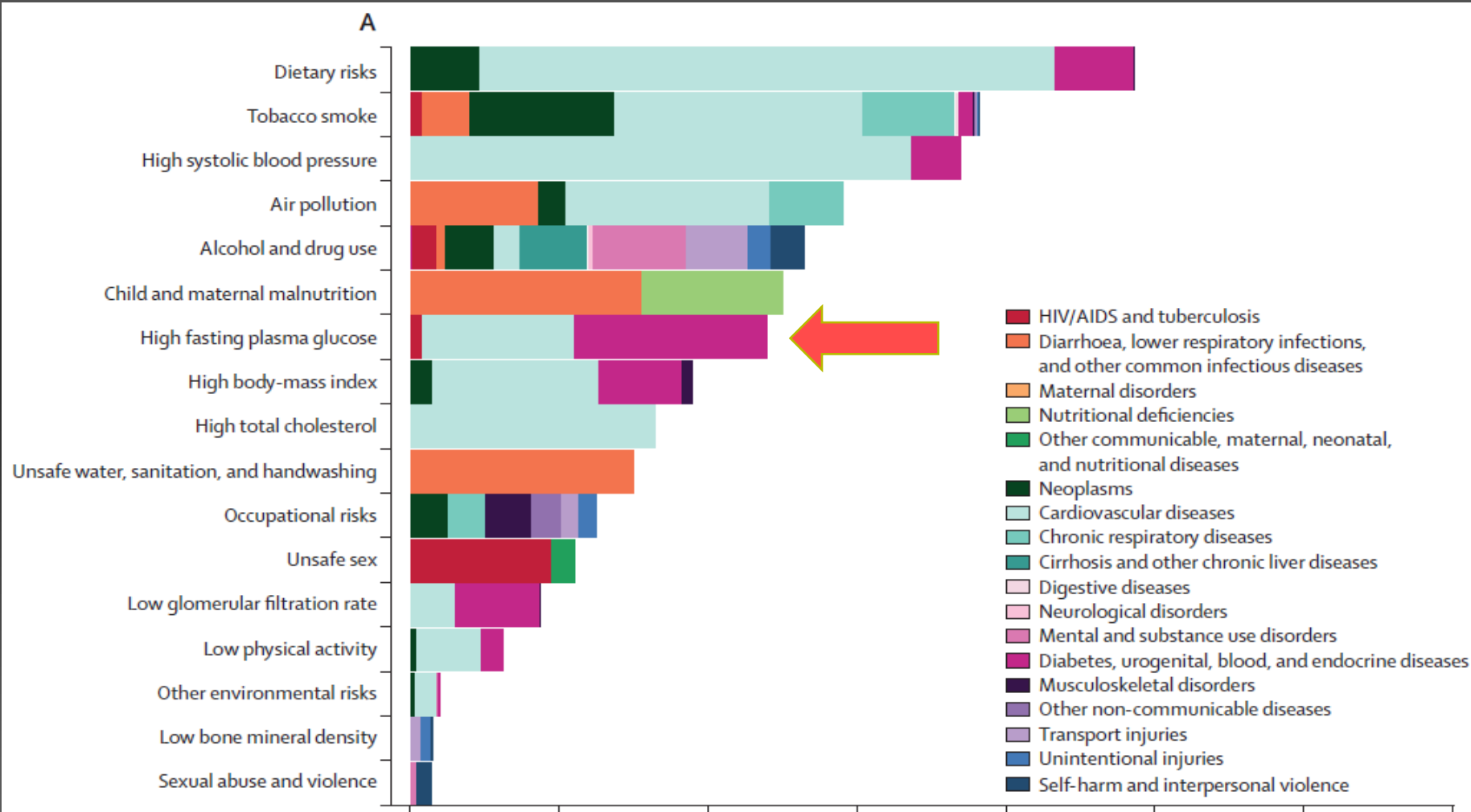


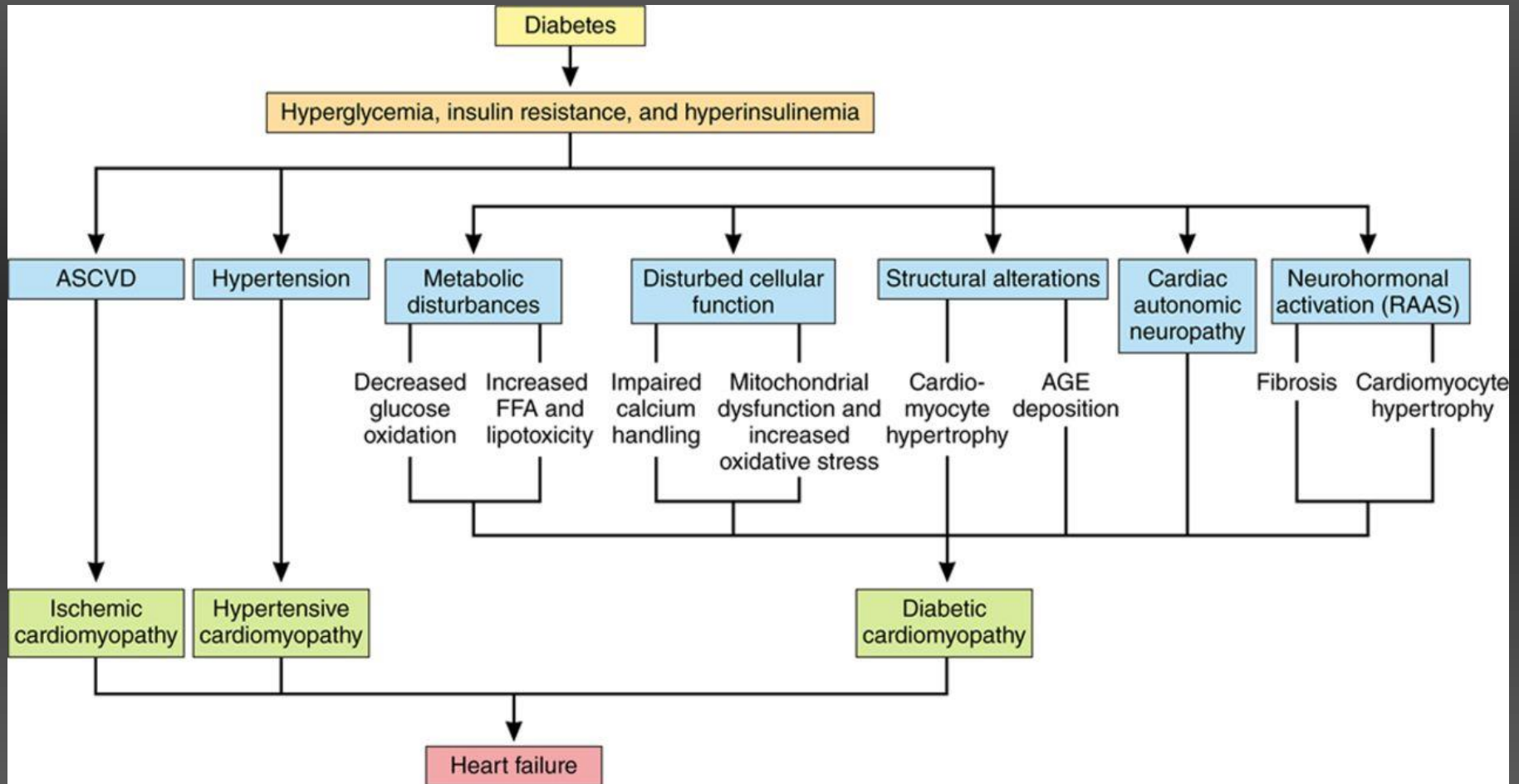
# Maladie coronaire du diabétique

**Y. Cottin (Dijon - FR)**

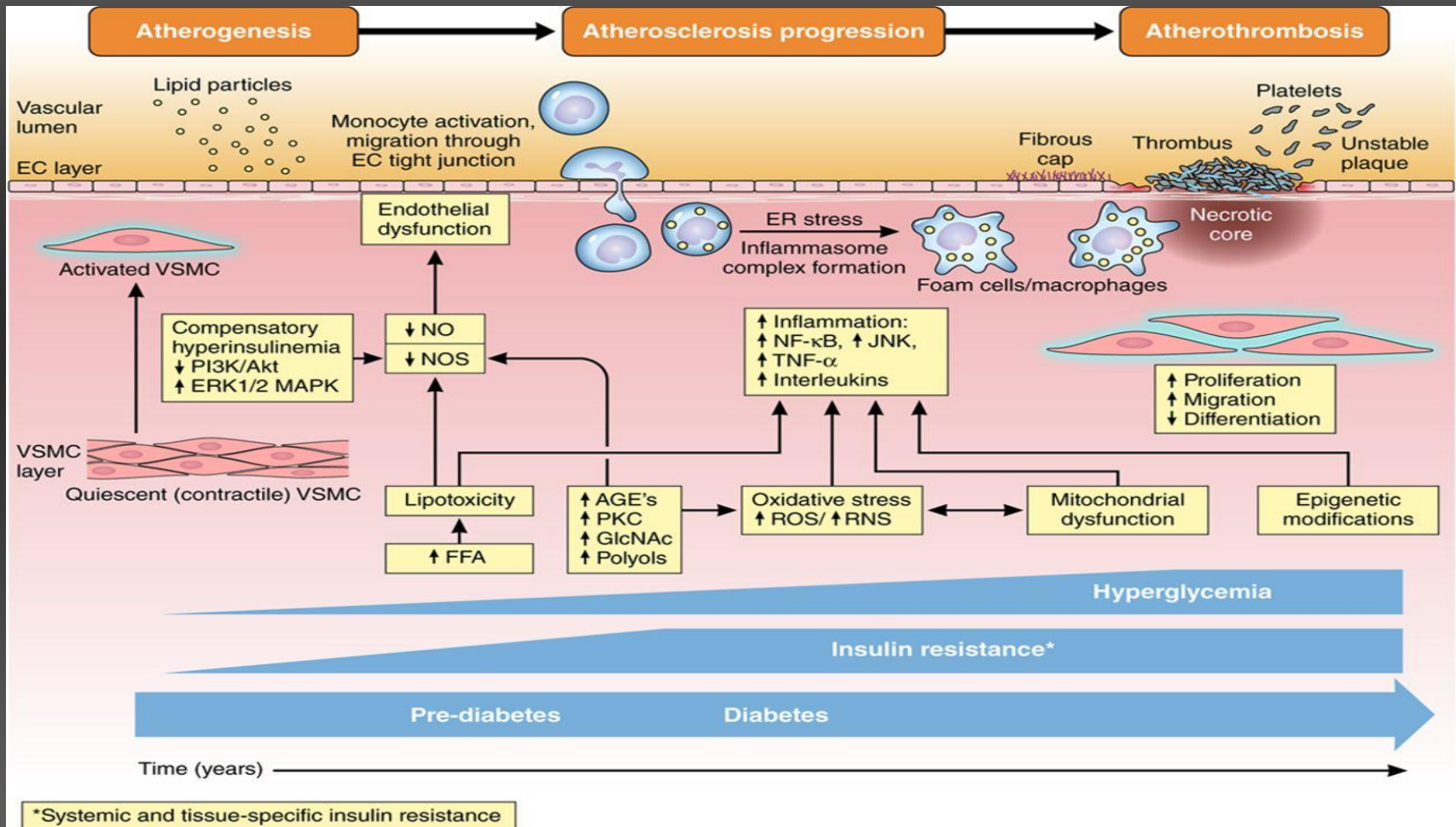
# Global, regional, and national comparative risk assessment of 79 behavioural, environmental and occupational, and metabolic risks or clusters of risks, 1990–2015: a systematic analysis for the Global Burden of Disease Study 2015



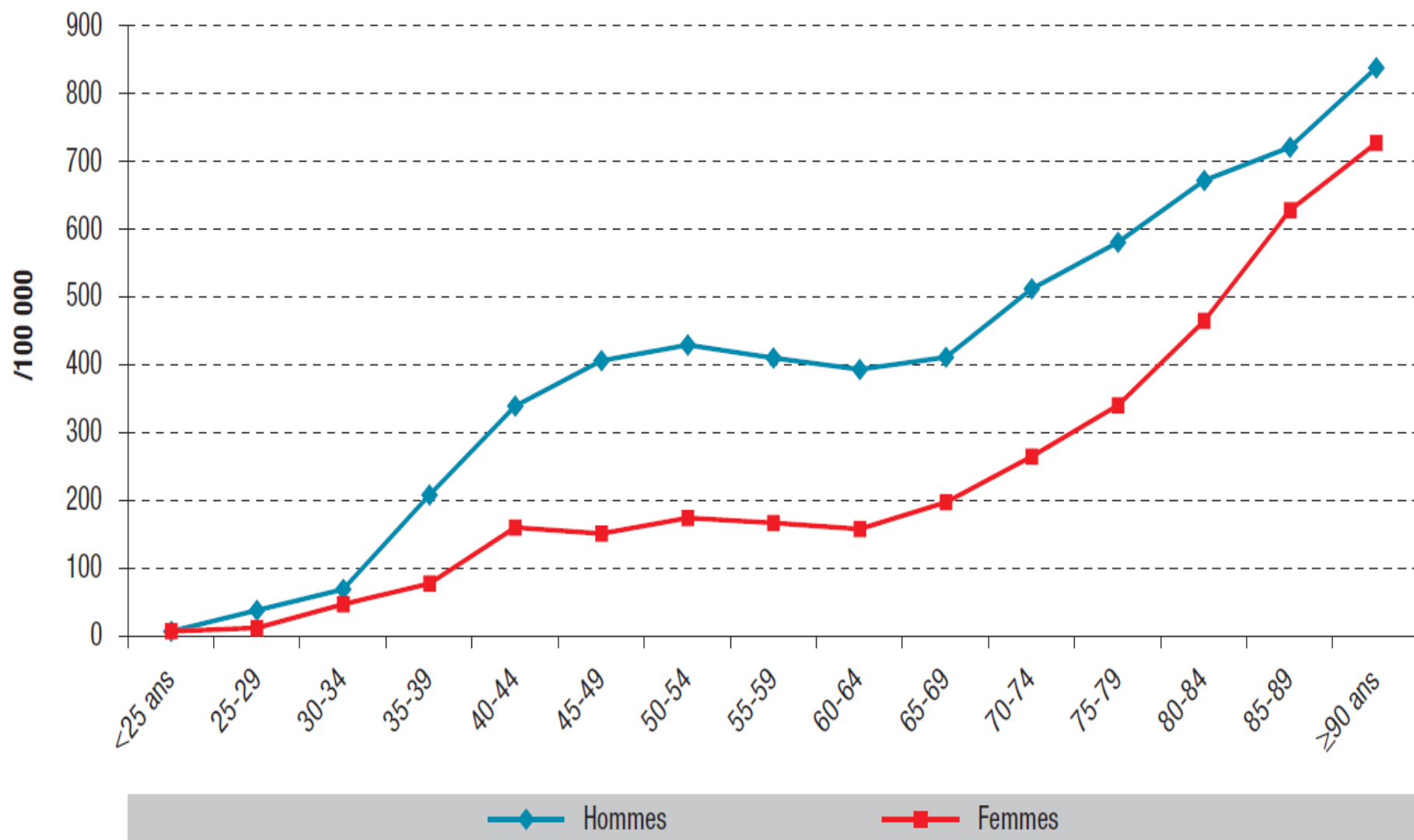
# Pathophysiologic mechanisms of heart failure in diabetes mellitus



# Clinical Update: Cardiovascular Disease in Diabetes Mellitus: Atherosclerotic Cardiovascular Disease and Heart Failure in Type 2 Diabetes Mellitus - Mechanisms, Management, and Clinical Considerations

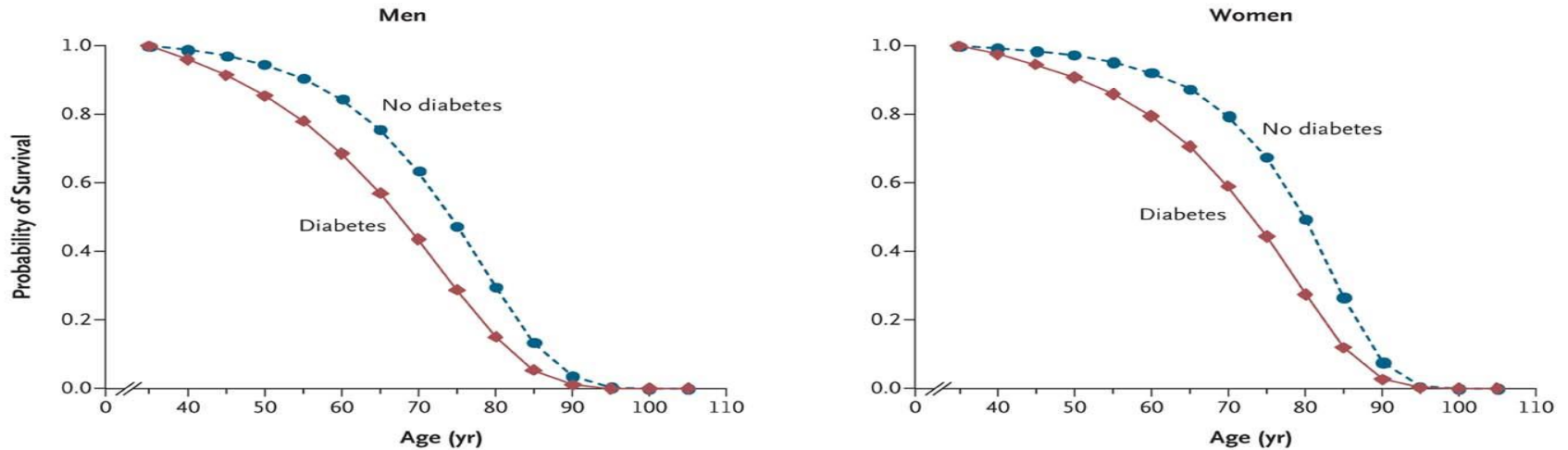


Taux de personnes diabétiques traitées pharmacologiquement hospitalisées pour infarctus du myocarde  
(pour 100 000 personnes diabétiques) selon le sexe et l'âge, France entière, 2013

