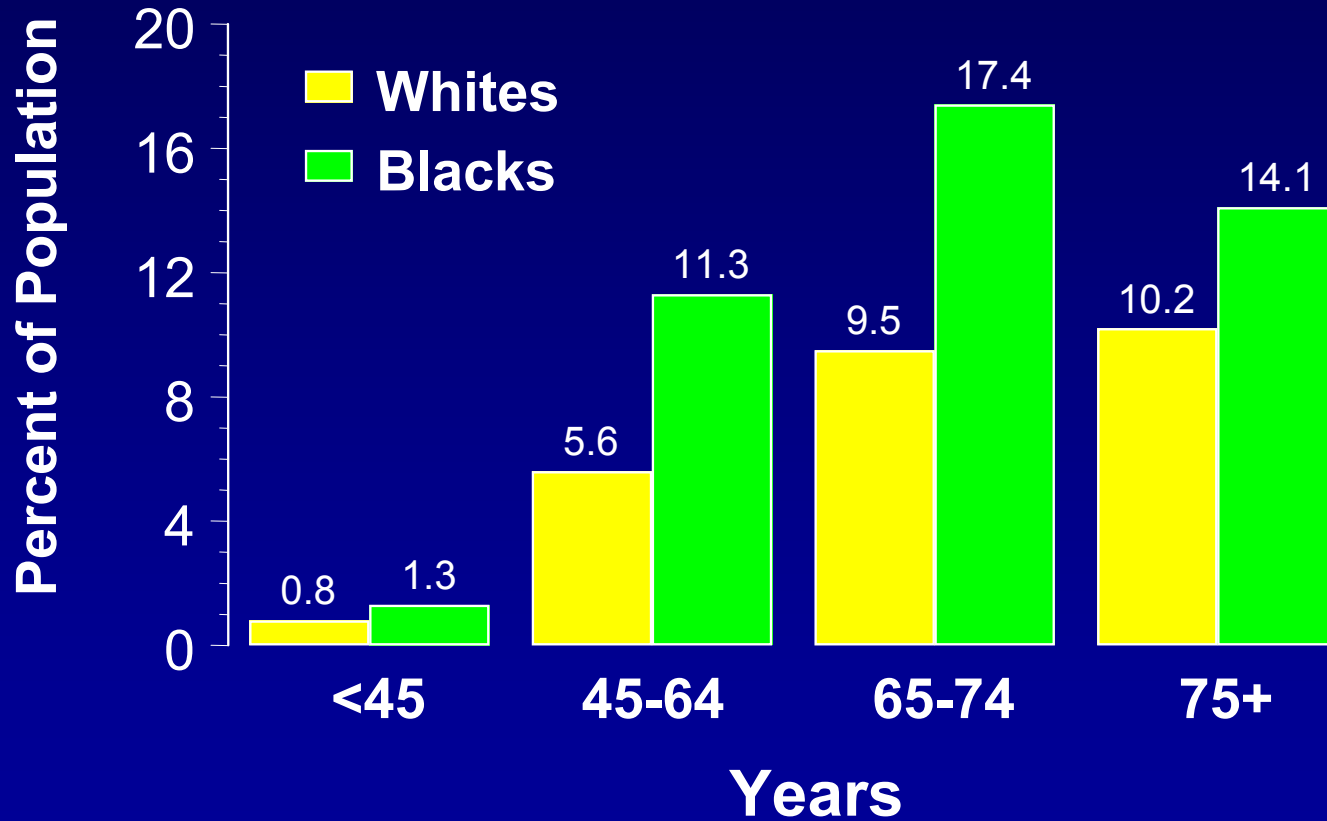


Duality of Risk in Diabetes Mellitus Microvascular and Macrovascular Disease

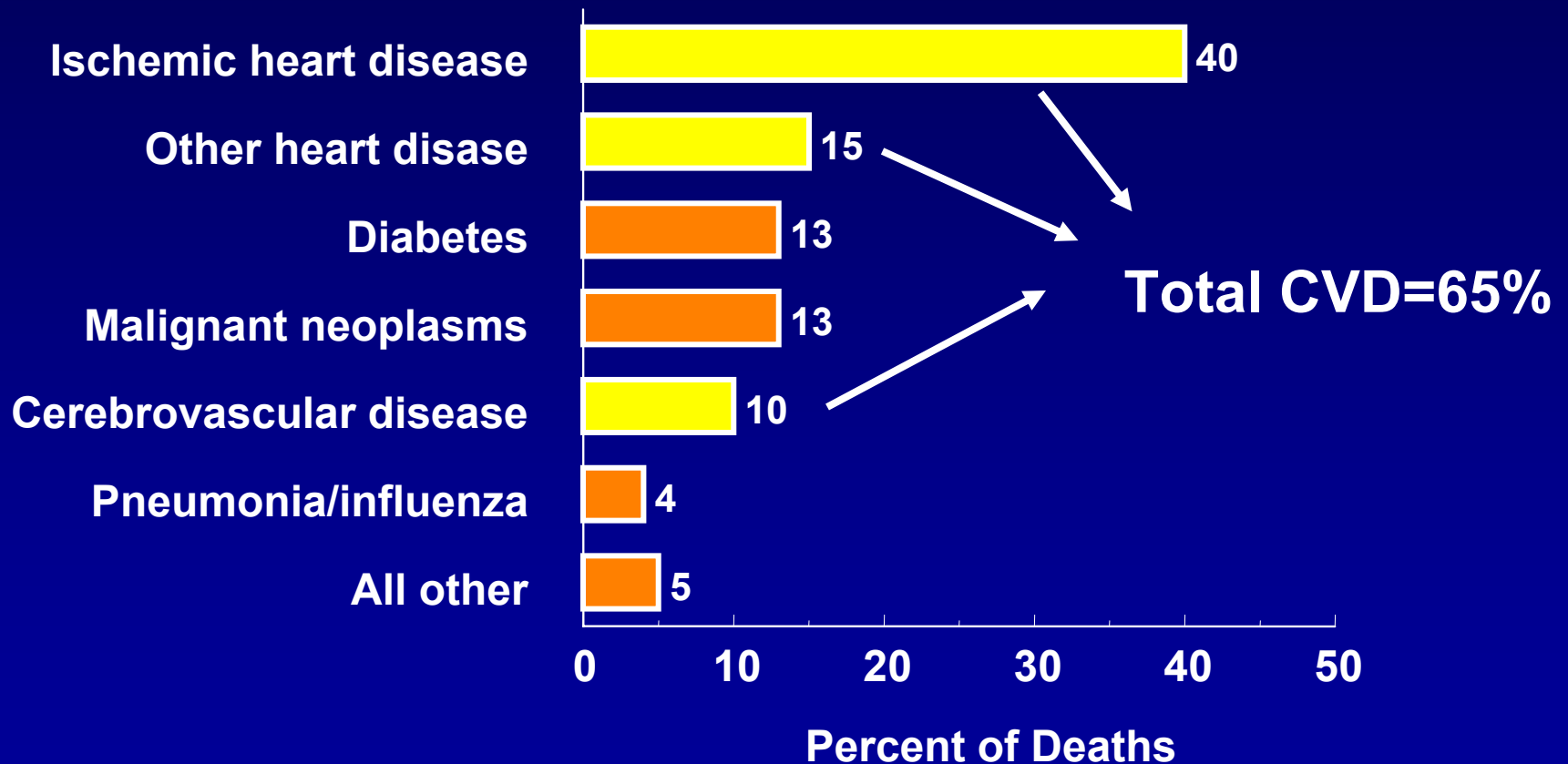
Peter W. F. Wilson, M.D.

**Section on Endocrinology, Diabetes and Medical Genetics
Medical University of South Carolina**

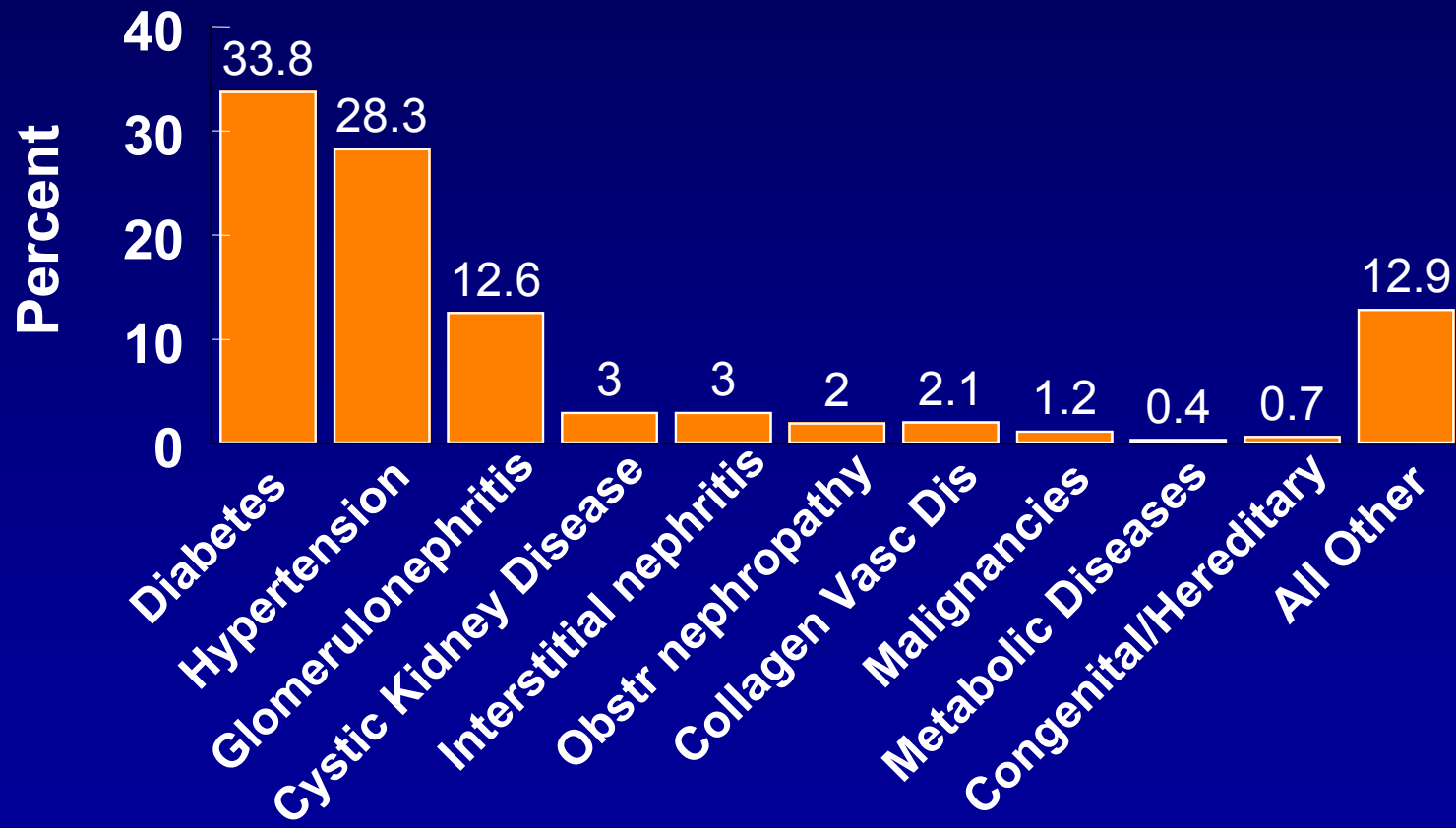
Estimated Percentage of Adults with Diagnosed Diabetes Mellitus by Age and Race U.S. 1993



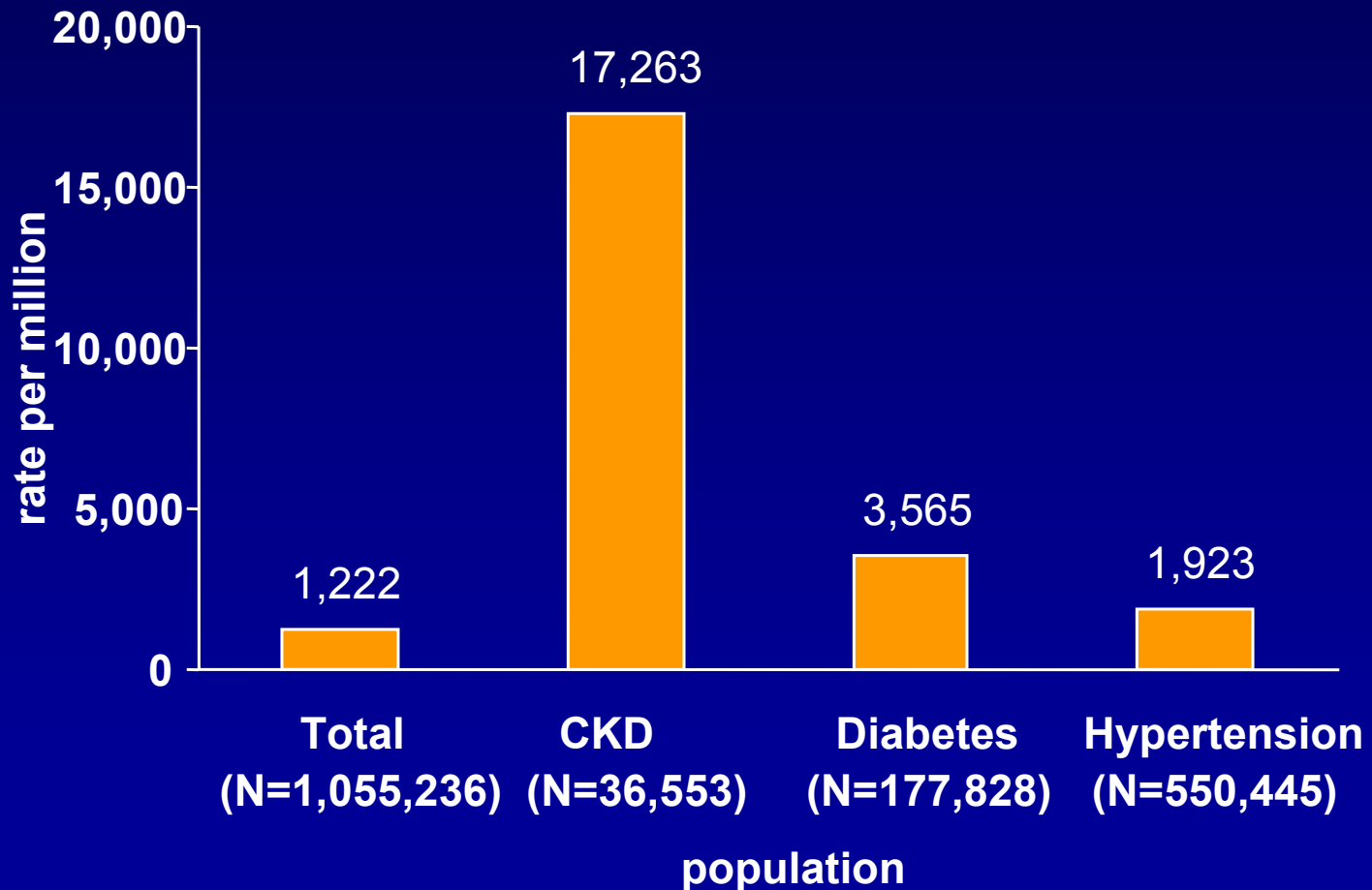
Approximate Distribution of Causes of Death in Persons with Diabetes, Based on U.S. Studies



