

# Metabolic Syndrome and Angioplasty

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# Metabolic Syndrome

## Definition

### Elevated Waist Circumference

- Men (>40 inches), Women (>35 inches)

### Elevated Triglycerides (>150)

### Reduced HDL

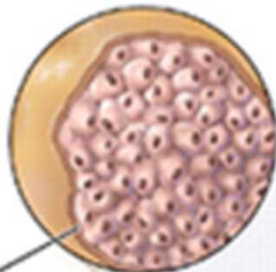
- (Men <40, Women <50)

### Elevated BP (>130/85 or on BP meds)

### Elevated Fasting Glucose (≥100 or on meds)

**PANCREAS**

- Ⓡ β-cell growth
- Ⓡ β-cell survival
- Ⓡ Glucose sensing



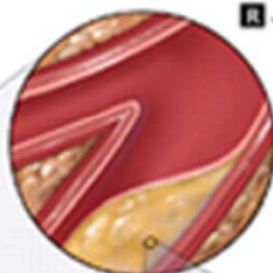
Islet

- Ⓢ ↑ Sympathetic tone
- Ⓡ ↓ Hepatic glucose output via vagal n.

- Ⓡ ↑ Glucose oxidation
- Ⓡ ↓ FFA oxidation

**MYOCARDIUM**

- Ⓡ ↓ Plaque formation



**ARTERIES**

- Ⓡ ↓ Plaque formation

**LIVER**

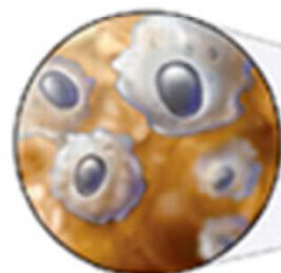
- Ⓢ ↑ FFA, TG secretion
- Ⓡ ↓ Glucose production
- Ⓡ ↑ Lipoprotein uptake

**MACROPHAGES**

- Ⓡ ↑ Survival



**INSULIN**



**MACROPHAGES**

- Ⓢ ↑ Fat infiltration

**FAT**

- Ⓢ ↑ TG synthesis
- Ⓡ ↓ Lipolysis

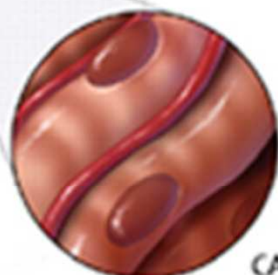


**RESISTANCE VESSELS**

- Ⓡ Vasodilation
- Ⓢ Vasoconstriction

**MUSCLE**

- Ⓡ ↑ Glucose uptake
- Ⓡ ↑ Glycogen synthesis



**CAPILLARIES**

- Ⓡ ↑ Capillary recruitment
- Ⓡ ↑ Transendothelial insulin transport



CONTRIBUTIONS

# Metabolic Syndrome and the Carotid Artery Structure in Institutionalized Elderly Subjects

## Three-City Study

Pe Empana, Mahmoud Zureik, Jerome Gariépy, Dominique Courbon, Jean Francois Dartigues, Karen Ritchie, Christopher J. Everson, Pierre Ducimetiere

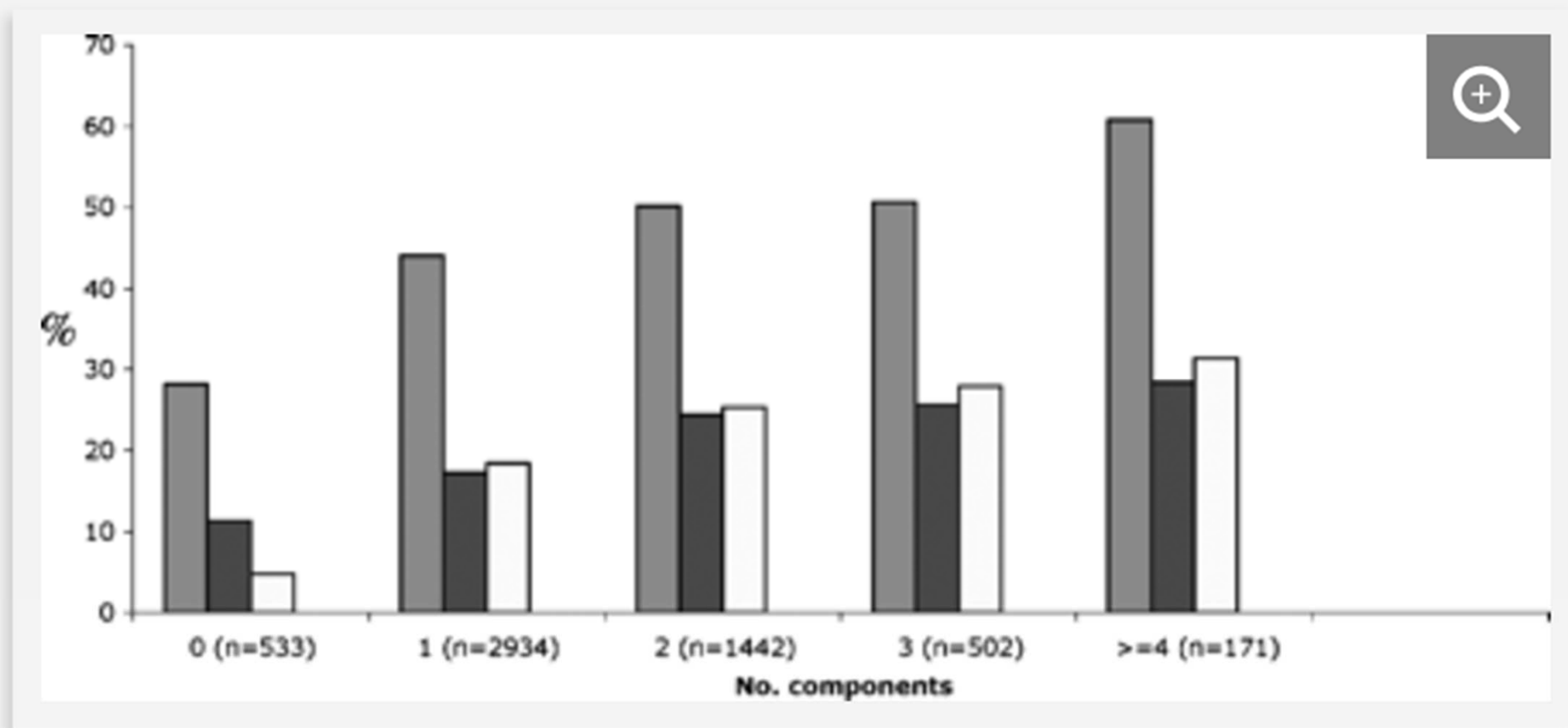
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**DOI** <https://doi.org/10.1161/01.STR.0000257983.62530.75>

