

# **The ideal management of diabetic dyslipidemia**

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# Asia-Pacific is in jeopardy



Ageing

Cardio- and Cerebrovascular diseases

Diabetes and Metabolic syndrome

# Type 2 Diabetes prevalence is projected to reach 150 Million by 2025 in Asia

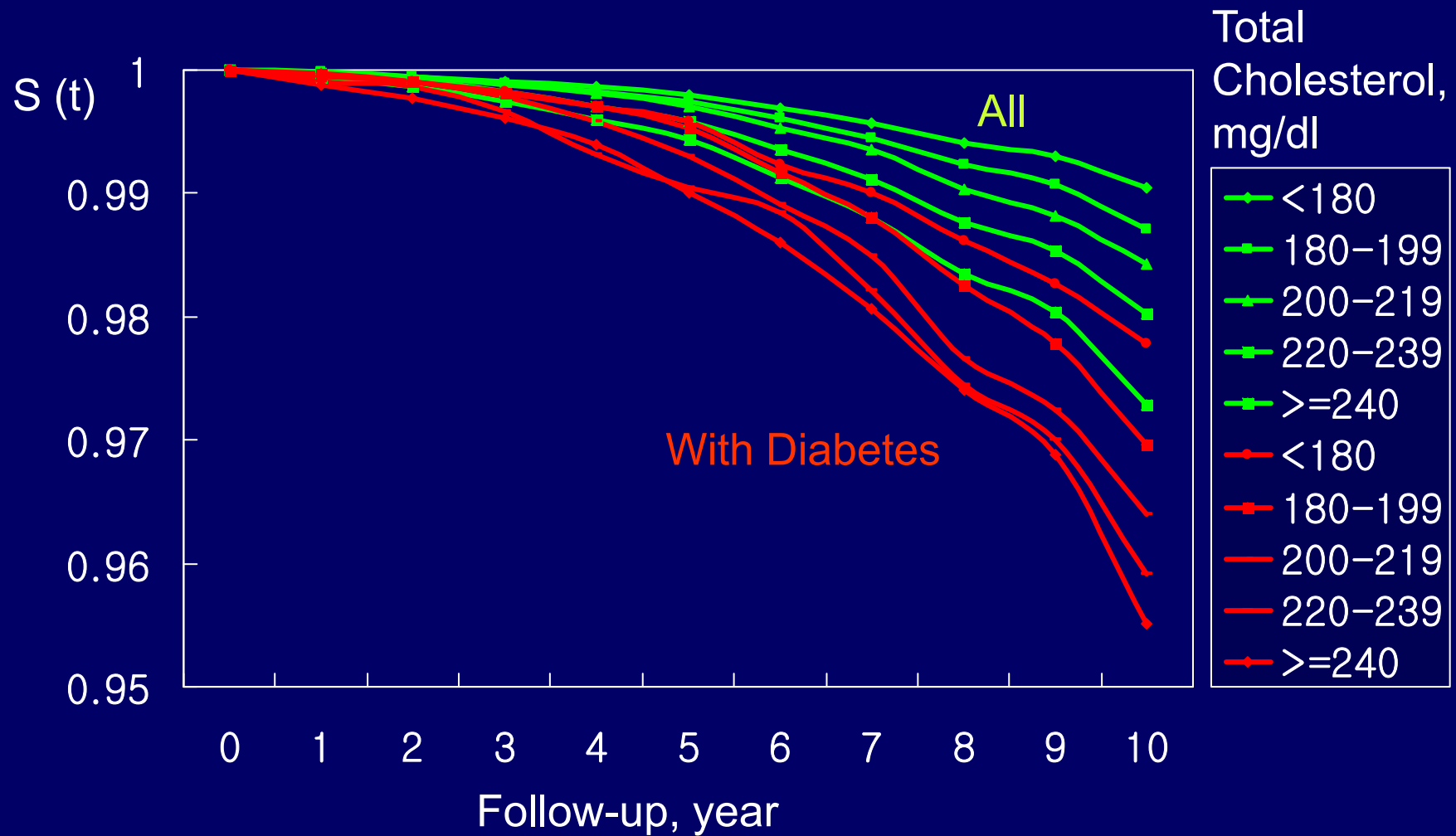
- About 33 million adults diagnosed with diabetes in China and OAI\* in 2000
  - 17 million women and 16 million men
- Between 1995 and 2025, the prevalence of diabetes in adults will increase by 68% in China and 41% in OAI and the number of people with diabetes will increase by 134% in China and over 150% in OAI



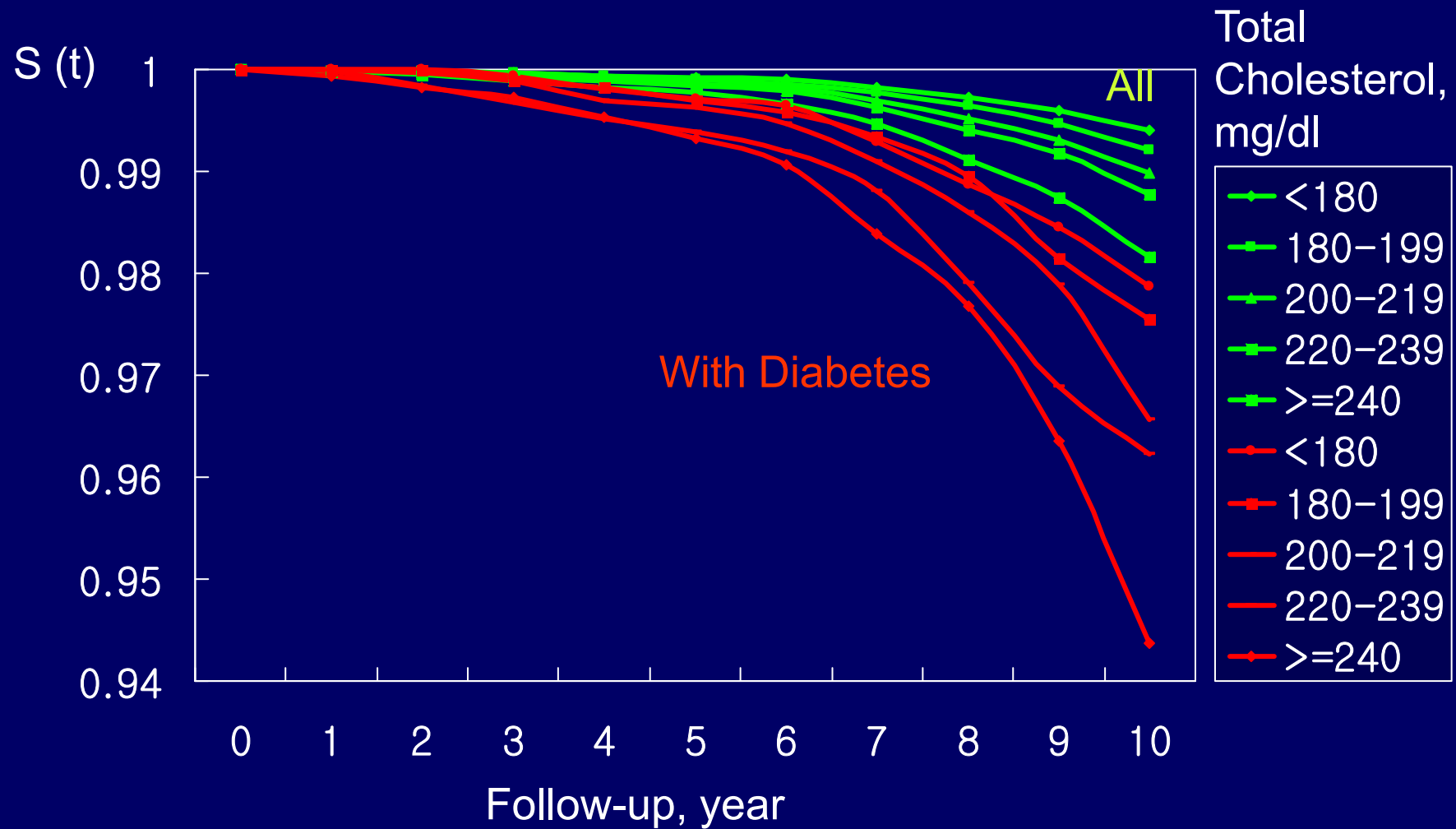
Subjects Aged  $\geq 20$  years  
Based on the UN Population Data

\* Other Asia and islands, not including Japan and India

# Survival Curve of IHD in Korean Men



# Survival Curve of IHD in Korean Women



# The comparison of metabolic syndrome and major risk factors described in NCEP-III

## IDF criteria of the metabolic syndrome

- High waist circumference

*Plus any two of*

- ↑ Triglycerides  $\geq 150$  ‡
- ↓ HDL cholesterol
  - Men  $< 40$  ‡
  - Women  $< 50$  ‡
- ↑ Blood pressure  $\geq 130/85$  ‡
- ↑ FPG  $\geq 100$  ‡

## NCEPIII criteria of the Risk factors

- NA (mg/dl)
- $< 40$  (mg/dl)
- $\geq 140/90$  ‡ (mmHg)
- Diabetes (mg/dl)

‡; specific treatment for these conditions

*International Diabetes Federation (2005)*

# Prevalence of Metabolic Syndrome in Korea

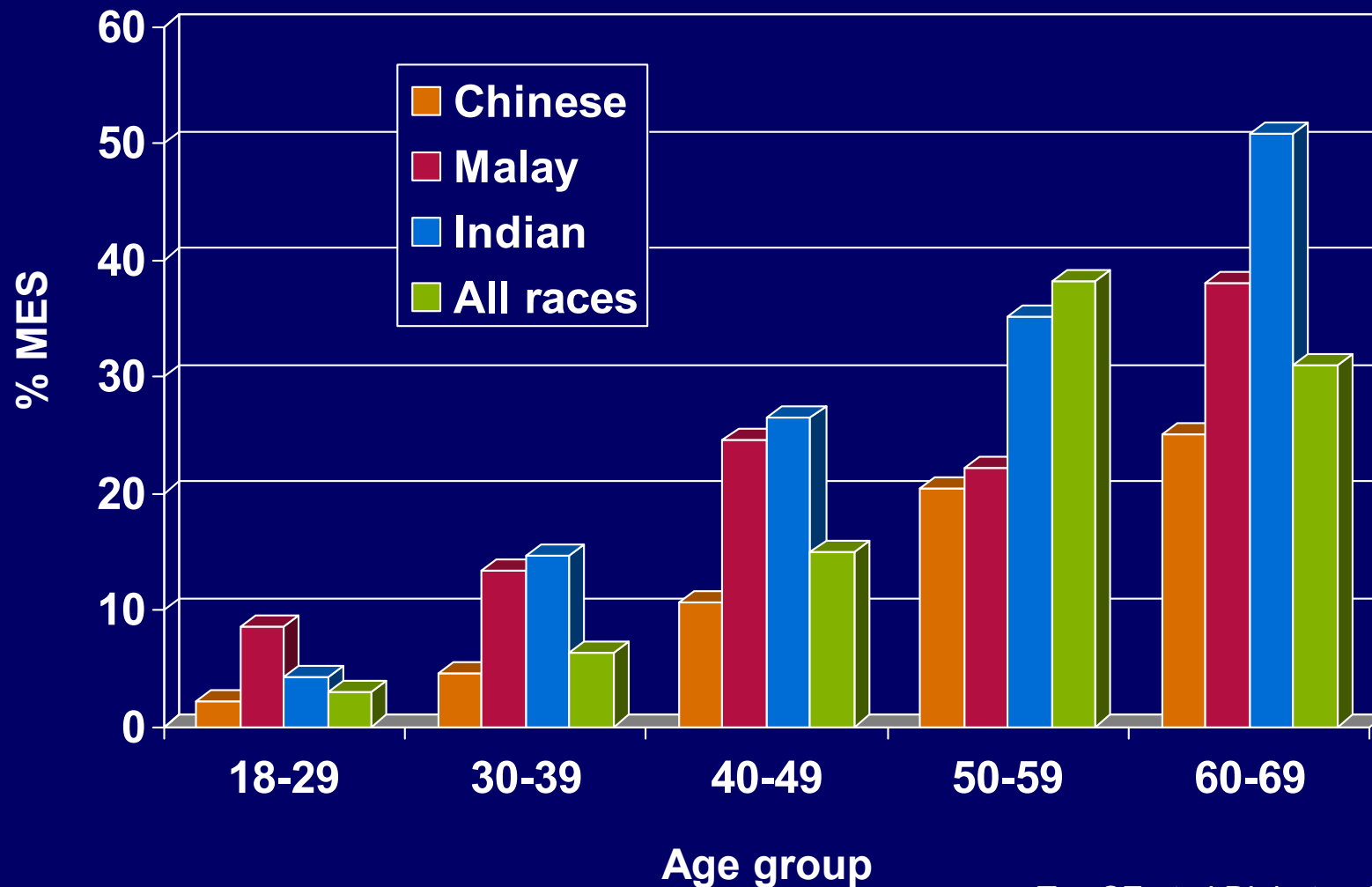
## ATP-III

- 1998 ; **16.0 %**
  - male : 14.2%, female : 17.7%
- 2000 ; **19.90 %**
  - male : 17.3%, female : 22.1%
- 2004 ; **19.48 %**
  - male : 18.6%, female : 20.1%

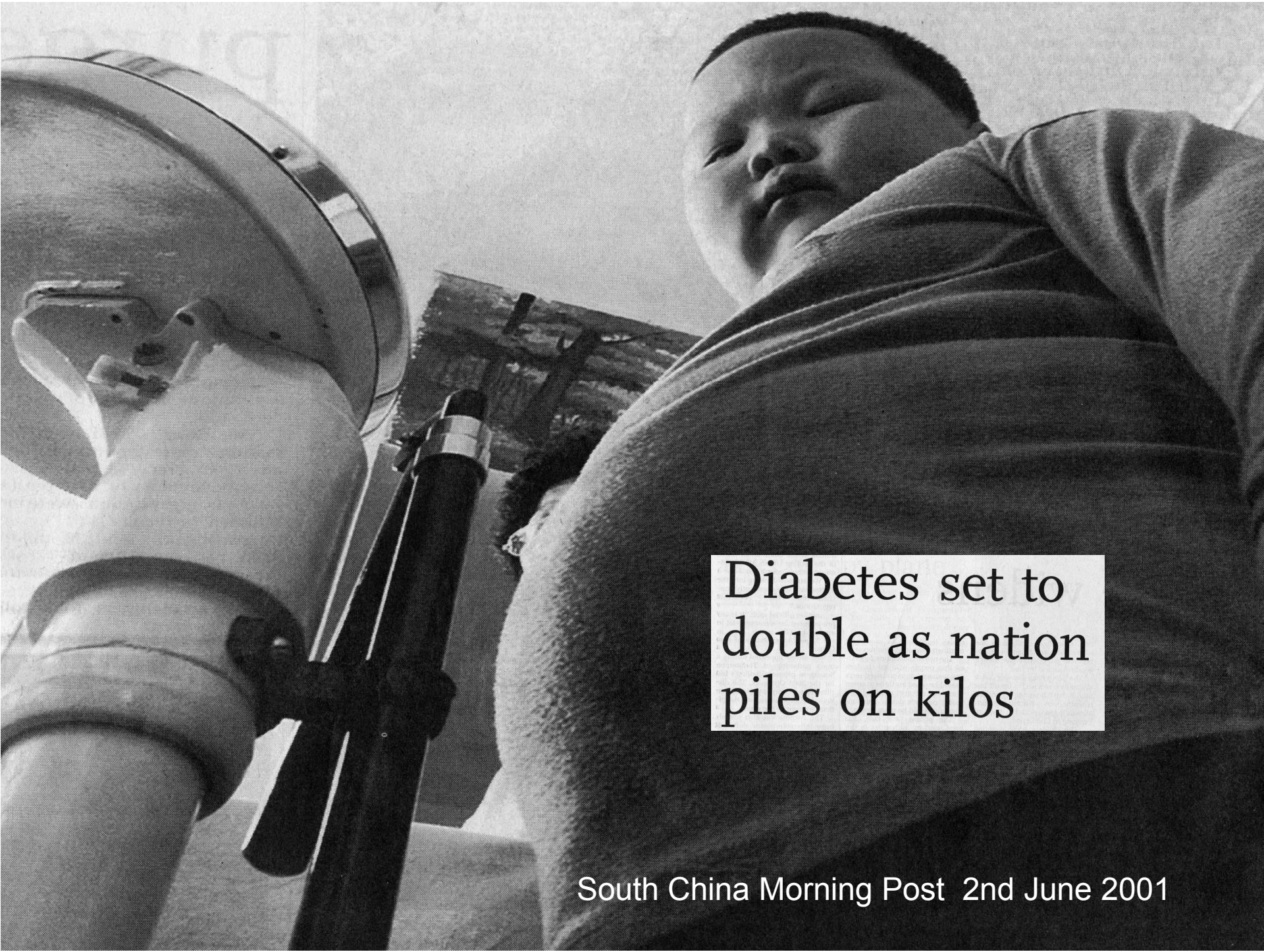
## IDF definition

- (defined by central obesity (waist circumference 90 cm for men and 85 cm for women))
- 1998;
  - male : **13.5 %**
  - female : **15.0 %**

## Metabolic Syndrome (Asian guideline) in Singapore (Relationship with Age)







Diabetes set to  
double as nation  
piles on kilos

South China Morning Post 2nd June 2001

## **Prevalence of Metabolic Syndrome in Korean Teen Age Group (12-19 years)**

- **1998 (n=1317) ; 6.8 % (boys; 6.6 % girls; 6.9 %)**
- **2001 (n=848) ; 9.2 % (boys; 12.5 %, girls; 5.8%)**

Diagnostic criteria by Cook et al.

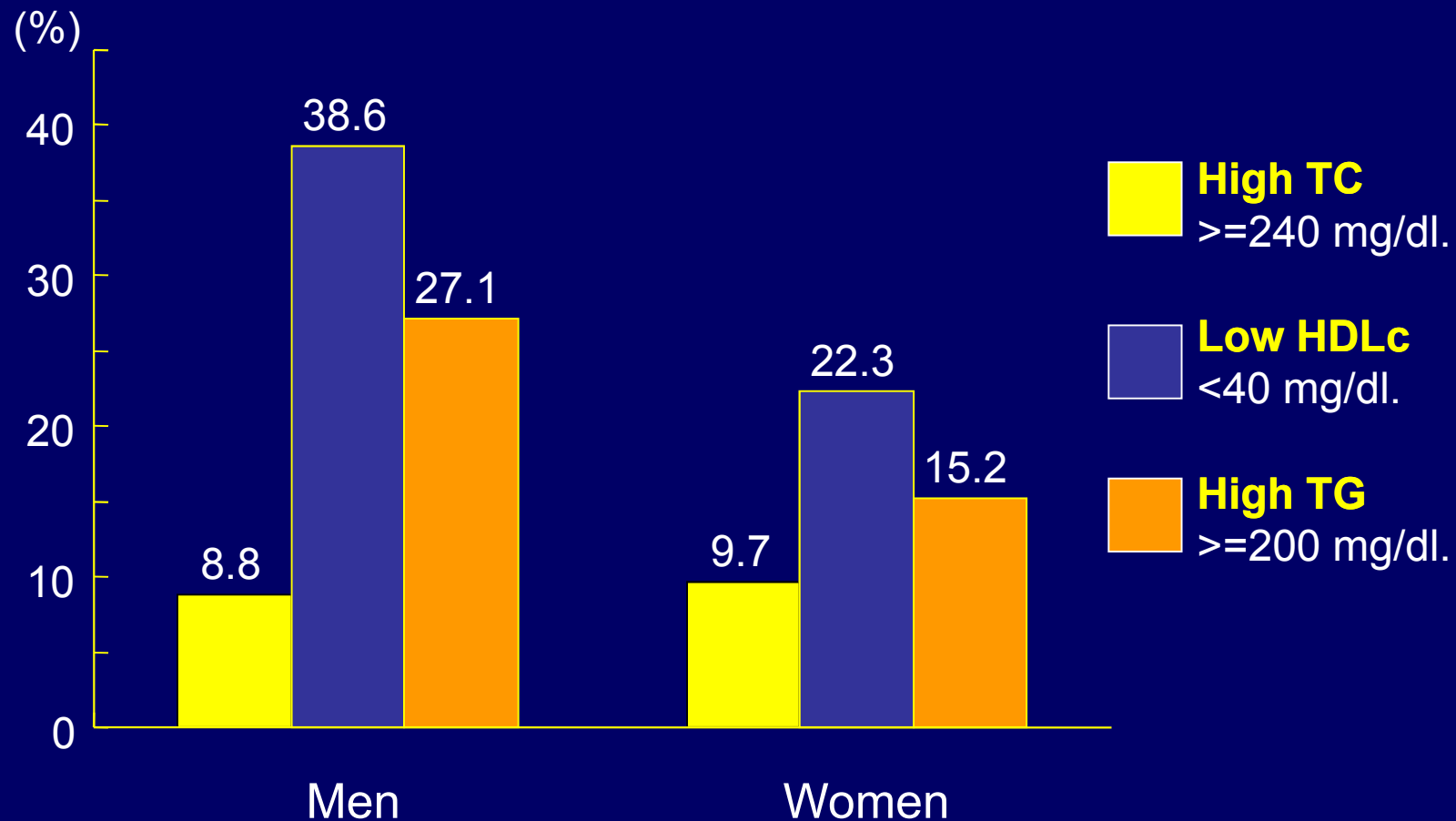
Subjects who had at least three of the following five risk factors

- (1) abdominal obesity (waist circumstamces  $\geq$  90<sup>th</sup> percentile)
- (2) elevated blood pressure ( $\geq$  90th percentile)
- (3) high triglyceride  $\geq$  1.24 mmol/L (110 mg/dL),
- (4) low HDLc  $\leq$  1.03 mmol/L (40 mg/dL)
- (5) high fasting glucose  $\geq$  6.1 mmol/L (110 mg/dL).

