



*Welcomes You To*

**THE CONVERGENCE OF  
TYPE 2 DIABETES &  
CARDIOVASCULAR DISEASE**



Convergence of Diabetes &  
Cardiovascular Disease

# Acknowledgments

*Major support for this activity is provided through an educational grant from:*



*Additional support is provided through an educational grant from:*



# Presenter Disclosure Information

**Alan Zajarias, M.D., F.A.C.C.**

**The following relationships exist related to this presentation:**

*Nothing to disclose*

# Program Overview

**Cardiovascular disease and diabetes are closely related and as a result, the ACC is conducting a large initiative over the next two years to increase this awareness and to provide further education to medical professionals.**

# Learner Objectives

The overall goal of this program is to enhance participants' competence by providing the most up-to-date information on the correlation of type 2 diabetes and cardiovascular disease.

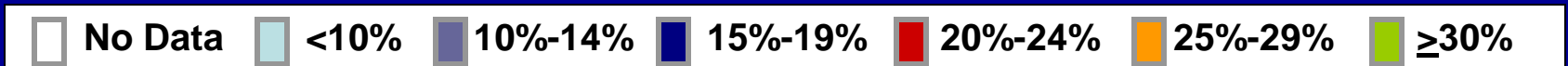
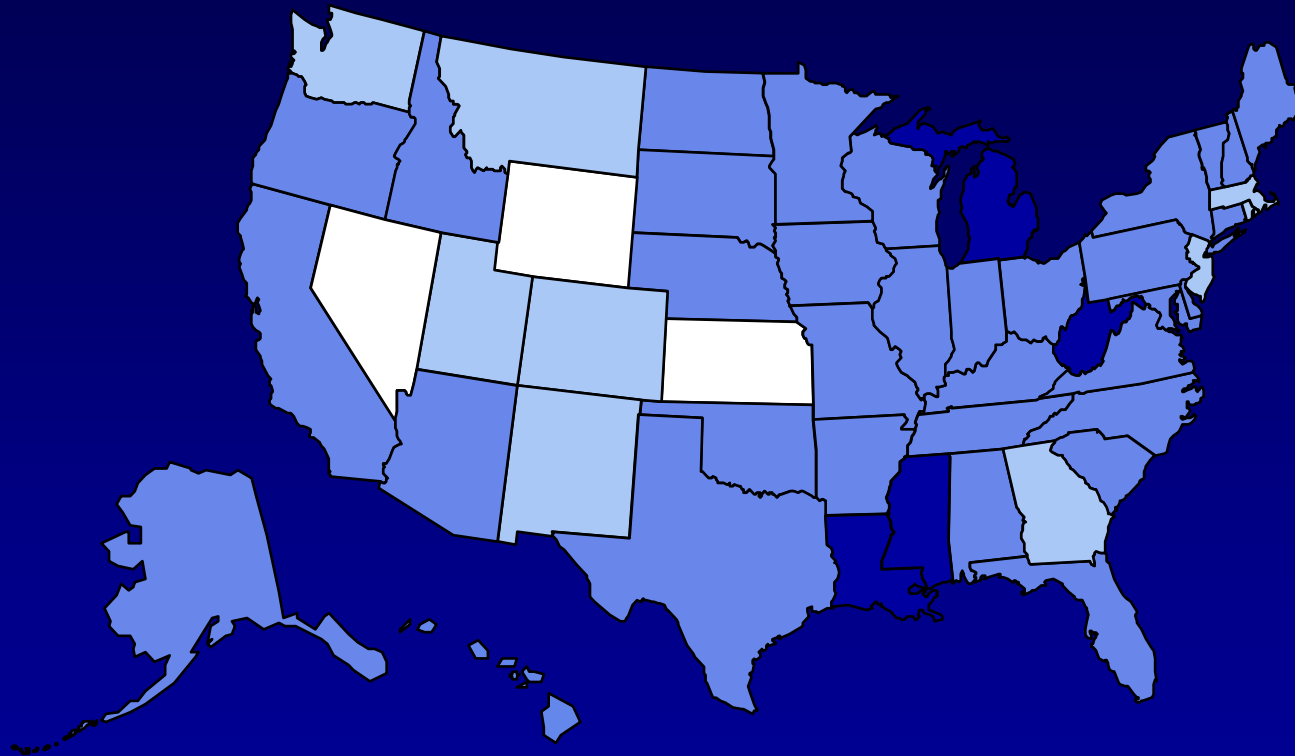
Upon completion of this program, attendees should be able to —

- Describe the prevalence of CV disease in patients with diabetes
- Identify patients with known diabetes and those at risk for diabetes, who are at significantly increased risk for CV disease based on the most current screening and treatment guidelines
- Apply modifiable and controllable risk factor strategies in the daily management of patients with diabetes and/or CV disease, to achieve evidence-based optimal outcomes



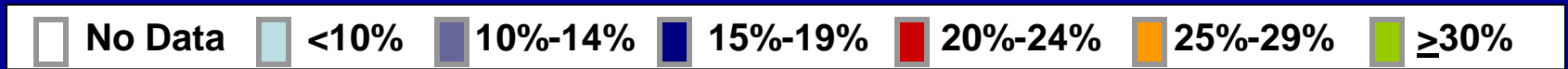
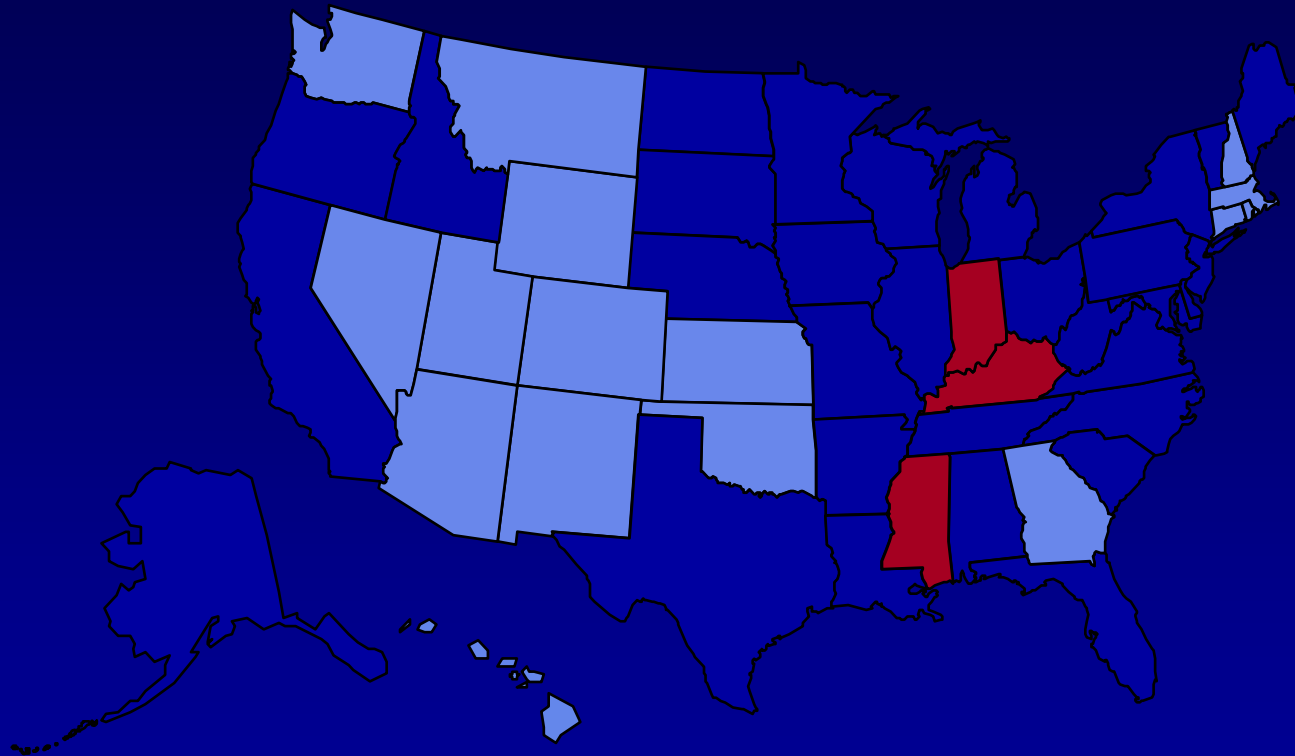
# Obesity Trends\* Among U.S. Adults: BRFSS - 1991

(\*BMI  $\geq 30$ , or  $\sim 30$  lbs overweight for 5'4" woman)



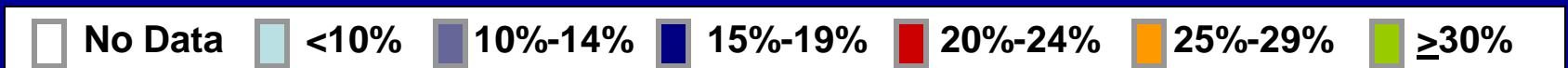
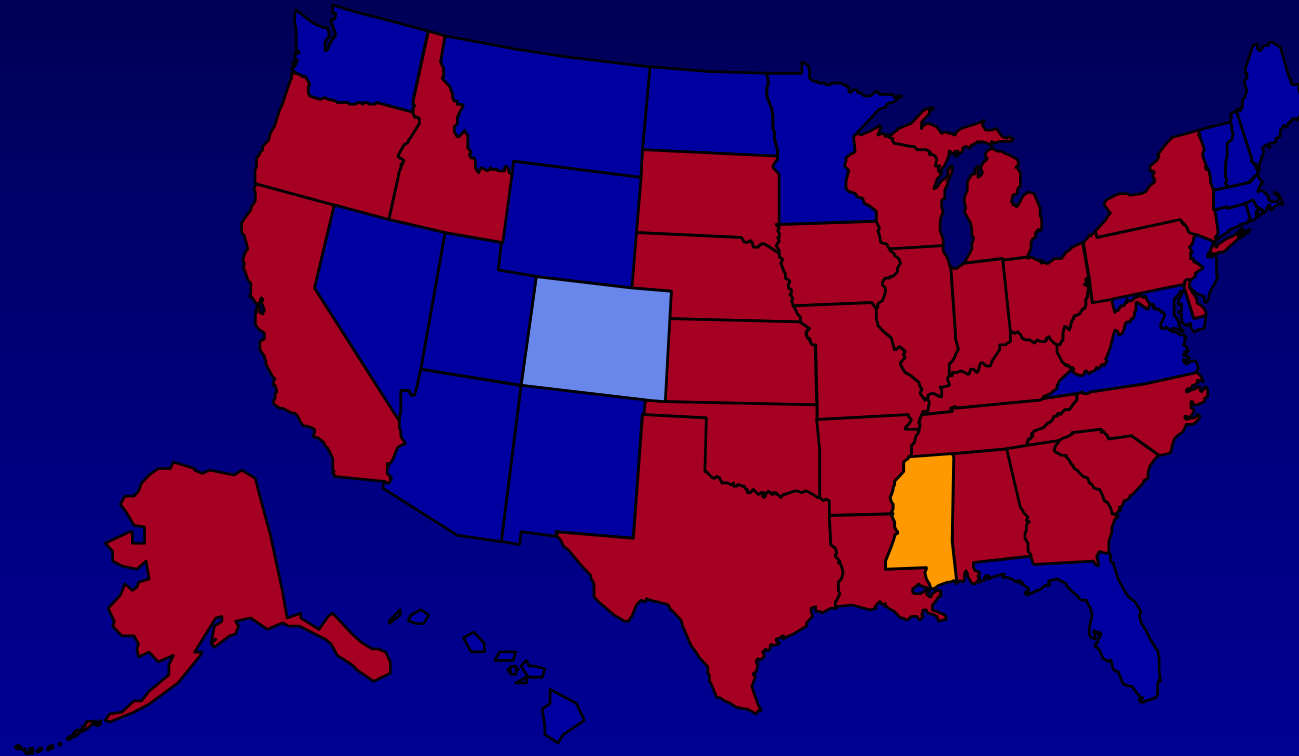
# Obesity Trends\* Among U.S. Adults: BRFSS - 1997

(\*BMI  $\geq 30$ , or  $\sim 30$  lbs overweight for 5'4" woman)



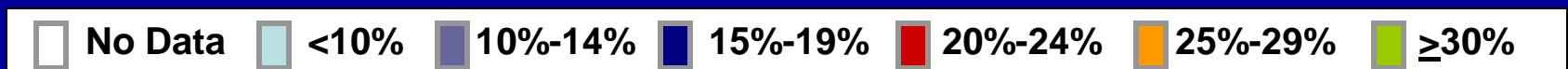
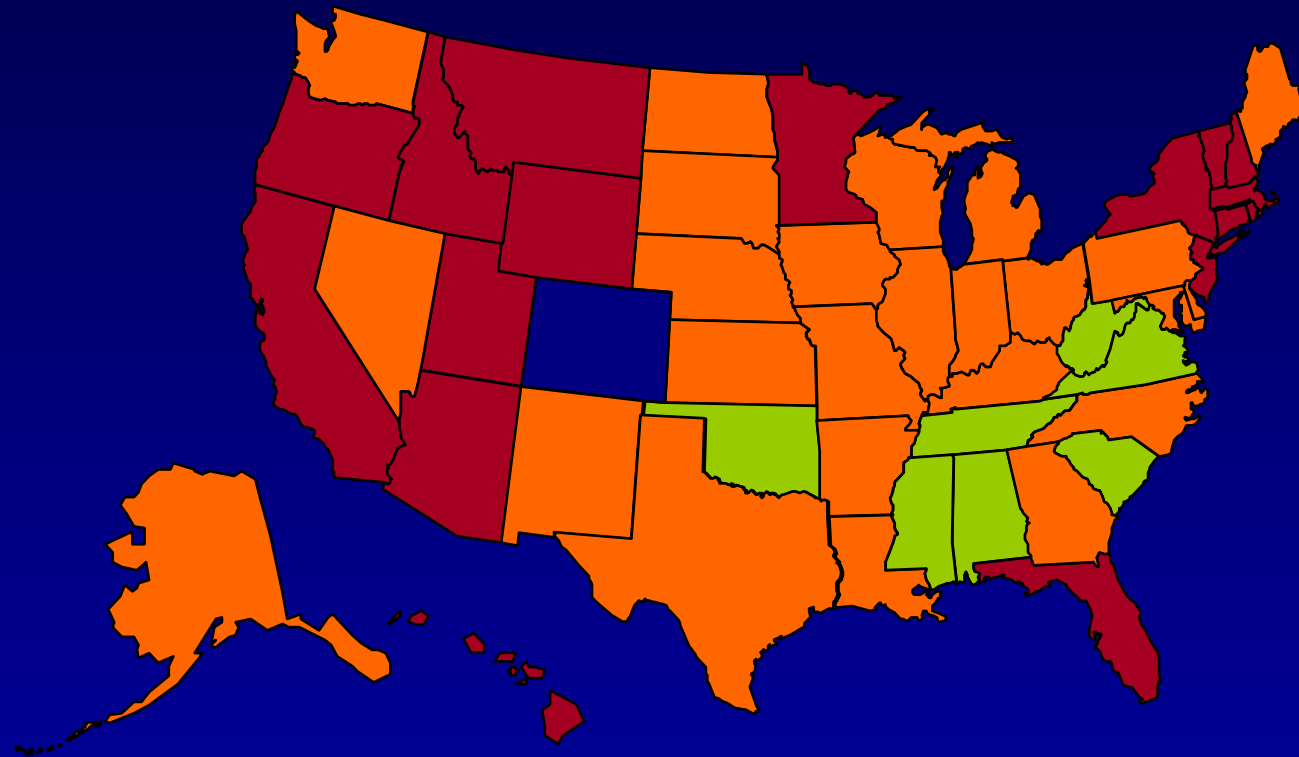
# Obesity Trends\* Among U.S. Adults: BRFSS - 2001

(\*BMI  $\geq 30$ , or  $\sim 30$  lbs overweight for 5'4" woman)

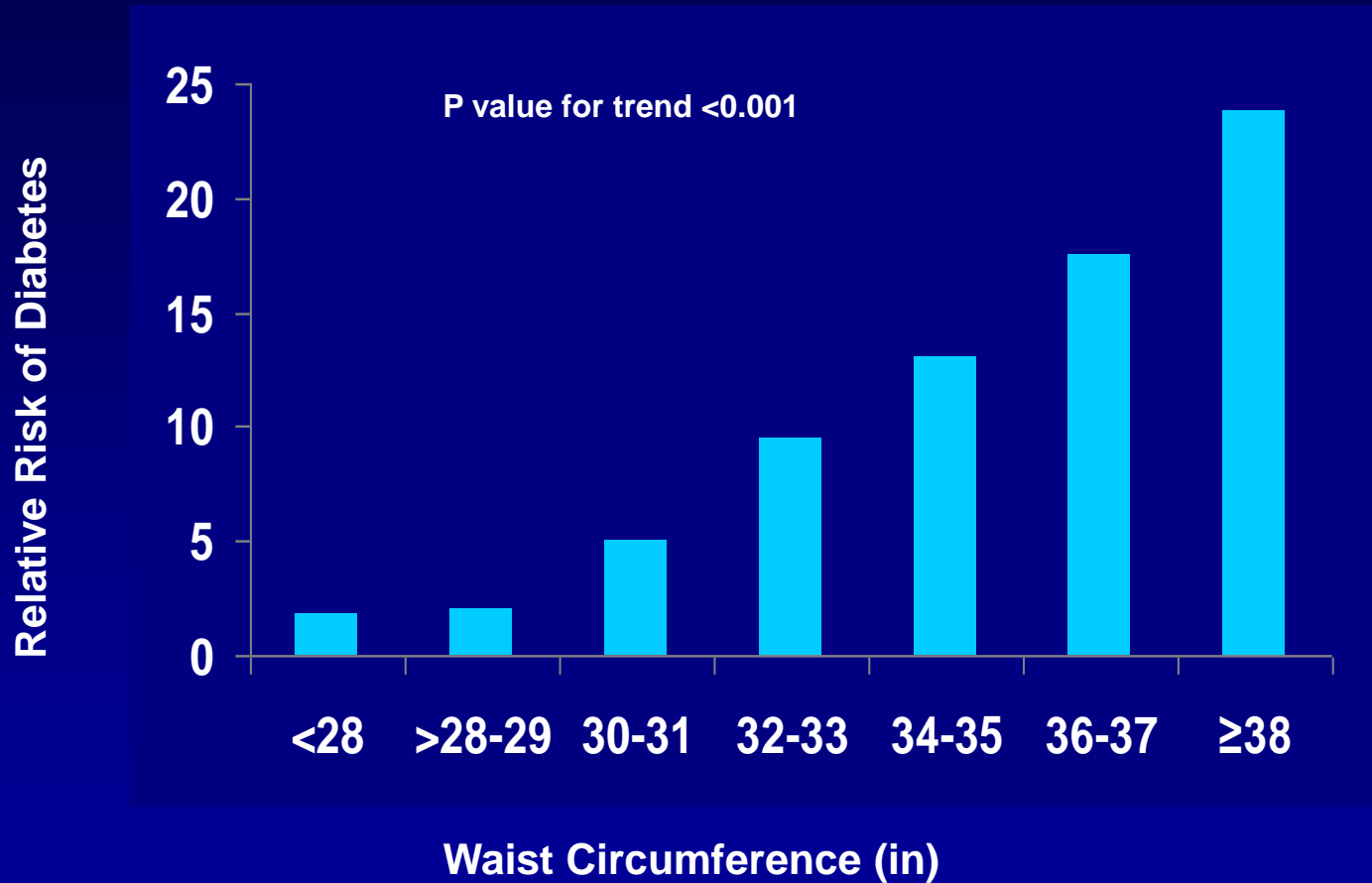


# Obesity Trends\* Among U.S. Adults: BRFSS - 2008

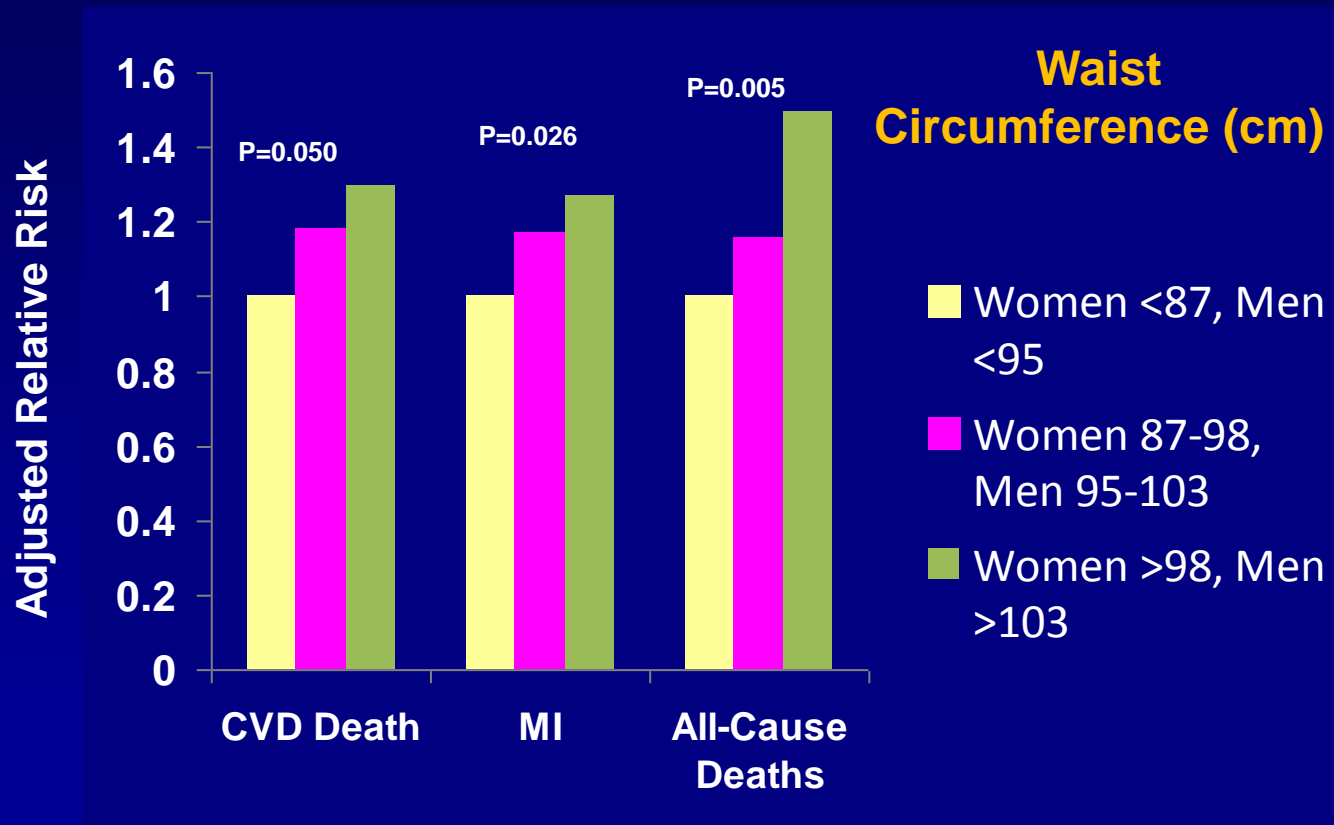
(\*BMI  $\geq 30$ , or  $\sim 30$  lbs overweight for 5'4" woman)