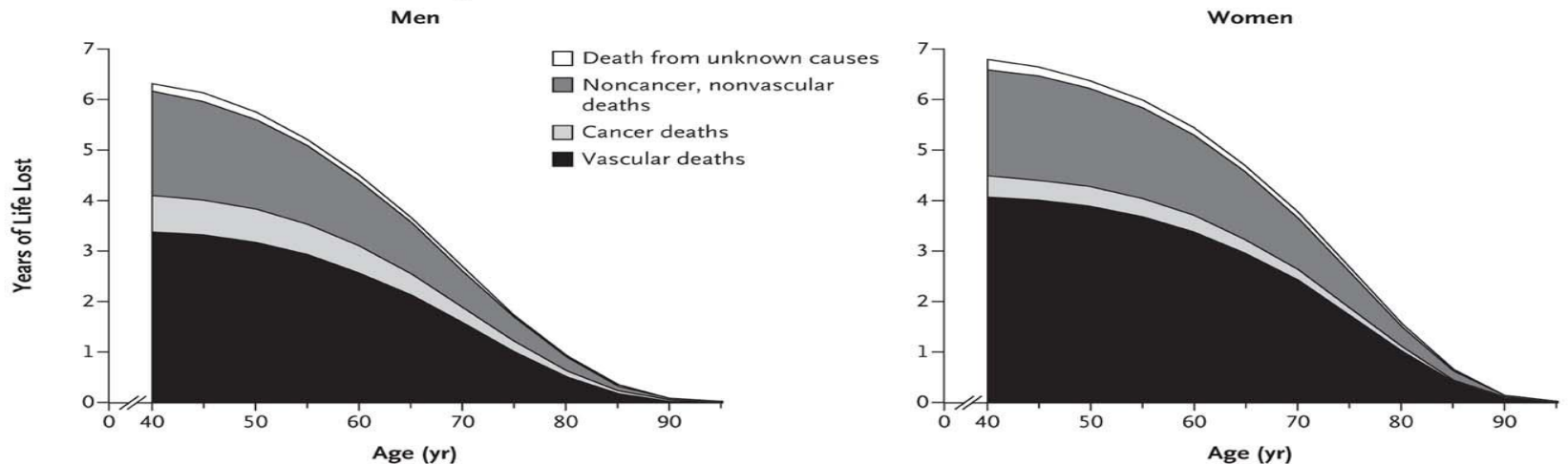


# Diabetes Mellitus, Fasting Glucose, and Risk of Cause-Specific Death

**A Estimated Survival**

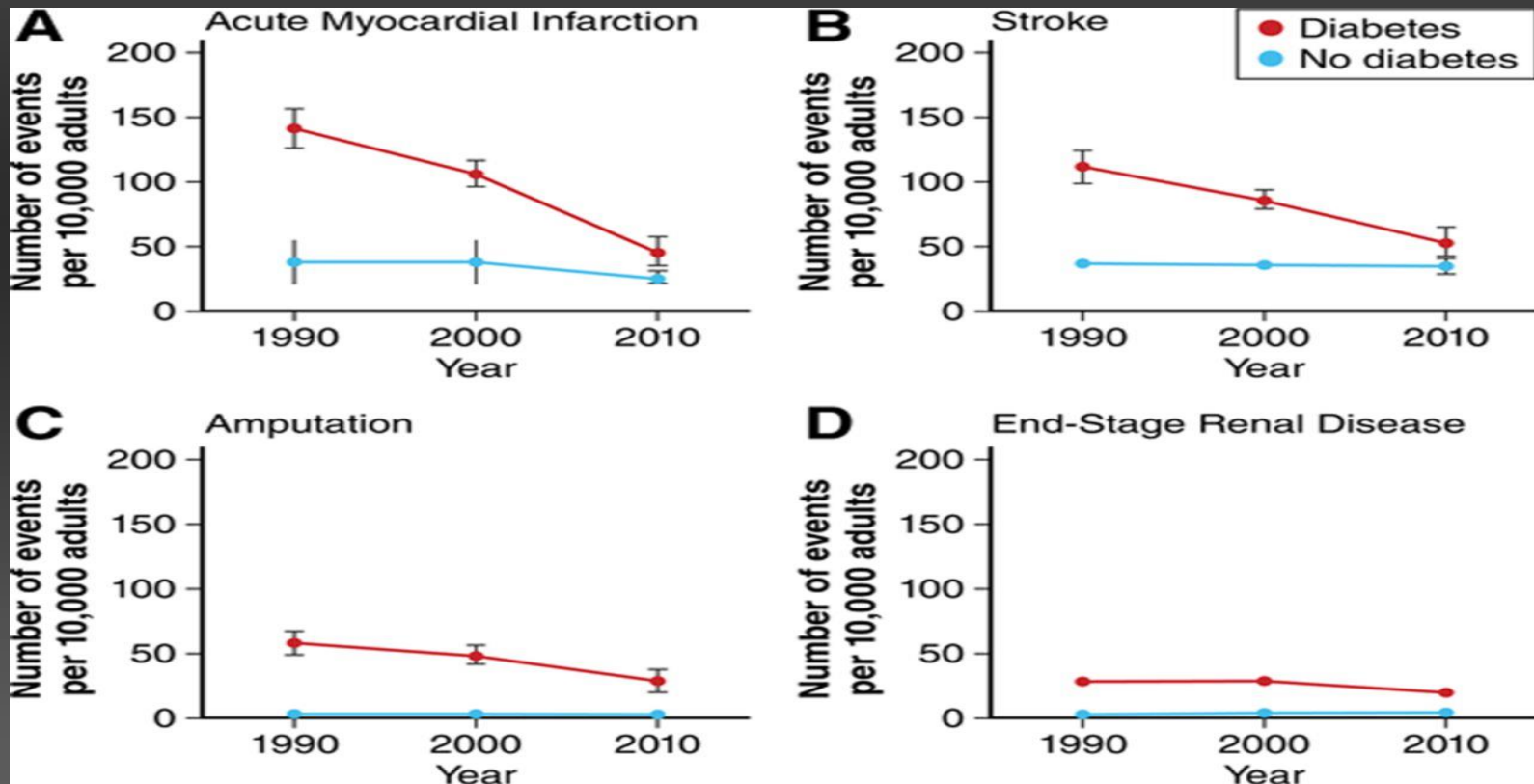


**B Estimated Future Years of Life Lost Owing to Diabetes**



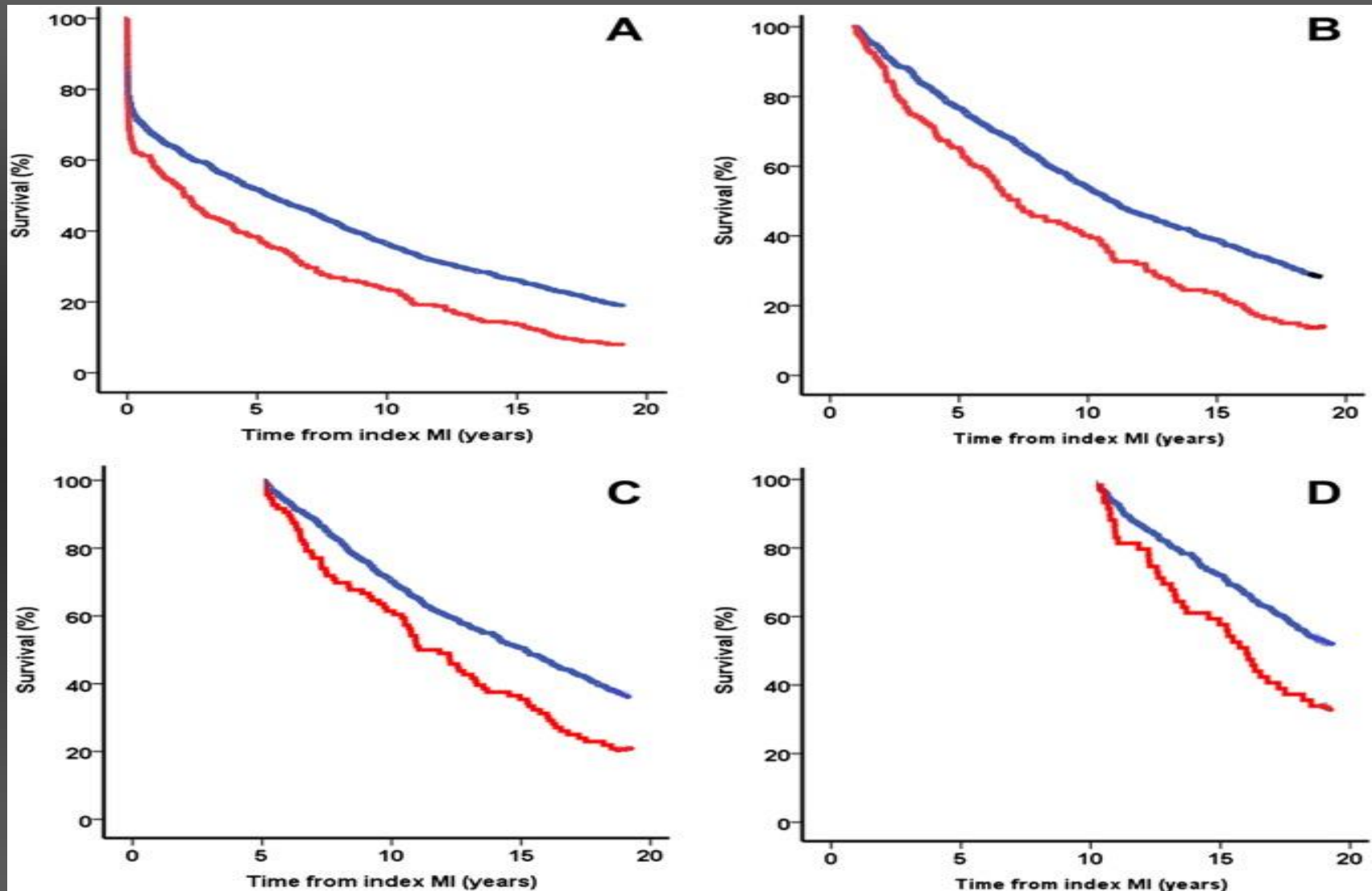
# Clinical Update: Cardiovascular Disease in Diabetes Mellitus: Atherosclerotic Cardiovascular Disease and Heart Failure in Type 2 Diabetes Mellitus - Mechanisms, Management, and Clinical Considerations

Rates of vascular diseases are decreasing in persons with diabetes mellitus but are still higher than in persons without diabetes mellitus: 20 years of surveillance.





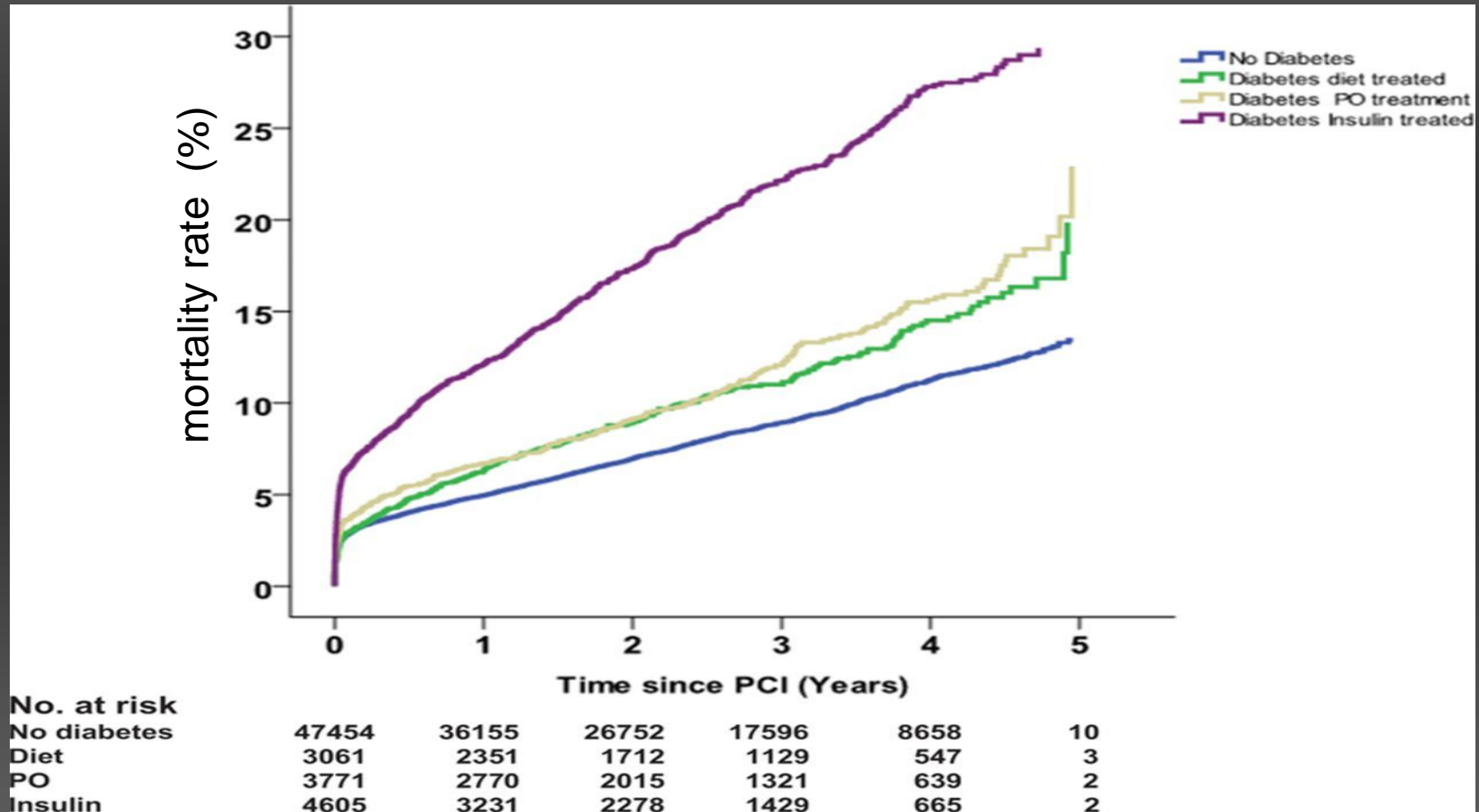
# An evaluation of 20 year survival in patients with diabetes mellitus and acute myocardial infarction



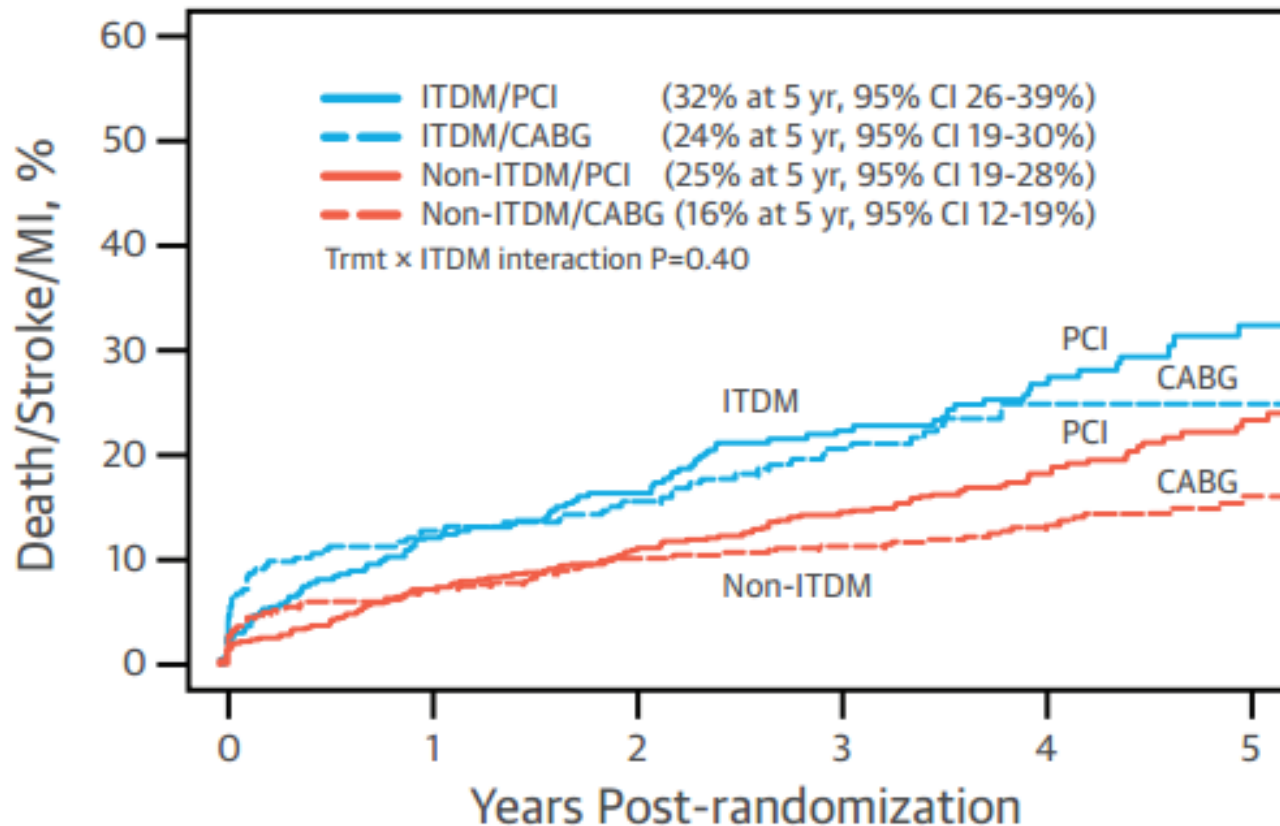


# High Event Rate After a First Percutaneous Coronary Intervention in Patients With Diabetes Mellitus

## Results From the Swedish Coronary Angiography and Angioplasty Registry

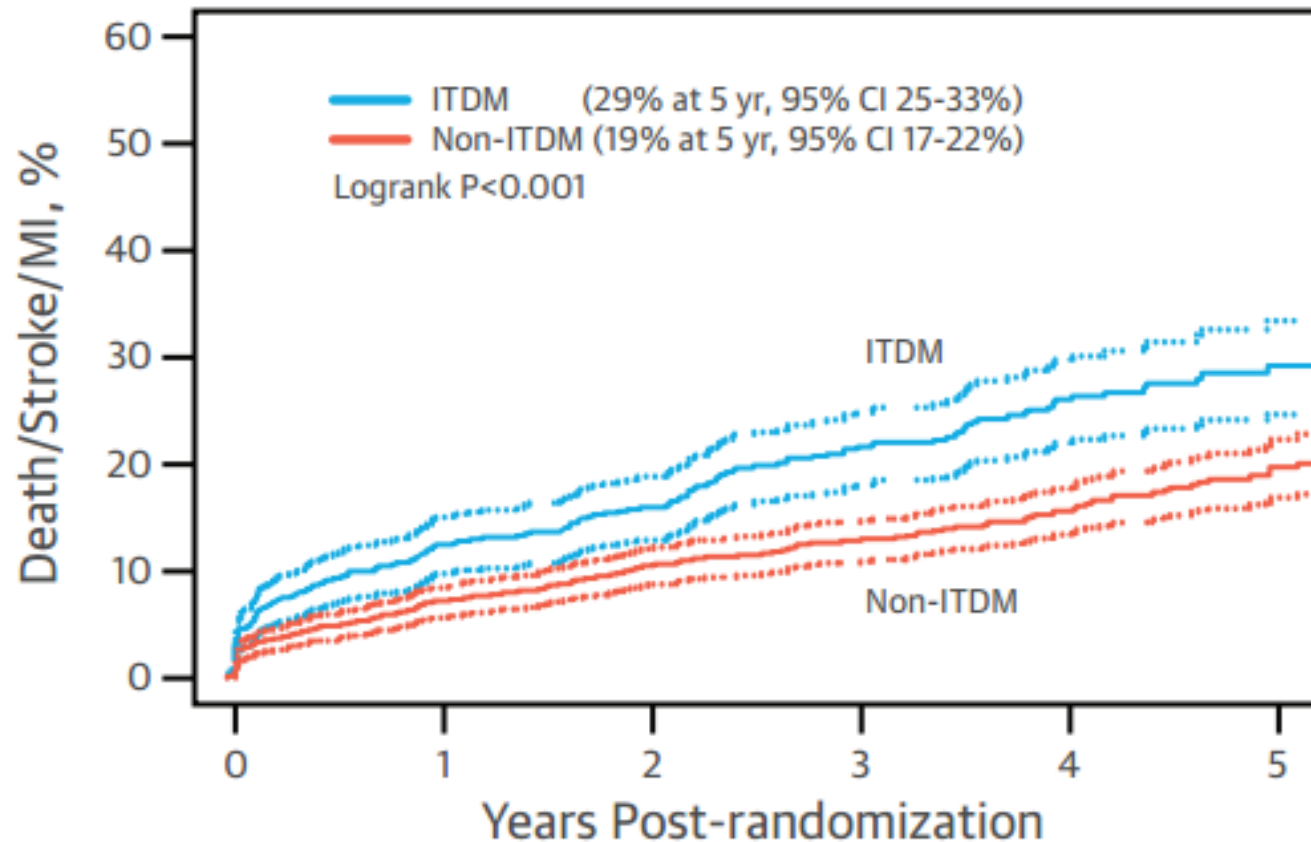


## Long-term outcome of PCI versus CABG in insulin and non-insulin-treated diabetic patients: results from the FREEDOM trial



