

# T2DM and cardiovascular risk

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NUFFIELD DEPARTMENT OF  
**PRIMARY CARE**  
HEALTH SCIENCES

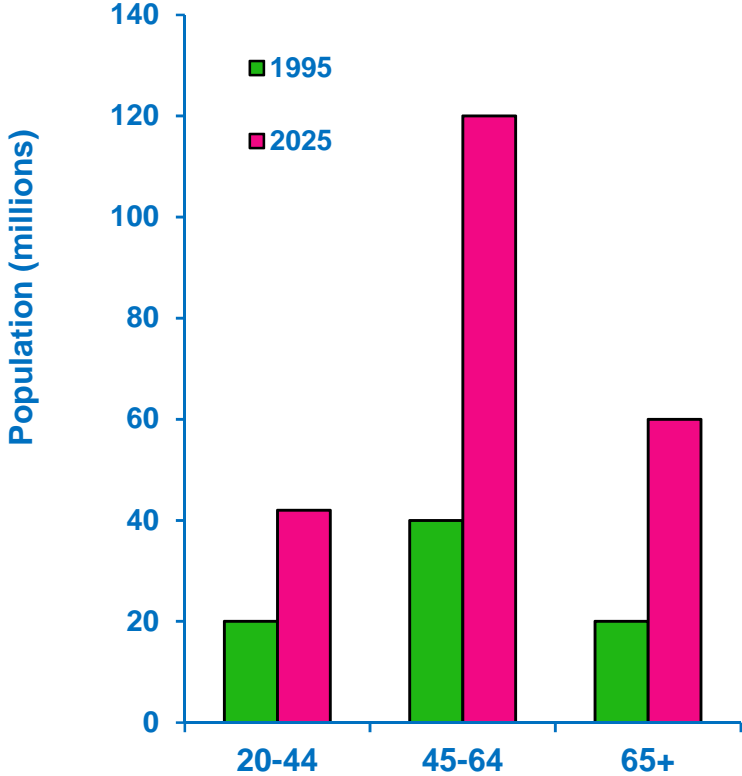


# Competing interests

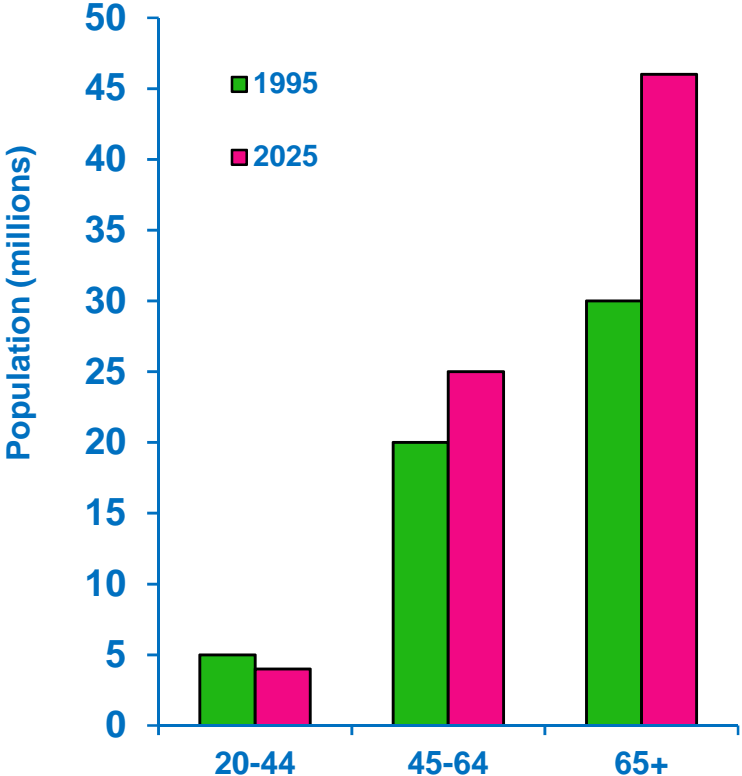
Speaker or congress sponsorship disclosures in past 5 years:  
Amgen, Bayer, Boehringer Ingelheim, Daichi Sankyo, Merck,  
Novartis, Pfizer, Roche, Takeda

# Projected increases in Diabetes Mellitus in Asia, US and Europe (1995-2025)

### Asian countries

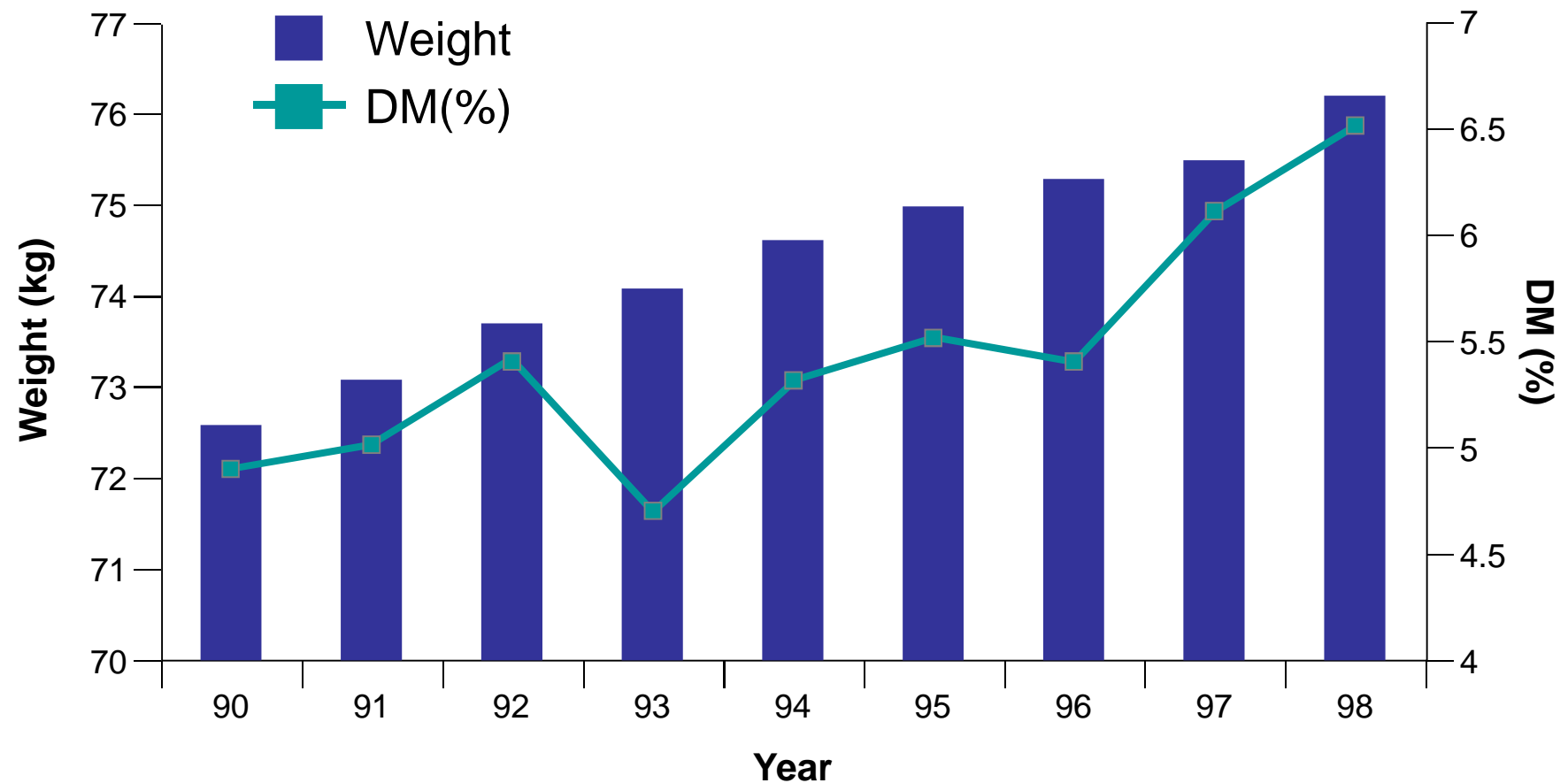


### US and Europe

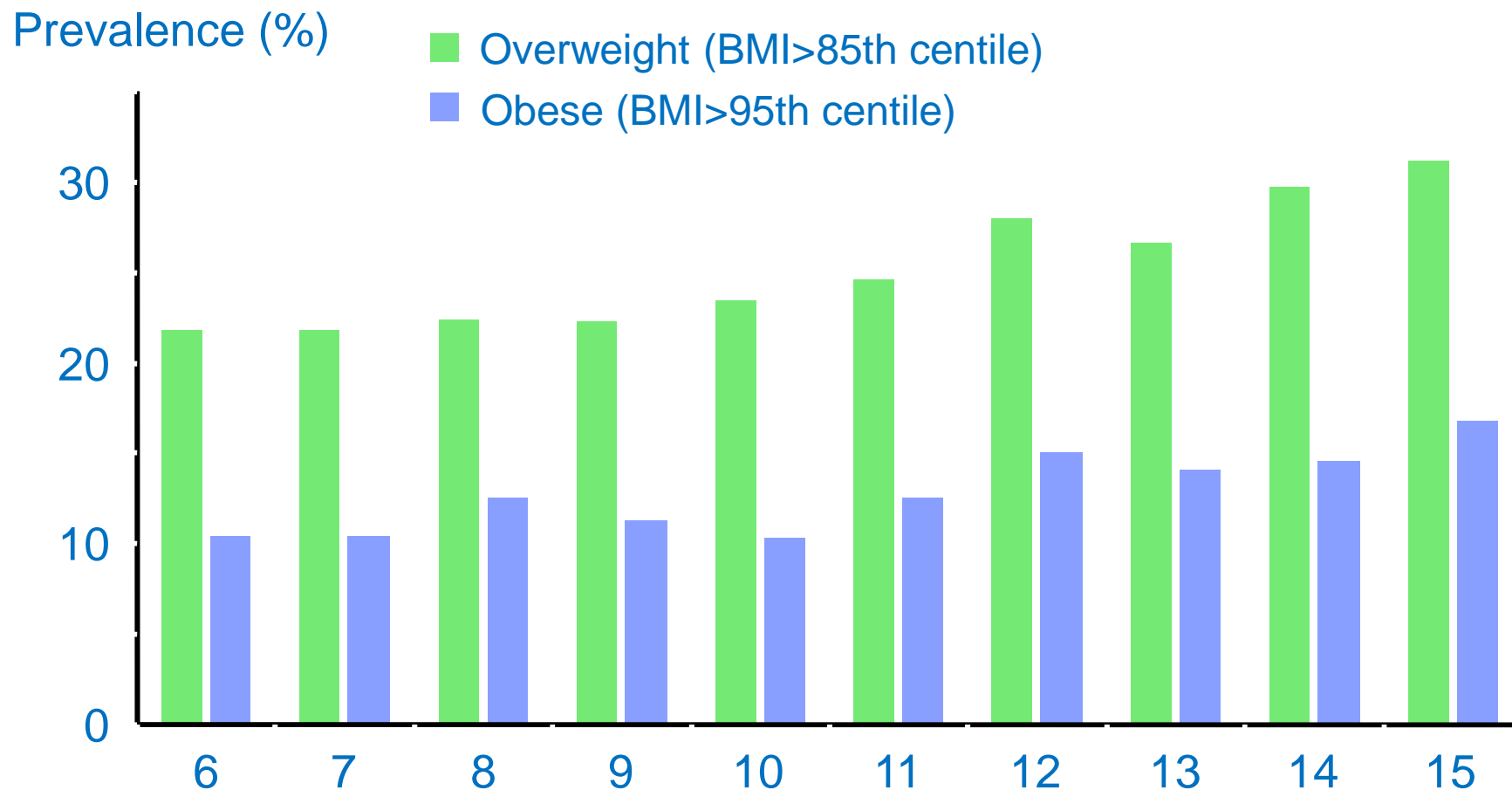


Age group (years)