Stroke. 2007;38:893-899

Originally published February 26, 2007



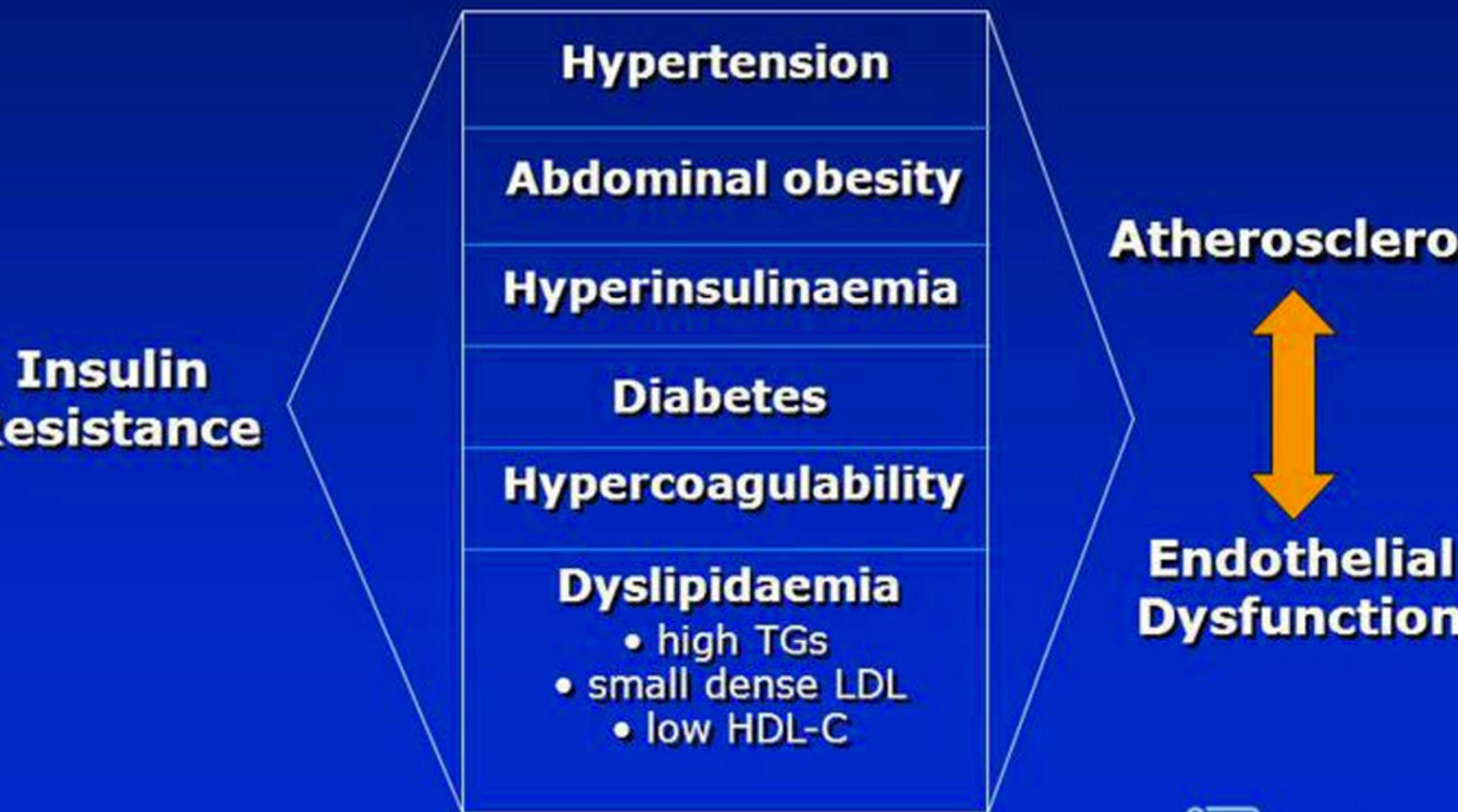


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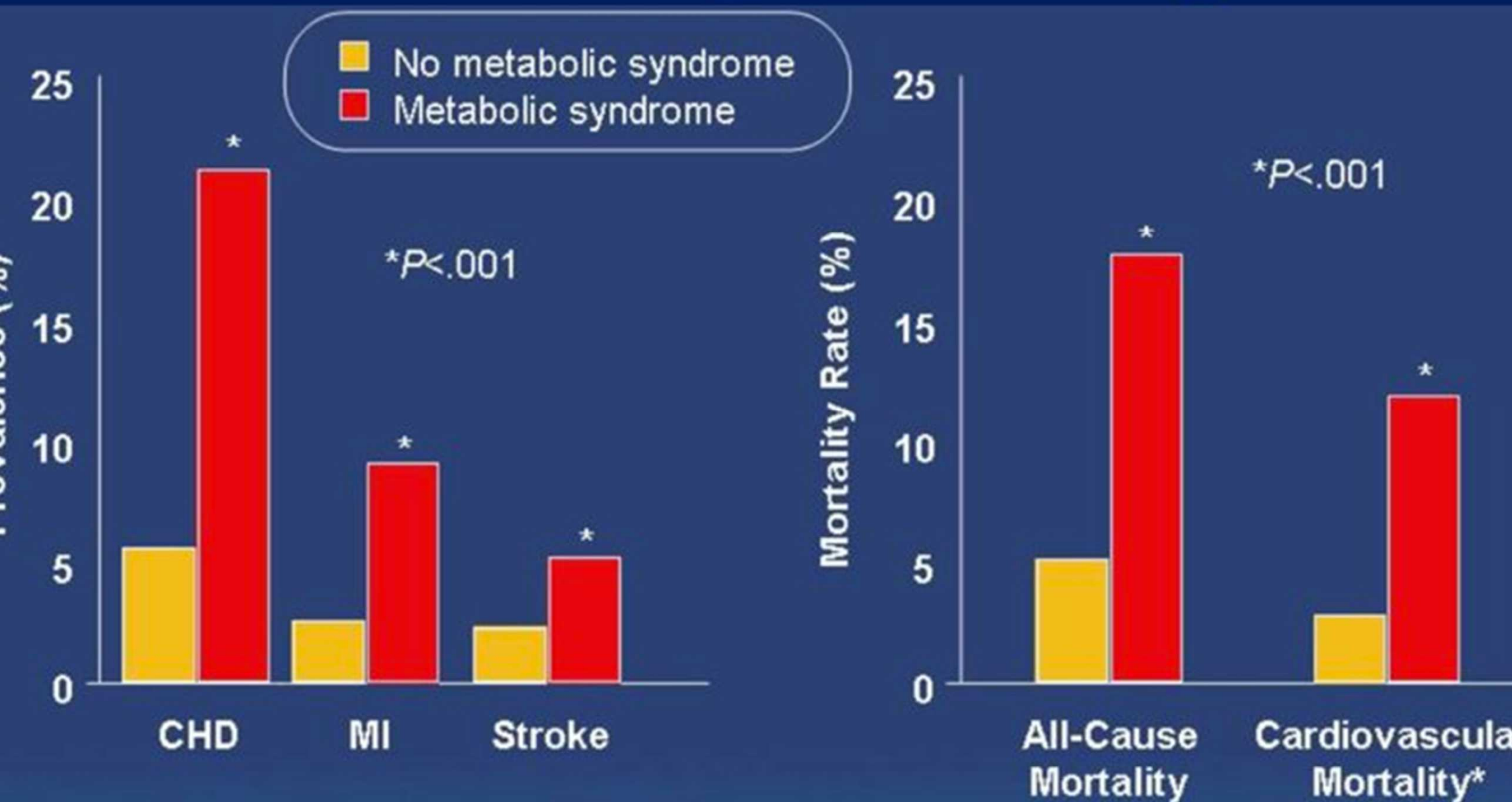
frequency of plaques, high CCA-IMT level (upper quintile), and high carotid lumen diameter (upper quintile) according to the number of components of the metabolic syndrome in the study. The Three City Study. Bars represent respectively carotid plaques (gray), high (5th quintile) intima-media thickness (dark gray), and high (5th quintile) lumen diameter (white).