Non-ITDM/PCI N	629	573	530	412	264	137
Non-ITDM/CABG N	653	574	532	436	302	143
ITDM/PCI N	322	274	241	191	129	58
ITDM/CABG N	293	239	214	163	101	57

## Long-term outcome of PCI versus CABG in insulin and non-insulin-treated diabetic patients: results from the FREEDOM trial



ITDM N	602	512	447	342	221	103
Non-ITDM N	1248	1138	1043	819	537	248

# Long-term outcome of PCI versus CABG in insulin and non-insulin-treated diabetic patients: results from the FREEDOM trial

**TABLE 5** 5-Year Kaplan-Meier Estimated Event Rates for the Primary Endpoint (Death/Stroke/MI)

Group*	Non-ITDM			ITDM			Treatment × Insulin Interaction p Value
	PCI	CABG	PCI vs. CABG	PCI	CABG	PCI vs. CABG	
SYNTAX ≤22 (208, 231, 123, 93)	19.7 (13.0-24.4)	14.1 (9.5-20.75)	1.18 (0.71-1.96)	29.7 (20.2-42.3)	26.3 (17.7-38.0)	0.84 (0.47-1.48)	0.39
SYNTAX 23-32 (305, 255, 138, 129)	23.1 (17.8-29.7)	14.3 (10.1-20.0)	1.61 (1.04-2.49)	35.5 (26.8-46.0)	21.8 (15.2-30.7)	1.56 (0.95-2.57)	0.93
SYNTAX ≥33 (114, 125, 64, 54)	30.4 (20.9-42.8)	20.0 (12.8-30.4)	1.58 (0.88-2.81)	28.9 (19.3-42.0)	25.9 (15.3-41.9)	1.27 (0.61-2.64)	0.65

Values are HR (95% CI). The 95% CI and HR are based on adjudicated events for the primary endpoint (death/stroke/MI) using all available follow-up and interaction p value for treatment by insulin dependency status, at each level of angiographic complexity. p Values were derived from Cox regression test of treatment × subgroup interaction using all available follow-up data (i.e., >5 years). \*Numbers in parentheses indicate PCI n, CABG n for each stratum.

# Coronary Thrombosis and Major Bleeding After PCI With Drug-Eluting Stents. Risk Scores From PARIS

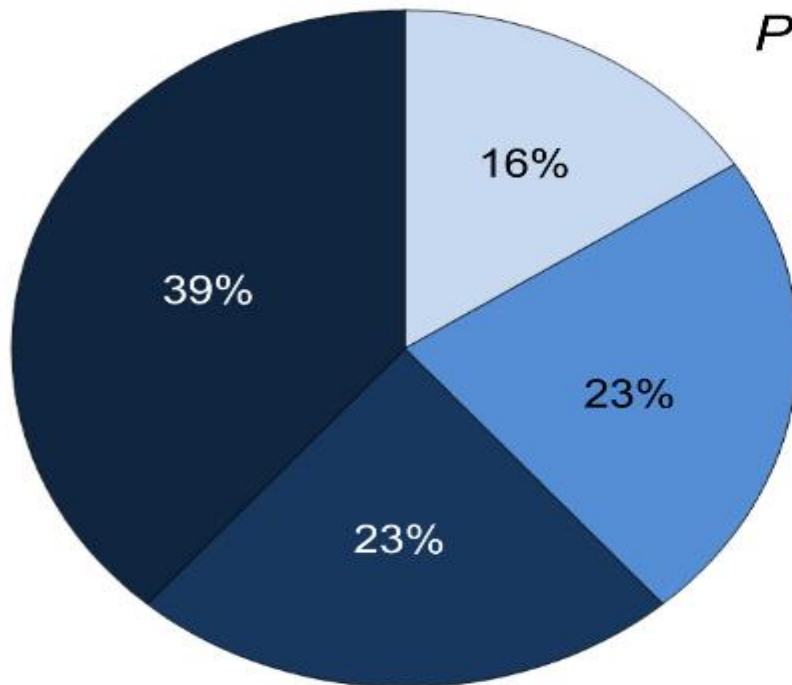
<b>TABLE 4 Integer Risk Score for Major Bleeding</b>	
Parameter	Score
Age, yrs	
<50	0
50–59	+1
60–69	+2
70–79	+3
≥80	+4
BMI, kg/m <sup>2</sup>	
<25	+2
25–34.9	0
≥35	+2
Current smoking	
Yes	+2
No	0
Anemia	
Present	+3
Absent	0
CrCl <60 ml/min	
Present	+2
Absent	0
Triple therapy on discharge	
Yes	+2
No	0
Abbreviations as in <a href="#">Table 1</a> .	

<b>TABLE 5 Integer Risk Score for Coronary Thrombotic Events</b>	
Parameter	Score
Diabetes mellitus	
None	0
Non-insulin-dependent	+1
Insulin-dependent	+3
Acute coronary syndrome	
No	0
Yes, Tn-negative	+1
Yes, Tn-positive	+2
Current smoking	
Yes	+1
No	0
CrCl <60 ml/min	
Present	+2
Absent	0
Prior PCI	
Yes	+2
No	0
Prior CABG	
Yes	+2
No	0
Tn – troponin; other abbreviations as in <a href="#">Table 1</a> .	

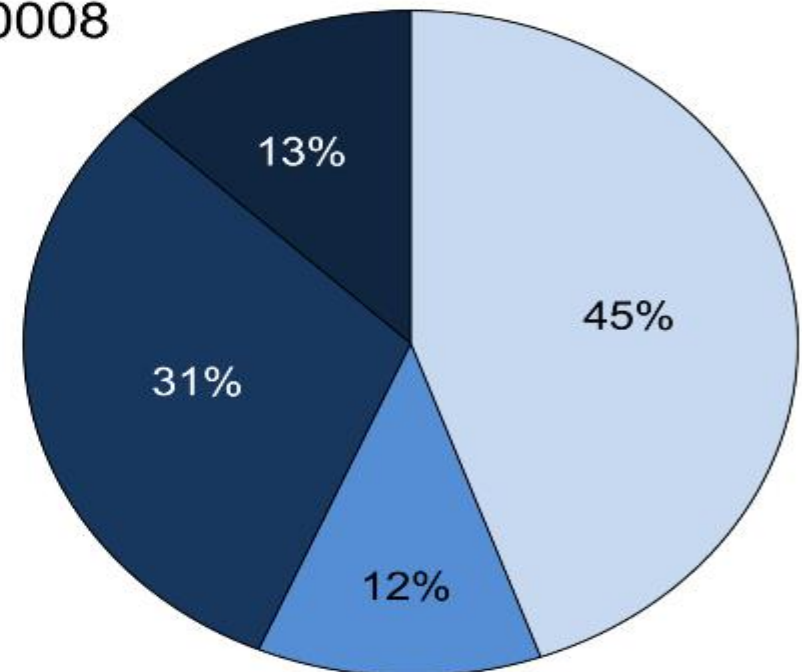
# Pathology of Human Coronary and Carotid Artery Atherosclerosis and Vascular Calcification in Diabetes Mellitus

142 sudden coronary death cases

Type 2 Diabetes



Non-diabetes

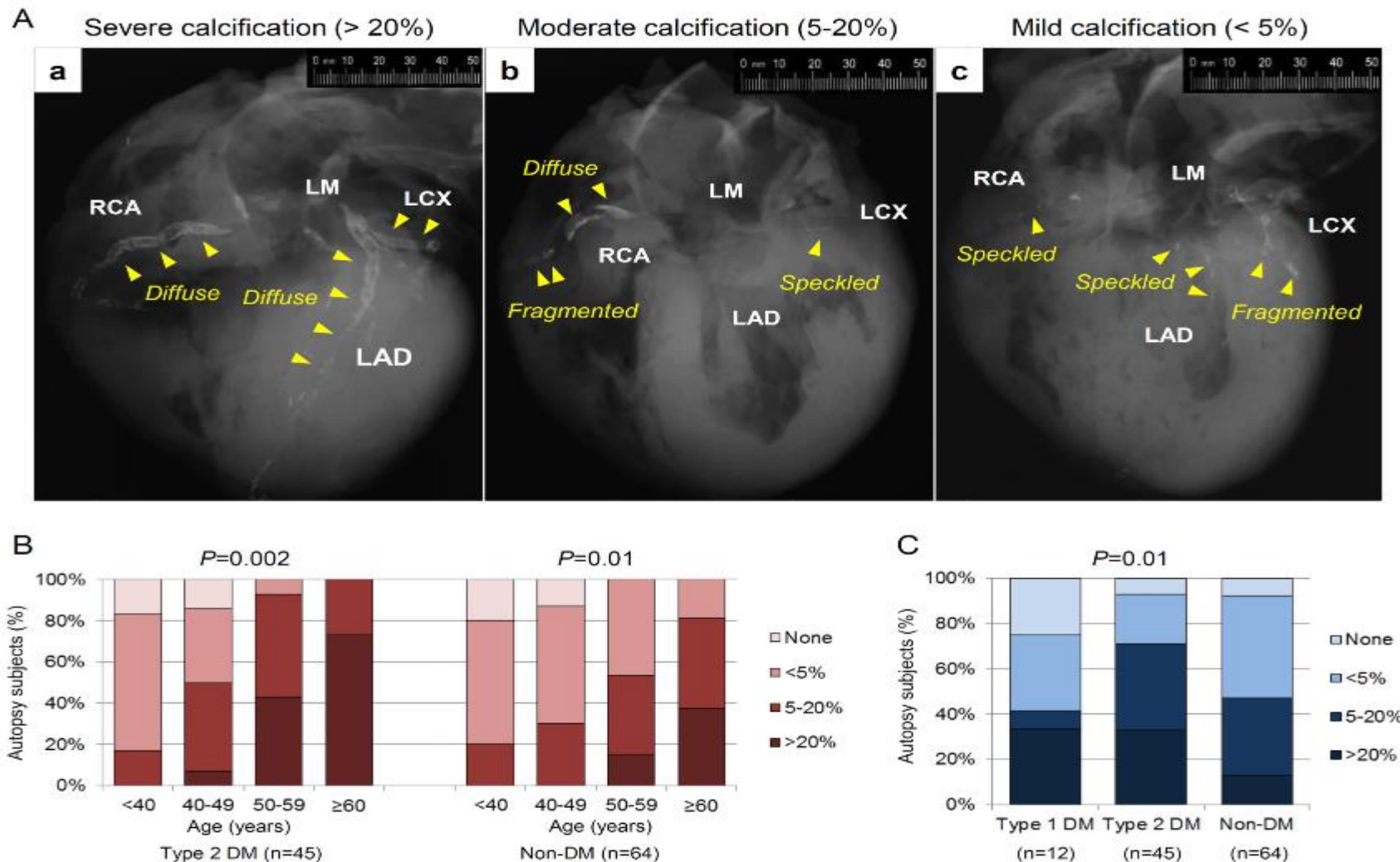


$P=0.0008$

□ None    ■ 1 healed rupture    ■ 2 healed ruptures    ■ ≥3 healed ruptures

# Pathology of Human Coronary and Carotid Artery Atherosclerosis and Vascular Calcification in Diabetes Mellitus

142 sudden coronary death cases

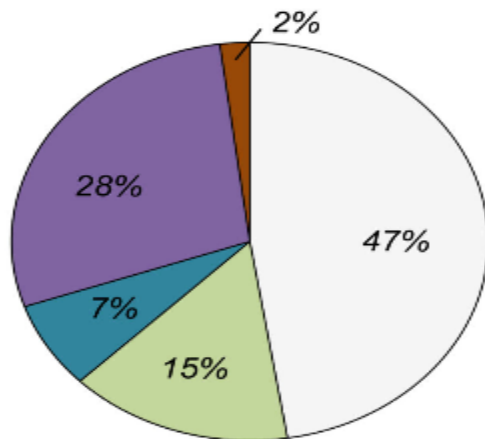




# Pathology of Human Coronary and Carotid Artery Atherosclerosis and Vascular Calcification in Diabetes Mellitus

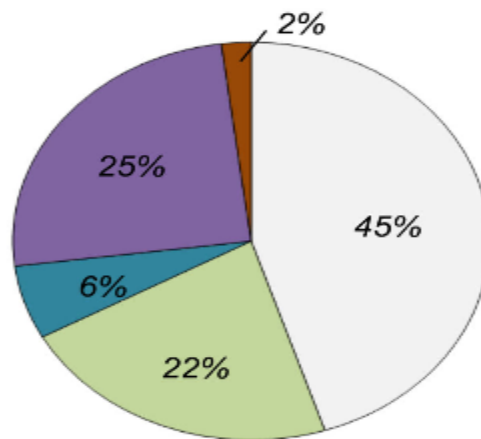
## Non-diabetes

HbA1c: <8%

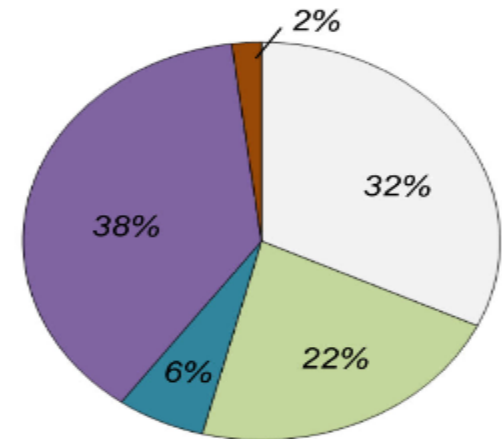


## Diabetes

HbA1c: 8 to <12%



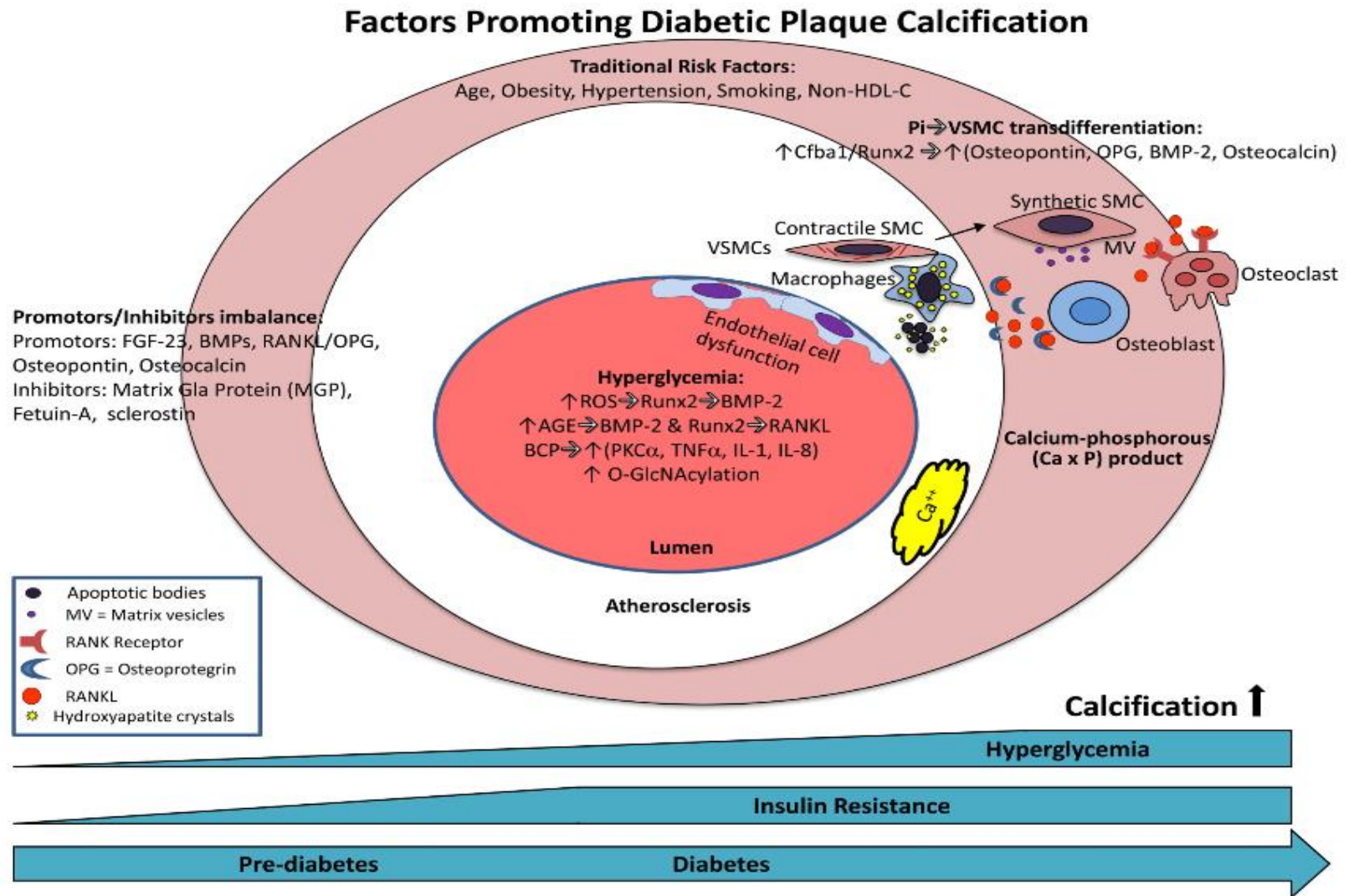
HbA1c: ≥12%



- No calcification
- Microcalcification
- Fragmented calcification
- Sheet calcification
- Nodular calcification