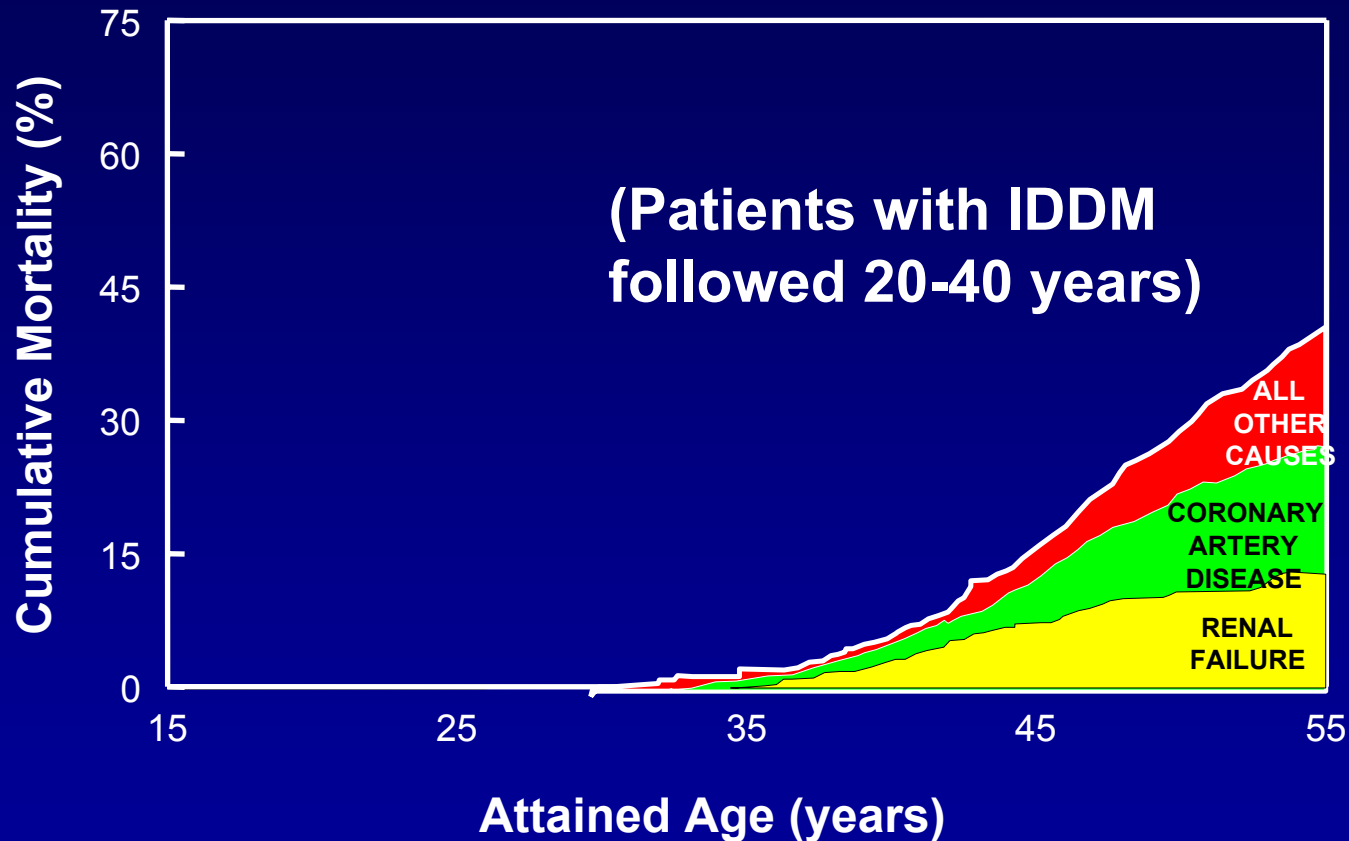
Percent distribution of New Cases of Treated End Stage Renal Disease by Primary Diagnosis, U.S., 1988-91



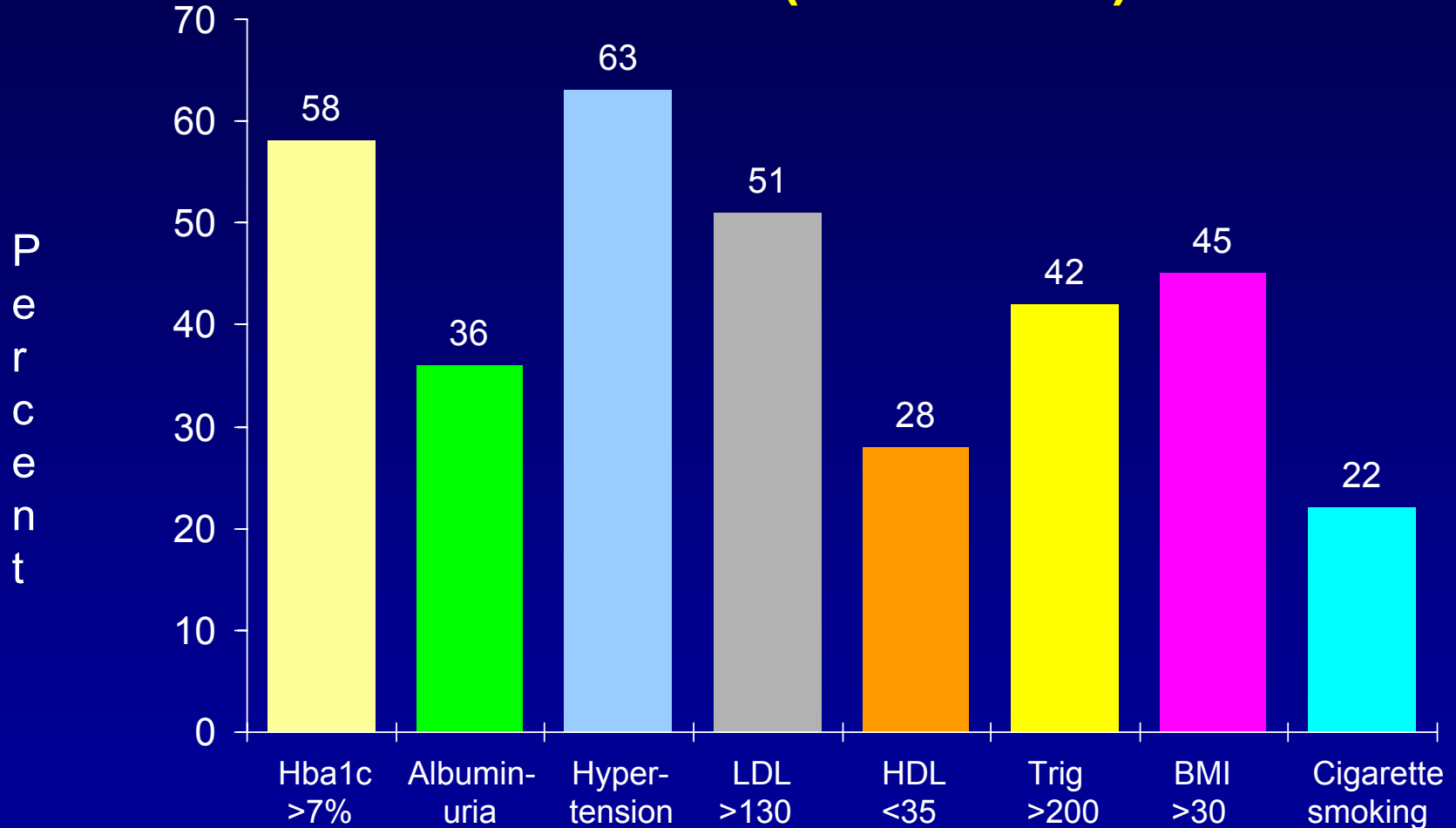
Incidence of ESRD in 1999-2001 (According to Status in 1997-1998)



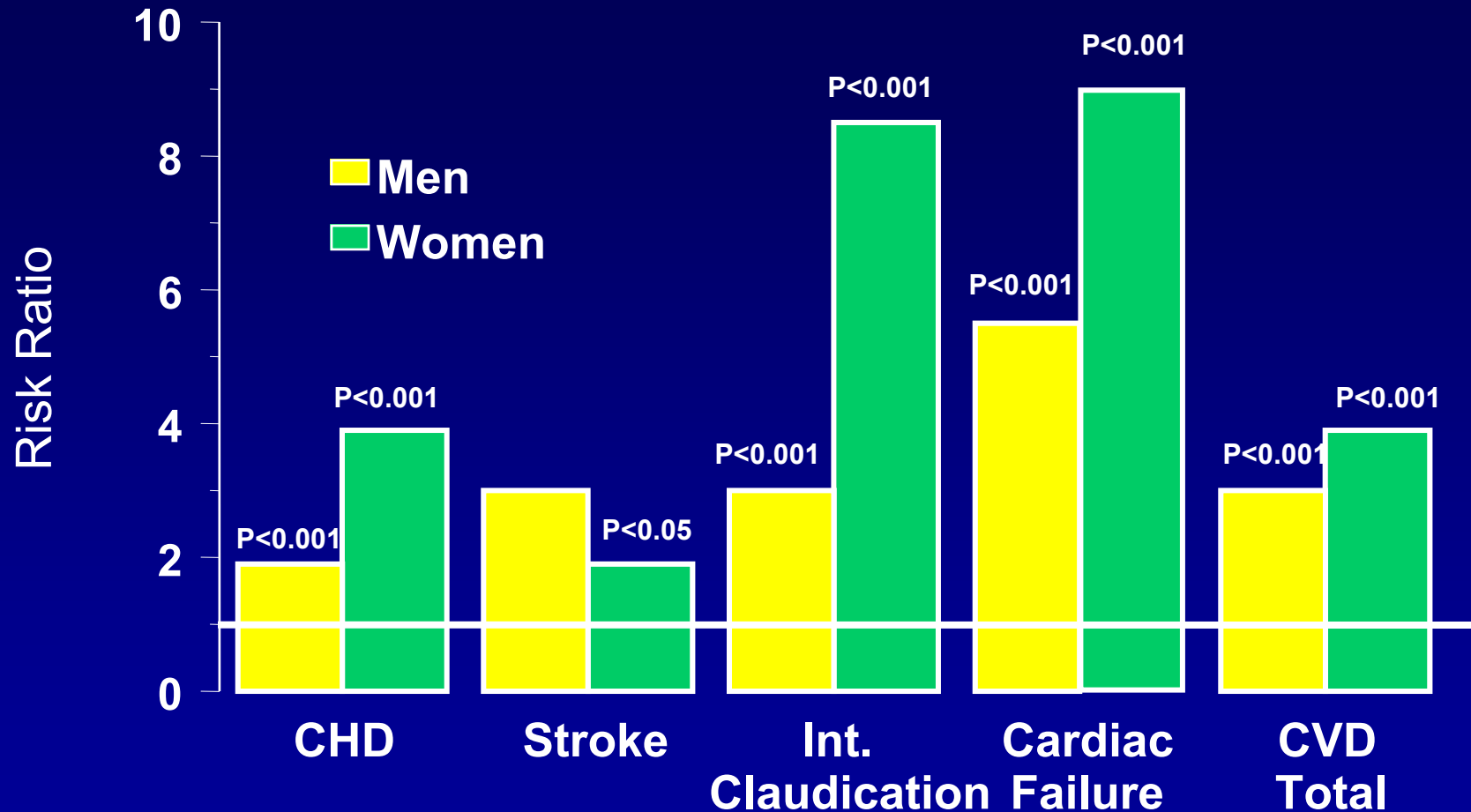
Cumulative Mortality Due to Coronary Artery Disease and Other Causes of Death



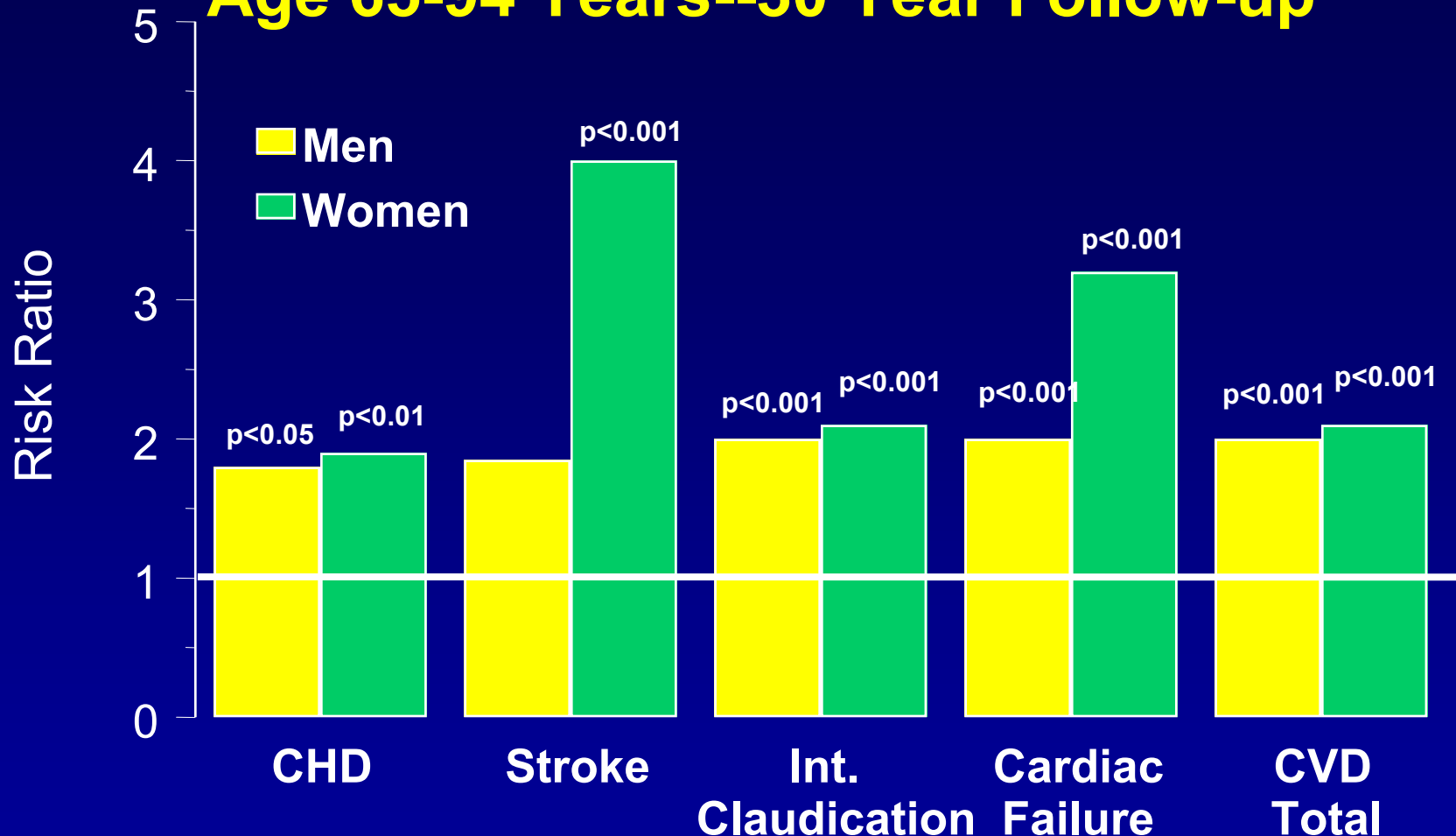
Risk Factors for Complications in Type 2 Diabetes NHANES III (1991-1994)



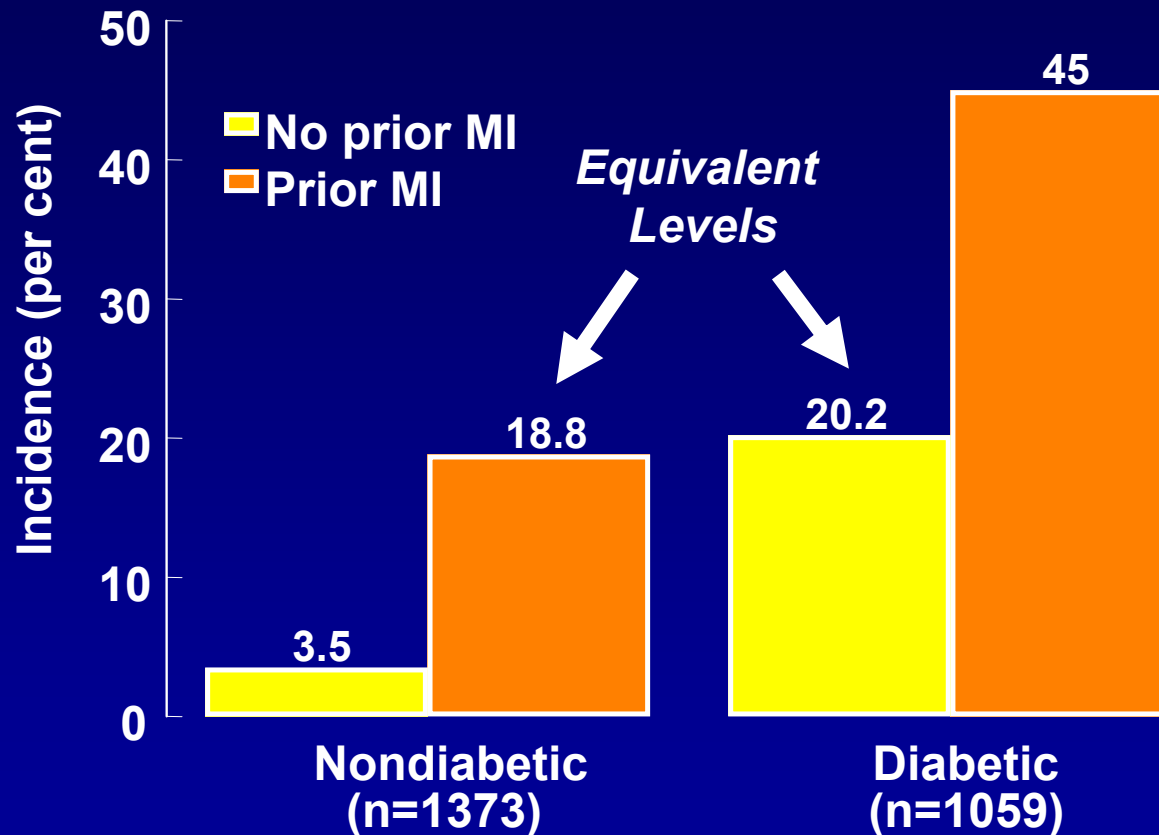
Diabetes and CVD Risk in Framingham Cohort Age 35-64 Years--30 Year Follow-up