# Abdominal Adiposity Is Associated With Increased Risk of Diabetes

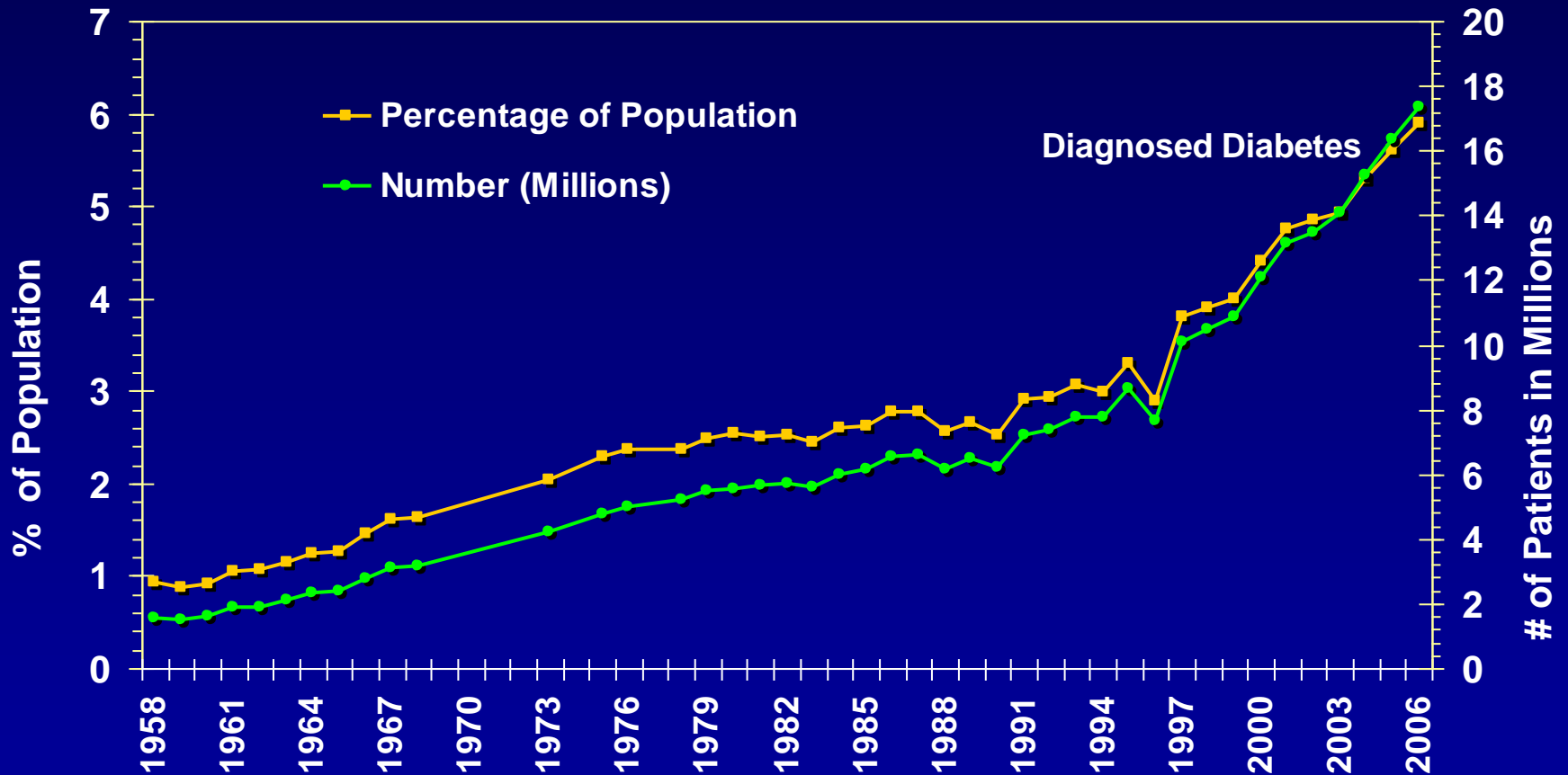


# Abdominal Adiposity Is Associated With Increased Risk of CV Events



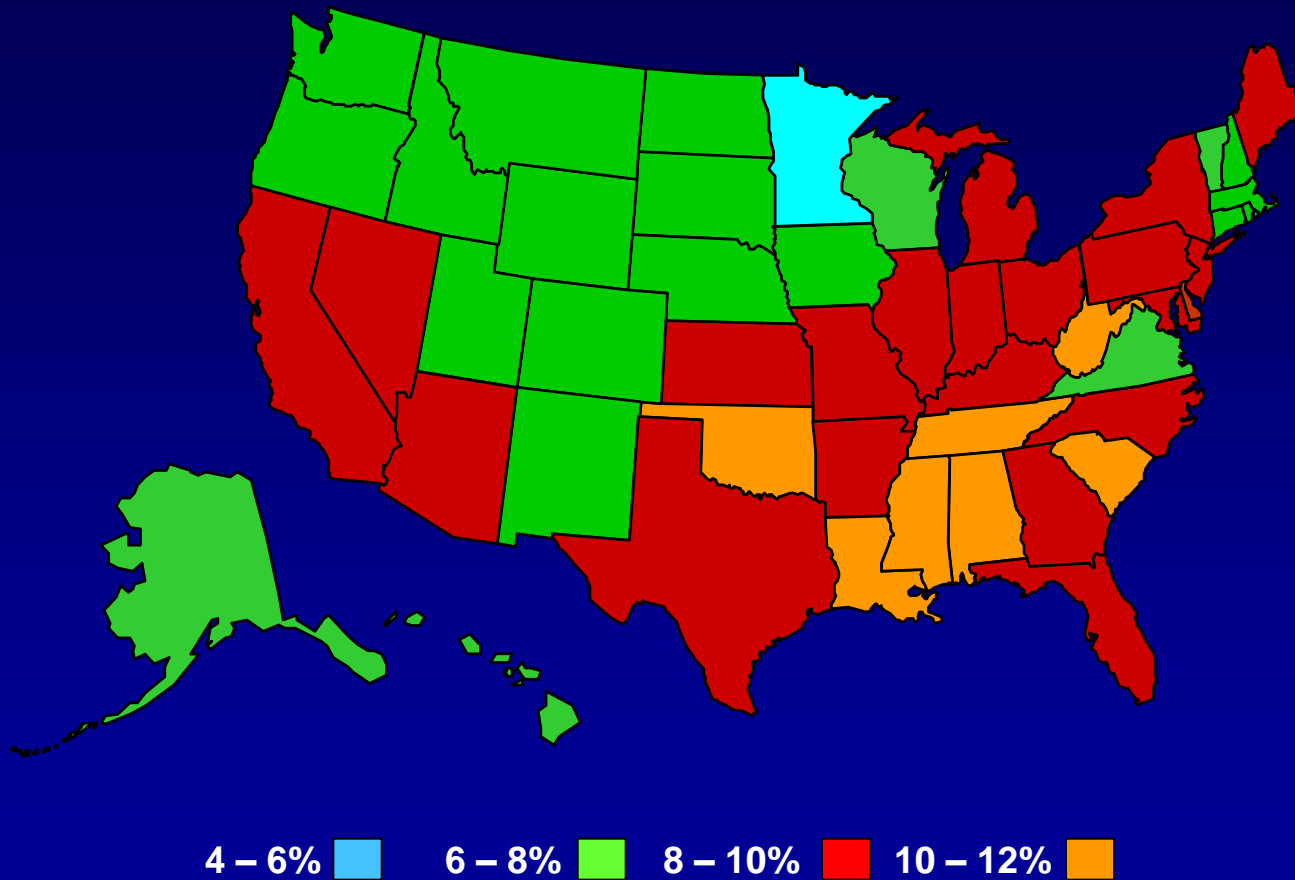
# Diabetes: A Growing Challenge

## Prevalence in the United States

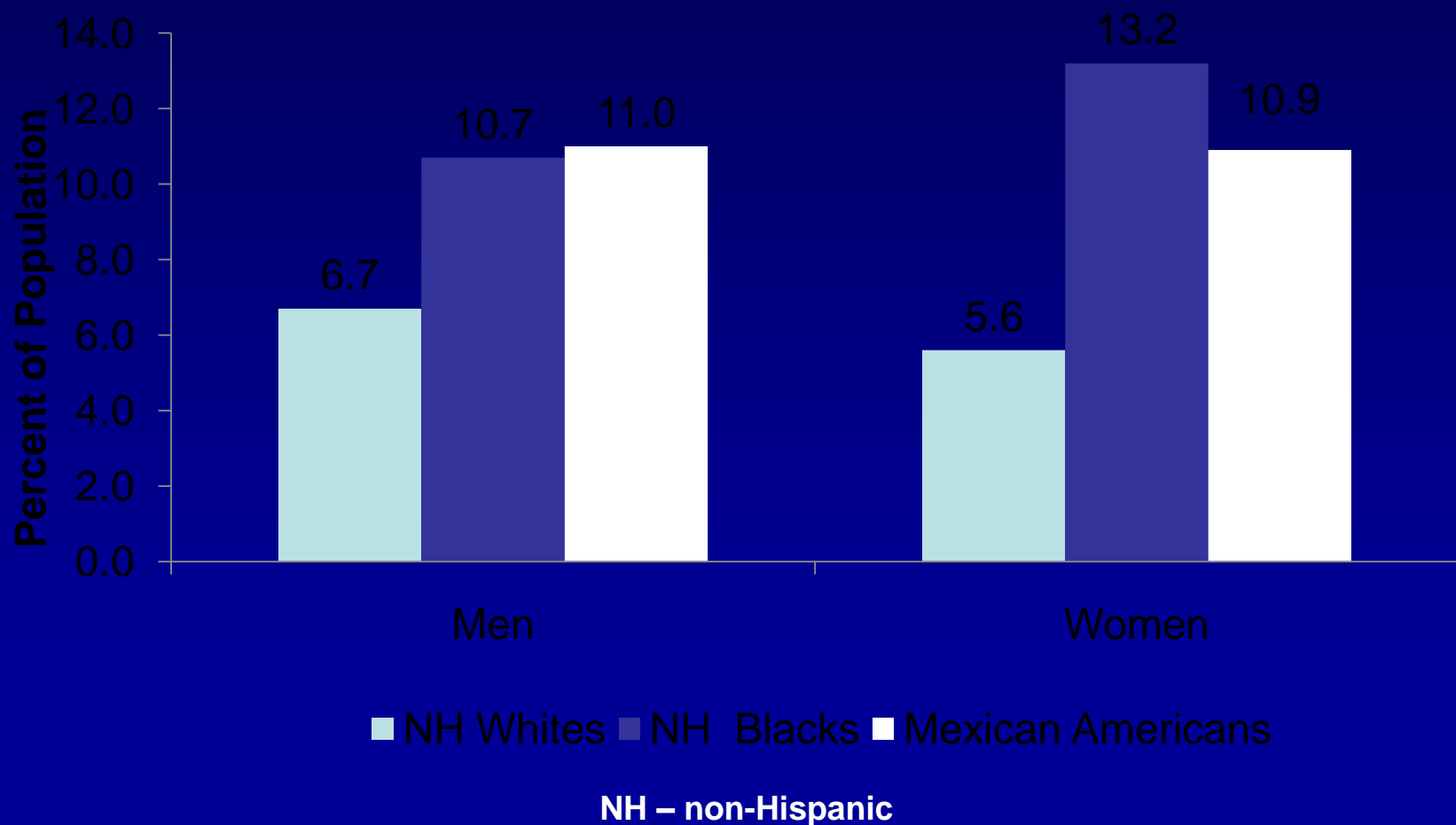


# Diagnosed Diabetes in the US: 2008

CDC BRFSS: Self-Reported Diabetes: 8.2% Nationwide



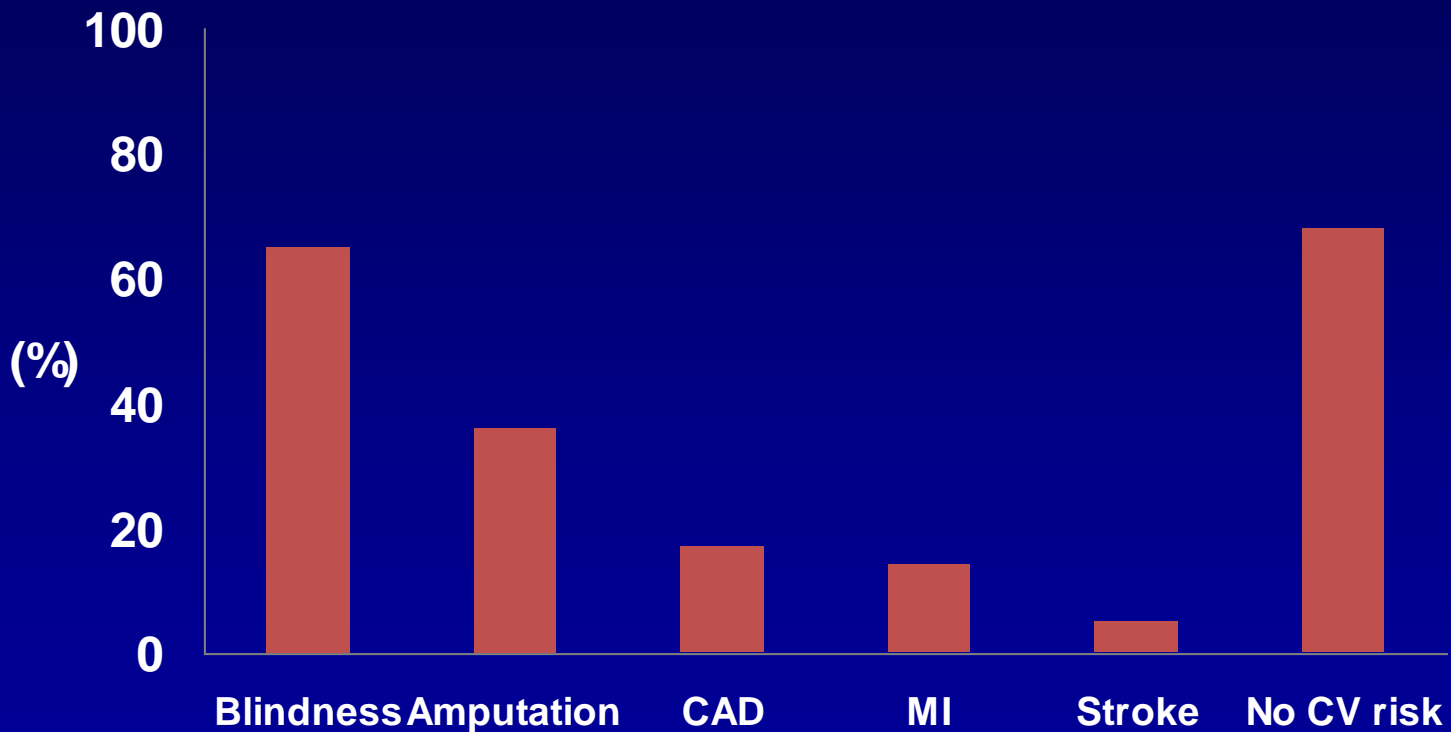
# Age-Adjusted Prevalence of Physician-Diagnosed Diabetes in Adults Age 18 and Older by Race/Ethnicity and Sex



(NHANES: 1999-2004). Source: NCHS and NHLBI. Briefel and Johnson. Annu Rev Nutr. 2004;24:401-431

# Patient Beliefs About Diabetes Risks

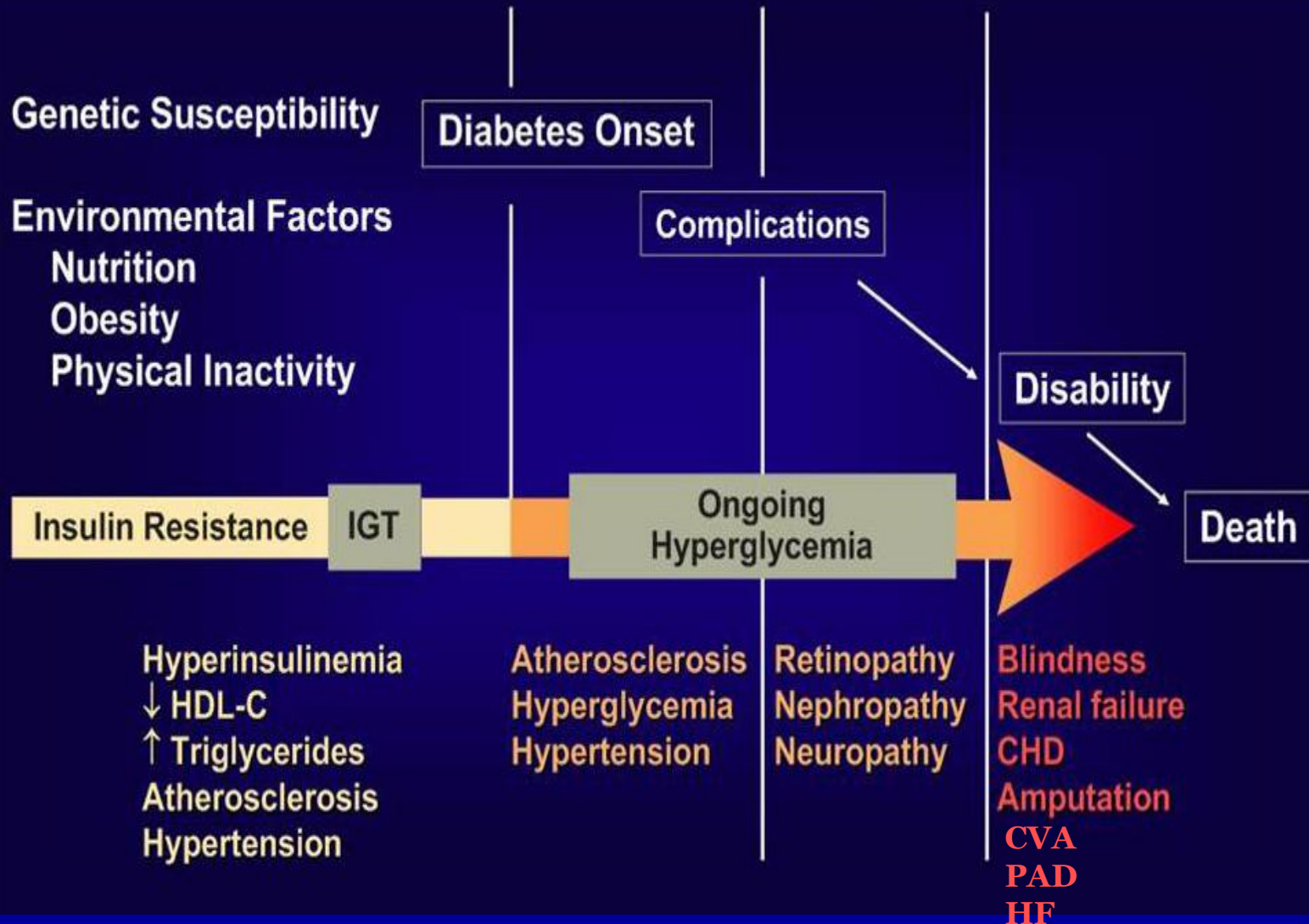
ACC/ADA Diabetes Knowledge Survey (n=2008)