# Diabetes and obesity trends in the USA from 1990–1998



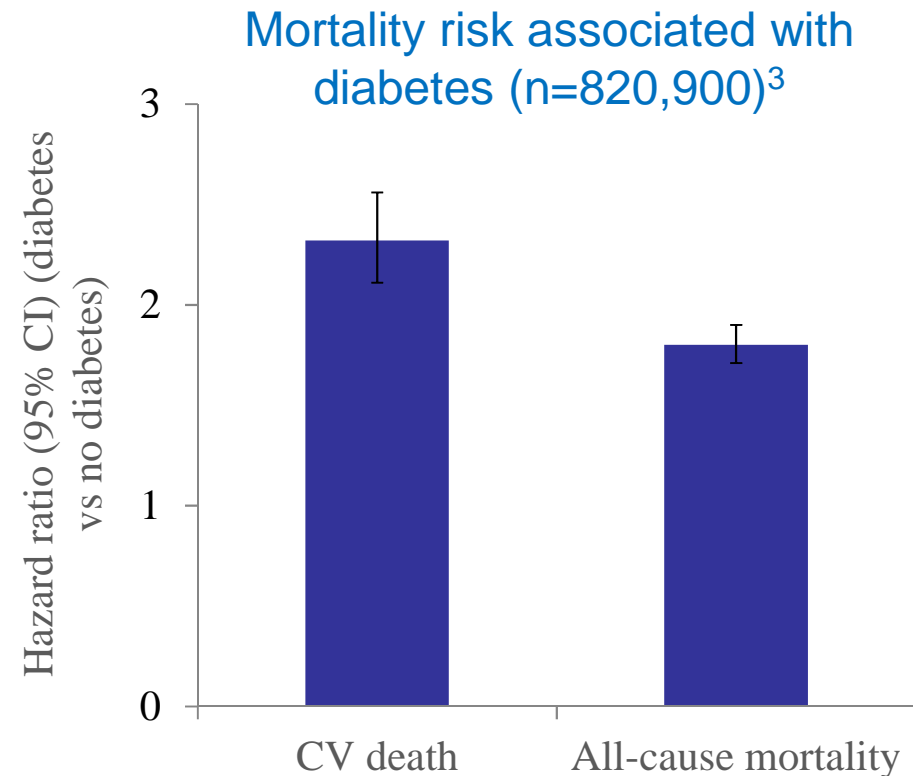
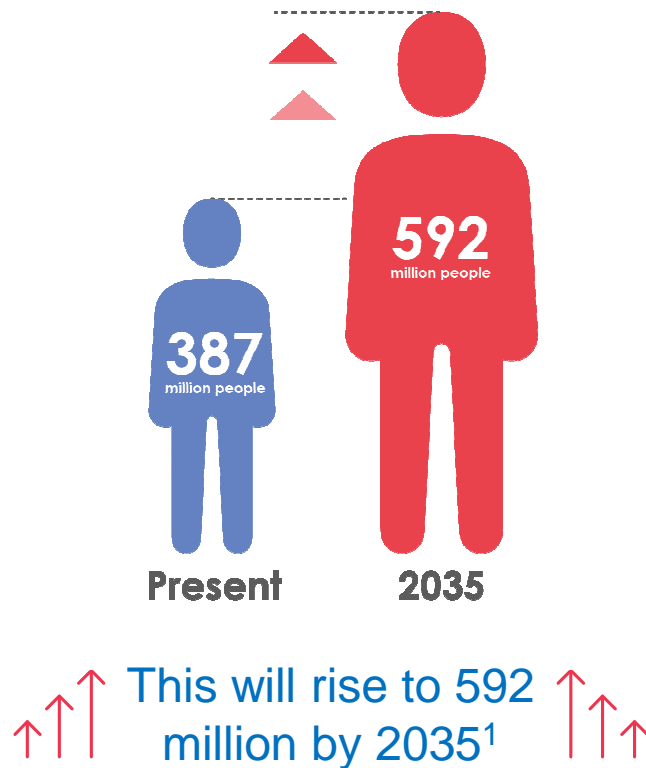
# Prevalence of overweight and obesity in UK children and adolescents



*Adapted from Reilly & Dorosty . Lancet 1999; 354: 1874-1875*

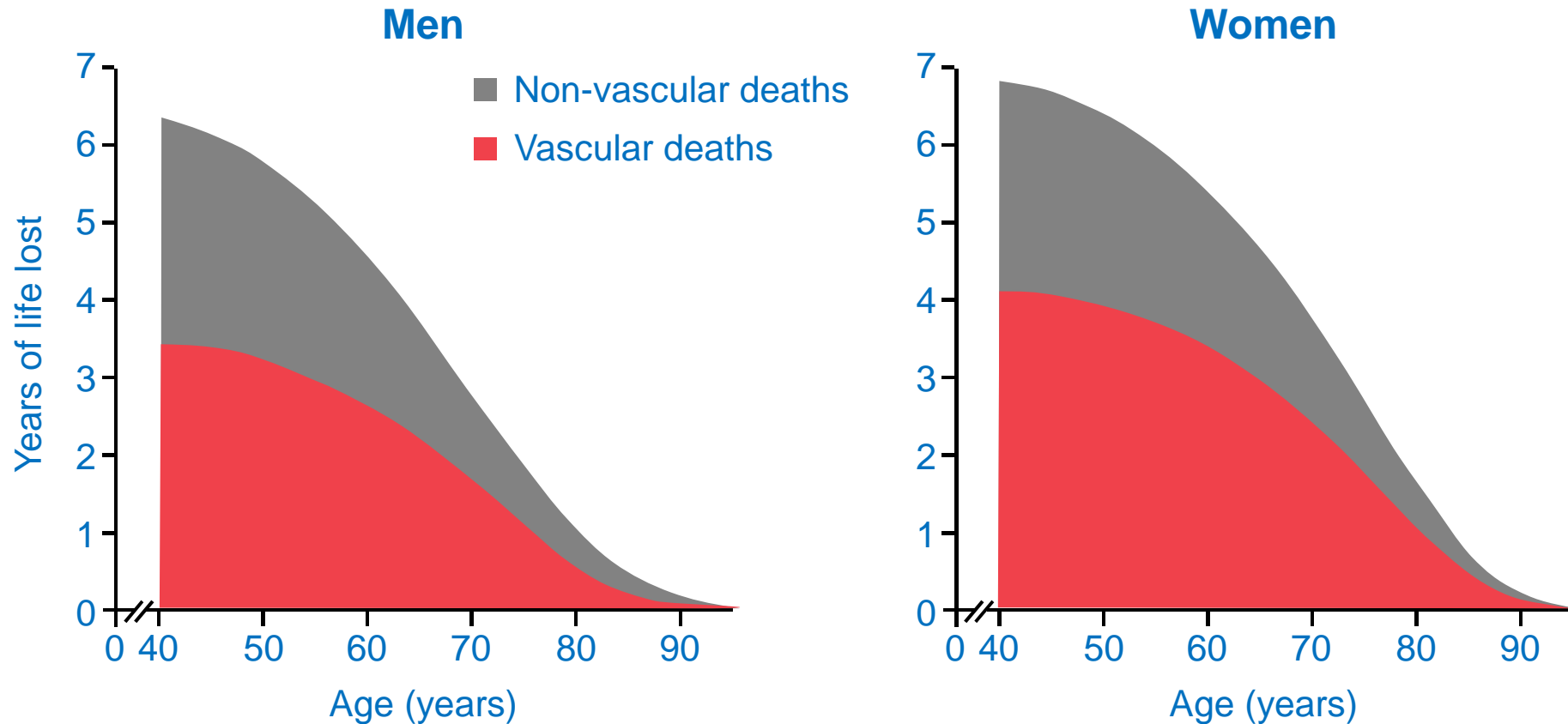
# Type 2 diabetes is increasingly prevalent

- Globally, 387 million people are living with diabetes<sup>1</sup>
- At least 68% of people >65 years with diabetes die of heart disease<sup>2</sup>



1. IDF Diabetes Atlas 6th Edition 2014 <http://www.idf.org/diabetesatlas>; 2. Centers for Disease Control and Prevention 2011; 3. Seshasai et al. N Engl J Med 2011;364:829-41

# Diabetes is associated with significant loss of life years



On average, a 50-year-old individual with diabetes and no history of vascular disease will die 6 years earlier compared to someone without diabetes