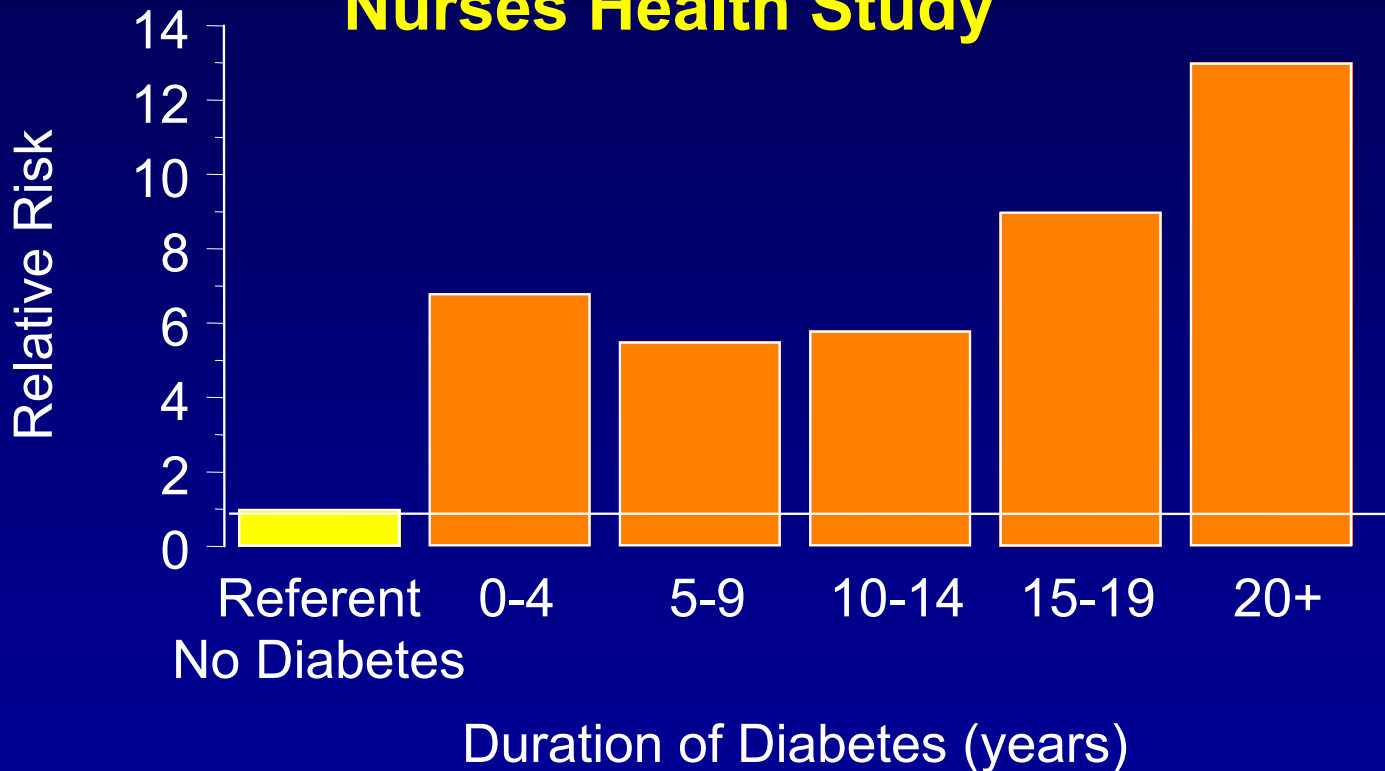
Diabetes and CVD Risk in Framingham Cohort Age 65-94 Years--30 Year Follow-up



Incidence of Myocardial Infarction Finnish East-West Study Diabetics and Non-Diabetics



Relative Risk of Combined Nonfatal MI and Fatal CHD Diabetic vs Nondiabetic Women, by Diabetes Duration Nurses Health Study

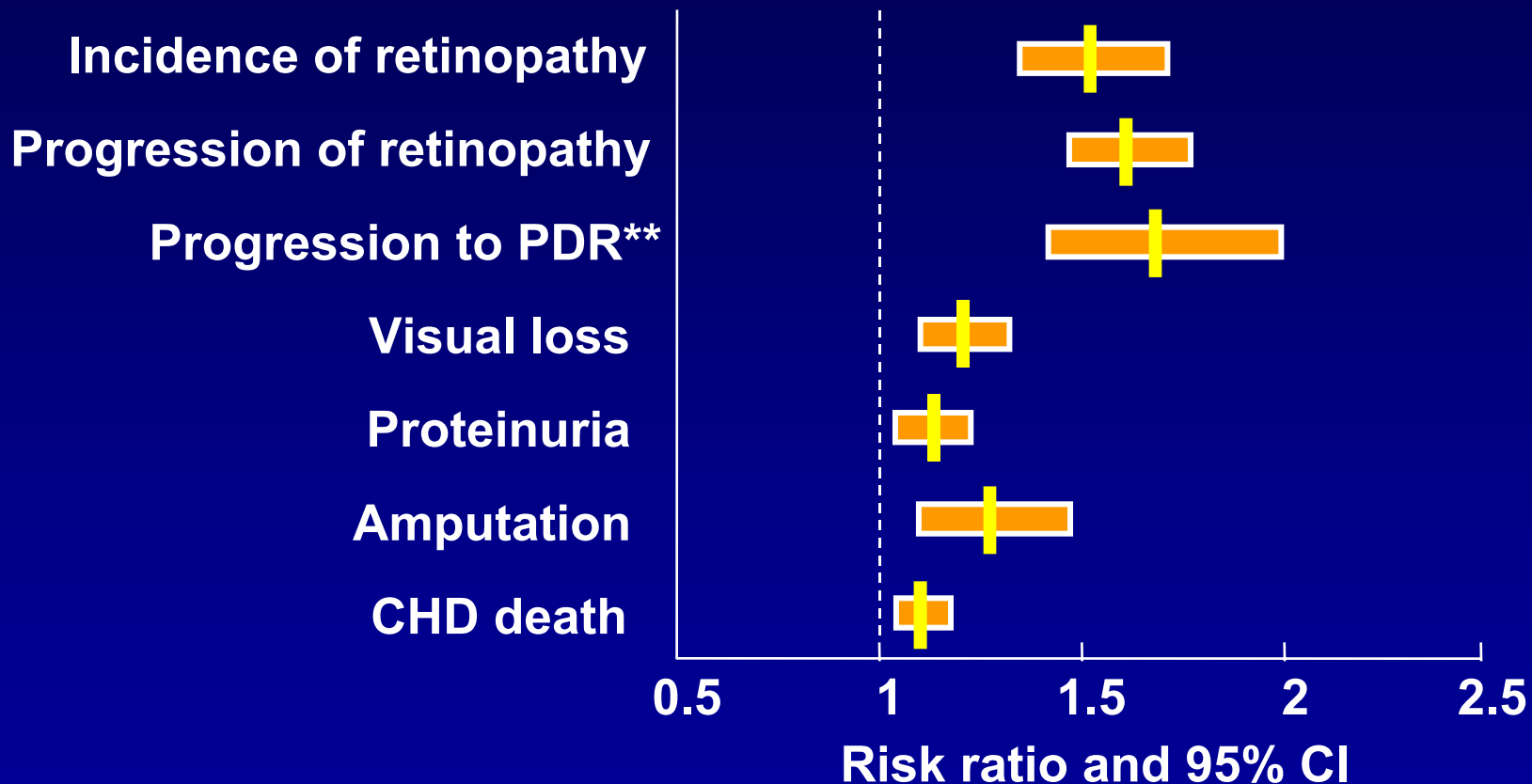


Manson Arch Int Med 1991; 151: 1141
Diabetes in America 1995, p 438

Glycemia and Vascular Risk

- **Observational Studies**
Epidemiology studies (WESDR)
- **Type I Diabetes**
DCCT
- **Type II Diabetes**
UKPDS
Steno-2

WESDR: Hyperglycemia and the Risk for Vascular Complications in Older-Onset Diabetes



* Wisconsin Epidemiology Study of Diabetic Retinopathy

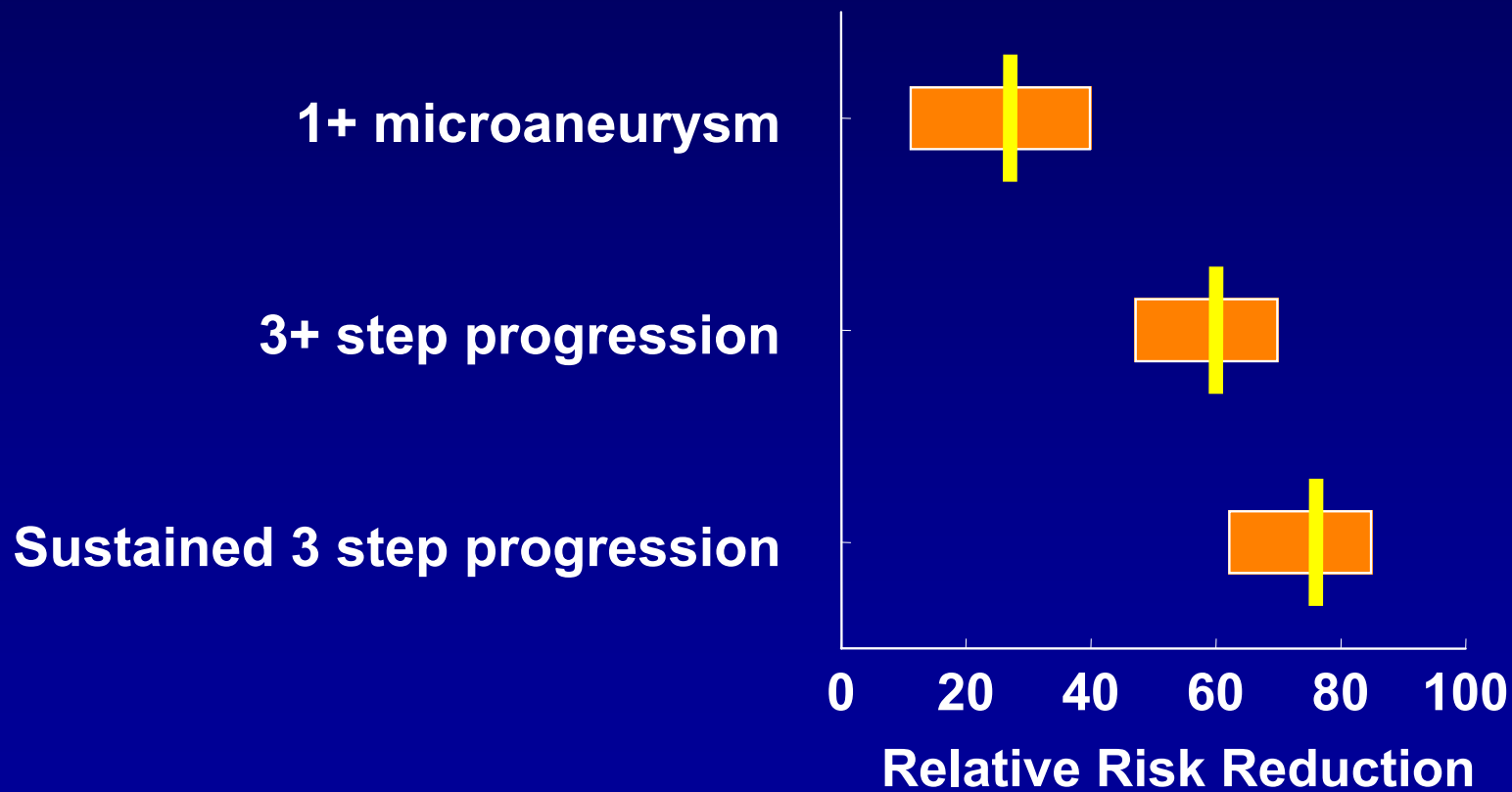
** PDR = proliferative diabetic retinopathy.

Klein R. Diabetes Care 1995; 18: 258

Diabetes Control and Complications Trial (DCCT) CVD Risk Factors and Outcomes

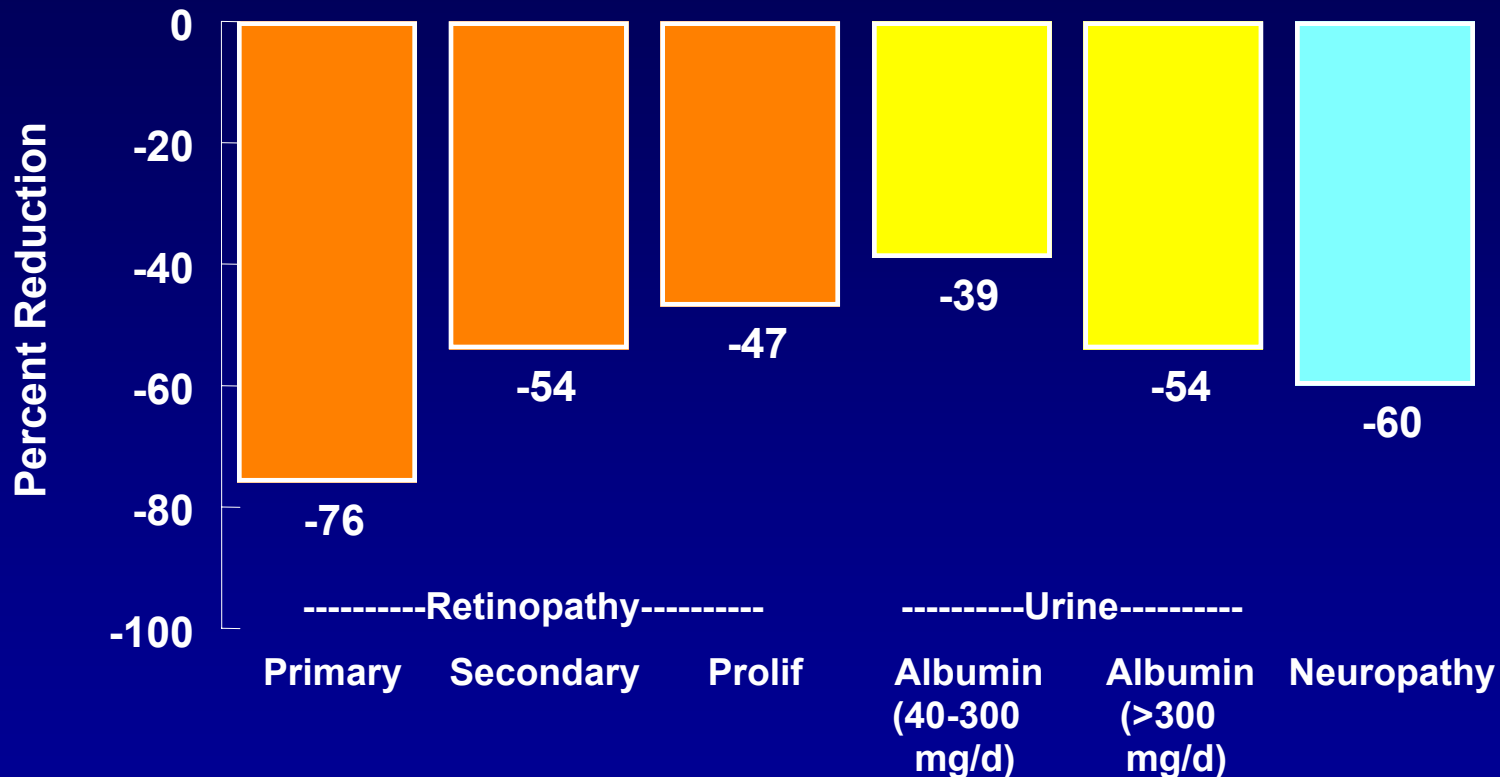
- **1441 Type I Diabetes Mellitus patients**
 - 13-39 years at onset of trial
 - No hypertension, elevated cholesterol, or obesity
 - 611 conventional diabetes Rx (mean HbA_{1C} 9%)
 - 618 intensive diabetes Rx (mean HbA_{1C} 7.2%)
- **Outcomes associated with Intensive Rx**
 - Greater risk of hypoglycemia
 - Improved cholesterol, LDL-C, and triglycerides (P=0.01)
 - Hypertension risk not increased (P=ns)
 - CVD risk increased 2X (P=0.08)