Diabetes Research and Clinical Practice , Volume 75 , Issue 1 , Pages 111 - 114

Korean National Health and Nutrition Examination Survey 1998 and 2001

# Dyslipidemia in Diabetics



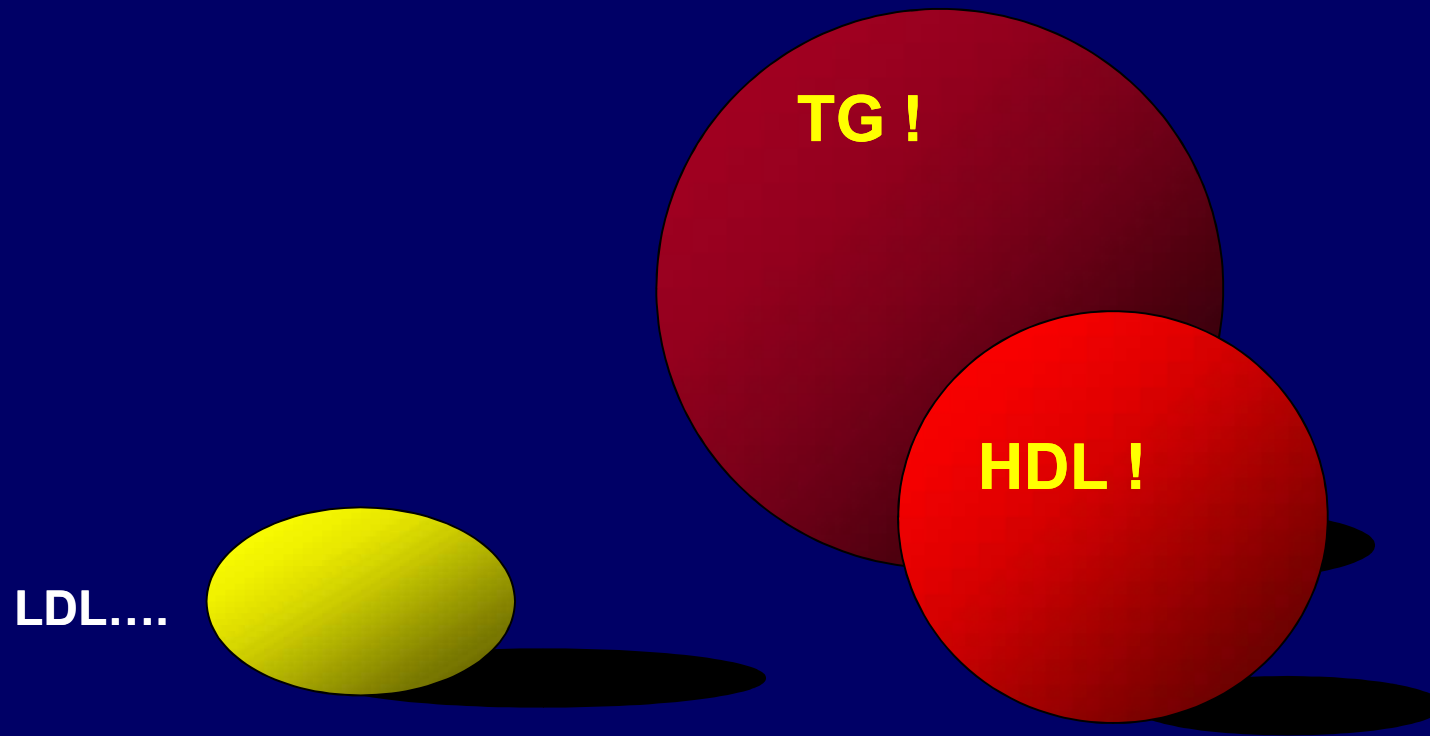
# Dyslipidemia in Diabetes

## *Framingham Heart Study*

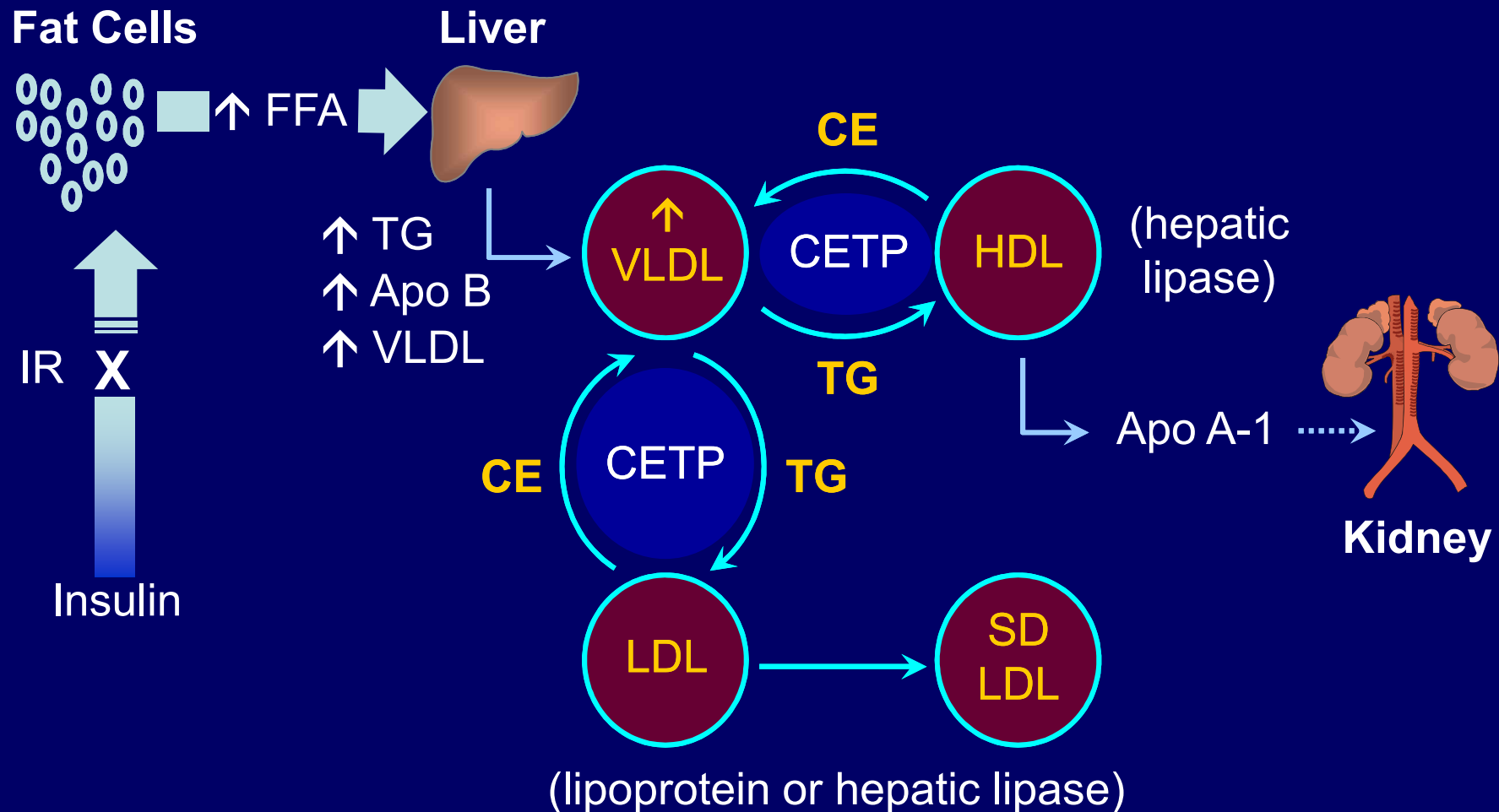
	MEN		WOMEN	
	Normal	DM	Normal	DM
Increased cholesterol	14%	13%	21%	24%
Increased LDLc	11%	9%	16%	15%
Decreased HDLc	12%	21%	10%	25%
Increased triglycerides	9%	19%	8%	17%

Garg A et al. *Diabetes Care* 1990;13:153-169.

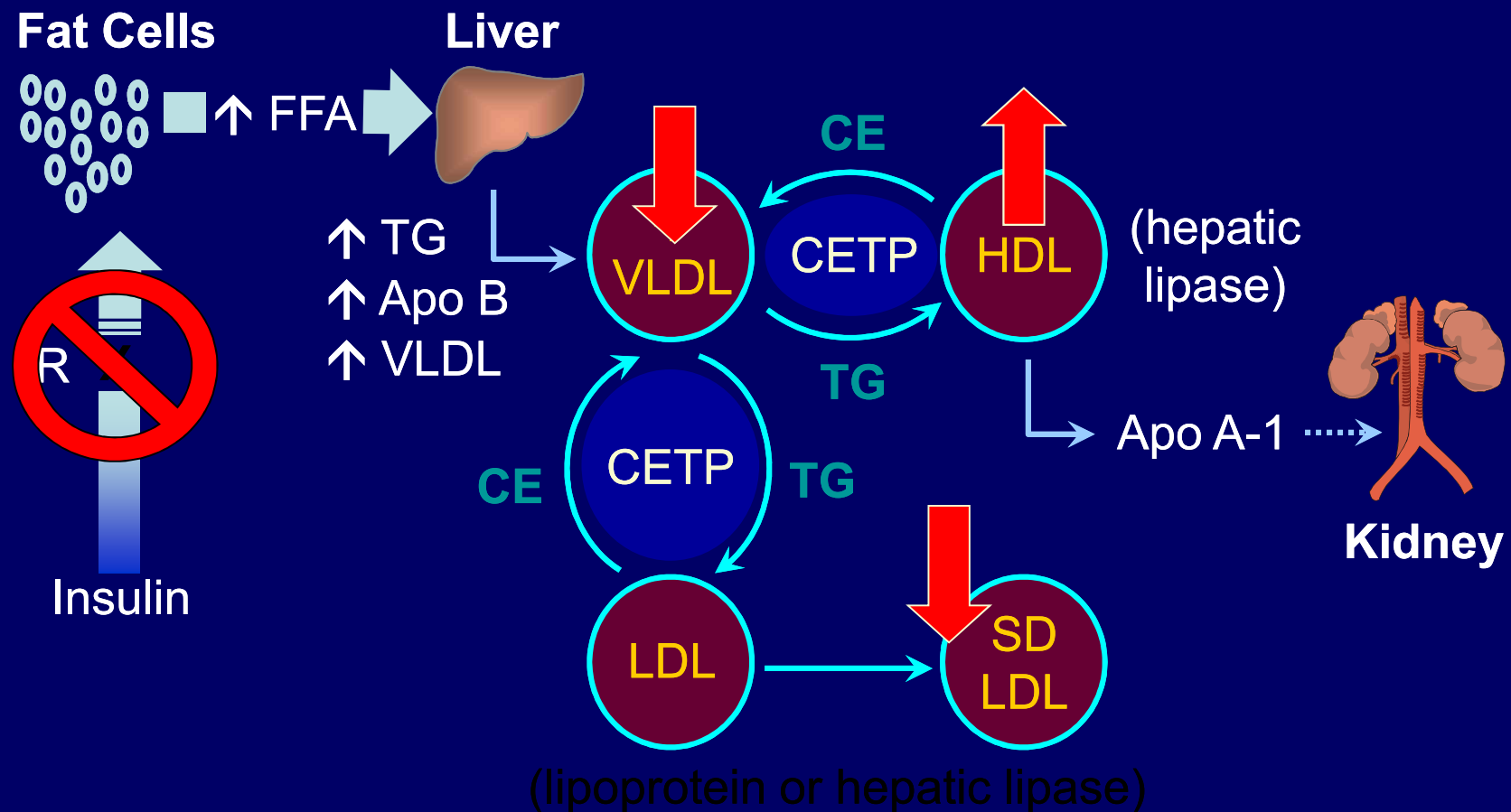
**Is LDL nothing in Diabetic conditions ?**  
**Are TG and HDL more important ?**



# Diabetic Dyslipidemia (High TG and Low HDLc)



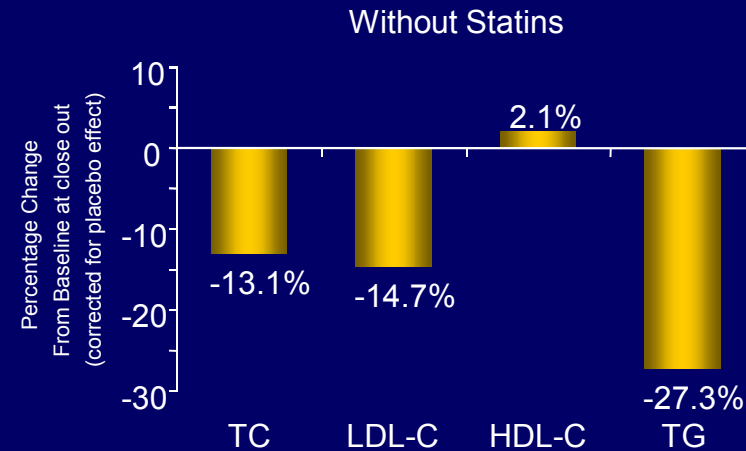
# Fibrates activate PPAR $\alpha$ and may reverse insulin resistance







The Fenofibrate Intervention and Event Lowering in Diabetes (FIELD) Trial



## Fenofibrate Treatment Effect

Relative Risk Reduction (95% CI)

*P*

### CHD Events

Unadjusted

11% (-5 to 25)

0.16

Adjusted for statin use\*

19% (4 to 32)

0.01

### Total CVD Events

Unadjusted

11% (1 to 20)

0.035

Adjusted for statin use\*

15% (5 to 24)

0.004

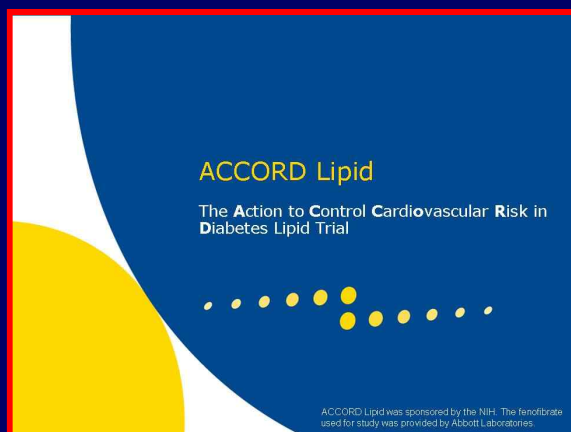
\* Non-randomised comparison adjusting for on-study statin use



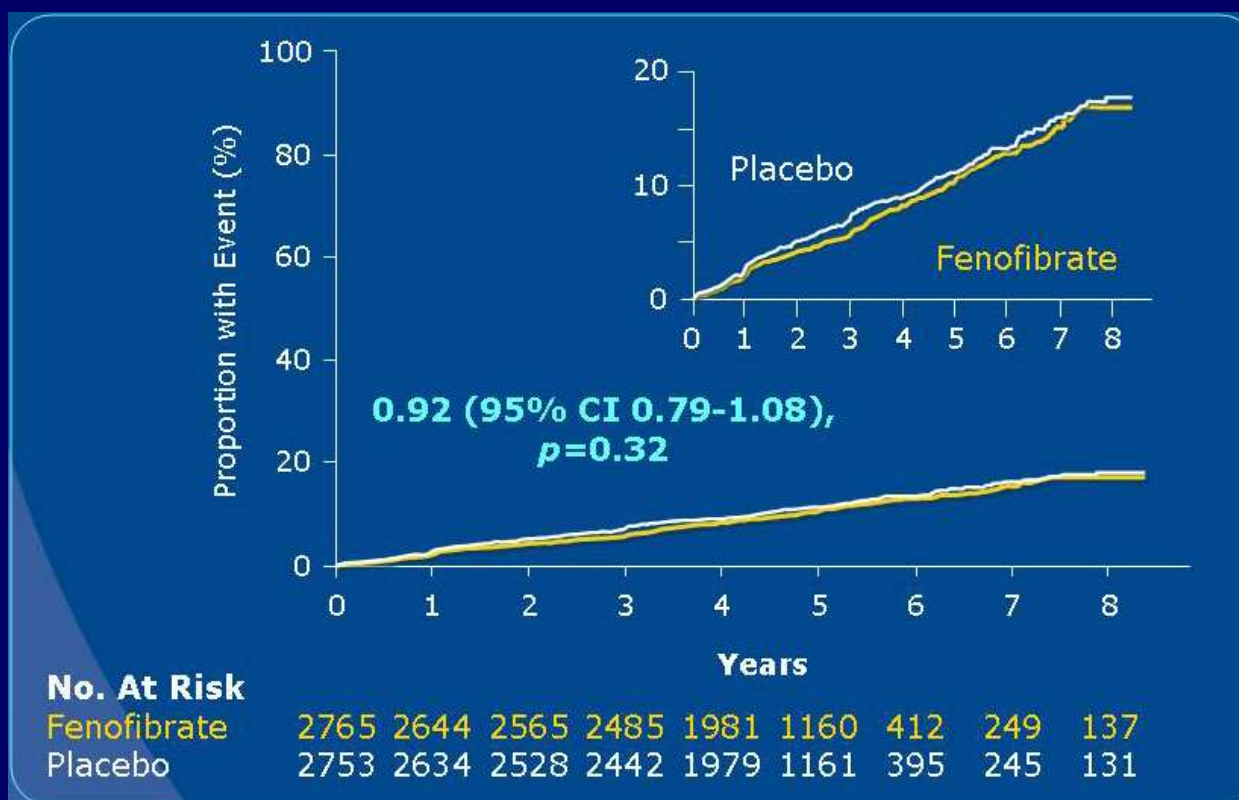
# Baseline Characteristics of FIELD study

	Total Population (n = 9,795)
Male/Female, %	62.7/37.3
No Prior CVD, %	78.3
Diabetes management with diet plus one oral hypoglycemic agent %	59.5
Median duration of diabetes, years	5
Median HbA1c, %	6.9
Diabetic complications	
Retinopathy, %	8.3
Nephropathy, %	2.8
Lipid parameters, mg/dl	
TC (mean)	194
LDL-C (mean)	119
HDL-C (mean)	42
TG (median)	153
Dyslipidemic*, %	37