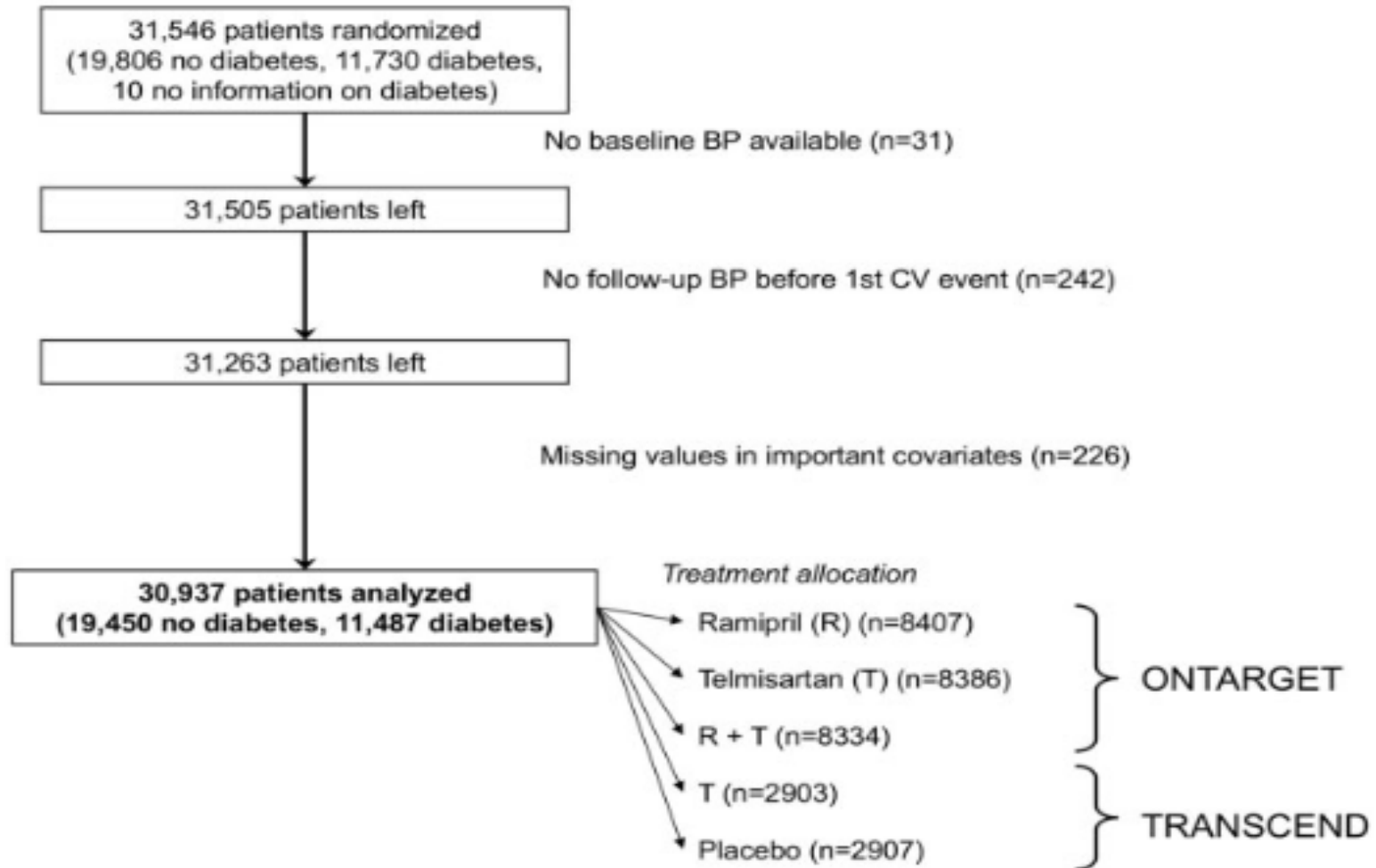
Type of calcification	<i>P</i> value
No calcification	<0.0001
Microcalcification	0.002
Fragmented calcification	0.53
Sheet calcification	0.0005
Nodular calcification	0.86

# Pathology of Human Coronary and Carotid Artery Atherosclerosis and Vascular Calcification in Diabetes Mellitus



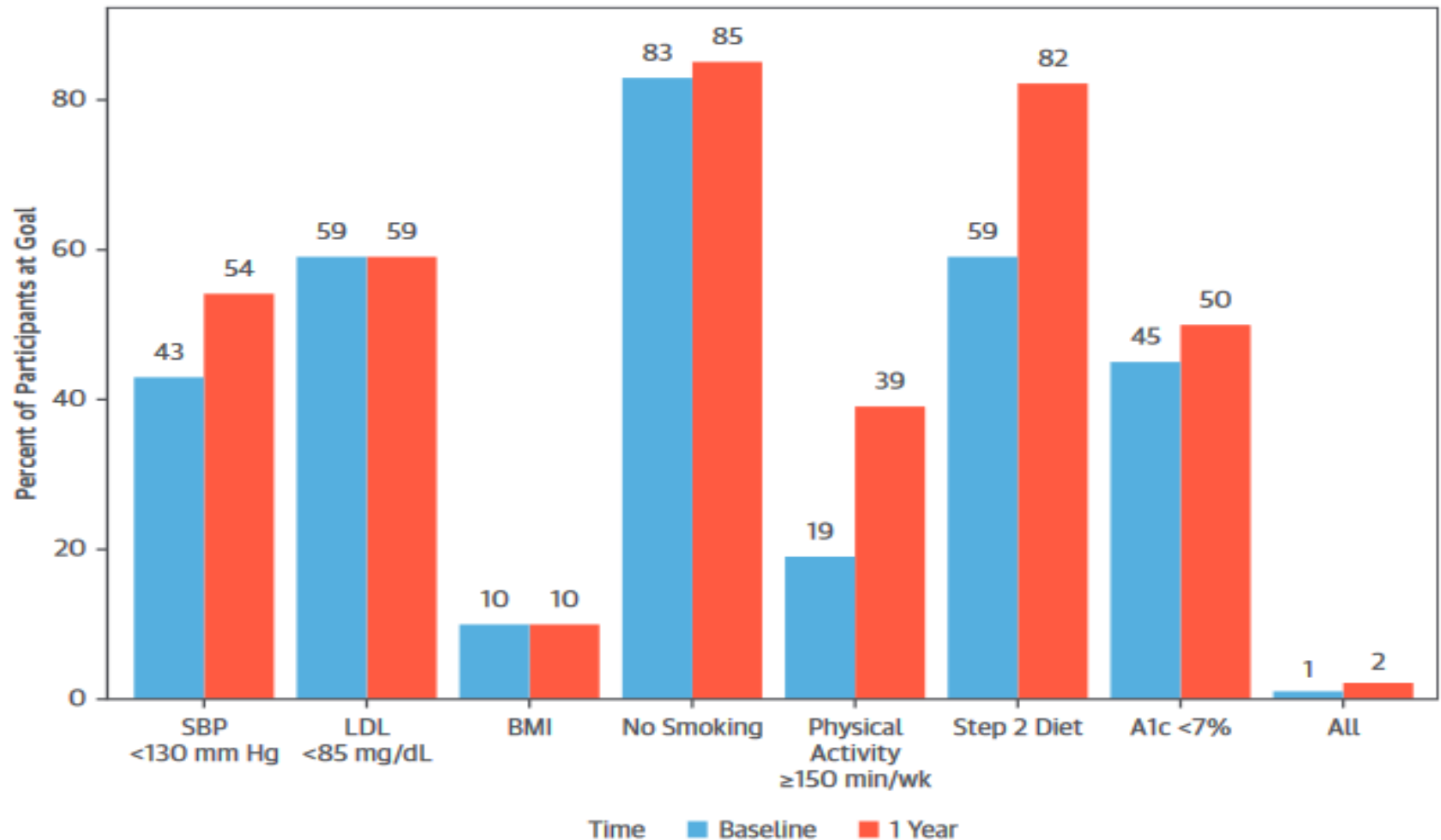
# Cardiovascular outcomes and achieved blood pressure in patients with and without diabetes at high cardiovascular risk

## Study Flow



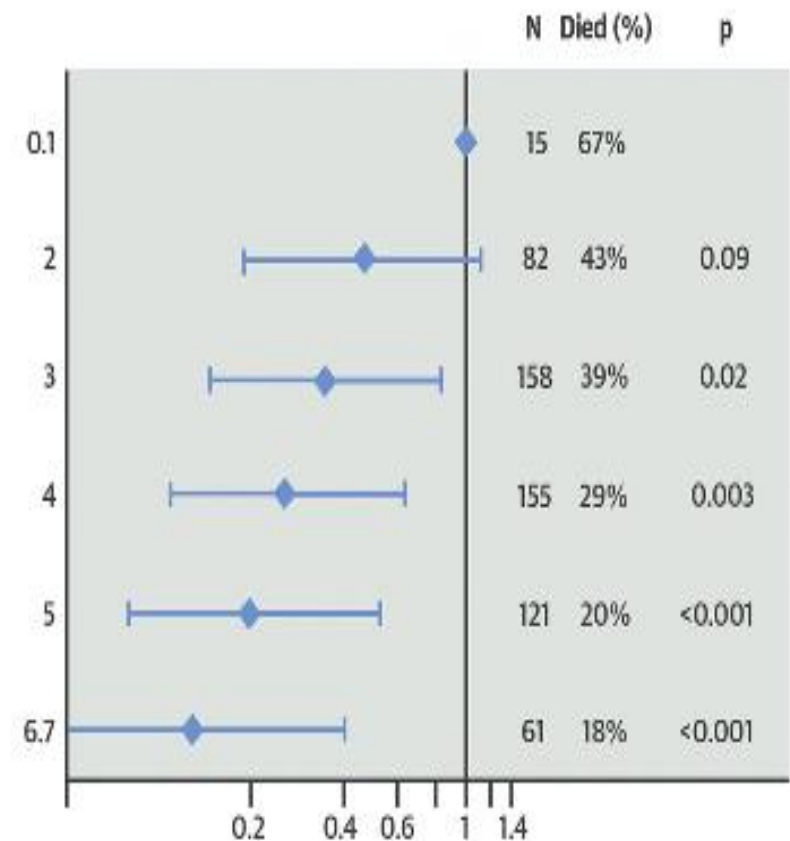
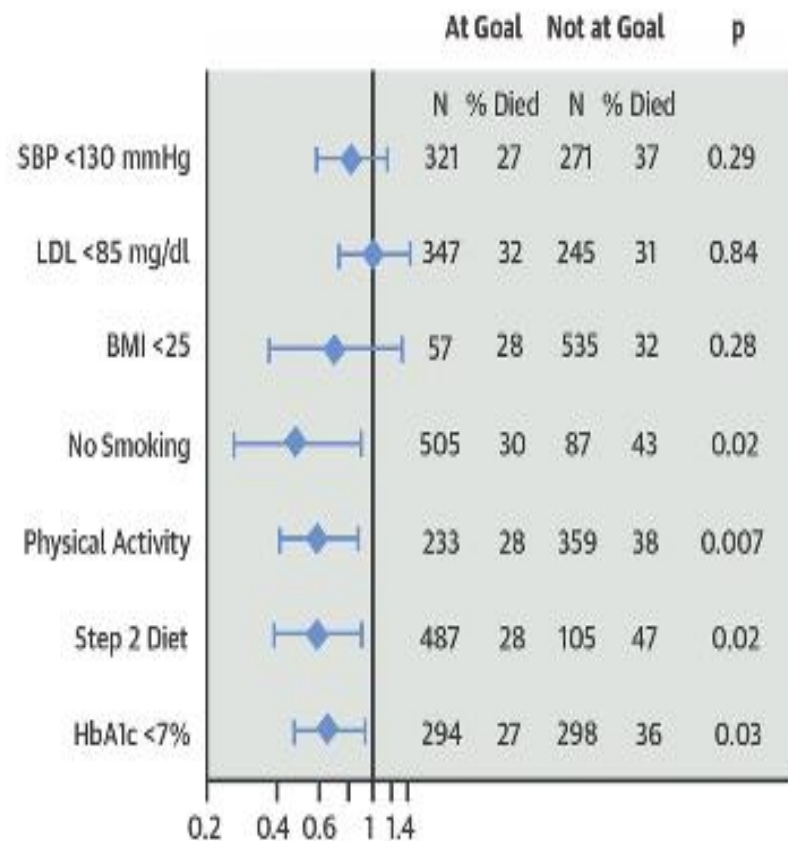
# Lifestyle, Glycosylated Hemoglobin A1c, and Survival Among Patients With Stable Ischemic Heart Disease and Diabetes

690 patients with DM followed in the COURAGE // a mean follow-up of  $7.0 \pm 4.2$  years



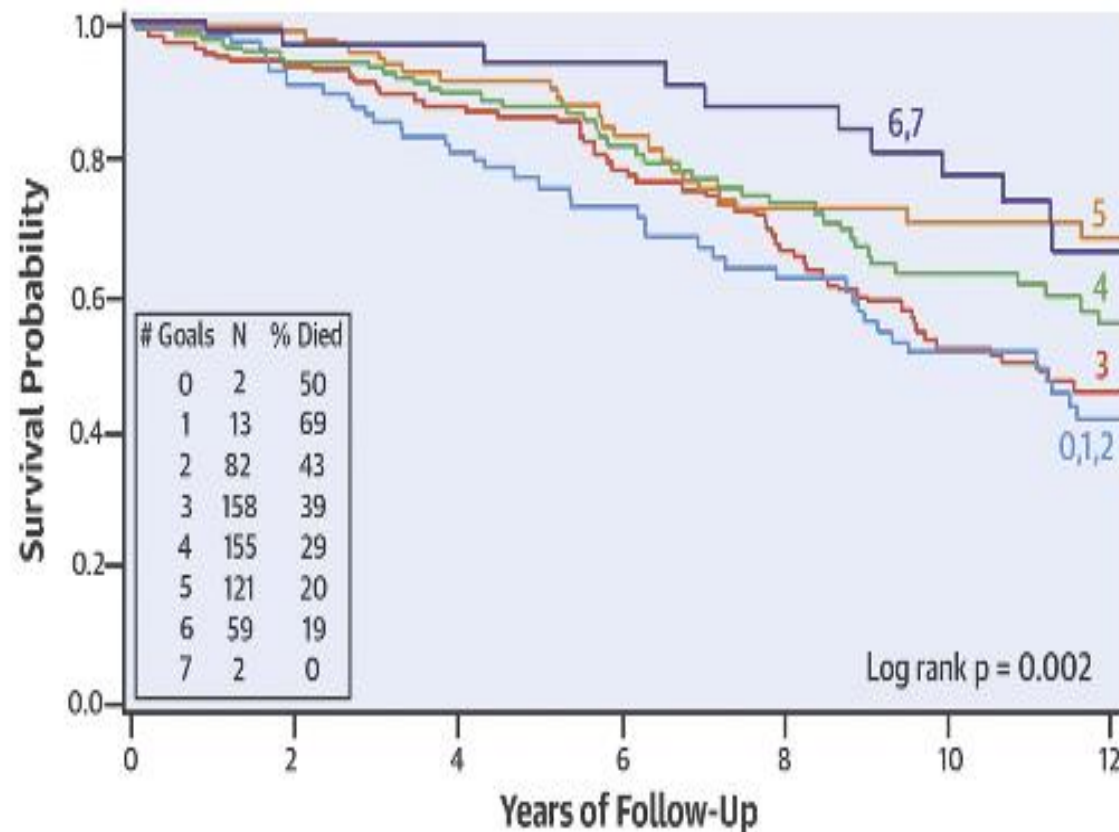
# Lifestyle, Glycosylated Hemoglobin A1c, and Survival Among Patients With Stable Ischemic Heart Disease and Diabetes

## Death Rate Associated With Achieving Individual and Number of Goals



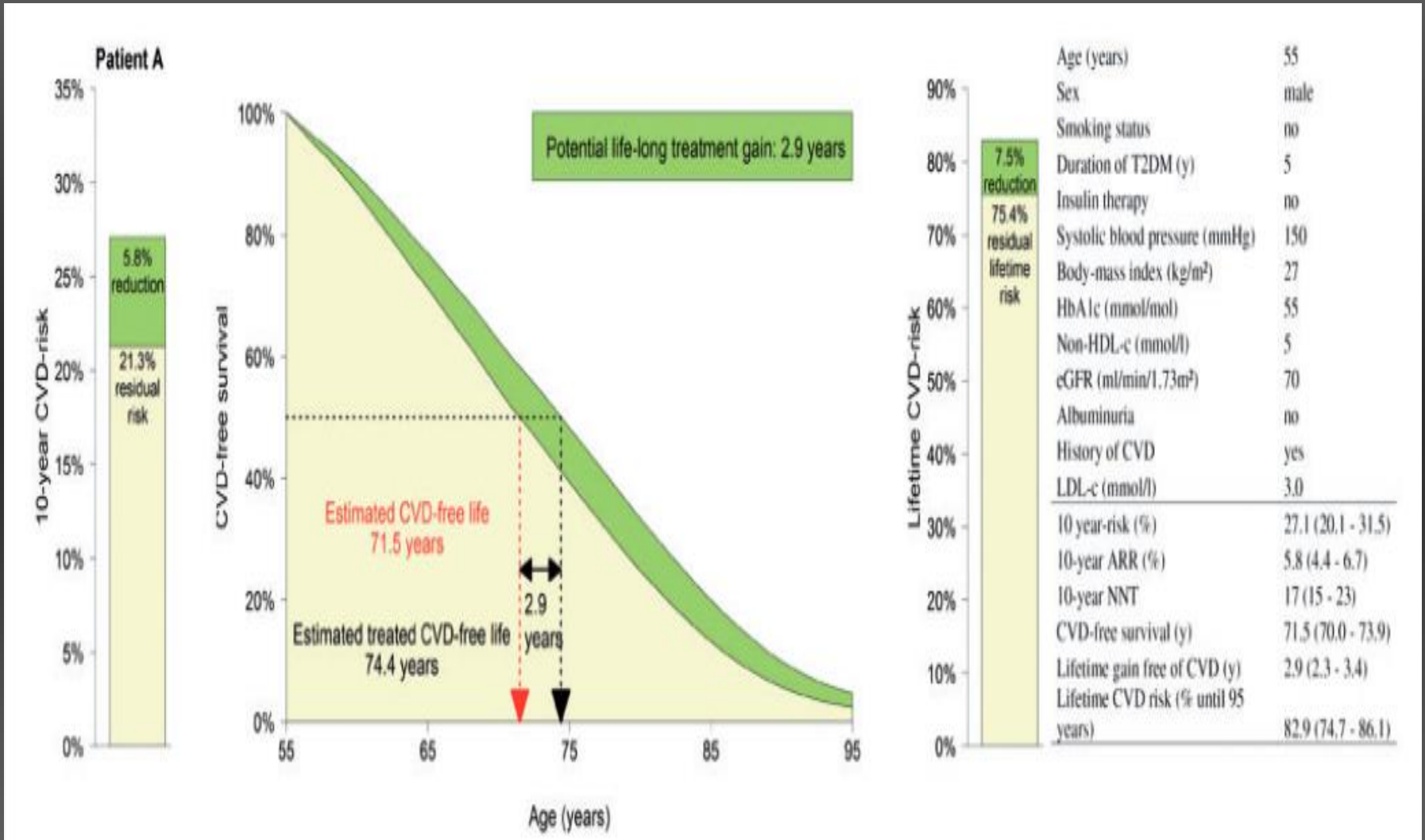
# Lifestyle, Glycosylated Hemoglobin A1c, and Survival Among Patients With Stable Ischemic Heart Disease and Diabetes