Risk Reduction in Incidence and Progression of Retinopathy DCCT Primary Prevention Group

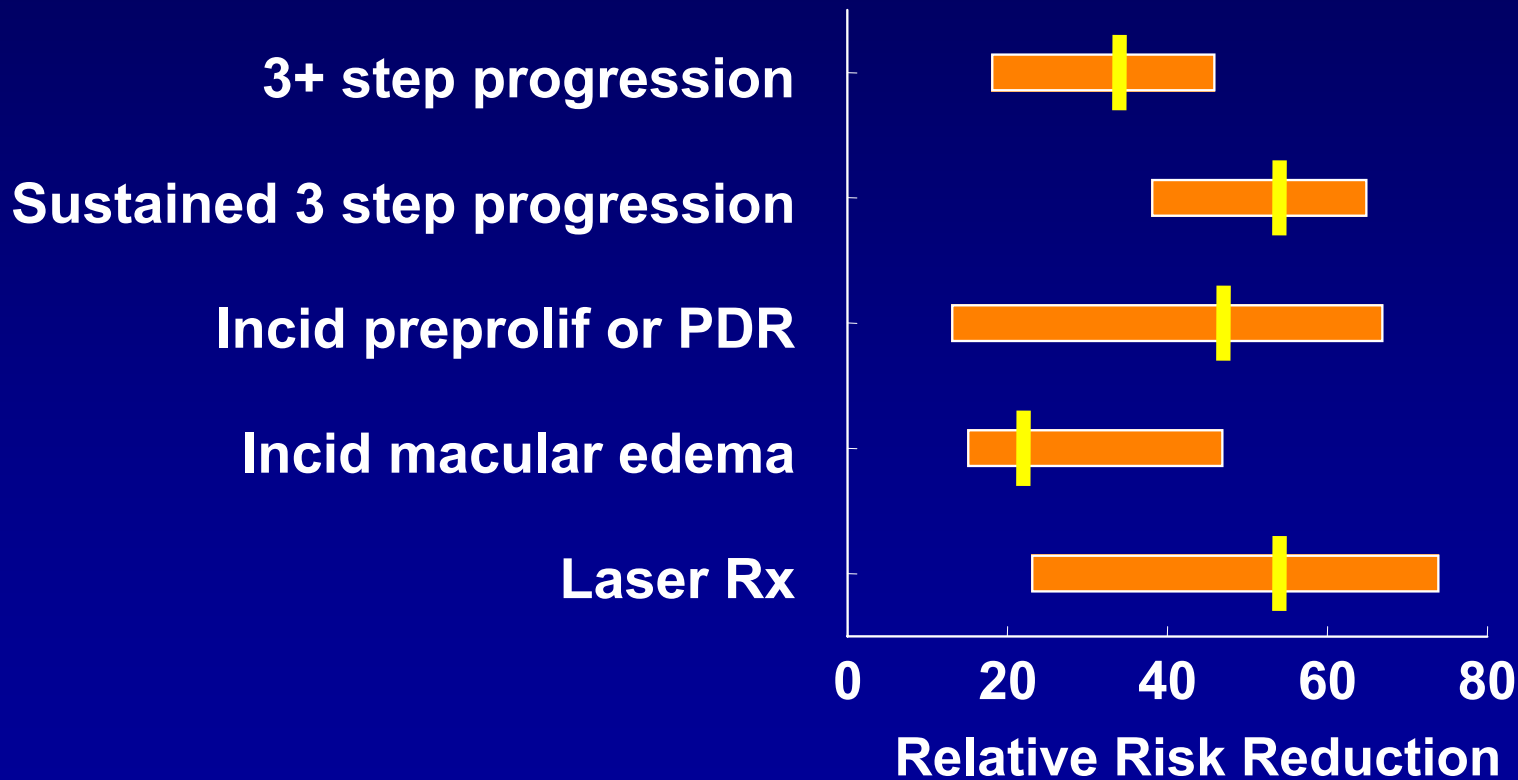


Diabetics Control and Complications Trial

Impact of Tight Glycemic Control on Events



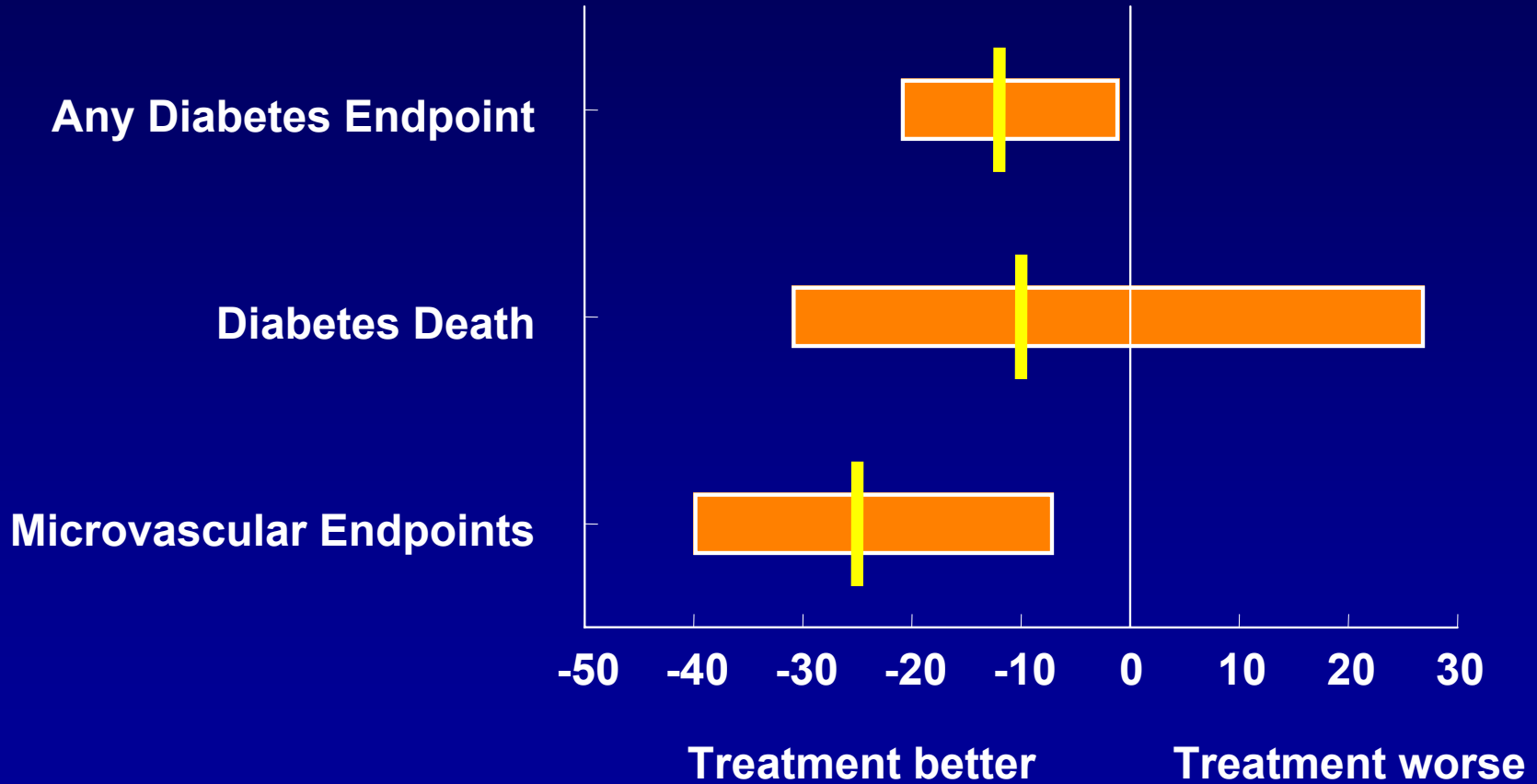
Risk Reduction in Incidence and Progression of Retinopathy DCCT Secondary Prevention Group



United Kingdom Prospective Diabetes Study (UKPDS) and CHD Prevention

- **3867 newly diagnosed non-obese Type 2 DM**
- **Median age 54 years at onset of trial**
- **1138 conventional diabetes initial Rx diet**
Drugs added if fasting glucose >15 mmol/L [270 mg/dl]
- **2729 intensive treatment diabetes**
Initial Rx oral agents or insulin for fasting glucose <6 mmol/L [128 mg/dl] then add others as needed)
Rx (mean HbA_{1c} 7.2%)

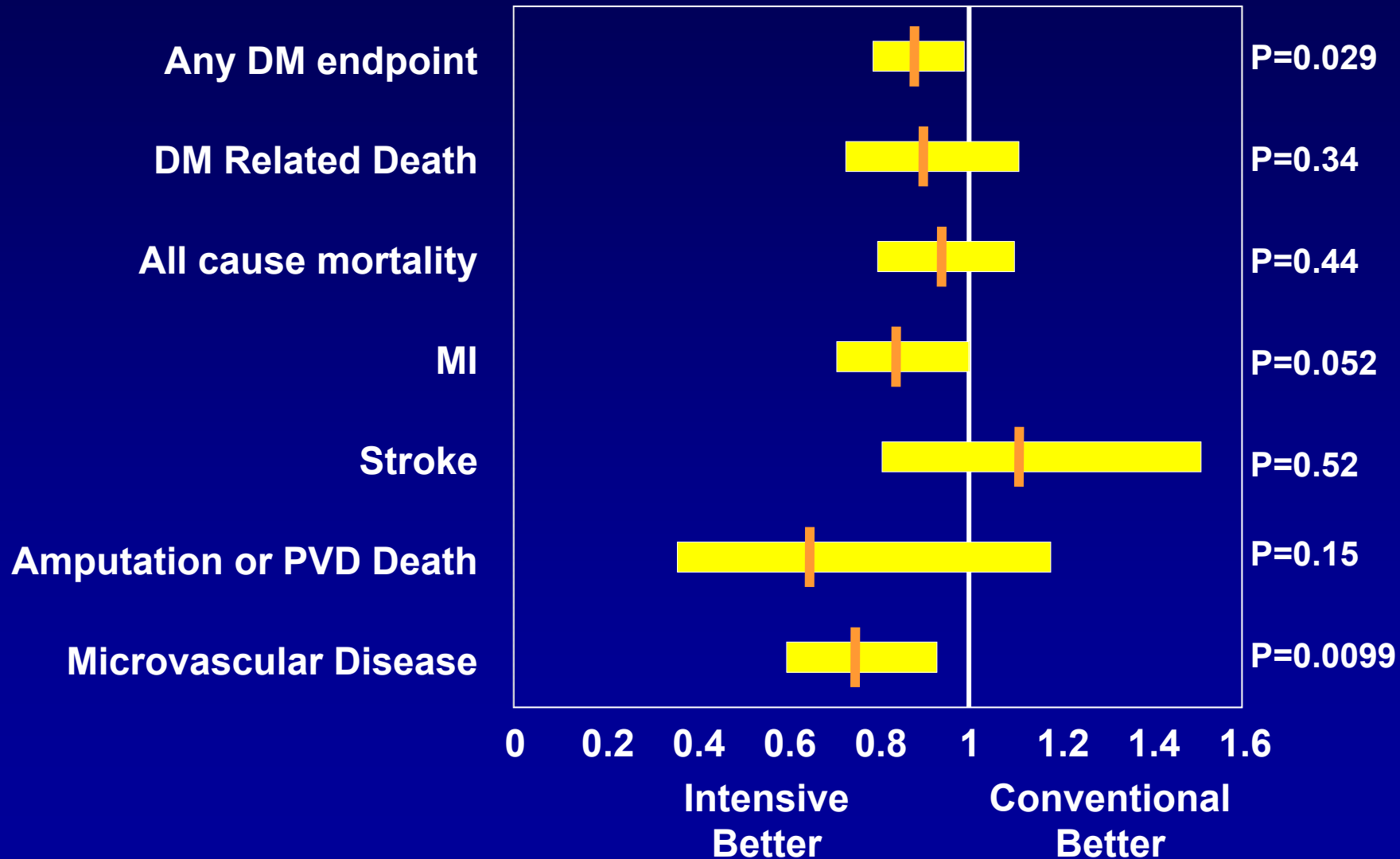
Intensive Blood Glucose and Vascular Disease in UKPDS



Risk Factors for Coronary Artery Disease: UKPDS

Risk Factor	Increment/Decrement	CAD Risk
	<i>For every:</i>	
HbA1c	1% decrease	Decrease 11%
SBP	10 mmHg decrease	Decrease 15%
LDL	39 mg/dl decrease	Decrease 57%
HDL	3.9 mg/dl increase	Decrease 15%

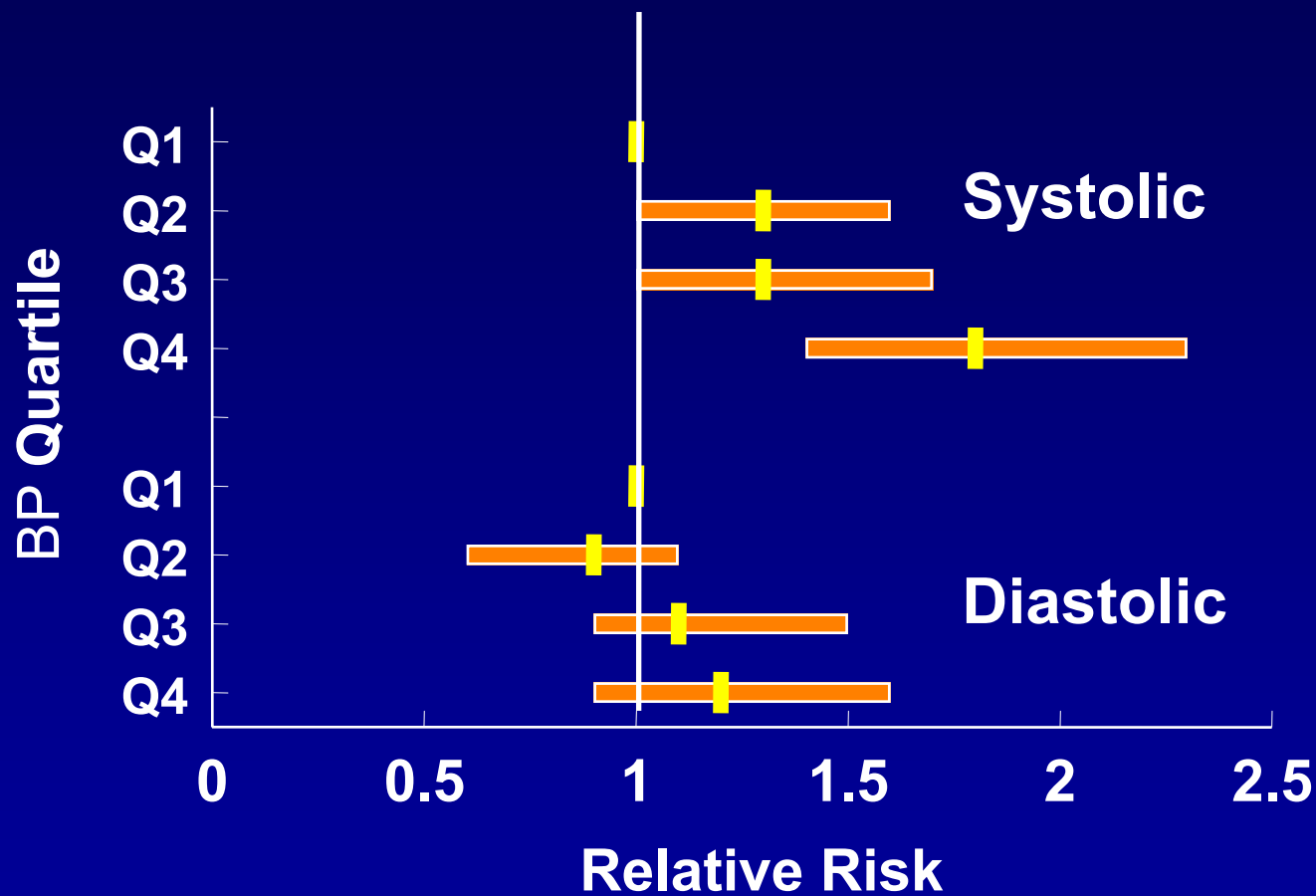
UKPDS Micro and Macro CVD Results: Intensive vs Conventional Therapy for Blood Glucose