\*TG > 150 mg/dL and HDL < 40 mg/dL for men or < 50 mg/dL for women

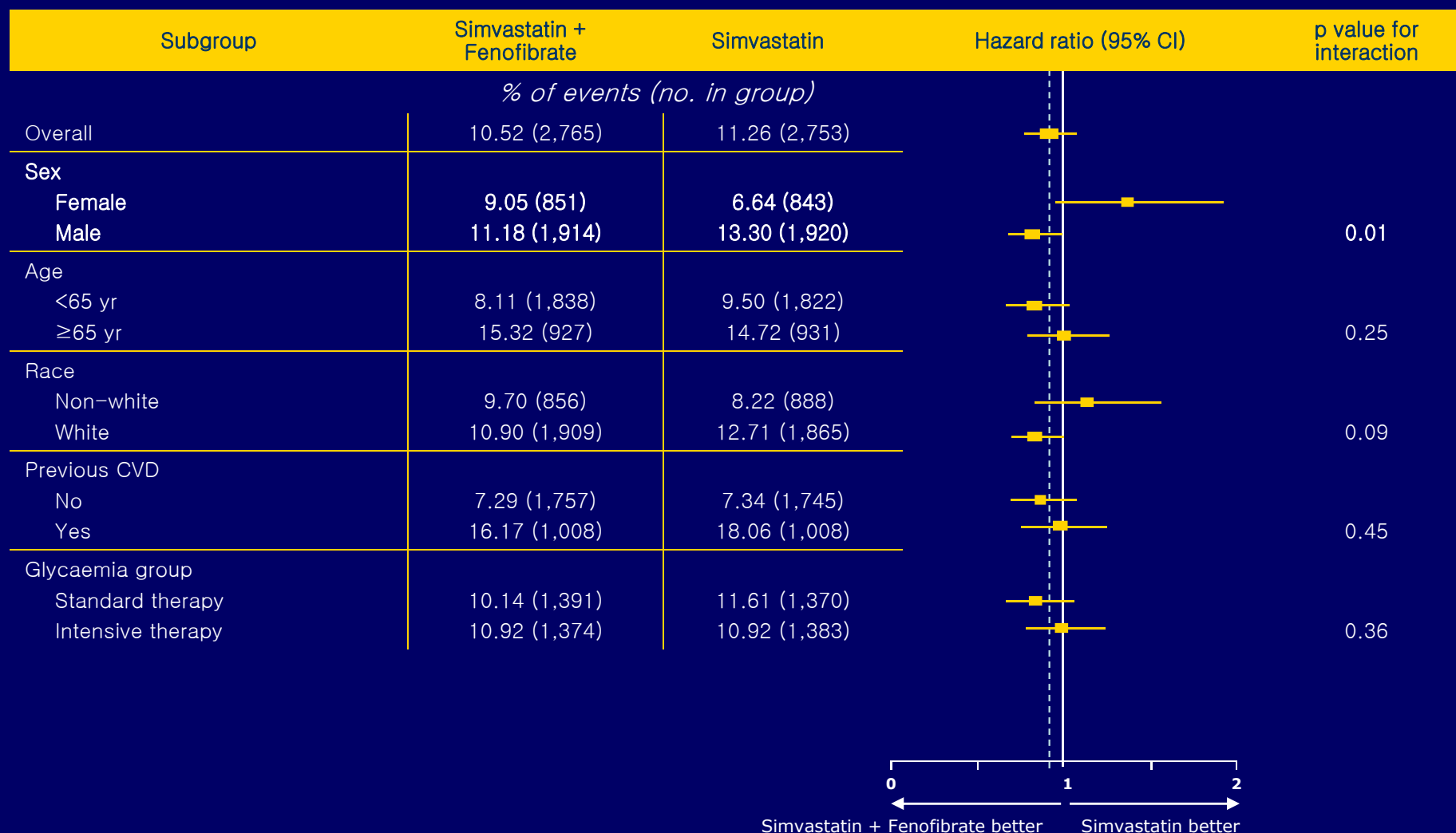


Lipid levels at study close	Simvastatin + Fenofibrate (n=2,765)	Simvastatin (n=2,753)	p value
Mean LDL-C (mg/dL)	81.1	80.0	p=0.16
Mean HDL-C (mg/dL)	41.2	40.5	p=0.01
Median triglycerides (mg/dL)	147.0	170.0	p=0.001

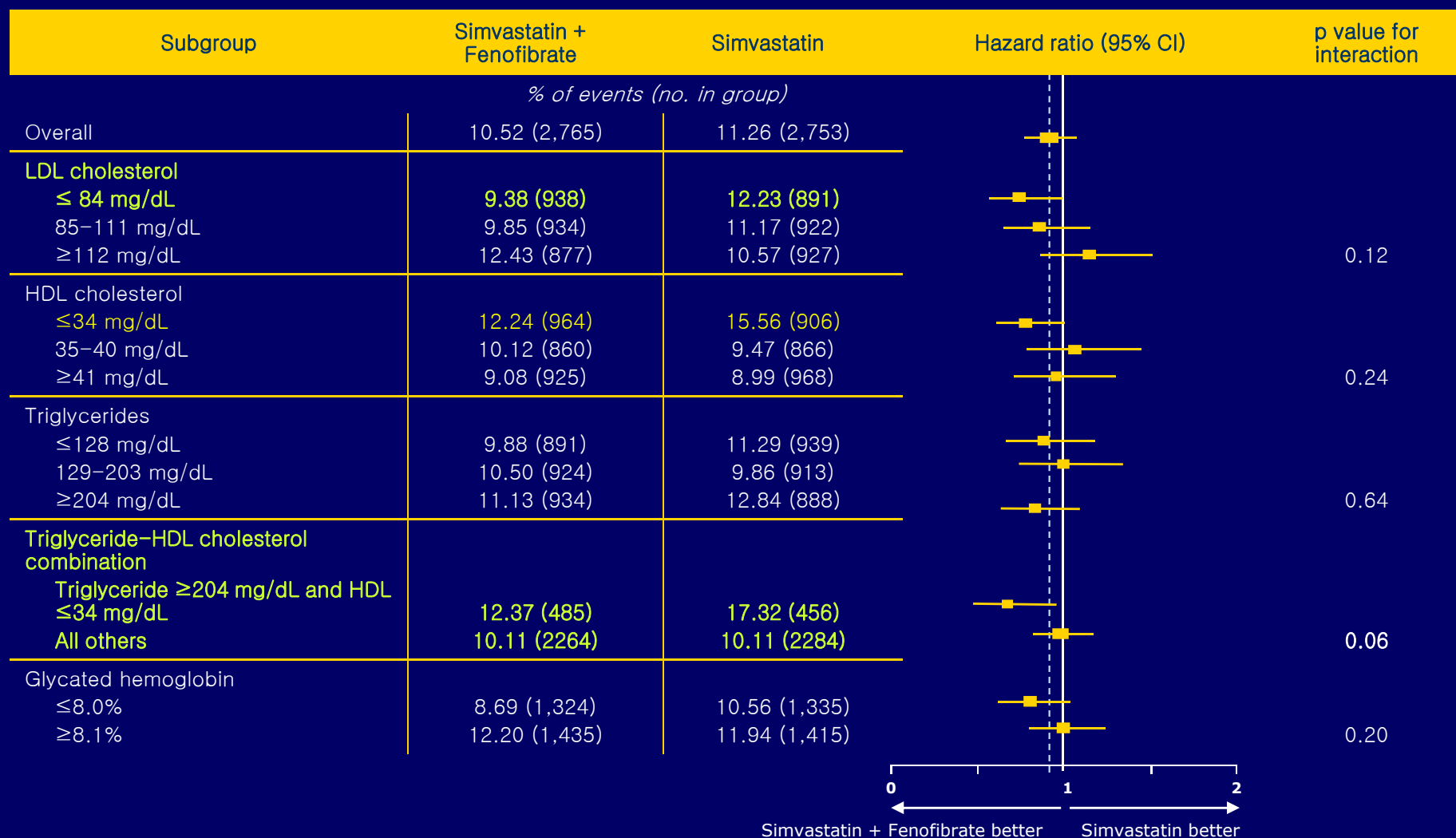


Baseline demographics	Simvastatin + Fenofibrate (n=2,765)	Simvastatin (n=2,753)	Overall (n=5,518)
Mean age – yr	62.2	62.3	62.3
Women – n (%)	851 (30.8)	843 (30.6)	1694 (30.7)
Race/ethnicity – n (%)			
White	1909 (69.0)	1865 (67.7)	3774 (68.4)
Black	392 (14.2)	442 (16.1)	834 (15.1)
Hispanic	213 (7.7)	194 (7.0)	407 (7.4)
Cigarette-smoking status – n (%)			
Current	410 (14.8)	393 (14.3)	803 (14.6)
Former	1292 (46.7)	1254 (45.6)	2546 (46.2)
Previous CVD – %	36.5	36.6	36.5
Median duration of diabetes – yrs	10	9	9
Mean HbA1c – %	8.3	8.3	8.3
Mean fasting serum glucose – mg/dL	176.5	175.1	175.8
Mean SBP – mmHg	133.8	134.0	133.9
Mean DBP – mmHg	73.9	74.0	74.0
Mean BMI– kg/m <sup>2</sup>	32.2	32.4	32.3
Mean total cholesterol	174.7	175.7	175.2
Mean LDL-C	100.0	101.1	100.6
Mean HDL-C	38.0	38.2	38.1
Median TG	164	160	162

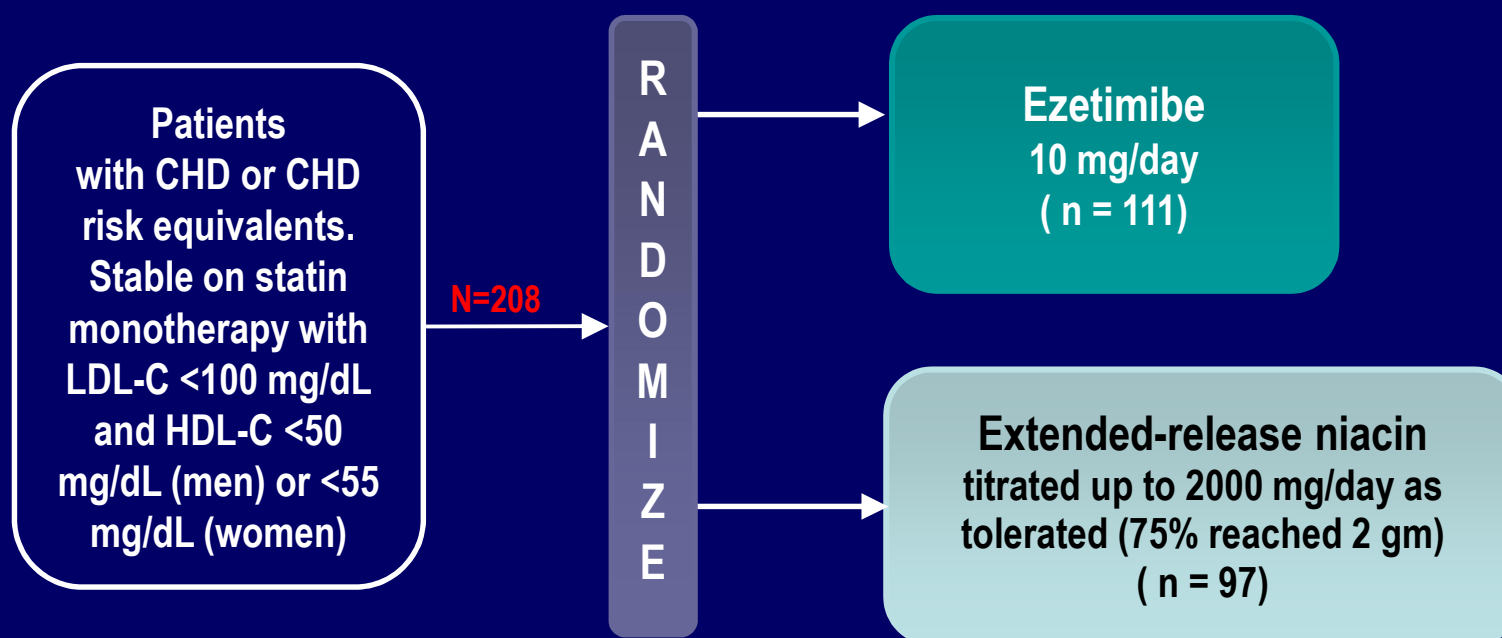
# Primary endpoint in pre-specified subgroups in ACCORD



# Primary endpoint in pre-specified subgroups in ACCORD



# ARBITER 6-HALTS -- Trial Design



- **Primary end point:** change in the mean common carotid IMT between treatment groups
- **Secondary end points** - change in lipid values
  - composite of major adverse cardiovascular events
- **Duration:** 14 months

CHD = clinical atherosclerotic coronary or vascular disease.

CHD risk equivalent = (diabetes mellitus, multiple coronary risk factors with a Framingham Risk Score >2% per year, an elevated coronary calcium score (>400 for men; >200 for women).

For internal use only. Not to be used with Health Care Professionals

Devine et al. *Cardiovasc Drugs Ther.* 2007;21:221.

# ARBITER-6: Results – lipid parameters

	Baseline		2 Months		8 Months		14 Months	
	Ezetimibe	Niacin	Ezetimibe	Niacin	Ezetimibe	Niacin	Ezetimibe	Niacin
Total Cholesterol	146.6 ± 23.3	143.6 ± 24.0	120.2 ± 20.6	131.0 ± 22.9	122.4 ± 21.5	133.6 ± 25.5	127.8 ± 22.8	136.7 ± 29.3
P value	0.90		0.001		<0.001		0.025	
HDL-C	43.3 ± 8.5	42.5 ± 8.6	42.2 ± 8.5	48.9 ± 10.6	41.1 ± 9.0	50.7 ± 11.6	40.5 ± 7.9	49.9 ± 12.2
P value	0.59		<0.001		<0.001		<0.001	
LDL-C	83.7 ± 19.9	80.5 ± 17.2	60.1 ± 16.1	66.2 ± 18.1	61.6 ± 17.2	67.1 ± 19.5	66.1 ± 18.8	70.5 ± 23.9
P value	0.34		0.013		0.013		0.12	
Triglycerides	122 (87-162)	126 (94-163)	100 (78-140)	88 (69-125)	107 (78-153)	88 (66-123)	113 (84-150)	90 (69-138)
P value	0.56		0.033		0.019		0.018	
Glucose	104.0 ± 27.8	104.1 ± 18.9	109.6 ± 39.5	109.1 ± 23.9	108.2 ± 27.7	107.6 ± 28.1	110.4 ± 33.4	107.4 ± 24.9
P value	0.20		0.51		0.53		0.34	
C-reactive protein	1.9 (0.8-3.6)	1.3 (0.8-4.0)	1.2 (0.6-3.0)	1.1 (0.6-3.1)	1.3 (0.6-2.9)	1.1 (0.5-2.4)	0.6 (0.6-3.1)	1.0 (0.4-2.9)
P value	0.51		0.093		0.067		0.42	

% change	LDL –C	HDL-C	TG
Niacin	- 12	+ 17	- 29
Ezetimibe	- 21	- 6	- 7

## ARBITER-6: cIMT endpoint result

	Ezetimibe (N=111)	Niacin (N=97)	P Value
<b>Baseline</b>			
Mean thickness (mm)	0.8957±0.1484	0.9001±0.1558	0.83
Maximal thickness (mm)	1.0065±0.1548	1.0092±0.1650	0.90
<b>Change from baseline to 8 mo</b>			
Mean thickness (mm)	0.0014±0.0020	-0.0102±0.0030	0.001
P value for change from baseline	0.48	0.001	
Maximal thickness (mm)	-0.0028±0.0031	-0.0128±0.0043	0.057
P value for change from baseline	0.38	0.004	
<b>Change from baseline to 14 mo</b>			
Mean thickness (mm)	0.0007±0.0035	0.0142±0.0041	0.01
P value for change from baseline	0.84	0.001	
Maximal thickness (mm)	-0.0009±0.0039	-0.0181±0.0050	0.006
P value for change from baseline	0.81	<0.001	

Taylor et al. N Engl J Med 2009;361



- Are TG and HDL important in diabetic condition ?  
YES, especially when LDL is promptly controlled
- Is LDL less important in diabetic conditions ?

## What is important risk for CVD in diabetic condition ? (UKPDS: 23)

Position in model	Coronary artery disease (n=280)		Fatal or non-fatal myocardial infarction (n=192)	
	Variable	p-value	Variable	p-value
1.	<b>LDL chol</b>	<0.001	<b>LDL chol</b>	0.0022
2.	<b>HDL chol</b>	0.001	Diastolic BP	0.0074
3.	HbA <sub>1c</sub>	0.002	Smoking	0.025
4.	Systolic BP	0.0065	<b>HDL chol</b>	0.026
5.	Smoking	0.056	HbA <sub>1c</sub>	0.053

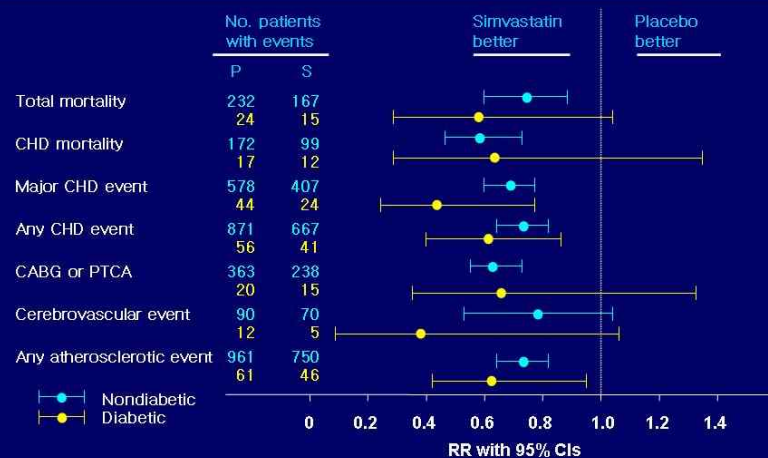
2,693 white patients with type 2 diabetes mellitus

\*Stepwise multivariate Cox models

Turner RC et al. *BMJ* 1998;316:823–8

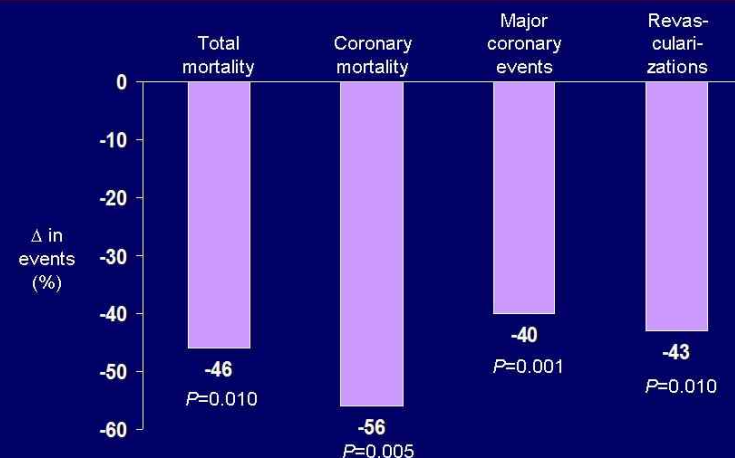
# 4S

## Secondary Prevention: CHD Risk Reduction in the 4S Subgroup of Patients With Diabetes



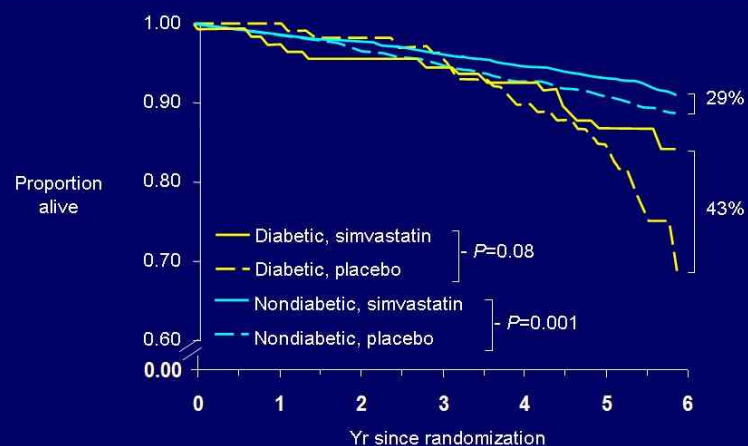
Pyörälä K et al. *Diabetes Care*. 1997;20:614-620.

## 4S: Treatment Benefit in Subgroup With Impaired Fasting Glucose (FG 110-125 mg/dL)



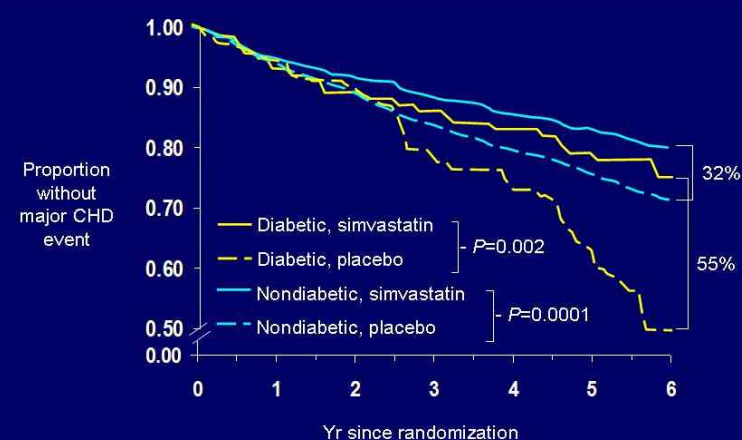
Haffner SM et al. *Diabetes*. 1998;(suppl 1):A54. Abstract.

## 4S: Total Mortality Reduction in a Subgroup of Patients With Diabetes



Pyörälä K et al. *Diabetes Care*. 1997;20:614-620.

## 4S: Major CHD Event Reduction in a Subgroup of Patients With Diabetes



Pyörälä K et al. *Diabetes Care*. 1997;20:614-620.