<0.001

# The Metabolic Syndrome and Associated CVD Risk Factors



# CV Morbidity and Mortality

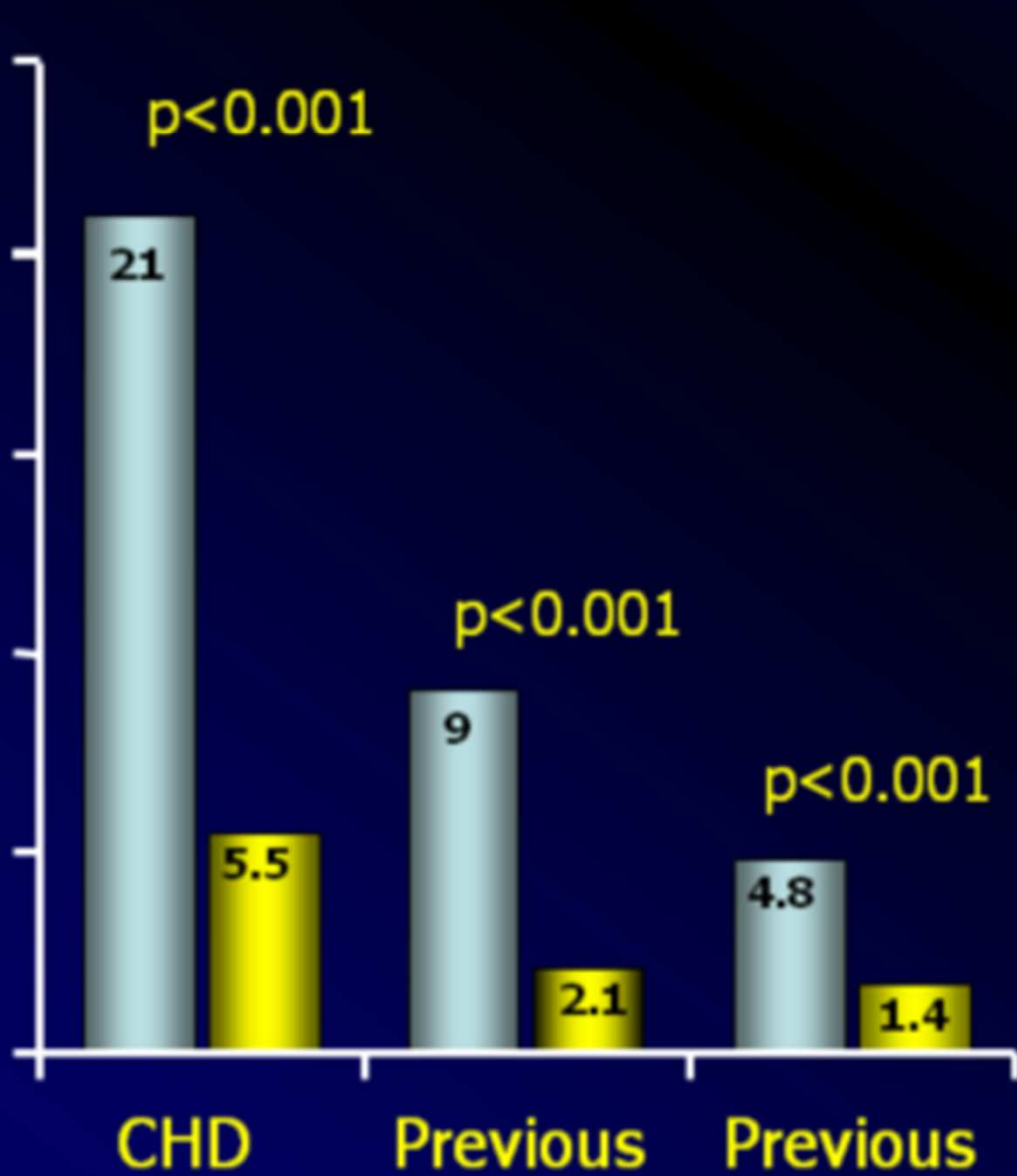


\* Cardiovascular mortality was defined using ICD-9 (codes 390-459) before 1997 and ICD-10 (codes 100-199)