# Diabetes and CVD

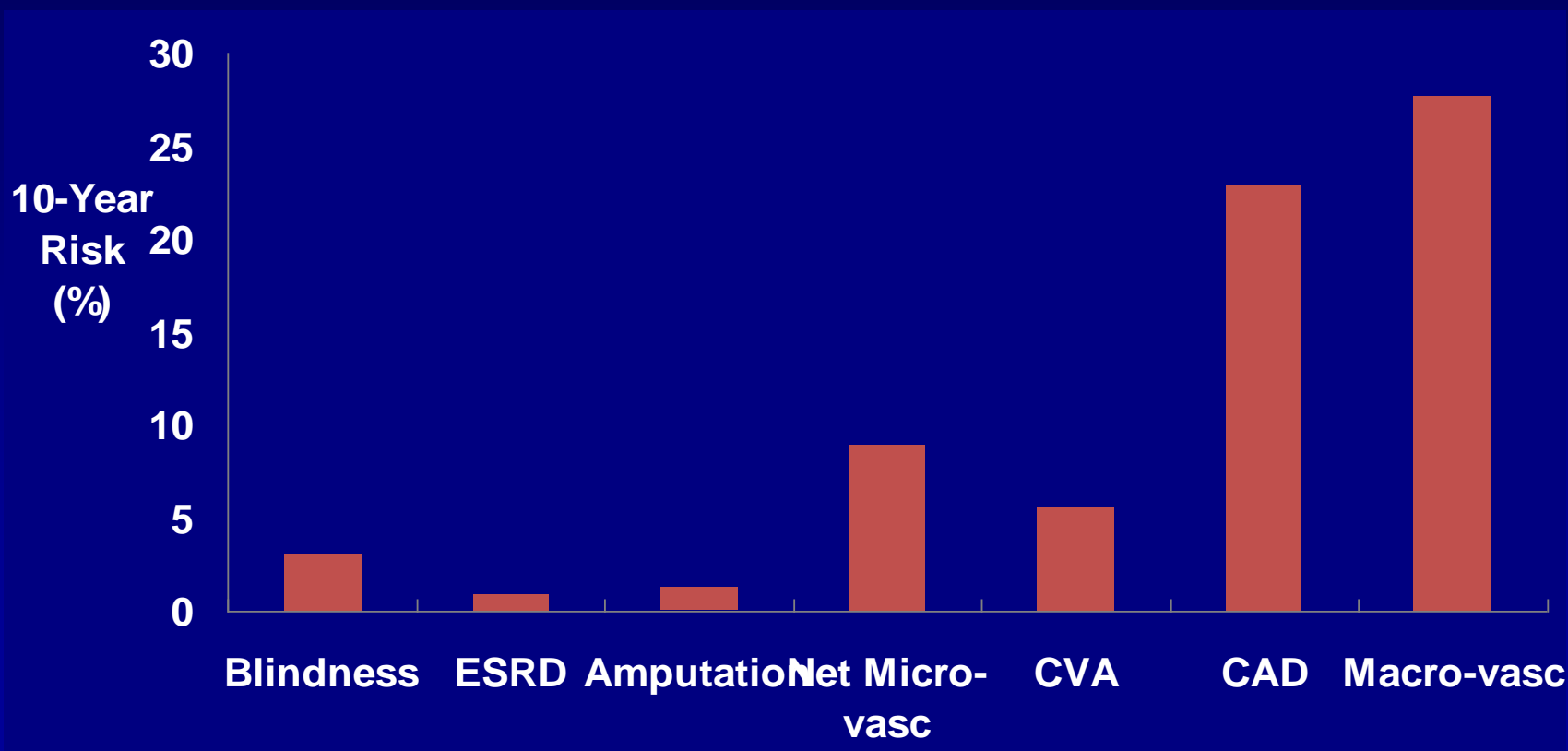
- Atherosclerotic complications responsible for
  - 80% of mortality among patients with diabetes
  - 75% of cases due to coronary artery disease (CAD)
  - Results in >75% of all hospitalizations for diabetic complications
- 50% of patients with type 2 diabetes have preexisting CAD. (This number may be less now that more younger people are diagnosed with diabetes.)
- 1/3 of patients presenting with myocardial infarction have undiagnosed diabetes mellitus

# The Continuum of CV Risk in Type 2 Diabetes



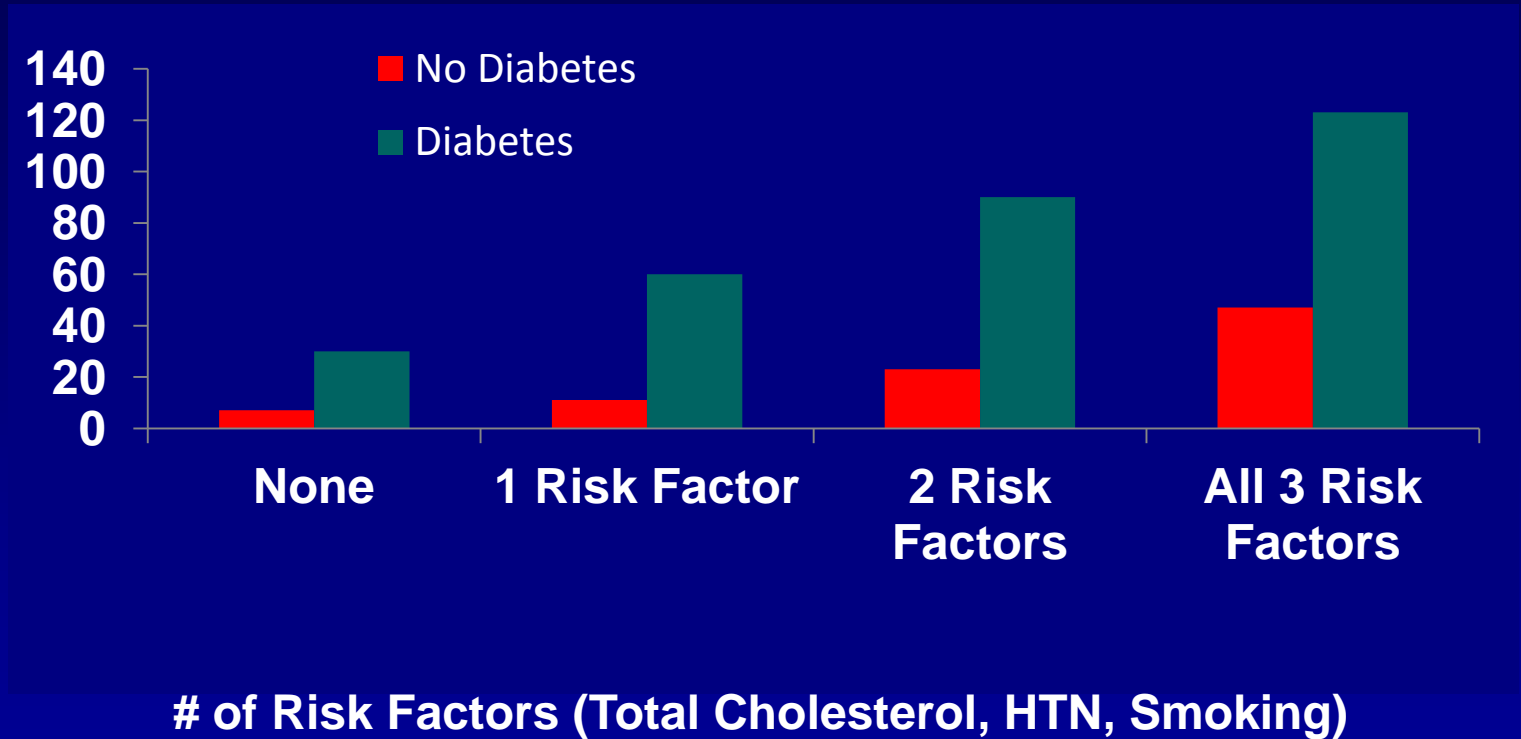
# Diabetes Mellitus: A Cardiovascular Disease

United Kingdom Prospective Diabetes Study (n=3867)



# Age-Adjusted CVD Death Rates (MRFIT)

Age-Adjusted CVD Death Rate  
per 10,000 Person Years

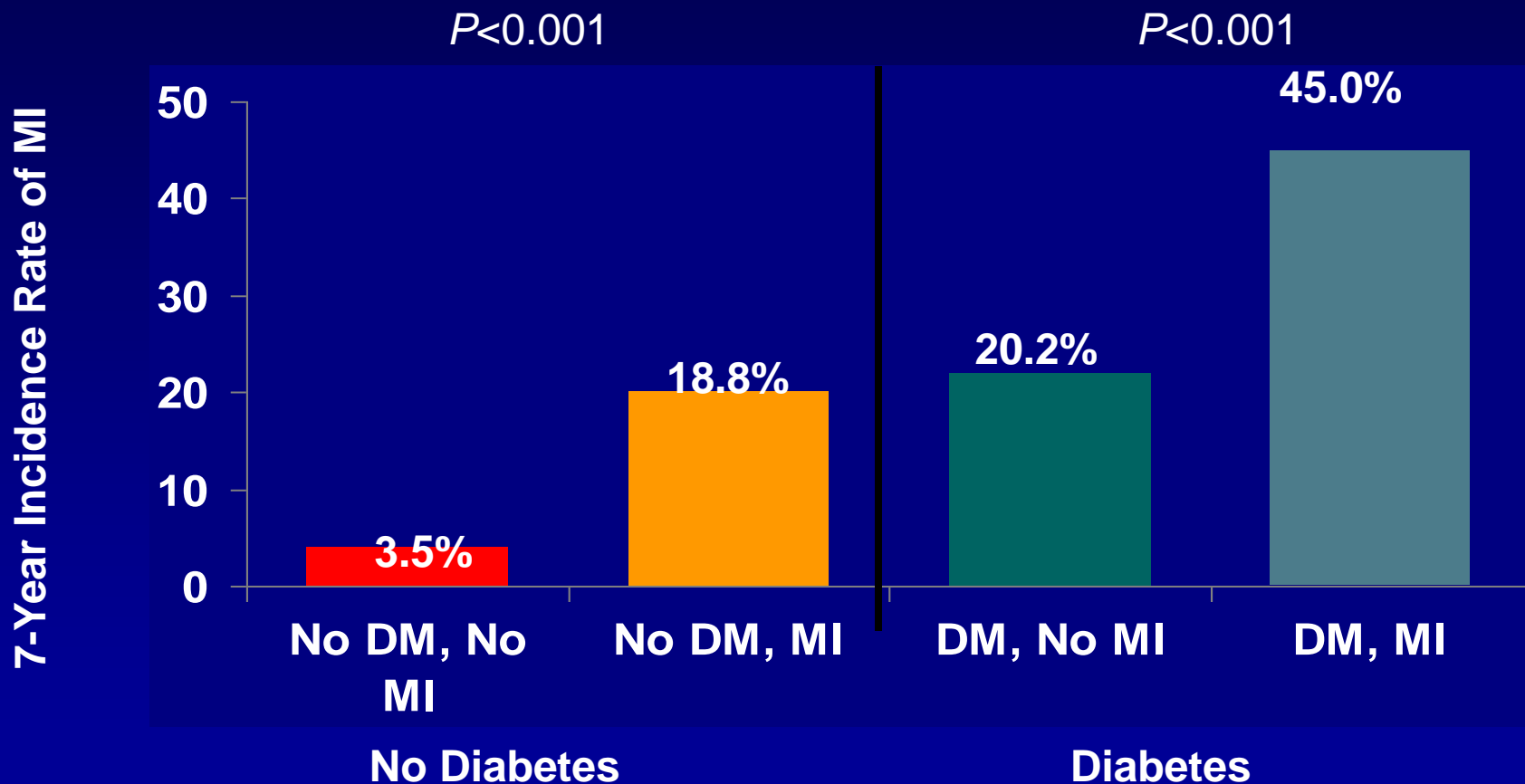


CVD=cardiovascular disease

MRFIT=multiple risk factor intervention trial

# Type 2 Diabetes and CHD

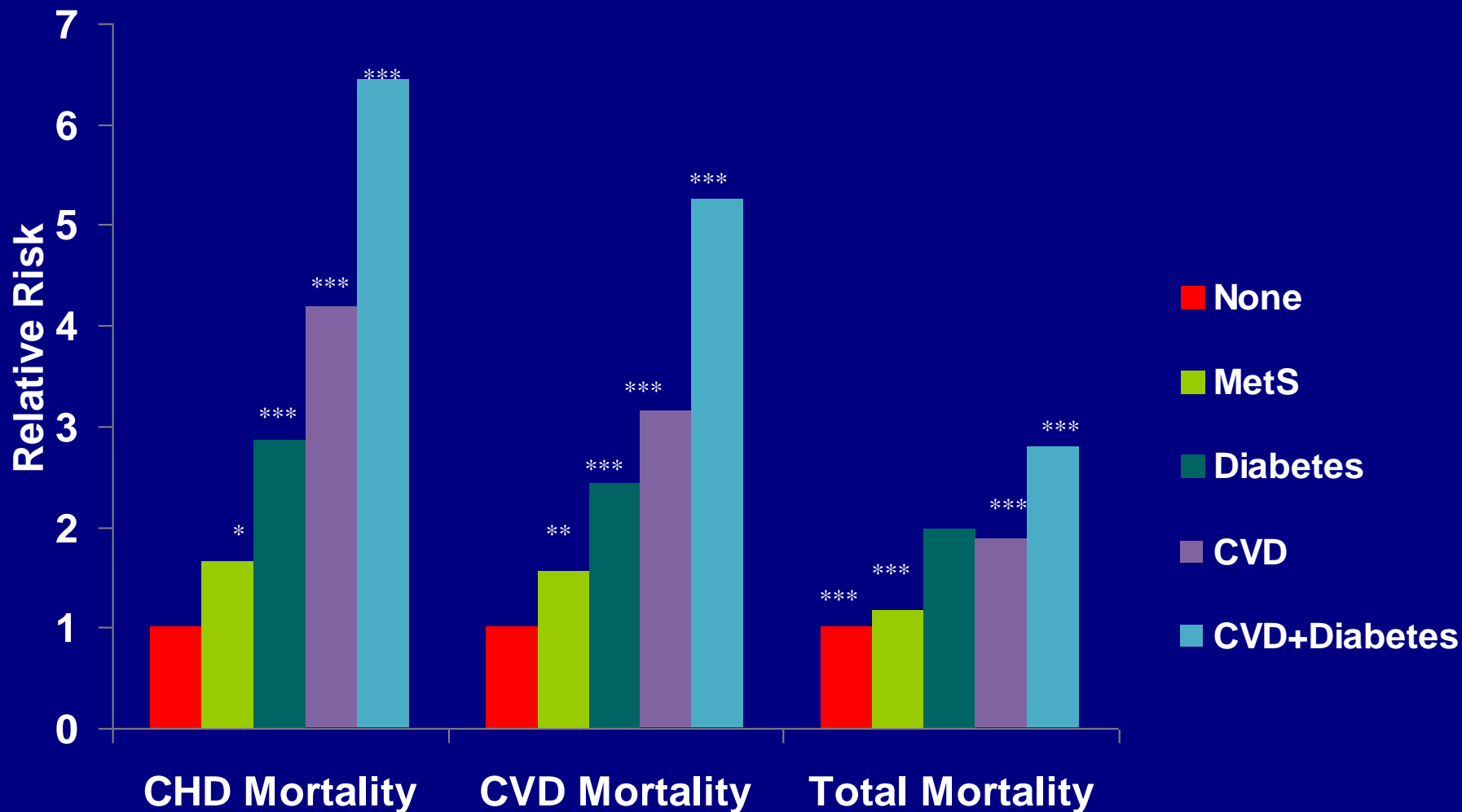
## 7-Year Incidence of Fatal/Nonfatal MI (East West Study)



CHD=coronary heart disease; MI=myocardial infarction; DM=diabetes mellitus

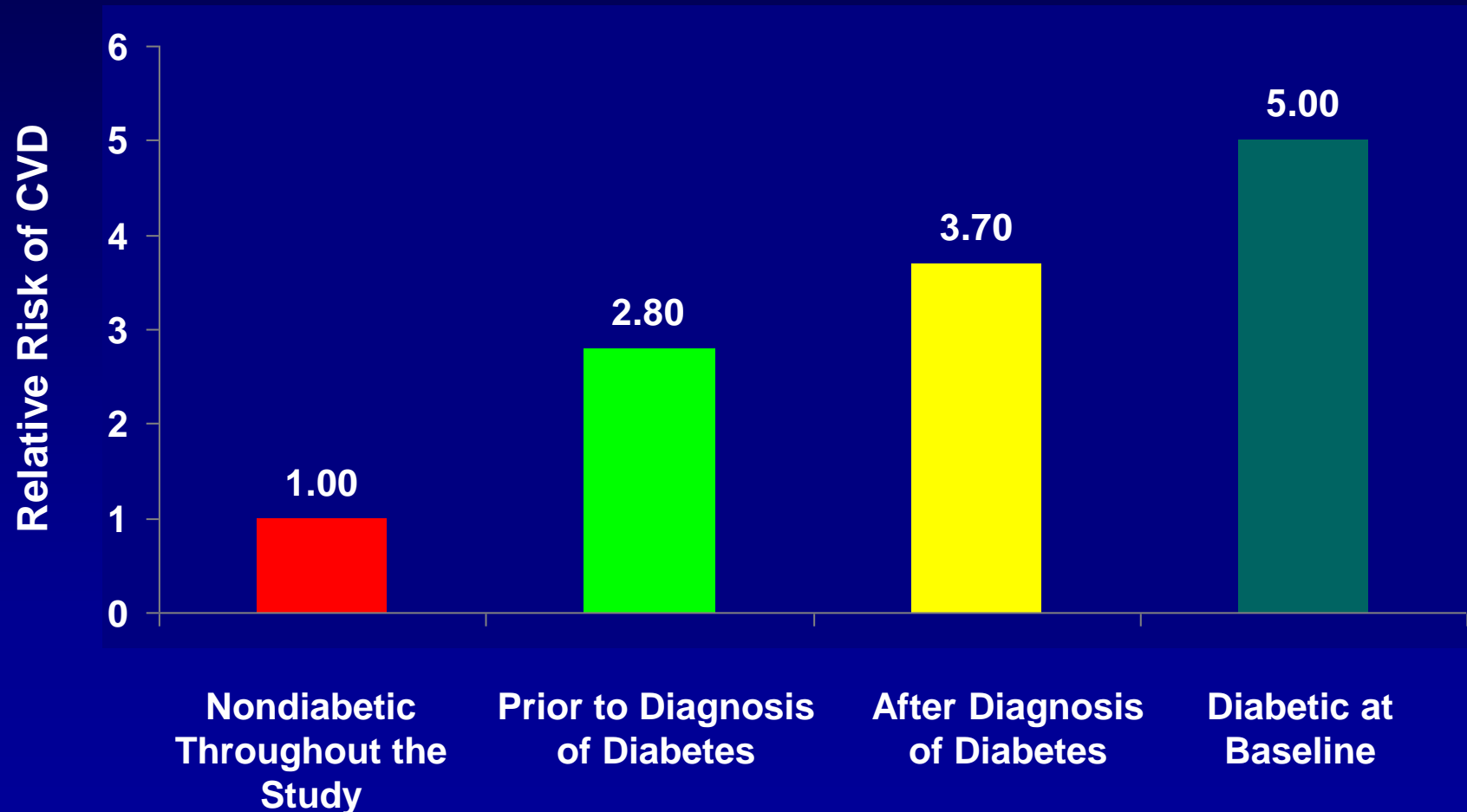
# Cardiovascular Disease (CVD) and Total Mortality: U.S. Men and Women Ages 30-74

(Risk-factor Adjusted Cox Regression) NHANES II Follow-up (n=6255)

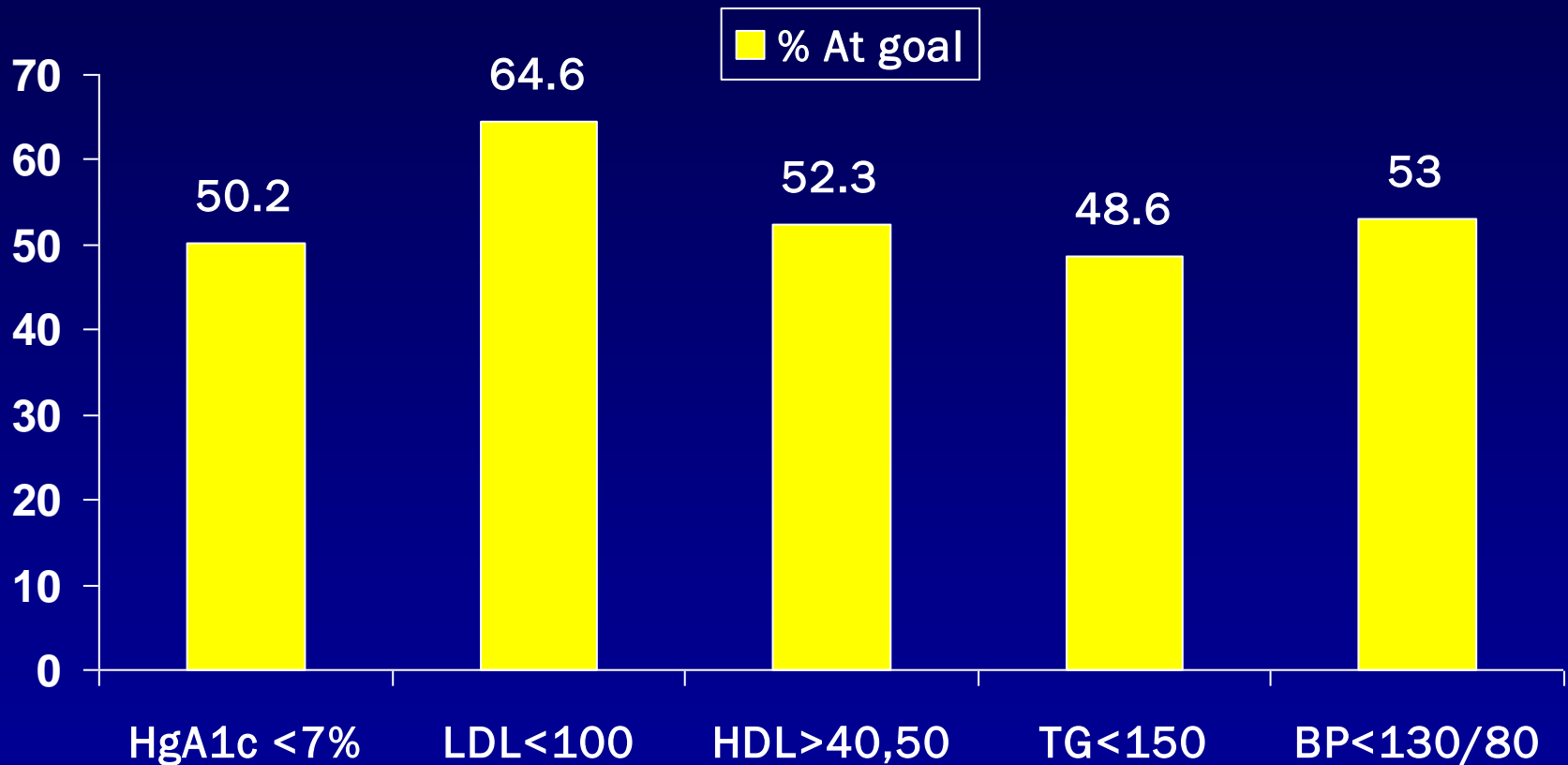


\* p<.05, \*\* p<.01, \*\*\*\* p<.0001 compared to none

# Nurses' Health Study: Elevated Risk of CVD Prior to Clinical Diagnosis of Type 2 Diabetes



# Under-Treatment of Cardiovascular Risk Factors Among U.S. Adults with Diabetes



# Summary

- Prevalence of obesity is increasing
- The number of patients with diabetes is increasing
- There is increased mortality and morbidity associated with diabetes
  - Primarily attributable to cardiovascular disease
- Patients with diabetes underestimate the risk of the disease