# HPS

## Heart Protection Study Diabetes Sub-Study

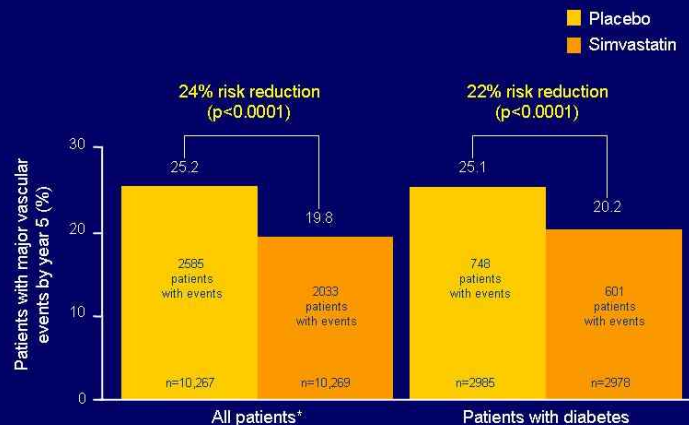
- Almost 6000 men and women, aged 40–80 years with diabetes mellitus
  - 1981 persons with history of CHD
  - 3982 persons with no history of CHD
- People randomized to simvastatin 40 mg or placebo
- Mean duration of follow-up 5 years
- Objective—to evaluate the long-term benefits of simvastatin and/or antioxidants in people with diabetes with or without CHD regardless of cholesterol level
- Primary endpoints—*first* major coronary events\* and *first* major vascular events\*\*
- Statin not considered clearly indicated or contraindicated by patients' primary physicians

\*Nonfatal MI or death from coronary disease

\*\*Major coronary events, stroke of any type, and coronary or noncoronary revascularizations

Adapted from Heart Protection Study Collaborative Group *Eur Heart J* 1999;20:725-741; Heart Protection Study Collaborative Group *Lancet* 2002;360:7-22; Heart Protection Study Collaborative Group *Lancet* 2003;361:2005-2016.

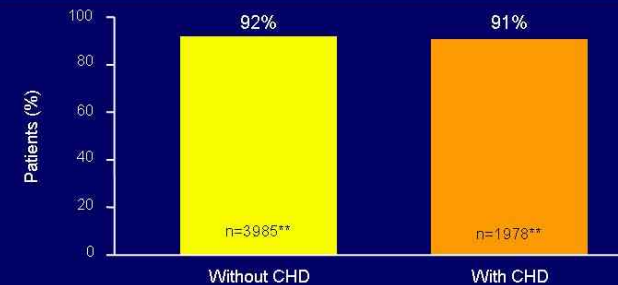
## First Major Vascular Events All Patients vs. Patients with Diabetes



\*Includes patients with CHD, occlusive disease of noncoronary arteries, diabetes, or treated hypertension

Adapted from Heart Protection Study Collaborative Group *Lancet* 2002;360:7-22; Heart Protection Study Collaborative Group *Lancet* 2003;361:2005-2016.

## Impact of Simvastatin on LDL-C Nine Out of 10 Patients with Diabetes Achieved Goal (LDLc <115mg/dl) \*



- Results from the five-year Heart Protection Study (HPS) of almost 6000 patients with diabetes with or without CHD indicated that 92% of patients with diabetes, but without CHD, and 91% of patients with CHD who received simvastatin 40 mg achieved the European Guidelines LDL-C treatment goal of <3 mmol/L (115 mg/dl)\*\*\*

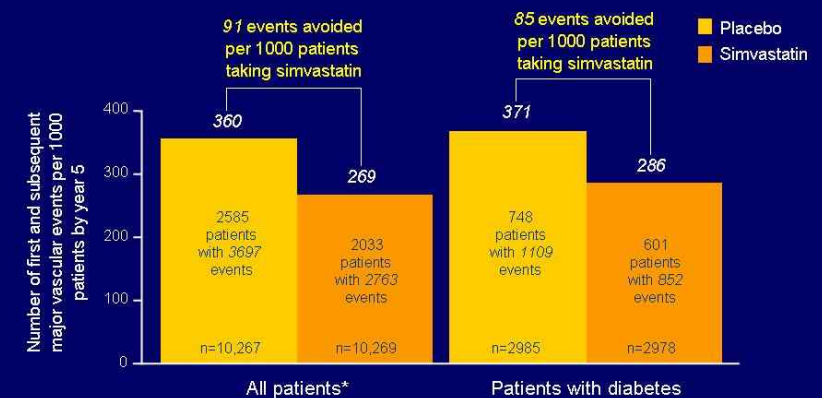
\*By the four-month point in HPS

\*\*These populations differ from those reported in later HPS publications (3982 and 1981) because three patients were reclassified after the four-month point. The percentages of patients achieving LDL-C goal are not affected.

\*\*\*Based on random sampling of patients with diabetes

Adapted from Armitage J, Collins R *Heart* 2000;84:357-360.

## First and Subsequent Major Vascular Events All Patients vs. Patients with Diabetes

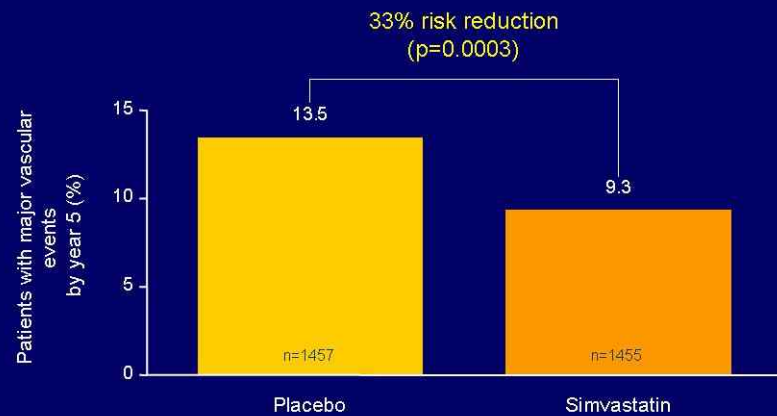


\*Includes patients with CHD, occlusive disease of noncoronary arteries, diabetes, or treated hypertension

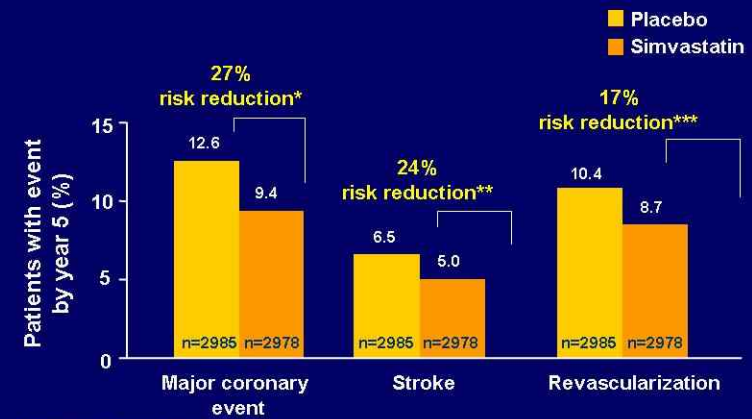
Adapted from Heart Protection Study Collaborative Group *Lancet* 2003;361:2005-2016.

# HPS

## *Impact of Simvastatin in Patients with Diabetes and No Prior CVD* **Major Vascular Events**



## *Impact of Simvastatin in Patients with Diabetes* **Major Coronary Events, Stroke, and Revascularization**



\*p<0.0001; \*\*p<0.01; \*\*\*p=0.02

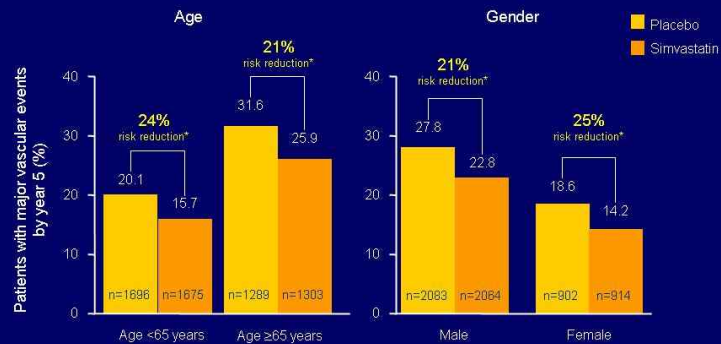
Adapted from Heart Protection Study Collaborative Group *Lancet* 2003;361:2005-2016.

Adapted from Heart Protection Study Collaborative Group *Lancet* 2003;361:2005-2016.



# HPS

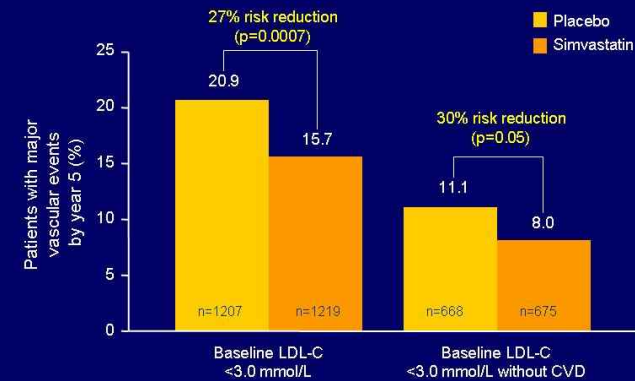
## Impact of Simvastatin in Patients with Diabetes By Age and Gender



\*p<0.05

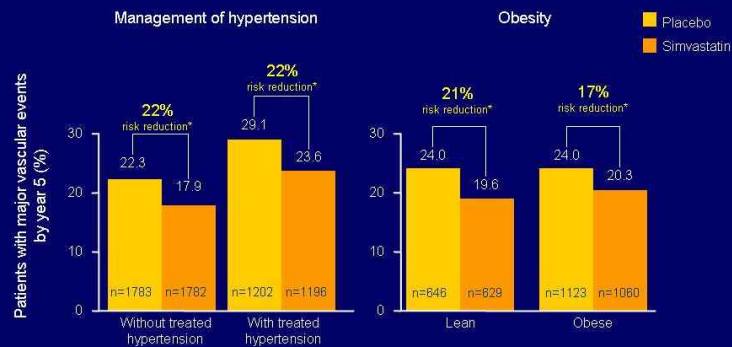
Adapted from Heart Protection Study Collaborative Group *Lancet* 2003;361:2005-2016.

## Impact of Simvastatin in Patients with Diabetes With Low LDL-C



Adapted from Heart Protection Study Collaborative Group *Lancet* 2003;361:2005-2016.

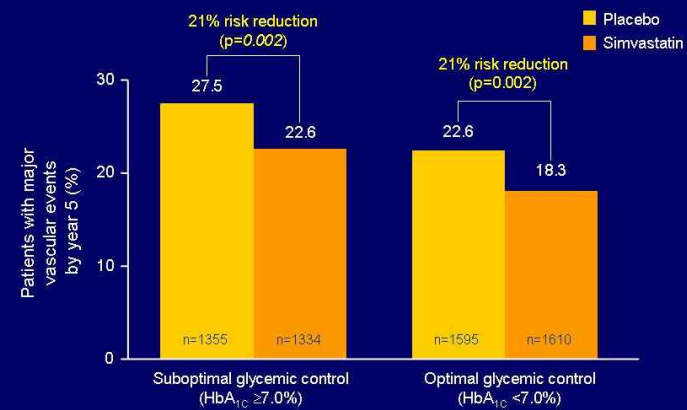
## Impact of Simvastatin in Patients with Diabetes with or without Treated Hypertension or Obesity



\*p<0.05

Adapted from Heart Protection Study Collaborative Group *Lancet* 2003;361:2005-2016.

## Impact of Simvastatin in Patients with Diabetes With or without Optimal Glycemic Control



Adapted from Heart Protection Study Collaborative Group *Lancet* 2003;361:2005-2016.

- Are TG and HDL important in diabetic condition ?  
YES, especially when LDL is promptly controlled
- Is LDL less important in diabetic conditions ?  
NO. Lowering LDLc with (simva)statin can reduce CVD incidence and save lives.
- Is LDLc a good marker to reflect LDL-burden under (pre)diabetic conditions ?

# Lipoproteins vs. Severity of Metabolic Syndrome

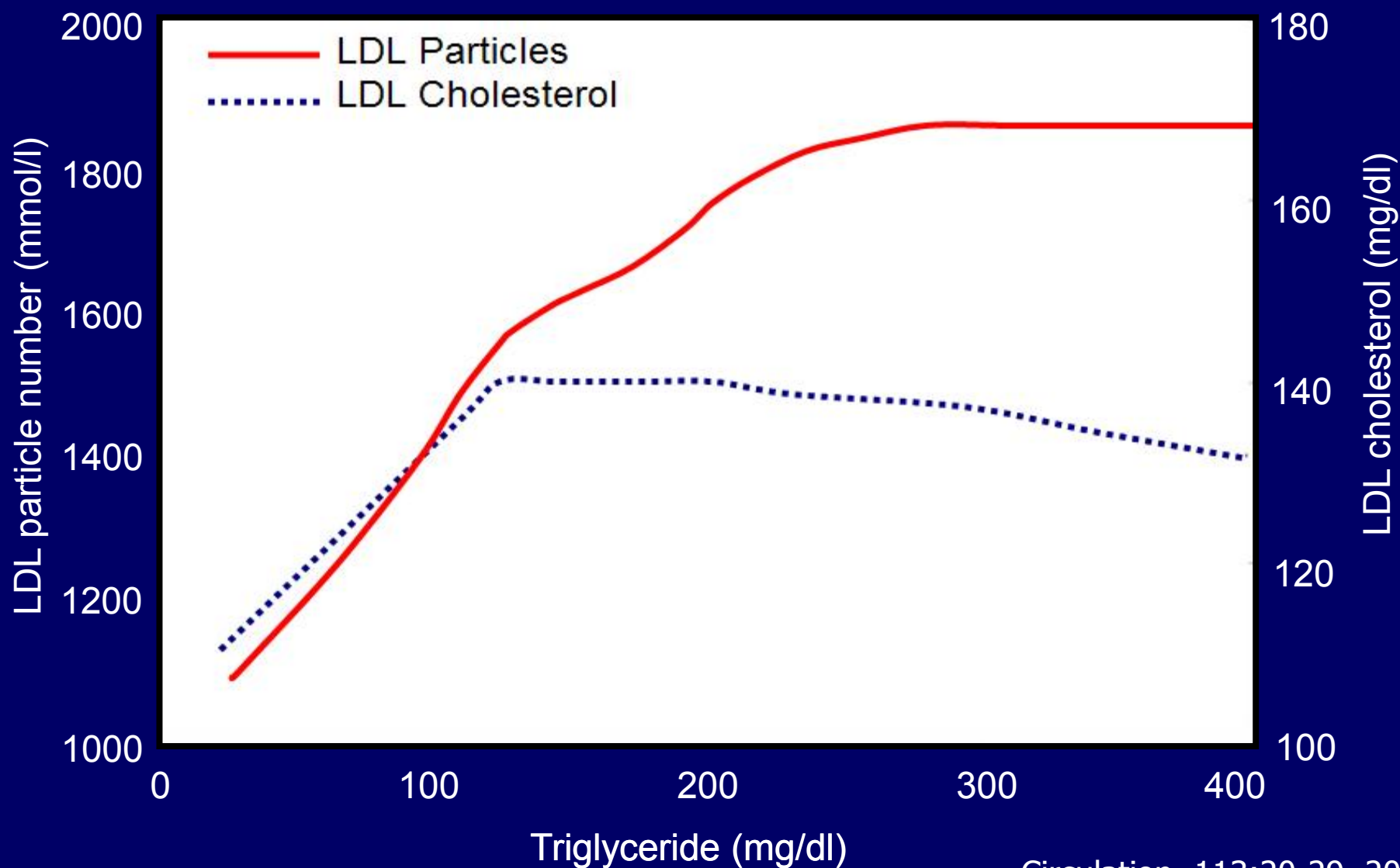
## A Prominent Feature of the Metabolic Syndrome in the Framingham Heart Study

**TABLE 4. Plasma Levels of NMR-Determined Lipoprotein Measures and Biochemical Lipid Measures With Increasing Number of MetSyn Features\***

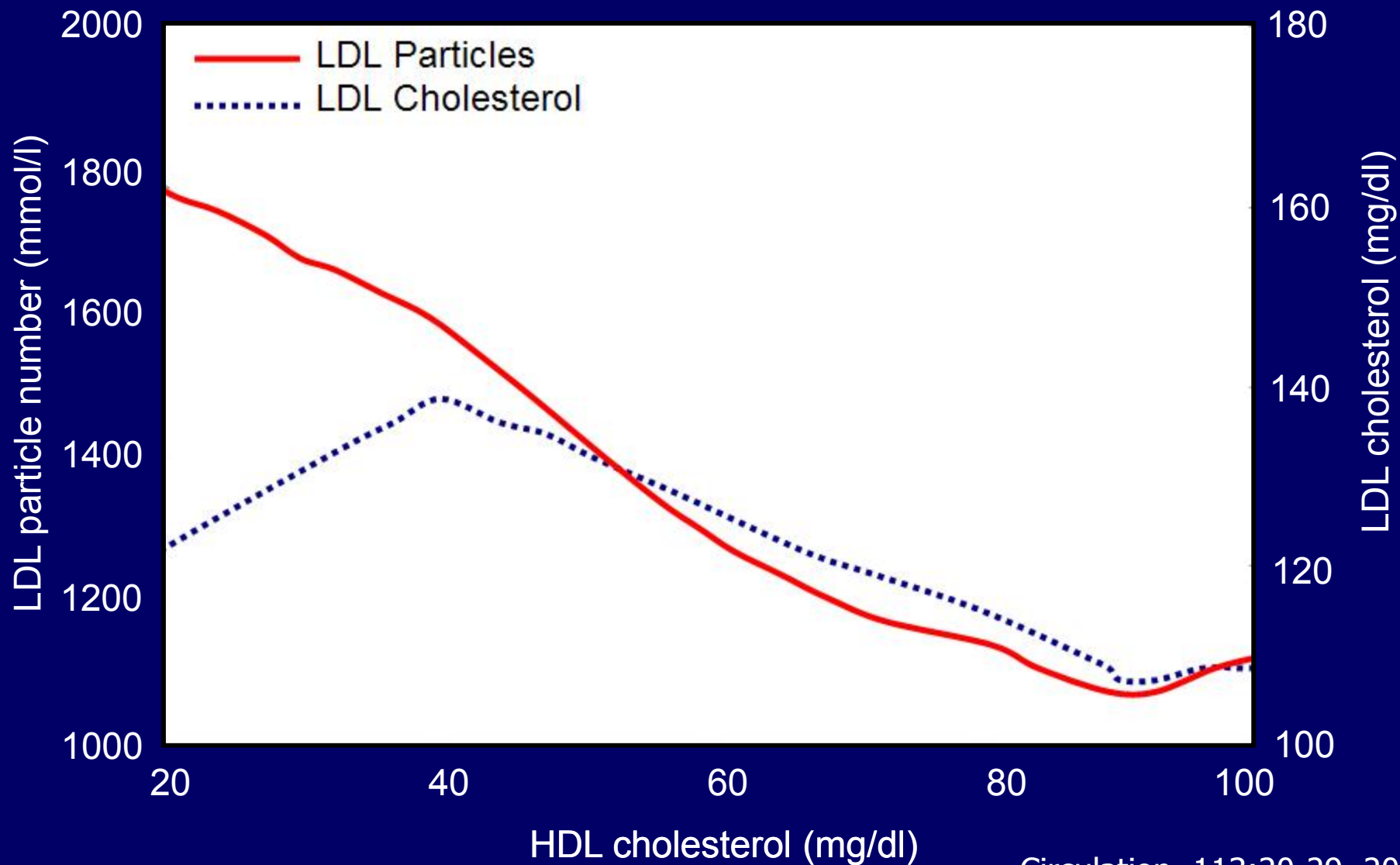
	No. of Components of MetSyn						<i>P</i> for Trend
	0	1	2	3	4	5	
Women	n=562	n=464	n=298	n=134	n=102	n=29	
NMR-derived lipoprotein measures							
Total LDL particle No., nmol/L	1169±16	1344±17	1496±22	1600±32	1678±37	1663±69	<0.0001
Small LDL particles, nmol/L	428±15	591±16	756±20	918±30	1090±34	1187±64	<0.0001
Large LDL particles, nmol/L	714±12	716±13	697±17	618±25	529±28	419±53	<0.0001
Biochemical lipid measures							
LDL-C, mg/dL	117±1	128±2	135±2	137±3	138±3	133±6	<0.0001
ApoB, mg/dL	84±1	92±1	101±1	110±2	111±2	113±4	<0.0001
Triglycerides, mg/dL	71±2	84±2	121±2	154±4	188±4	211±8	<0.0001
HDL-C, mg/dL	66±1	57±1	51±1	45±1	40±1	36±2	<0.0001
Men	n=286	n=407	n=335	n=233	n=113	n=30	
NMR-derived lipoprotein measures							
Total LDL particle No., nmol/L	1290±23	1485±19	1554±21	1690±25	1783±36	1767±69	<0.0001
Small LDL particles, nmol/L	574±26	813±21	991±24	1232±29	1396±41	1361±79	<0.0001
Large LDL particles, nmol/L	684±17	630±14	520±16	411±19	336±27	362±52	<0.0001
Biochemical lipid measures							
LDL-C, mg/dL	127±2	137±2	135±2	137±2	135±3	136±6	0.01
ApoB, mg/dL	90±1	99±1	103±1	111±1	115±2	115±4	<0.0001
Triglycerides, mg/dL	71±3	96±3	133±3	178±4	214±5	231±10	<0.0001
HDL-C, mg/dL	52±1	48±1	43±1	37±1	33±1	32±2	<0.0001