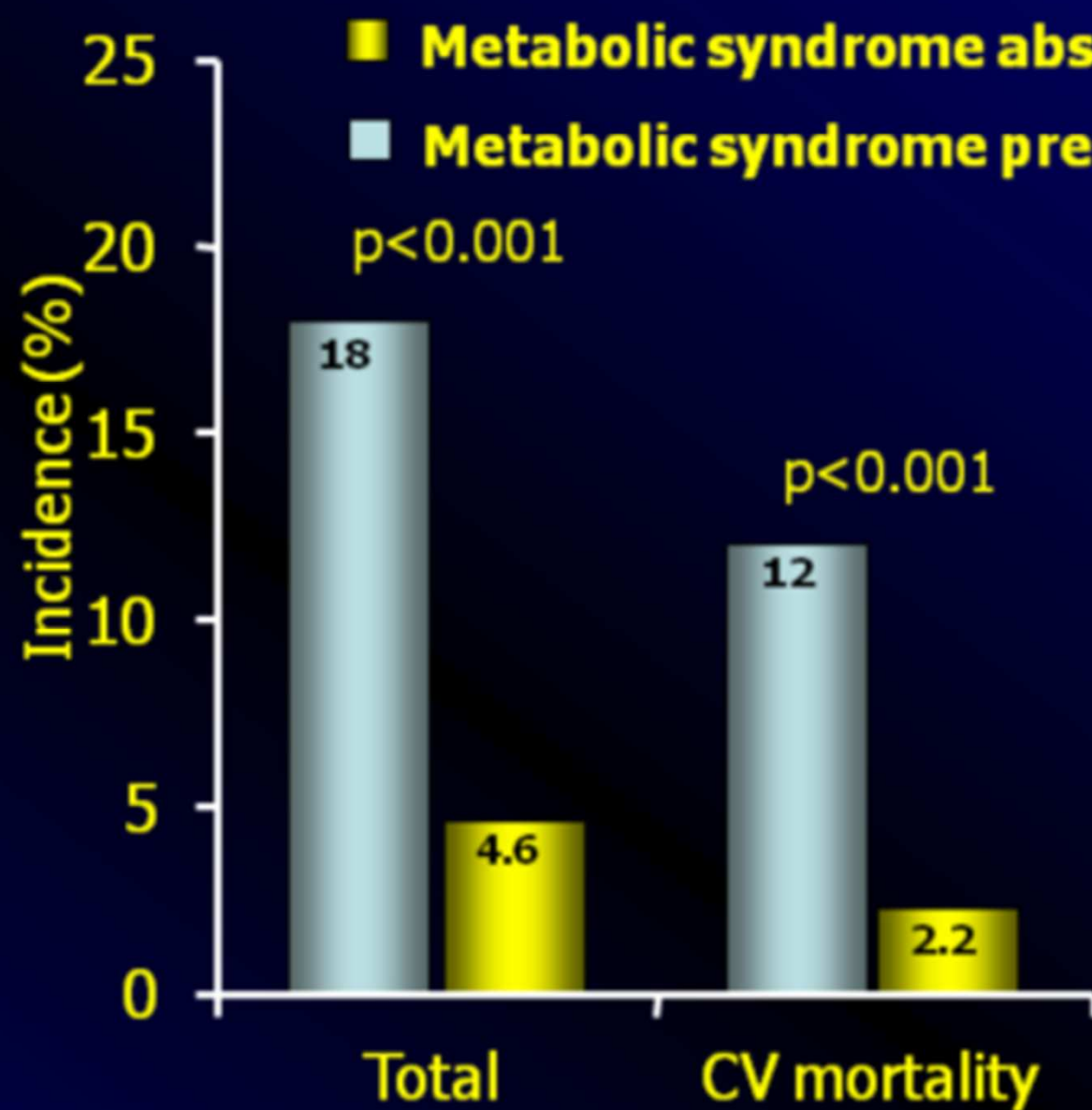


# Morbidity and mortality

## Morbidity



## Mortality



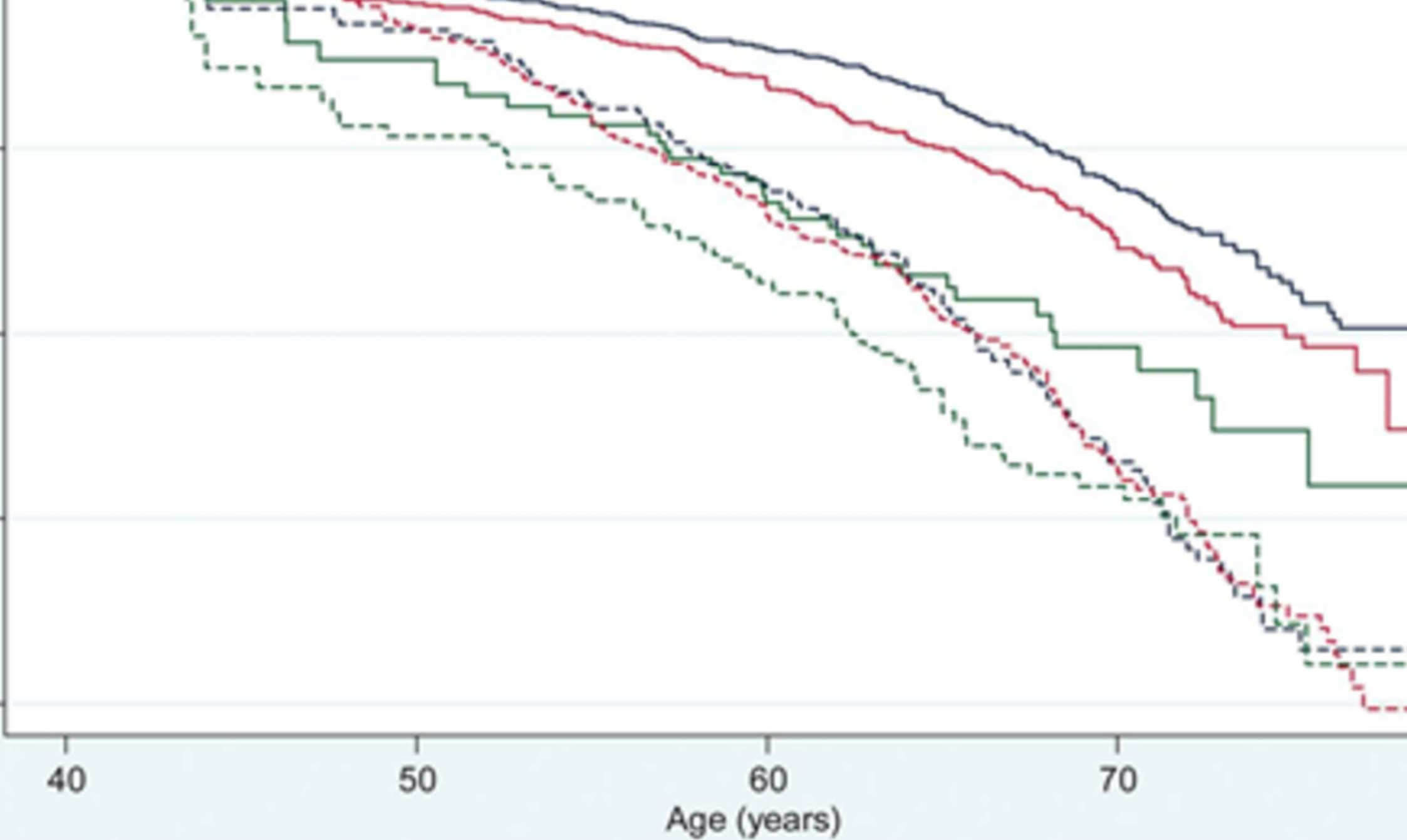


# Metabolically healthy obesity and the risk of cardiovascular disease and type 2 diabetes: Whitehall II cohort study

Marino Hinnouho ; Sébastien Czernichow; Aline Dugravot; Hermann Nabi-Brunner; Mika Kivimaki; Archana Singh-Manoux

Heart J (2014) 36 (9): 551-559. DOI: <https://doi.org/10.1093/eurheartj/ehu>

Published: 26 March 2014 **Article history** ▼



— Metabolically healthy-normal weight

— Metabolically healthy-overweight

- - - - Metabolically unhealthy-normal weight

- - - - Metabolically unhealthy-overweight



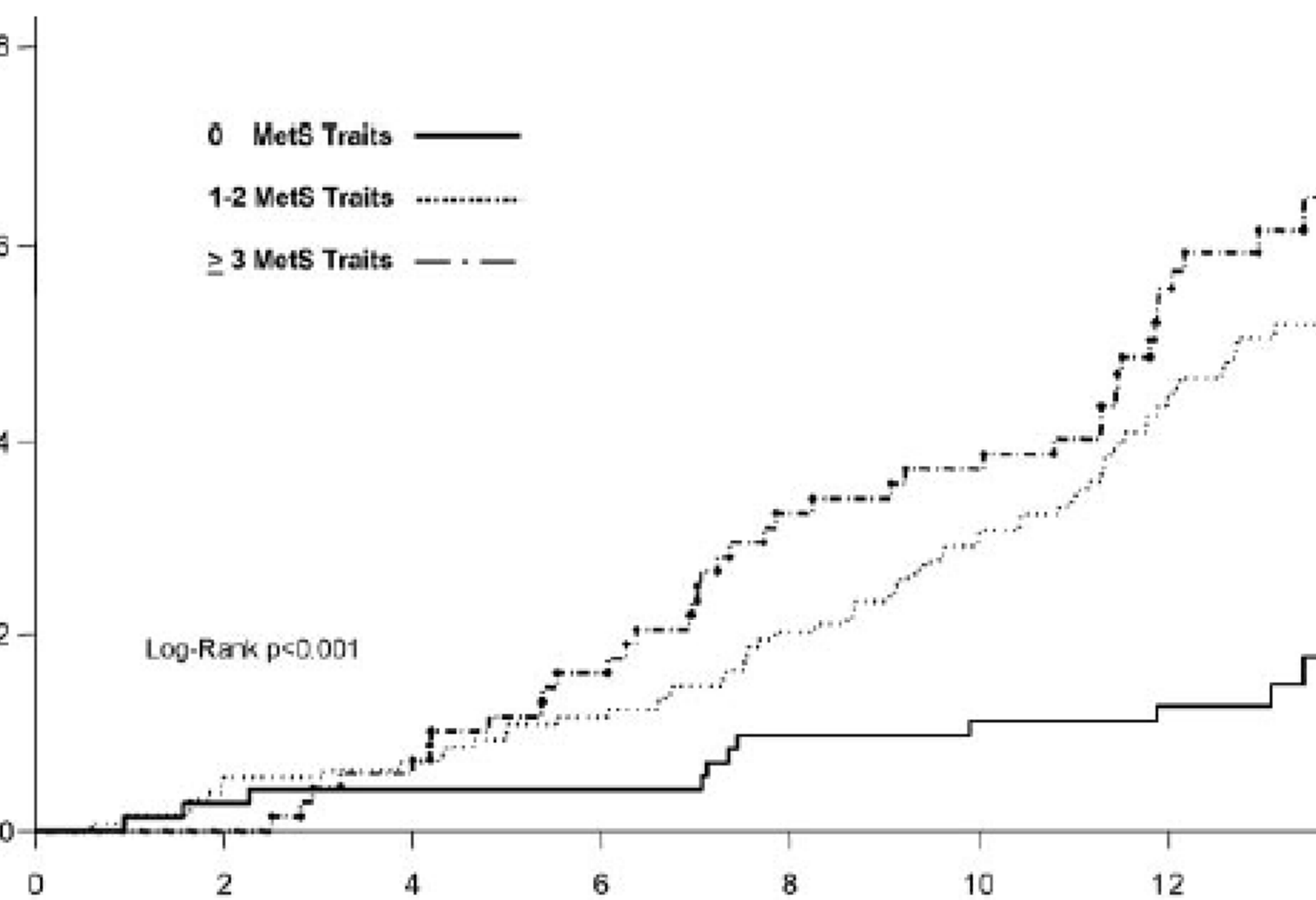
# Metabolic Syndrome, Inflammation, and Risk of Symptomatic Peripheral Artery Disease in Women

## A Prospective Study

David Conen, MD, MPH; Kathryn M. Rexrode, MD, MPH; Mark A. Creager, MD;  
Paul M. Ridker, MD, MPH; Aruna D. Pradhan, MD, MPH