# Summary of Care: ABC's for Providers



Convergence of Diabetes &  
Cardiovascular Disease

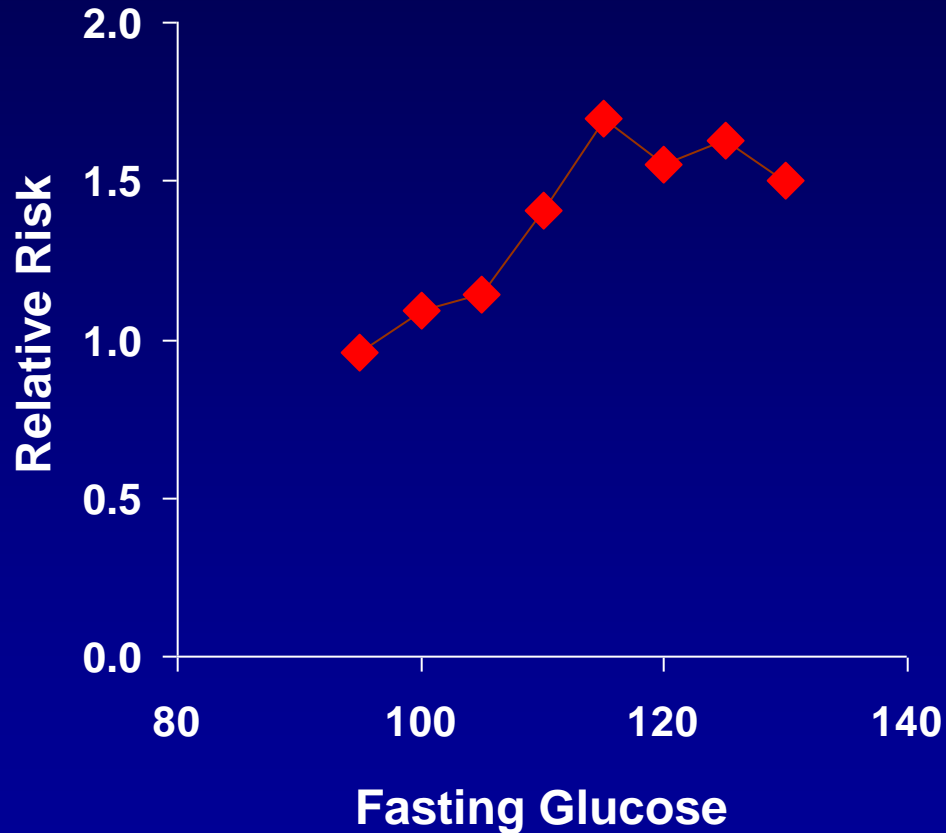
<b>A</b>	<b>A1c Target Aspirin Daily</b>
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# A1c Target

## Aspirin Daily

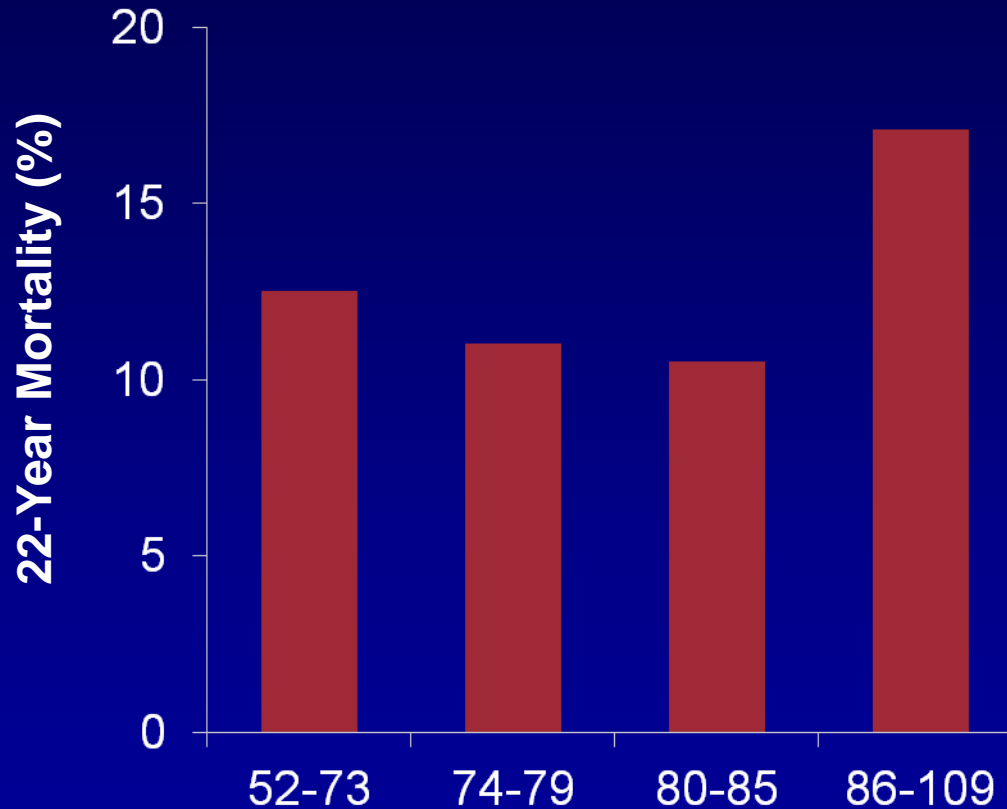
- A1c Target: Glucose lowering to achieve normal to near normal plasma glucose, as defined by the HbA1c <7%
- Aspirin Daily: Secondary prevention or primary prevention in higher risk patients with diabetes

# CAD Event Risk vs. Fasting Glucose (CARE)



CAD=coronary artery disease; CARE=Cholesterol and Recurrent Events trial.

# CV Mortality vs. FBG: 22-Year Follow-Up

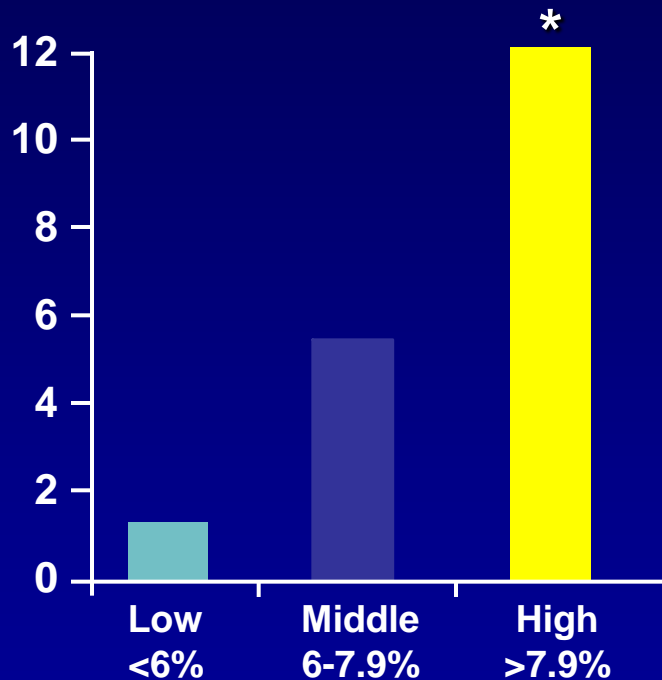


FBG=fasting blood glucose

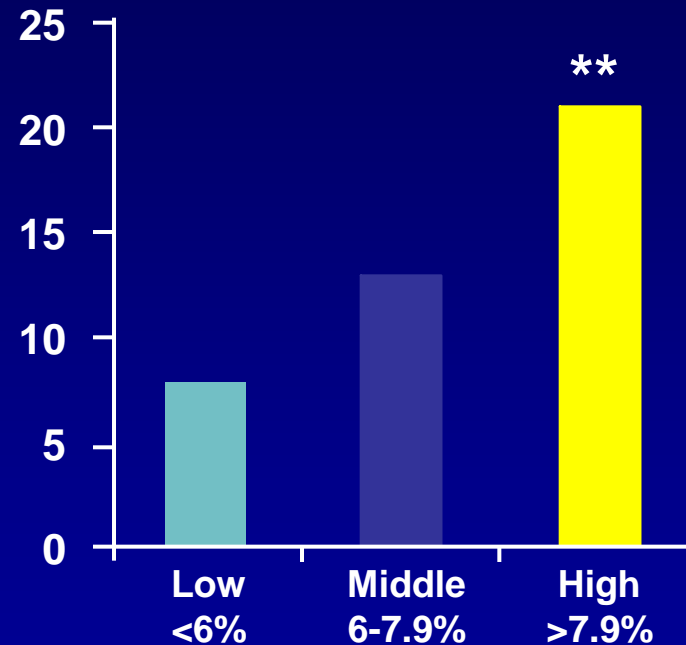
FBG

# Type 2 Diabetes: A1C Predicts CHD

CHD Mortality Incidence  
(%) in 3.5 Years



All CHD Events Incidence  
(%) in 3.5 Years



A1C=hemoglobin A1C

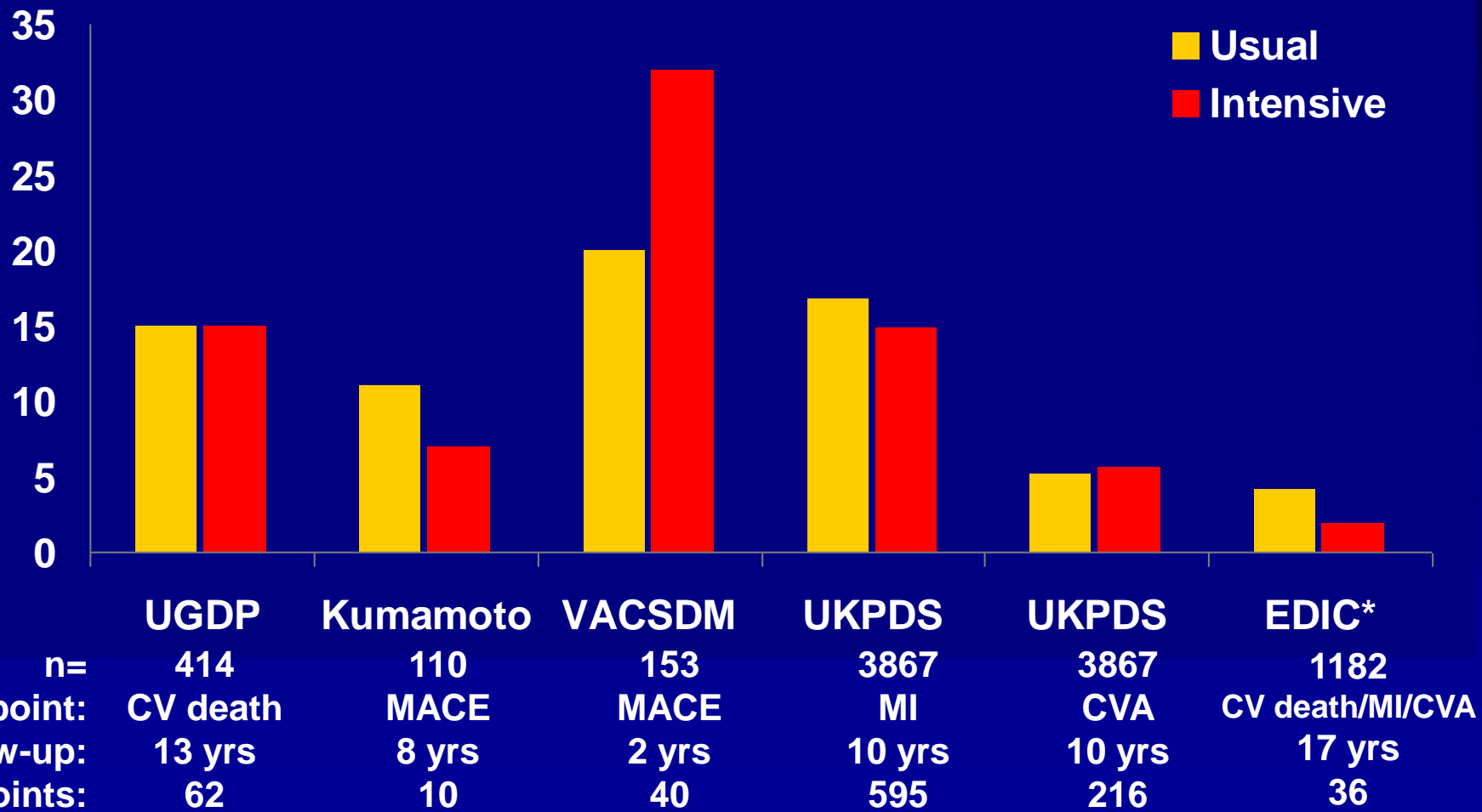
\* $P < 0.01$  vs lowest tertile

\*\* $P < 0.05$  vs lowest tertile

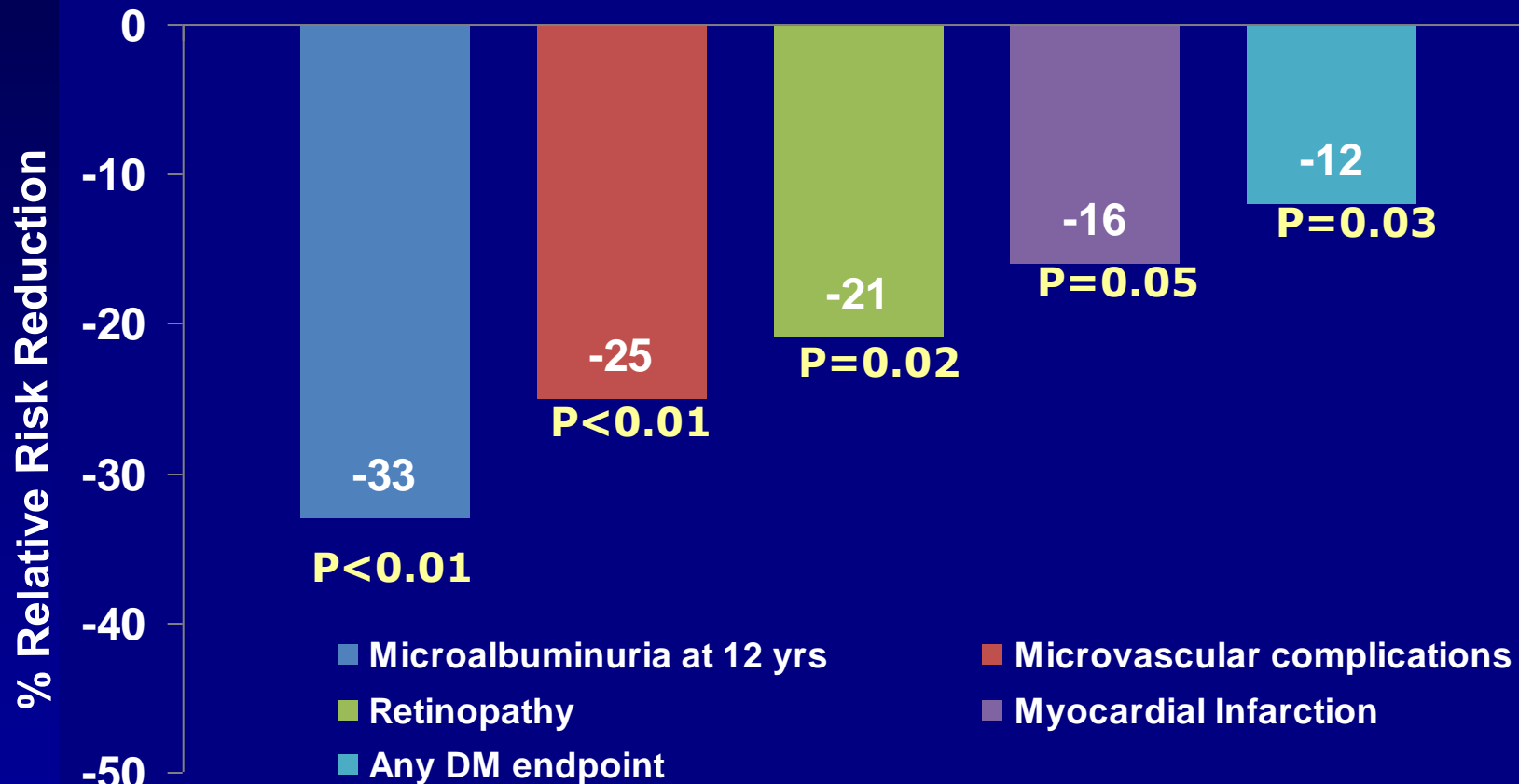
# Impact of Glycemic Control on Clinical Outcomes

- Proven efficacy for microvascular complications
- Uncertain effects on cardiovascular outcomes
  - Most trials to date not designed nor powered to assess CVD effects

# Impact of Glycemic Control on Cardiovascular Outcomes



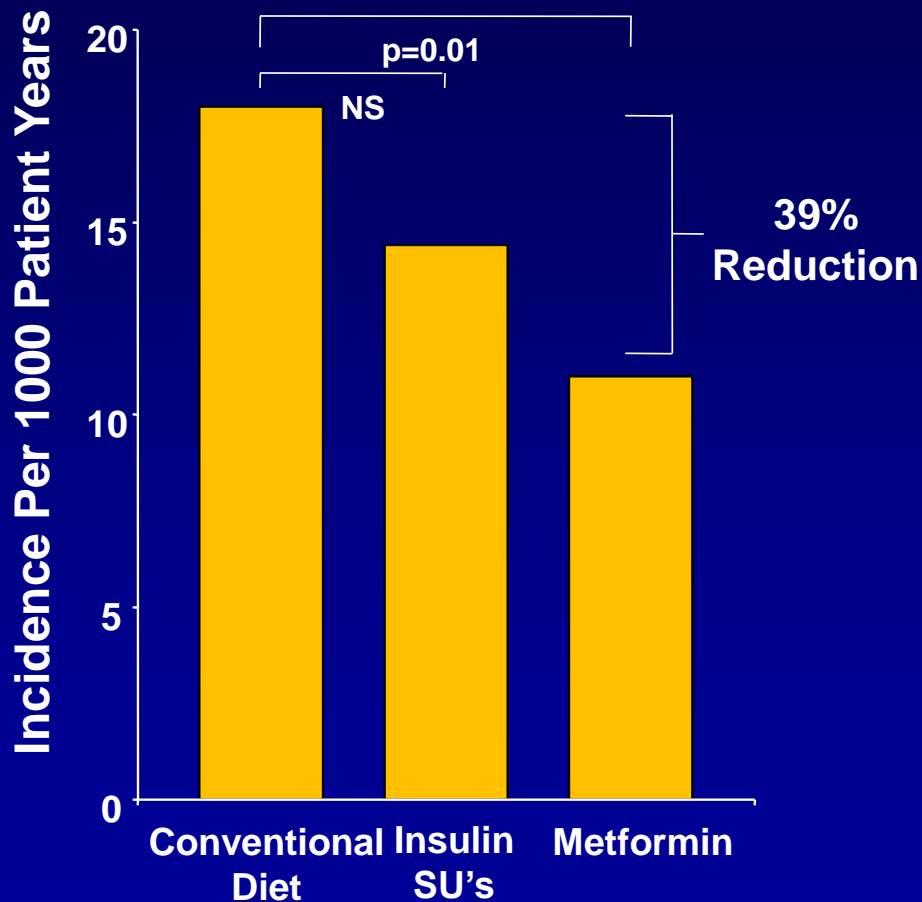
# UKPDS Relative Risk Reduction for Intensive vs. Less Intensive Glucose Control



Over 10 years, HbA<sub>1c</sub> was 7.0% (6.2-8.2) in the intensive group (n=2,729) compared with 7.9% (6.9-8.8) in the conventional group (n=1,138).