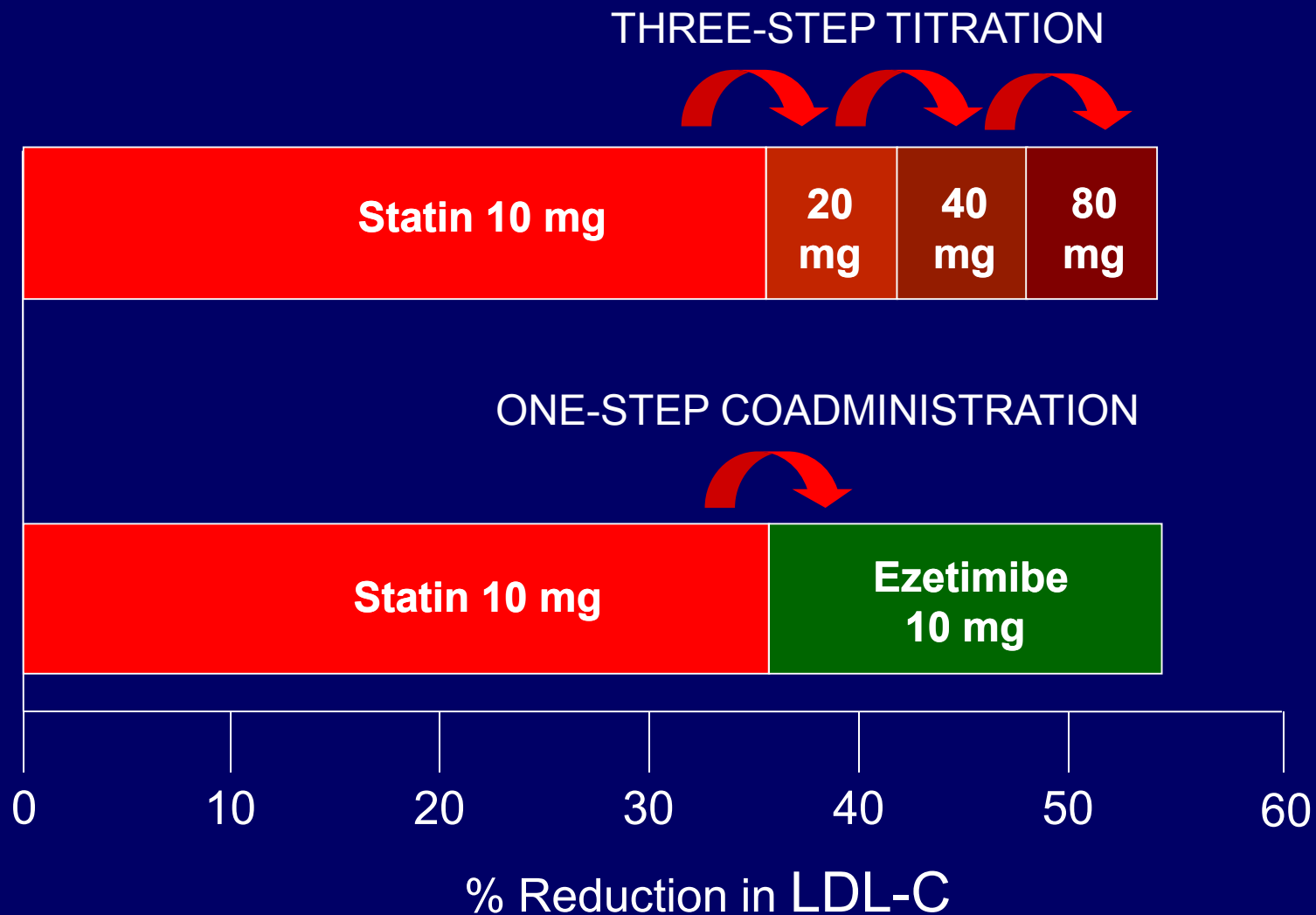
## Relations of total LDL particle number and LDL cholesterol value to the Triglyceride level



## Relations of total LDL particle number and LDL cholesterol value to the HDL cholesterol level

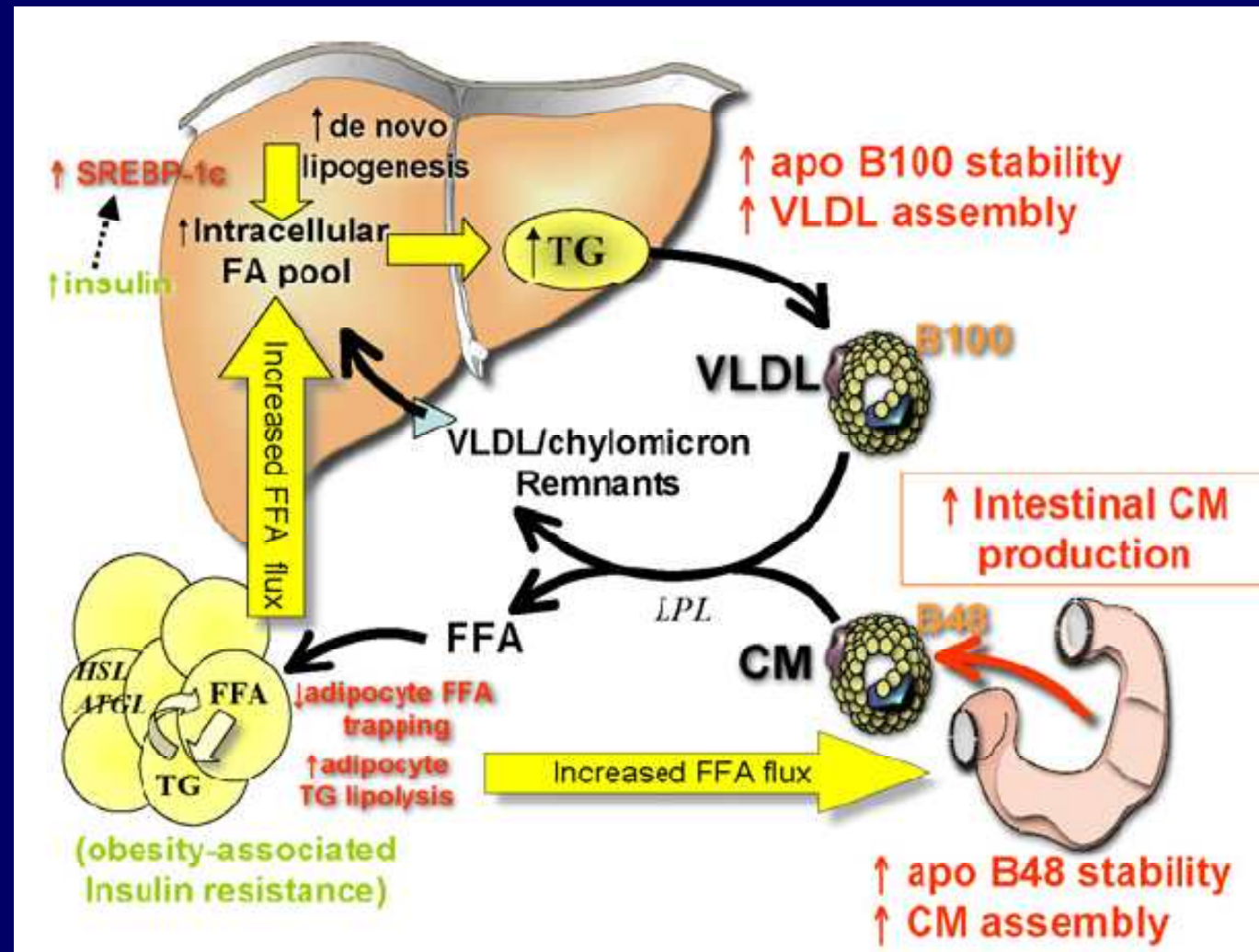


# One more way for LDLc reduction with ezetimibe

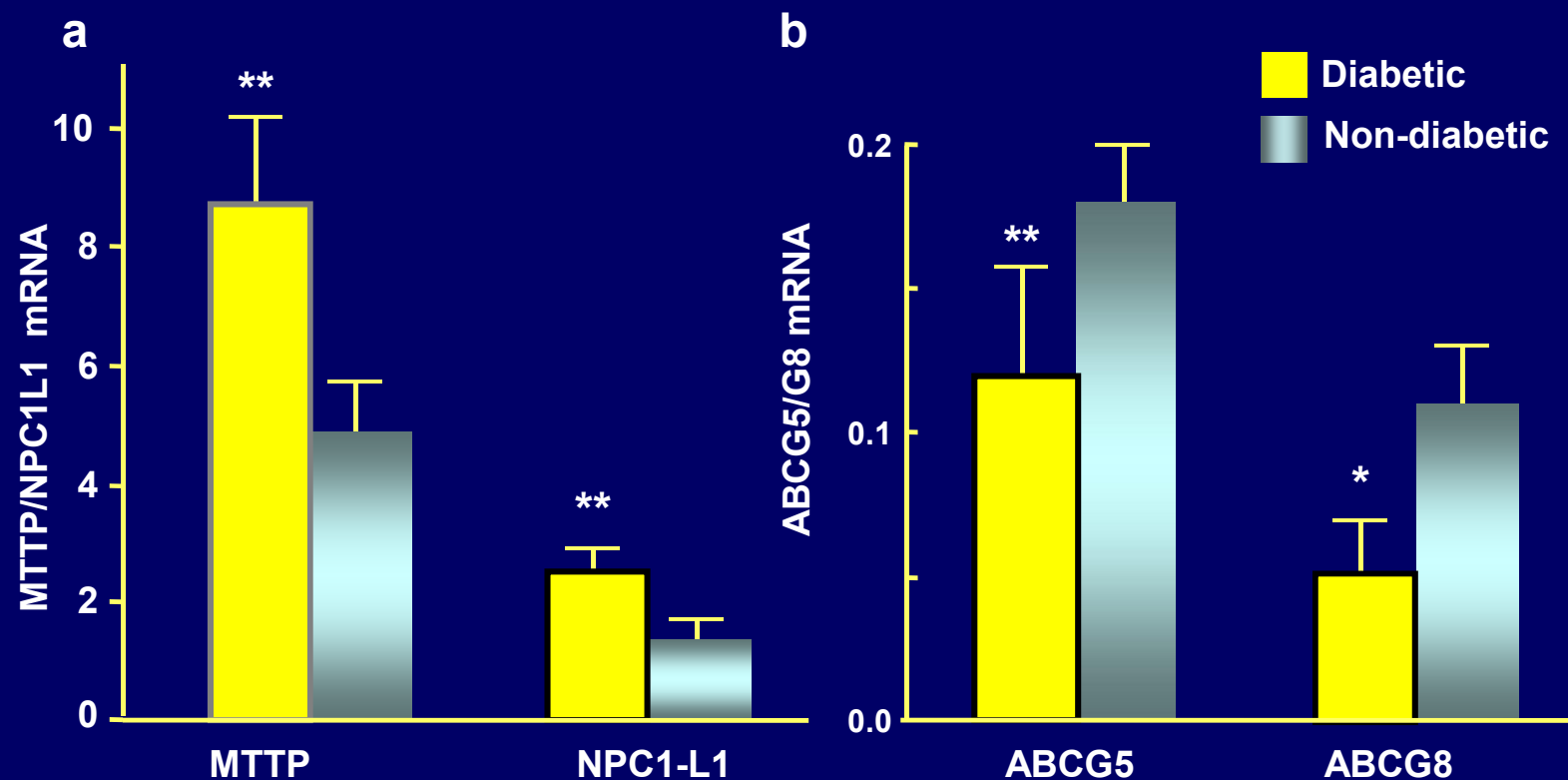


- Are TG and HDL important in diabetic condition ?  
YES, especially when LDL is promptly controlled
- Is LDL less important in diabetic conditions ?  
NO.  
On the contrary, lowering LDLc with (simva)statin can reduce CVD incidence and save lives.
- Is LDLc a good marker to reflect LDL-burden under (pre)diabetic conditions ?  
Measured LDL cholesterol becomes less liable when TG and HDL cholesterol level are abnormal.

## Diabetic condition increases intestinal chylomicron production



## Increased Chylomicron (ApoB48) Synthesis in DM



T2DM: increased MTTP and NPC1L1 mRNA  
decreased ABCG5/8 mRNA

(MTTP: 8.76 vs 4.87,  $p < 0.02$ , NPC1L1: 2.47 vs 1.39,  $p < 0.02$ , ABCG5/8: 0.12 vs 0.17,  $p < 0.04$ )

# Cholesterol in Plaque from 2 sources

Intestinal absorption



Chylomicrons  
Apo B48

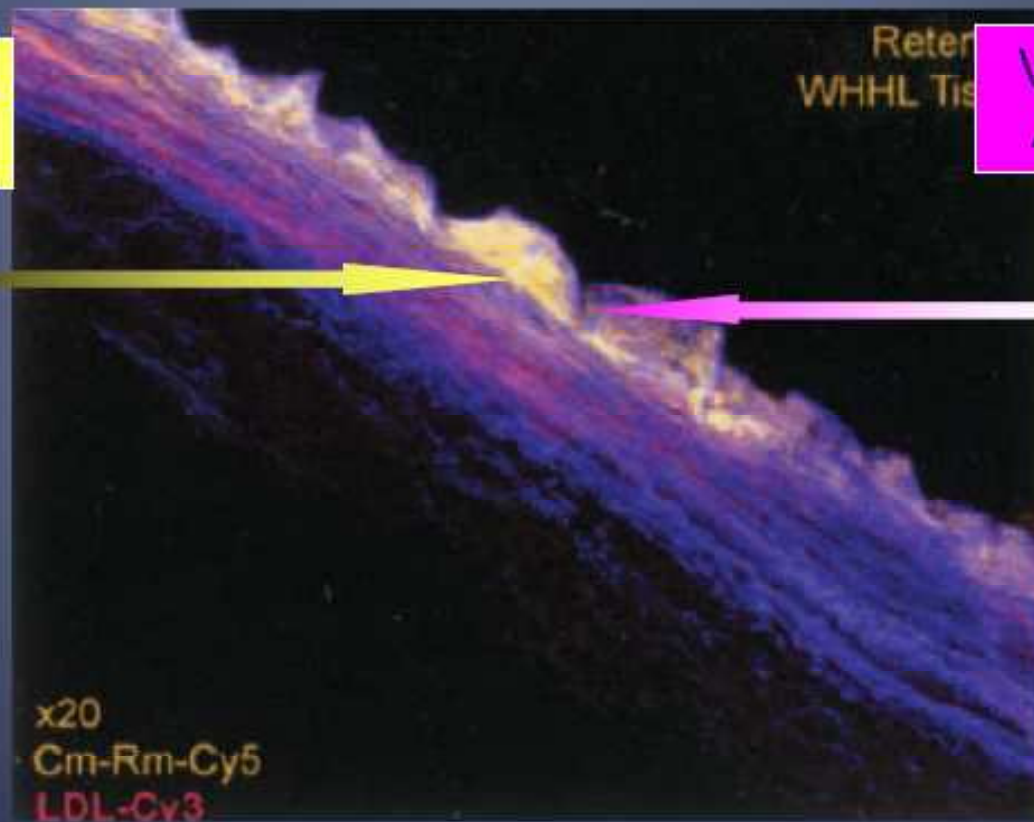
80%

Hepatic synthesis



VLDL, LDL  
Apo B100

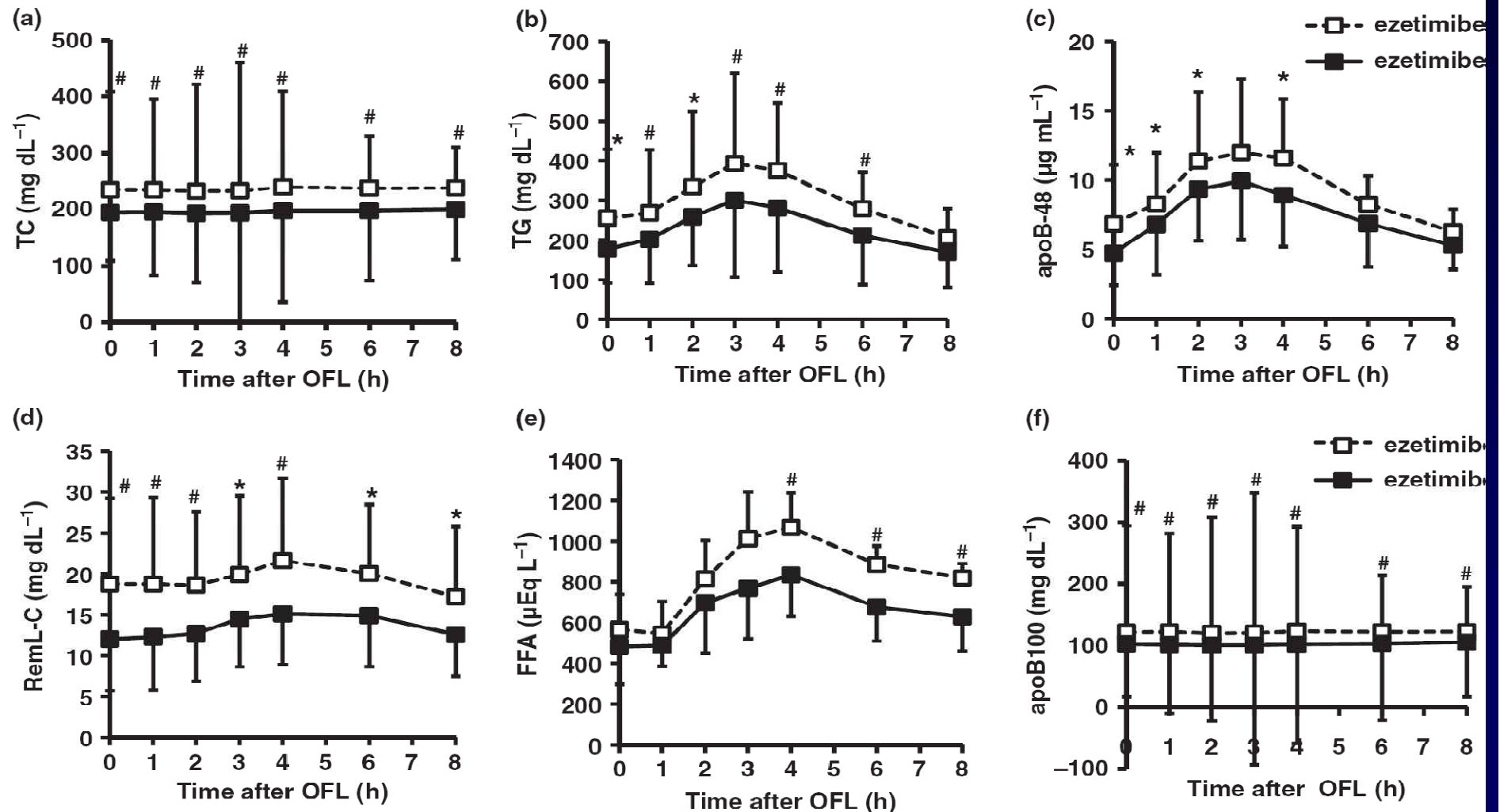
20%



Proctor et al. *Arterioscler Thromb Vasc Biol.* 2003;23:1595-1600

# Ezetimibe improves postprandial hyperlipidemia

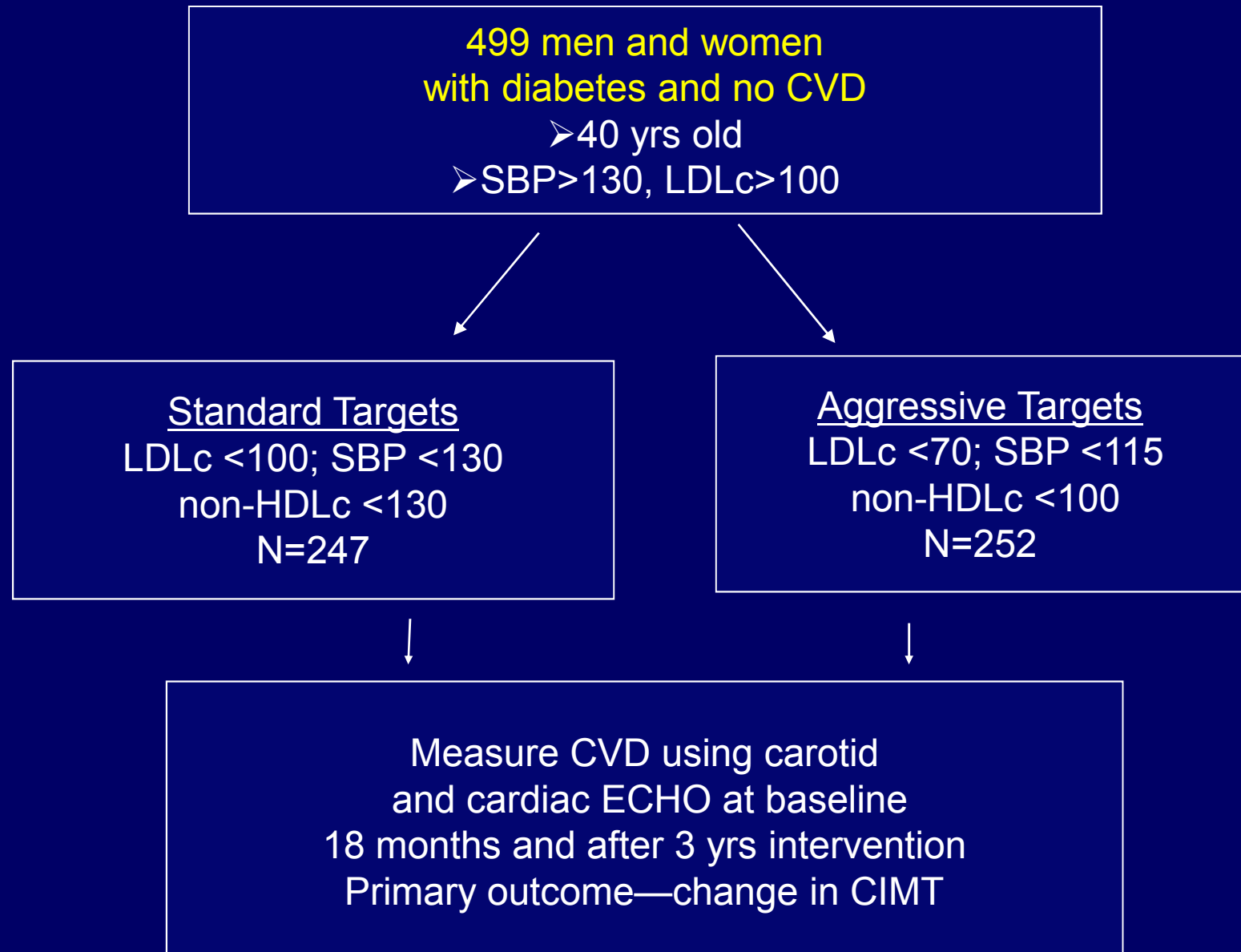
Oral fat loading (OFL) test before and after administration of ezetimibe.