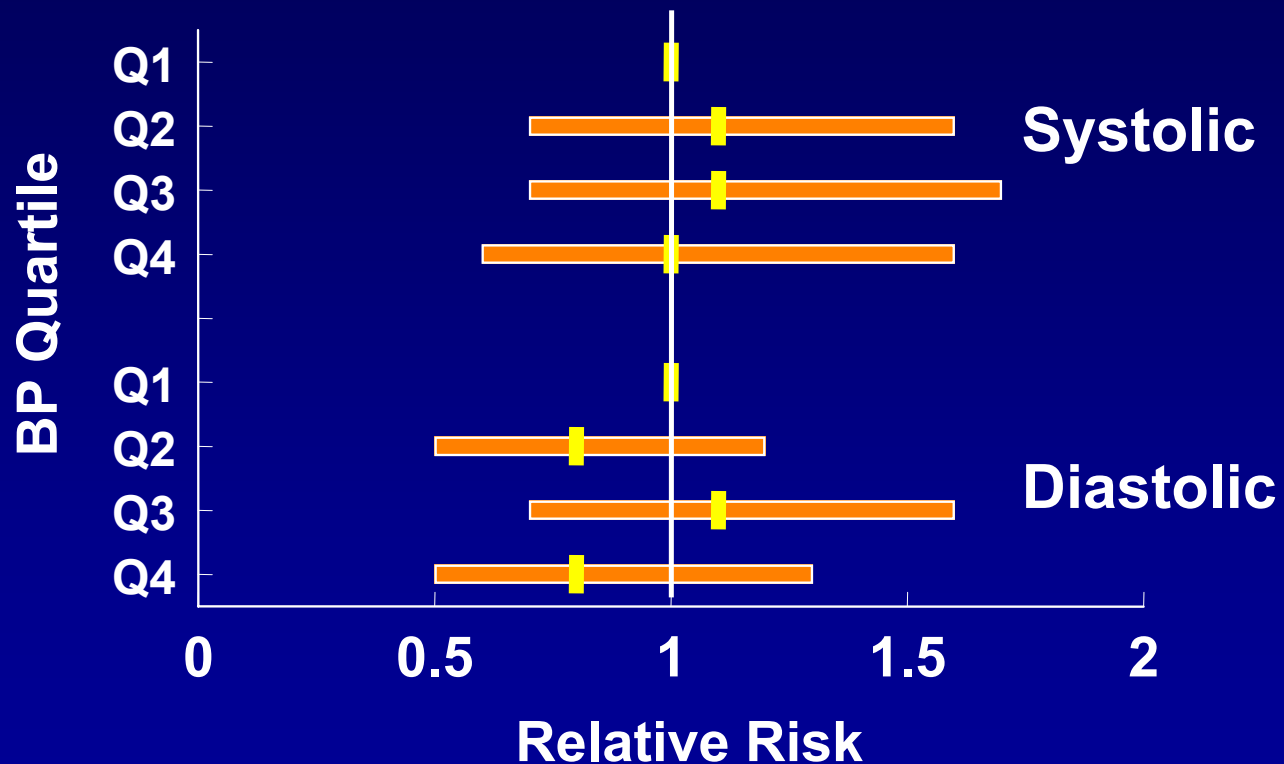
Blood Pressure and Vascular Risk In Diabetes Mellitus

- **WESDR**
Wisconsin Epidemiologic Study of Diabetic Retinopathy
- **SHEP**
Systolic Hypertension in Elderly Program
- **SYSEUR**
Systolic Hypertension in Europe
- **HOT**
Hypertension Optimal Treatment
- **HOPE**
Heart Outcomes Prevention Evaluation
- **RENAAL**
Reduction of Endpts in NIDDM Angio II Antag Losartan

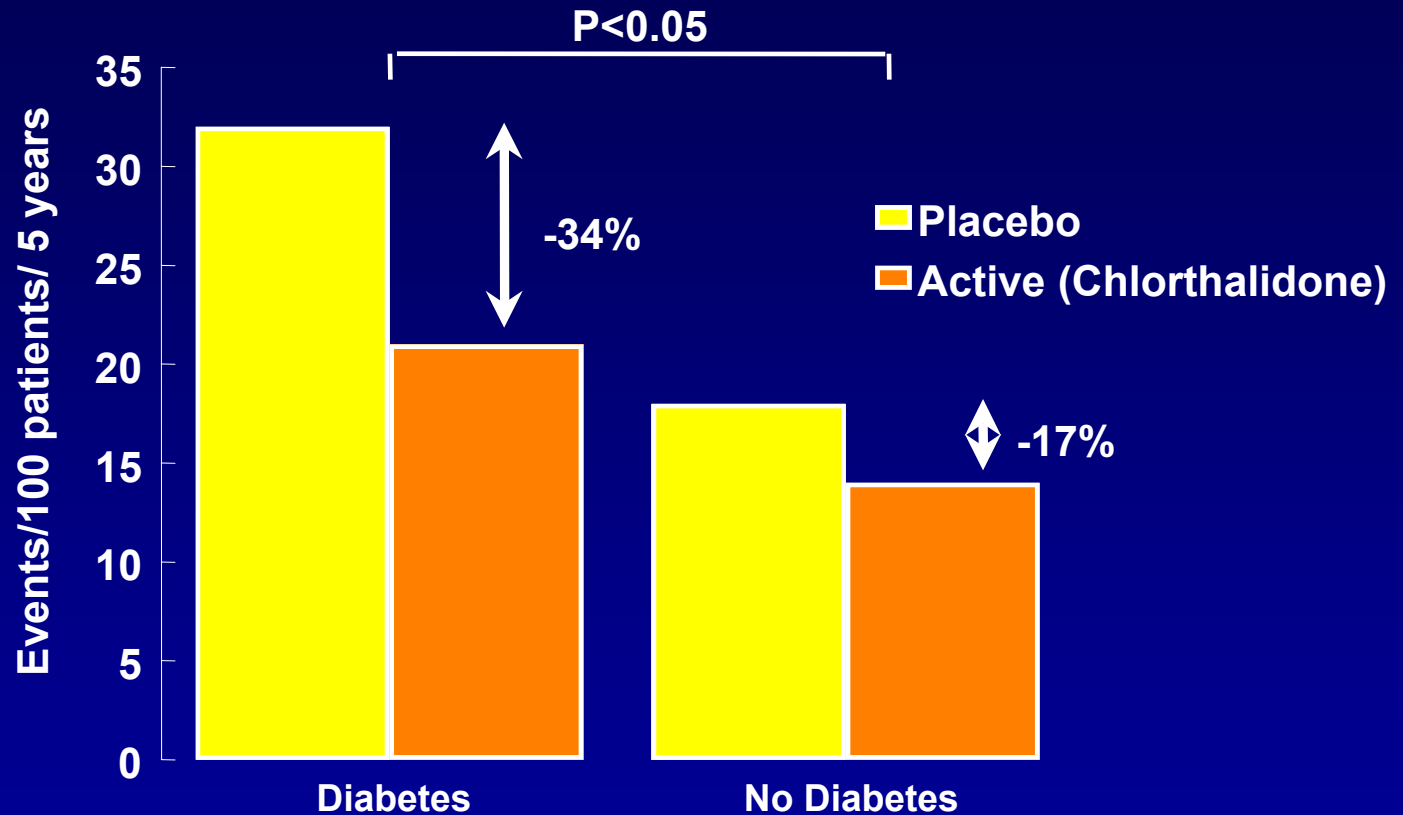
Blood Pressure and 4 Yr Retinopathy Progression Younger Onset Diabetes in WESDR



Blood Pressure and 4 Yr Retinopathy Progression Older Onset Diabetes not Using Insulin in WESDR



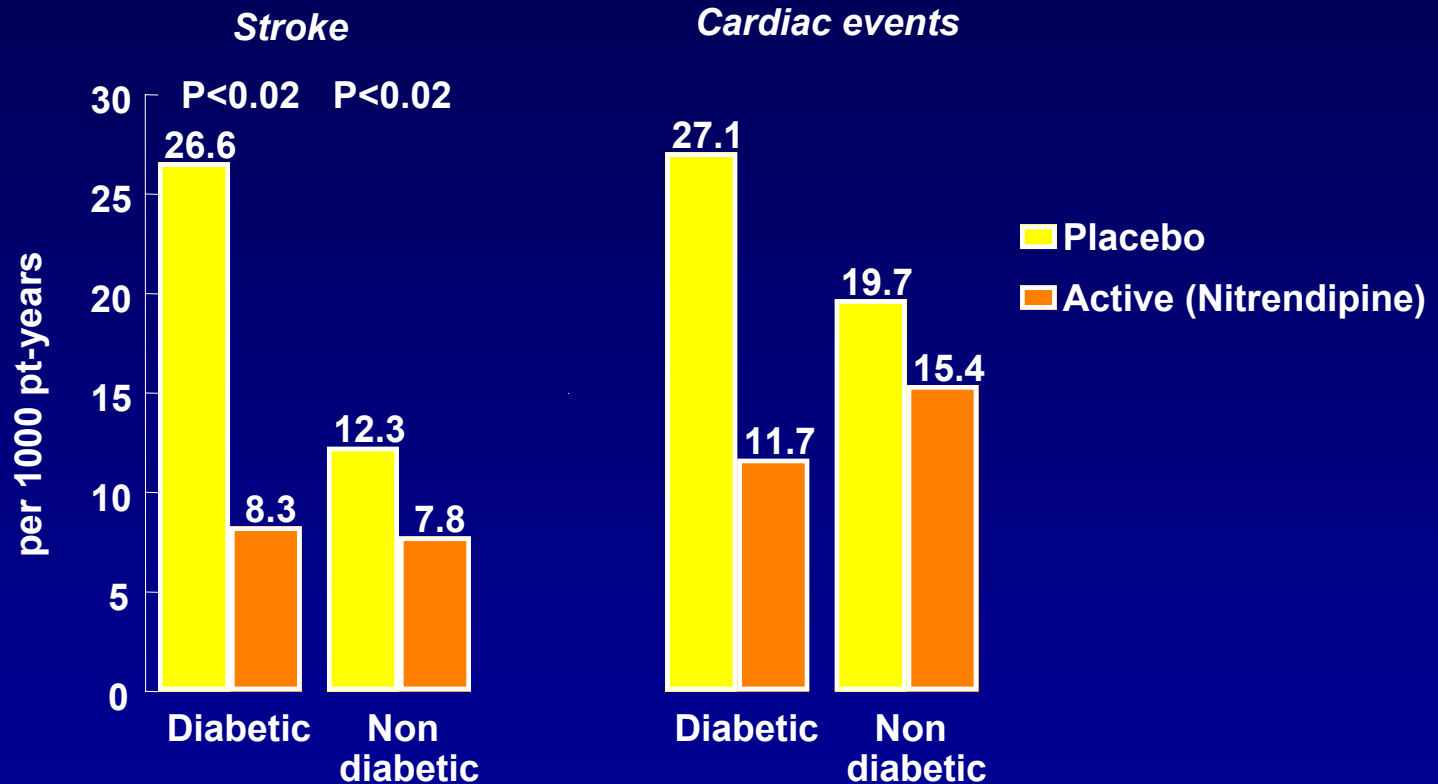
Major CVD Event Rate in SHEP



Curb JAMA 1996; 276: 1886

Events --MI, sudden cardiac death, CABG, angioplasty, CVA, aneurysms, endarterectomy

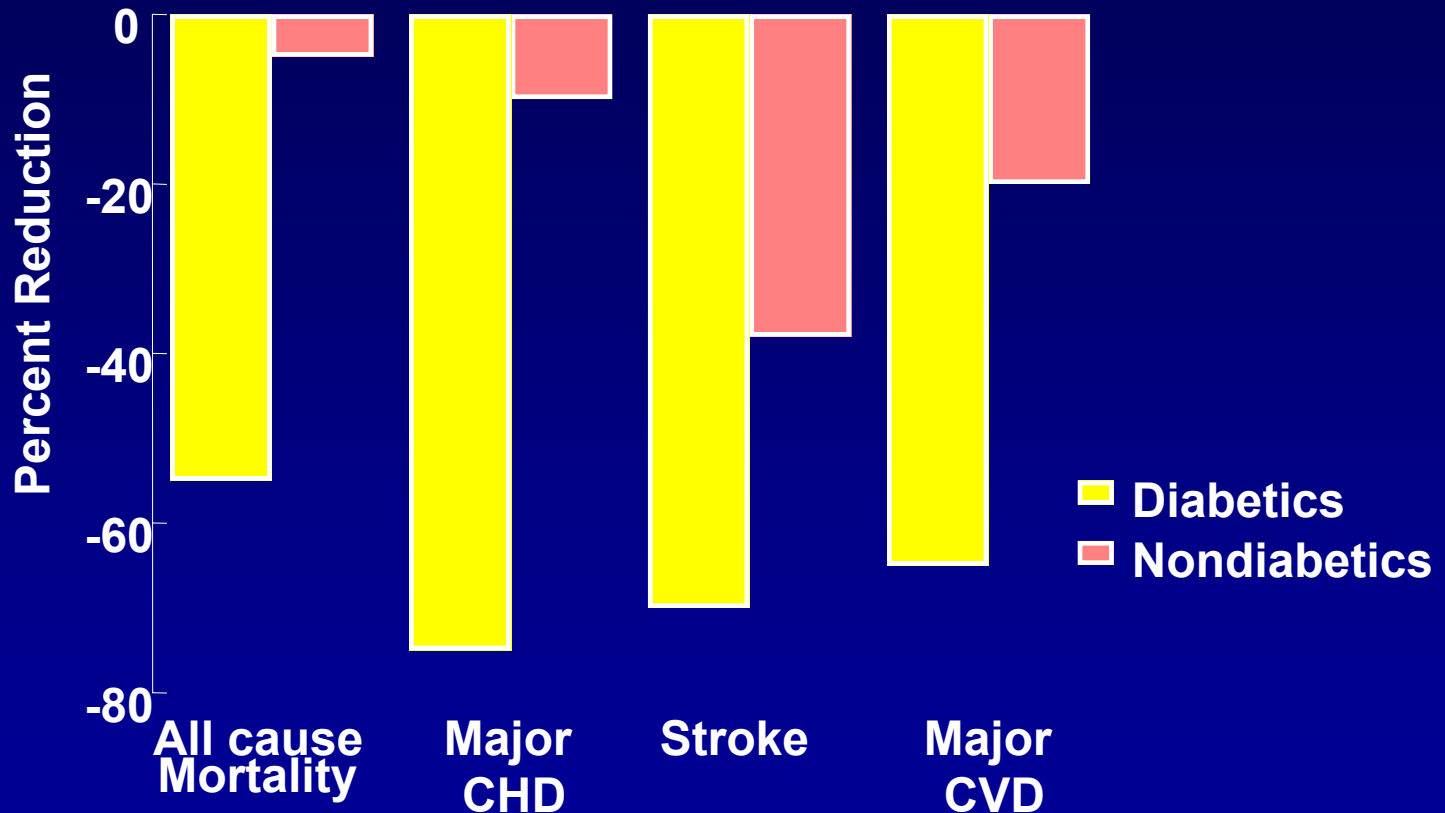
SYSEUR Hypertension Therapy in Diabetics and Nondiabetics



