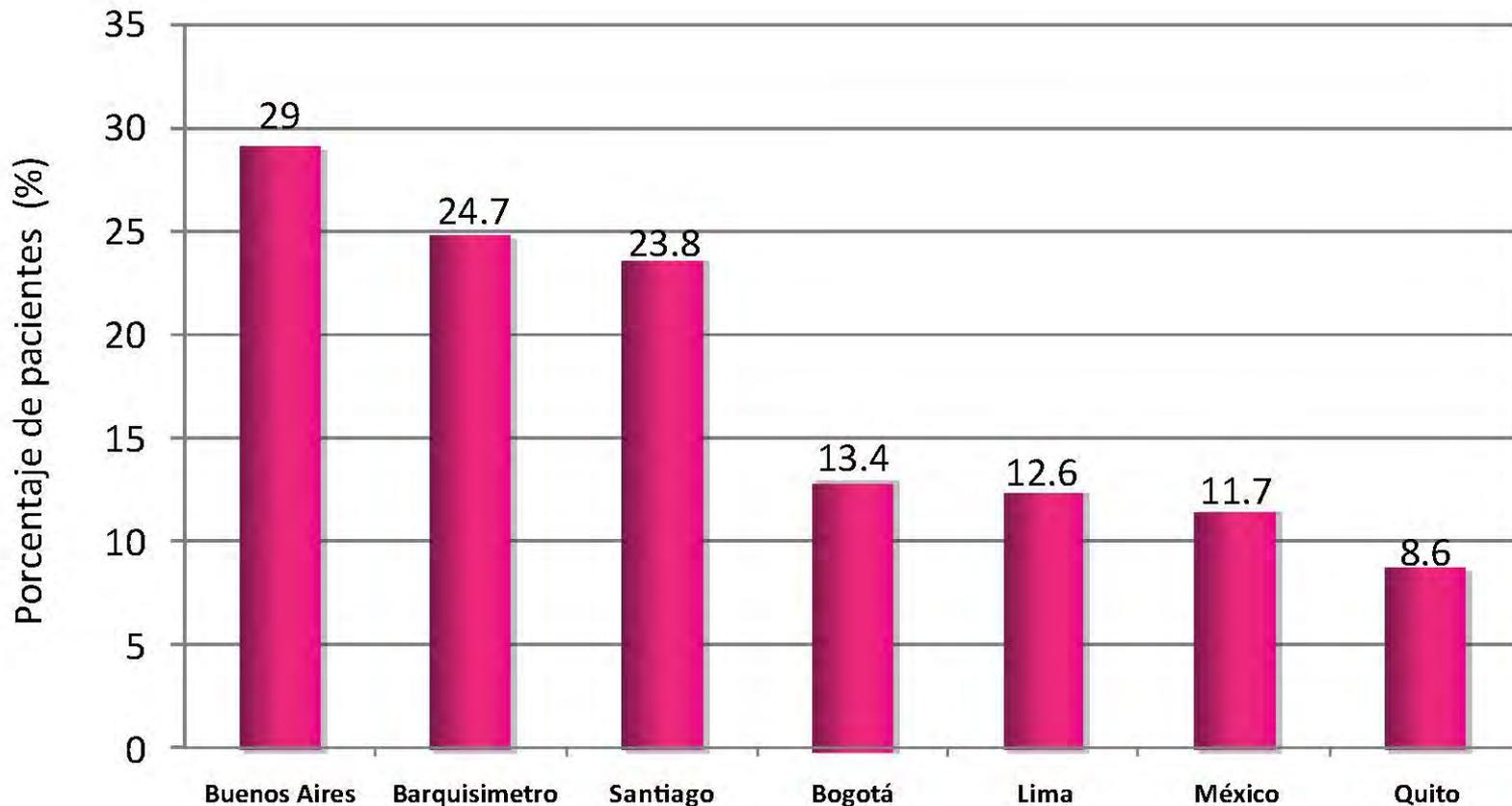


DIABETES, HIPERTENSION Y RIÑÓN

Doctor Mario A. Aguilar Joya
Internista Diabetologo

Diabetes, hipertension arterial y nefropatia

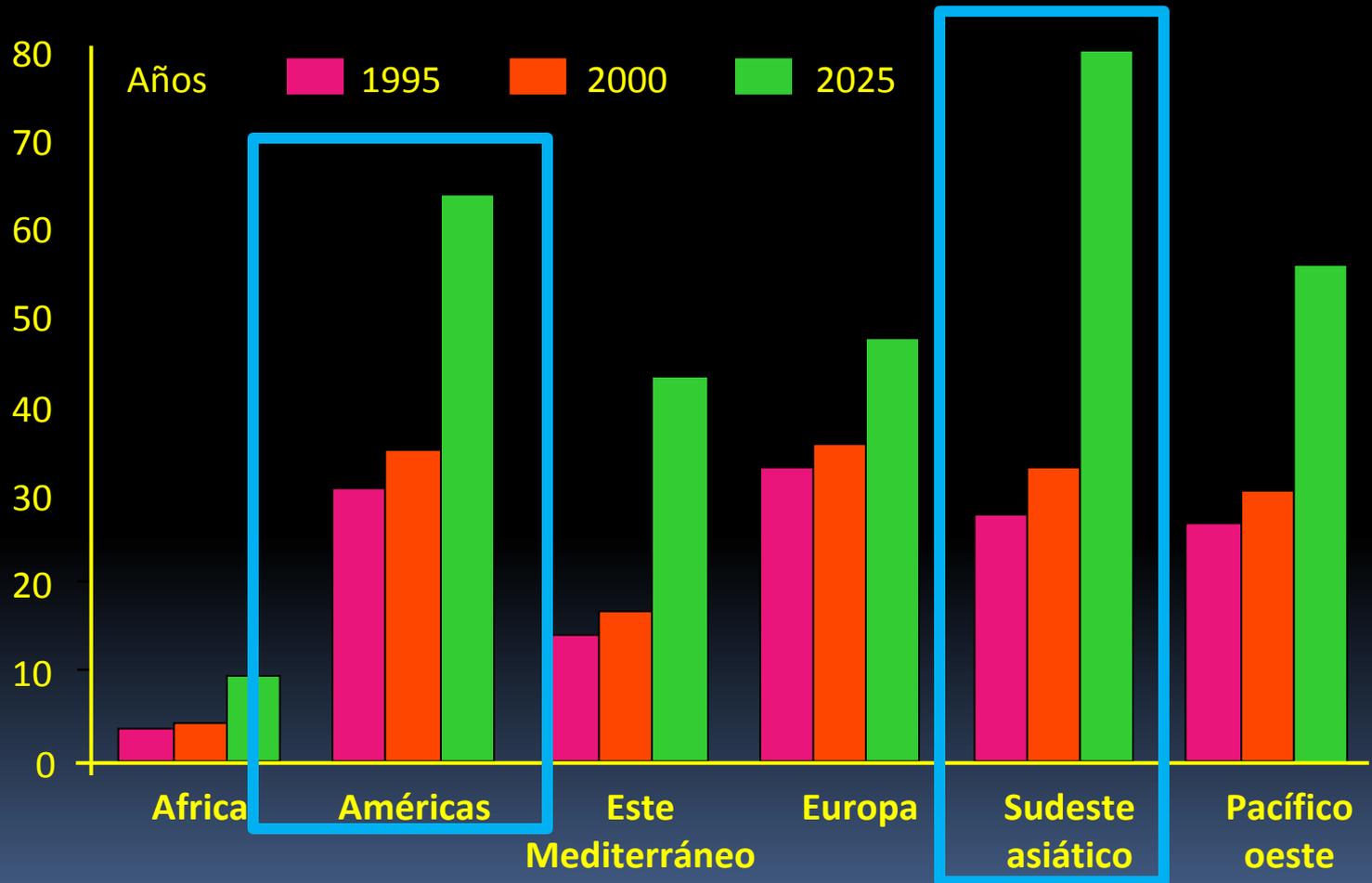
PREVALENCIA DE HIPERTENSIÓN ARTERIAL – ESTUDIO CARMELA



Diabetes
mellitus
insulin
type
resistance
weight
secretion
deficiency
metabolic
sugar
transplants
symptoms
health
treatment
healthy
diseases
suffer
cardiovascular
congenital
genetic
blood
defects
body
complications
success
forms