## Time to Death by Count of Goals Achieved





# Prediction of individual life-years gained without cardiovascular events from lipid, blood pressure, glucose, and aspirin treatment based on data of more than 500 000 patients with Type 2 diabetes mellitus





# Prediction of individual life-years gained without cardiovascular events from lipid, blood pressure, glucose, and aspirin treatment based on data of more than 500 000 patients with Type 2 diabetes mellitus

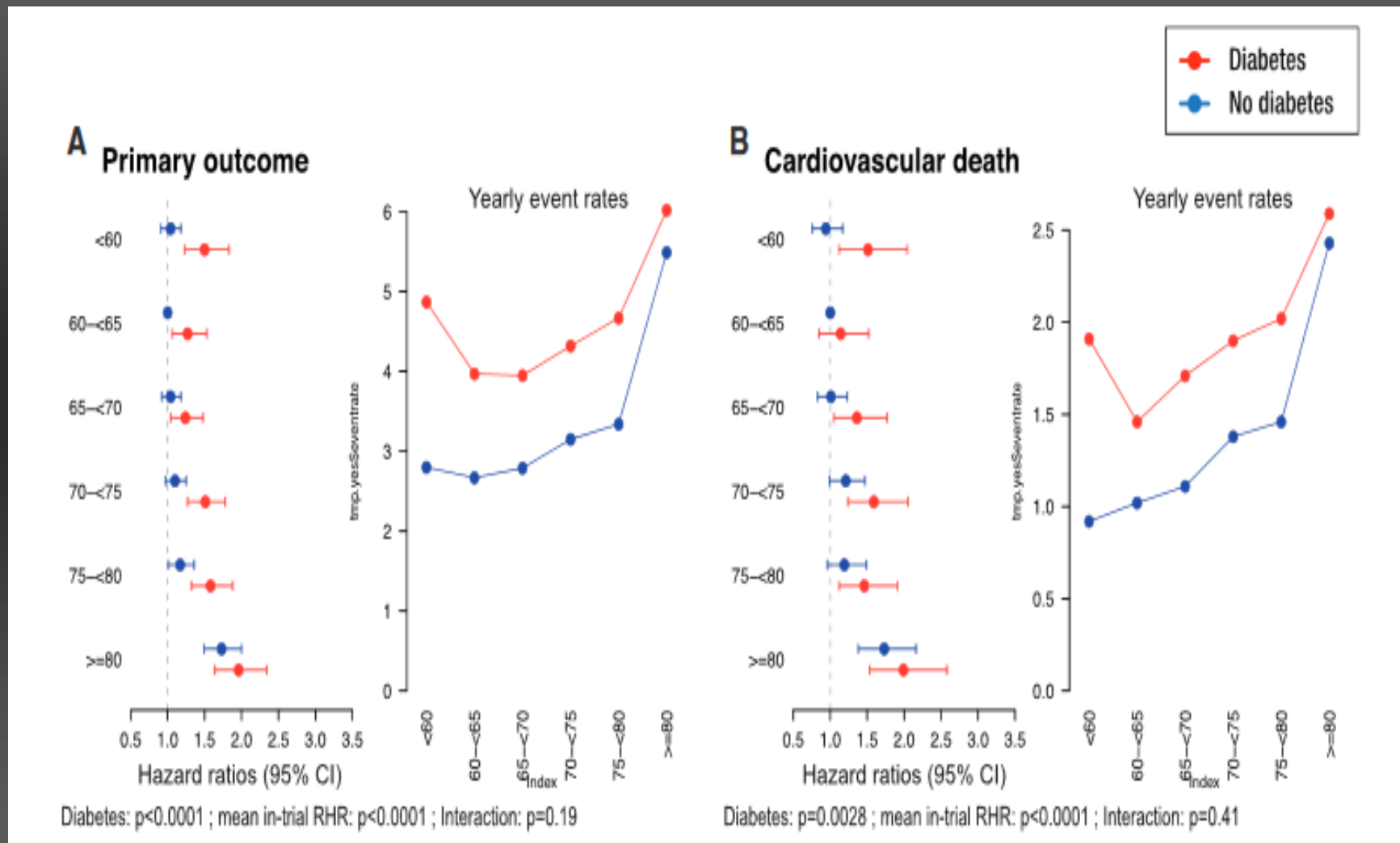
**Table 2** Hazard ratios derived from a multi-variable model used in the Diabetes Lifetime-perspective prediction model

	Cox proportional hazard function A (vascular events), HR (95% CI)	Cox proportional hazard function B (non-vascular mortality), HR (95% CI)
Male sex <sup>a</sup>	0.91 (0.88–0.94) <sup>a</sup>	0.89 (0.87–0.91) <sup>a</sup>
Current smoking <sup>a</sup>	1.04 (1.00–1.09) <sup>a</sup>	1.46 (1.43–1.50) <sup>a</sup>
Duration of T2DM (years)	1.02 (1.01–1.02)	1.01 (1.01–1.01)
Insulin therapy <sup>a</sup>	1.02 (0.98–1.06) <sup>a</sup>	1.04 (1.01–1.07) <sup>a</sup>
Systolic blood pressure (mmHg) <sup>b</sup>	1.06 (0.95–1.17) <sup>b</sup>	1.01 (0.93–1.10) <sup>b</sup>
Body mass index (kg/m <sup>2</sup> ) <sup>b</sup>	0.88 (0.81–0.97) <sup>b</sup>	0.89 (0.84–0.95) <sup>b</sup>
HbA1c (mmol/L) <sup>b</sup>	1.15 (1.05–1.26) <sup>b</sup>	1.00 (1.00–1.00)
Non-HDL-c (mmol/L) <sup>b</sup>	1.16 (1.10–1.23) <sup>b</sup>	0.96 (0.92–1.00) <sup>b</sup>
eGFR (mL/min/1.73 m <sup>2</sup> ) <sup>b</sup>	0.64 (0.60–0.69) <sup>b</sup>	0.99 (0.99–0.99)
Micro-albuminuria	1.18 (1.14–1.22)	1.17 (1.14–1.20)
Macro-albuminuria	1.23 (1.18–1.28)	1.24 (1.20–1.28)
History of cardiovascular disease	9.99 (9.63–10.36) <sup>a</sup>	0.25 (0.24–0.26) <sup>a</sup>

<sup>a</sup>Age-dependent variables. Hazard ratios are shown for the median age of 65 years.

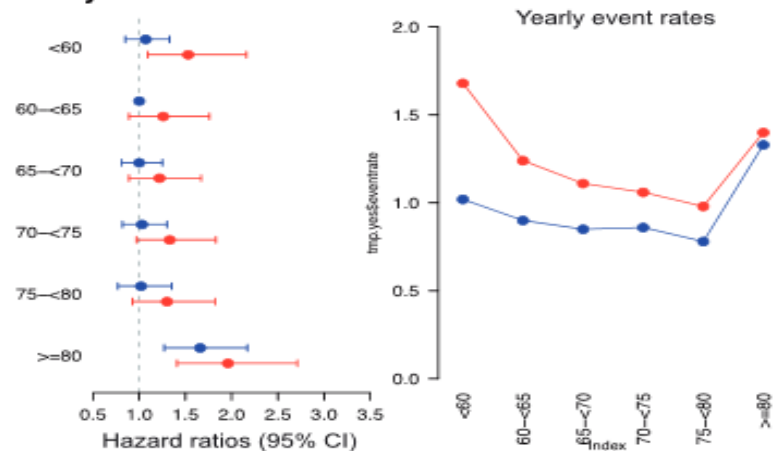
<sup>b</sup>Transformed variables. Hazard ratios are shown for the 75th percentile vs. the 25th percentile (systolic blood pressure: 150 mmHg vs. 128 mmHg; body mass index: 33 kg/m<sup>2</sup> vs. 26 kg/m<sup>2</sup>; HbA1c: 59 mmol/L vs. 44 mmol/L; eGFR: 96 mL/min vs. 68 mL/min; and non-HDL-c: 4.5 mmol/L vs. 3.0 mmol/L).

# Resting heart rate and cardiovascular outcomes in diabetic and non-diabetic individuals at high cardiovascular risk analysis from the ONTARGET/TRANSCEND trials

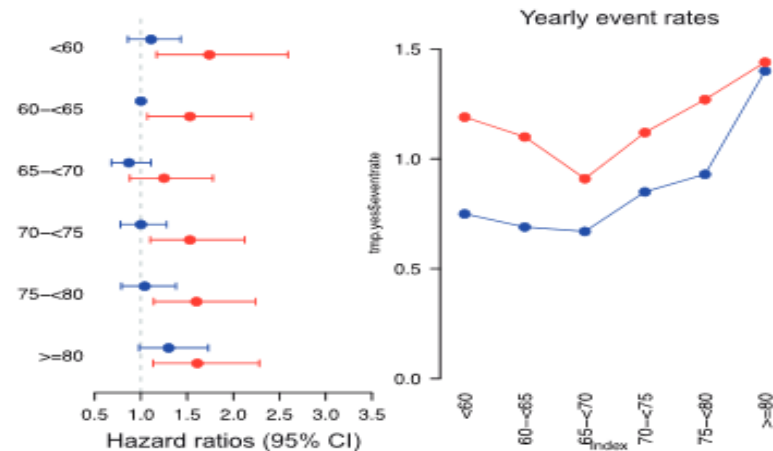


# Resting heart rate and cardiovascular outcomes in diabetic and non-diabetic individuals at high cardiovascular risk analysis from the ONTARGET/TRANSCEND trials

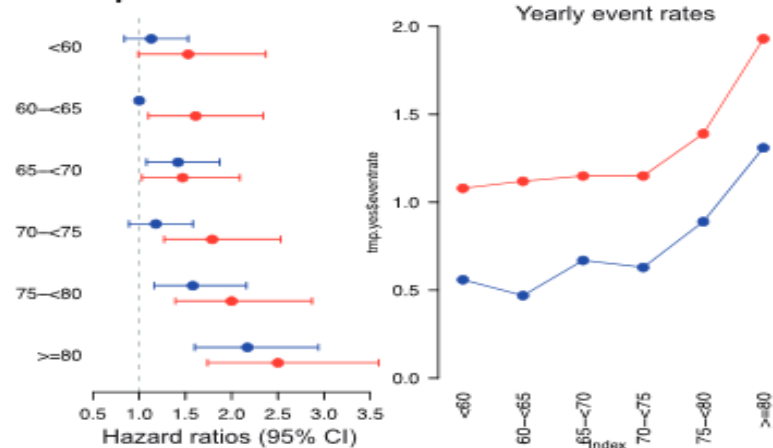
## C Myocardial infarction



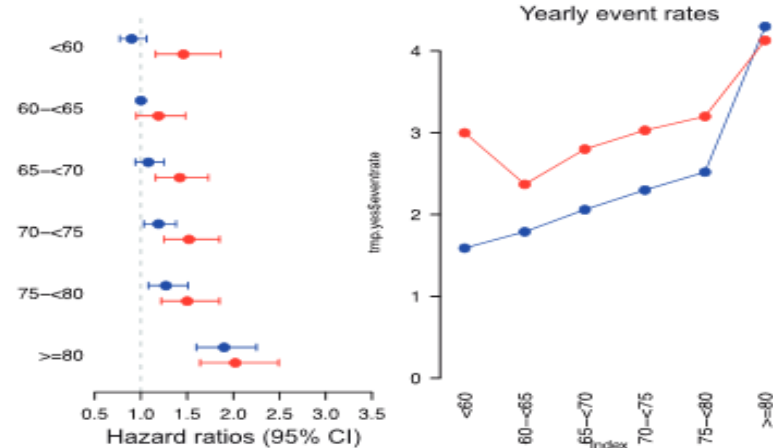
## D Stroke



## E Hospitalization for CHF

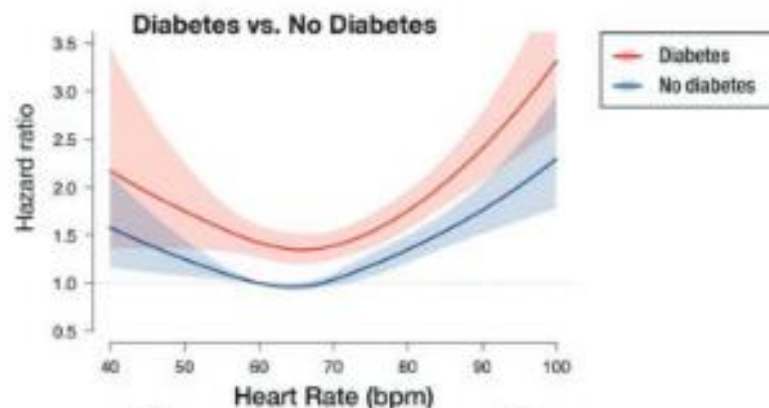


## F All-cause death



# Resting heart rate and cardiovascular outcomes in diabetic and non-diabetic individuals at high cardiovascular risk analysis from the ONTARGET/TRANSCEND trials

## Heart Rate as Cardiovascular Outcome Marker:



## Mechanisms of Higher Heart Rate

### Vasculature

- Oxidative stress ↑
- Endothelial dysfunction
- Arterial stiffness
- Altered arterial shear stress
- Plaque stability
- Microalbuminuria
- Cognitive dysfunction

### Heart

- Oxygen consumption ↑
- Oxygen delivery ↓
- Coronary perfusion ↓
- Diastolic length
- Maladaptive hypertrophy
- Tachycardiomyopathy