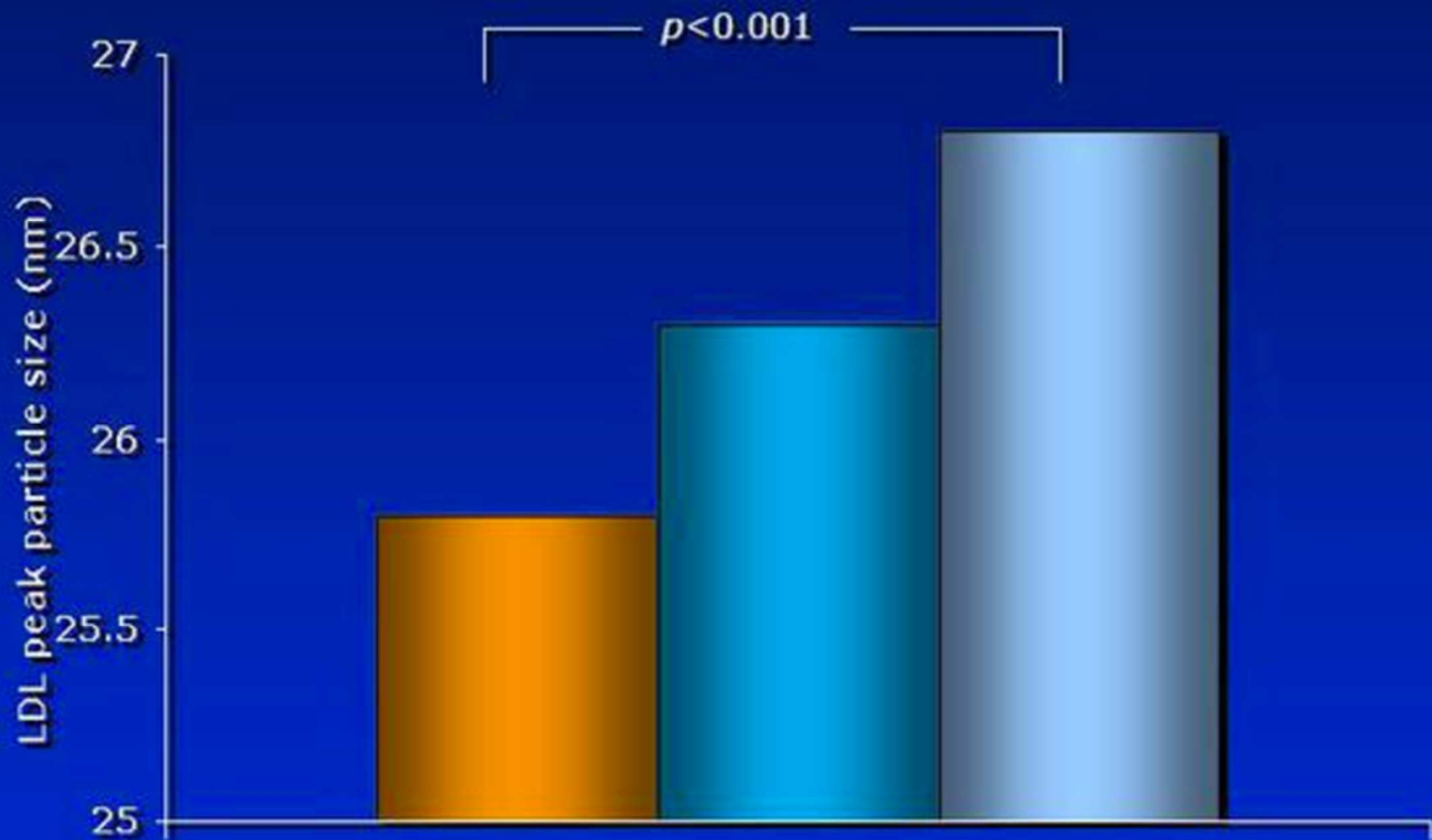
**Background**—The metabolic syndrome (MetS) is associated with incident myocardial infarction and stroke and is associated with subclinical inflammation; however, prospective data pertaining to MetS and future peripheral artery disease (PAD) are sparse, with few studies examining the role of inflammation. We therefore evaluated the relationship between MetS, inflammation, and incident PAD.

**Methods and Results**—We conducted a prospective cohort study among 27 111 women free of baseline cardiovascular disease who were participating in the Women's Health Study. Subjects were followed for incident symptomatic PAD (n=114; median cohort follow-up 13.3 years). We used Cox proportional hazards models to compare PAD risk in women with and without MetS. We also evaluated relationships between MetS and subclinical inflammation, measured by high-sensitivity C-reactive protein and soluble intercellular adhesion molecule-1 and adjusted for traditional risk markers in multivariable models. Women with MetS had a 62% increased risk of future PAD (hazard ratio 1.62, 95% confidence interval 1.10 to 2.38). After multivariable adjustment, MetS remained significantly associated with incident PAD (adjusted hazard ratio 1.48, 95% confidence interval 1.01 to 2.18), with a 21% risk increase per additional MetS-defining factor (adjusted hazard ratio 1.21, 95% confidence interval 1.06 to 1.39). In women with and without MetS, respectively, median levels of high-sensitivity C-reactive protein were 4.0 versus 1.5 mg/L ( $P<0.0001$ ), and median levels of soluble intercellular adhesion molecule-1 were 374 versus 333 ng/mL ( $P<0.0001$ ). When high-sensitivity C-reactive protein and soluble intercellular adhesion molecule-1 were added to multivariable models, risk associated with MetS was substantially attenuated and no longer significant (hazard ratio 1.14, 95% confidence interval 0.75 to 1.73).





# AIR: LDL Particle Size Is Related to the Metabolic Syndrome



■ **Metabolic Syndrome (n=62)**

■ **No Metabolic syndrome but 1 or more risk factors (n=252)**

# Plaque Characteristics

Metabolic Syndrome Plaques (versus plaques of patients without metabolic syndrome)

- Longer lesions
- more plaque burden
- greater necrotic core
- more calcification
- more MACE events over time

# ASA/Plavix resistance

Metabolic Syndrome associated with reduced response to Plavix in CAD patients

- Wu *J Geriatr Cardiol* 2015
- Feldman *Am Heart J* 2014
- Paul *Int J Appl Basic Med Res* 2013

# Coronary Stenting

2x increased mortality after PCI

MACE events increased 30%

Restenosis increased 35%

*Xu Atherosclerosis 2012*



# Peripheral Interventions

Controversial

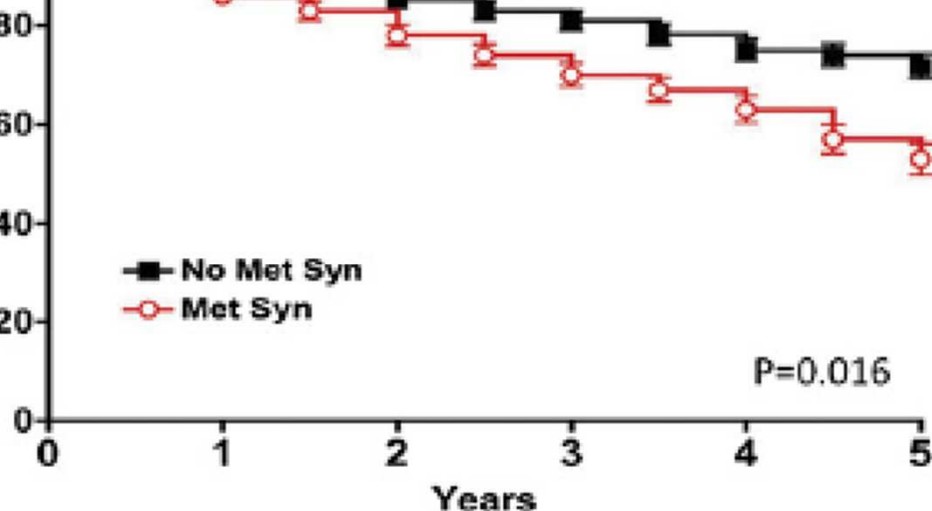
One study showed no difference in PAD interventions in CLI patients with metabolic syndrome, unless they also had overt DM

# Peripheral Interventions

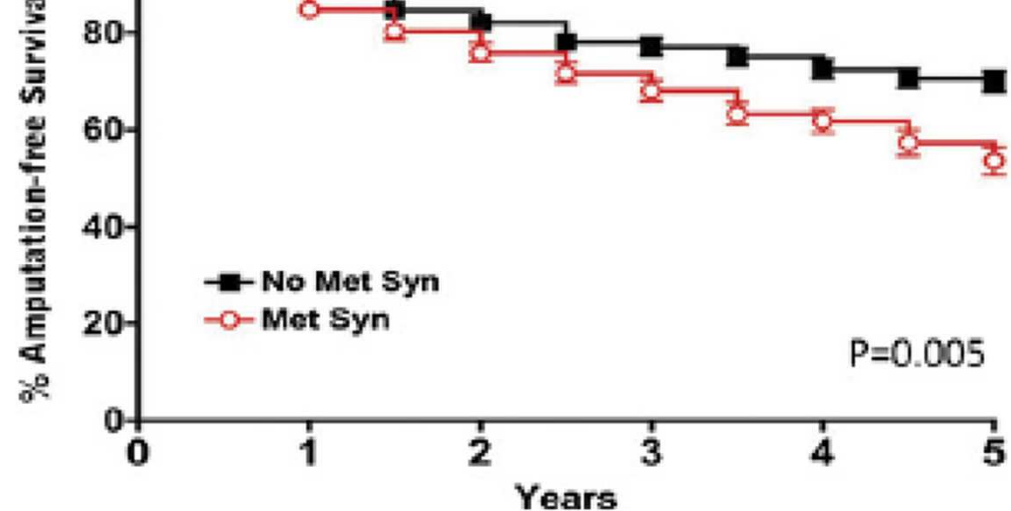
Review of SFA treatments in 1018 limbs

Metabolic Syndrome associated with

- more complex lesions
- more complex treatments
- equivalent mortality
- more limb events
- worsened clinical failure
- lower amputation free survival