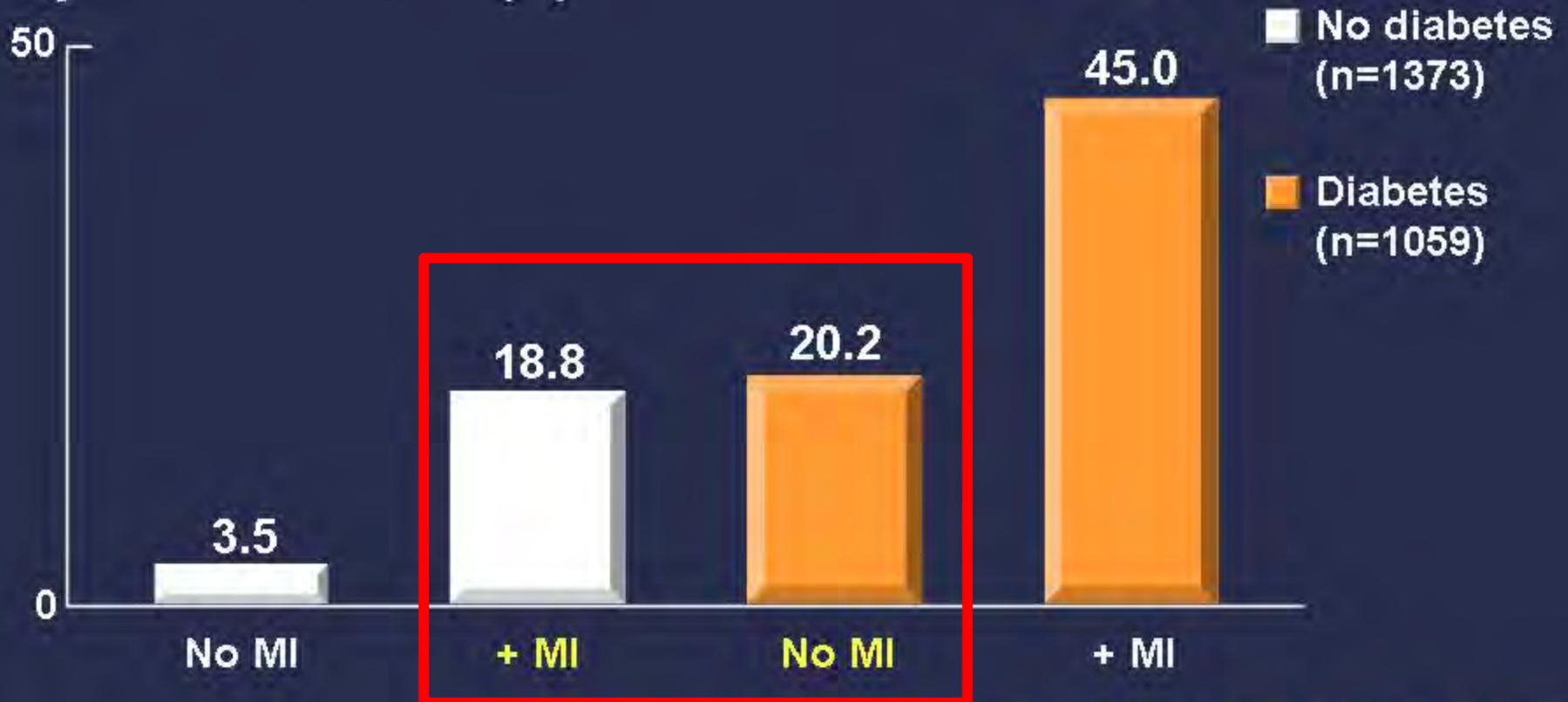
Tasas mundiales futuras de DM

Epidemia en ascenso

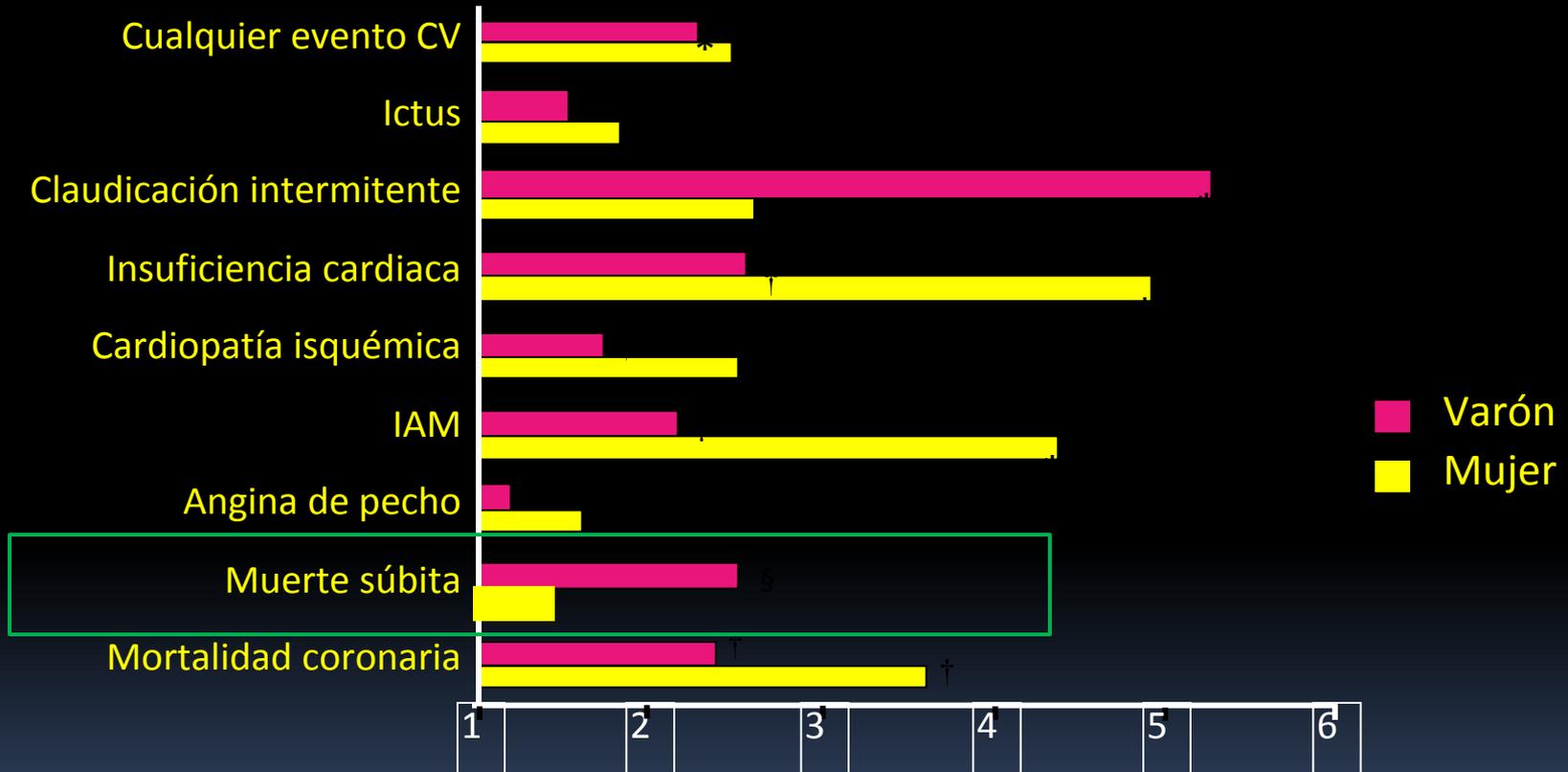


Diabetes as a risk equivalent of CAD

7-year incidence of myocardial infarction (%)



Diabetes tipo 2 aumenta el riesgo de Enfermedad Cardiovascular

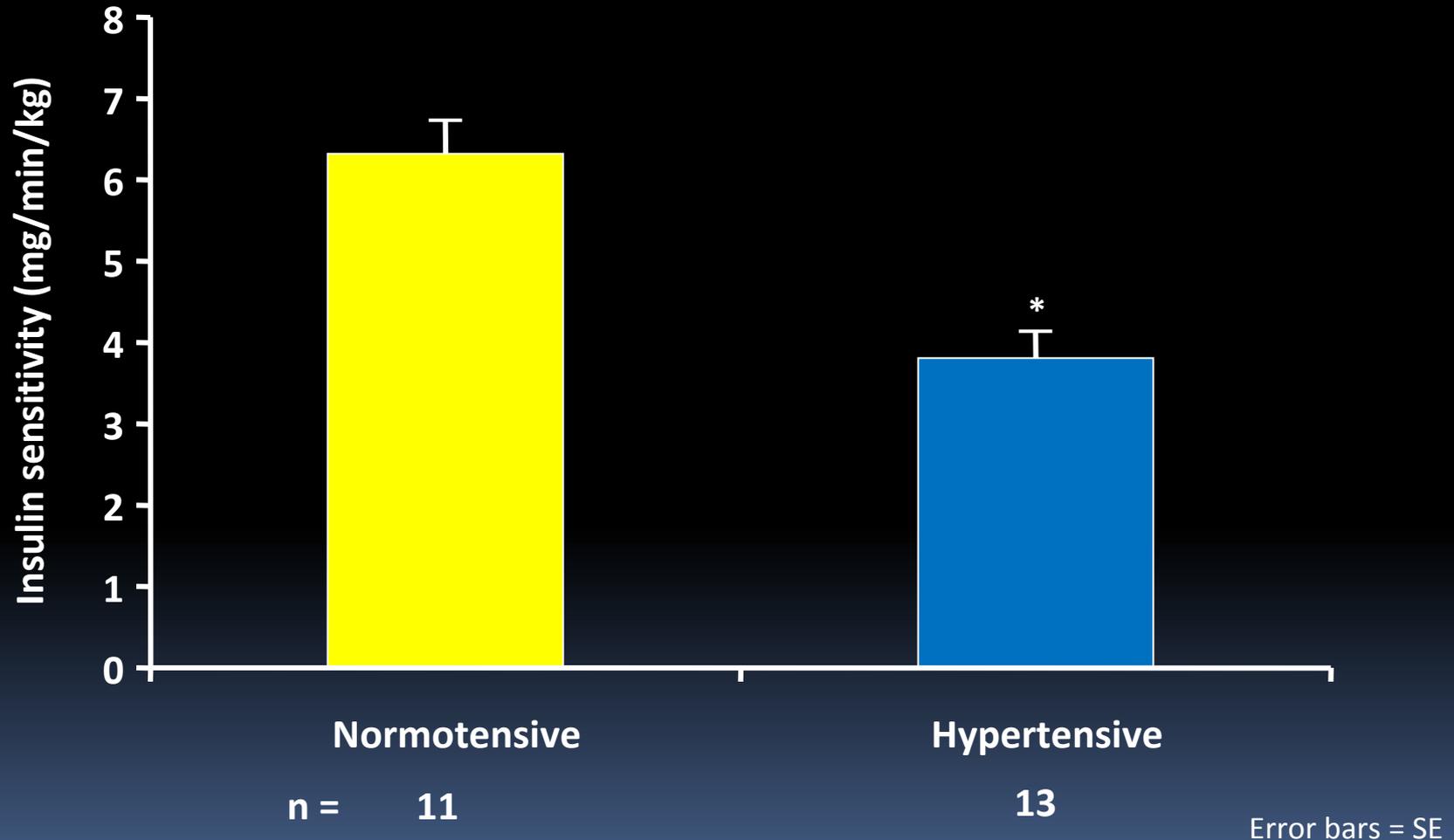


* $P < 0,001$; † $P < 0,05$;

‡ $P < 0,01$; § $P < 0,1$

Riesgo relativo ajustado por edad
(1 = riesgo para las personas sin diabetes)

Hipertension esta asociado con Resistencia Insulina



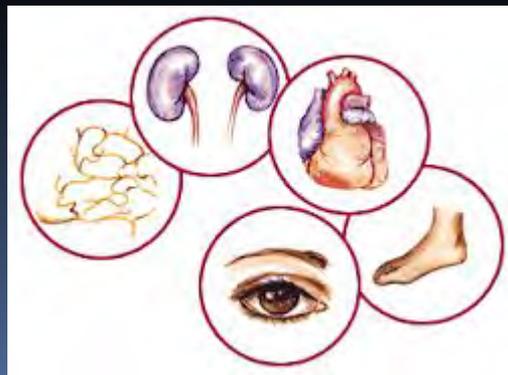
< 0.001 vs. normotensive

Ferrannini E, et al. *N Engl J Med* 1987; 6:350-357.