\*P < 0.05, #P < 0.01.



# SANDS Trial Design



# SANDS (Stop Atherosclerosis in Native Diabetics Study) Trial

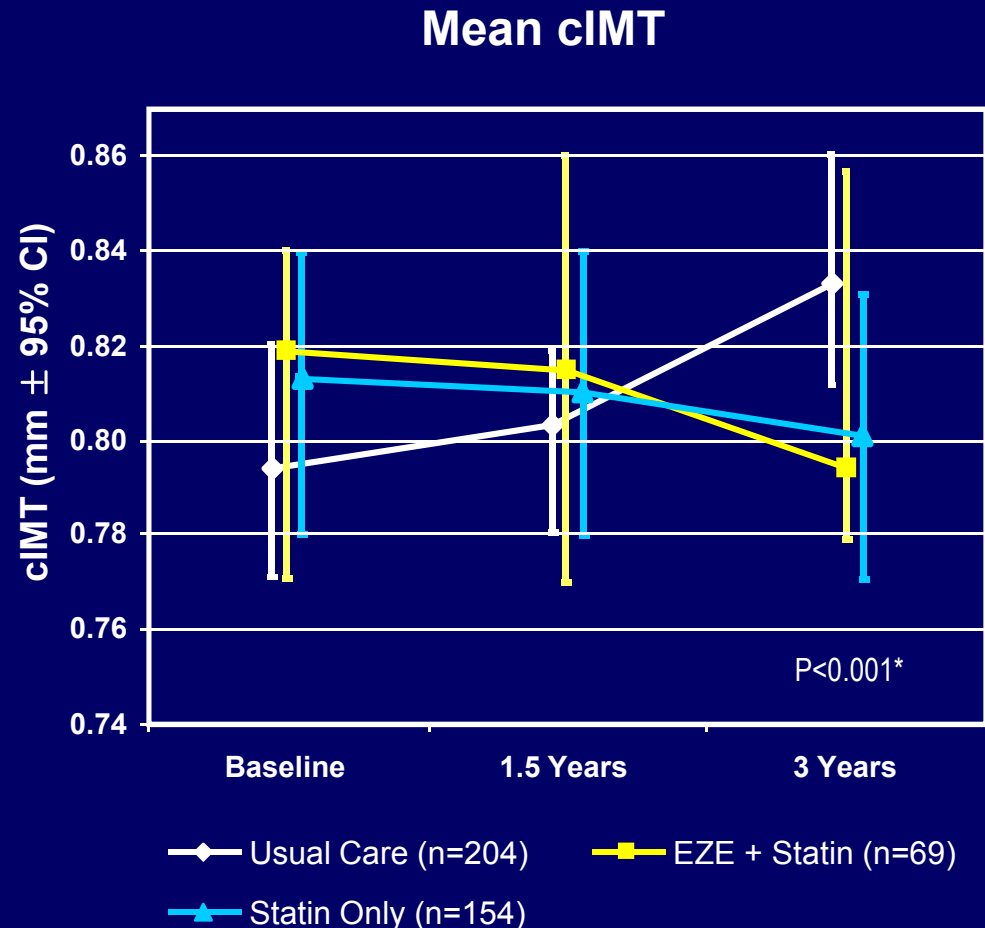
- Study population:
  - Native Americans (>40 years of age) with type 2 diabetes (N=499)
  - **Lipid lowering therapy at enrollment:**
    - 37% - 44% on statins
    - 4% - 7% on fibrates
    - 0 – 2% on niacin
    - 0 – 2% on fish oil

Tx arm	Baseline LDL-C (mg/dL)	Endpoint LDL-C (mg/dL)	Change (%)
Usual care	102	103	+ 0.9
Aggressive Tx			
Statin only	101	68	– 32
EZE + statin	108	78	– 31

- Treatment duration: 3 years
- Primary endpoint: mean change in cIMT

\*P-value for change in cIMT for both active treatment arms vs usual care group

Fleg JL et al. *J Am Coll Cardiol.* 2008;52:2198.



## Potential benefits of ezetimibe on statin

- Dual inhibition ; inhibition of cholesterol absorption from terminal ileum
- Avoidance of statin tolerance
- Inhibition of chylomicron formation in terminal ileum
- Lower the postprandial hyperTGemia.

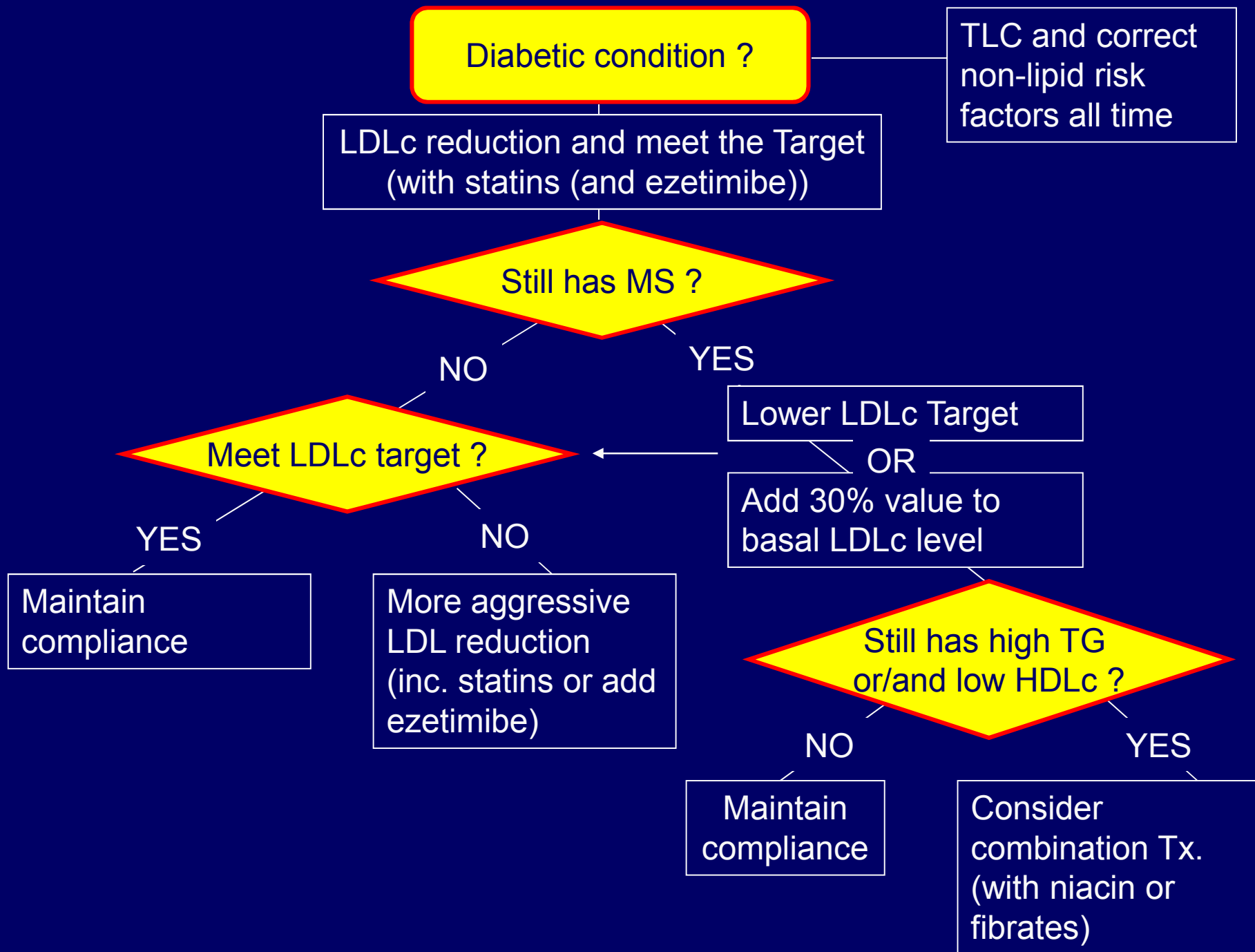
# Who will be the prince for 'princess statin' ?

EZ

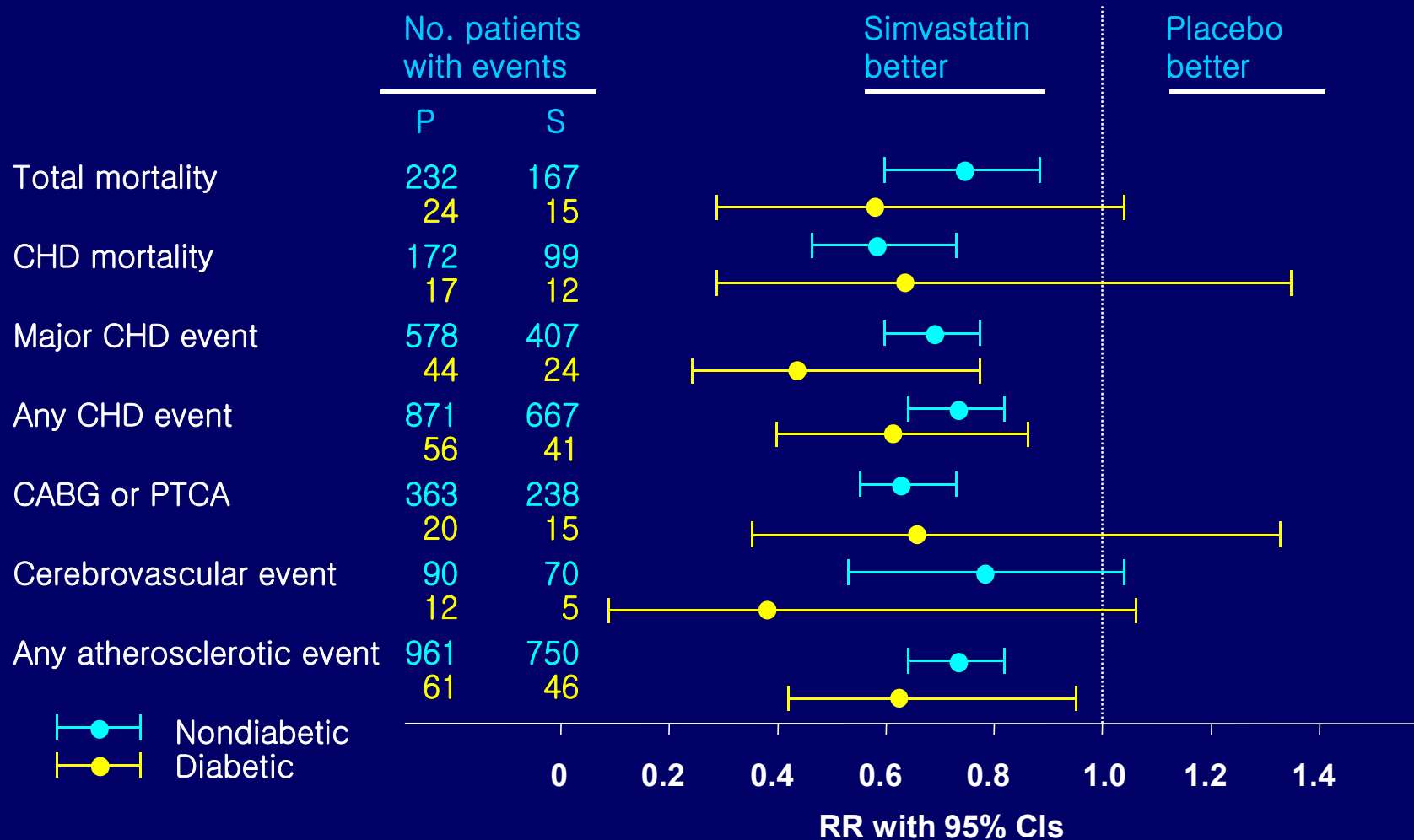


Nia

Sta

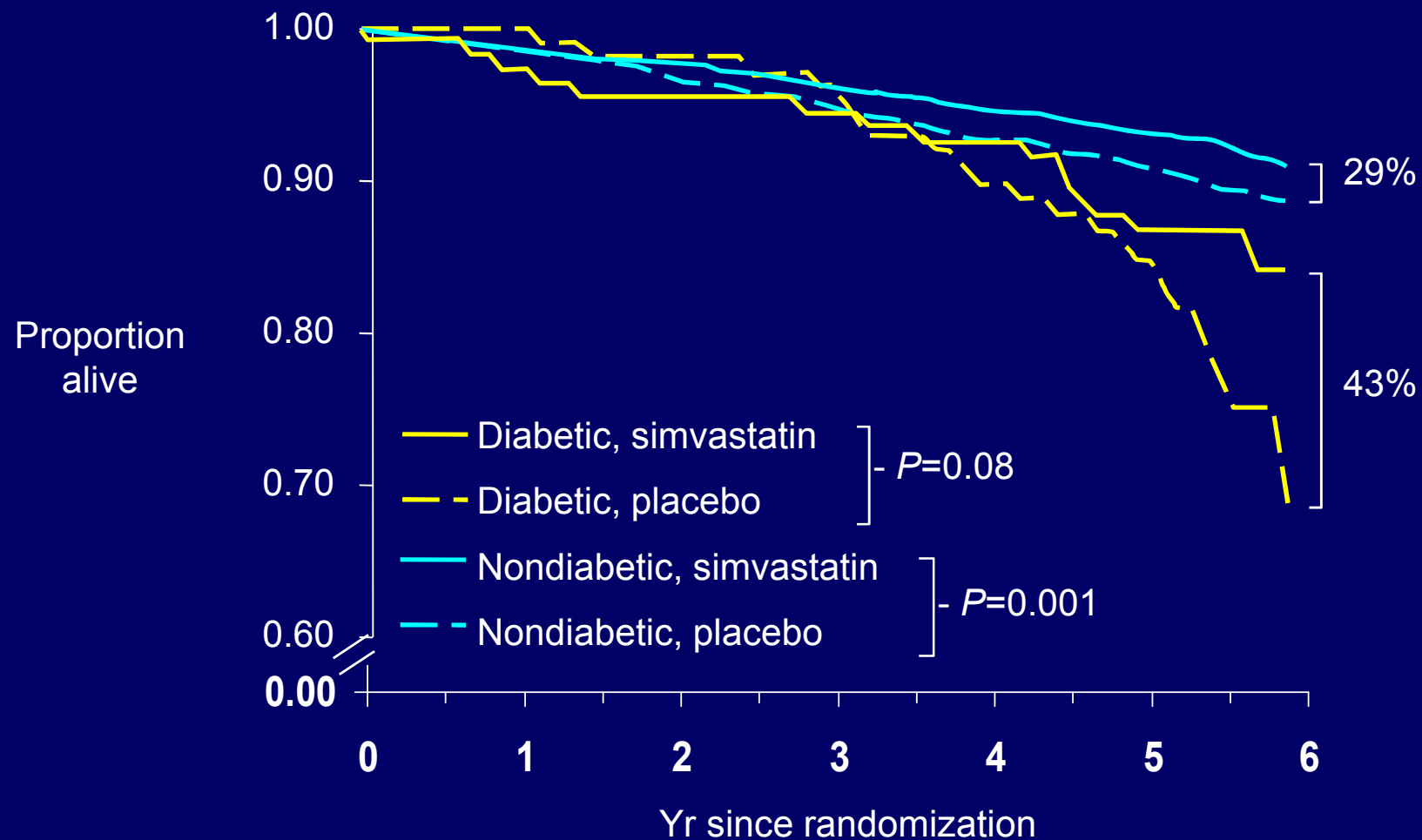


## Secondary Prevention: CHD Risk Reduction in the 4S Subgroup of Patients With Diabetes

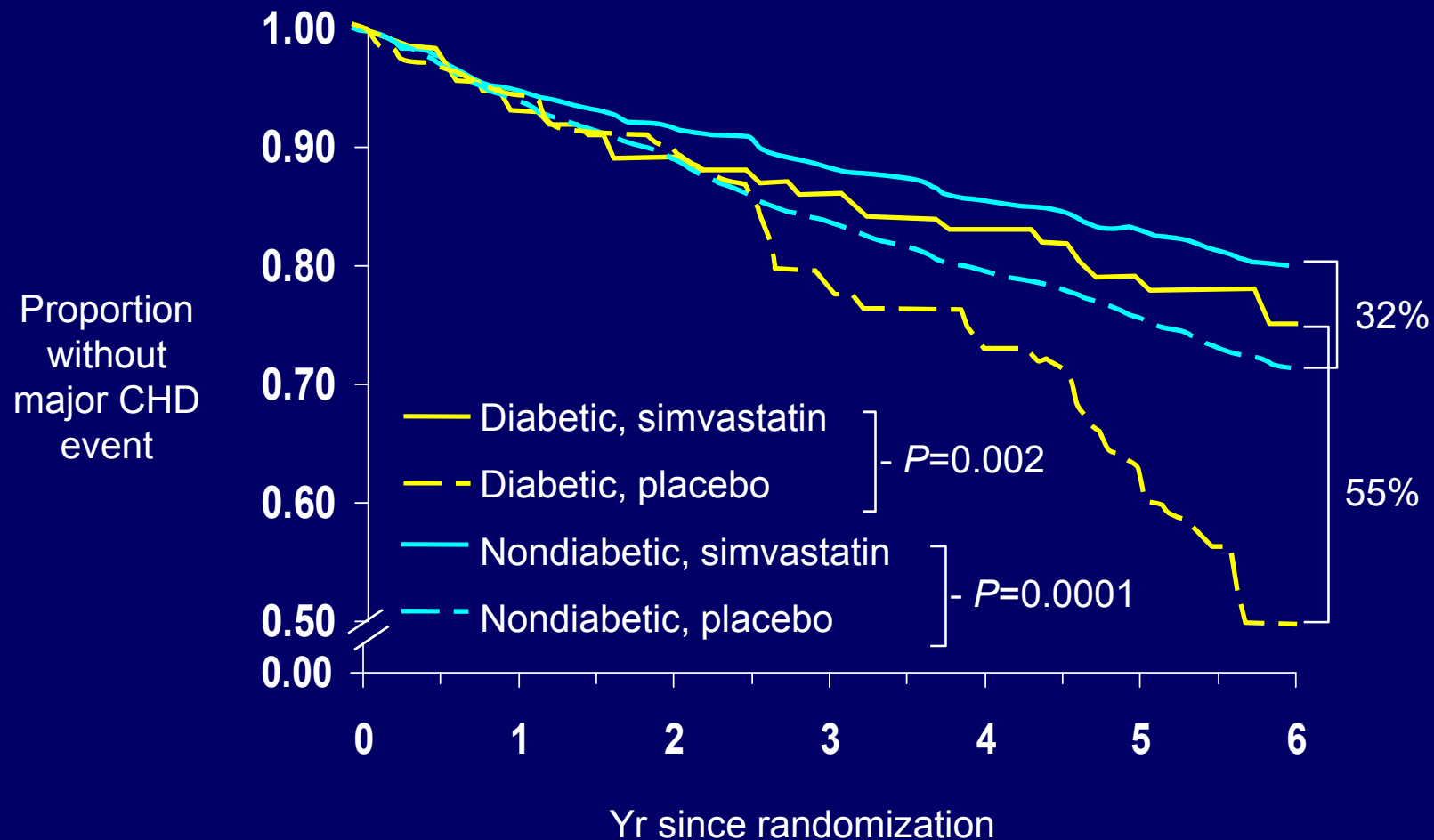


Pyörälä K et al. *Diabetes Care*. 1997;20:614-620.