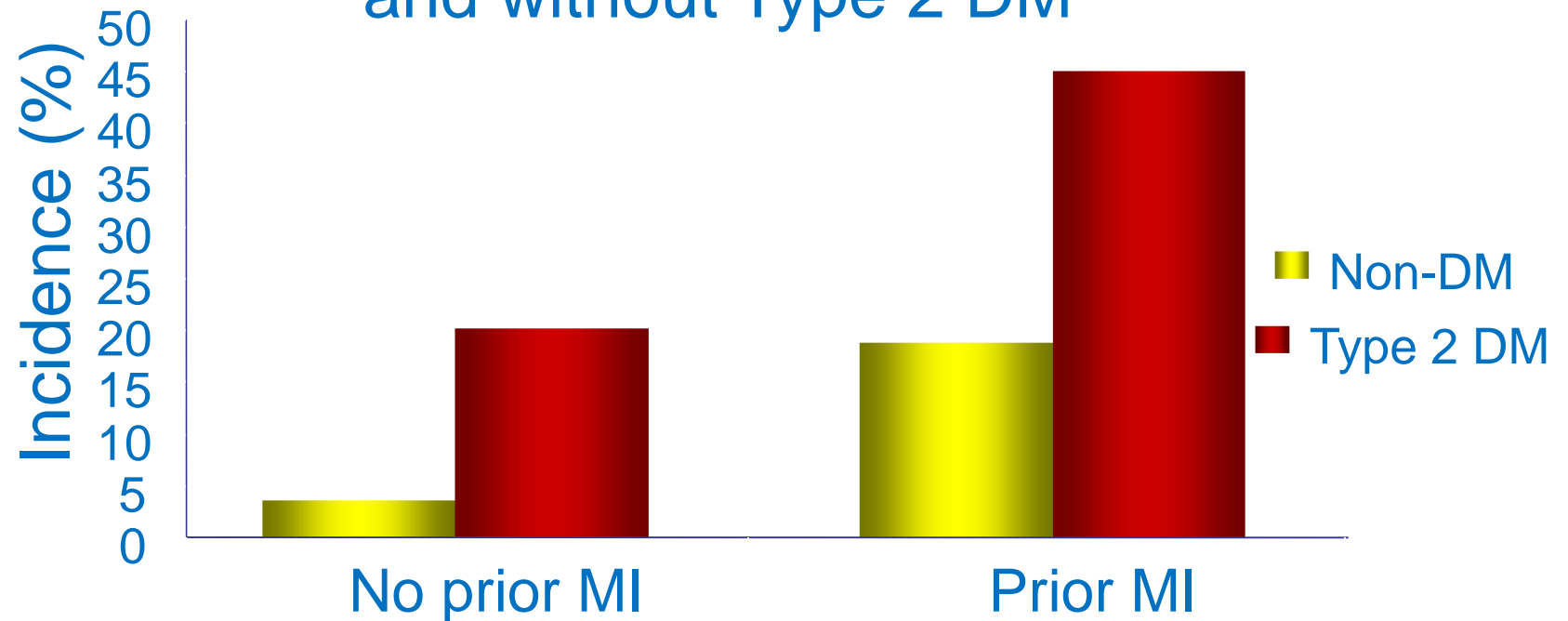
**Is diabetes a CVD risk equivalent?**



**Evidence that diabetes confers a  
SIMILAR risk of CV events to prior  
CHD**

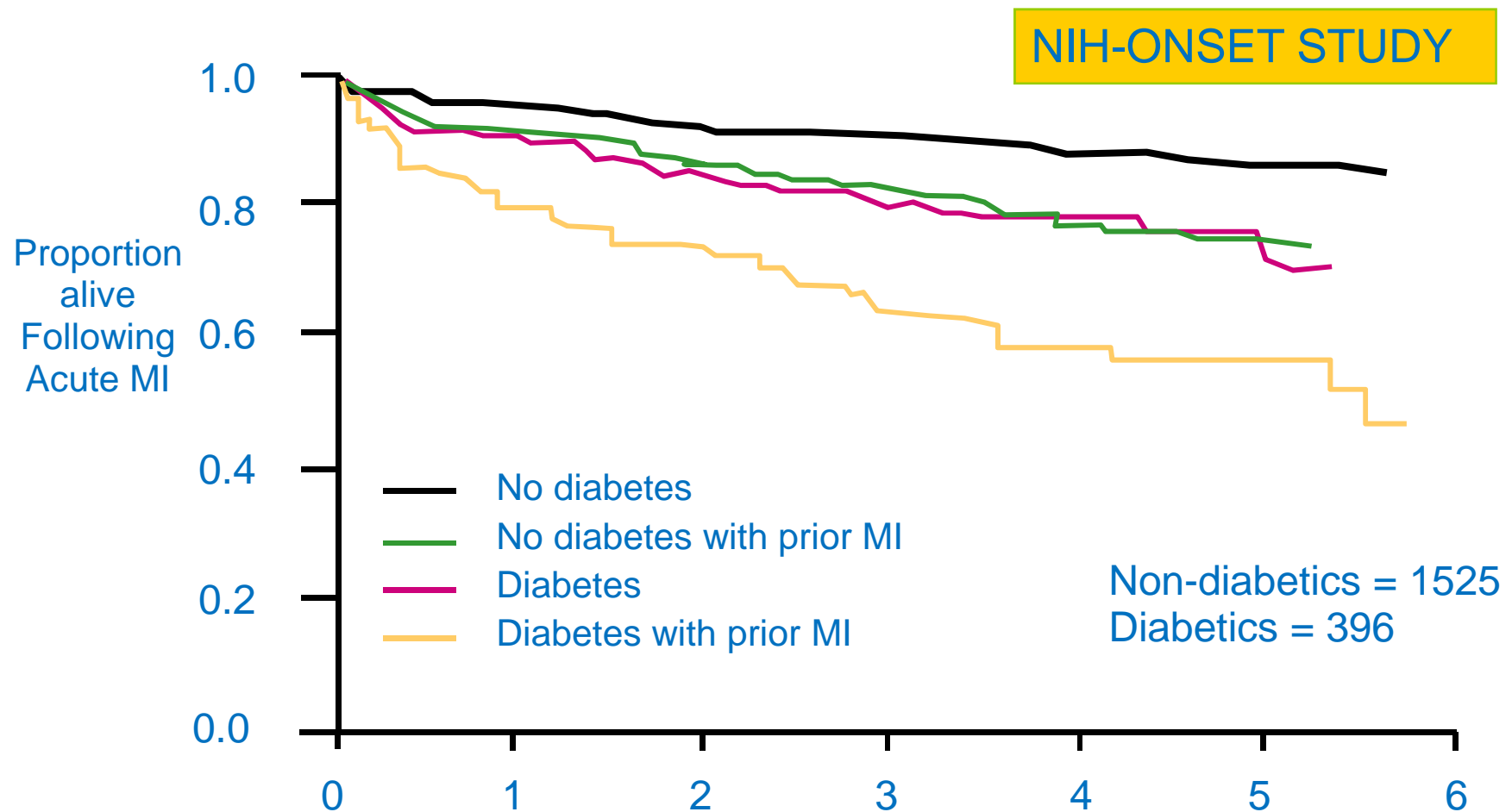
# Finnish East West Study

Fatal & nonfatal MI in subjects with and without Type 2 DM



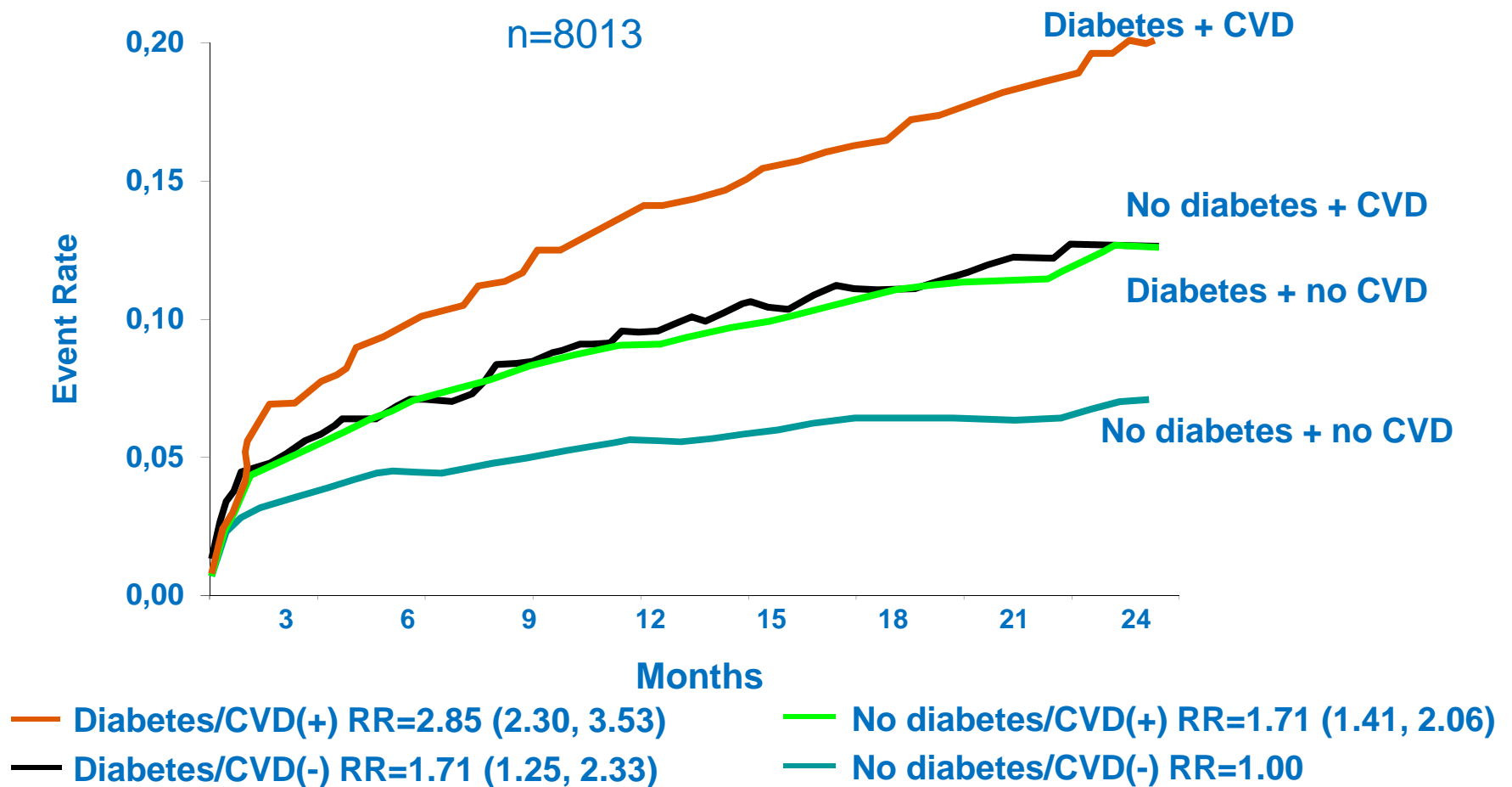
7-year incidence of fatal and nonfatal MI in 1373 nondiabetic and 1059 diabetic subjects ( $p < 0.001$ )

# Diabetes and long-term survival following acute MI: Comparability of risk with prior MI



# Diabetics at High Risk of Cardiovascular Mortality in ACS: OASIS Registry

OASIS = Organization to Assess Strategies for Ischemic Syndromes



Adapted from Malmberg K et al. *Circulation*. 2000;102:1014

# HOPE: CHD risk is similar in people with diabetes and prior CHD

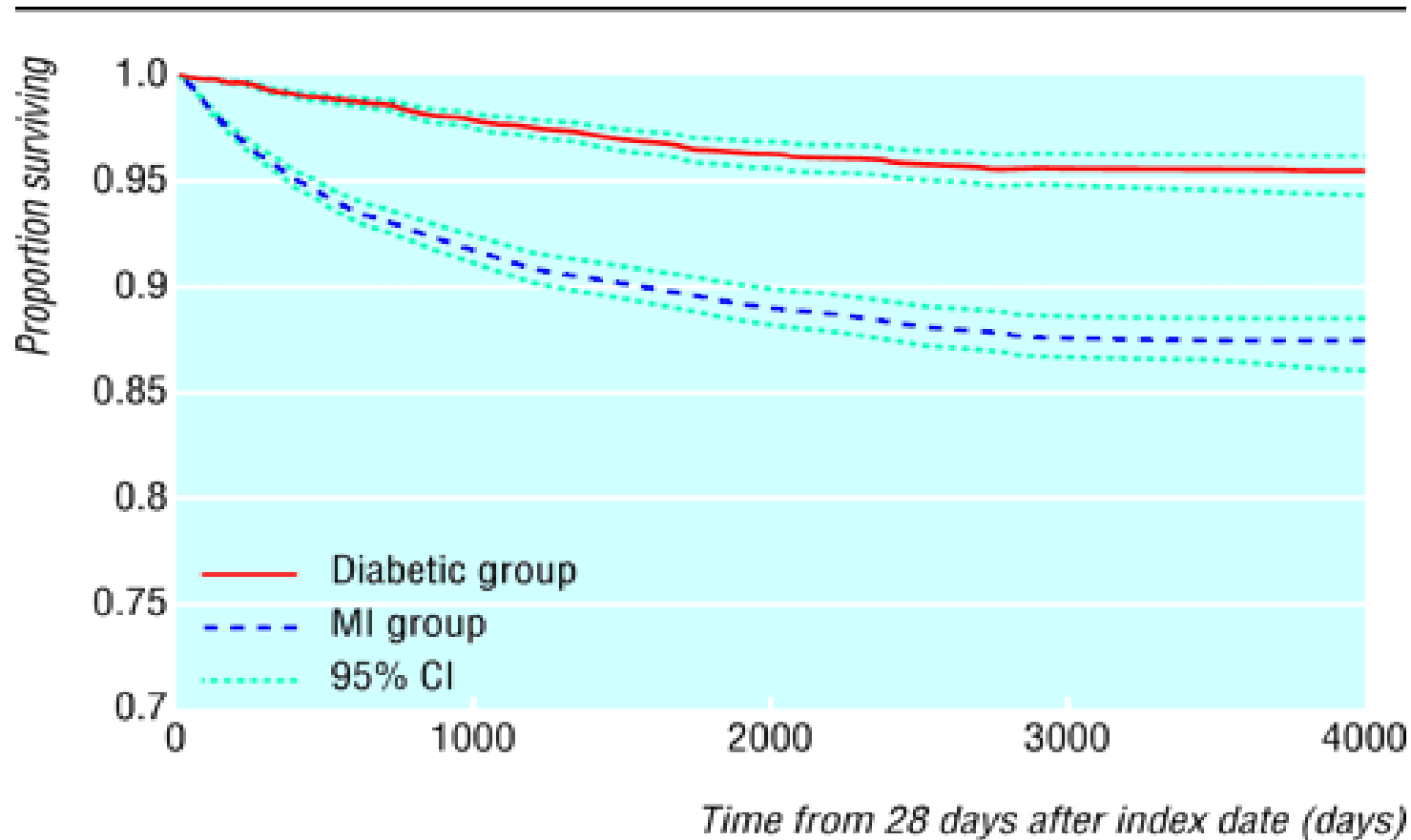
|             | No. patients | Incidence of composite outcome in placebo group (%) |
|-------------|--------------|---|
| Overall     | 9297         | 17.8  |
| CVD         | 8162         | 18.7  |
| No CVD      | 1135         | 10.2  |
| Diabetes    | 3577         | 19.8  |
| No diabetes | 5720         | 16.5  |