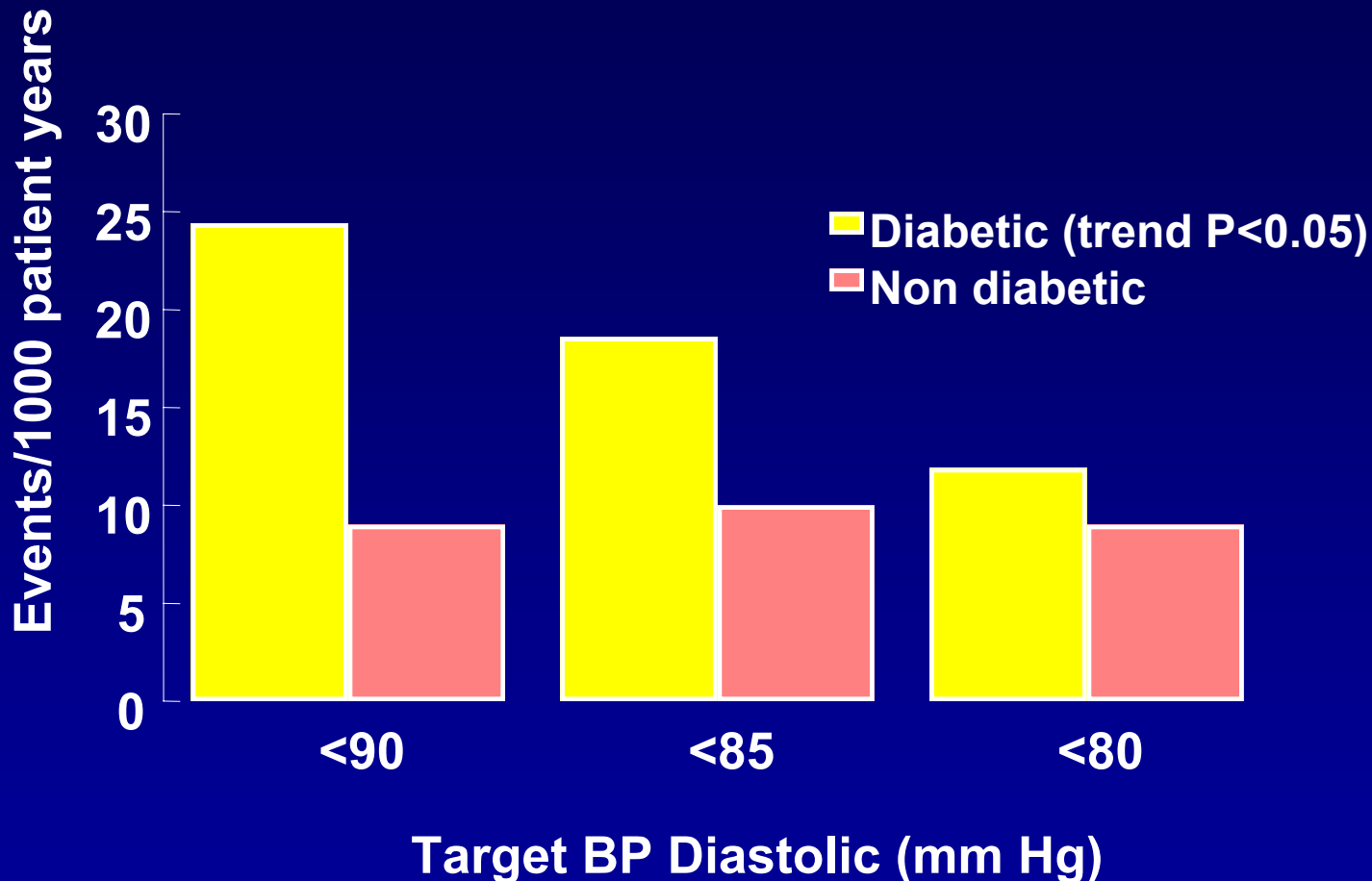
Tuomilehto NEJM 1999; 340: 677

492 diabetics, 4203 nondiabetics

Percent Reduction in Endpoints in SYSEUR Trial in Diabetics and Non Diabetics

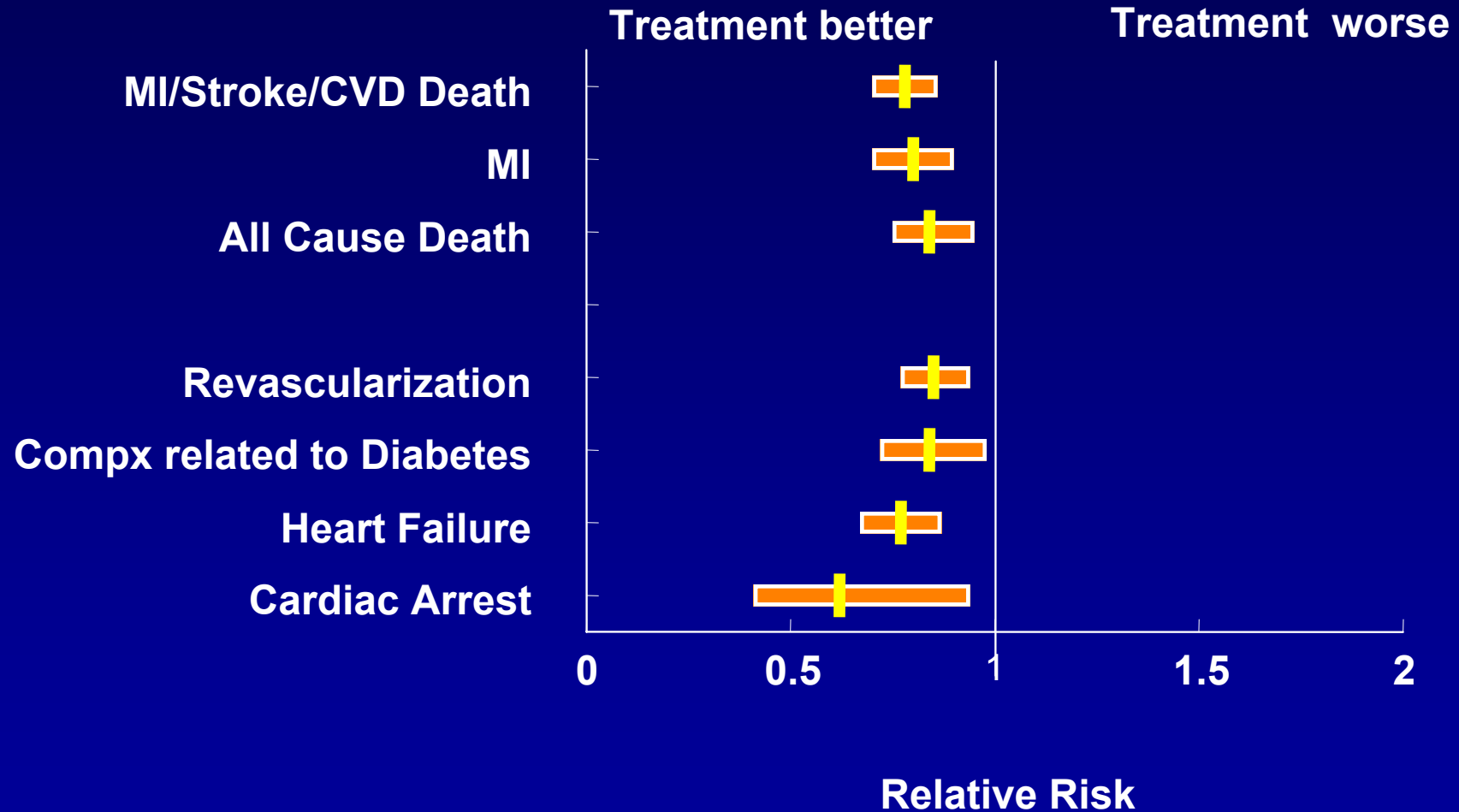


Major CVD Events in HOT Trial According to Diastolic Blood Pressure

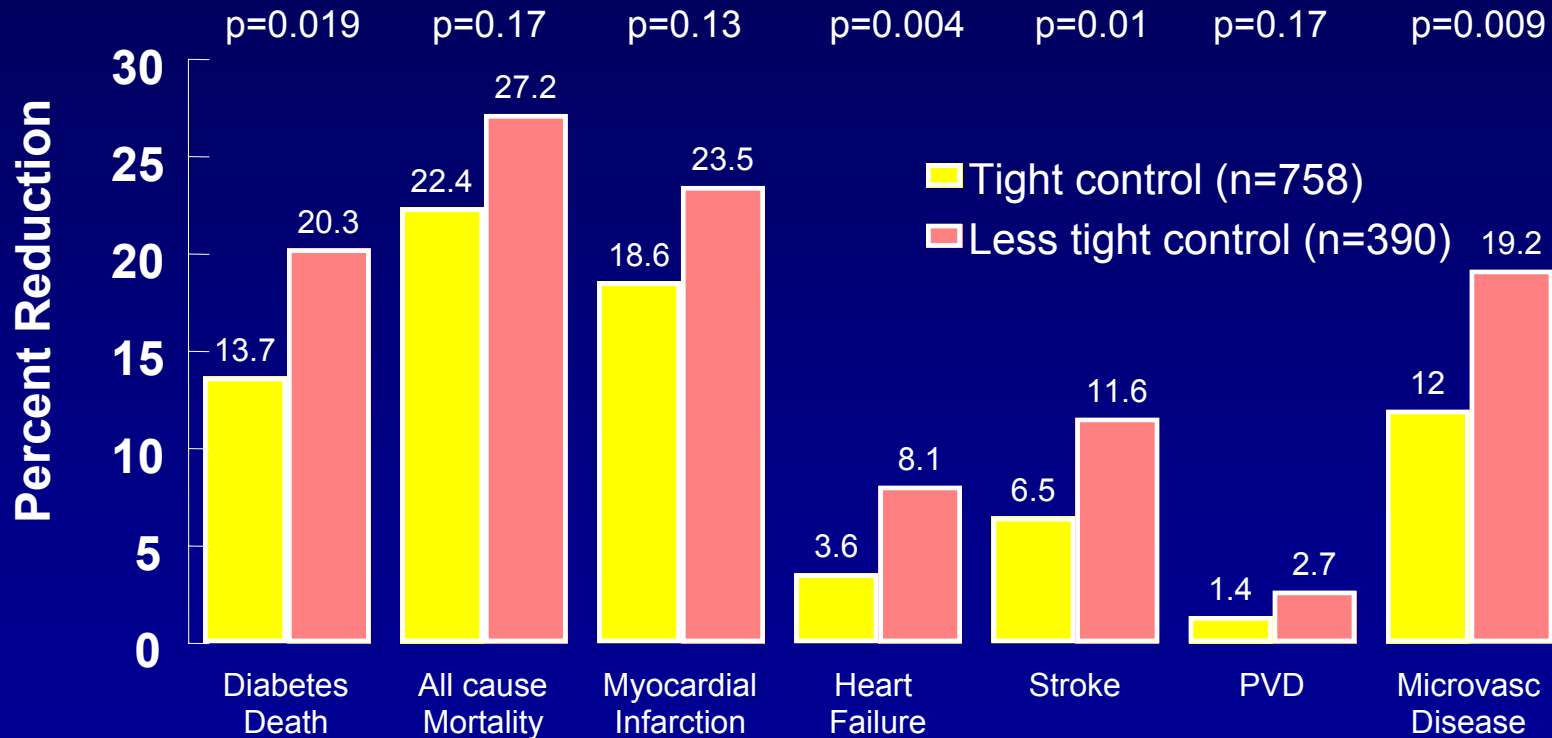


ACE Inhibition and CVD in High Risk Patients

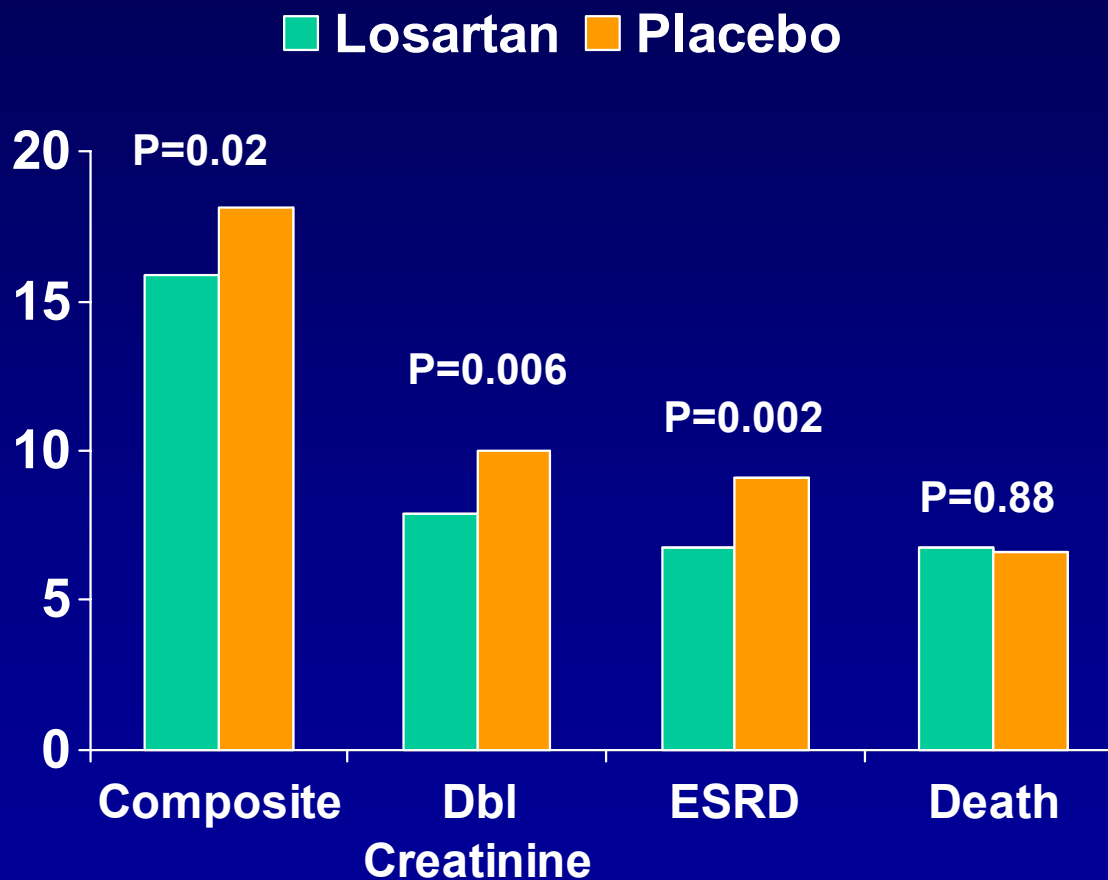
HOPE Results



Percent Reduction in Endpoints with BP 144/82 in UKPDS



Endpoint Incidence in the RENAAAL Study 1513 Type 2 Diabetics over 3.4 years



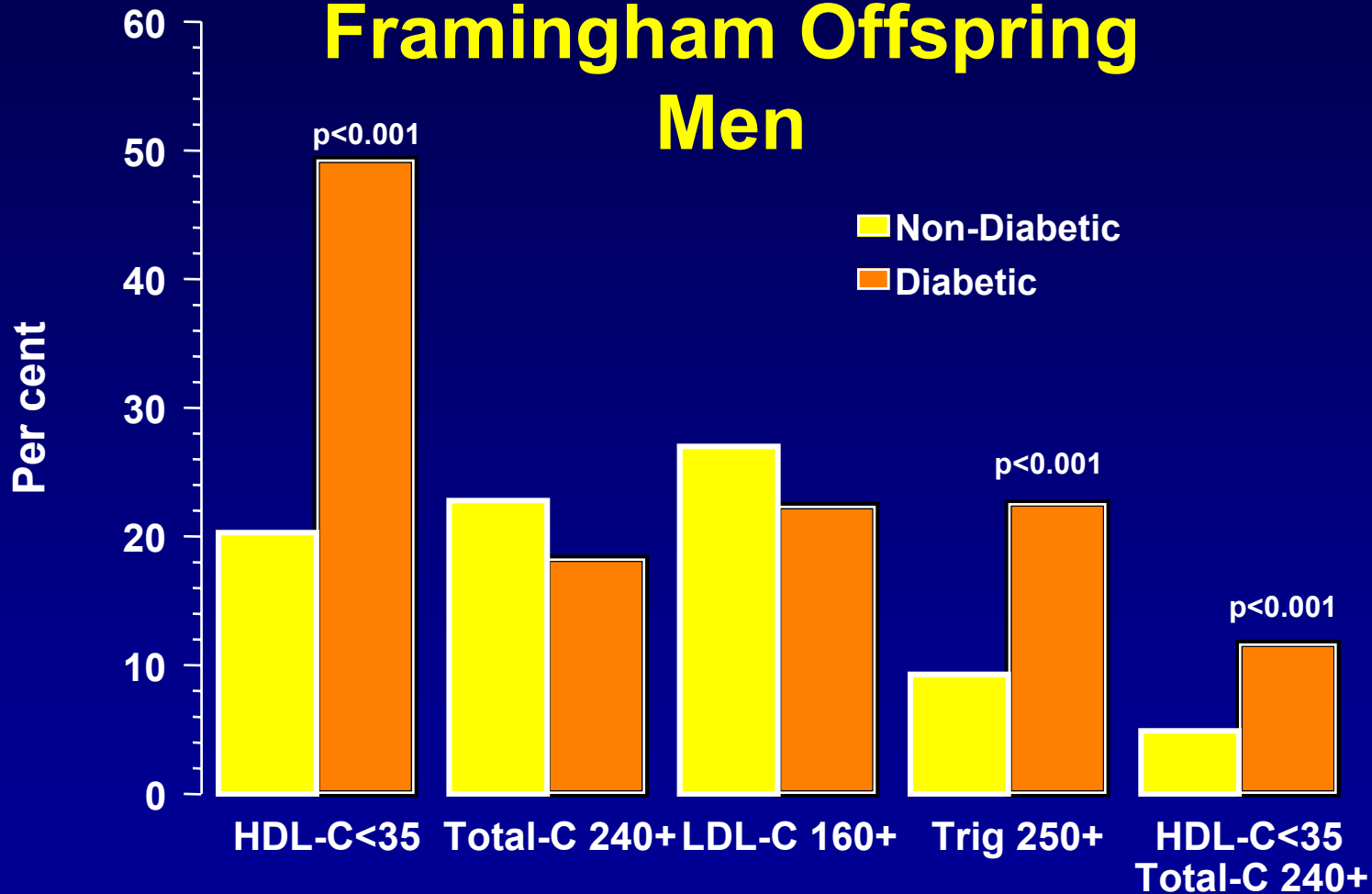
Reduction of Endpoints in NIDDM
with Angio II Antag Losartan