**EVENTS**

## Density

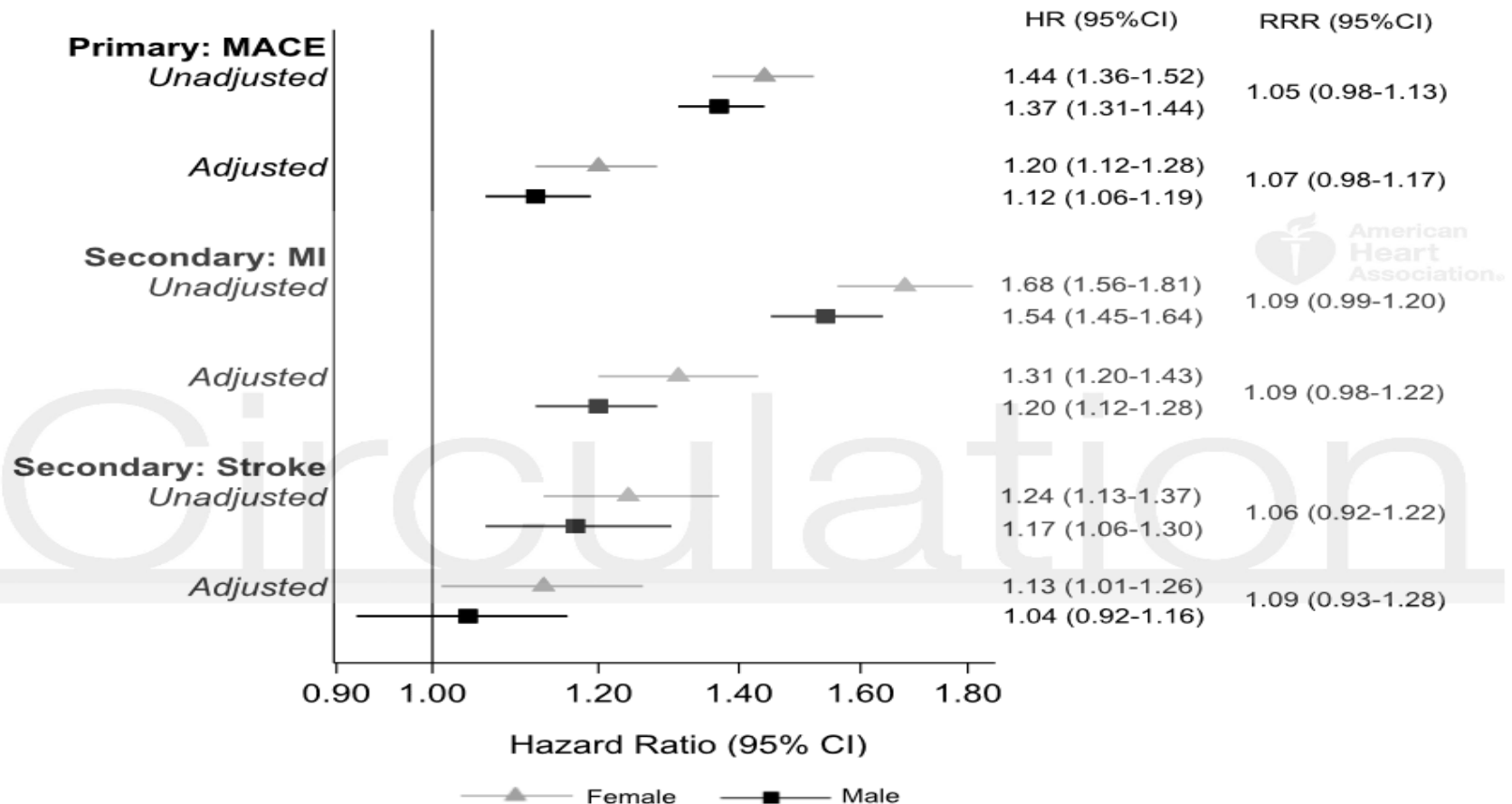


## Diabetes

- Autonomic Dysfunction
- Augmentation of CV risk factors

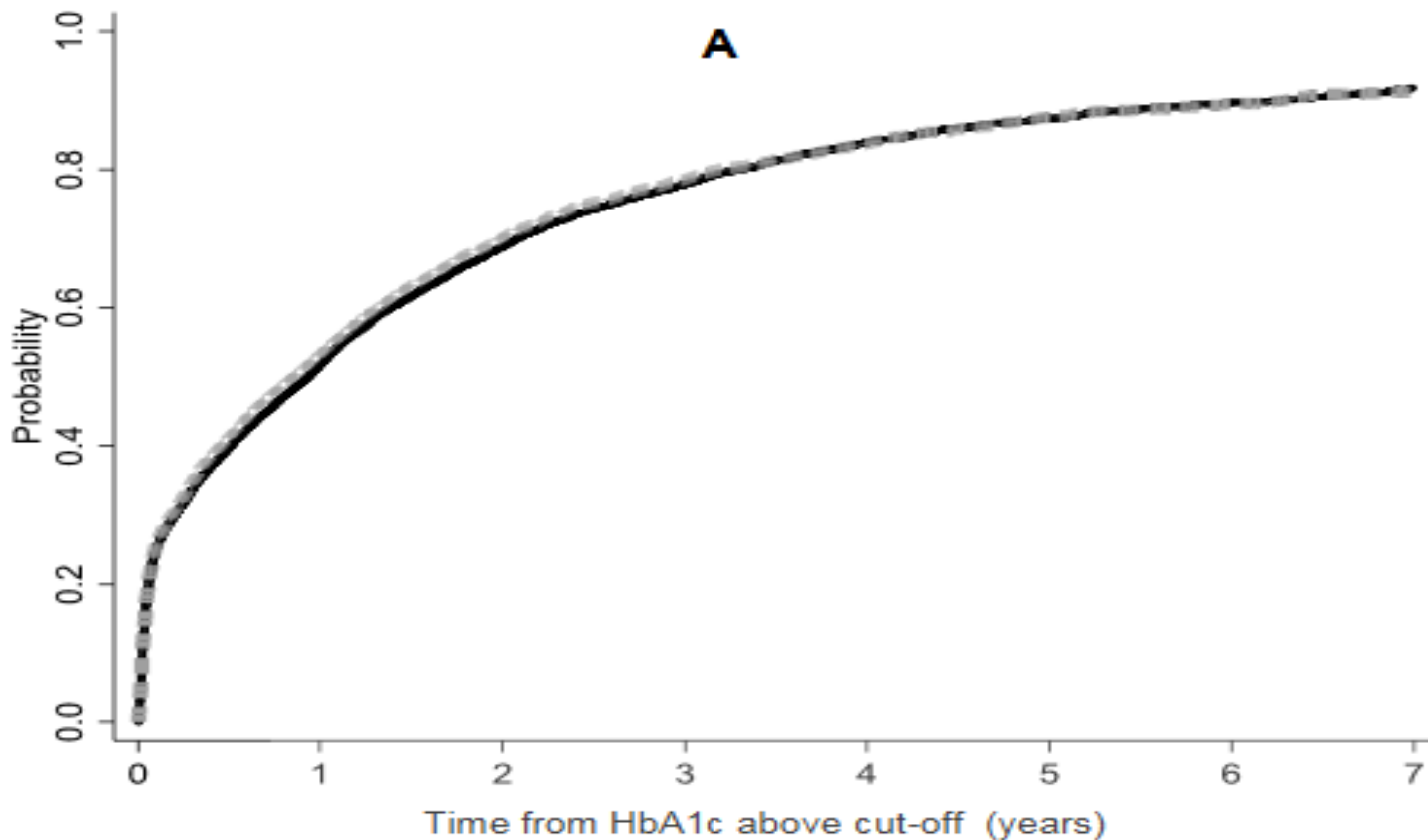
# Cardiovascular Risk and Risk Factor Management in Type 2 Diabetes: A Population-Based Cohort Study Assessing Sex Disparities

Type 2 diabetes (N=63,718; 29,348 (46.1%) women and 34,370 (53.9%) men)  
And Controls (N=277,176; 130,524 (47.1%) women and 146,652 (52.9%) men)



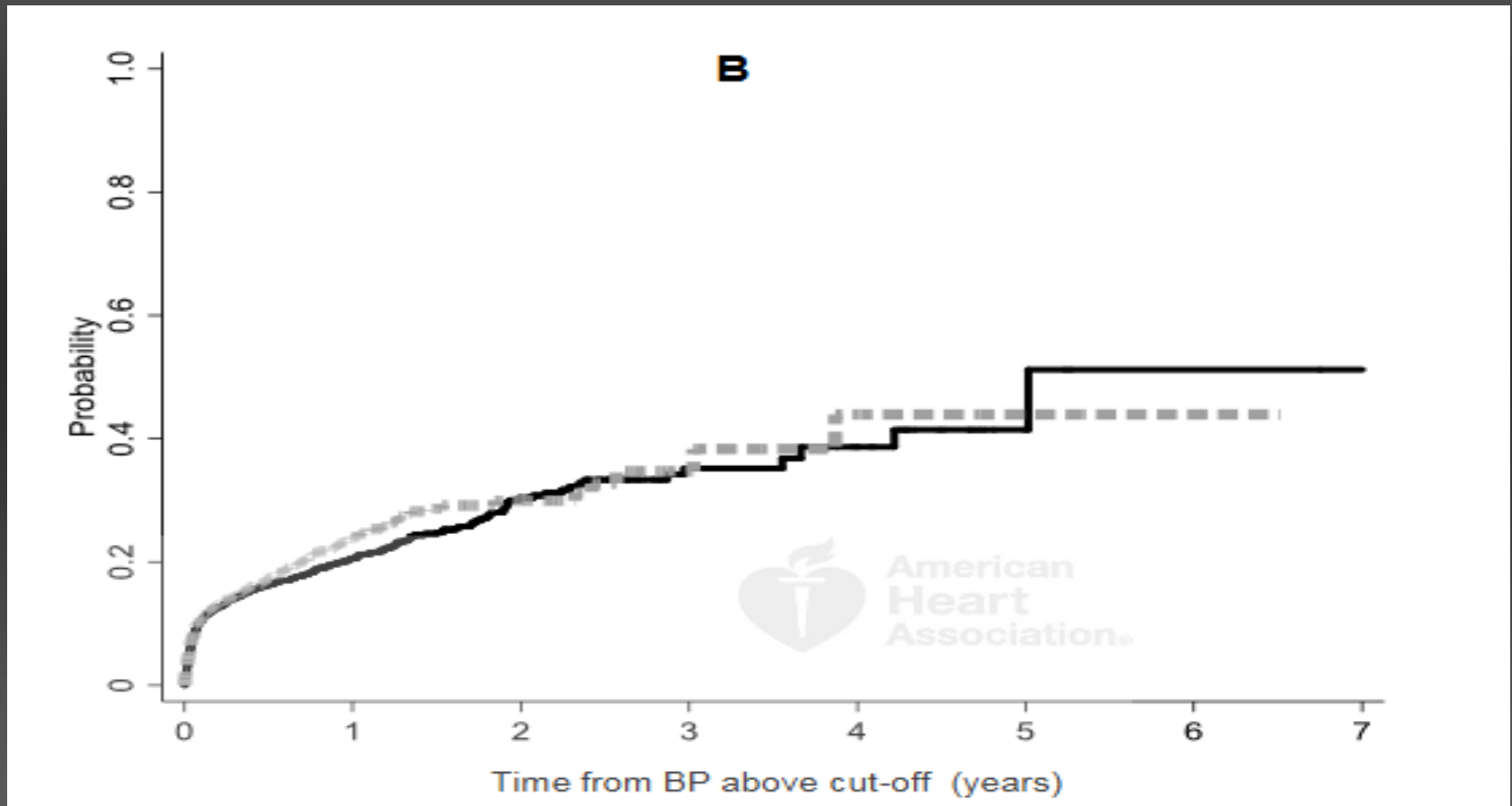
# Cardiovascular Risk and Risk Factor Management in Type 2 Diabetes: A Population-Based Cohort Study Assessing Sex Disparities

Comparison of the proportion of men and women undergoing intensification of drug regimens in relation to the time that their risk factors : HbA1c >7%



# Cardiovascular Risk and Risk Factor Management in Type 2 Diabetes: A Population-Based Cohort Study Assessing Sex Disparities

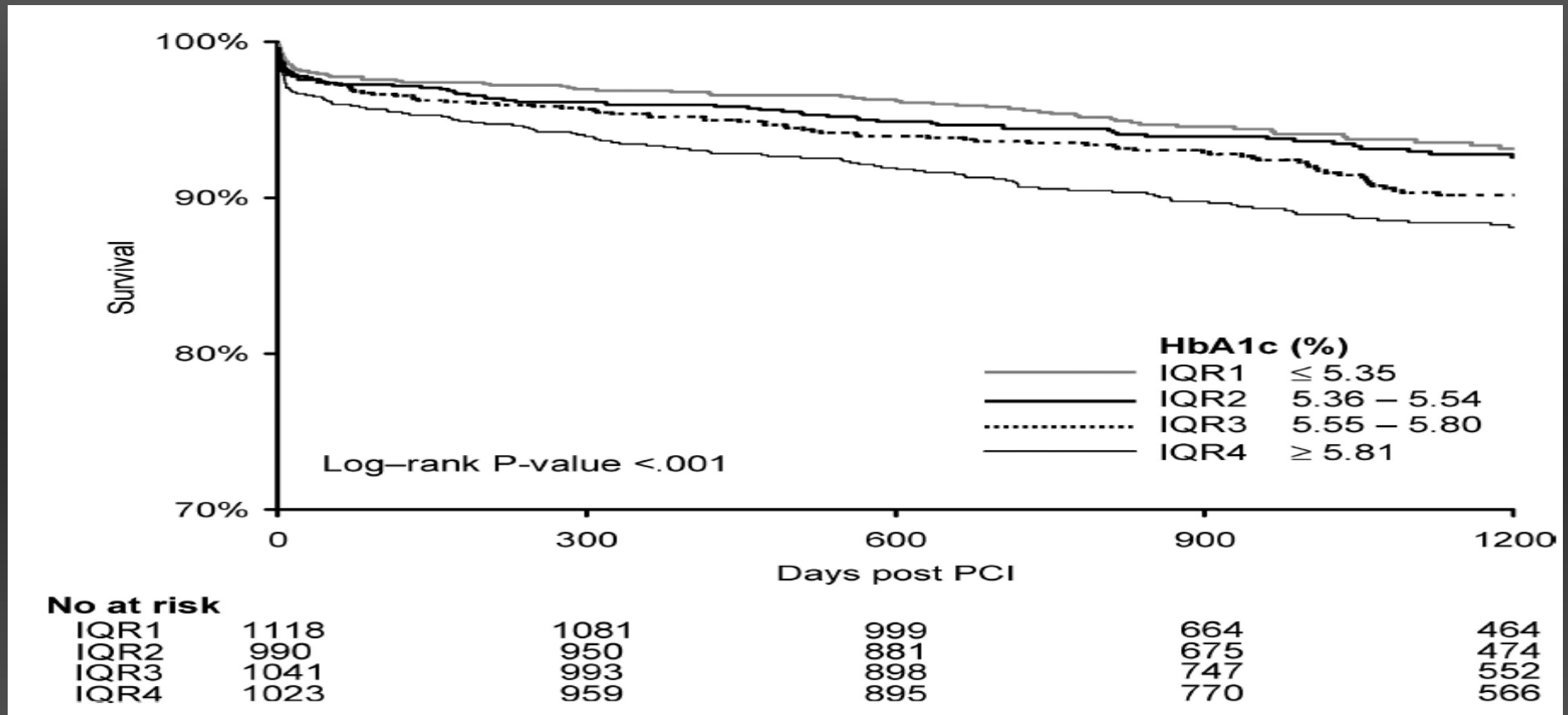
Comparison of the proportion of men and women undergoing intensification of drug regimens in relation to the time that their risk factors : BP >140/80 mmHg





# Prognostic value of admission glycosylated hemoglobin and glucose in nondiabetic patients with ST-segment-elevation myocardial infarction treated with percutaneous coronary intervention

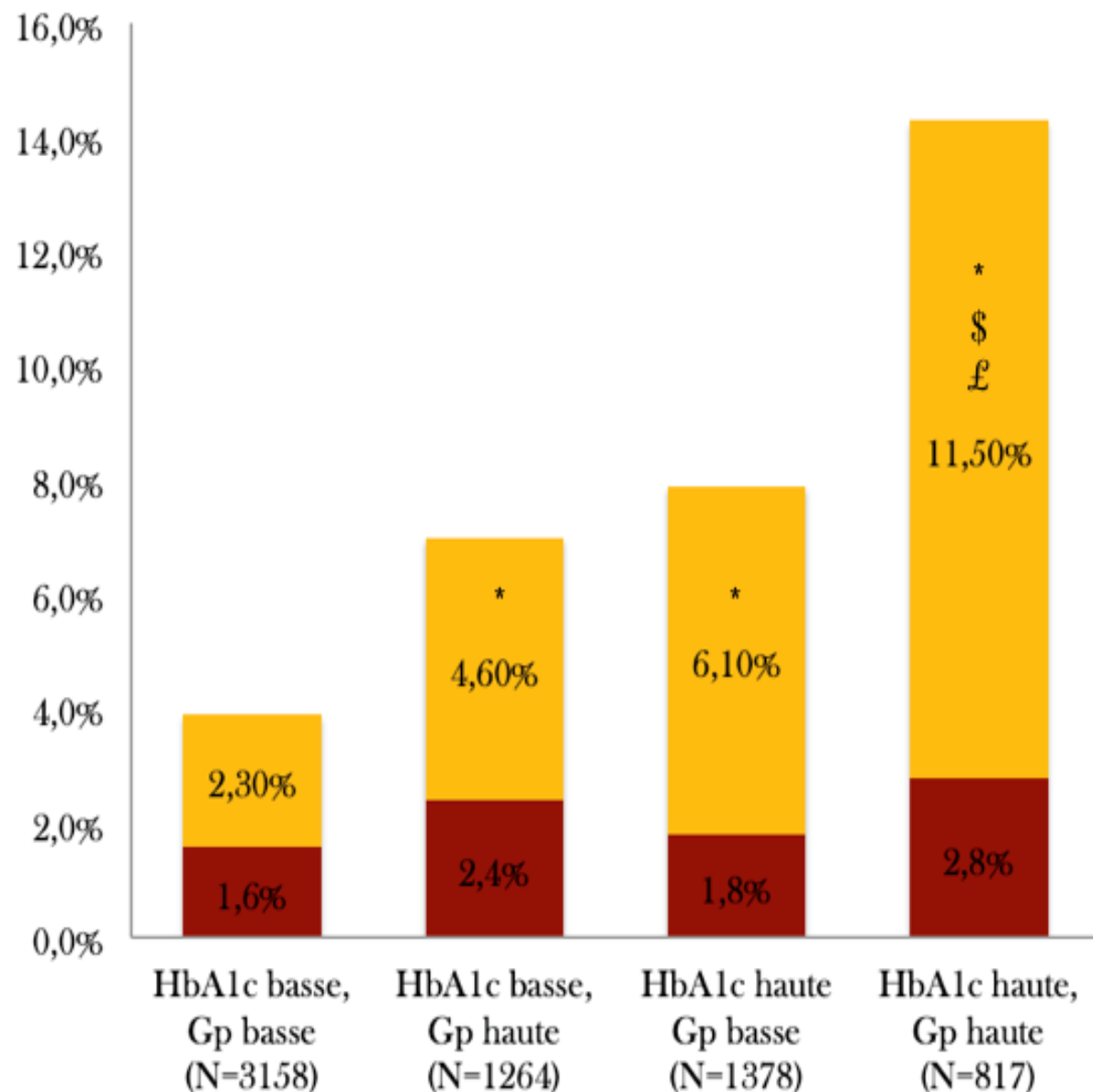
4176 patients non diabétiques STEMI



HbA1c élevée → facteur prédictif de mortalité à long terme (suivi : 3 ans)