Afección Aterotrombótica HTA y DM (Estudio SARA)

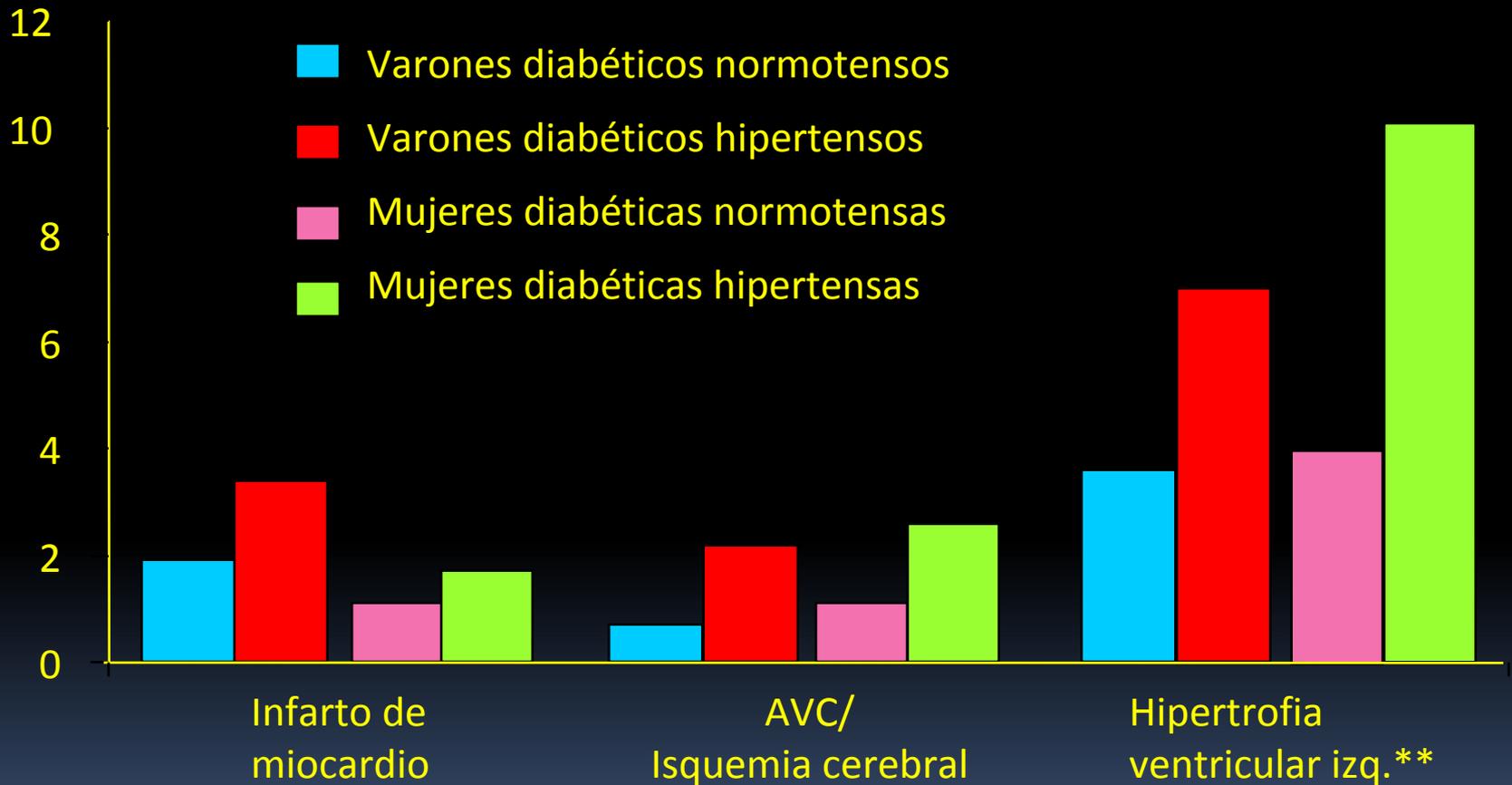
Afectación AT (%)	DM	No DM	p
▪ Enf. Coronaria	32,5	10,6	0.0001
▪ Enf. Arterial Periférica	10,0	2,3	0.0001
▪ Ictus	2,5	0,9	0.0001

Diabetes e Hipertensión Arterial



Hipertensión y Diabetes Tipo 2

Población de muy alto riesgo

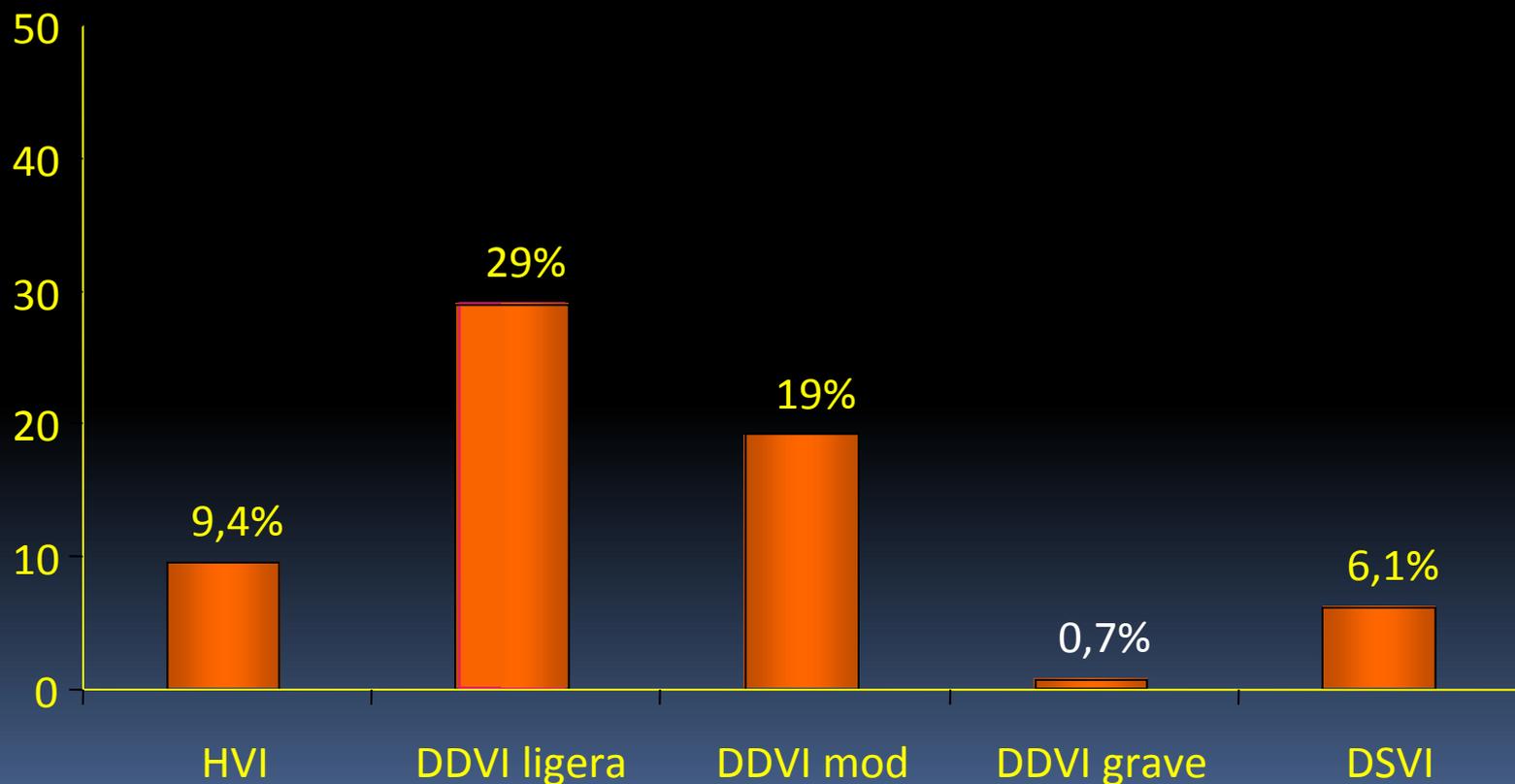


* $P < 0.05$, Hipertensos vs Normotensos.

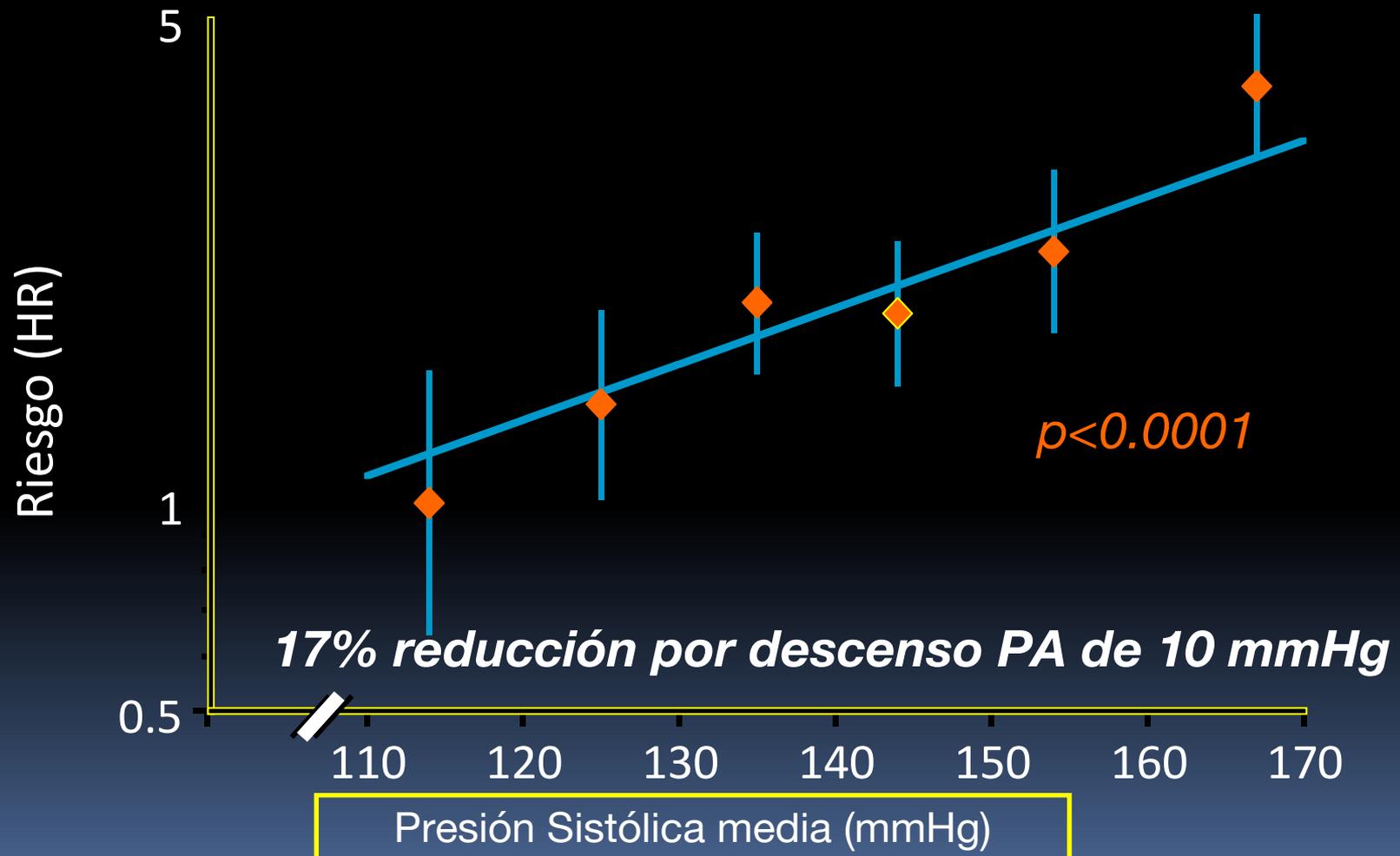
** HVI en ECG.