Brenner N Engl J Med 2001; 345; 866

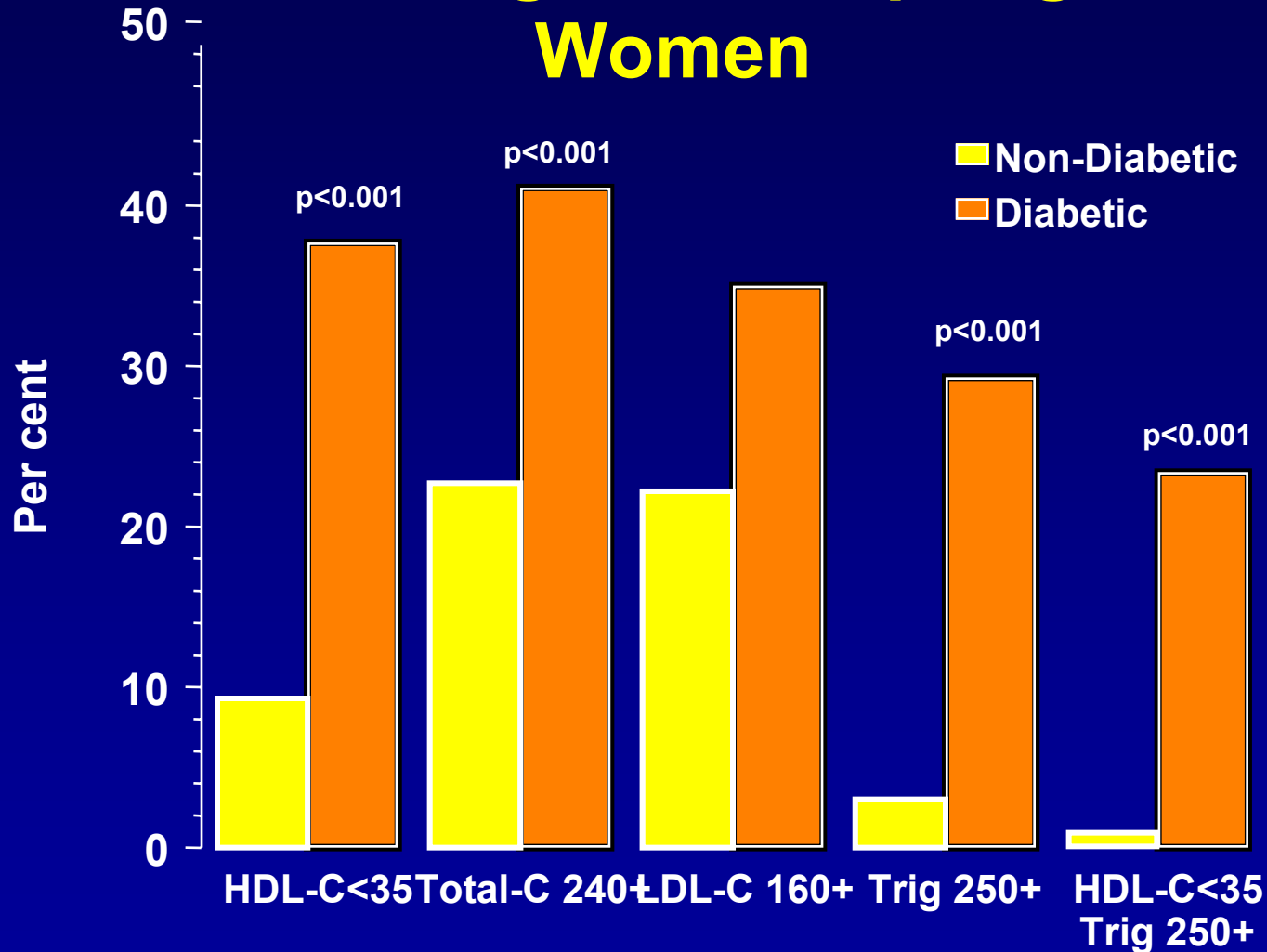
Dyslipidemia and Vascular Risk In Diabetes Mellitus

- **Observational Studies**
- **Lipid Intervention Trials**

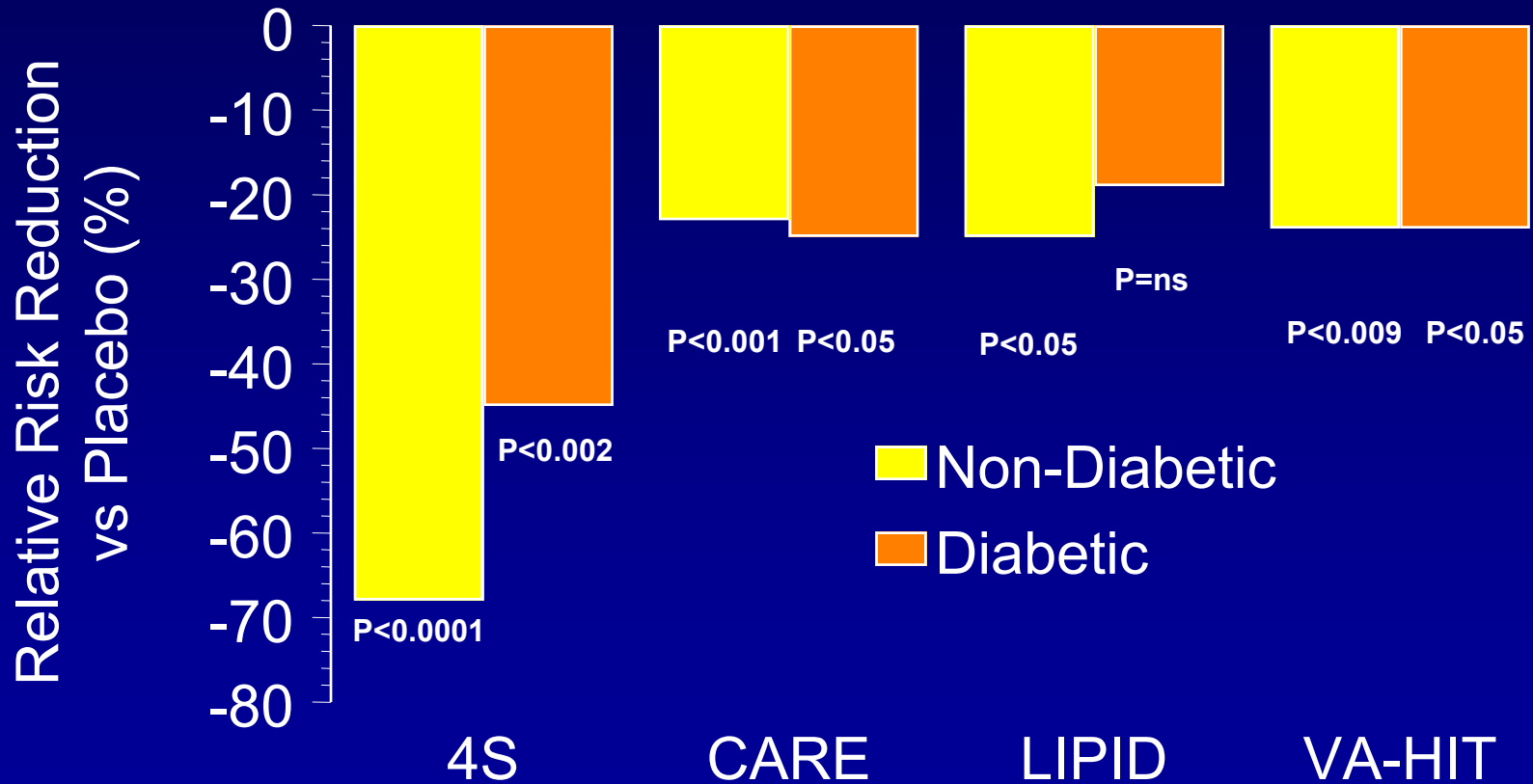
Diabetes and Lipid Extremes Framingham Offspring Men



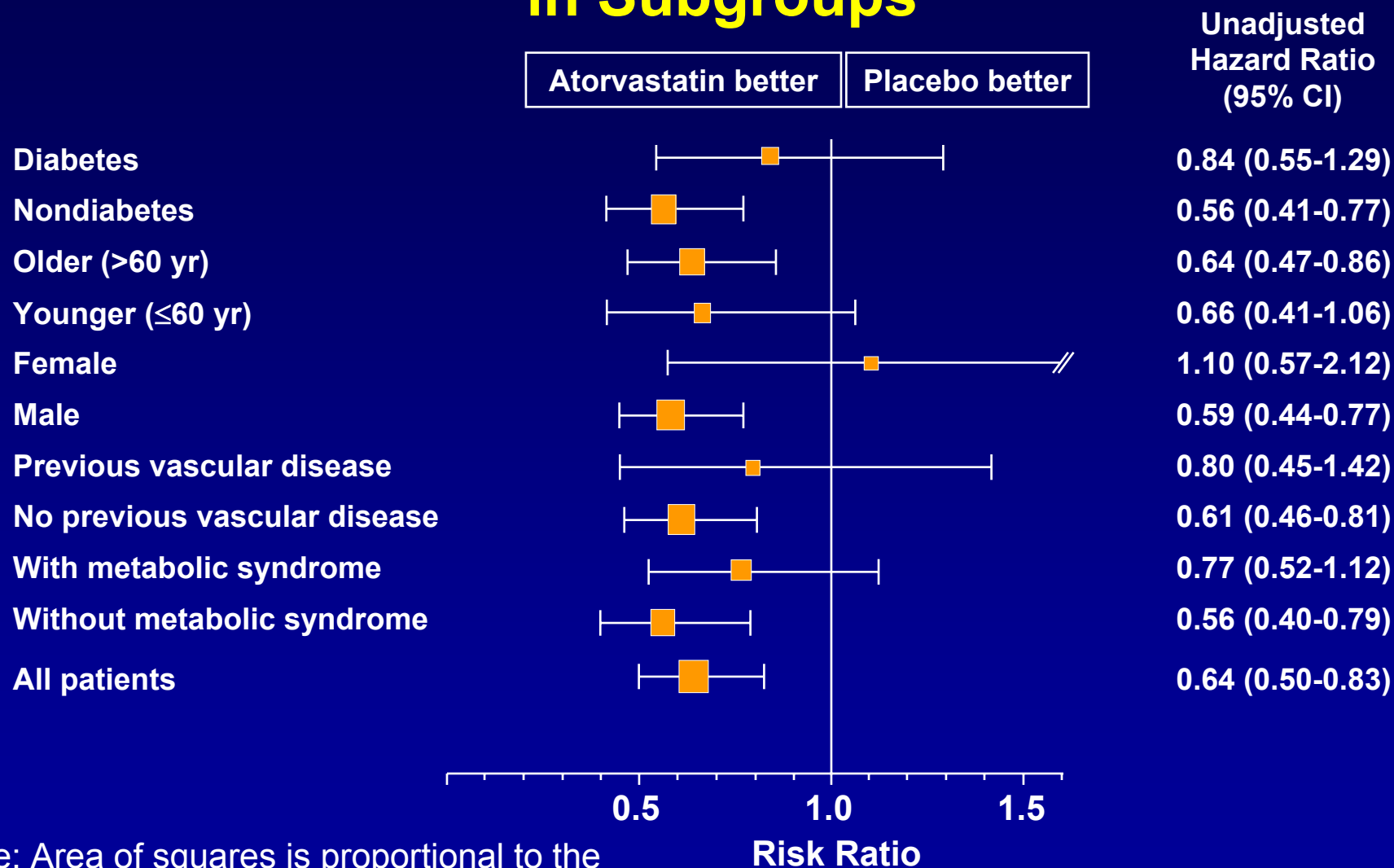
Diabetes and Lipid Extremes Framingham Offspring Women



Reduction in CVD Relative Risk Results from Secondary Prevention Trials

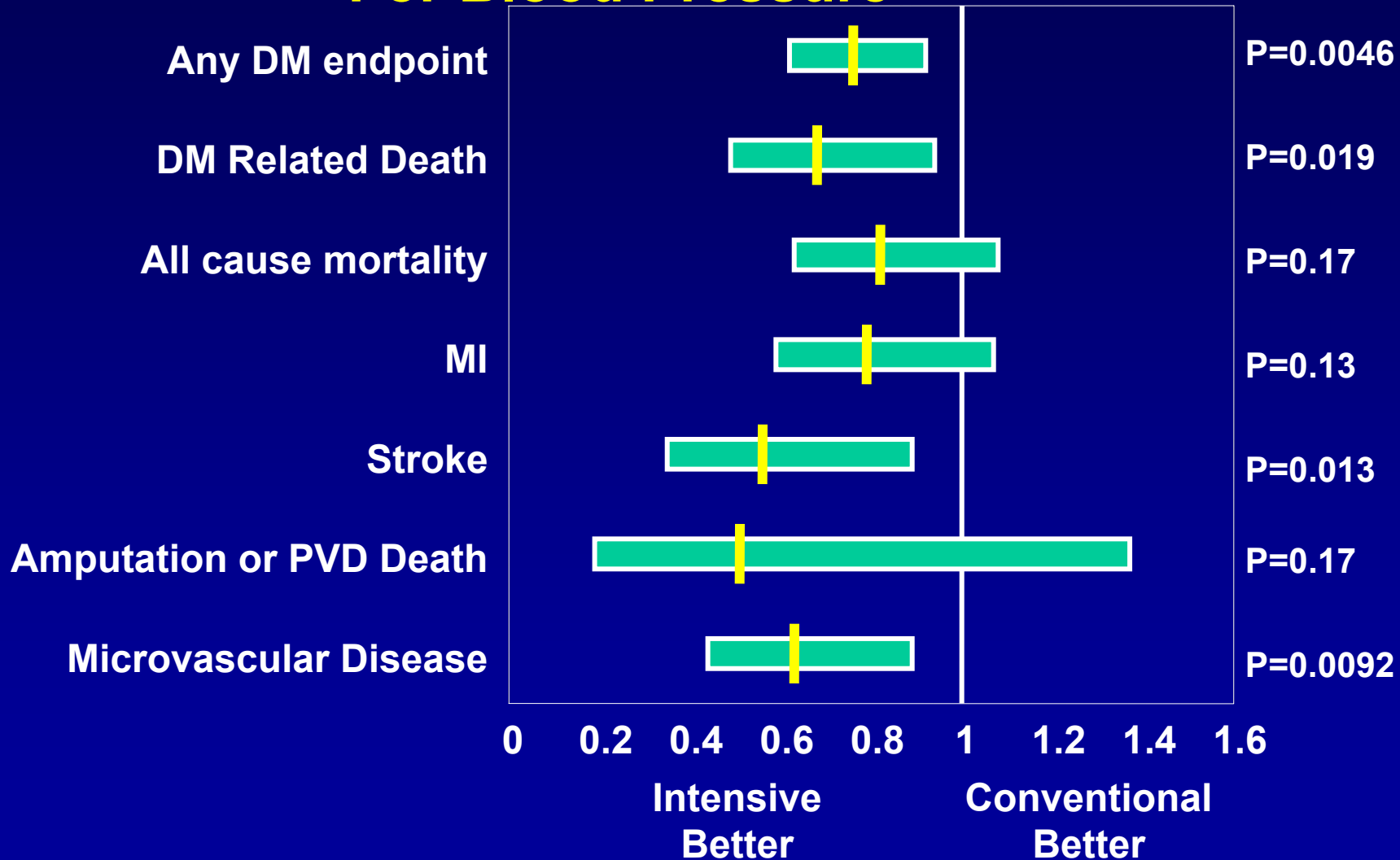


ASCOT-LLA: Primary End Point in Subgroups



Note: Area of squares is proportional to the amount of statistical information.