→ y compris en multivariée OR (IC95%) 1.2 (1.0-1.3) ;  $p < 0.01$

Figure 3. *Mortalité toutes causes et CV à un an.*



Mortalité non CV :  $p=0.079$

Mortalité CV :  $p<0.001$

\* $p<0.05$  vs HbA1c basse, Gp basse

\$ $p<0.05$  vs HbA1c basse, Gp haute

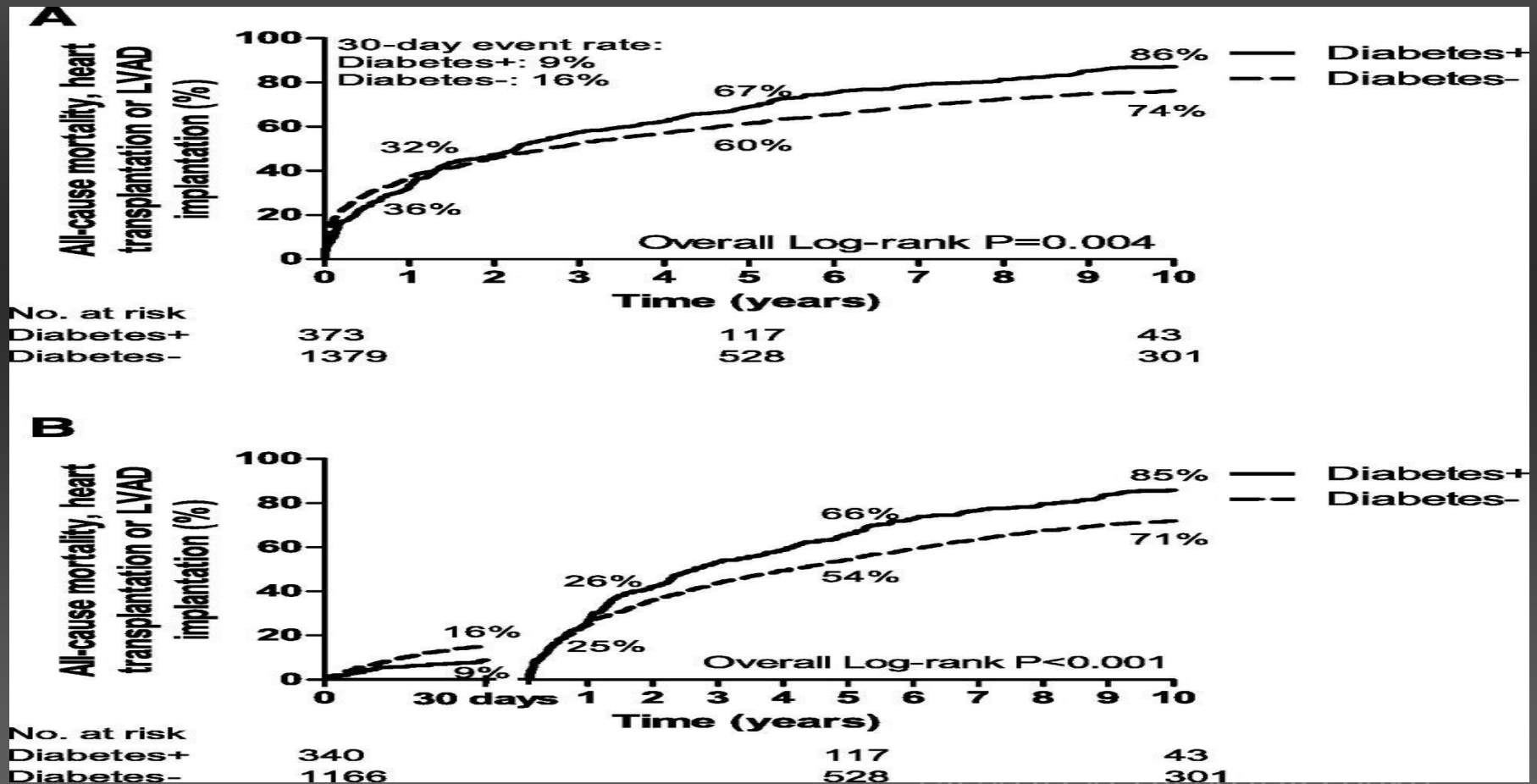
£ $p<0.05$  vs HbA1c haute, Gp basse

■ Mortalité non CV à un an

■ Mortalité CV à un an

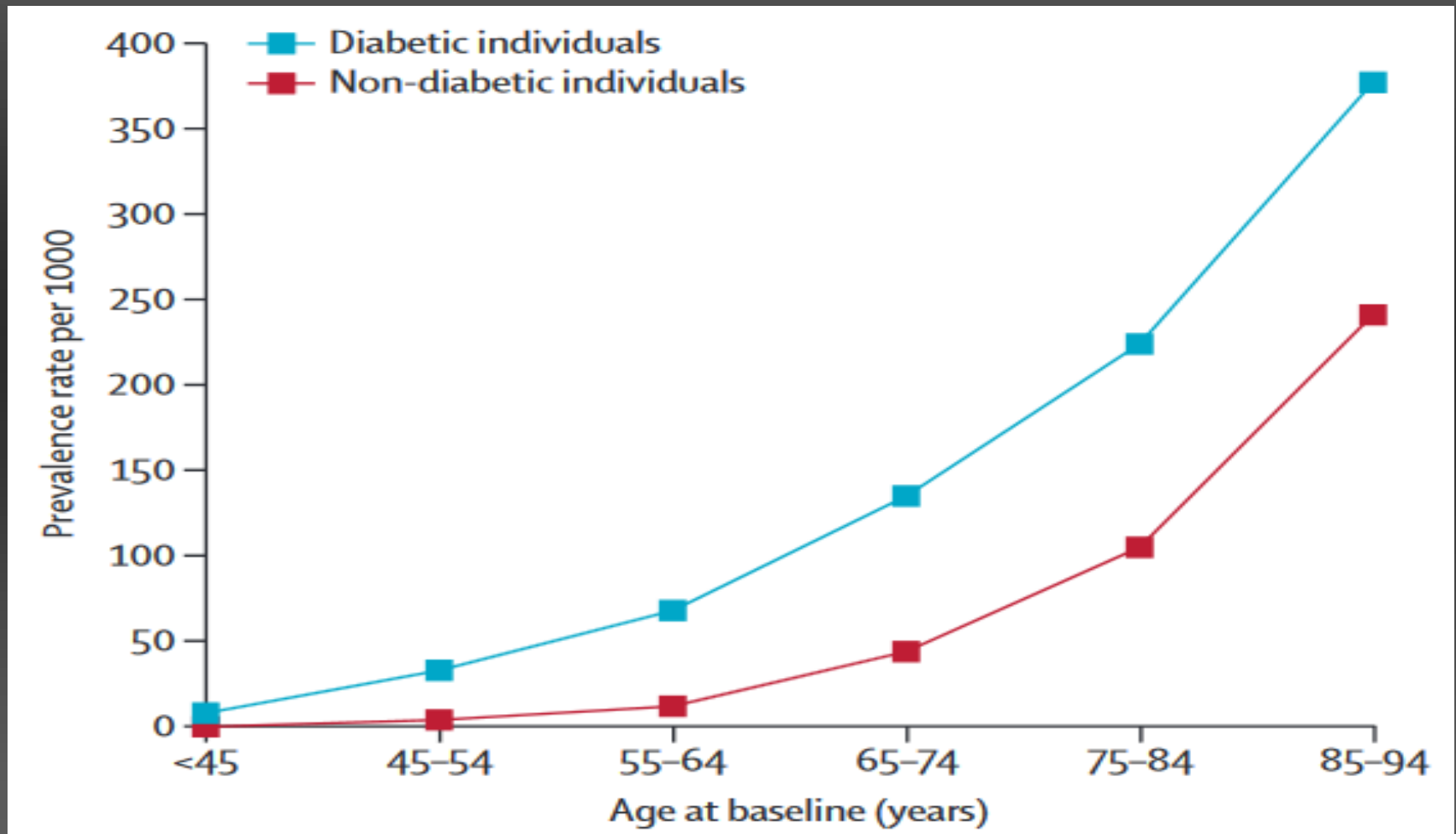
# Short- and long-term prognosis of patients with acute heart failure with and without diabetes: changes over the last three decades

This prospective registry included all consecutive patients aged 18 years and older admitted to the Intensive Coronary Care Unit with acute HF in the period of 1985-2008. A total of 1,810 patients were included; 384 patients (21%) had diabetes

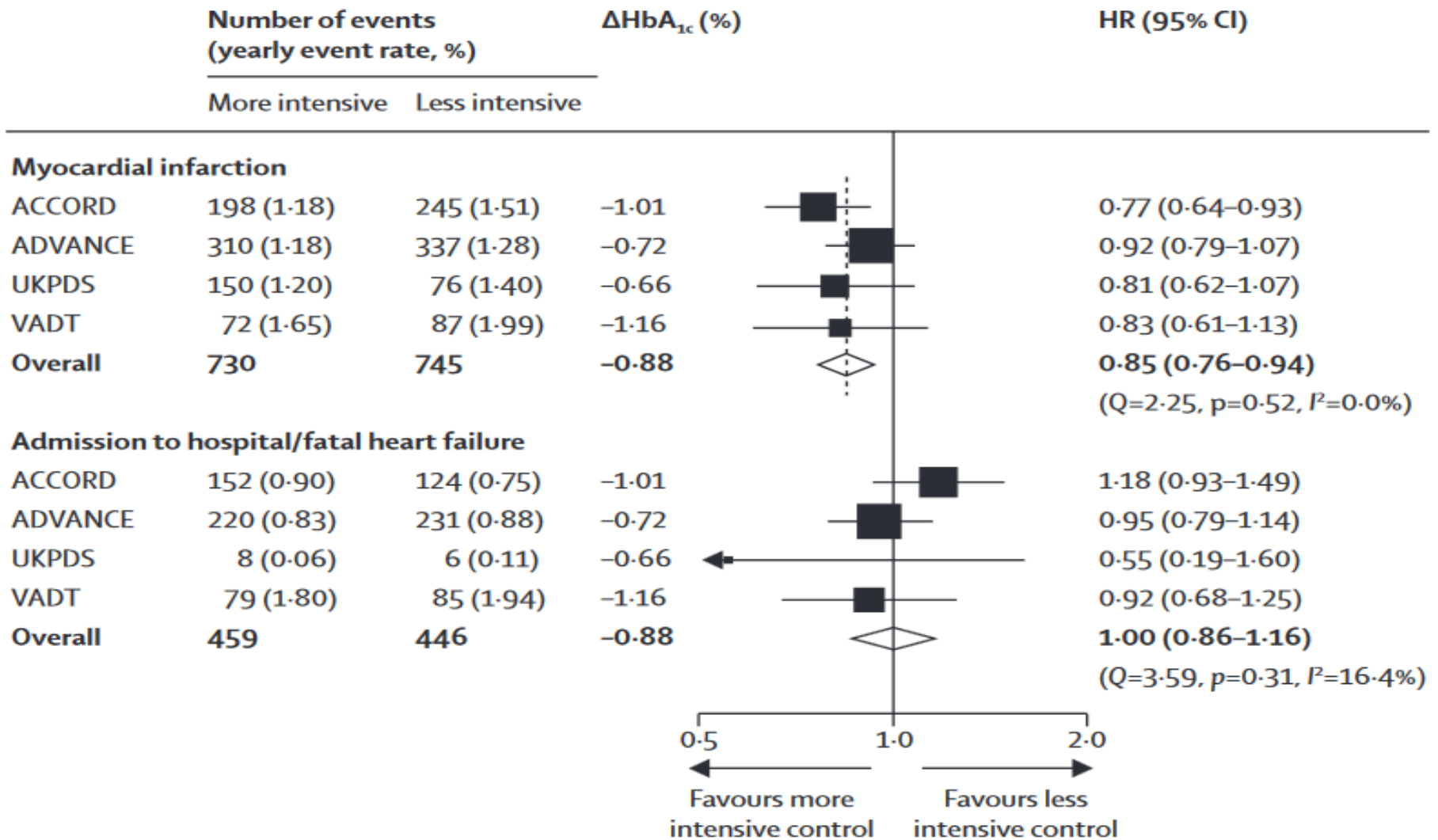


# Heart failure in diabetes: effects of anti-hyperglycaemic drug therapy

Age-associated prevalence of heart failure in diabetic and non-diabetic individuals



# Heart failure in diabetes: effects of anti-hyperglycaemic drug therapy



# Suspected Heart Failure

## Clinical History

Symptoms  
Functional limitation  
Prior cardiac disease  
Risk factors  
Exacerbating factors  
Comorbidities  
Drugs

## Physical Examination

Vital signs  
Weight  
Volume status  
Heart  
Lung  
Abdomen  
Peripheral Vascular

## Initial Investigations

Chest radiograph  
Electrocardiogram  
Lab work (CBC, electrolytes, renal function, urinalysis, glucose, thyroid function)

## Still Suspect Heart Failure?

NO

Not heart failure;  
workup other  
diagnoses

YES

## Assess Natriuretic Peptides\*

NT-proBNP > 125 pg/ml  
BNP > 50 pg/ml  
(if available)

YES

## Assessment of Ventricular Function

Echocardiogram<sup>†</sup>

## Additional Diagnostic Investigations

Cardiac catheterization  
Cardiopulmonary  
exercise testing  
Others (CMR, MIBI, MUGA, CT scan)

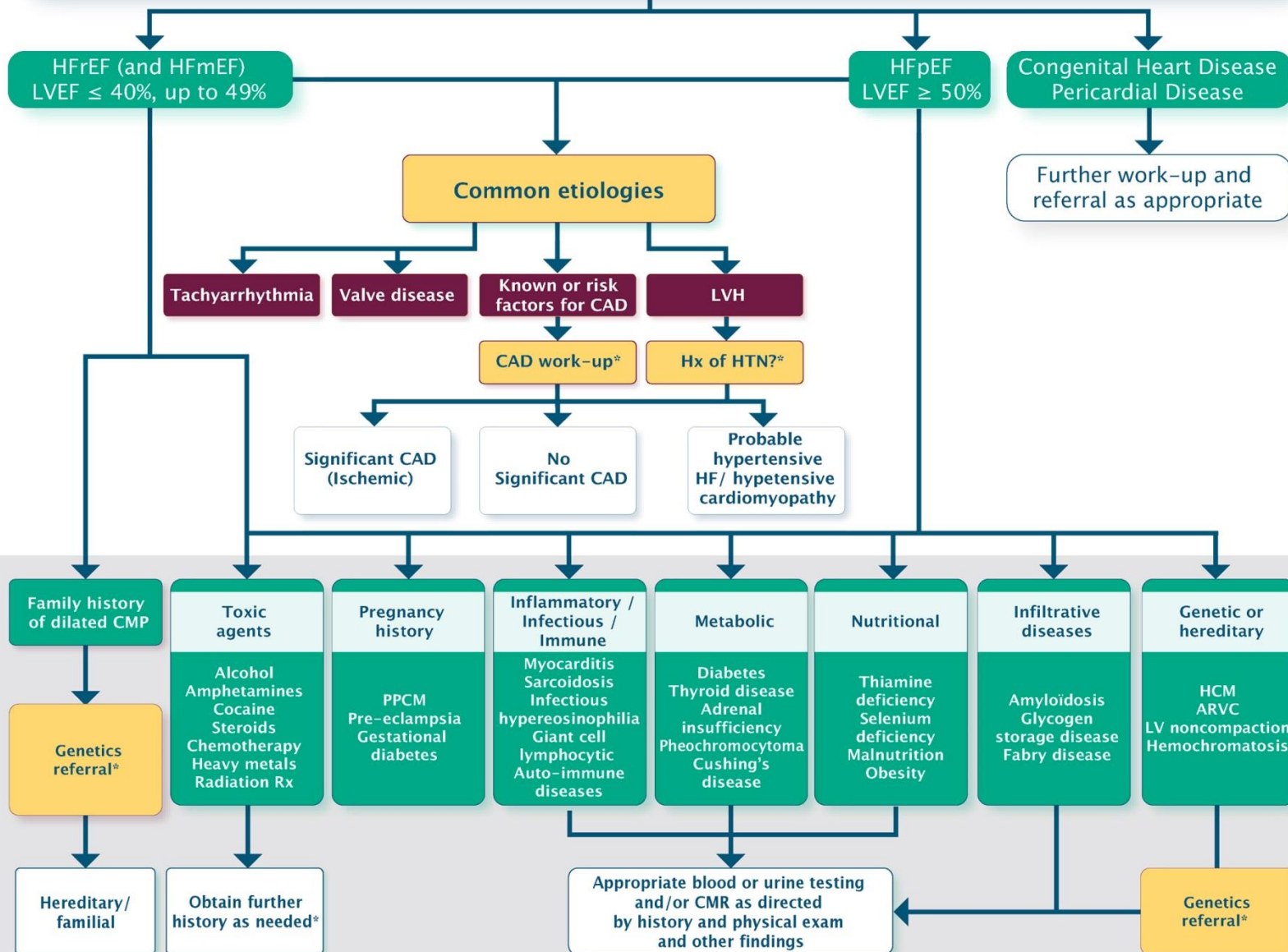
Heart failure likely,  
treat accordingly