Afectación Cardíaca en Diabéticos Asintomáticos

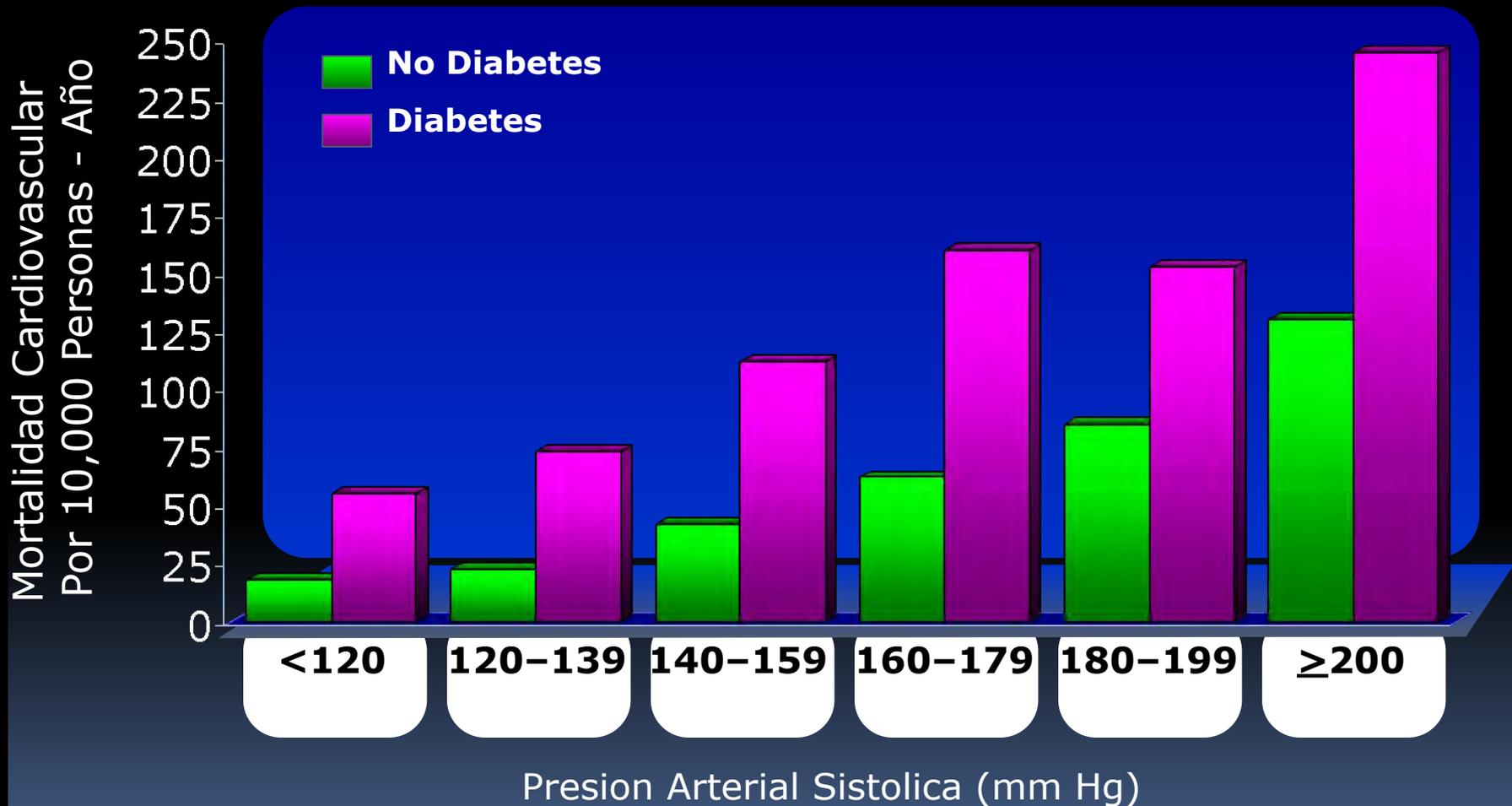
54,8% de diabéticos asintomáticos tienen ya algún grado de disfunción VI (48% diastólica ligera o moderada)



Relación entre Control PA y Muertes relacionadas con Diabetes



Diabetes es un Multiplicador Mayor de Riesgo Cardiovascular en Pacientes con Hipertension: Presion Arterial Sistolica y Mortalidad Cardiovascular



Stamler J, et al. *Diabetes Care*. 1993;16:434-444.

Objetivos de Presión Arterial en HTA (JNC-7/ESH-ESC 2007)

- **Objetivo General del Tratamiento:**

PA < 140/90 mm Hg

- **Pacientes con Diabetes**

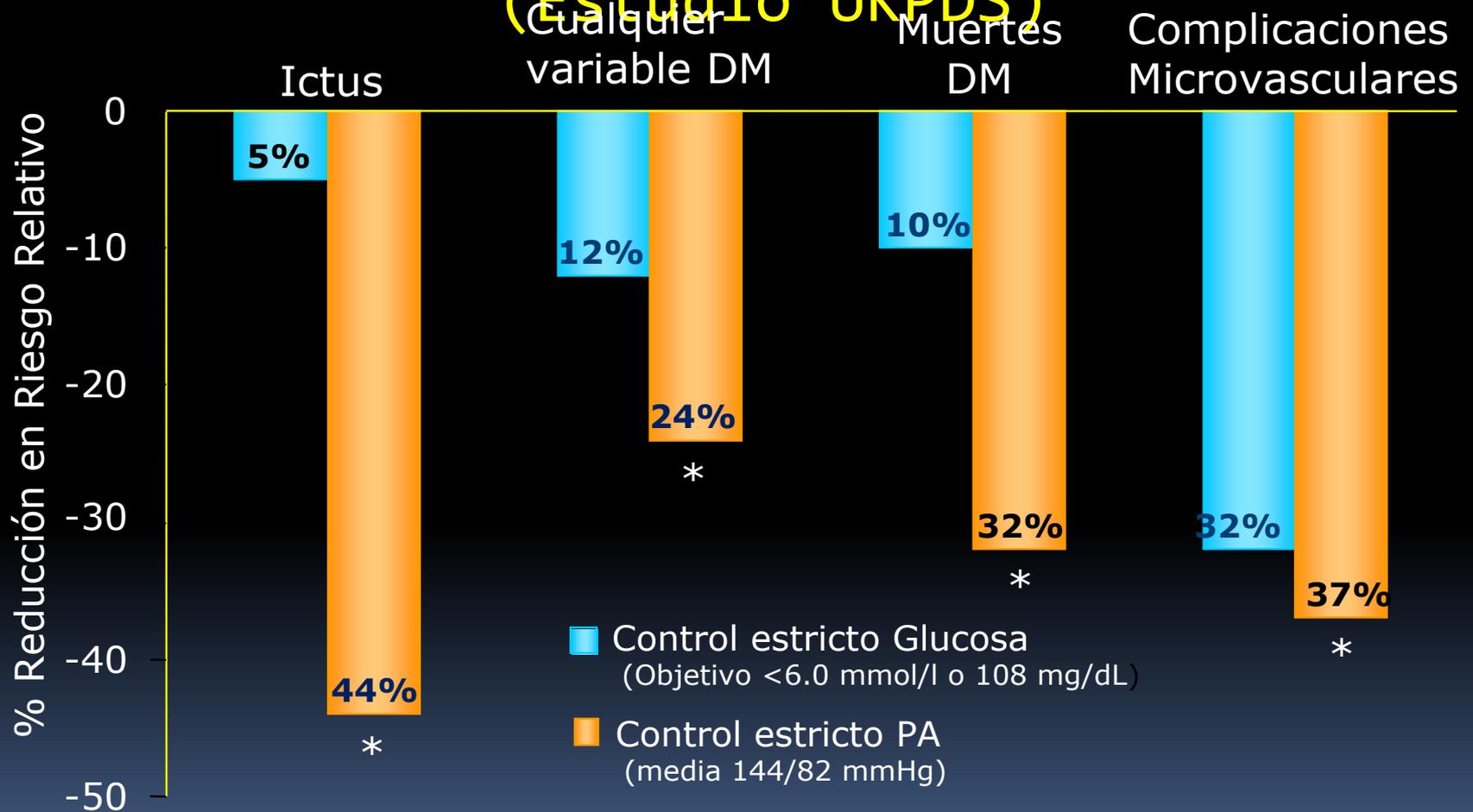
PA < 130/80 mm Hg

- **Pacientes con IRC y proteinuria > 1g/24h:**

PA < 125/75 mm Hg

Control estricto Glucosa vs PA en DM2

(Estudio UKPDS)



*p < 0.05 comparado con control estricto Glu

Control de Presion Arterial en pacientes con Diabetes Tipo 2 (UKPDS)

Control Estricto (144/82 mmHg)

vs.

Control Menos Estricto (154/87 mmHg)

Results:

24% Reduccion del Riesgo en cualquier resultado final de DMT2 $P = 0.0046$

32% Reduccion del Riesgo en muertes relacionadas a diabetes $P = 0.019$

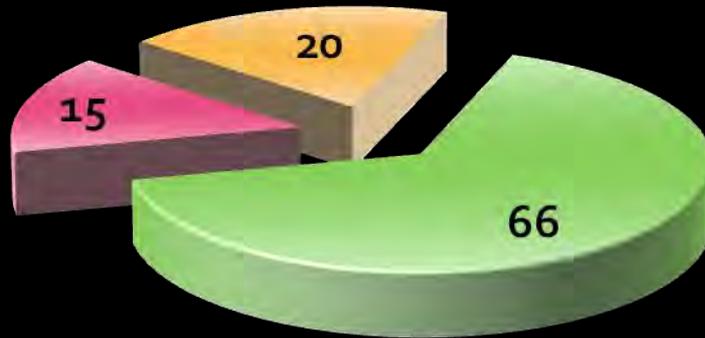
44% Reduccion del Riesgo en ACV $P = 0.013$

34% Reduccion del Riesgo en daño macrovascular $P = 0.019$

37% Reduccion del Riesgo en daño microvascular $P = 0.0092$

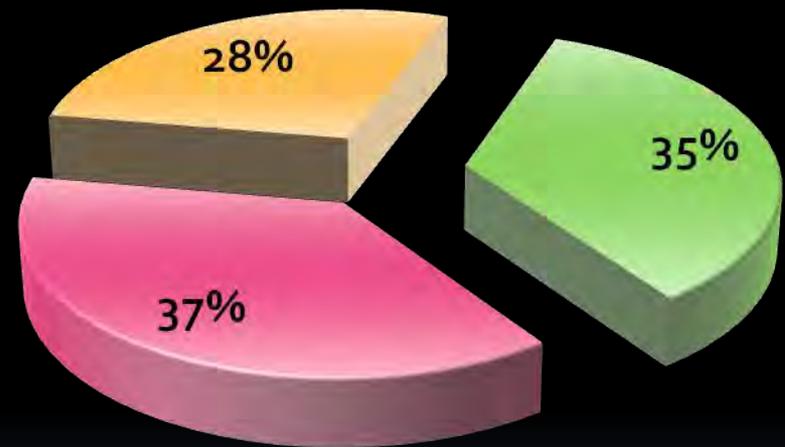
¿Que tan bien se trata la HTA en Diabeticos?