UKPDS Micro and Macro CVD Results: Intensive vs Conventional Therapy For Blood Pressure

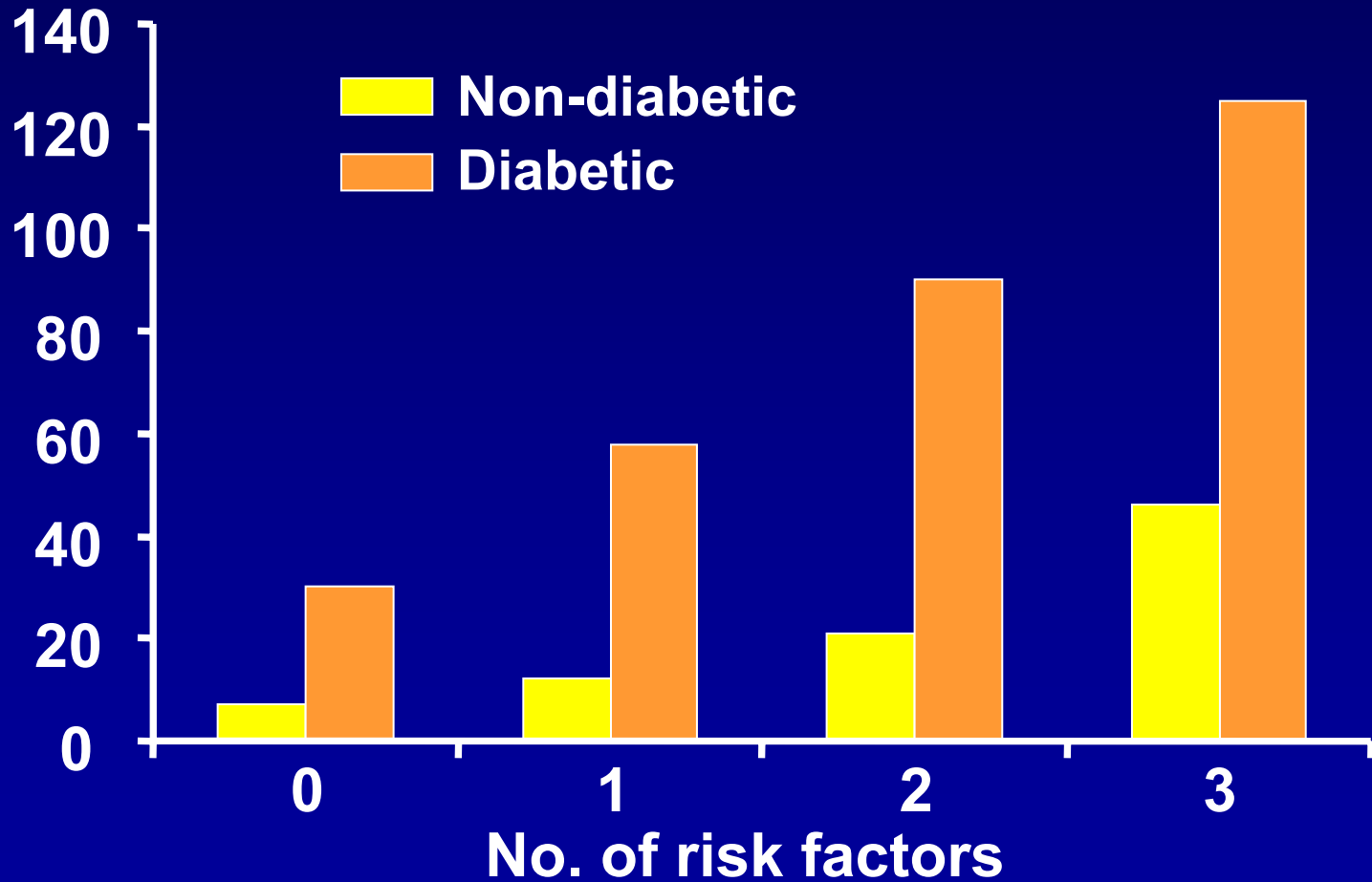


Multifactorial Issues

- **Observational Data**
- **Clinical Trials**

Type 2 Diabetes is a Significant Risk Factor for CAD Death

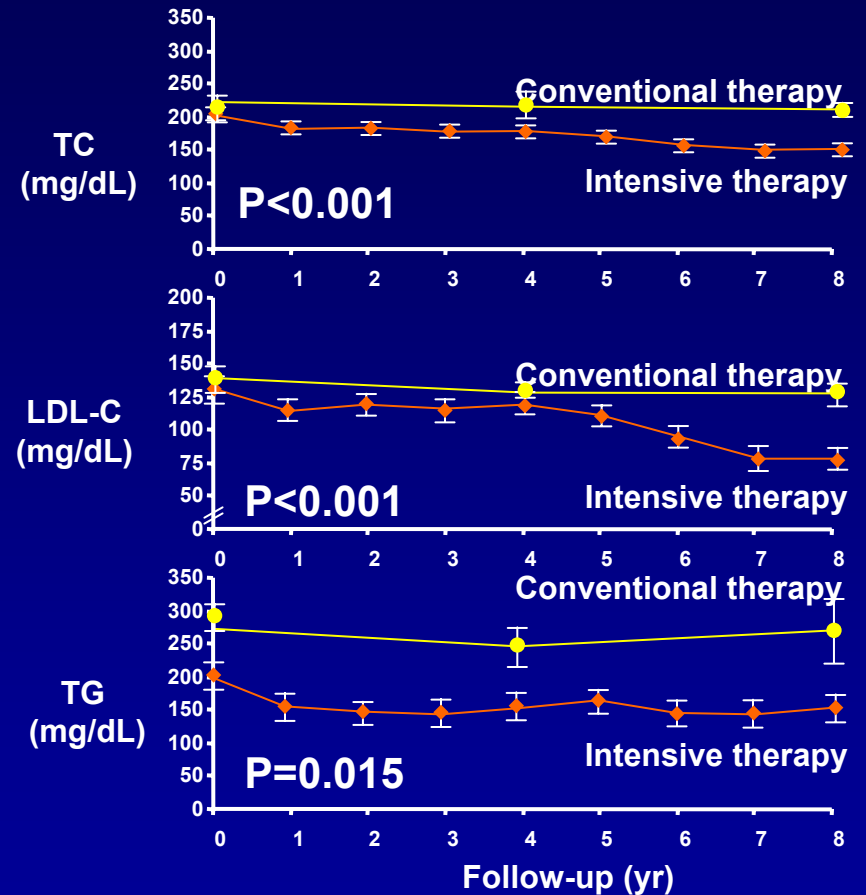
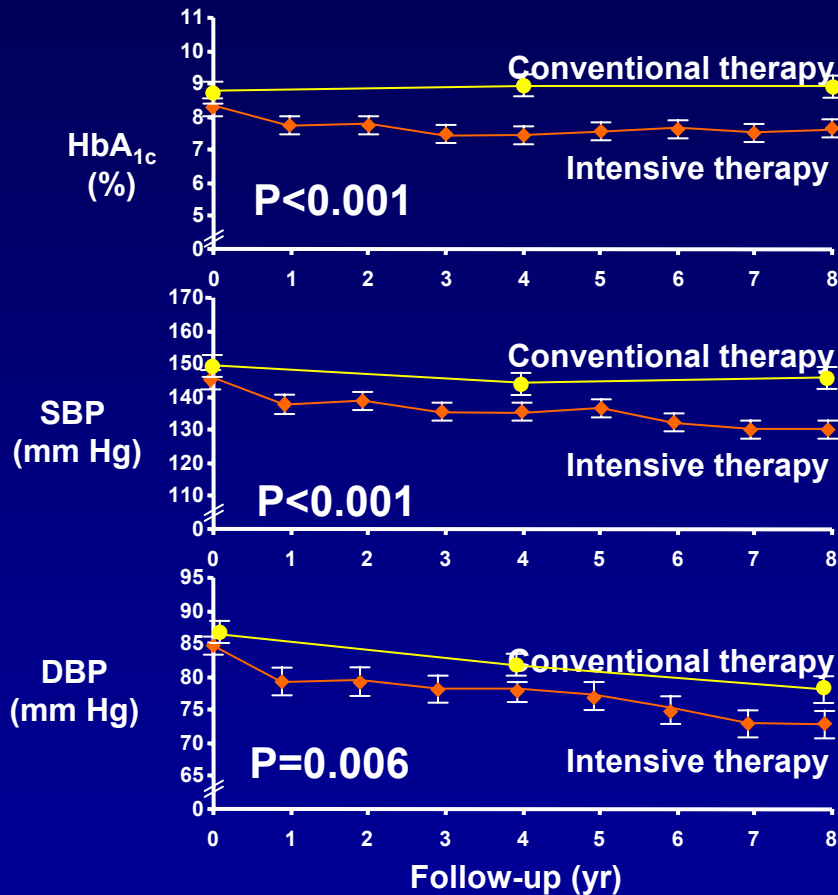
Death rate /100 000 patient-years



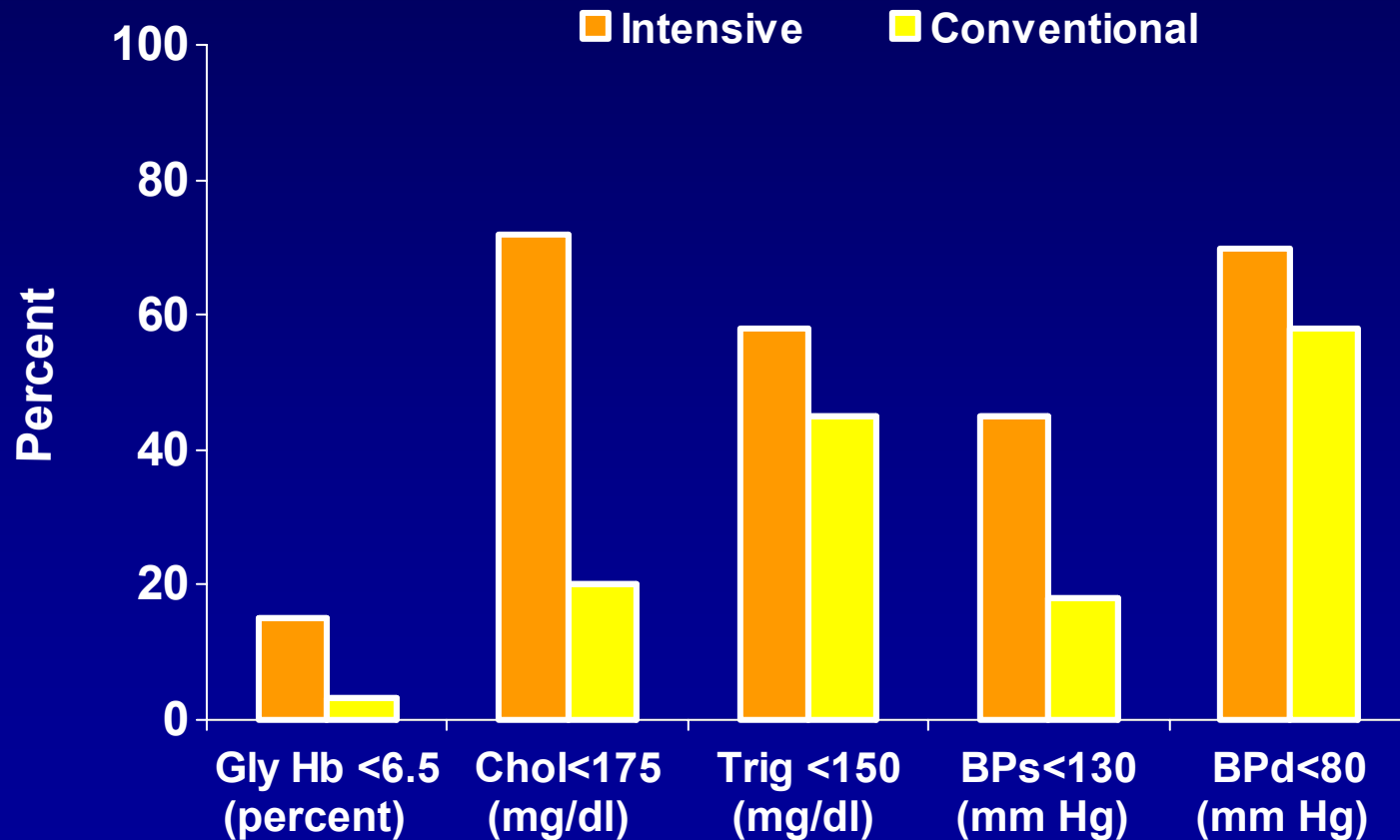
Multifactorial Intervention and CVD in Patients with Type 2 DM (Steno-2)

- **160 adults with Type 2 Diabetes Mellitus**
Mean age 55 years at entry
Mean follow-up 7.8 years, all (aspirin, ACE, vitamins)
80 conventional diabetes Rx
80 intensive diabetes Rx
total diet fat <30%, sat fat<10%, exercise 30 min for 3-5 x/wk,
smoke cessation program, glucose Rx to HbA_{1c} <7.5 later
<6.5, BP step Rx, elevated cholesterol Rx statin, trig >350
mg/dl fibrate Rx)
- **Outcomes**
Composite CVD death, nonfatal MI, nonfatal stroke
Revascularization, amputation

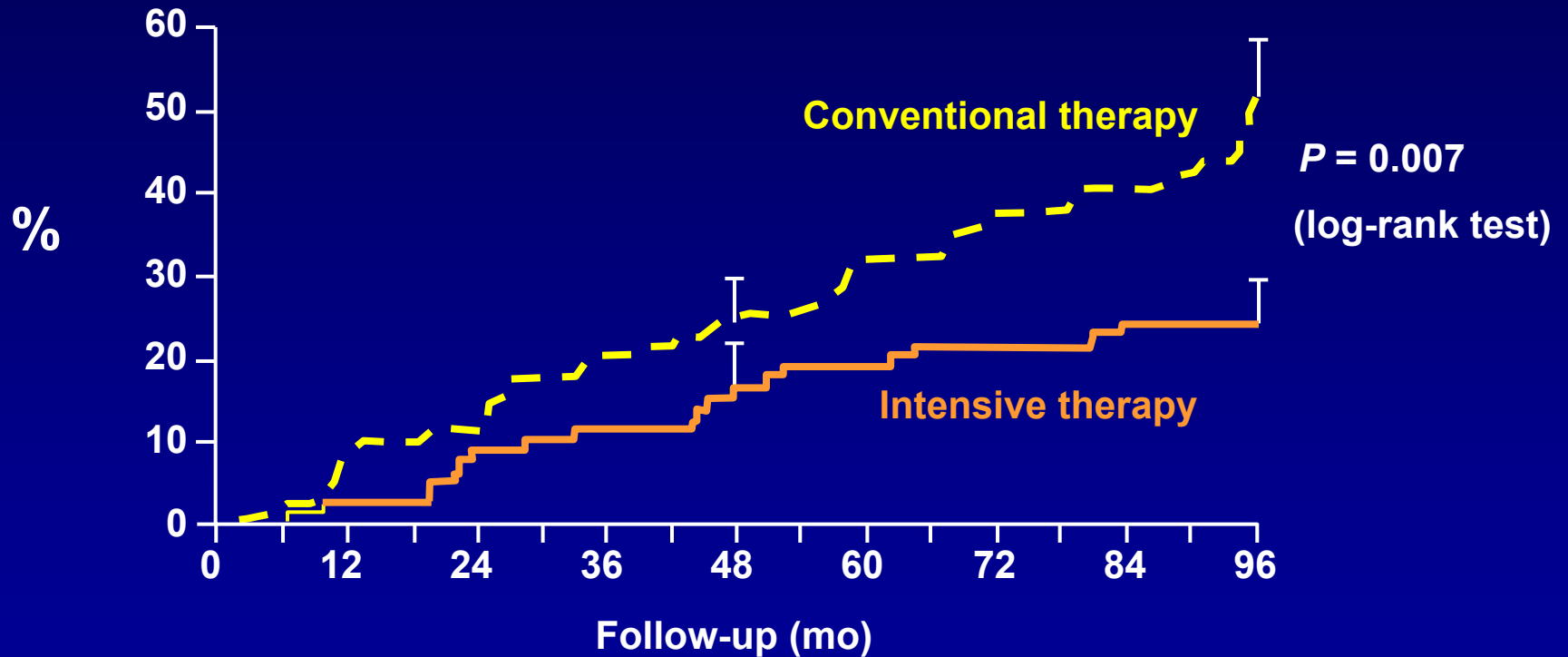
Steno-2: Effect of Therapies on Selected Risk Factors



Goals Reached for Selected Risk Factors in Intensive vs Conventional Therapy Steno-2 Trial



Intensive vs Conventional Diabetes Therapy to Prevent CVD in Steno-2



Microvascular Disease in Diabetes Mellitus

- **Eye and Kidney Disease**

Role of glycemic control

Blood pressure control important

Lipids less important

Macrovascular Disease in Diabetes Mellitus

- **Event Rate**
 - 2X risk of non-diabetic men
 - 3X risk of non-diabetic women
 - Lipids especially abnormal in women
 - CHD risk equivalent by US guidelines
 - Worse prognosis after CVD events
- **Interventions**
 - Blood pressure therapy very important
 - Lipids—treatment effective as in non-diabetics
 - Glucose—mild effects for lg vessel disease