Composite outcome: MI, stroke, or death from cardiovascular causes

Yusuf et al. *N Engl J Med* 2000;342:145

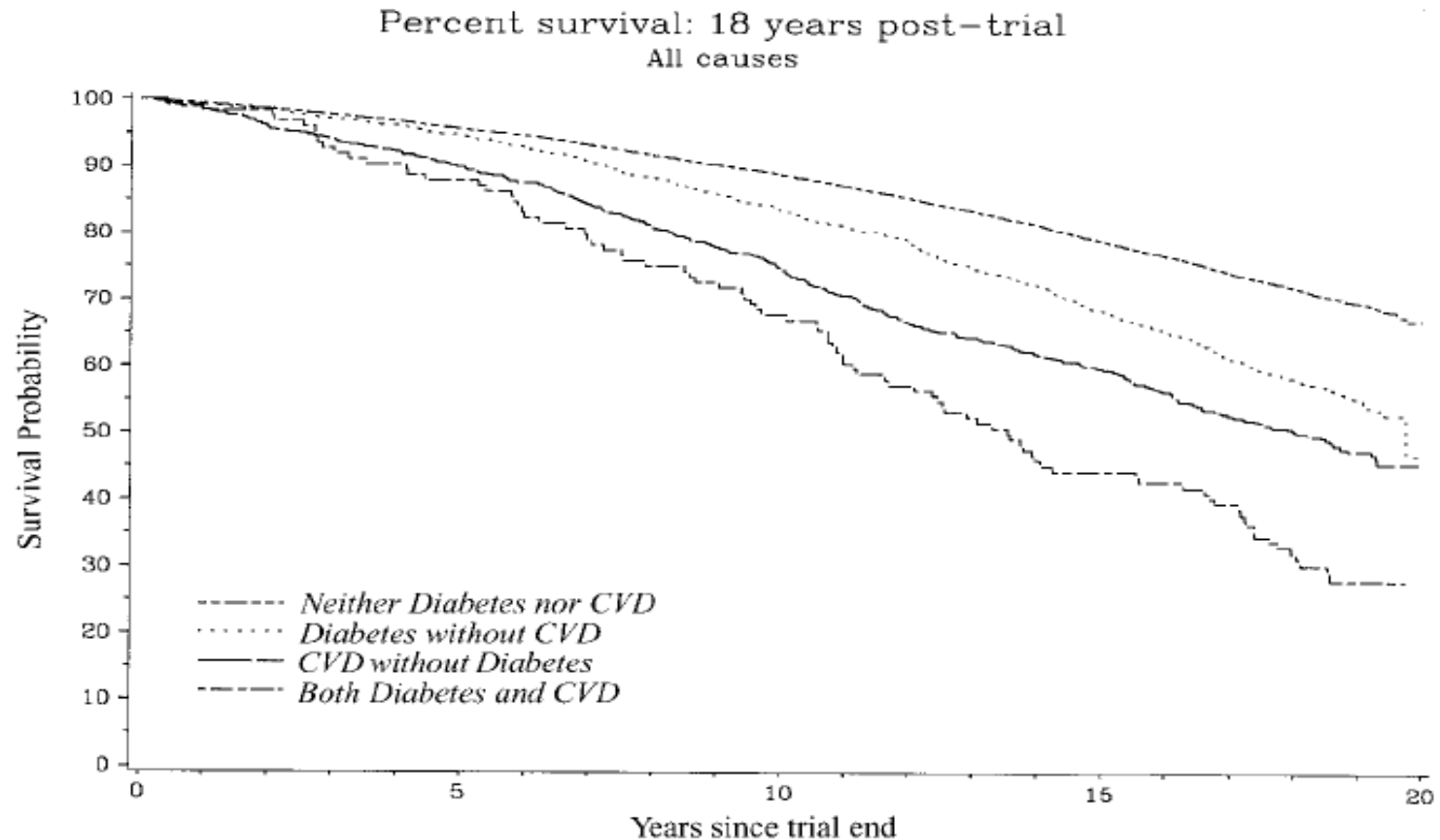
**Evidence that diabetes confers a  
LOWER risk of CV events than prior  
CHD**

# Lower risk of CV events with diabetes vs prior CHD



Kaplan-Meier survival curve: time to hospital admission for MI

# MRFIT: Lower risk of CHD death with diabetes vs prior CHD



Kaplan-Meier curves for post-trial total mortality

Eberly et al. *Diabetes Care* 2003;26:848



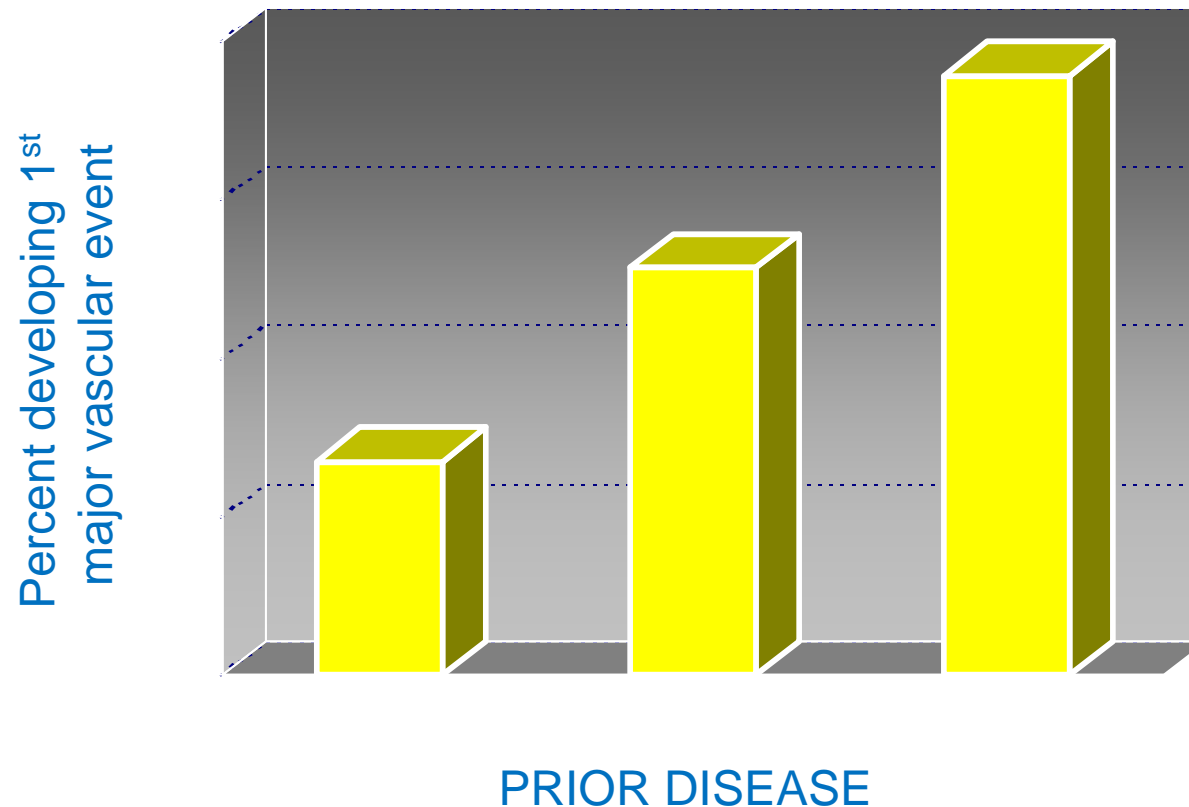
# Lower risk of CHD death with diabetes versus prior CHD

| Study/<br>Patients   | Follow-up | RR CHD death* |      |      |
|----------------------|-----------|---------------|------|------|
|                      |           | Diabetes      | CHD  | Both |
| Nurses' Health Study | 20 yrs    | 8.7           | 10.6 | 25.8 |
| US male physicians   | 5 yrs     | 3.3           | 5.6  | 12.0 |

\*vs patients without diabetes or CHD

Hu et al. *Arch Intern Med* 2001;161:1717  
Lotufo et al. *Arch Intern Med* 2001;161:242

# HPS: % of Patients in HPS Placebo Group with Major Vascular Events\* by Prior Disease



\* CHD, Stroke, revascularization

Adapted from Collins et al. Lancet. 2003 Jun 14;361(9374):2005

**Why the discrepancies in reported risk?**

# **Influence of additional CVD risk factors with diabetes**

# UKPDS: Order of Importance for Prediction of CHD (Baseline Epidemiologic Data)

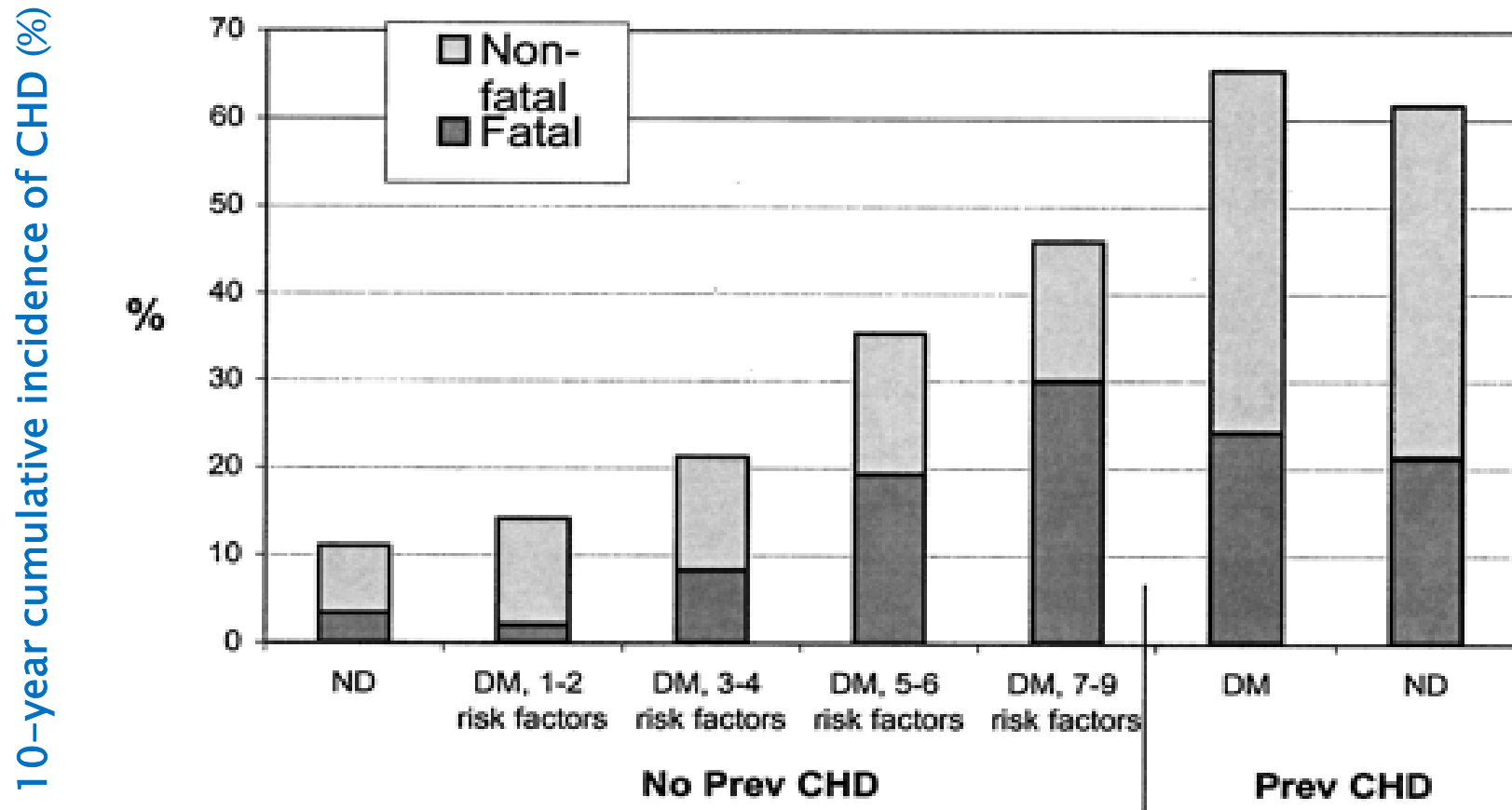
| Variable       | P-value |
|----------------|---------|
| 1. LDL-C       | <0.0001 |
| 2. HDL-C       | 0.0001  |
| 3. HbA1c       | 0.0022  |
| 4. Systolic BP | 0.0065  |
| 5. Smoking     | 0.056   |