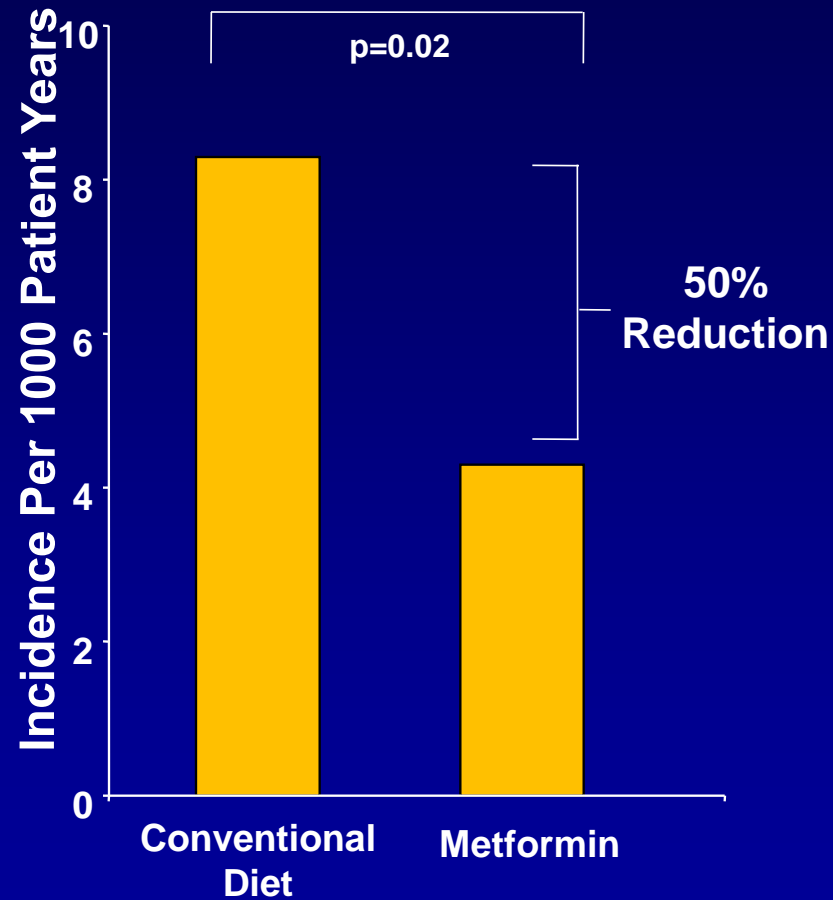
# UKPDS Metformin Sub-Study: CHD Events

## Myocardial Infarction



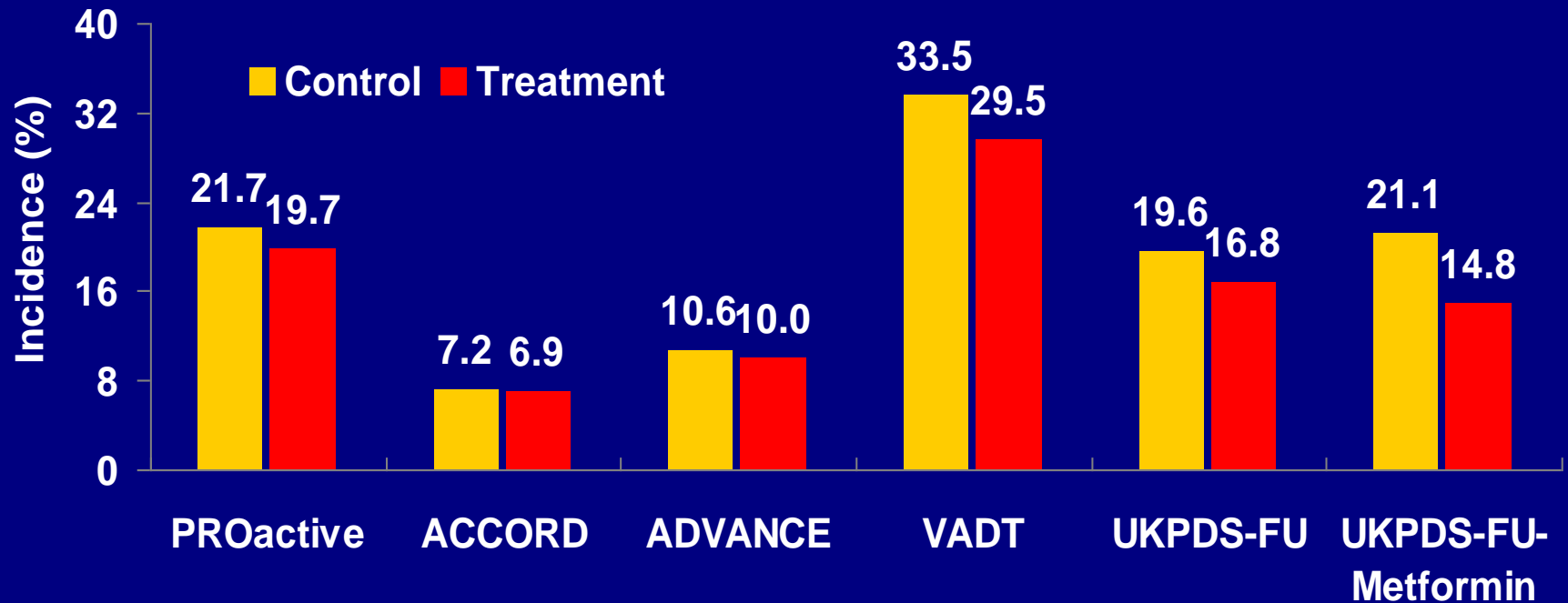
	Conventional Diet	Insulin SU's	Metformin
n=	411	951	342
#Events	73	139	39

## Coronary Deaths



	Conventional Diet	Metformin
n=	411	342
#Events	36	16

# CV Effects of Glucose Control in Recent Large-Scale Trials



Events (n):	358 vs. 301	371 vs. 352	590 vs. 557	264 vs. 235	319 vs. 678	126 vs. 81
RRR	0.9	0.9	0.94	0.88	0.85	0.67
95% CI	0.8-1.02	0.78-1.04	0.84-1.06	0.74-1.05	0.74-0.97	0.51-0.89

# 2009 ADA/AHA/ACC Statement Recommendations

- Goal of  $A1c < 7\%$  remains reasonable
  - for uncomplicated patients
    - *ACC/AHA Class I (A)*
  - and for those with macrovascular disease
    - *ADA Level B; ACC/AHA Class IIb (A)*
- Incremental microvascular benefit may be obtained from even lower goals
  - *ADA Level B; ACC/AHA Class IIa (C)*
- Less stringent goals may be appropriate for those with labile glucose control or with advanced micro- or macrovascular disease
  - *ADA Level C; ACC/AHA Class IIa (C)*

# A1c Target

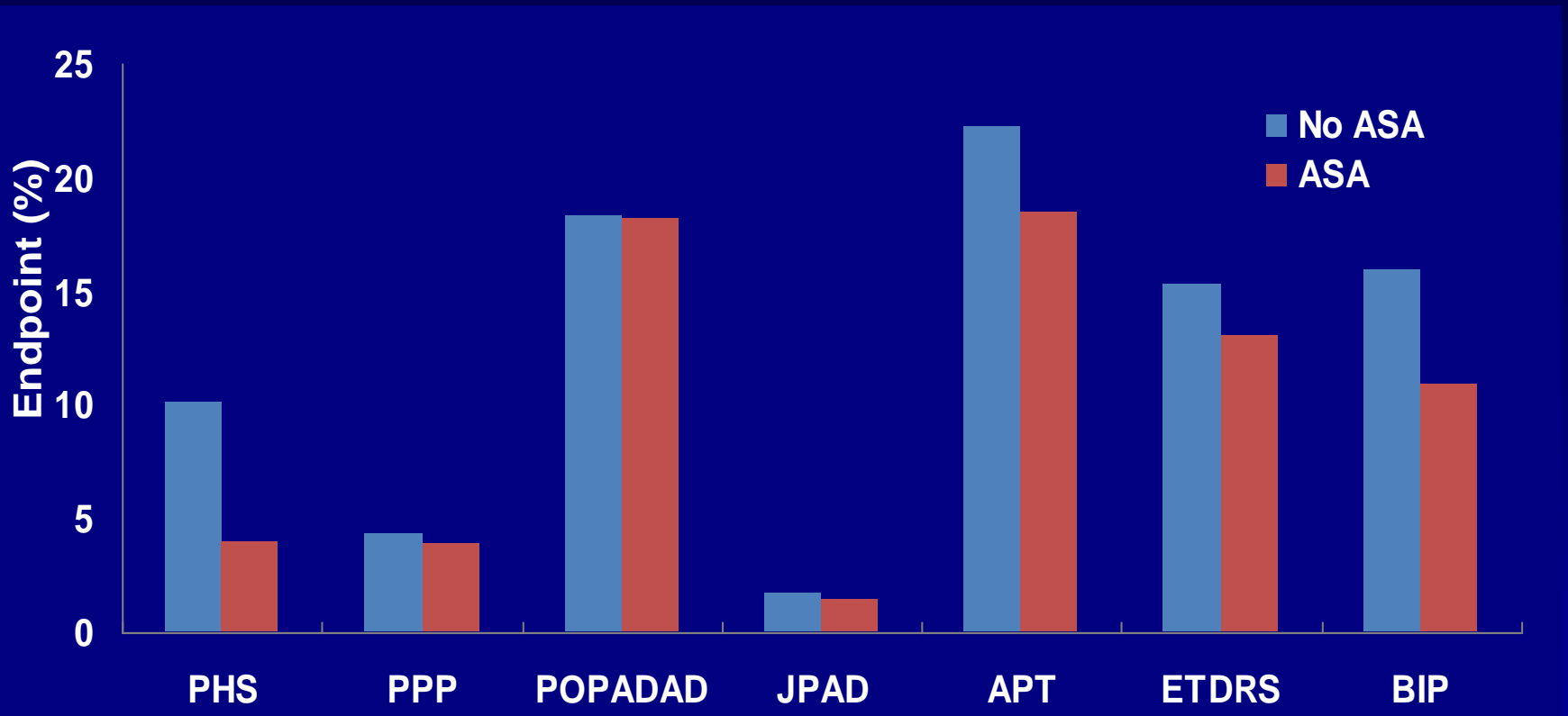
## Aspirin Daily

- A1c Target: Glucose lowering to achieve normal to near normal plasma glucose, as defined by the HbA1c  $<7\%$
- Aspirin Daily: Secondary prevention or primary prevention in higher risk patients with diabetes

# Aspirin Therapy

- Aspirin therapy 75-162 mg for secondary prevention in patients with diabetes with CVD
- Aspirin therapy 75-162 mg for type 1 or type 2 at increased CV risk (10 year risk > 10%)
  - Men > 50 or women > 60 and
    - Family History
    - Hypertension
    - Smoker
    - Dyslipidemia
    - Albuminuria

# Therapeutic Efficacy in Diabetes: ASA



n=	533	1031	1276	2539	4502	3711	2368
Endpoint	5yr MI	4yr MCE	7 yr MCE	4 yr MCE	1 yr MCE	7yr MI	5yr CVDeath
# Events	26 vs 11	20 vs 22	117 vs 116	86 vs 68	426 vs 403	283 vs 241	183 vs 133

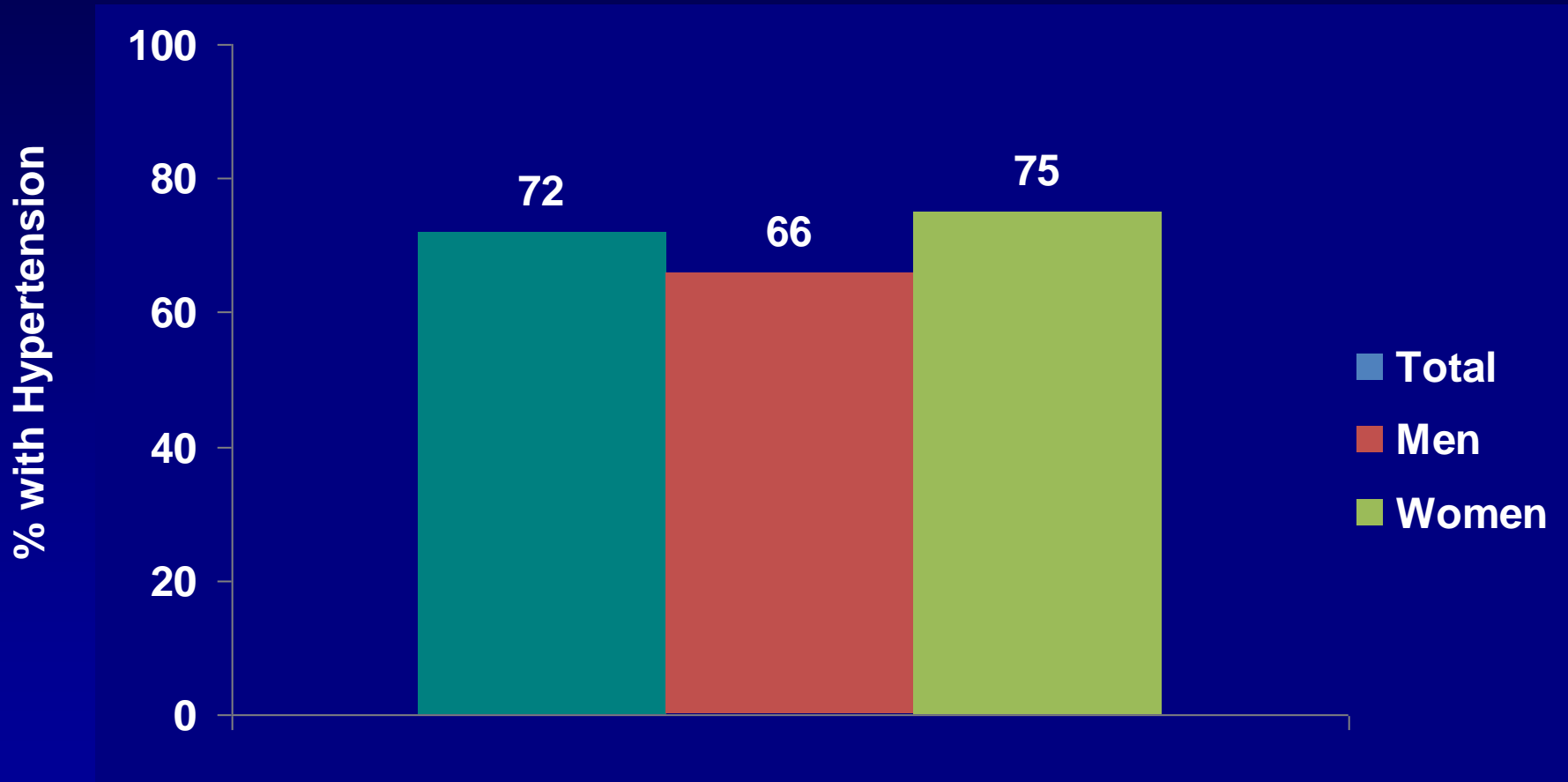
# Summary of Care: ABC's for Providers



Convergence of Diabetes &  
Cardiovascular Disease

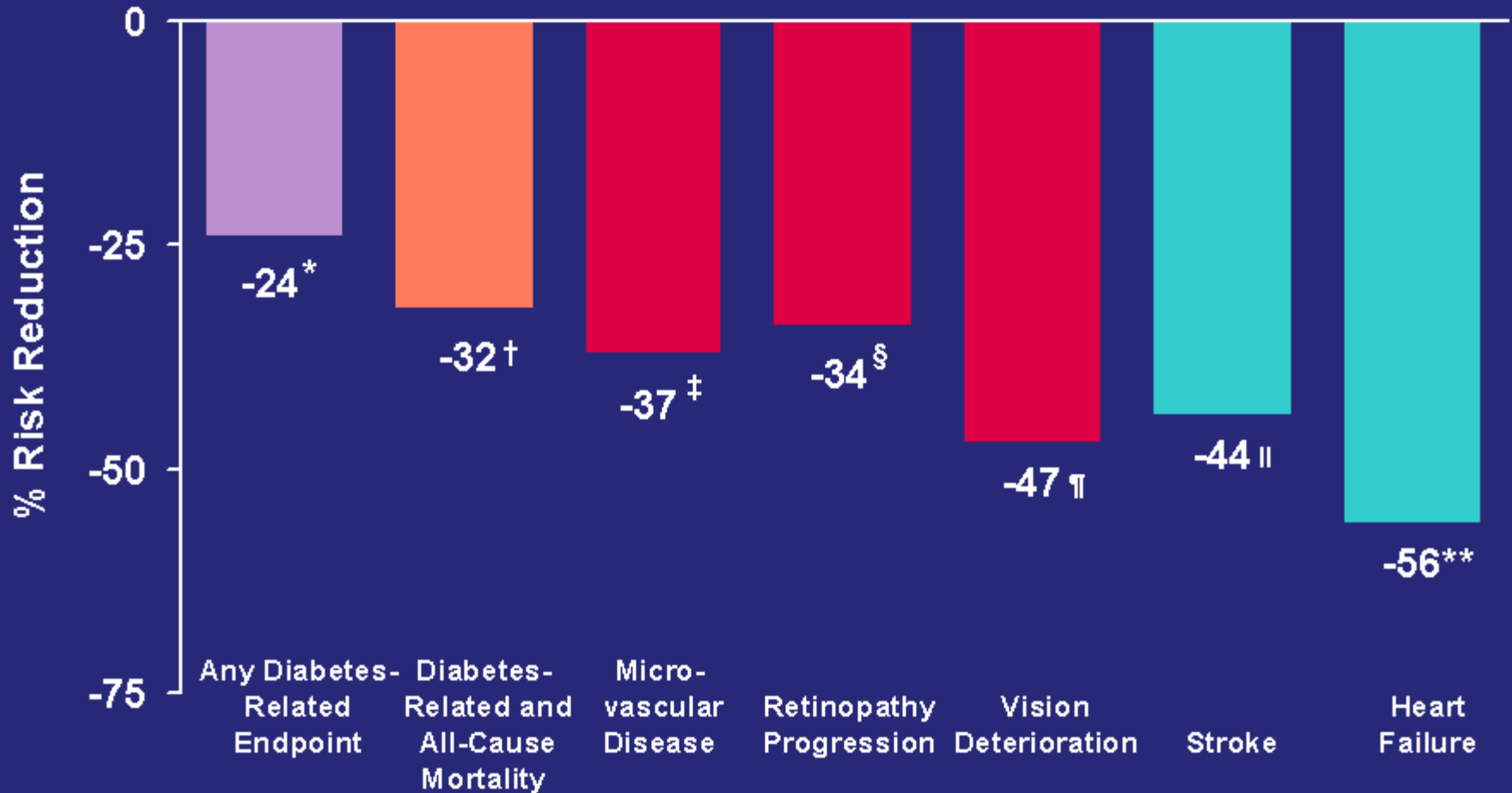
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# Prevalence of Hypertension\* in Adults with Diabetes: NHANES III 1988-1994



\*BP  $\geq$ 130/85 or therapy for hypertension

# UKPDS: Effects of Tight vs. Less-Tight Blood Pressure Control

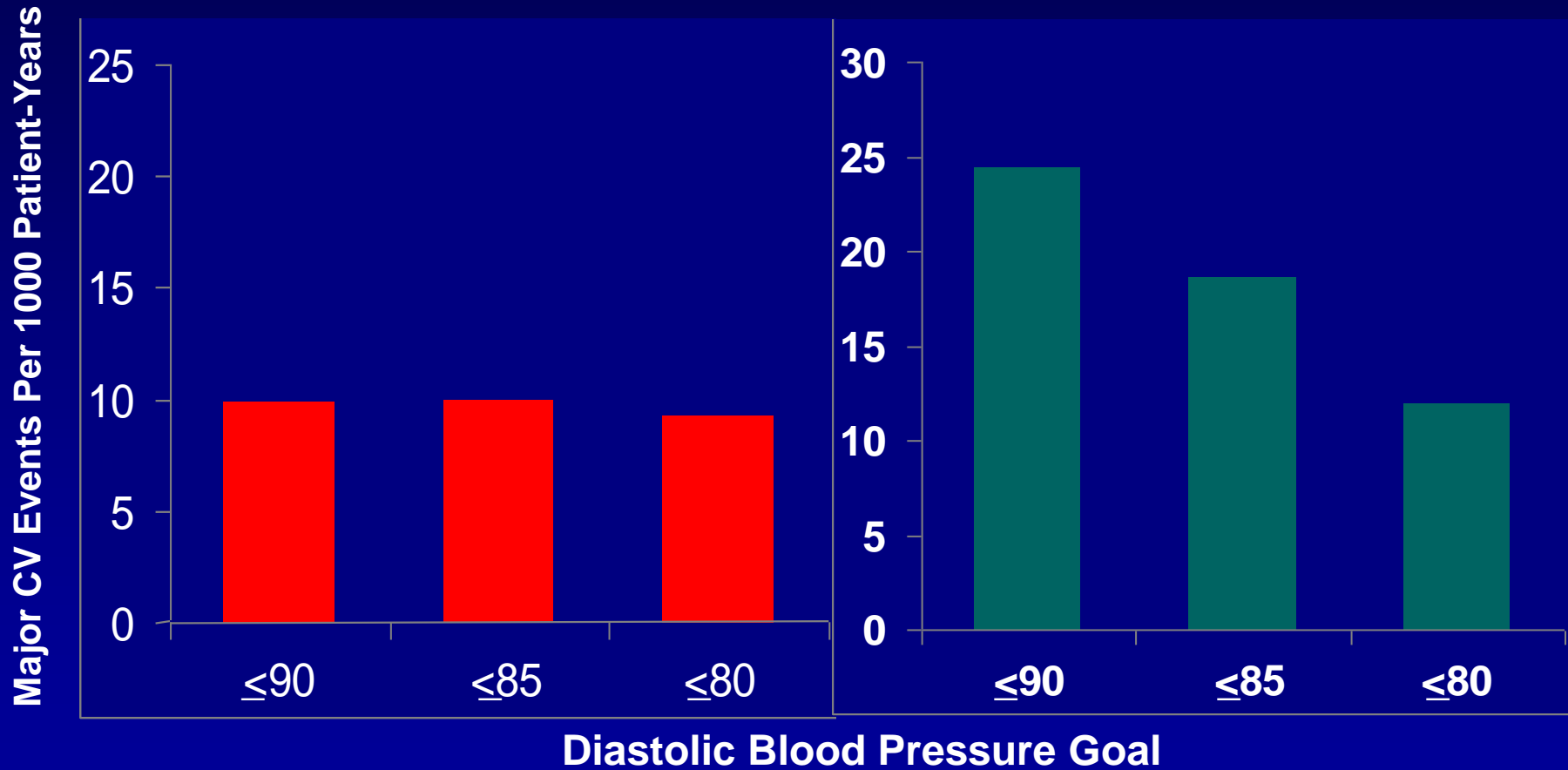


\* $P=0.0046$ ; † $P=0.019$ ; ‡ $P=0.0092$ ; § $P=0.0038$ ; ¶ $P=0.0036$ ; || $P=0.013$ ; \*\* $P=0.0043$

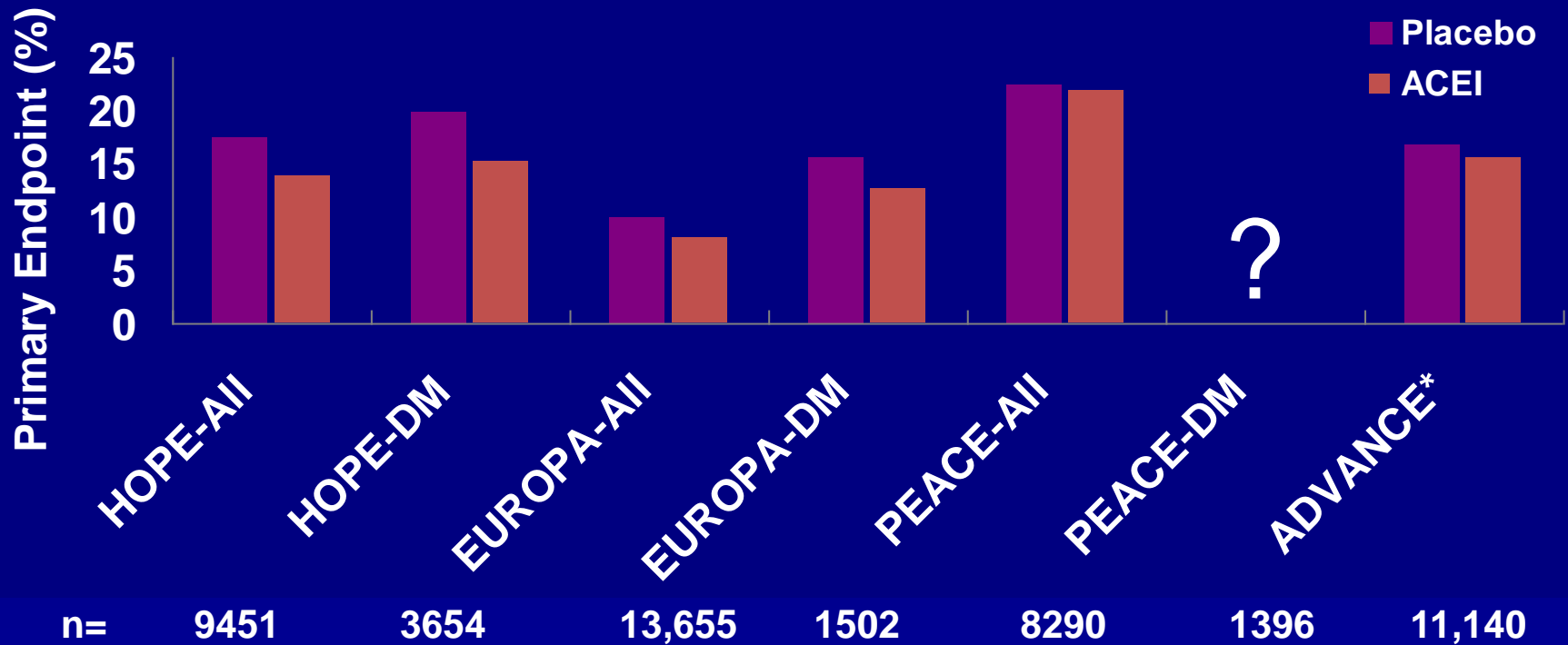
# HOT Trial: Effect of BP Control on CV Event Rate