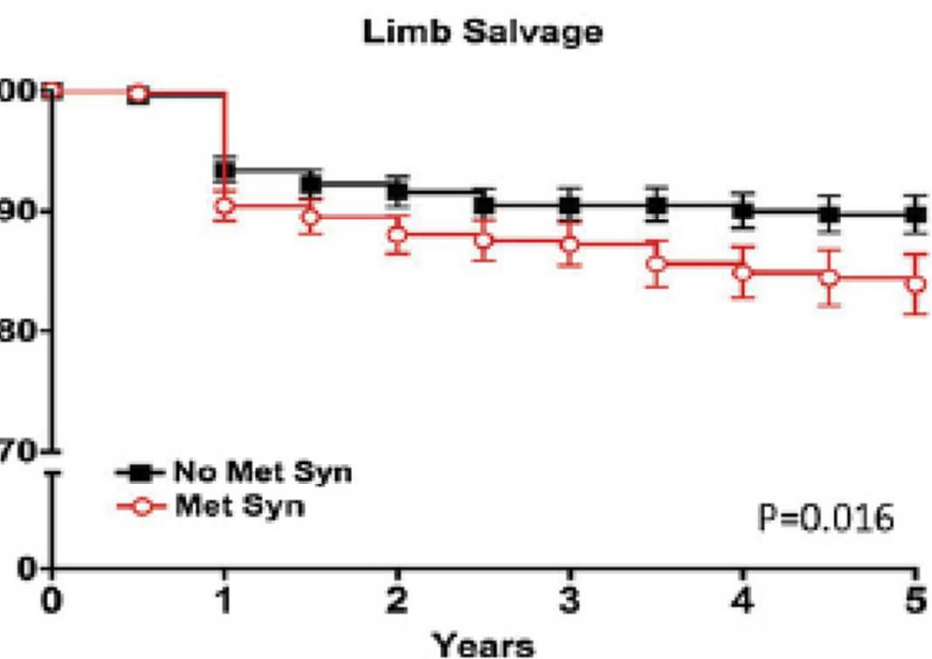


Year	0	1	2	3	4	5
No Metabolic Syndrome	408	380	335	304	263	223
Metabolic syndrome	330	296	259	216	171	126

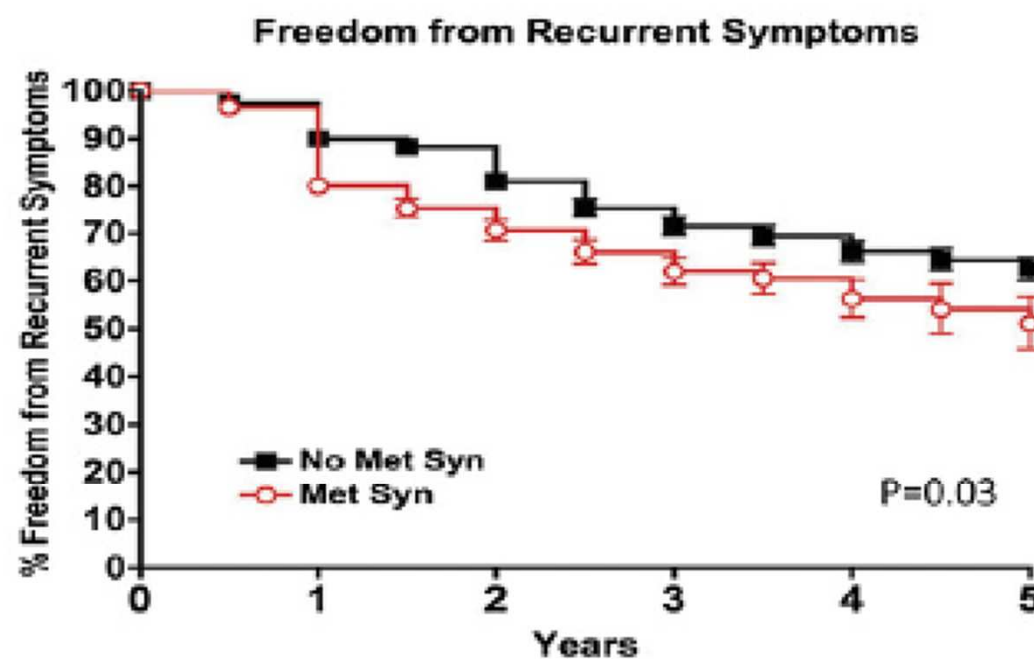


Year	0	1	2	3	4
No Metabolic Syndrome	545	542	456	404	374
Metabolic syndrome	474	472	373	314	251

**B**



Year	0	1	2	3	4	5
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Year	0	1	2	3	4
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# Iliac Interventions

Study of restenotic lesions more strongly associated with metabolic syndrome than gender, DM, multilevel disease, previous type of intervention, and even smoking

Davies *J Endovasc Ther* 2011

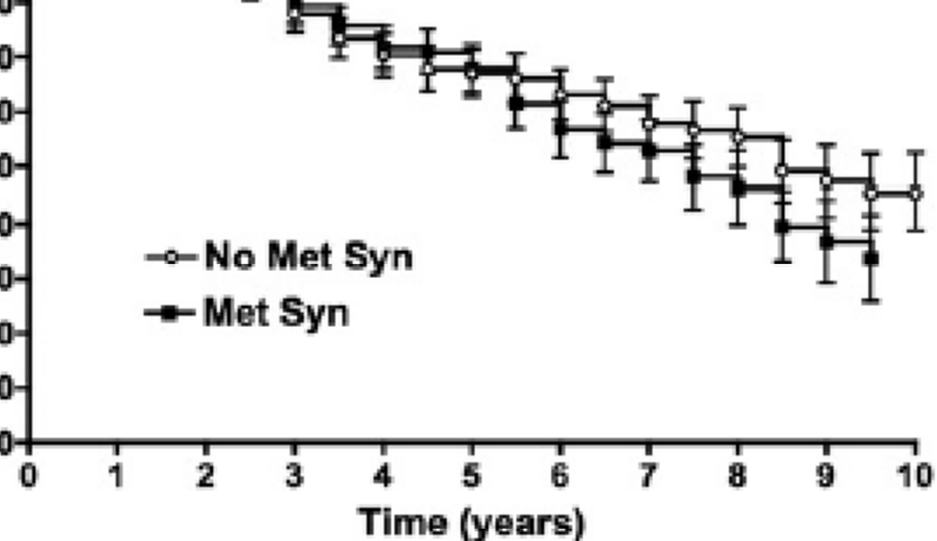


# Renal Interventions

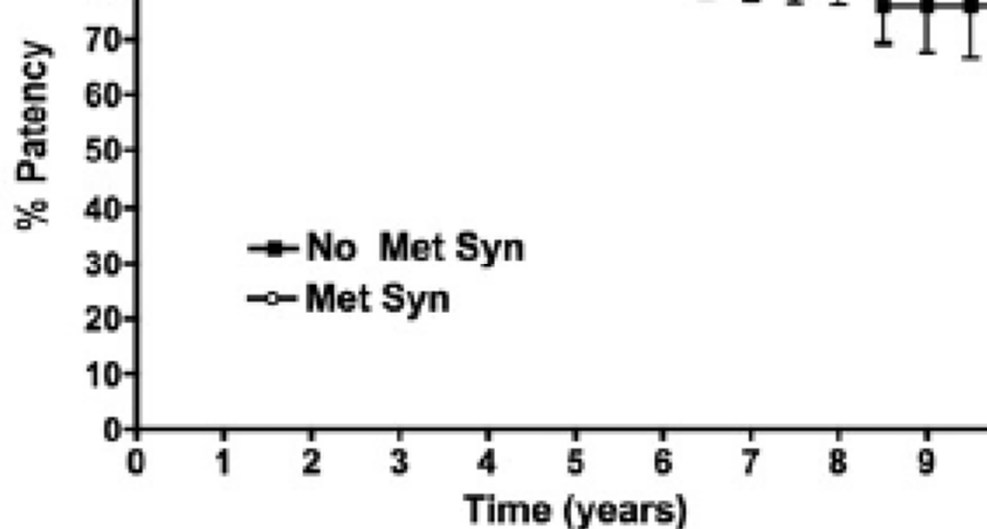
Study of 427 patients with Renal Artery Interventions

Outcomes of Metabolic Syndrome vs not

- Equal Morbidity/Mortality
- Higher restenosis rates
- Lower clinical benefit
- More progression to dialysis dependence
- Statins had no impact