## 4S: Total Mortality Reduction in a Subgroup of Patients With Diabetes

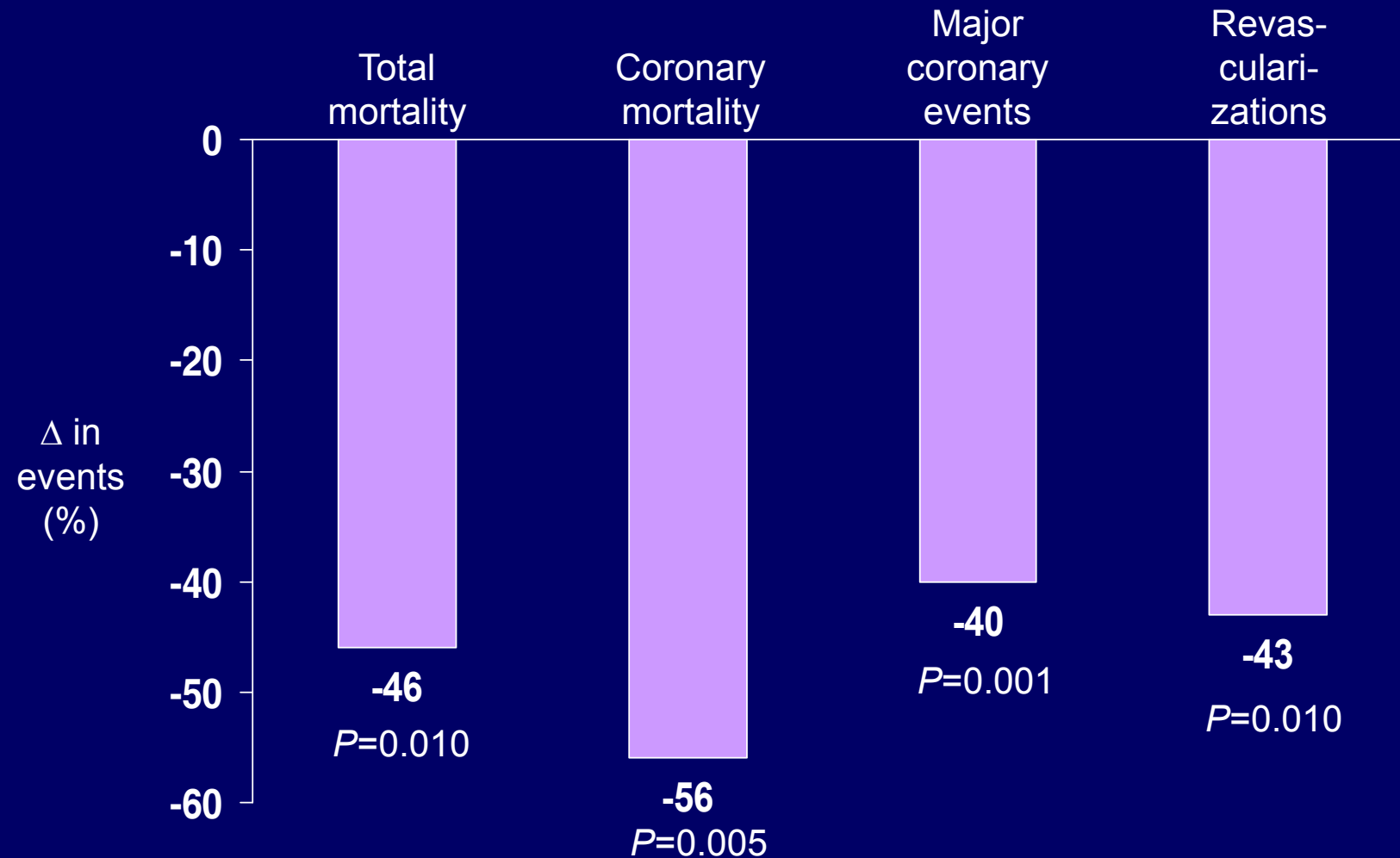


## 4S: Major CHD Event Reduction in a Subgroup of Patients With Diabetes





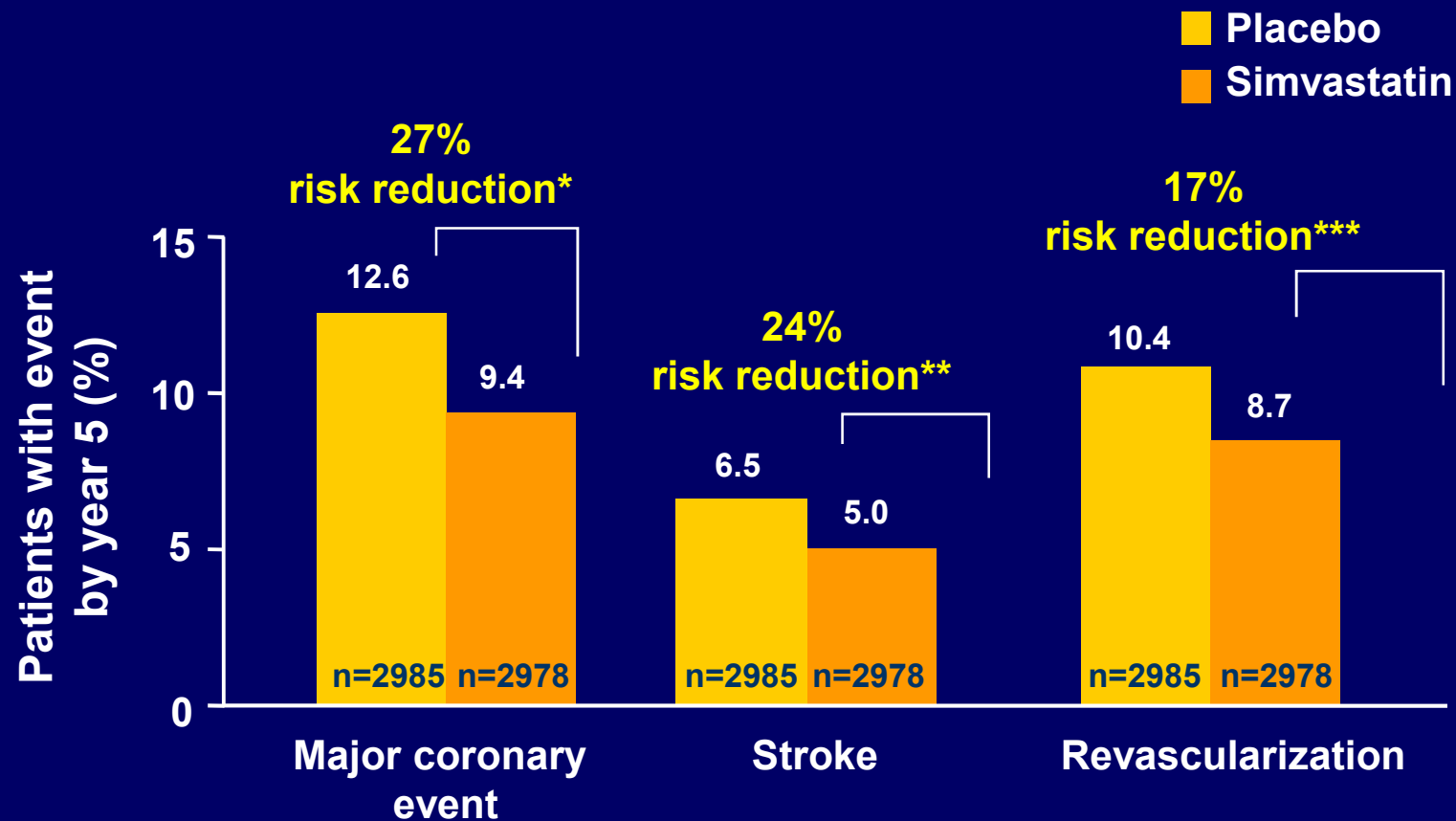
## 4S: Treatment Benefit in Subgroup With Impaired Fasting Glucose (FG 110-125 mg/dL)



Haffner SM et al. *Diabetes*. 1998;(suppl 1):A54. Abstract.

## *Impact of Simvastatin in Patients with Diabetes*

# **Major Coronary Events, Stroke, and Revascularization**

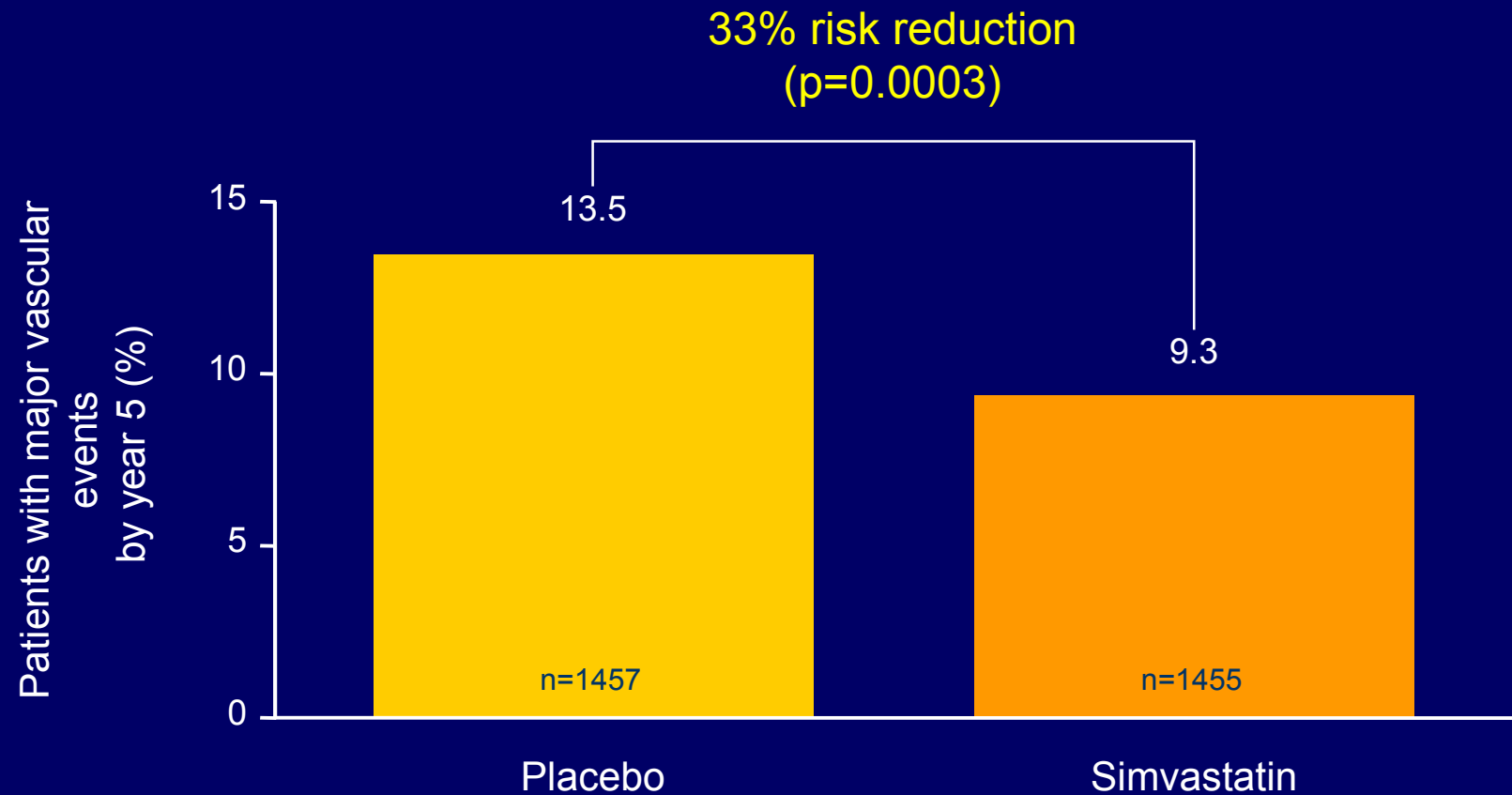


\*p<0.0001; \*\*p<0.01; \*\*\*p=0.02

Adapted from Heart Protection Study Collaborative Group *Lancet* 2003;361:2005-2016.

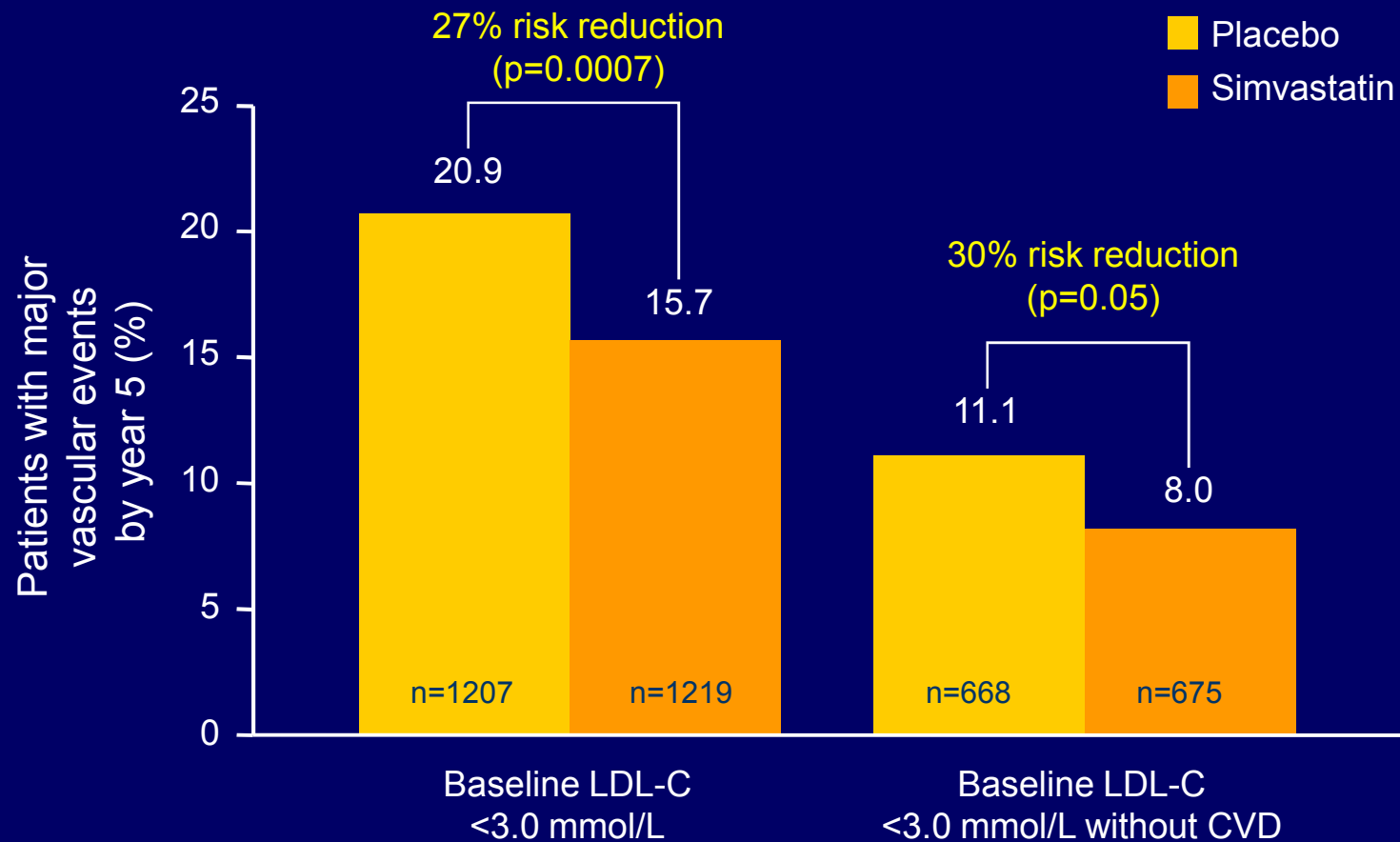
## ***Impact of Simvastatin in Patients with Diabetes and No Prior CVD***

### **Major Vascular Events**



Adapted from Heart Protection Study Collaborative Group *Lancet* 2003;361:2005-2016.

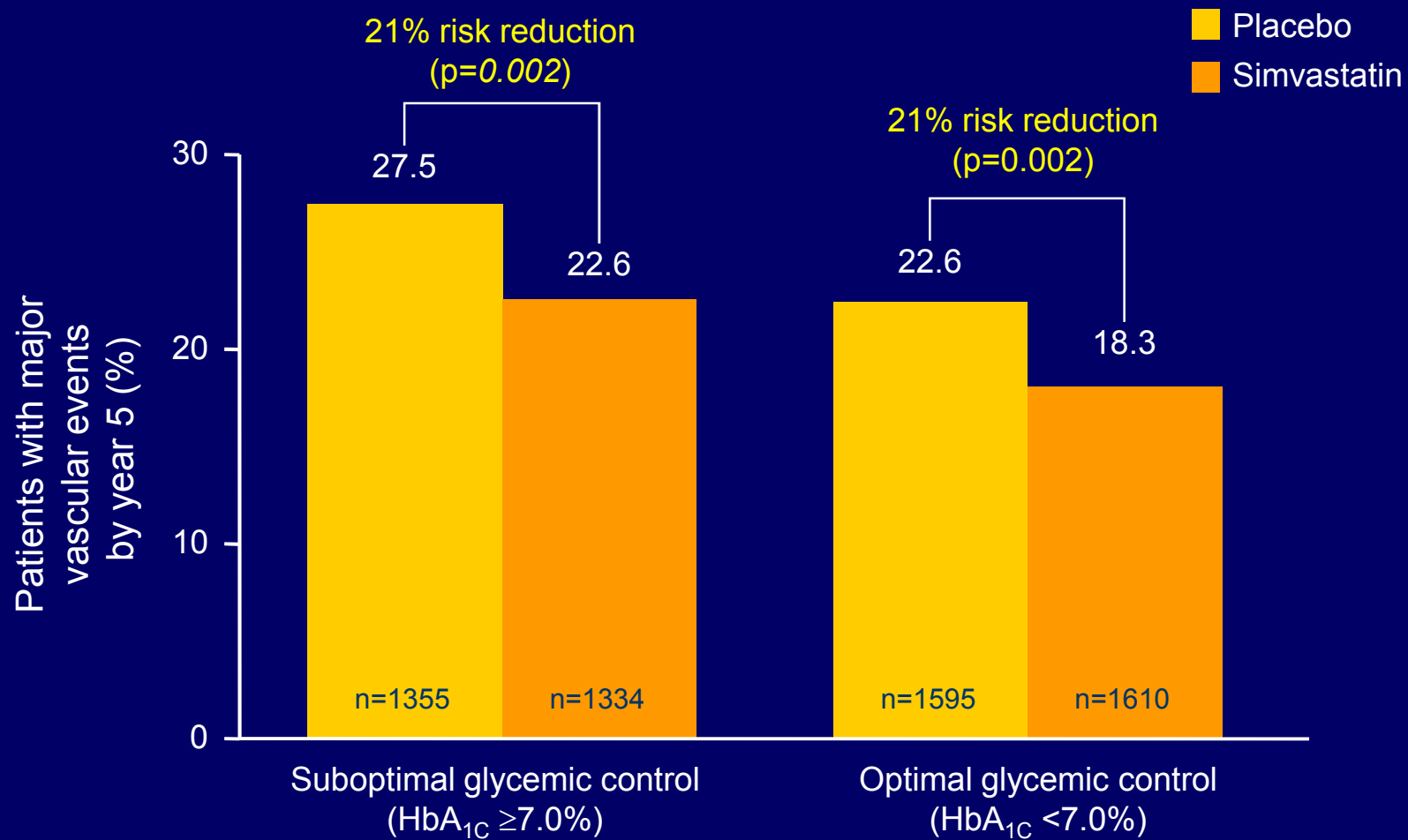
## Impact of Simvastatin in Patients with Diabetes With Low LDL-C



Adapted from Heart Protection Study Collaborative Group *Lancet* 2003;361:2005-2016.