Overall Study Cohorts

Patients with Diabetes



# Therapeutic Efficacy in Diabetes: ACE Inhibitors



\*Experimental therapy was ACEI plus indapamide

# Scientific Statements: Diabetes, CV Disease and Hypertension

- JNC VII Report on Diabetic Hypertension
  - BP goal (<130/80 mm Hg)
    - Commonly requiring combinations of  $\geq 2$  drugs
  - ACEIs, CCBs, Thiazide-diuretics,  $\beta$ -blockers, and ARBs shown to reduce CVD/CVA risk
  - ACEIs/ARBs reduce progression of diabetic nephropathy and reduce albuminuria
  - ARBs reduce progression of macroalbuminuria

# ADA Standards of Medical Care in Diabetes – 2010

- Treatment of hypertension
  - Target SBP<130 and DBP<80 mmHg
    - In patients with BP 130-139/80-89 may try three months of diet, weight management and exercise
  - ACEI or ARB for initial drug therapy
    - Especially with micro or macroalbuminuria, given benefit in both type 1 diabetes and type 2 diabetes
  - Multiple drug therapy is generally required to achieve BP control

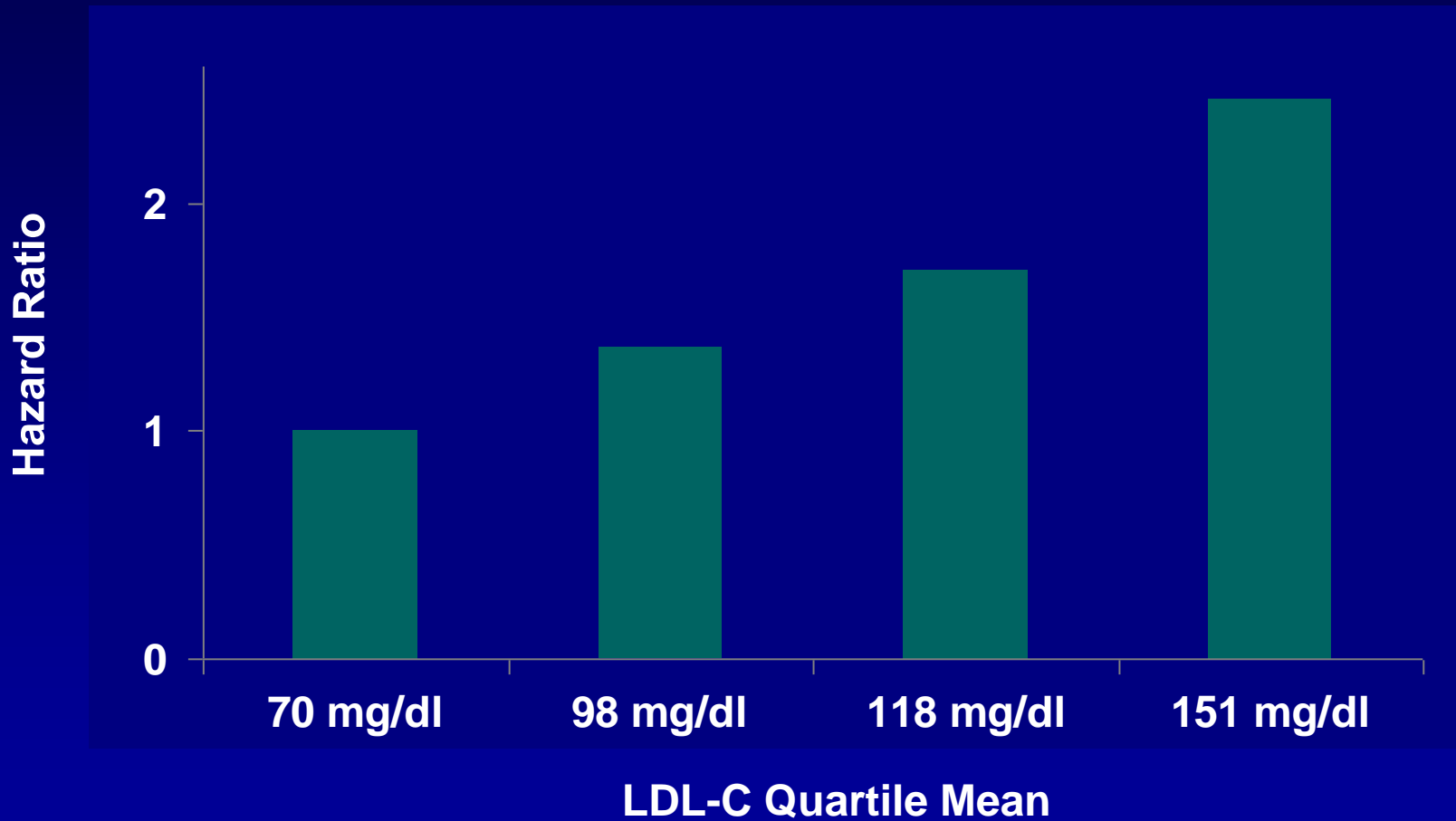
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# LDL-C as a Predictor of CAD in Patients with Diabetes



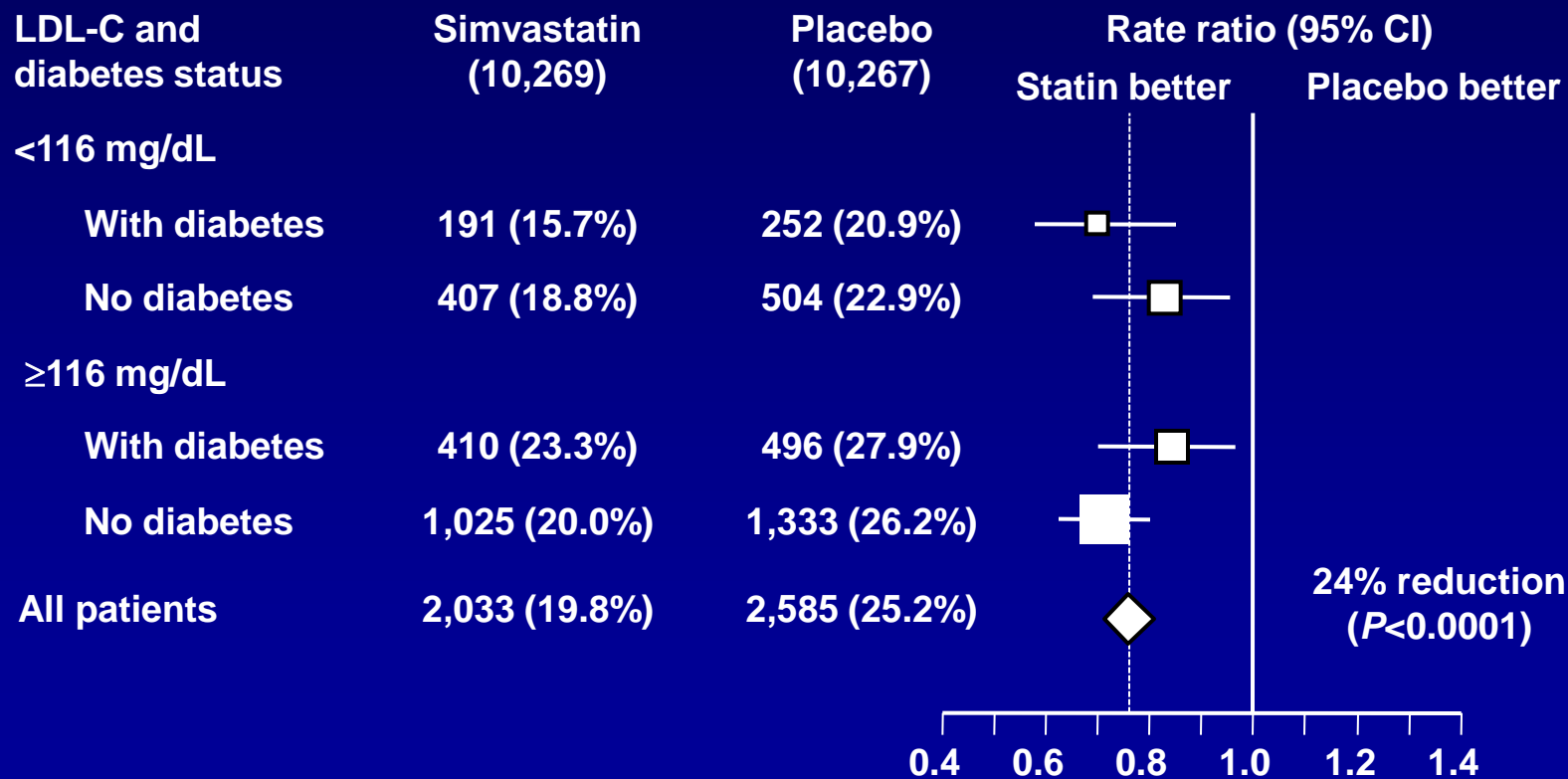
LDL=low-density lipoprotein cholesterol; CAD=coronary artery disease.

# Lipid Treatment Goals for Patients with Type 2 Diabetes

	ADA 2010 <sup>1</sup>	ATP III <sup>4</sup>
LDL (mg/dL)	<100 <70 highest risk	<100
TG (mg/dL)	<150	<150
HDL (mg/dL)	>50	*
Non HDL (mg/dL)	<130	<130

1. American Diabetes Association. *Diabetes Care*. 2010;33 (suppl 1) pgS12-S61
2. American Association of Clinical Endocrinologists Diabetes Guidelines. *Endocr Pract*. 2002;8(suppl 1):41-65.
3. The JNC 7 Report. *JAMA*. 2003;289(19):2560-2572.
4. NCEP ATP III Executive Summary. *JAMA*. 2001;285(19):2486-2497.

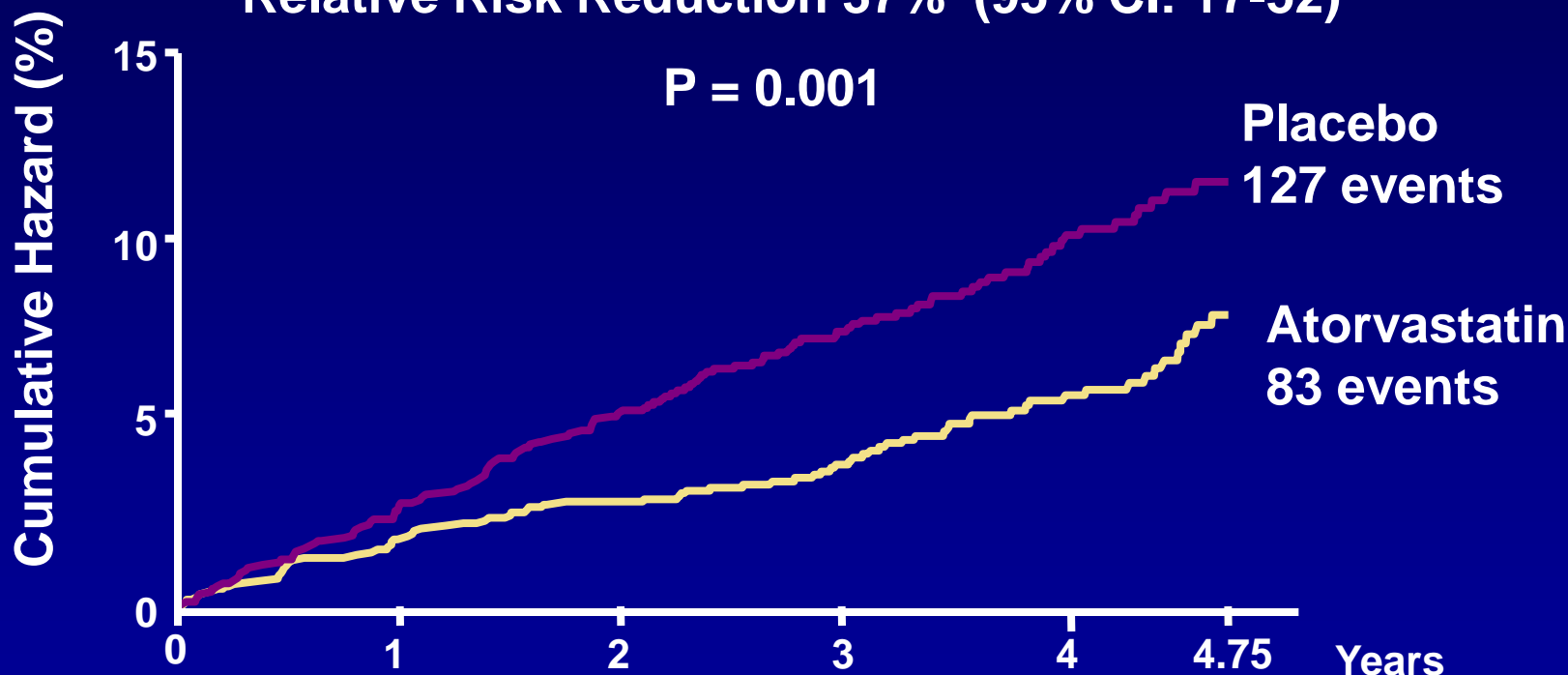
# HPS Substudy: First Major Vascular Event by LDL-C and Prior Diabetes Status



# CARDS: Primary Endpoint

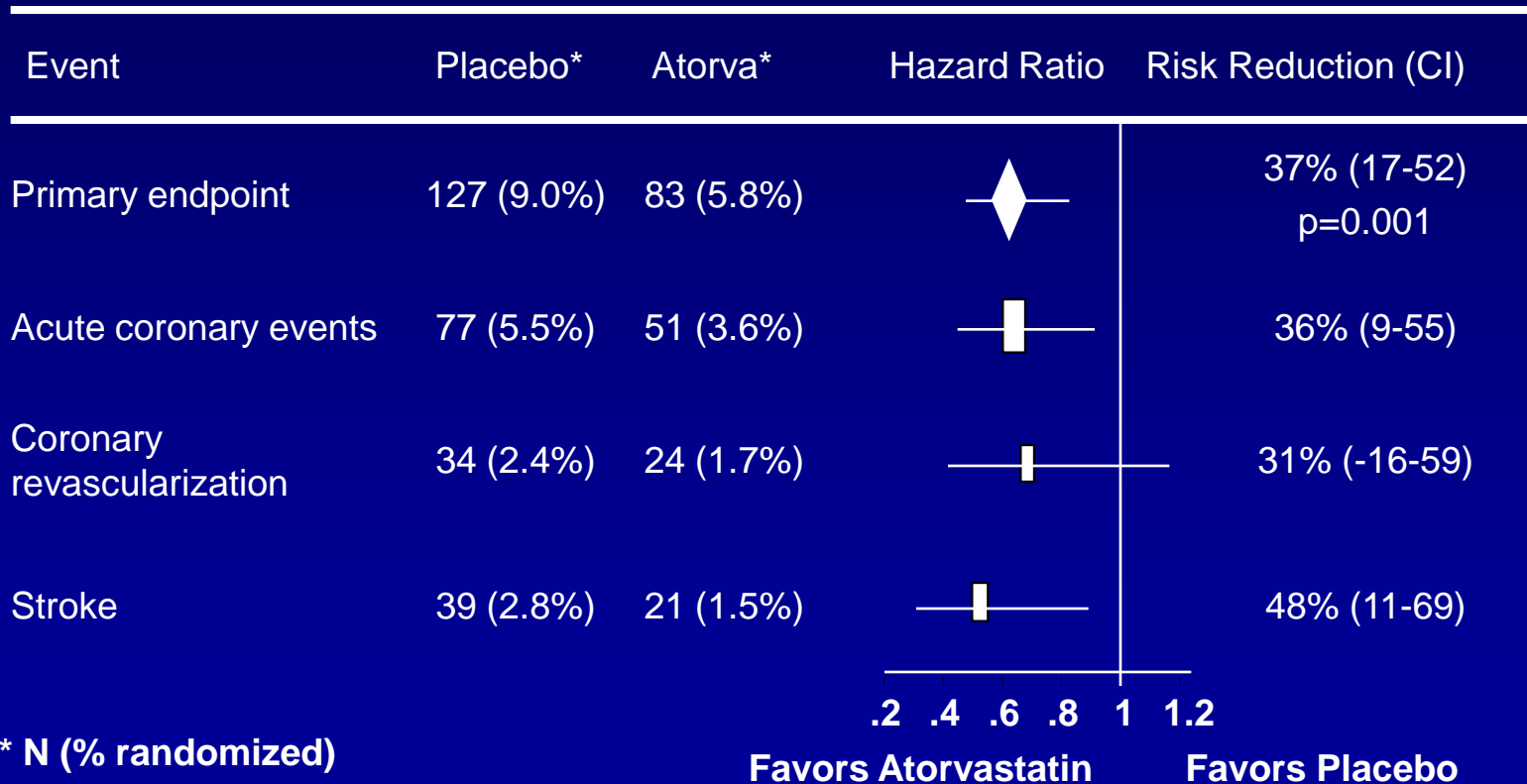
Relative Risk Reduction 37% (95% CI: 17-52)

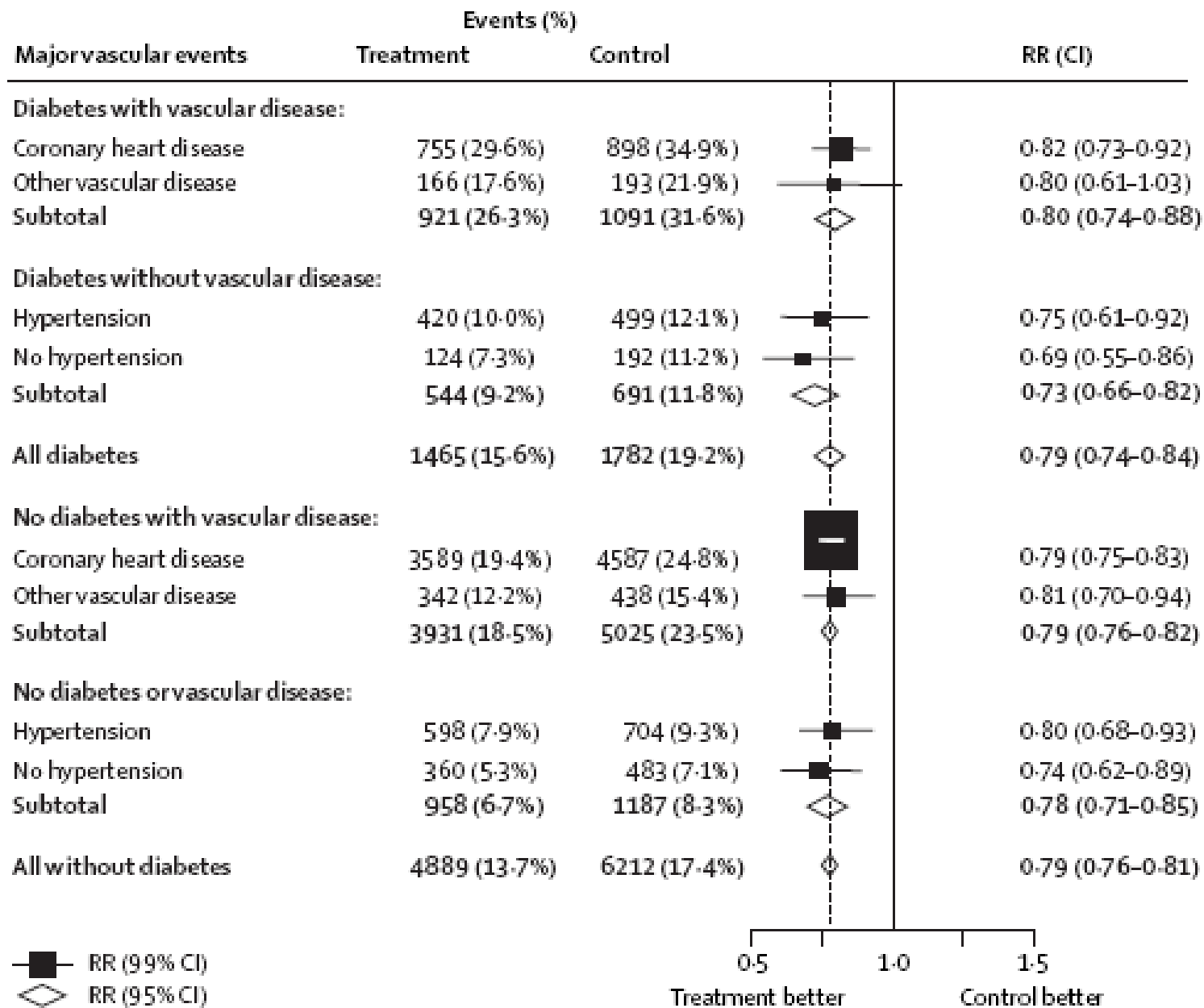
P = 0.001



Placebo	1410	1351	1306	1022	651	305
Atorva	1428	1392	1361	1074	694	328

# CARDS: Treatment Effect on the Primary Endpoint





# Reducing CVD Risk with Statin Therapy in Patients with Diabetes

- Number needed to treat to prevent 1 major CVD event
  - From meta-analysis
    - Without vascular disease 39
    - With vascular disease 19