Tratamiento y Control en Pacientes con Hipertension



- Tratado y Controlado
- Tratado y No Controlado
- No Tratado

Tratamiento y Control en Pacientes con HTA y Diabetes



- Tratado y Controlado
- Tratado y No Controlado
- No Tratado

The NEW ENGLAND JOURNAL of MEDICINE

REVIEW ARTICLE

MEDICAL PROGRESS

Uric Acid and Cardiovascular Risk

Daniel I. Feig, M.D., Ph.D., Duk-Hee Kang, M.D., and Richard J. Johnson, M.D.

N ENGL J MED 359;17 WWW.NEJM.ORG OCTOBER 23, 2008

Table 1. Cardiovascular Conditions and Risk Factors Associated with Elevated Uric Acid.

Hypertension and prehypertension

Renal disease (including reduced glomerular filtration rate and microalbuminuria)

Metabolic syndrome (including abdominal obesity, hypertriglyceridemia, low level of high-density lipoprotein cholesterol, insulin resistance, impaired glucose tolerance, elevated leptin level)

Obstructive sleep apnea

Vascular disease (carotid, peripheral, coronary artery)

Stroke and vascular dementia

Preeclampsia

Inflammation markers (C-reactive protein, plasminogen activator inhibitor type 1, soluble intercellular adhesion molecule type 1)

Endothelial dysfunction

Oxidative stress

Sex and race (postmenopausal women, blacks)

Demographic (movement from rural to urban communities, Westernization, immigration to Western cultures)

Table 2. Evidence Linking Uric Acid and Hypertension.

An elevated uric acid level consistently predicts the development of hypertension.

An elevated uric acid level is observed in 25–60% of patients with untreated essential hypertension and in nearly 90% of adolescents with essential hypertension of recent onset.

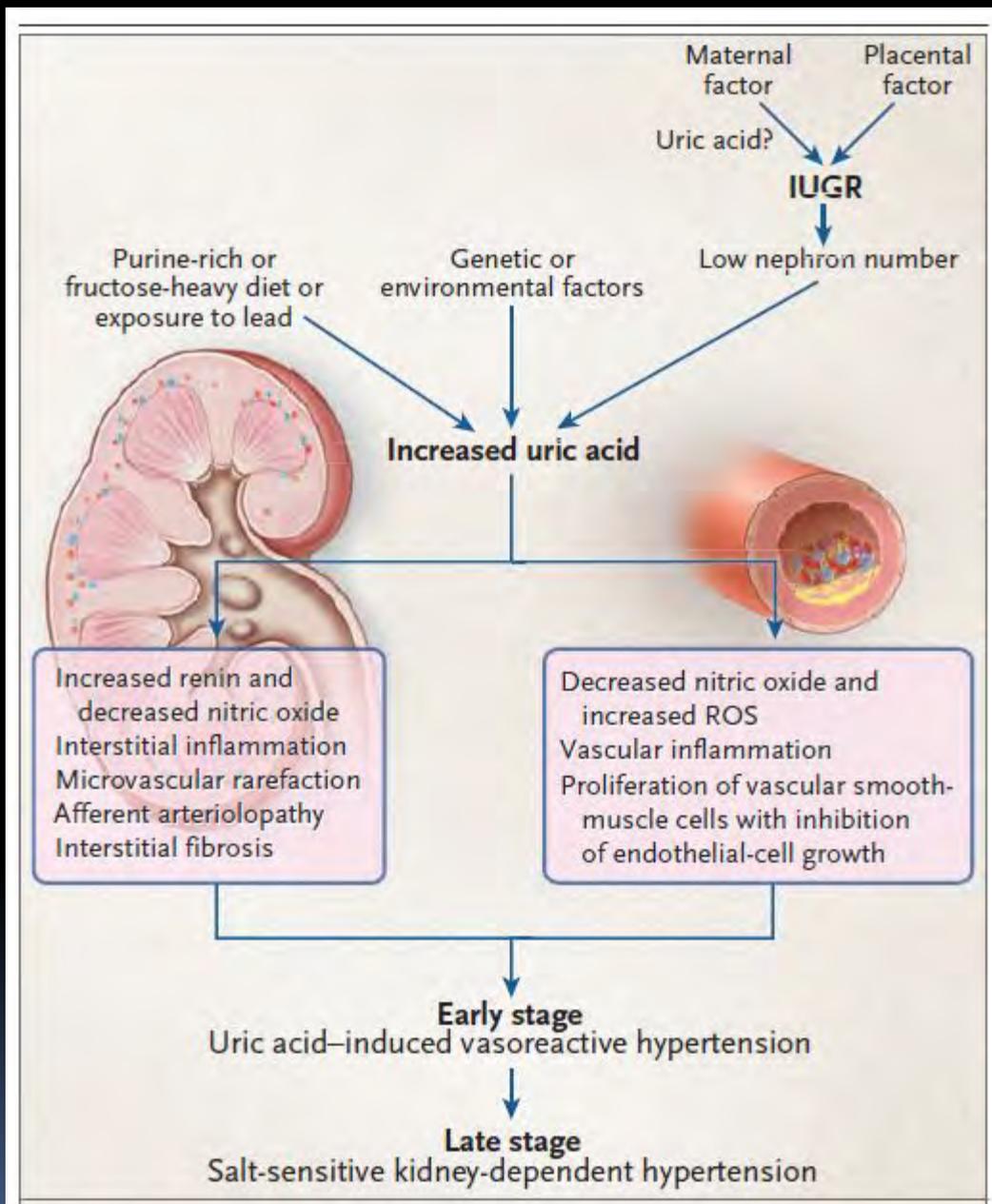
Raising the uric acid level in rodents results in hypertension with the clinical, hemodynamic, and histologic characteristics of hypertension.

Reducing the uric acid level with xanthine oxidase inhibitors lowers blood pressure in adolescents with hypertension of recent onset.

Table 3. Hyperuricemia and the Development of Hypertension.*

Study	No. of Patients	Relative Risk of Hypertension	95% CI
Kaiser Permanente, 1990 ⁵³	2062 adults	2.1 times greater at 6 yr (high vs. low quintile)	1.20–3.98
University of Utah, 1991 ⁴⁴	1482 adults	1.44 times greater per SD increment at 7 yr	1.03–2.01
Olivetti Heart, 1994 ⁴⁶	619 men	1.23 times greater per 1 mg/dl increase at 12 yr	1.07–1.39
CARDIA, 1999 ⁴²	5115 men	1.21 times greater per SD increment at 10 yr	1.03–1.41
Osaka Health Survey, 2001 ⁵⁶	6356 men	2 times greater at 10 yr (high vs. low quintile)	1.56–2.60
Hawaii–Los Angeles–Hiroshima, 2001 ⁴⁵	140 men	2.0 times greater at 15 yr (high vs. low quartile)	1.02–3.9
Osaka Factory, 2003 ⁴⁸	433 men	1.0 mg/dl, increased 27 mm Hg SBP at 5 yr	Not calculated
Osaka Health Survey, 2003 ⁵¹	2310 men	1.13 times greater per SD increment at 6 yr	1.06–1.21
Okinawa, 2004 ⁵⁰	4489 adults	1.46 times greater for men (uric acid \geq 7 mg/dl) and 1.94 for women (uric acid \geq 6 mg/dl) at 13yr	1.09–2.03 1.05–3.57
Bogalusa Heart, 2005 ⁴¹	679 children	Increased risk for diastolic hypertension at 11 yr	Not calculated
Framingham Heart, 2005 ⁵⁵	3329 adults	1.17 times greater per SD increment at 4 yr	1.02–1.33
Normative Aging, 2006 ⁵²	2062 men	125 times greater at 21 yr (uric acid >6.5 mg/dl)	1.08–1.34
ARIC, 2006 ⁴⁹	9104 adults	1.1 times greater per SD increment at 9 yr	1.02–1.14
Beaver Dam Health Survey, 2006 ⁵⁴	2520 adults	1.65 times greater at 10 yr (high vs. low quintile)	1.41–1.93
Health Professionals' Follow-up, 2006 ⁴³	750 men	1.02 times greater per SD increment at 8 yr	0.92–1.13
MRFIT, 2007 ⁴⁷	3073 men	1.1 times greater per SD increment at 6 yr	1.02–1.19

* To convert the values for uric acid to micromoles per liter, multiply by 59.48. ARIC denotes Atherosclerosis Risk in Communities, CARDIA Coronary Artery Risk Development in (Young) Adults, MRFIT Multiple Risk Factors Intervention Trial, and SBP systolic blood pressure.



**Coronary artery
disease**

**Atherosclerosis
and LVH**

Myocardial infarction

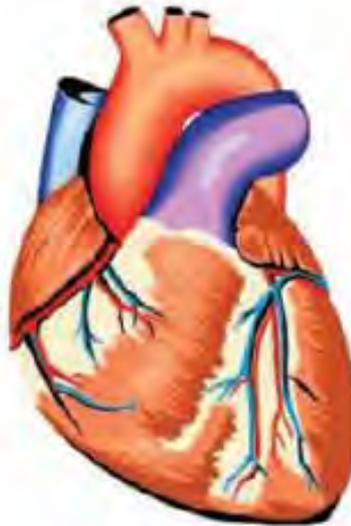
Endothelial dysfunction

Dilatation /remodelling

**Hypertension
Hyperlipidemia
Diabetes
Smoking**

Heart failure

End-stage heart disease





TRATAMIENTO FARMACOLOGICO

¿NO DA LO MISMO USAR CUALQUIER DROGA!