# Echocardiogram, ECG, plus recommended lab testing for all patients (CBC, creatinine, ferritin, TSH, troponin, NP)

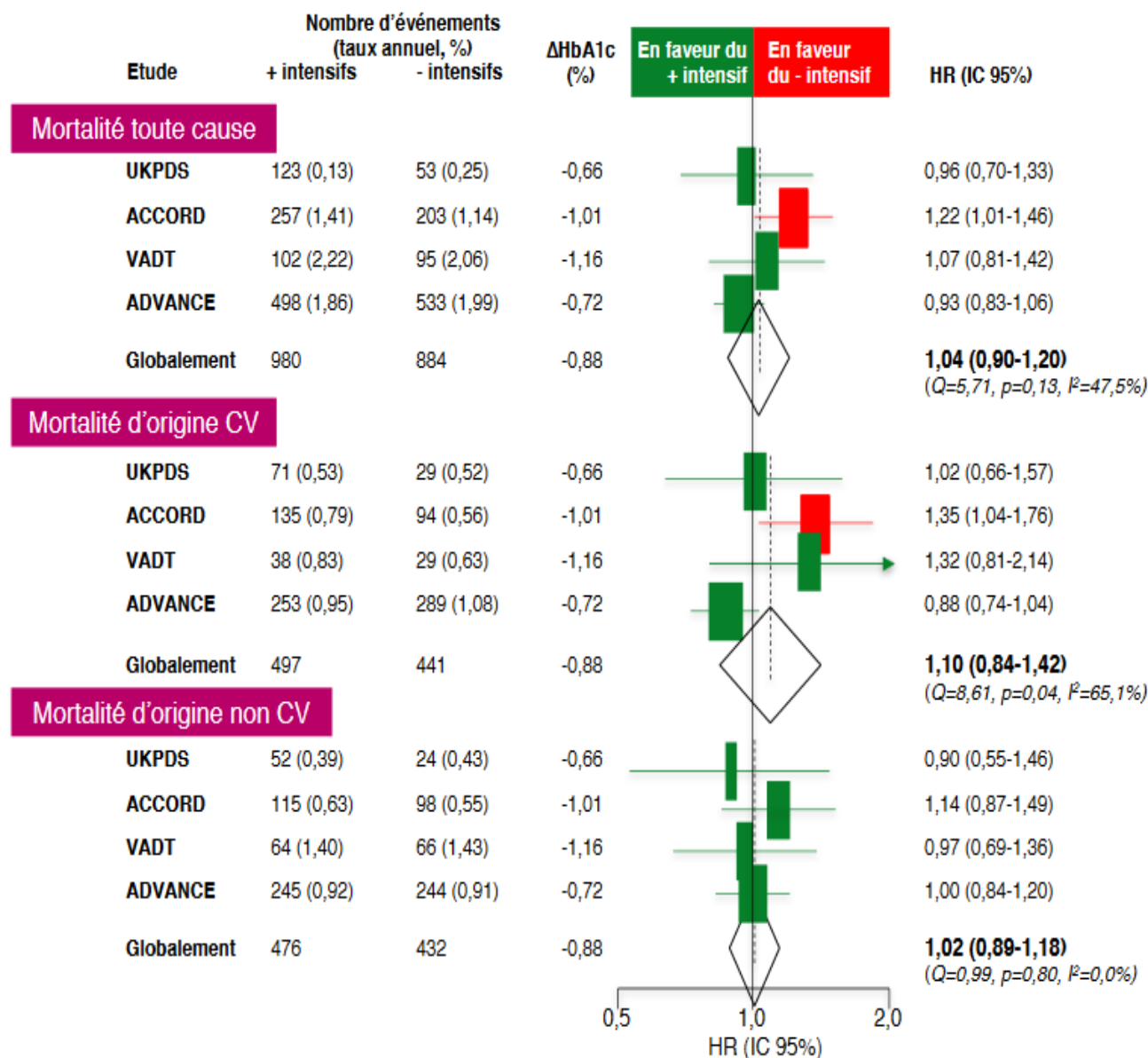
**MORE COMMON**

**LESS COMMON**

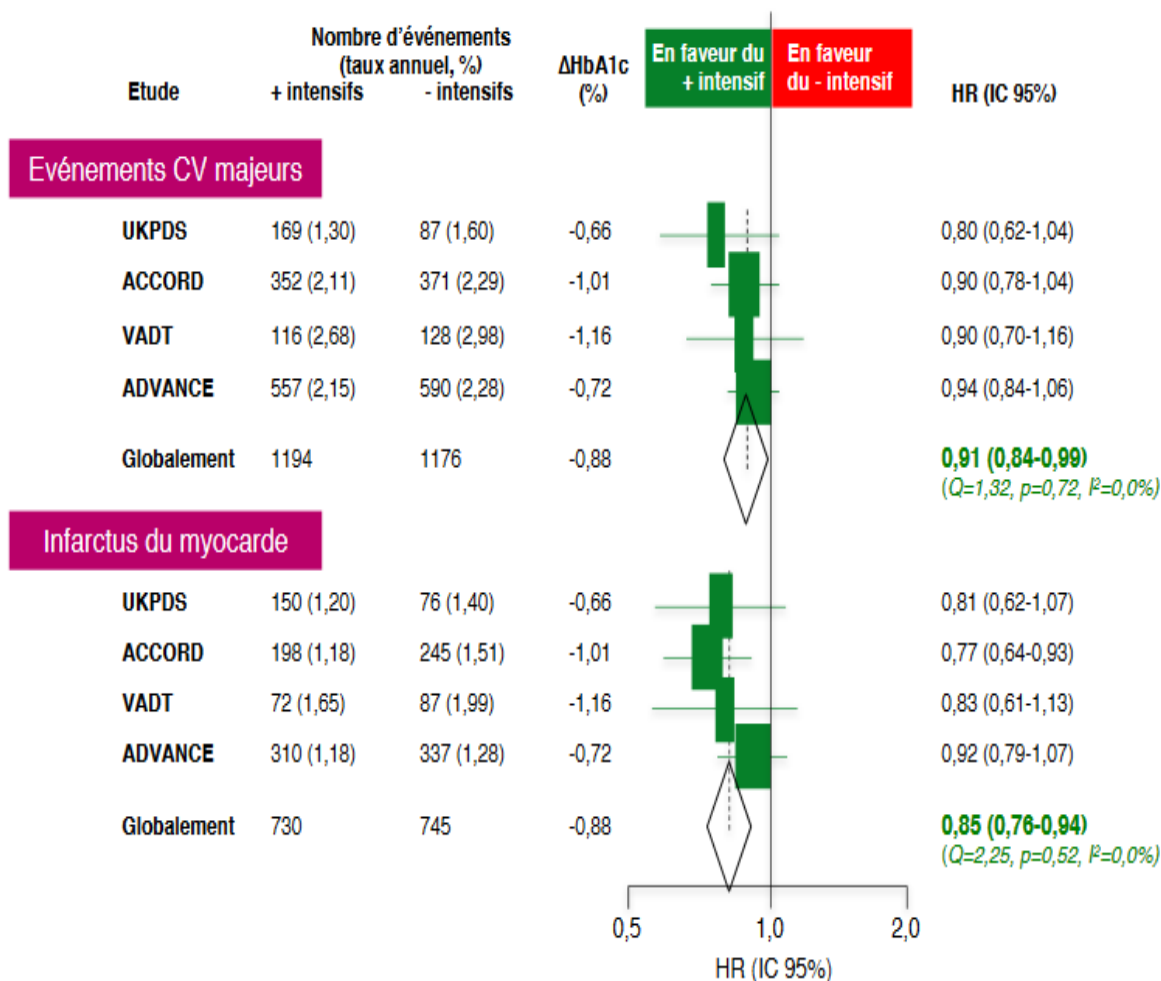




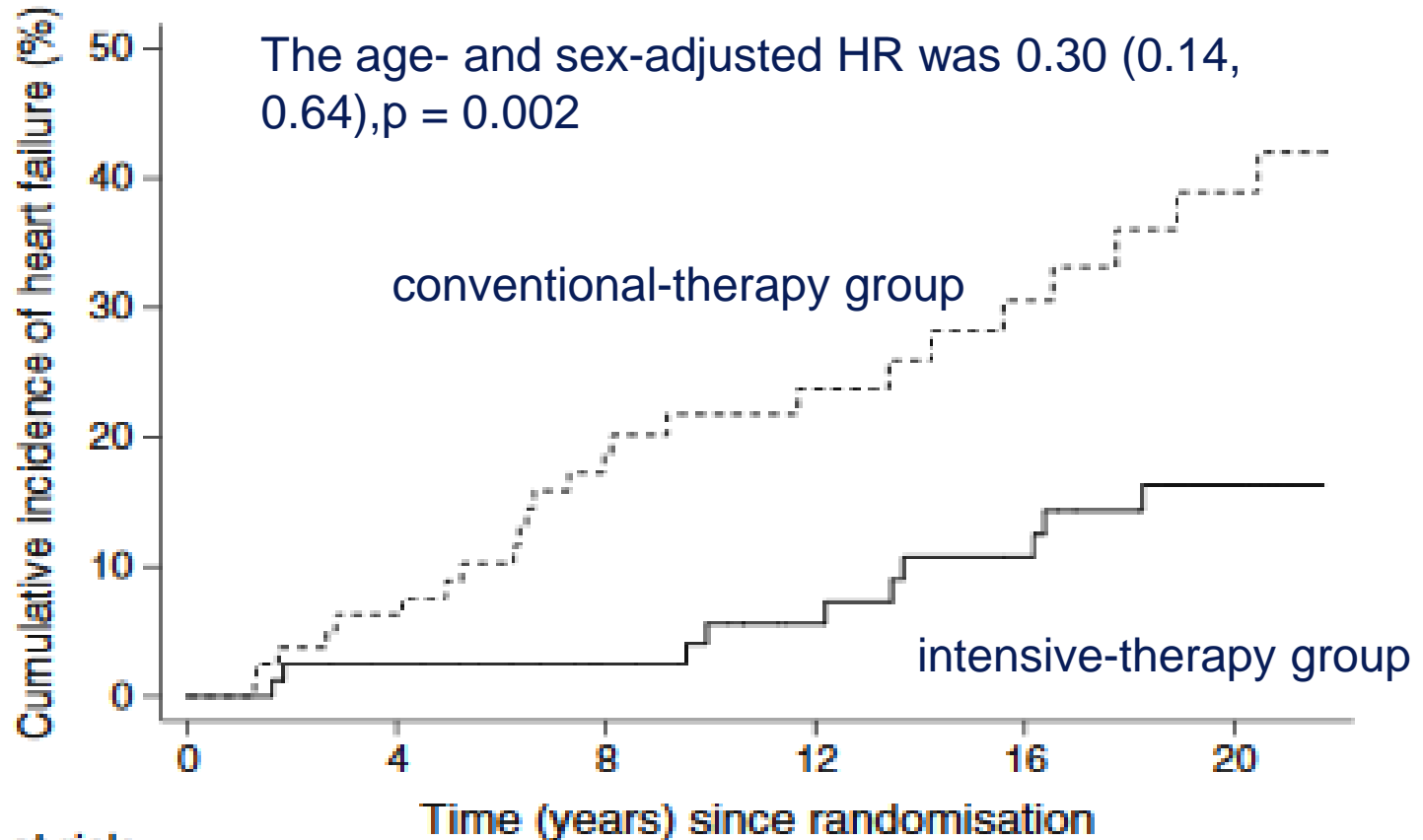
# Diabète de type 2 : contrôle glycémique et mortalité



# Diabète de type 2 : contrôle glycémique et événements cardiovasculaires



# Reduced risk of heart failure with intensified multifactorial intervention in individuals with type 2 diabetes and microalbuminuria: 21 years of follow-up in the randomised Steno-2 study

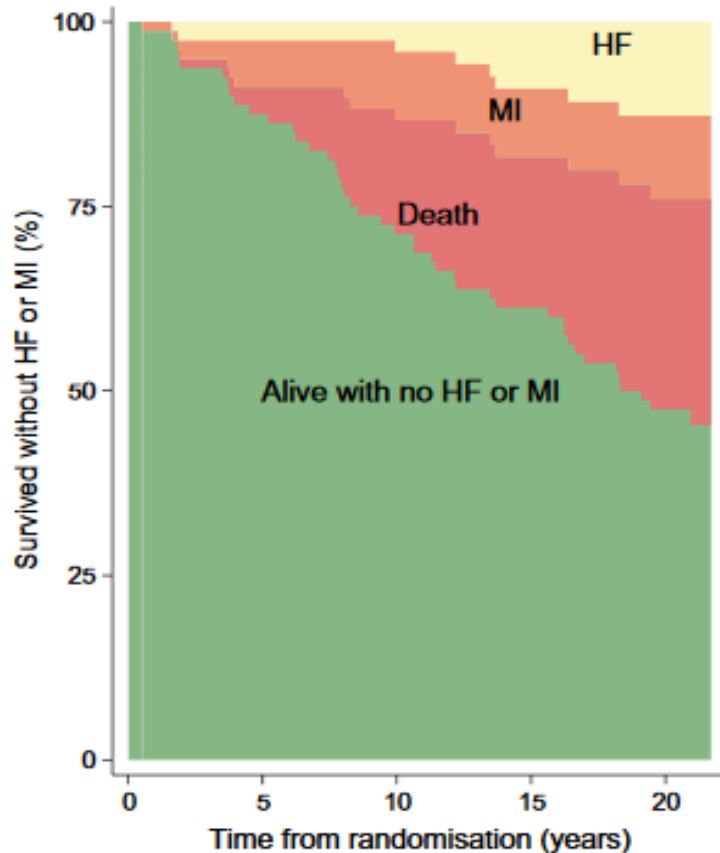


Number at risk

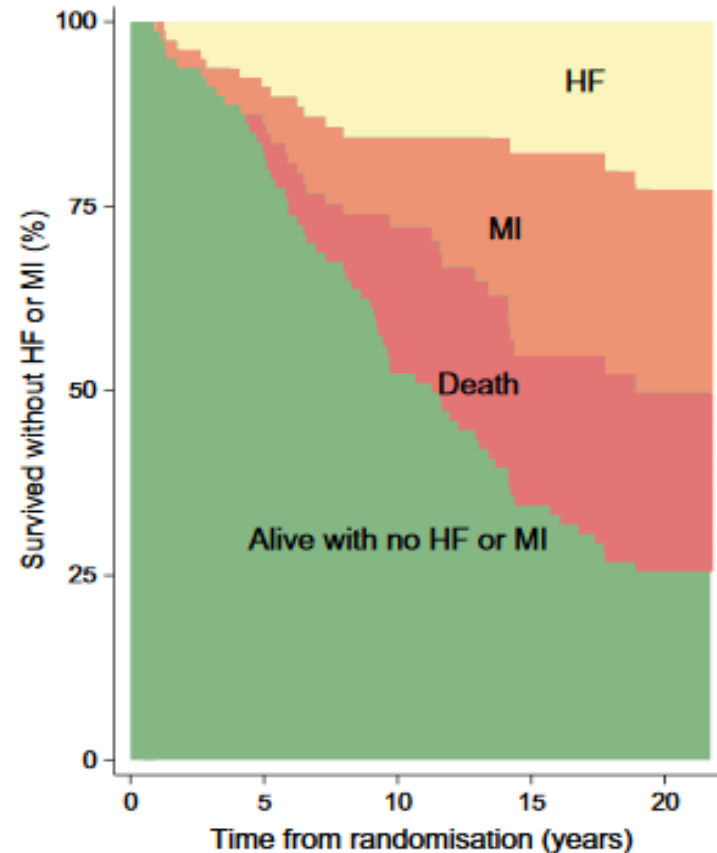
Intensive	80	75	65	56	51	40
Conventional	80	74	57	38	29	21

# Reduced risk of heart failure with intensified multifactorial intervention in individuals with type 2 diabetes and microalbuminuria: 21 years of follow-up in the randomised Steno-2 study

intensive-therapy group

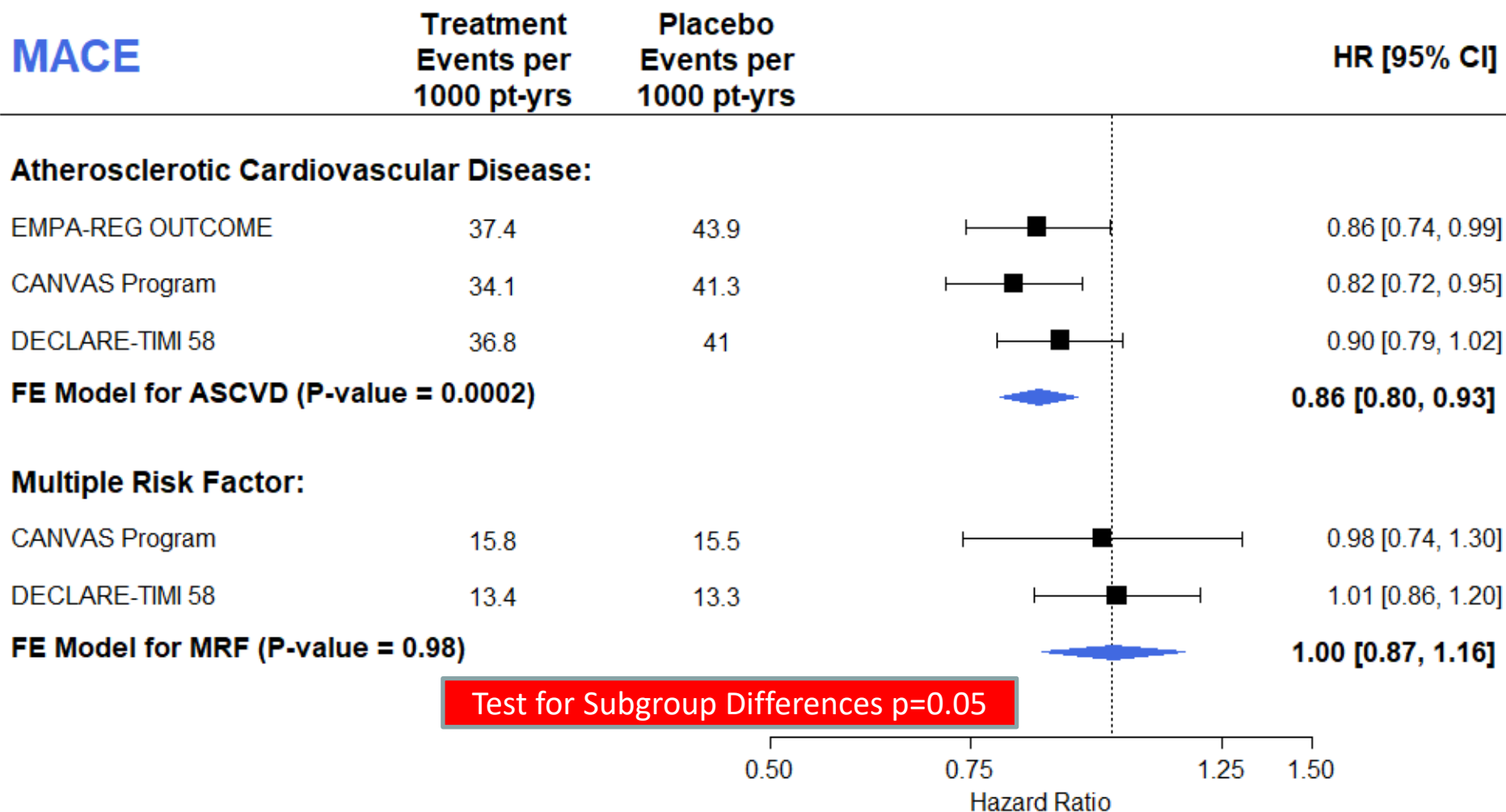


conventional-therapy group

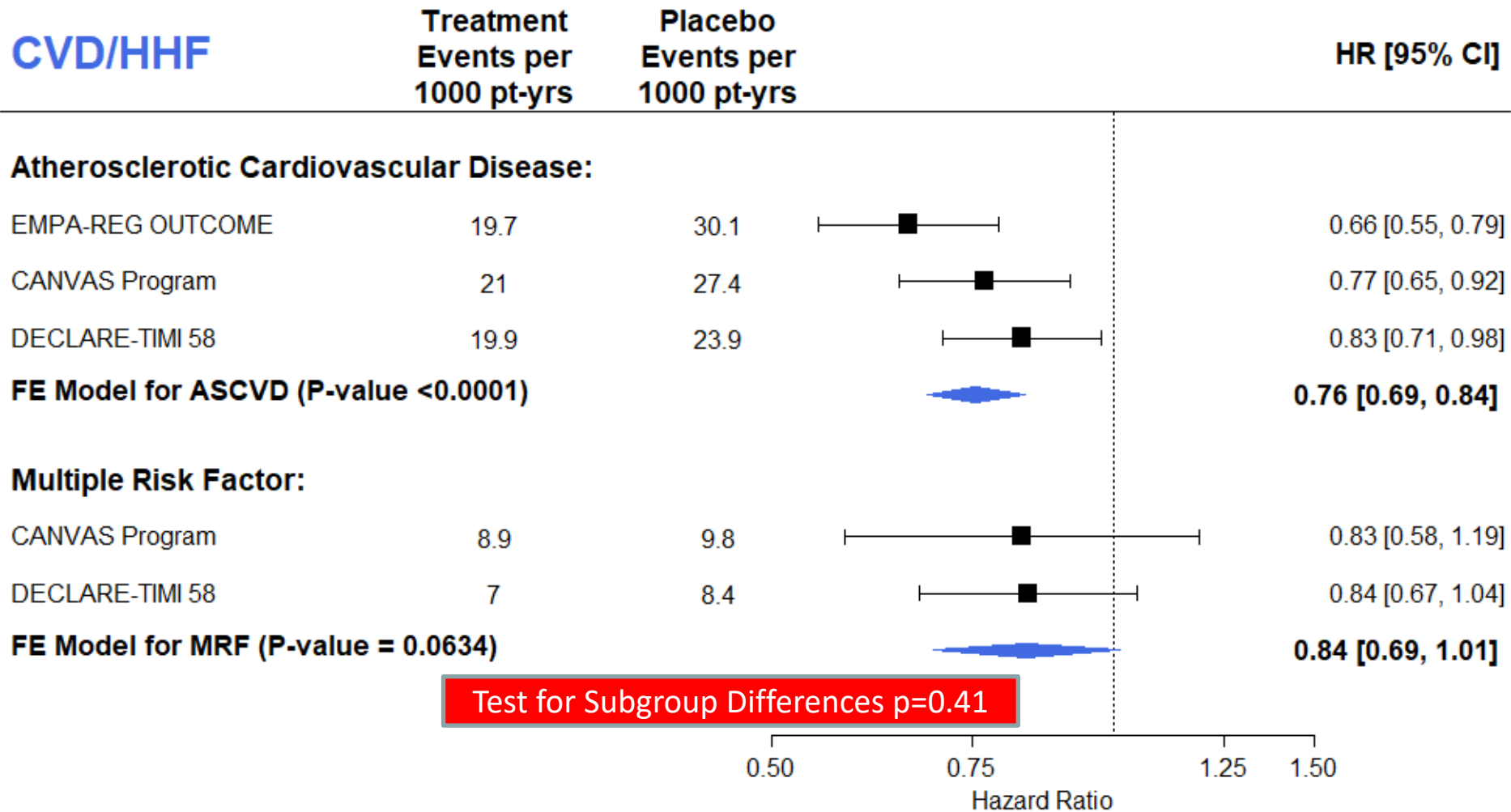


# Meta-Analysis of CVOTs: MACE by Presence of ASCVD

## MACE



# Meta-Analysis of CVOTs: CVD/HHF by Presence of ASCVD



# Post-SCA

Contrôle des Facteurs de risque  
Education Thérapeutique

Optimisation pharmacologique  
IEC/ARA II-Bétabloquants-Statine

Réduire le Risque Résiduel

Individualisation du risque

Anti-aggrégation  
Anticoagulation

Lipides

Diabétique

Voie Inflammatoire  
CRP us

## Prolongation :

- de Bithérapie anti-aggrégante
- Ticagrelor ?

## Introduction AOD :

Rivaroxaban

## LDL-Cs :

- Ezetrol
- PCSK9

## Hpertrigycéridémie :

- Icosapent éthyle

## Lp (a) :

- inhibiteur LP (a)

## Agonistes :

- GLP-1

## Inhibiteurs :

- SGLT-2

Canakinumab