# ADA 2010 Guidelines

- *Statin therapy should be added to lifestyle therapy, regardless of baseline lipid levels, for diabetic patients:*
  - *With overt CAD*
  - *Without CVD >40 and have  $\geq 1$  CVD risk factor*

# Specific Dyslipidemias: Elevated Triglycerides

## Non-HDL: Secondary Target

- $\text{Non-HDL} = \text{TC} - \text{HDL}$
- Non-HDL: secondary target of therapy when serum triglycerides are  $\geq 200$  mg/dL (esp. 200-499 mg/dl)
- Non-HDL goal: LDL goal + 30 mg/dL

# Specific Dyslipidemias: Low HDL Cholesterol

## Management of Low HDL

- LDL is primary target of therapy
- Weight reduction and increased physical activity (if the metabolic syndrome is present)
- Non-HDL is secondary target of therapy (if triglycerides  $\geq 200$  mg/dL)
- Consider nicotinic acid or fibrates (for patients with CHD or CHD risk equivalents)

# Summary of Care: ABC's for Providers

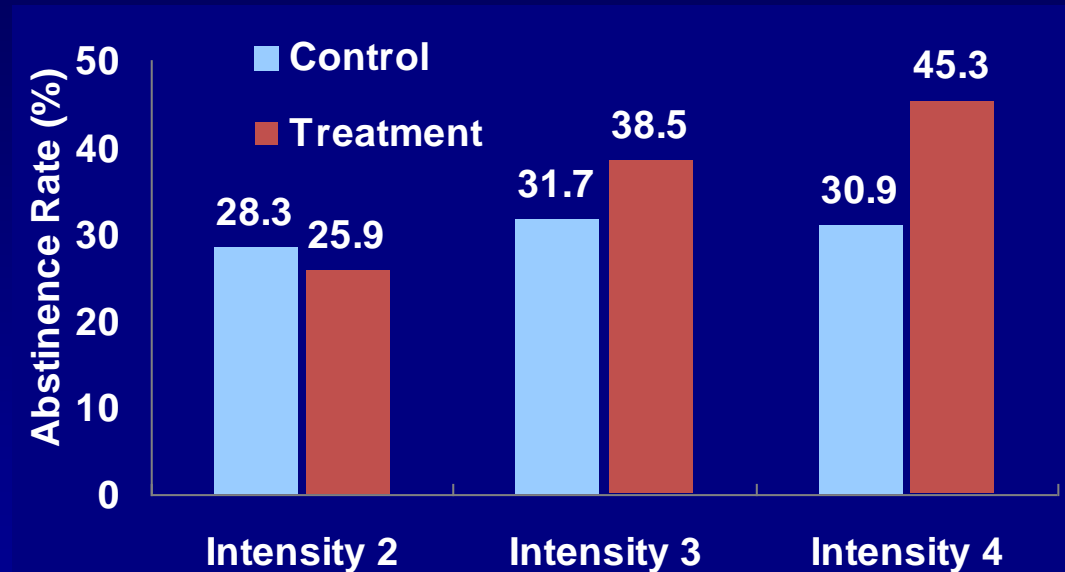


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# Effectiveness of Smoking Cessation Interventions for CVD Admissions

- Smoking cessation intervention
  - MI = “teachable moment”
  - JCAHO/CMS core measure for MI care
- Meta-analysis of 18 RCTs in CVD, by intensity of intervention
- Only extended support programs significantly improved abstinence



Summary OR	1.14	1.07	1.81
95% CI	0.9-1.4	0.7-1.6	1.5-2.2

# The 5 “A’s” for Effective Smoking Intervention

1. **ASK** about smoking
2. **ADVISE** to quit
3. **ASSESS** willingness to make a quit attempt
4. **ASSIST** if ready - offer therapy and consultation for quit plan and if not, then offer help when ready
5. **ARRANGE** follow up visits

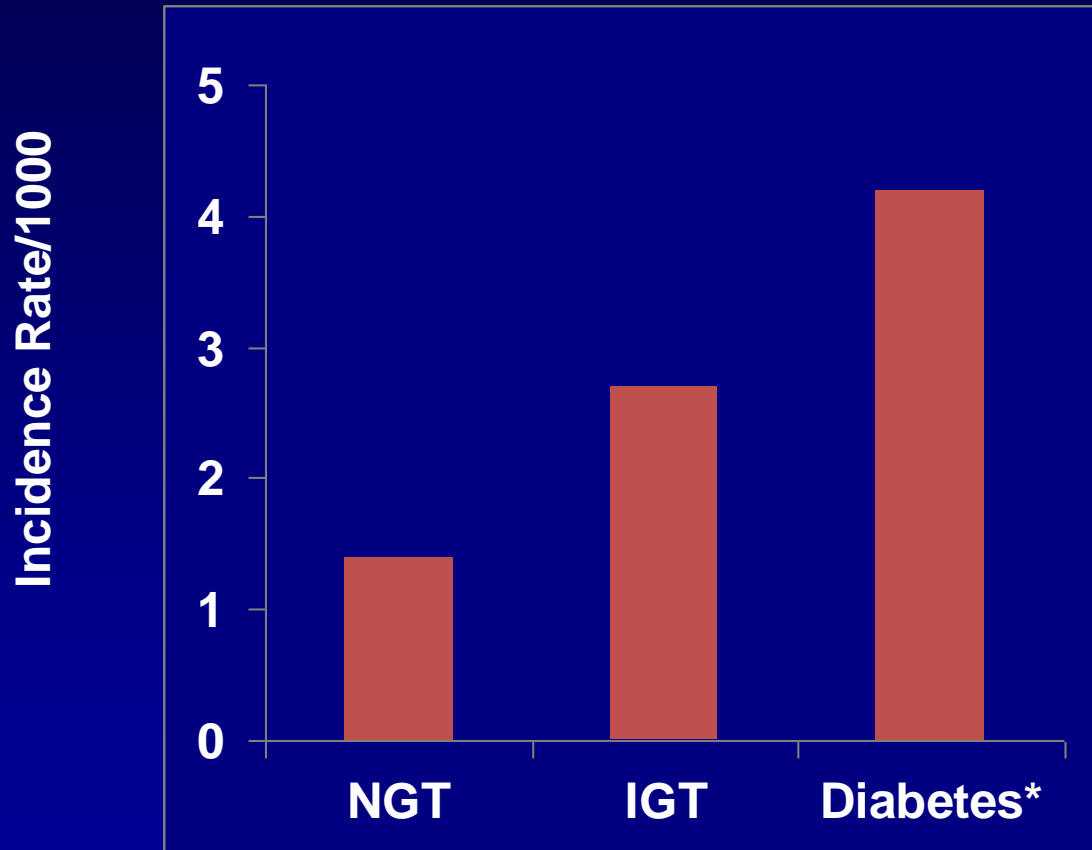
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# CHD Mortality Rates (by Degree of Glucose Tolerance)

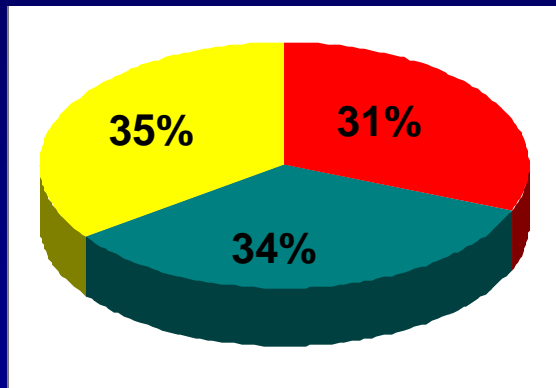


\*Indicates patients known to have diabetes prior to the study.

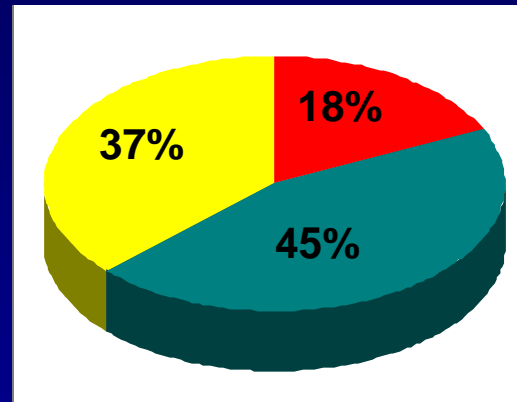
CHD=coronary heart disease; NGT=normal glucose tolerance; IGT=impaired glucose tolerance

# Most Cardiovascular Patients Have Abnormal Glucose Metabolism

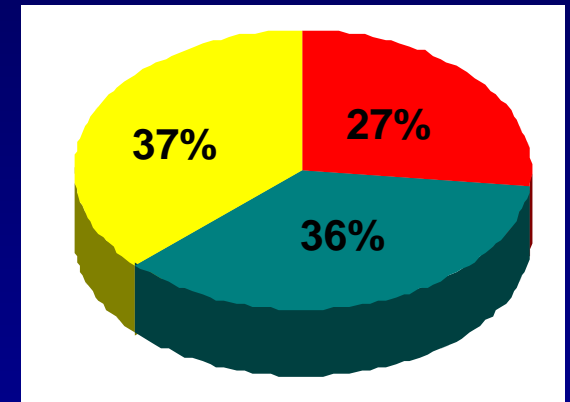
GAMI  
n = 164



EHS  
n = 1920



CHS  
n = 2263



- Normoglycemia
- Prediabetes
- Type 2 Diabetes

**GAMI = Glucose Tolerance in Patients with Acute Myocardial Infarction Study**

**EHS = Euro Heart Survey**

**CHS = China Heart Survey**

# Diagnostic Criteria for Metabolic Syndrome: Modified NCEP ATP III

≥3 Components Required for Diagnosis

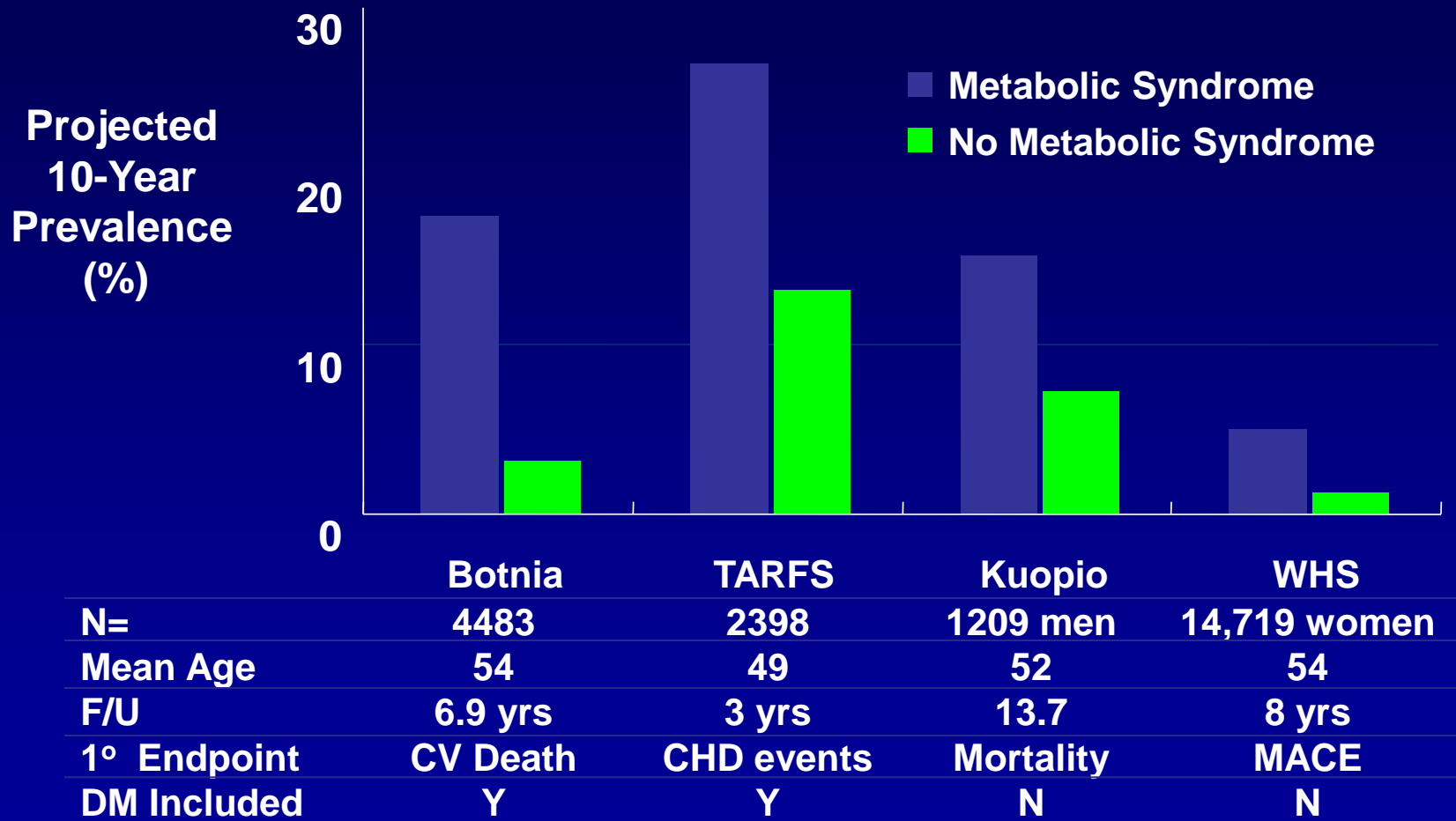
Components	Defining Level
Increased waist circumference Men Women	≥ 40 in ≥ 35 in
Elevated triglycerides	≥150 mg/dL (or Medical Rx)
Reduced HDL-C Men Women	<40 mg/dL <50 mg/dL (or Medical Rx)
Elevated blood pressure	≥130 / ≥85 mm Hg (or Medical Rx)
Elevated fasting glucose	≥100 mg/dL (or Medical Rx)

# IDF Criteria: Abdominal Obesity and Waist Circumference Thresholds

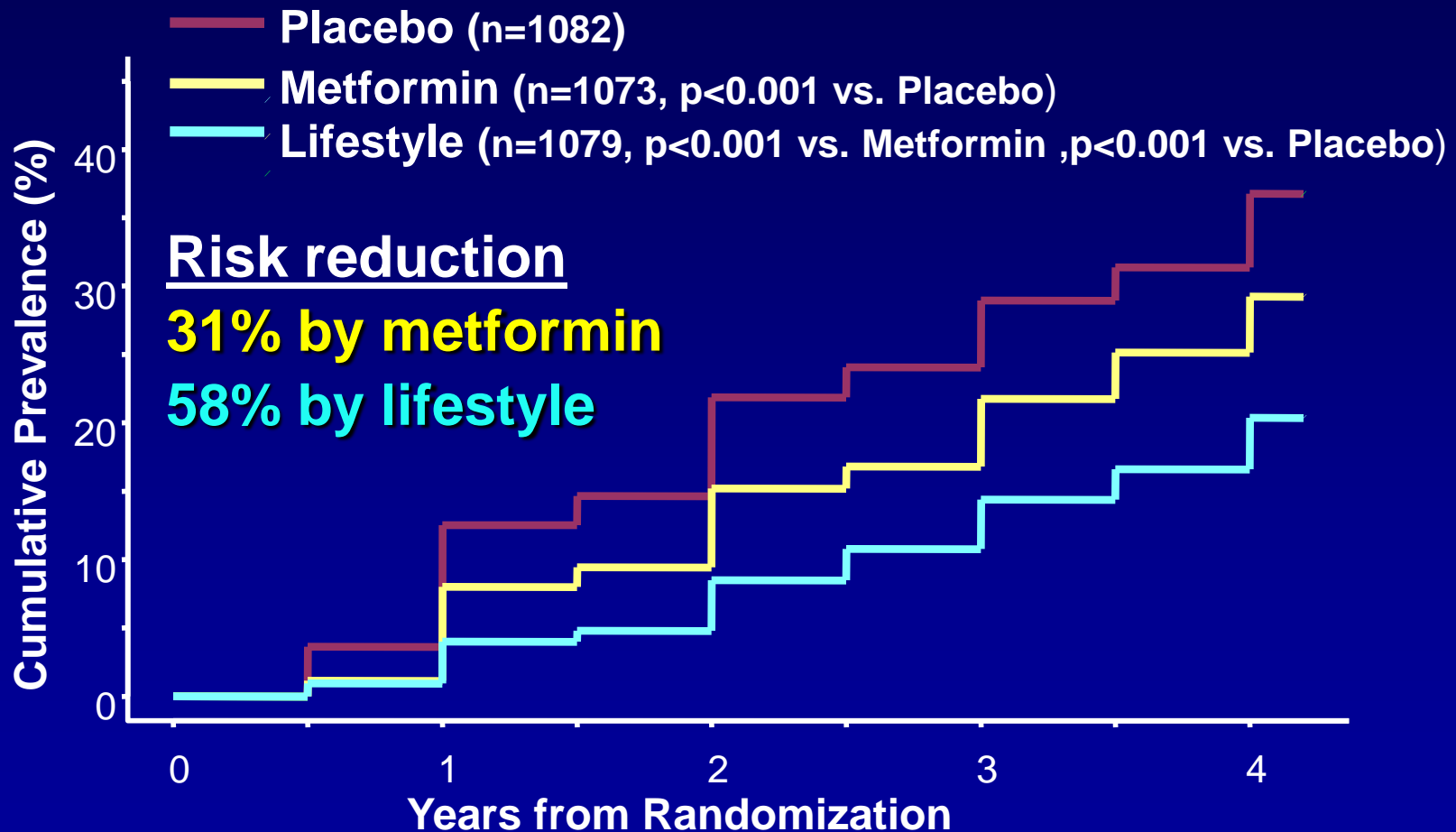
	Men	Women
Europid	≥ 94 cm (37.0 in)	≥ 80 cm (31.5 in)
South Asian	≥ 90 cm (35.4 in)	≥ 80 cm (31.5 in)
Chinese	≥ 90 cm (35.4 in)	≥ 80 cm (31.5 in)
Japanese	≥ 85 cm (33.5 in)	≥ 90 cm (35.4 in)

- AHA/NHLBI criteria: ≥ 102 cm (40 in) in men, ≥ 88 cm (35 in) in women
- Some US adults of non-Asian origin with marginal increases should benefit from lifestyle changes. Lower cutpoints (≥ 90 cm in men and ≥ 80 cm in women) for Asian Americans

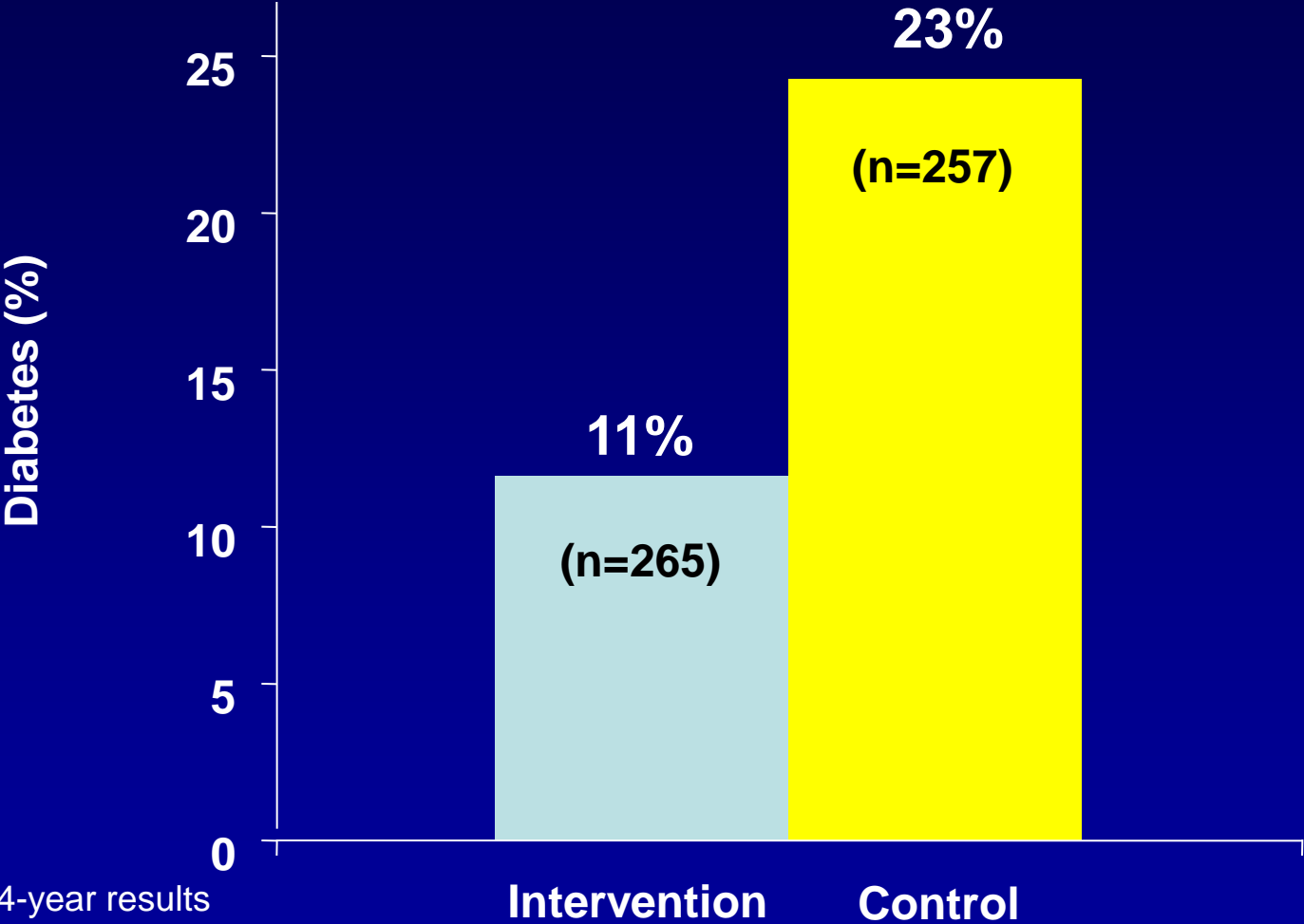
# 10-Year CVD Risk Estimates Associated with Metabolic Syndrome