N=2693 type 2 diabetes patients

UKPDS: United Kingdom Prospective Diabetes Study

Modified from Turner RC, et al. *BMJ*. 1998;316:823-28

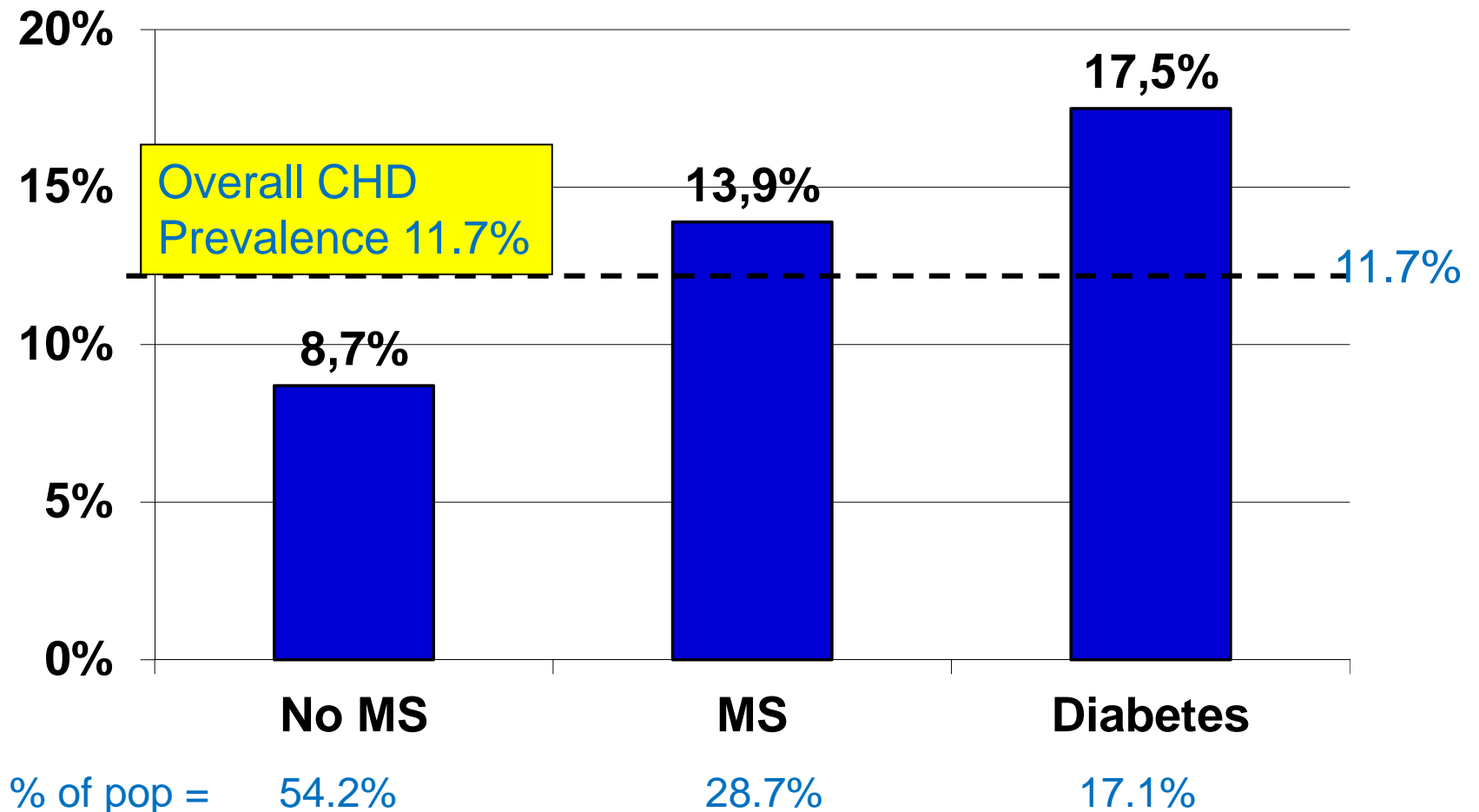
# CHD rates vary in people with diabetes with risk factors



DM, diabetes; ND, no diabetes; Prev, previous

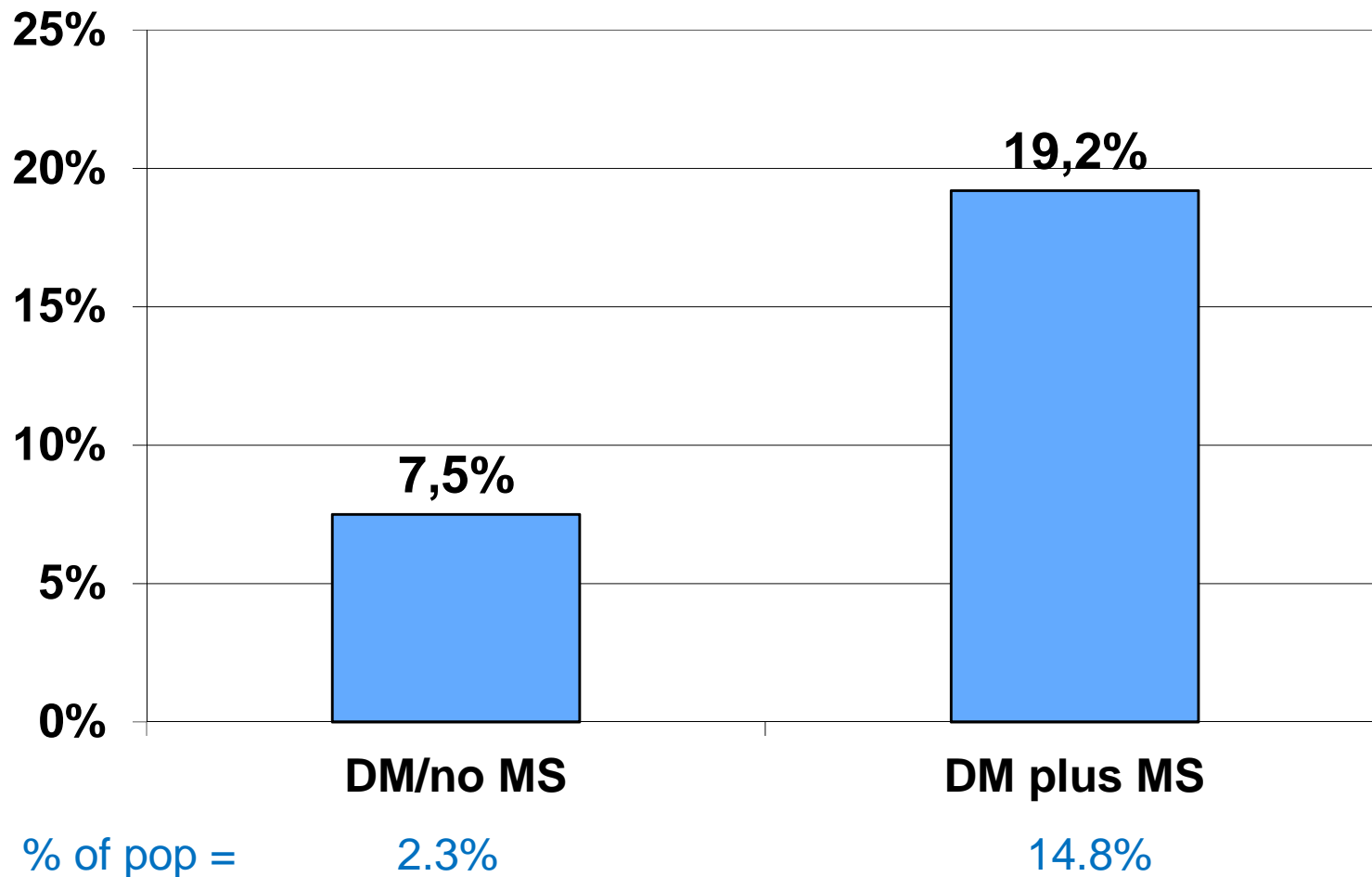
# Age-adjusted CHD prevalence & NCEP metabolic syndrome (MS) status

## NHANES population aged 50+



# Age-adjusted CHD prevalence & NCEP metabolic syndrome status in diabetes

NHANES population aged 50+





# **Effect of length of time with diabetes and CVD risk**

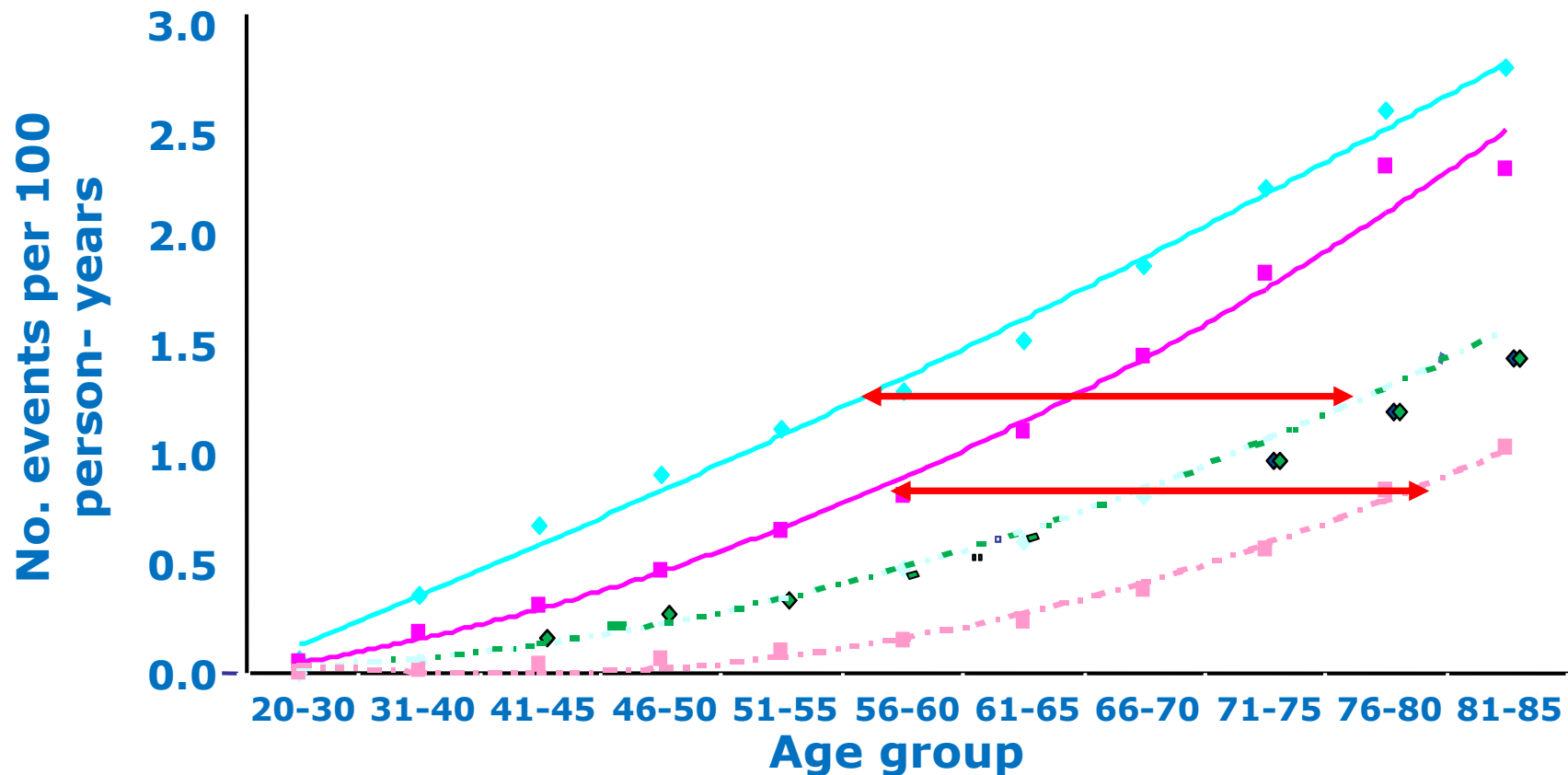
# Duration of diabetes increases risk of CHD events