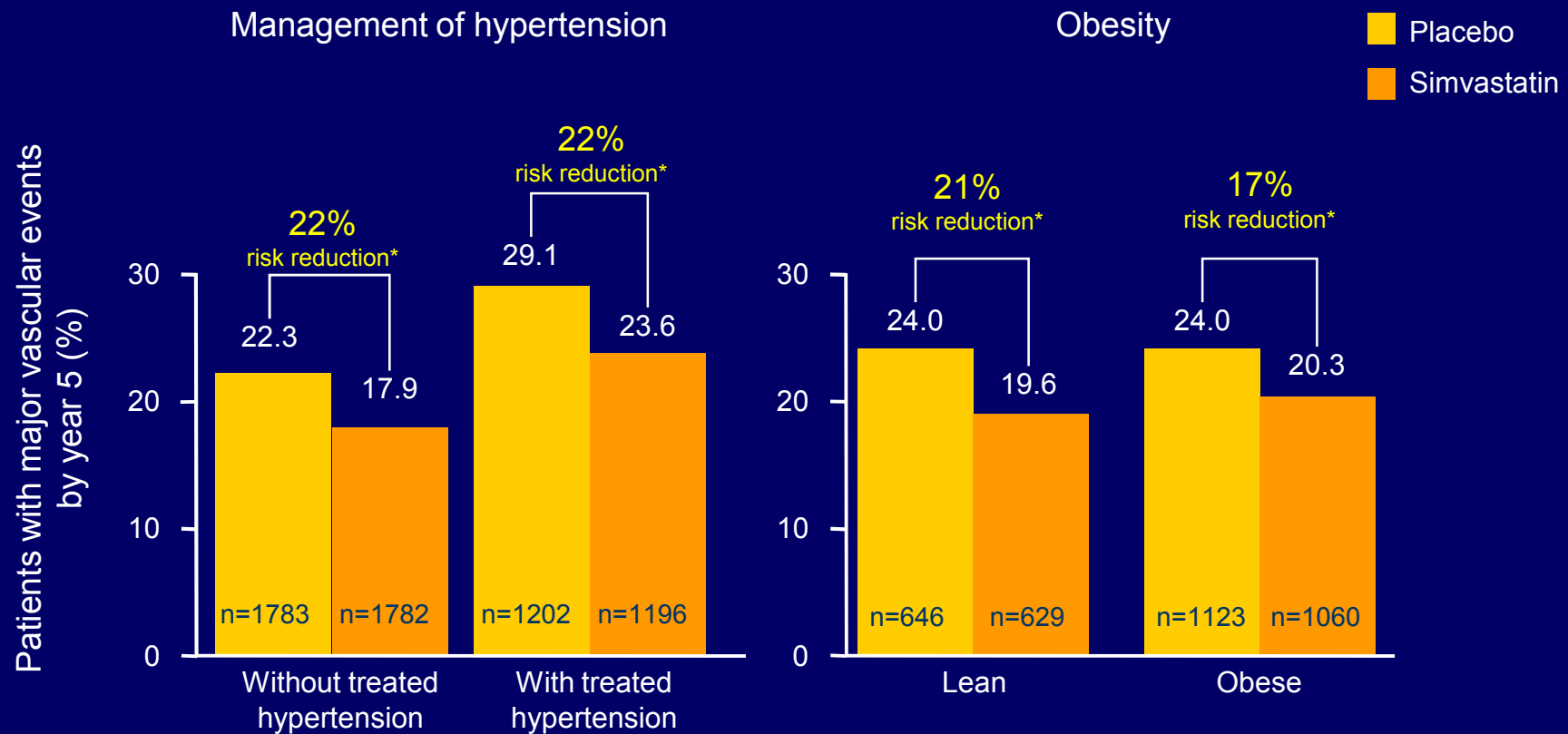
***Impact of Simvastatin in Patients with Diabetes***

***With or without Optimal Glycemic Control***



Adapted from Heart Protection Study Collaborative Group *Lancet* 2003;361:2005-2016.

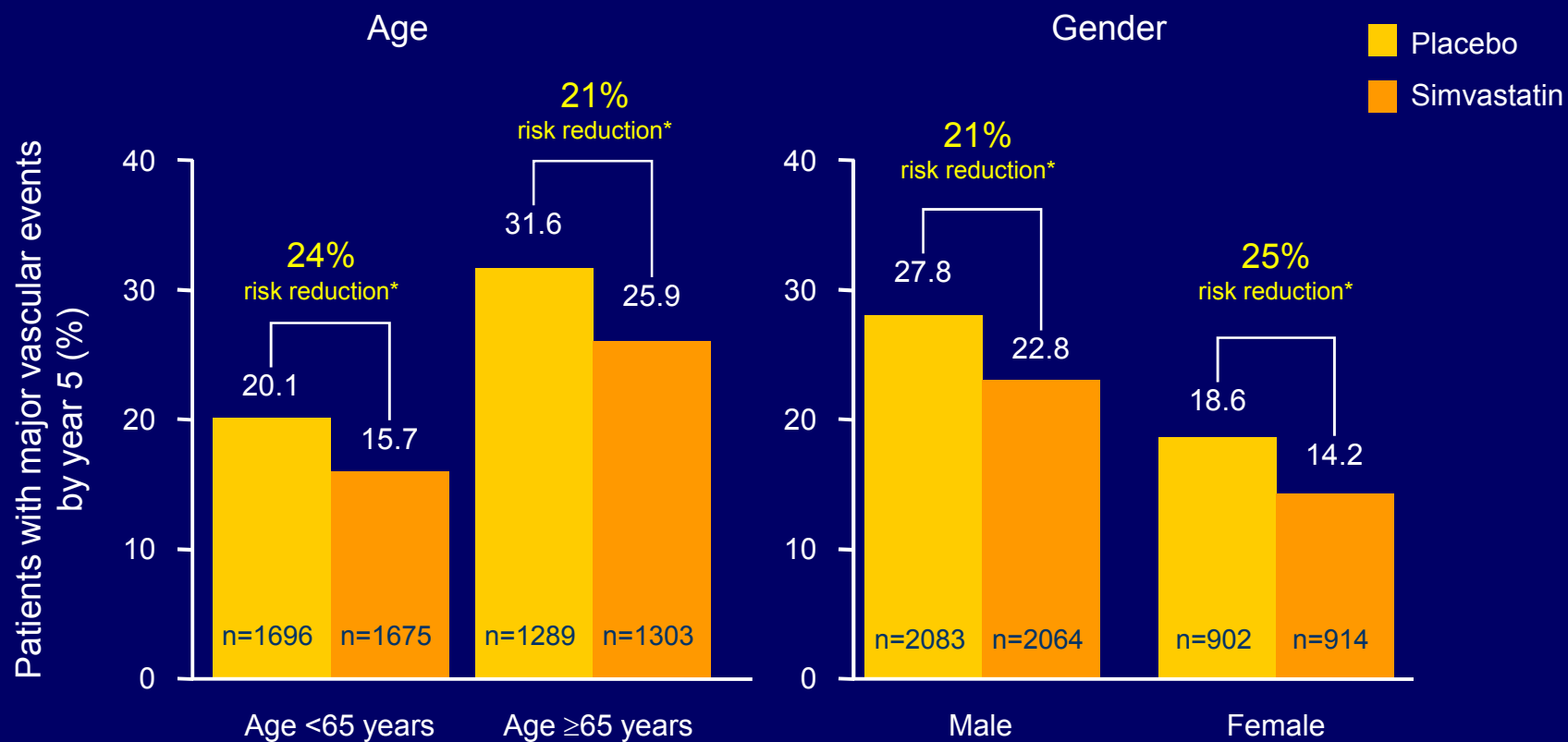
## Impact of Simvastatin in Patients with Diabetes with or without Treated Hypertension or Obesity



\*p<0.05

Adapted from Heart Protection Study Collaborative Group *Lancet* 2003;361:2005-2016.

## Impact of Simvastatin in Patients with Diabetes By Age and Gender



\*p<0.05

Adapted from Heart Protection Study Collaborative Group *Lancet* 2003;361:2005-2016.

## *Heart Protection Study*

# Diabetes Sub-Study

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- Almost 6000 men and women, aged 40–80 years with diabetes mellitus
  - 1981 persons with history of CHD
  - 3982 persons with no history of CHD
- People randomized to **simvastatin 40 mg** or placebo
- Mean duration of follow-up 5 years
- Objective—to evaluate the long-term benefits of simvastatin and/or antioxidants in people with diabetes with or without CHD regardless of cholesterol level
- Primary endpoints—*first* major coronary events\* and *first* major vascular events\*\*
- Statin not considered clearly indicated or contraindicated by patients' primary physicians

\*Nonfatal MI or death from coronary disease

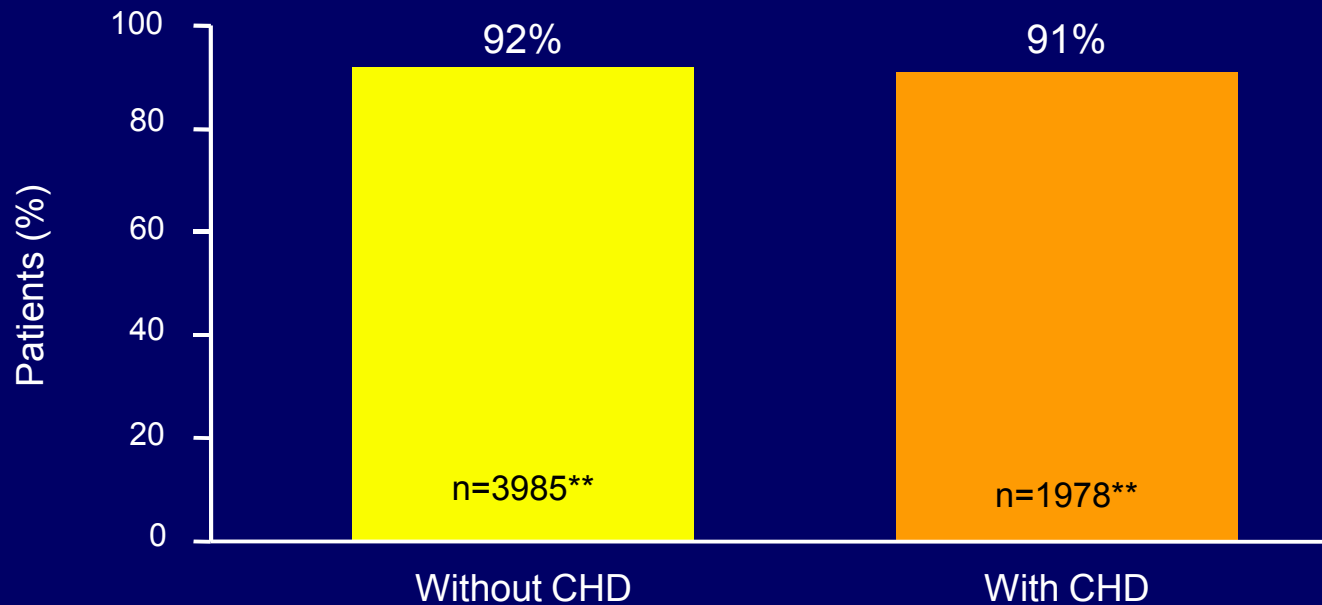
\*\*Major coronary events, stroke of any type, and coronary or noncoronary revascularizations

Adapted from Heart Protection Study Collaborative Group *Eur Heart J* 1999;20:725-741; Heart Protection Study Collaborative Group *Lancet* 2002;360:7-22; Heart Protection Study Collaborative Group *Lancet* 2003;361:2005-2016.



## ***Impact of Simvastatin on LDL-C***

### **Nine Out of 10 Patients with Diabetes Achieved Goal (LDLc <115mg/dl) \***



- Results from the five-year Heart Protection Study (HPS) of almost 6000 patients with diabetes with or without CHD indicated that 92% of patients with diabetes, but without CHD, and 91% of patients with CHD who received simvastatin 40 mg achieved the European Guidelines LDL-C treatment goal of <3 mmol/L (115 mg/dl)\*\*\*

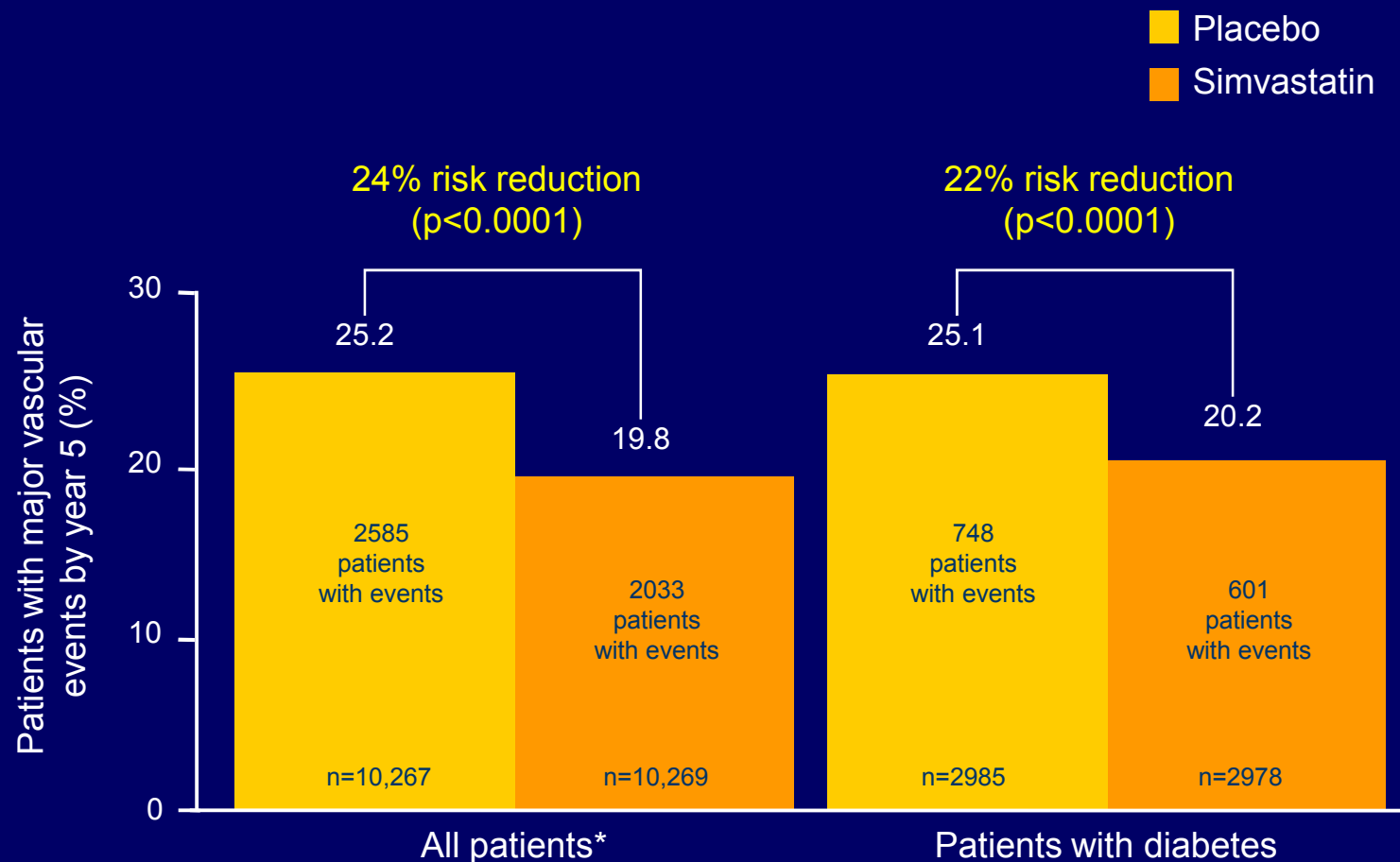
\*By the four-month point in HPS

\*\*These populations differ from those reported in later HPS publications (3982 and 1981) because three patients were reclassified after the four-month point. The percentages of patients achieving LDL-C goal are not affected.

\*\*\*Based on random sampling of patients with diabetes

Adapted from Armitage J, Collins R *Heart* 2000;84:357-360.

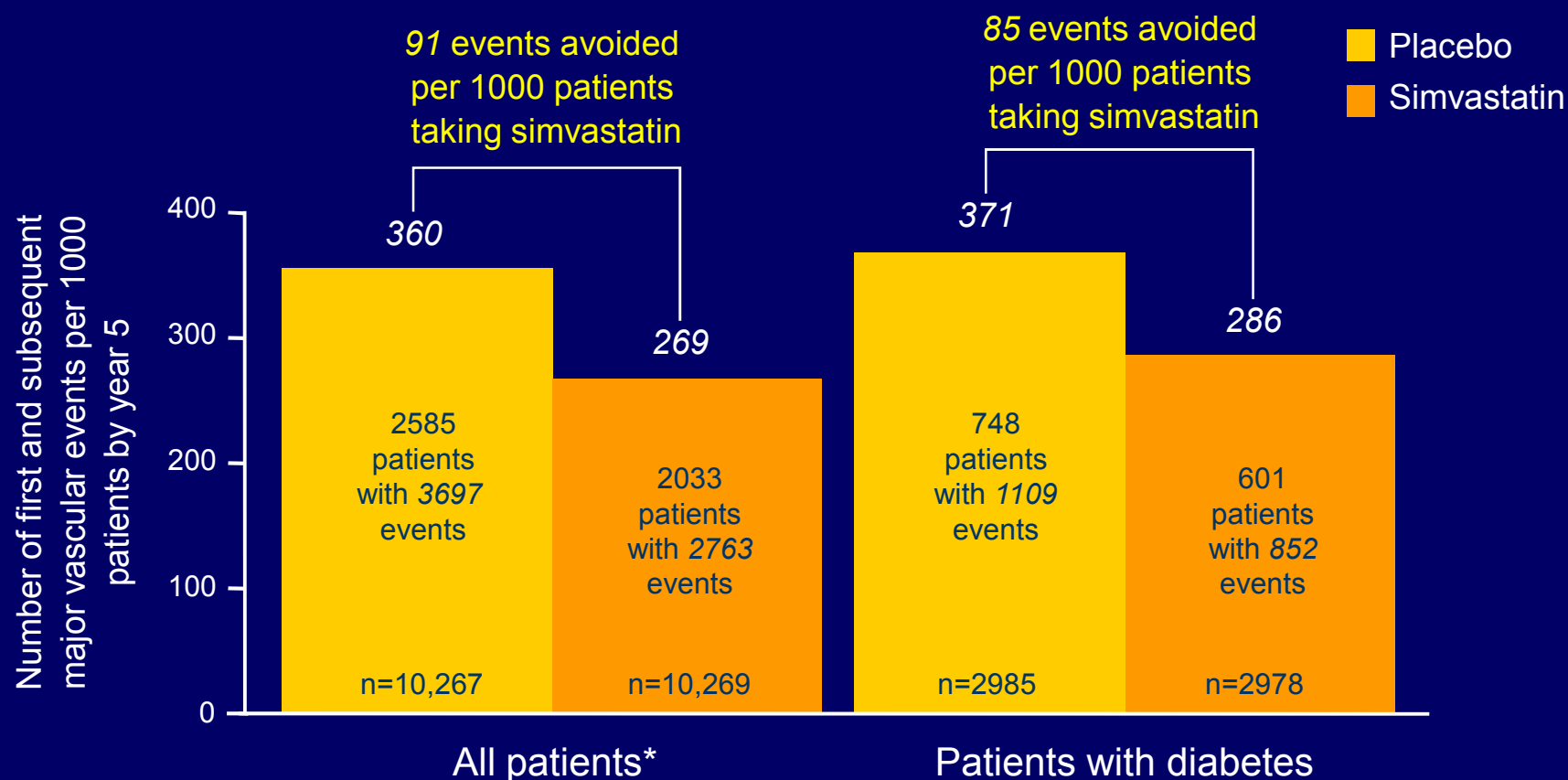
## First Major Vascular Events All Patients vs. Patients *with* Diabetes



\*Includes patients with CHD, occlusive disease of noncoronary arteries, diabetes, or treated hypertension

Adapted from Heart Protection Study Collaborative Group *Lancet* 2002;360:7-22; Heart Protection Study Collaborative Group *Lancet* 2003;361:2005-2016.

## First and Subsequent Major Vascular Events All Patients vs. Patients *with* Diabetes



\*Includes patients with CHD, occlusive disease of noncoronary arteries, diabetes, or treated hypertension  
Adapted from Heart Protection Study Collaborative Group *Lancet* 2003;361:2005-2016.