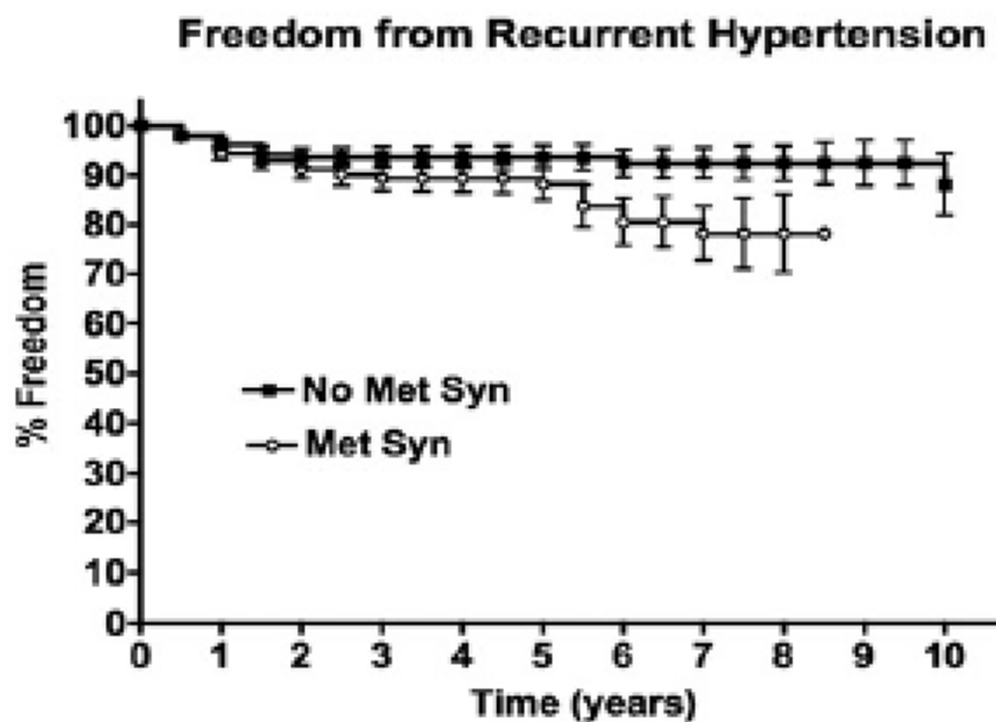
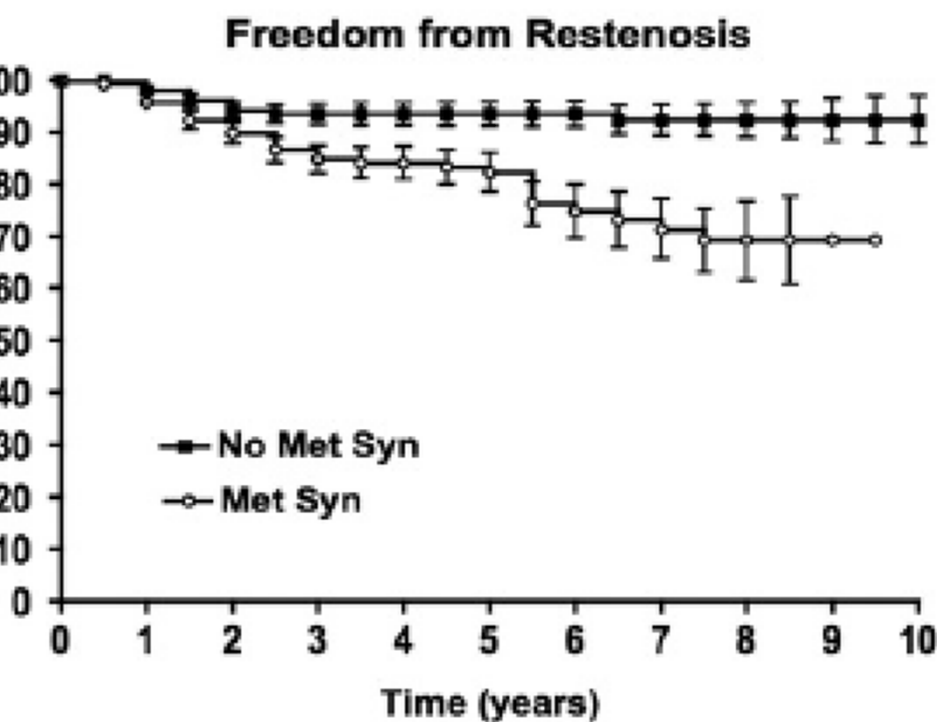


	0	1	2	3	4	5	6	7	8	9	10
No Met Syn	205	162	132	105	88	73	63	51	41	25	23
Met Syn	222	176	142	112	89	67	47	38	23	12	9



Year	0	1	2	3	4	5	6	7	8
No Met Syn	282	194	138	104	86	64	50	35	31
Met Syn	310	227	174	127	100	70	44	33	15

**B**



# Renal Reinterventions

Study of 80 restenotic lesions (19%) incidence in follow up study from larger group

Metabolic syndrome (73%) more common than hyperlipidemia or DM

Female gender, younger age strong predictors

Most patients with restenosis presented with hypertension suggesting clinical follow up is adequate