# Management Opportunity: Prevent Diabetes



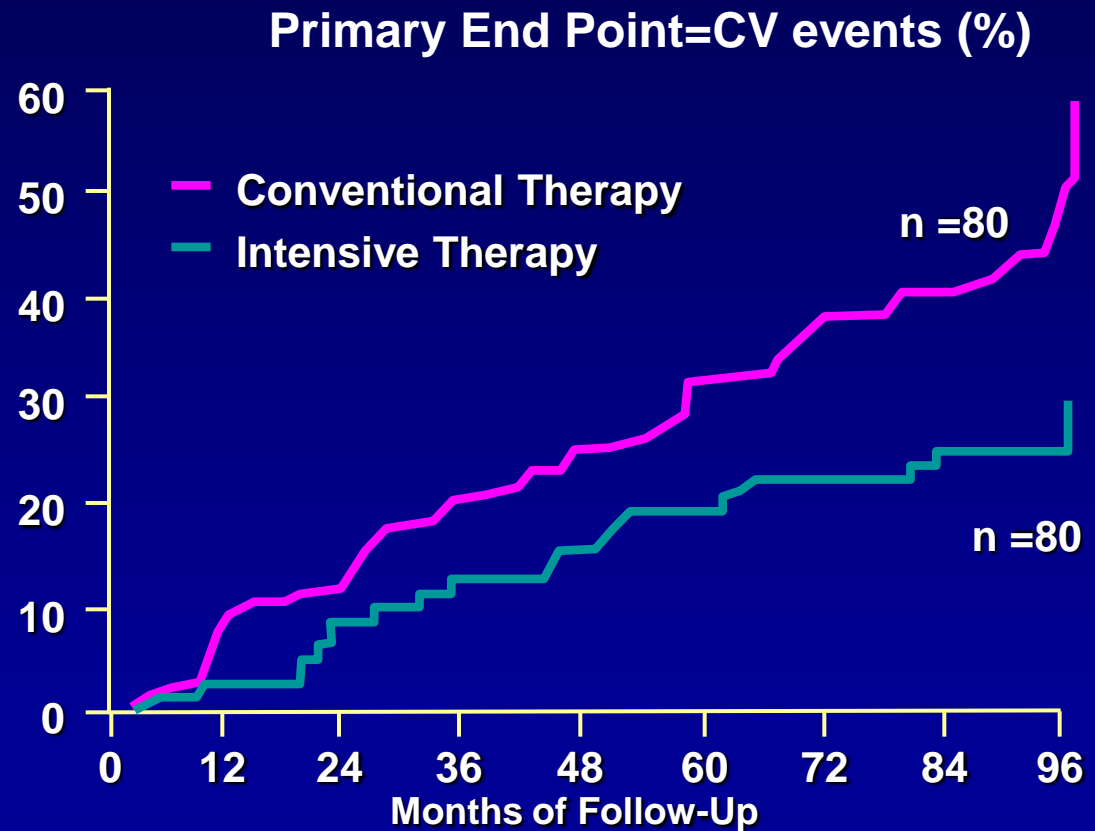
# Finnish Diabetes Prevention Study: Reduction in Risk for Diabetes\*



\* $P < 0.001$ ; 4-year results

# Benefit of Comprehensive, Intensive Management: STENO 2 Study

- Treatment Goals:
  - Intensive TLC
  - HgbA1c <6.5%
  - Cholesterol <175
  - Triglycerides <150
  - BP <130/80



# Summary of Care: ABC's for Providers



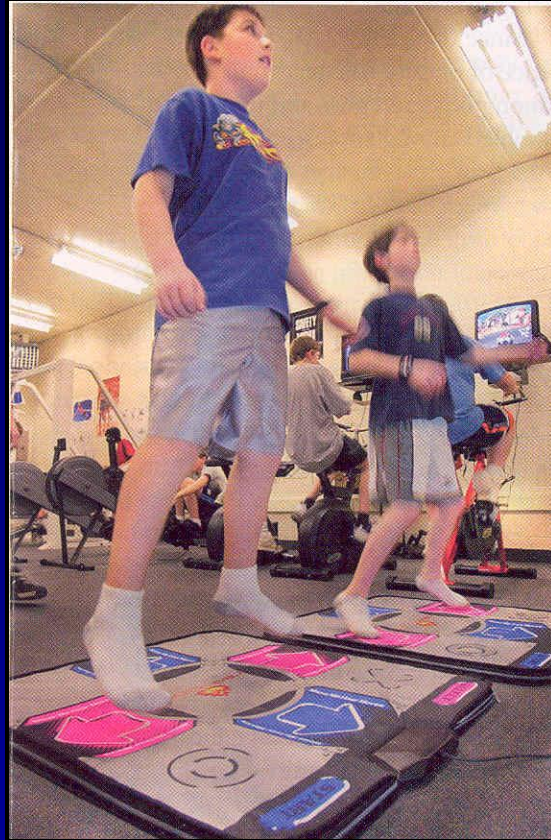
Convergence of Diabetes &  
Cardiovascular Disease

<b>A</b>	<b>A1c Target Aspirin Daily</b>
<b>B</b>	<b>Blood Pressure Control</b>
<b>C</b>	<b>Cholesterol Management Cigarette Smoking Cessation</b>
<b>D</b>	<b>Diabetes and Pre-Diabetes Management</b>
<b>E</b>	<b>Exercise</b>
<b>F</b>	<b>Food Choices</b>

# Physical Inactivity: A Call to Arms



10,000 Steps Daily



30 minutes most days

# Take an Exercise History and Encourage Increased Physical Activity

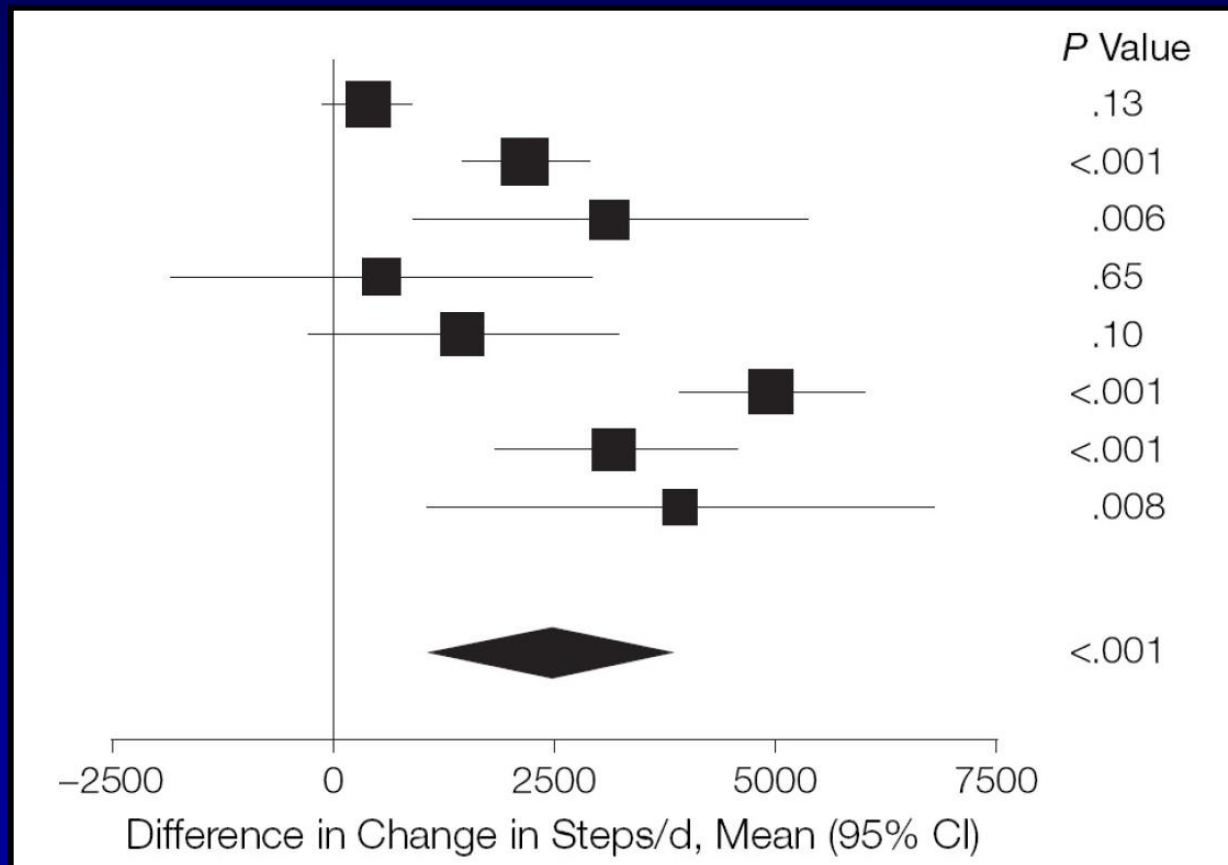
- Brisk walking is an ideal physical activity for those without orthopedic issues
- Walking uses the patient's increased body weight to increase energy expenditure
- Pedometers provide daily feedback - 10,000 Steps Per Day



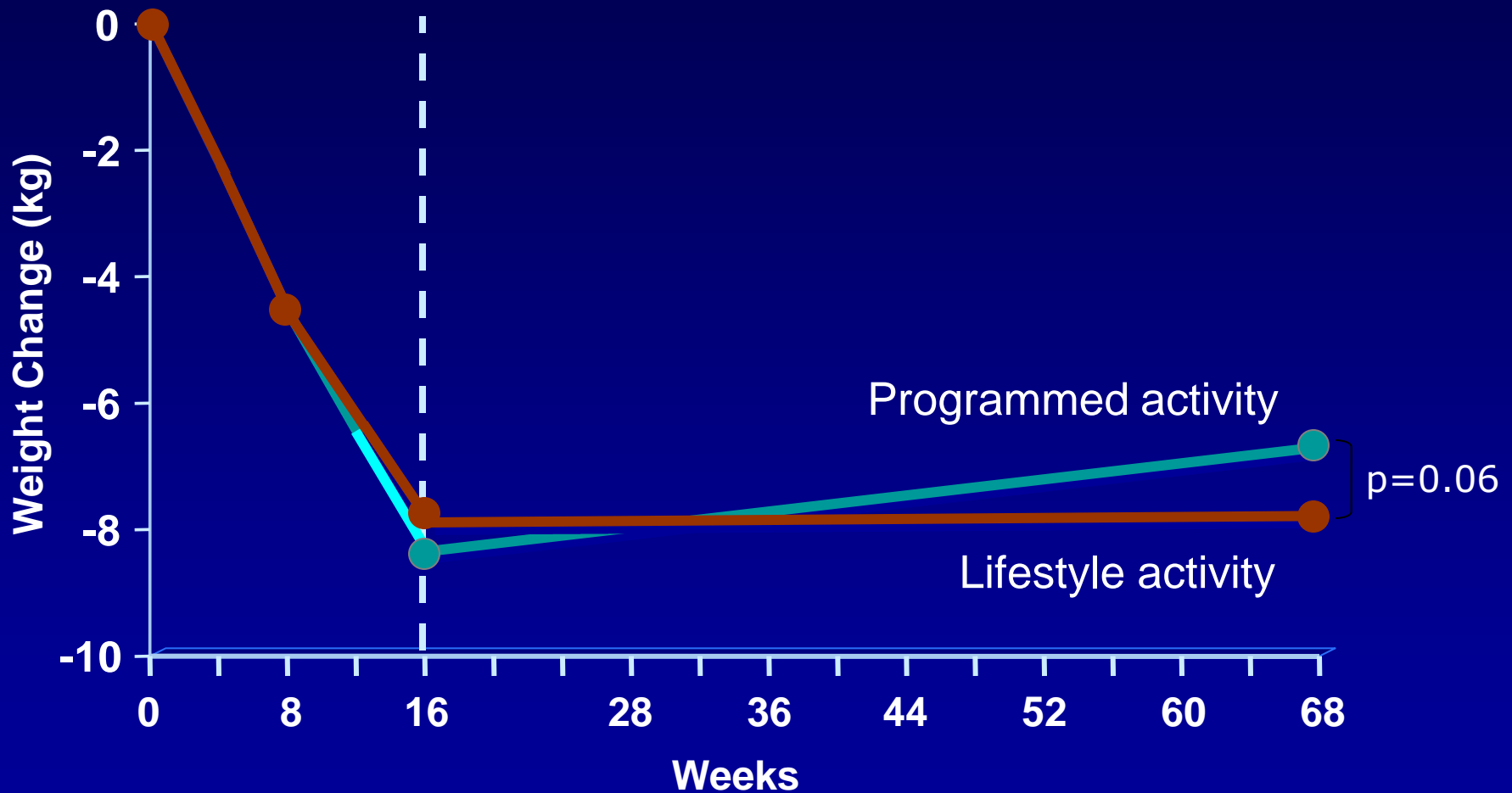
# RCT Trial Assessment of Pedometer Interventions

N=277; 8 Trials

Pedometer increased steps by 2500/day



# Lifestyle Activity as an Alternative to "Working Out"



# National Weight Control Registry

- Successful Losers: >10% Body weight for 1 year
- 3000 Registrants, 80% Women
- Average Loss = 30 kg; Time = 5.5 yrs
- How?
  - ~Low Fat Diet
  - ~Self-monitoring
  - ~Physical Activity
- 81% Reported More Physical Activity

# Physical Activity Recommendations



Mode of exercise	Frequency	Intensity	Duration	Class and level
Cardio-respiratory (large muscle)	3-7 d/week	Moderate intensity OR	150 min/week	1 (A)
Cardio-respiratory (large muscle)	3 d/week	Vigorous Intensity	90 min/week	1 (A)
Resistance	3 d/week	2-4 sets of 8-10 reps		1 (A)

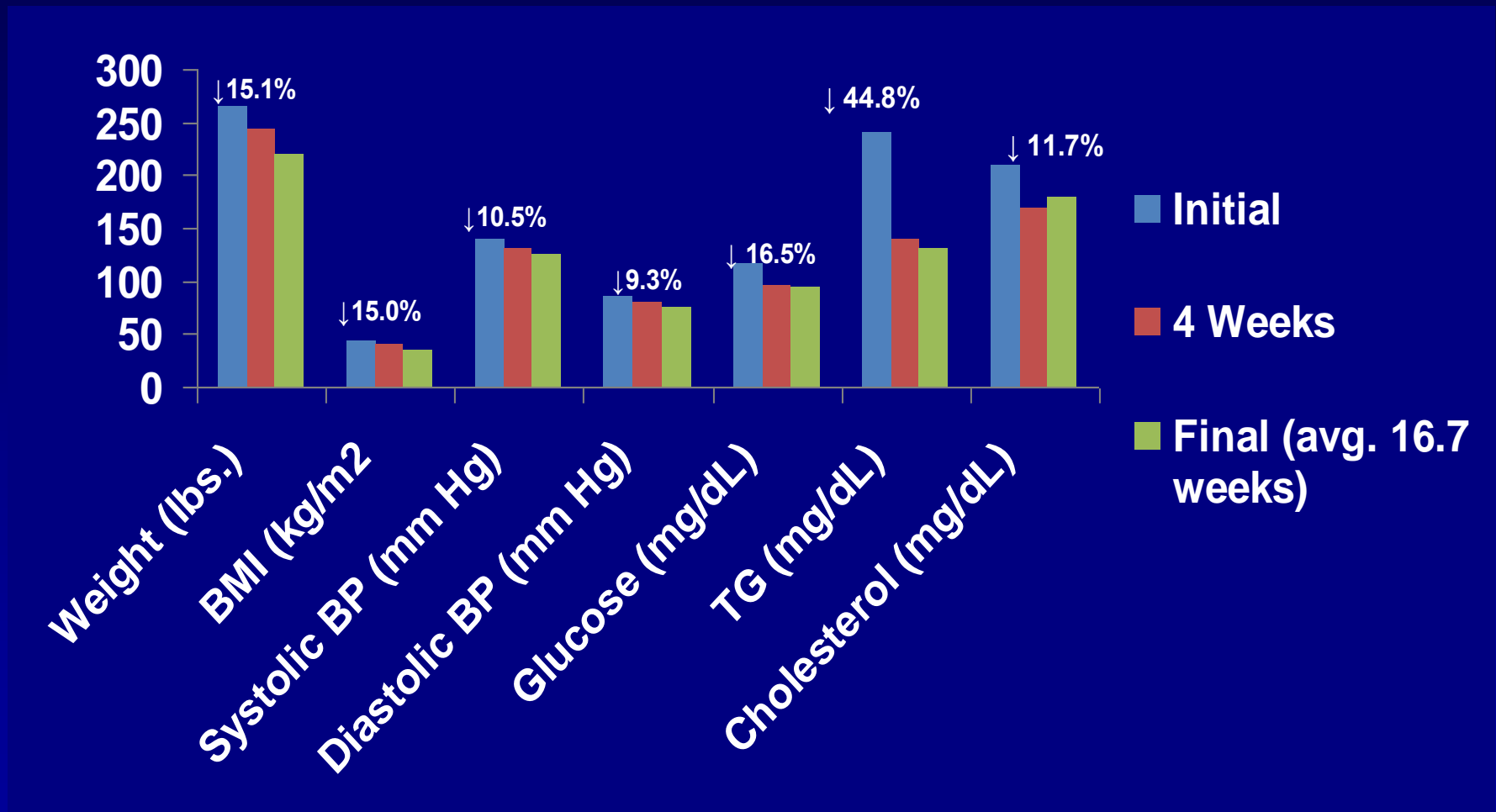
# Summary of Care: ABC's for Providers



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<b>F</b>	<b>Food Choices</b>

# Effect of Moderate Weight Loss On Cardiometabolic Risk Factors



Percent changes are initial visit to final visit.

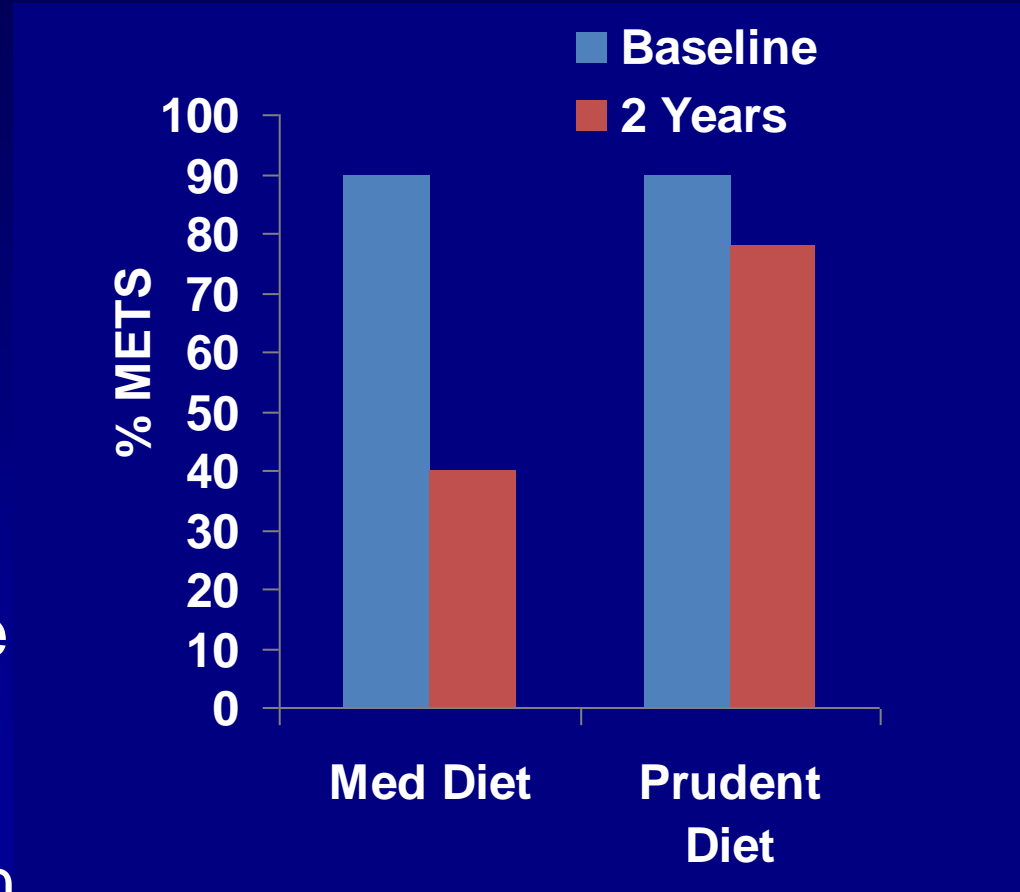
# ADA Nutritional Guidelines

- Patients with pre-diabetes should receive individualized Medical Nutrition Therapy (MNT)
- Weight loss recommended for all overweight or obese individuals who have or are at risk for diabetes
- Physical activity and behavior modification effective for weight loss and maintenance
- Fiber 14 g/1000 kcal intake
- Saturated fat 7% with minimal trans fat



# Effect of Mediterranean-Style Diet in the Metabolic Syndrome

- 180 pts with metabolic syndrome randomized to Mediterranean-style vs. prudent diet for 2 years
- Those in intervention group lost more weight (-4kg) than those in the control group (+0.6kg) ( $p < 0.01$ ), and significant reductions in CRP and IL-6



# Patient Education

- Educational Objectives
  - Ensure patients realize the link between metabolic syndrome and risk of heart disease
  - Reinforce the patient's role and control in disease management
    - Focus on significant impact even modest exercise and weight loss will have
  - Verify patients understand how to implement healthy changes to diet and physical activity level



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