Eficacia en la reducción
de la presión arterial



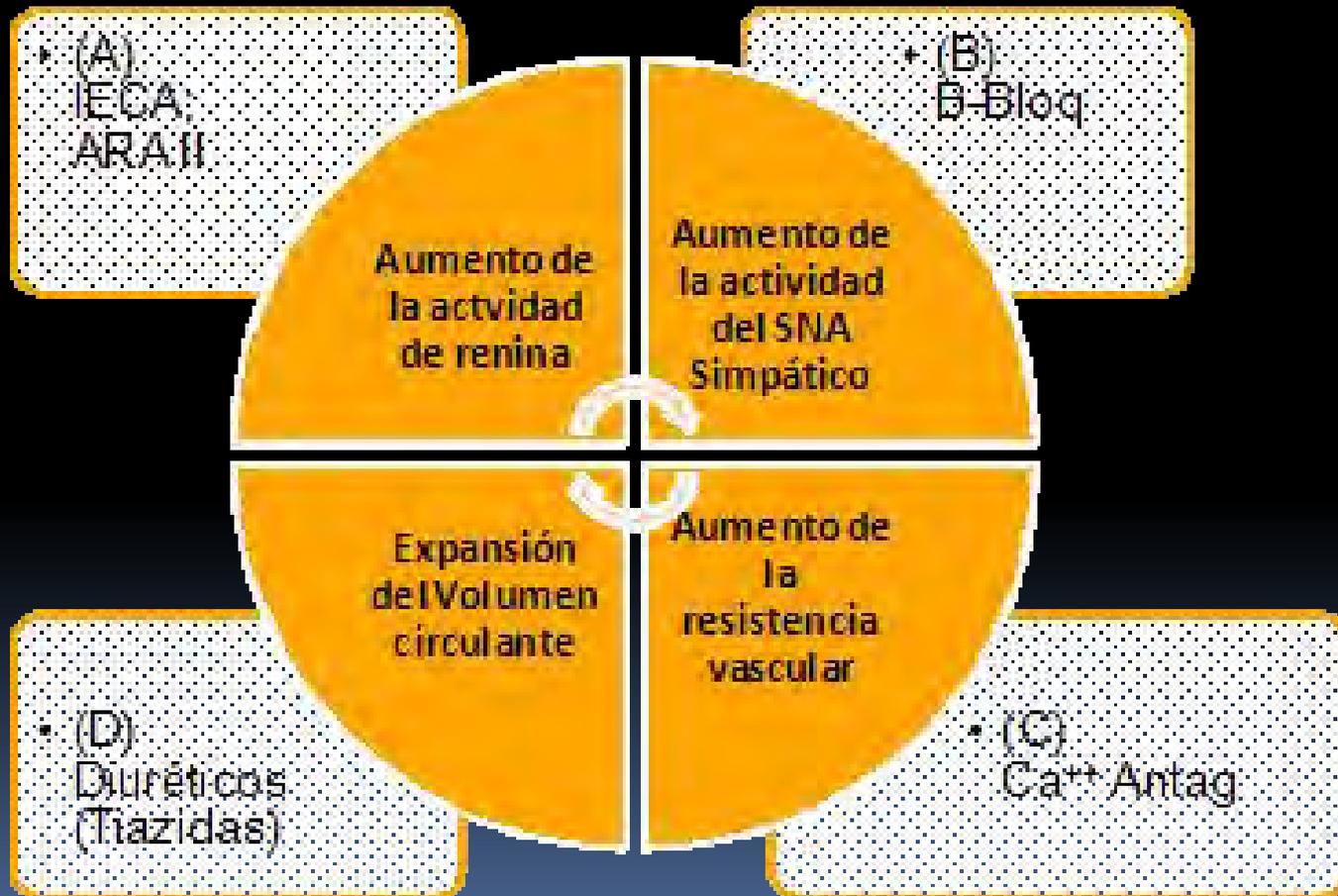
Mejorar la
adherencia

Lograr la
protección de
los órganos
blanco

No incrementar
otros factores de
riesgo

No perjudicar la
calidad de vida

No existe el Efecto de Clase (Cada Fármaco debe mostrar su Evidencia)



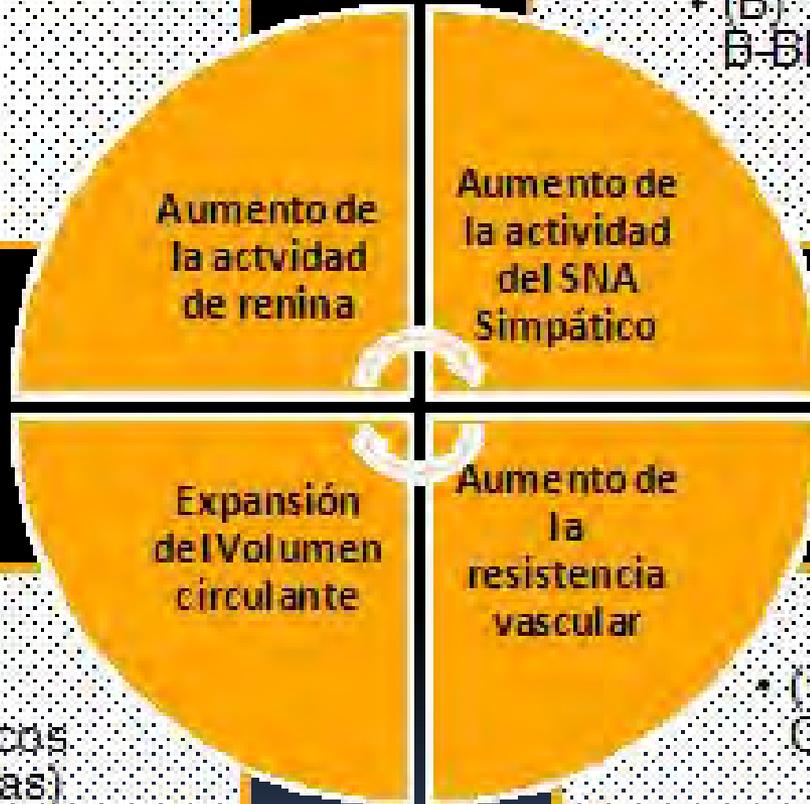
No existe el Efecto de Clase

Fosinopril
Lisinotril
Trandolapril

Candesartan
Irbesartan
Olmesartan



Atenolol
Metoprolol
Nebivolol
Bisoprolol



Hidroclorotiazida

(Indapamida, Espironolactona)

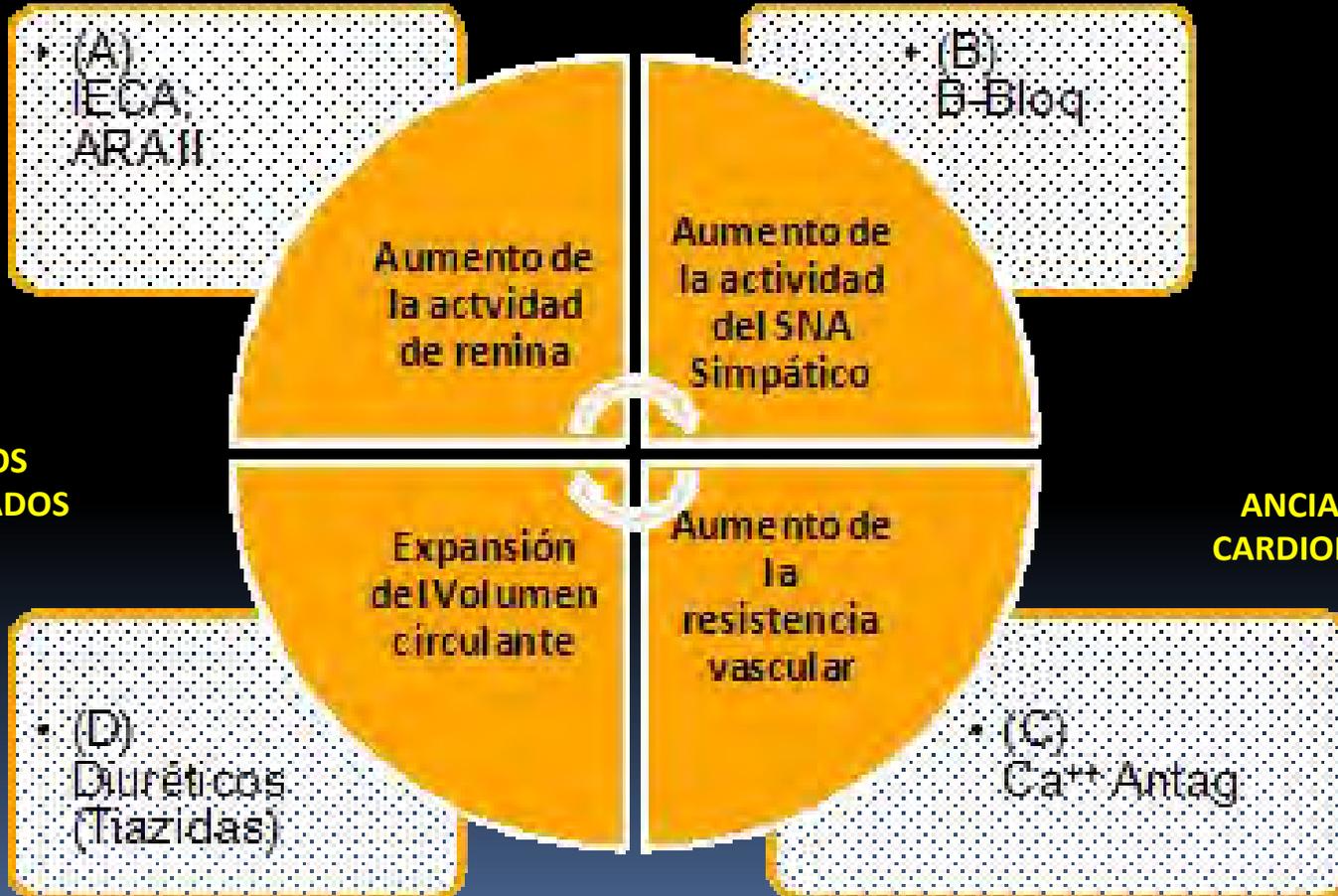
Verapamilo
Diltiazem

Amlodipina / Felodipina
Lercanidipino

(Cada Fármaco debe mostrar su Evidencia)