Risk of events for each 10-yr increase in diabetes duration

| Outcome   | Crude |           | Age and sex adjusted |           | Multivariable adjusted |           |
|-----------|-------|-----------|----------------------|-----------|------------------------|-----------|
|           | HR    | 95% CI    | HR                   | 95% CI    | HR                     | 95% CI    |
| CVD death | 1.50† | 1.02-2.21 | 1.30                 | 0.89-1.90 | 1.44                   | 0.97-2.15 |
| CHD death | 1.83‡ | 1.18-2.83 | 1.59 †               | 1.04-2.42 | 1.86 ‡                 | 1.17-2.93 |

†P < 0.05; ‡ P < 0.01

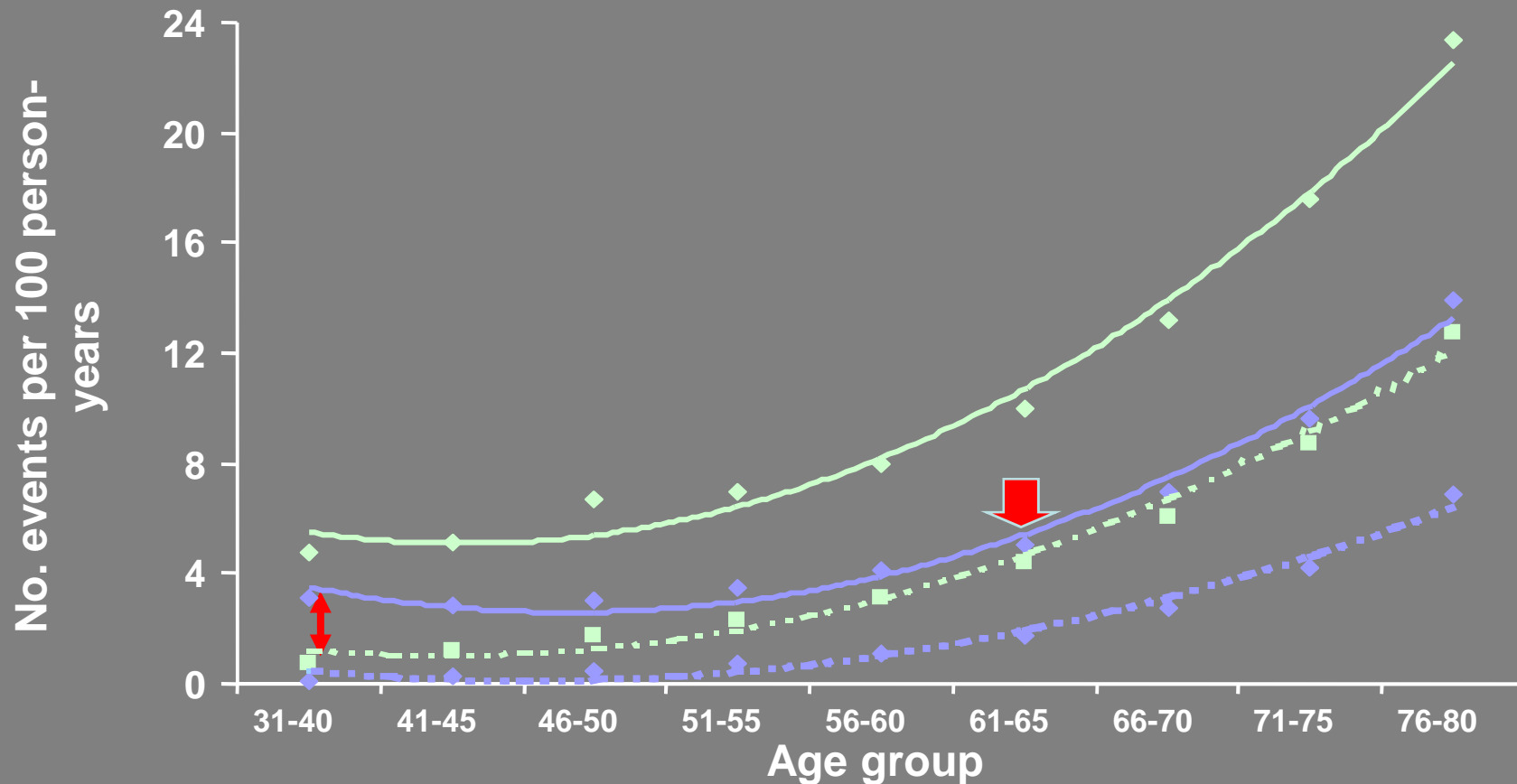
# ICES: Absolute Risk of AMI by Gender and Diabetes Status



**Diabetes:** — Men — Women    **No diabetes:** - - - Men - - - Women

All lines fitted according to a polynomial equation;  $R^2 = 0.99-1.00$  for each

# ICES: Age and Risk of CVD Events by DM and MI Status



Diabetes: — MI    - - - - No MI    No diabetes: — MI    - - - - No MI

All lines fitted according to a polynomial equation;  $R^2 = 0.99-1.00$  for each

# DM duration and CVD events

|                    |                | Men with <u>diabetes</u> without MI               |   | Men with MI                  |
|--------------------|----------------|---|---|------------------------------|
|                    | None<br>N=3197 | Late onset<br>N=307<br>Mean duration<br>1.7 years | Early onset<br>N=107<br>Mean duration<br>16 years | Without<br>diabetes<br>N=368 |
| CVD events (n=534) |                |   |   |                              |
| Age                | 1.00           | 1.59 (1.19,2.12)                                  | 2.61 (1.73,3.96)                                  | 2.35<br>(1.88,2.95)          |
| Adj                | 1.00           | 1.53 (1.15,2.06)                                  | 2.52 (1.65,3.84)                                  | 2.23<br>(1.76,2.83)          |

# **Effect of diabetes on severity of cardiovascular events**

# High mortality rate in diabetic patients after first MI

| Study                     | 1-yr mortality rate (%) |             |         |
|---------------------------|-------------------------|-------------|---------|
|                           | Diabetes                | No diabetes |         |
| Herlitz et al<br>(Sweden) | 25                      | 10          | P<0.001 |
| FINMONICA                 |                         |             |         |
| Men                       | 44.2                    | 32.6        | OR 1.36 |
| Women                     | 36.9                    | 20.2        | OR 1.83 |

Herlitz et al. *Cardiology* 1992;80:237

Miettinen et al. *Diabetes Care* 1998;21:69

# High mortality rate in diabetic patients after CABG

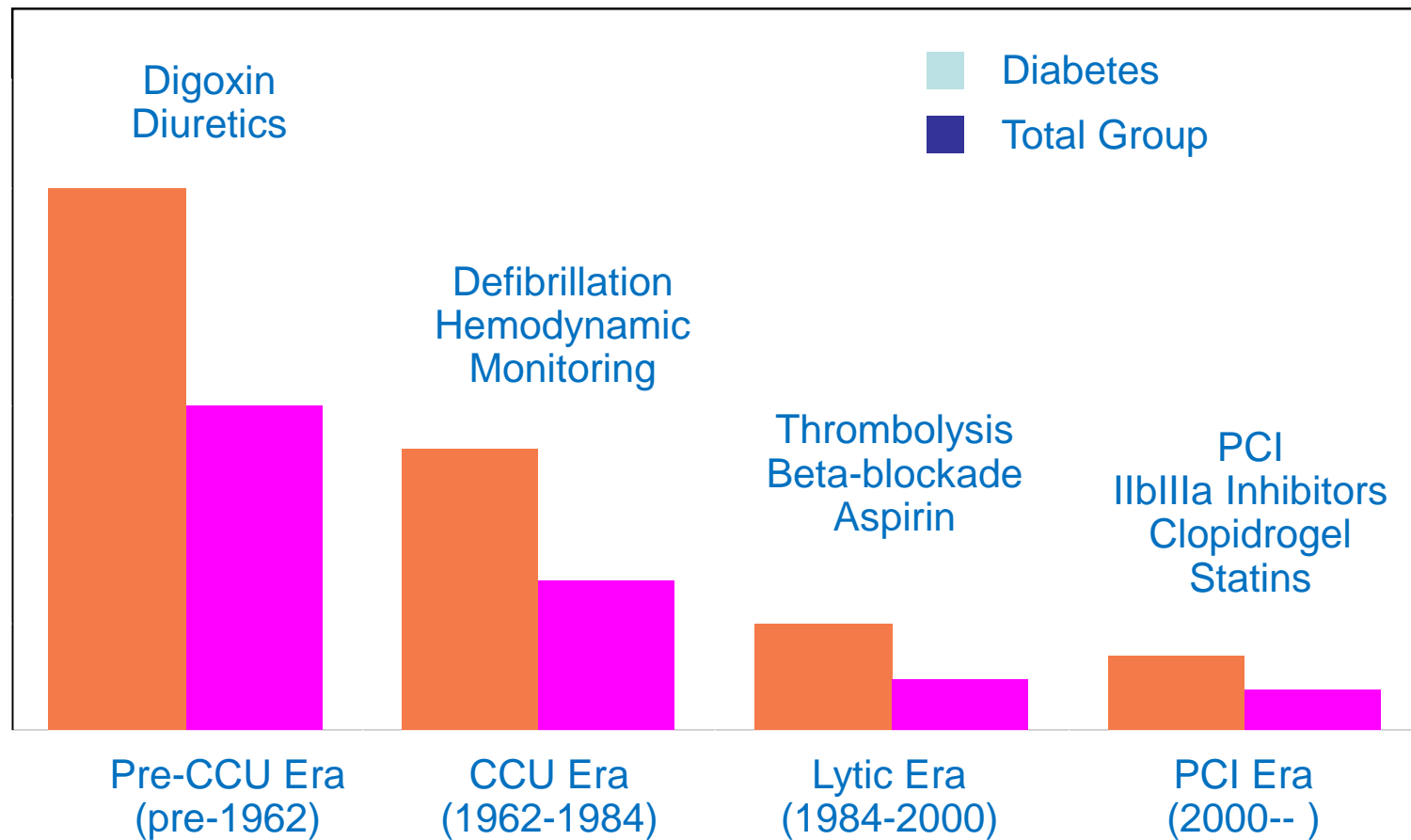
| Patients         | Survival rate (%) |           |
|------------------|-------------------|-----------|
|                  | 5-yr              | 10-yr     |
| With diabetes    | 78                | 50        |
| Without diabetes | 88                | 71        |
|                  | P ≤ 0.05*         | P ≤ 0.05* |