# Carotid Revascularization

Retrospective study of CEA and CAS

Metabolic Syndrome patients had higher stroke rate in  
CEA vs non metabolic

CAS stroke rate unaffected

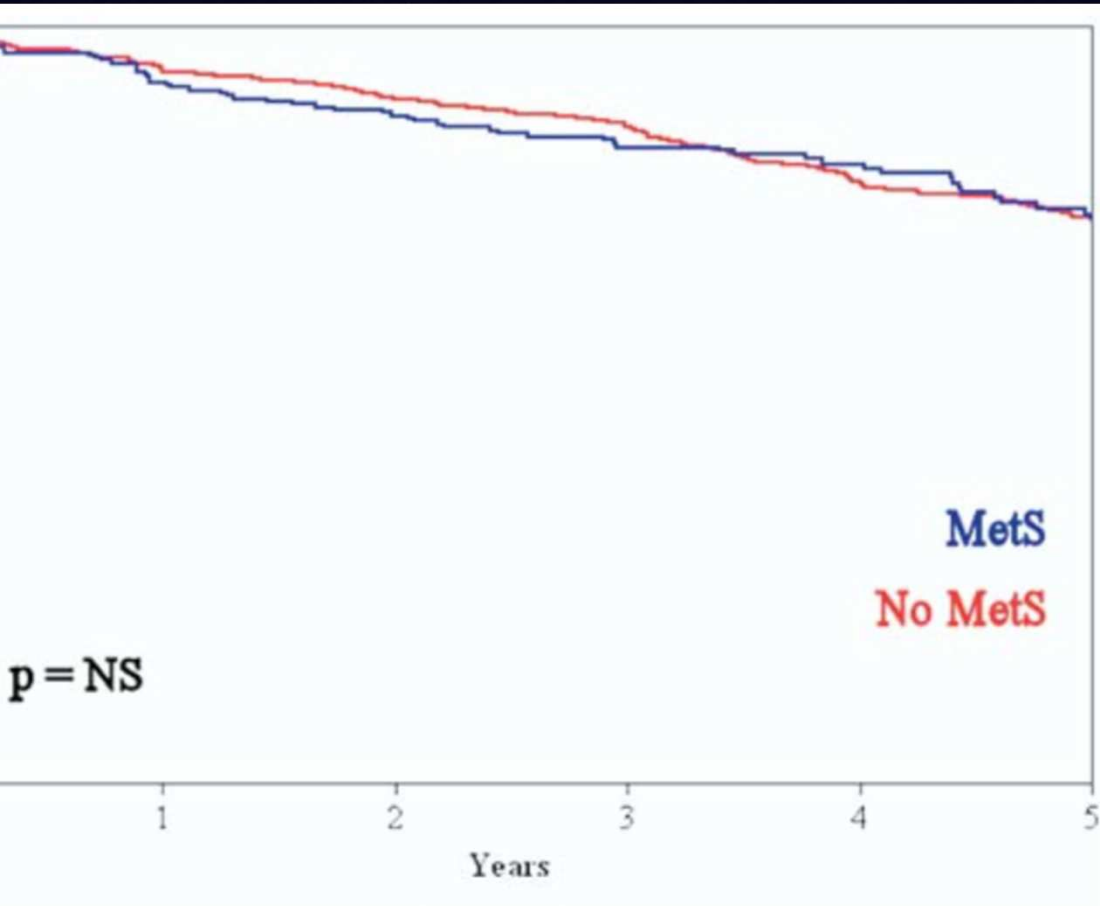
Higher rates of MAE and MI

DM + metabolic syndrome = worst outcomes

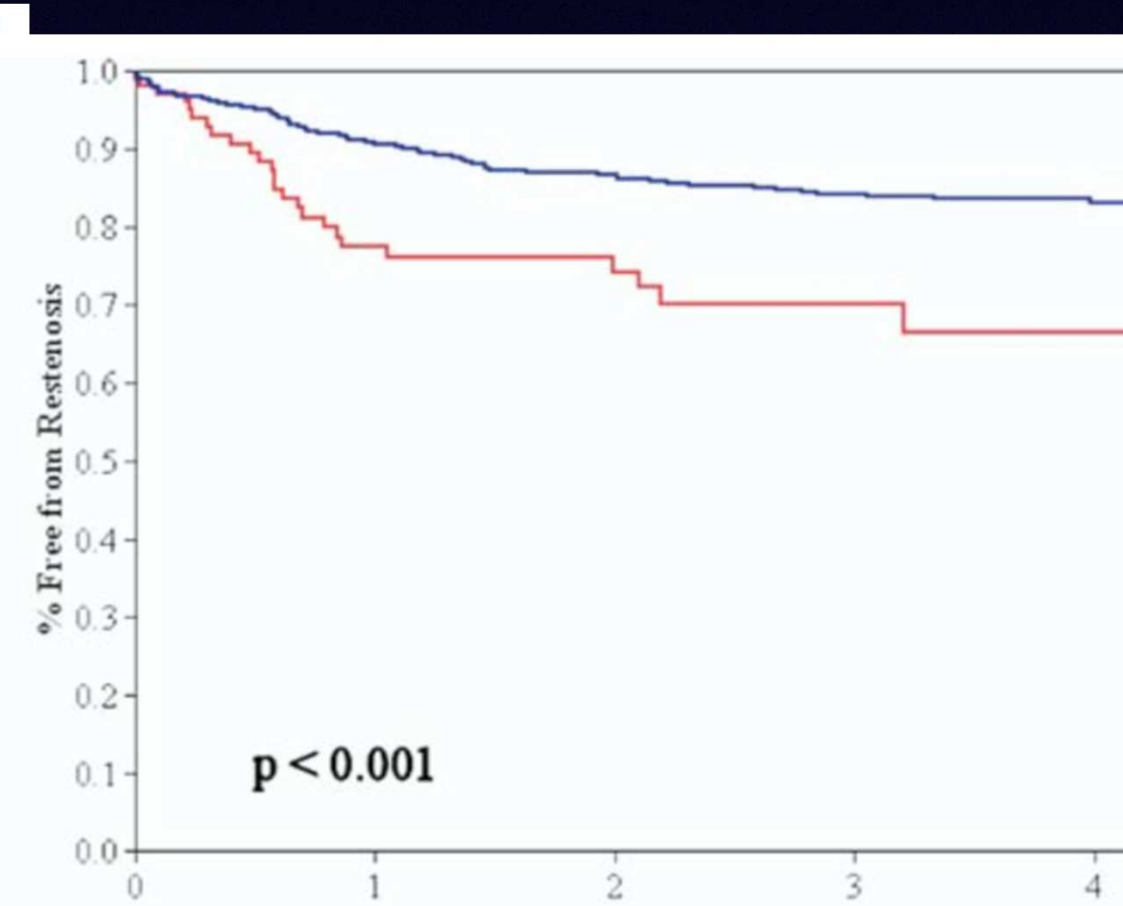
higher restenotic rates



# Carotid Revascularization



	0	0.5	1	1.5	2	2.5	3	3.5	4	4.5	5
MetS	617	597	584	559	494	450	383	324	288	250	
No MetS	276	260	245	236	205	180	156	135	119	100	
Total	893	857	829	795	699	630	539	459	407	350	



# Vascular Biology

High plasma levels of free fatty acids and glucose

Pro Inflammatory state

Pro Thrombotic state

Increased Intimal-Media thickness

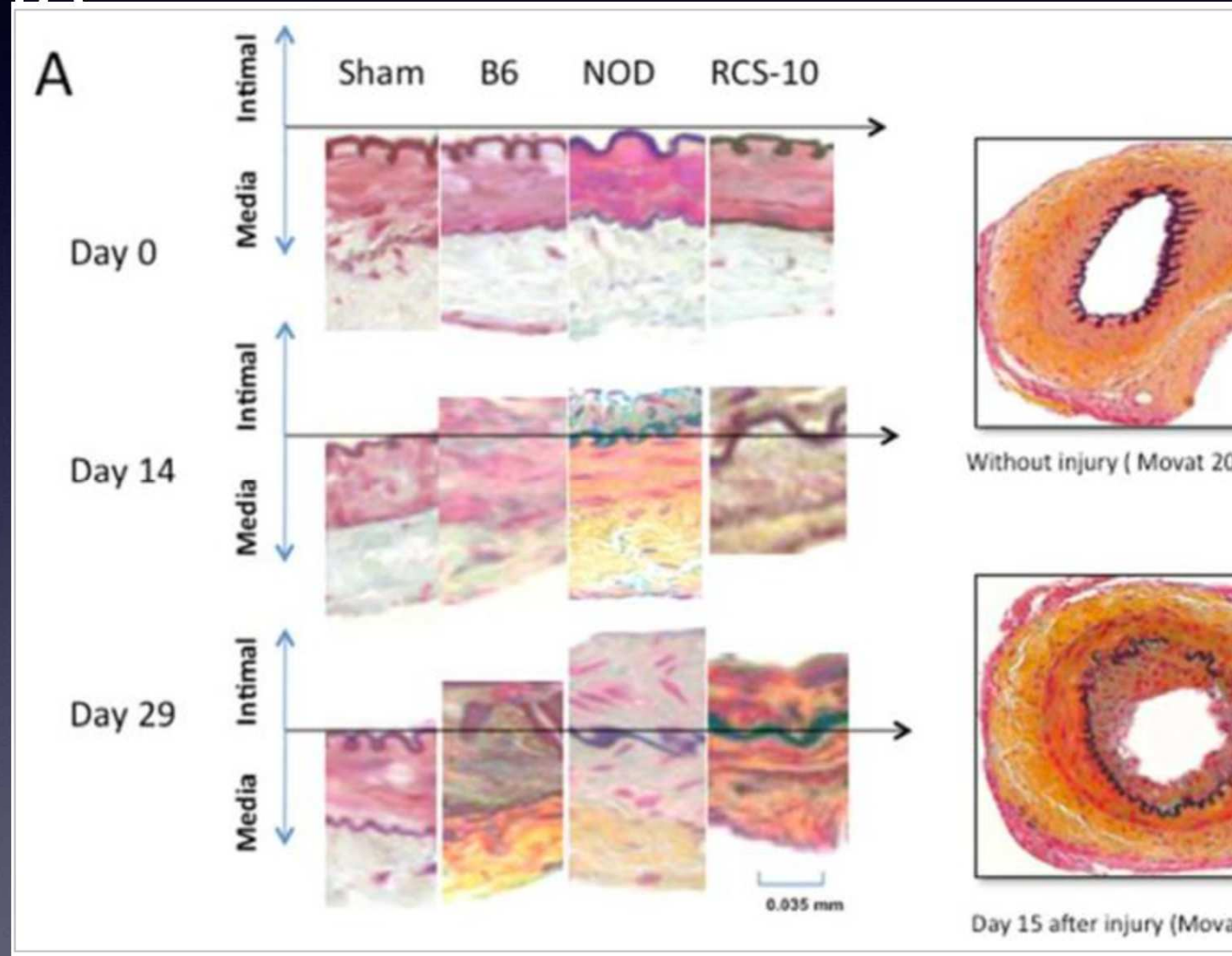
vascular wall thickness/stiffness

# Vascular Biology

Enhanced response to  
vascular injury

increased collagen  
deposition

reduced smooth  
muscle cell  
proliferation



# Summary

Metabolic Syndrome clearly impacts outcomes

Increasing obesity is largely responsible

Dietary choices are influential

Medical therapy has less impact

Little use however to clinician for decision making but perhaps important for patient counseling about outcomes expectations