**OBESOS
S. METABOLICO
DIABETES**

**JOVENES
TAQUICARDIA
HIPERADRENERGICOS**

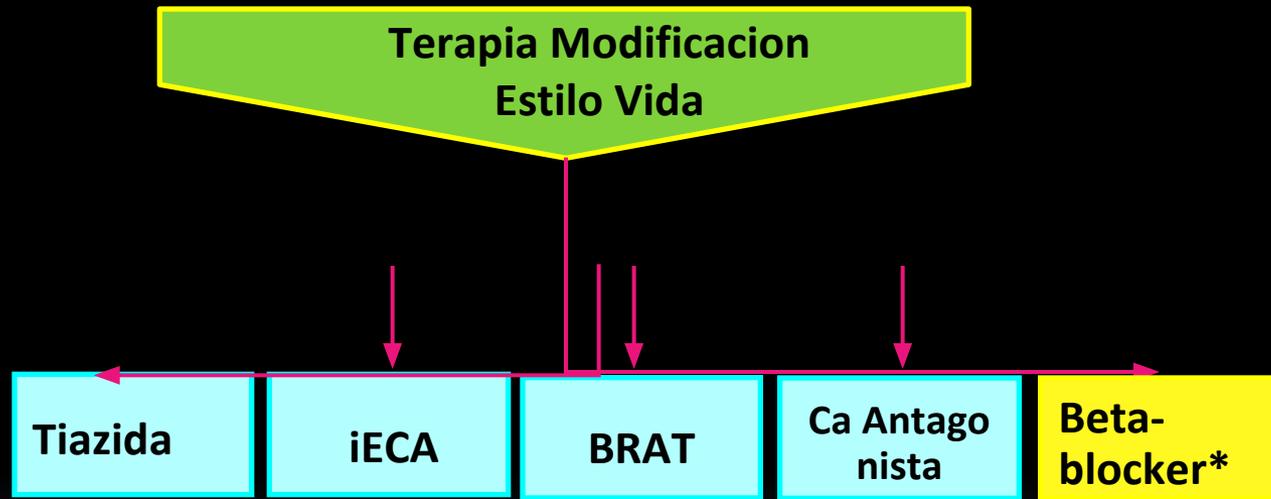


**ANCIANOS
EDEMATIZADOS**

**ANCIANOS
CARDIOPATAS**

TRATAMIENTO DE ADULTOS CON HIPERTENSION
SISTOLO - DIASTOLICA
SIN OTRA PATOLOGIA MEDICA

META <140/90 mmHg



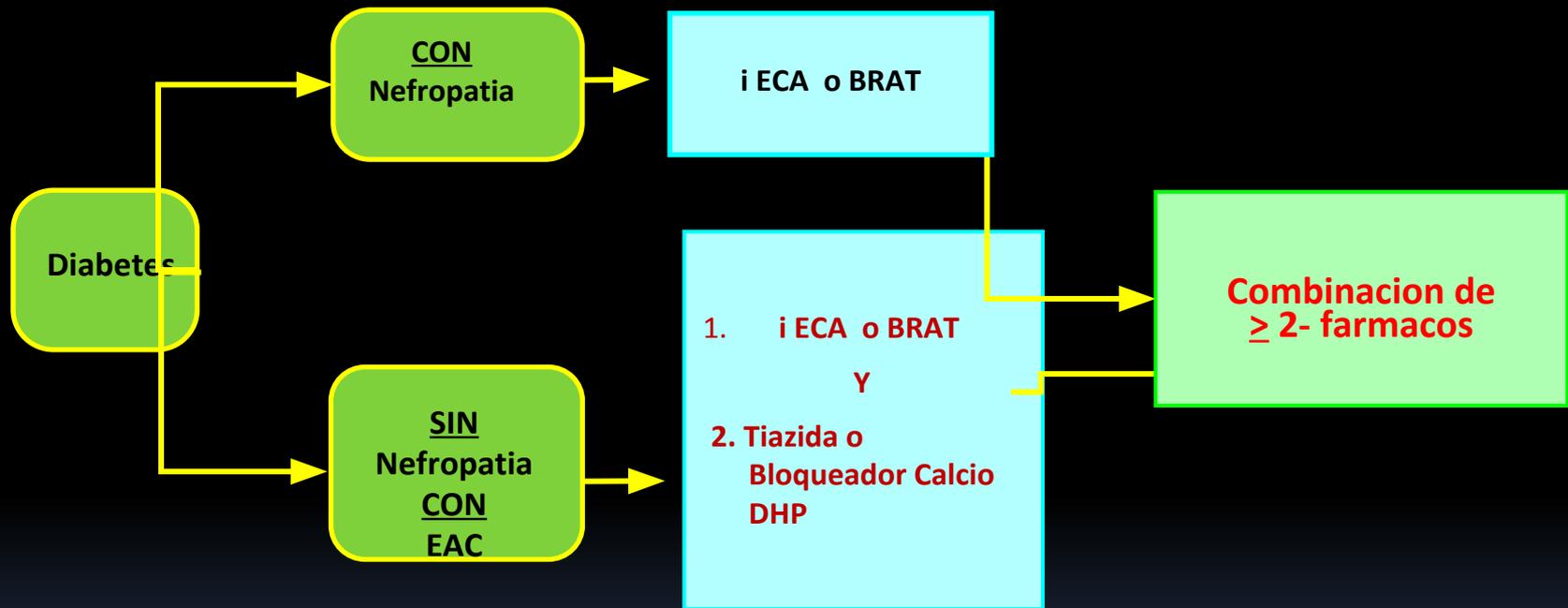
DOS FARMACOS ESTAN INDICADOS COMO TERAPIA INICIAL SI PRESION ARTERIAL ES ≥ 20 mmHg SISTOLICA o ≥ 10 mmHg DIASTOLICA

• BBs no indicados como 1ra linea en > 60 años, solamente con indicacion especifica

iECA, BRAT e Inhibidores Directos de Renina estan contraindicados en Embarazo

FARMACOTERAPIA PARA HIPERTENSION ARTERIAL EN PACIENTES CON DIABETES MELLITUS

NIVEL Y META DE TRATAMIENTO 130 / 80 mm Hg



MAS DE 3 FARMACOS PUEDEN SER NECESARIOS PARA EL CONTROL DE LA PRESION ARTERIAL

Tabla 1

Estrategia ABCS adoptada por el *Department of Health and Human Services* (DHHS) de Estados Unidos en su causa denominada «The Million Heart Initiative»⁴

A (AAS)	Administración de ácido acetilsalicílico a sujetos de alto riesgo
B (<i>Blood pressure</i>)	Control de la presión arterial
C (<i>Cholesterol</i>)	Control de los valores séricos de colesterol
S (<i>Smoking cessation</i>)	Abandono completo del tabaquismo activo y en lugares públicos

AAS: ácido acetilsalicílico.

Hipertensión Arterial y Diabetes en Ancianos



**POBLACIONES CON
MAYOR RIESGO ...**

DIABETICOS ANCIANOS

CONCEPTOS ERRONEOS ...

LOS ANTIHIPERTENSIVOS NO PRODUCEN NINGUN EFECTO BENEFICO EN PACIENTES MAYORES DE 65 AÑOS.

J FREY . LANCET 1974

EN PACIENTES MAYORES LOS TRATAMIENTOS ANTIHIPERTENSIVOS NO DEBEN SER ADMINISTRADOS A MENOS QUE LA PRESION ARTERIAL EXCEDA 200 / 100 mm HG.

BMJ 1978

NIVEL SOBRE EL CUAL HAY QUE TRATAR LA HTA EN ANCIANOS

$$\text{PAS } 100 + \text{EDAD (85)} = 185$$

GREOFFY ROSE

HIPERTENSION ARTERIAL EN ANCIANOS



**Un hombre es
tan viejo como sus arterias**

THOMAS SYDENHAM
MEDICO INGLES 1624 – 1689
65 Años

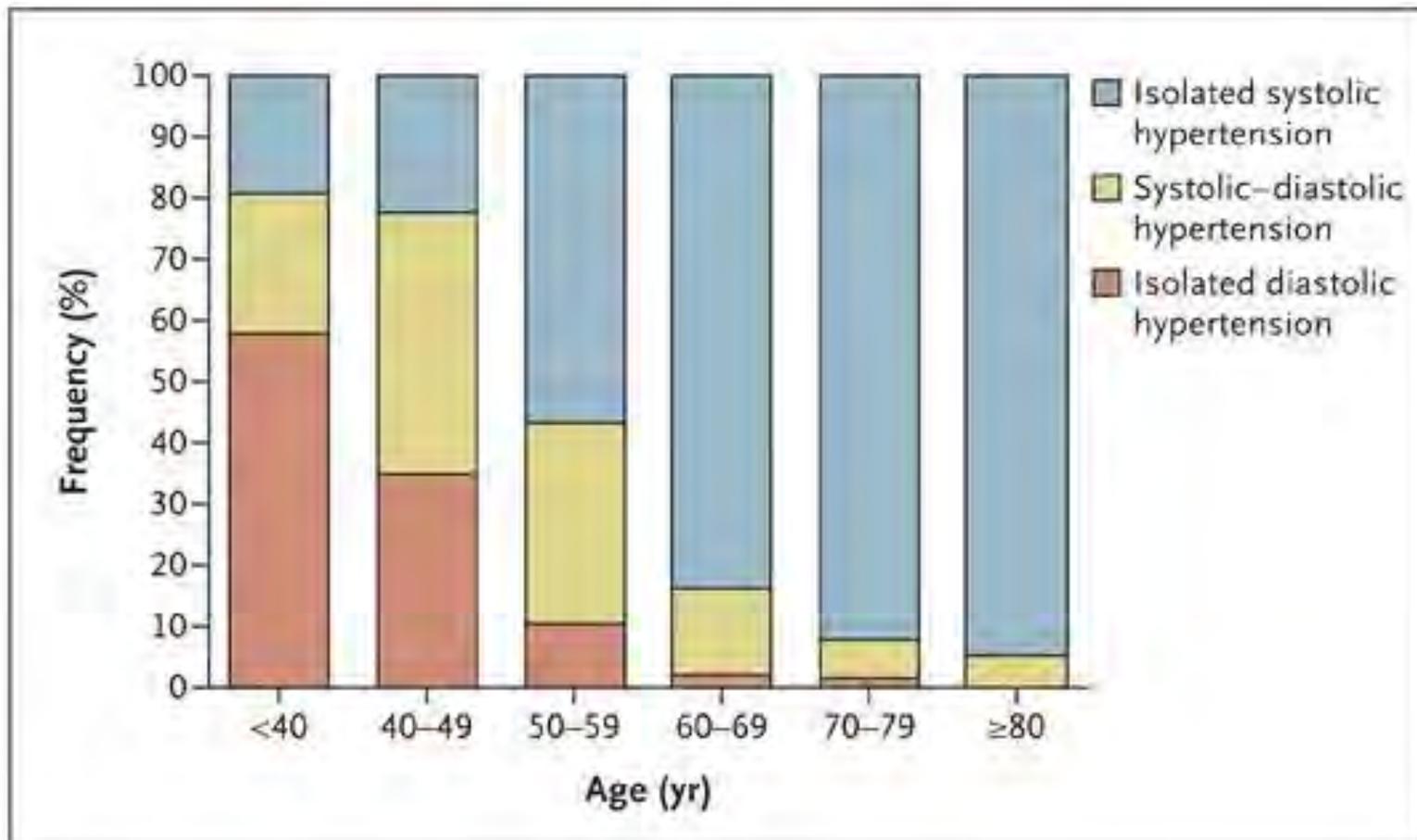


EXPECTATIVA DE VIDA DEPUES DE LOS 70 AÑOS

AÑOS	MUJERES	HOMBRES
70	16	13
75	13	10
80	9	7
85	6.5	5.3
90	4	3

NUNCA ES DEMASIADO TARDE PARA INICIAR TRATAMIENTO

Frequency of Untreated Hypertension According to Subtype and Age.