\*With diabetes vs without diabetes

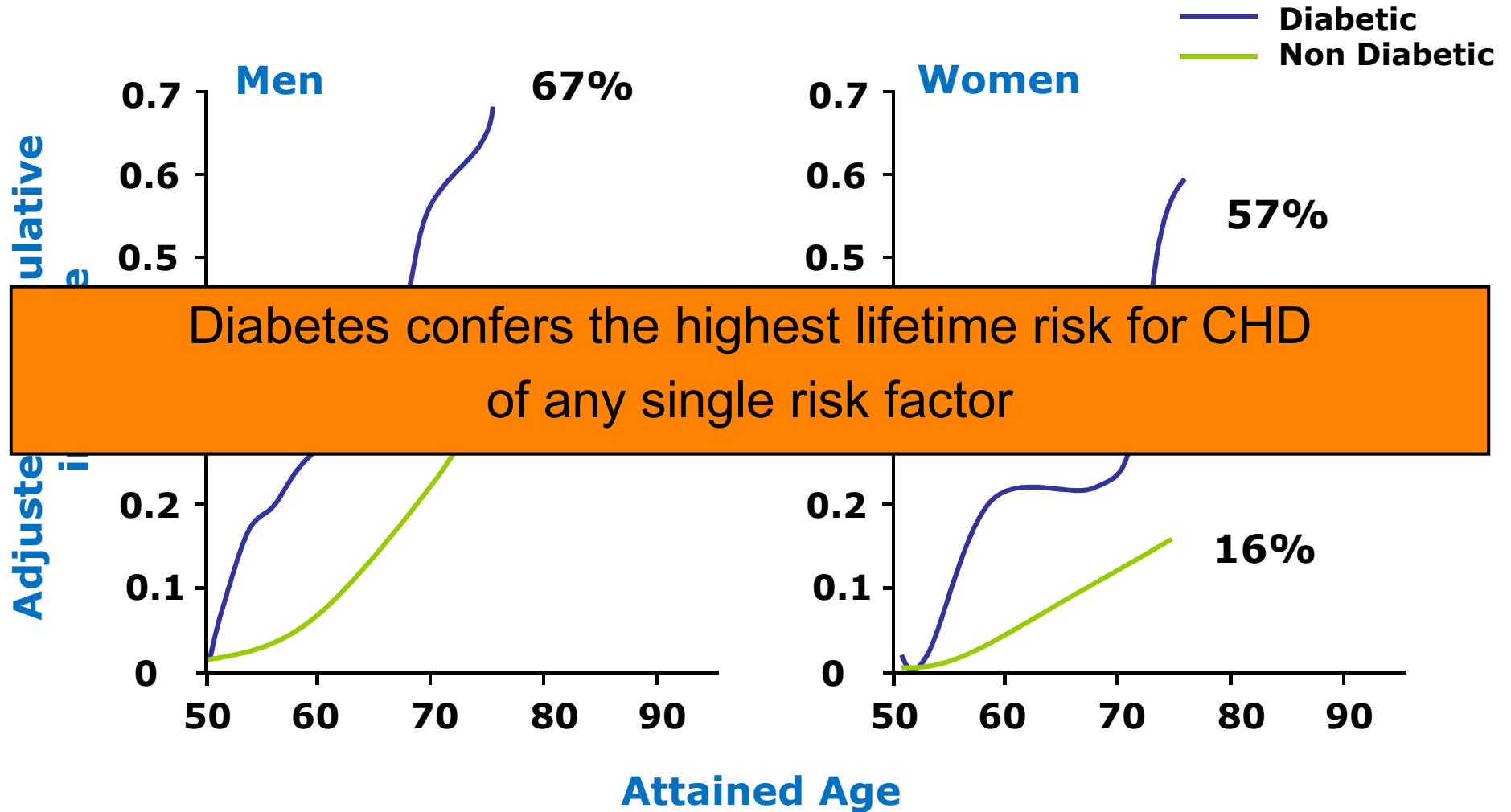


# Diabetes Confers a Doubling of Risk for Early MI Mortality Despite Advances in Cardiac Care

Early Mortality  
from Acute MI

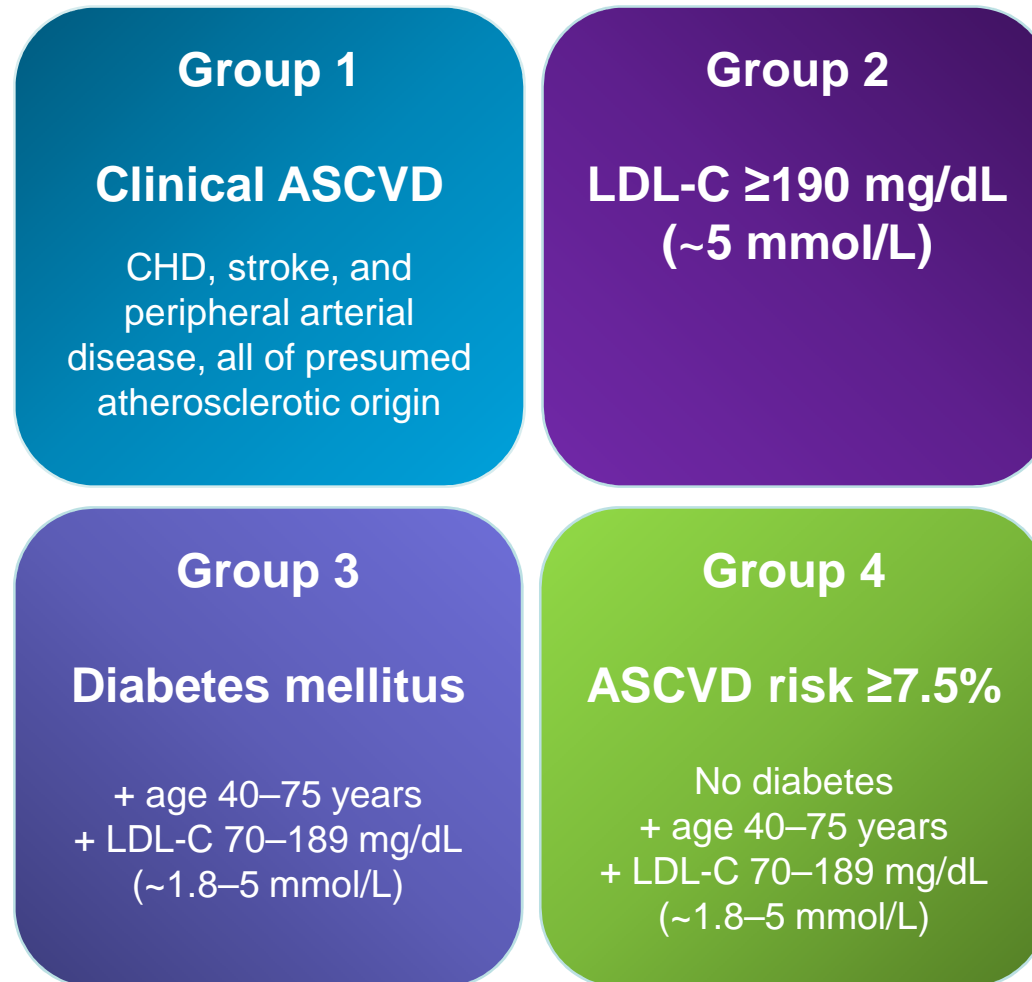


# Diabetes and Lifetime Risk for CHD

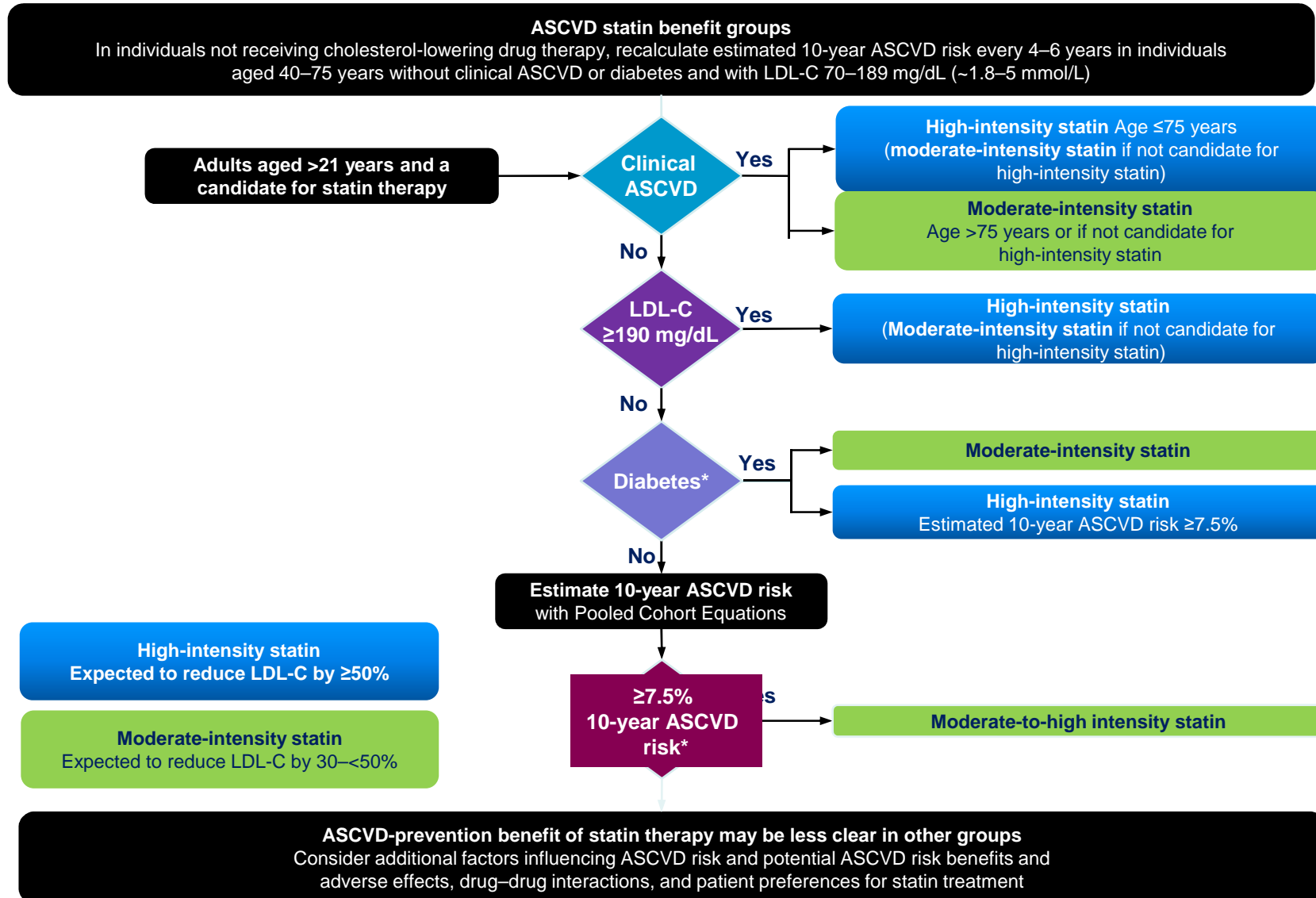


**How is diabetes considered in CVD  
guideline updates?**

# US Guidelines identify four statin benefit groups



# Treatment decision flow for four statin benefit groups



\*Aged 40–75 years

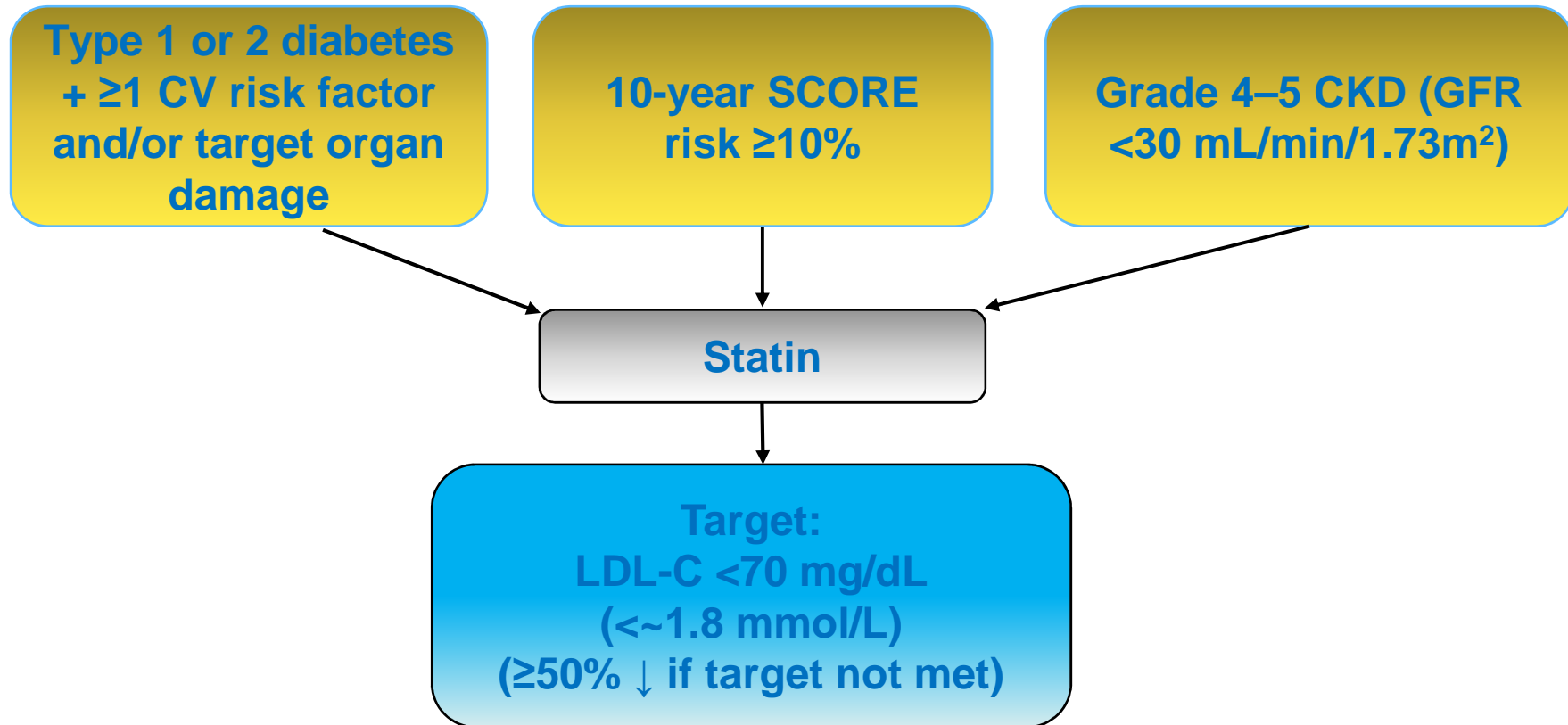
# Guidelines specify statin doses

| High-intensity therapy* | Moderate-intensity therapy† | Low-intensity therapy‡ |
|-------------------------|-----------------------------|------------------------|
| Atorvastatin 40–80 mg   | Atorvastatin 10–20 mg       | Simvastatin 10 mg      |
| Rosuvastatin 20–40 mg   | Rosuvastatin 5–10 mg        | Pravastatin 10–20 mg   |
|                         | Simvastatin 20–40 mg        | Lovastatin 20 mg       |
|                         | Pravastatin 40–80 mg        | Fluvastatin 20–40 mg   |
|                         | Lovastatin 40 mg            | Pitavastatin 1 mg      |
|                         | Fluvastatin XL 80 mg        |                        |
|                         | Fluvastatin 40 mg BID       |                        |
|                         | Pitavastatin 2–4 mg         |                        |

\*LDL-C reduced by ~≥50%;

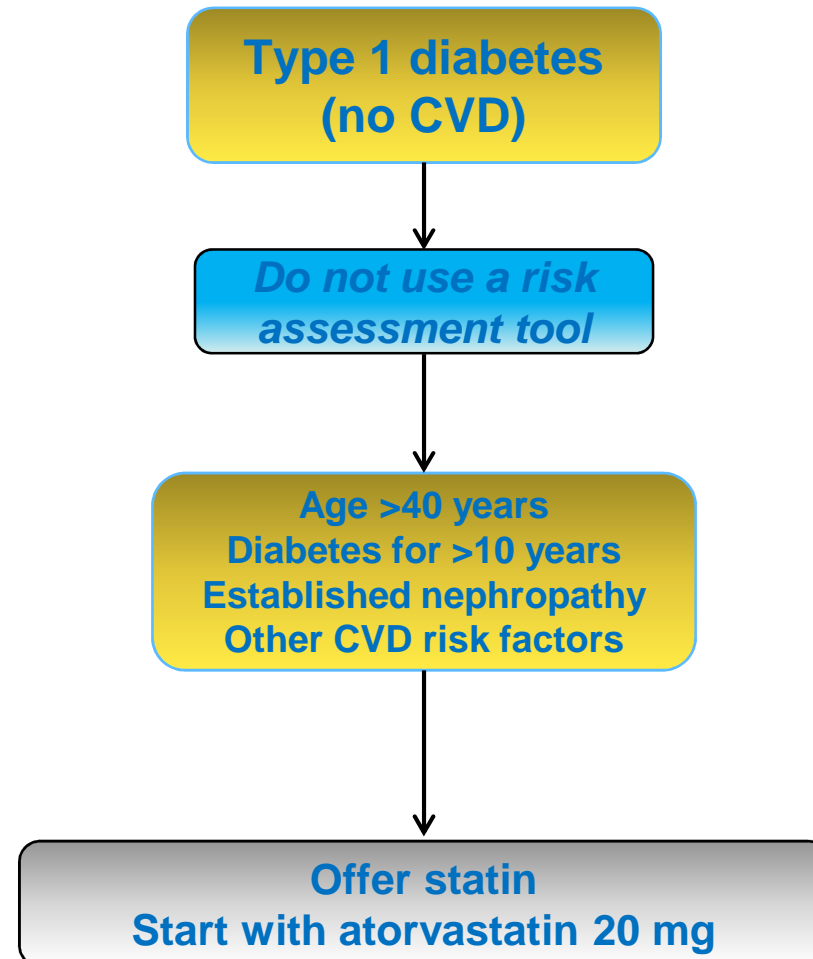
†LDL-C reduced ~30–50%; ‡ LDL-C reduced ~<30%  
 BID, twice-daily dosing

# ESC: Other very high risk groups



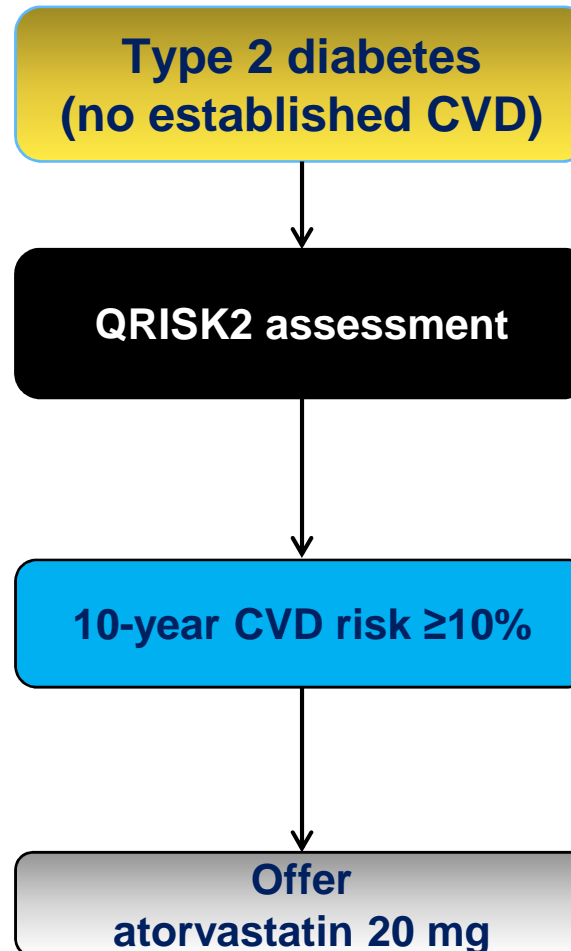
CKD, chronic kidney disease;  
CV, cardiovascular;  
GFR, glomerular filtration rate

# NICE lipid guidelines: Type 1 diabetes

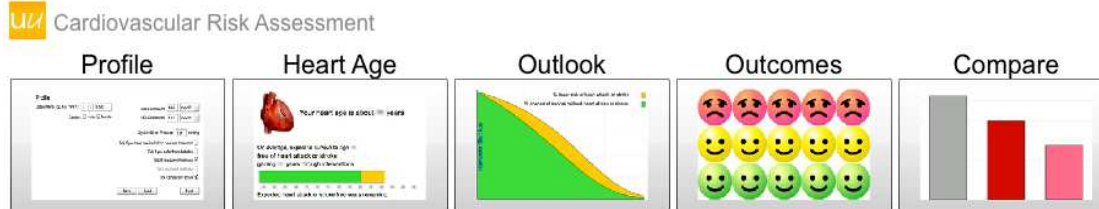
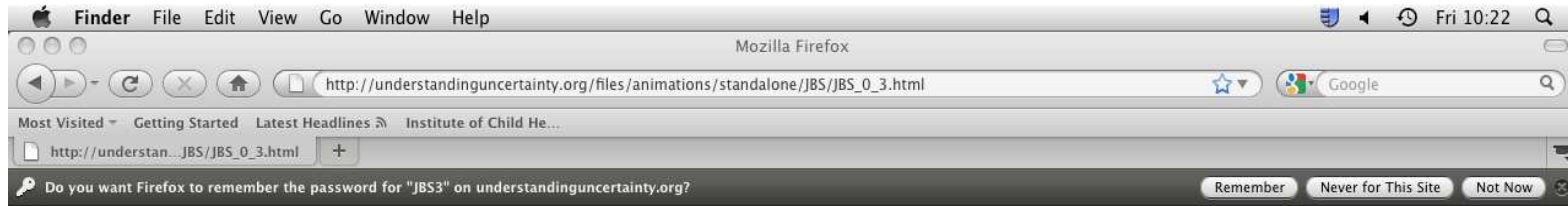




# NICE lipid guidelines: Type 2 diabetes



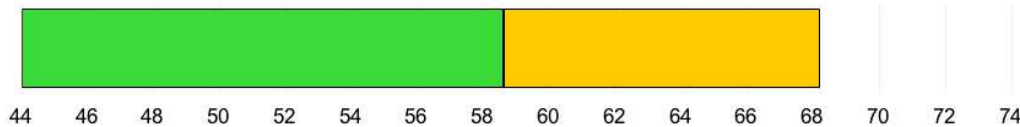
# Should we use lifetime CVD risk estimation?



**45 year old male**

Your heart age is about 68 years

On average, expect to survive to age 68  
free of heart attack or stroke  
gaining 9.6 years through interventions



Expected heart attack or stroke free years remaining

## Interventions

Systolic Blood Pressure

150 → 150

Treat?

Total Cholesterol

6 → 4.5

HDL Cholesterol

1.16 → 1.16

Stop smoking

Physically active

# Diabetes is a major risk factor for CVD

- Most diabetes patients are at high risk for atherosclerotic CVD
- If diabetes patients suffer CVD it is more severe
- CV risk factor modification (cholesterol and bp-lowering) are important components of CV risk reduction in diabetes
- Badging diabetes as a CHD risk equivalent is pragmatic and may increase the likelihood of appropriate CVD primary and secondary prevention