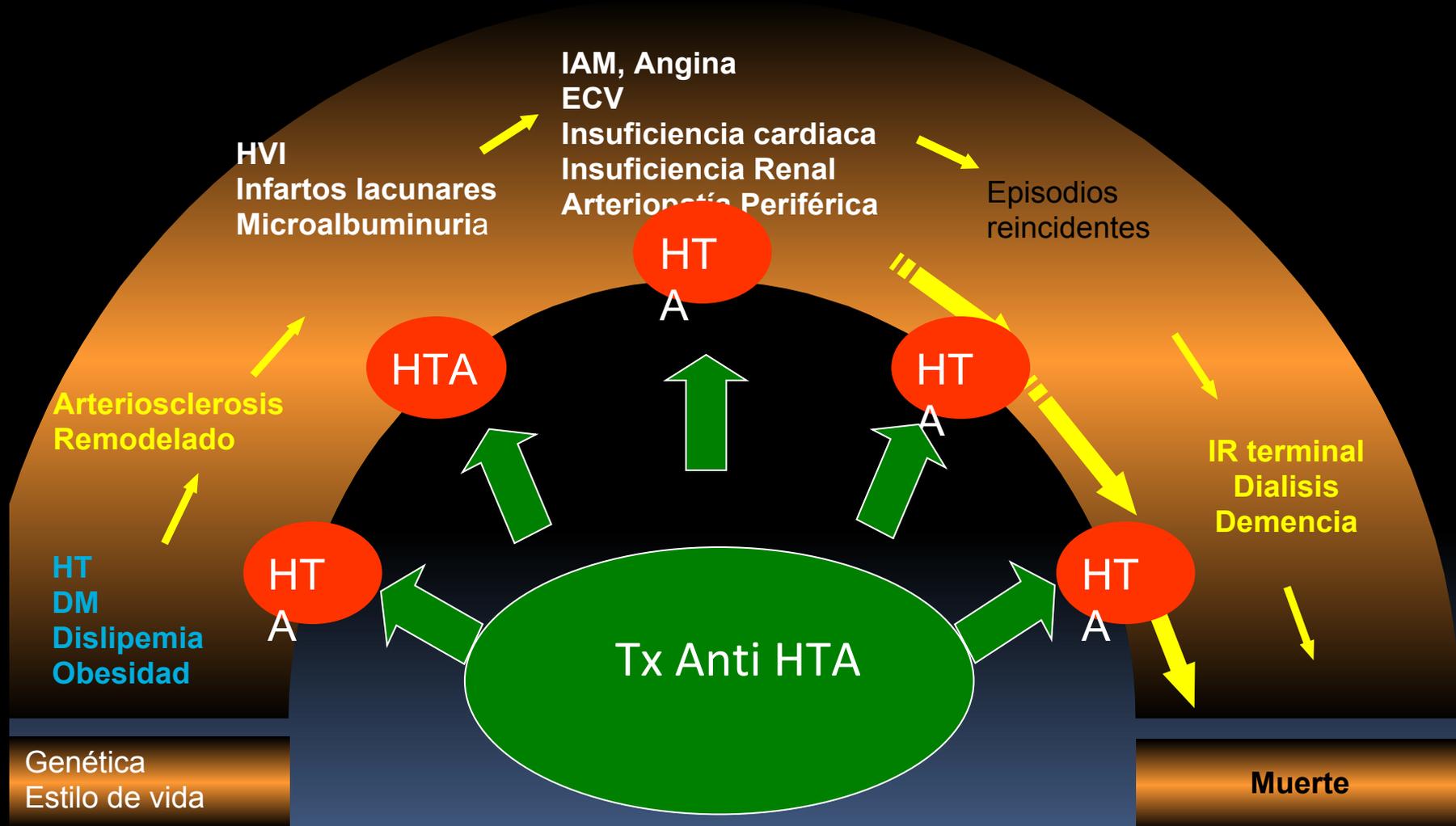




Protección a órgano blanco en el
continuum CV.

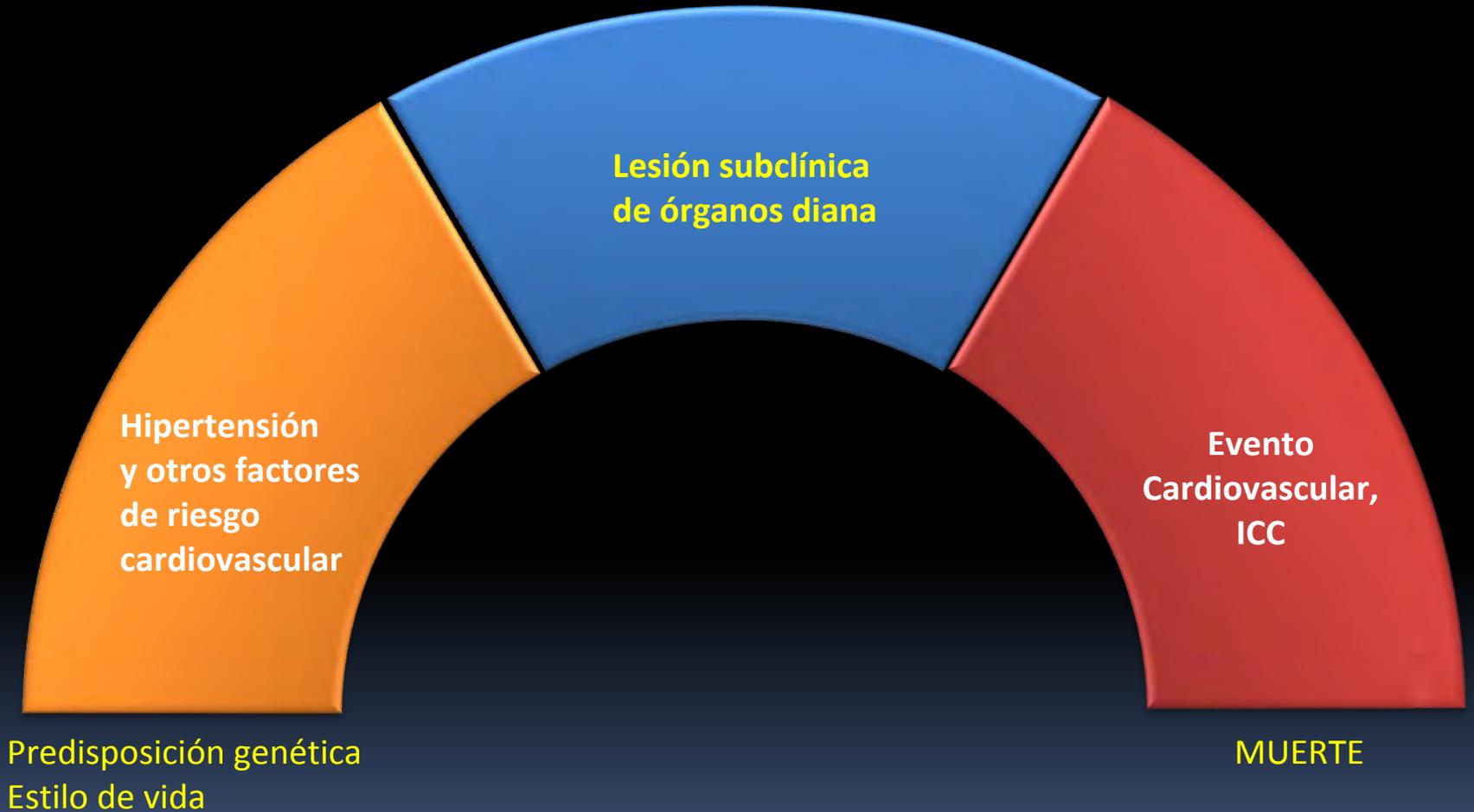
Énfasis en Bloqueadores de
Receptores de Angiotensina

Historia Natural del Riesgo Cardiovascular

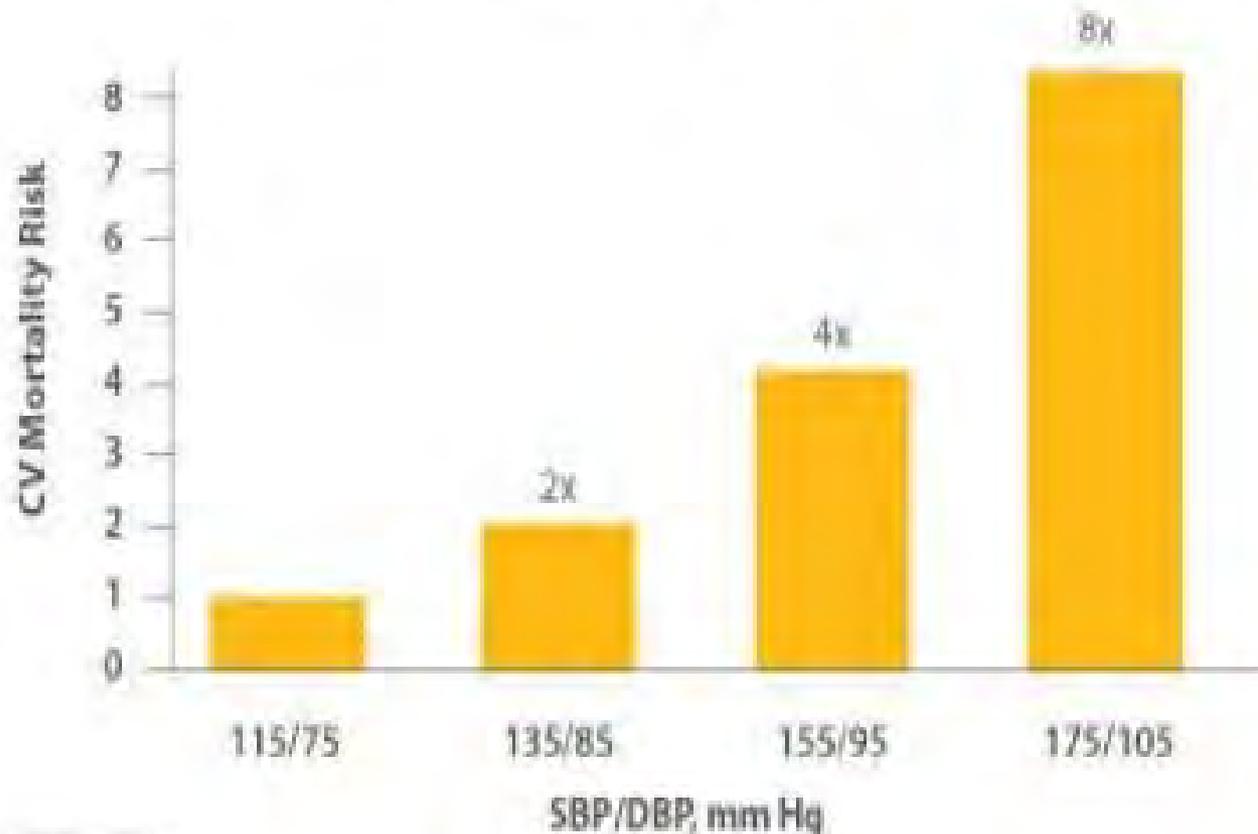


Adaptado de Dzau V y Braunwald E. Am Heart J 1991; 121:1244

El Continuum CV en 3 etapas significativas



Cardiovascular Mortality Risk Doubles With Each 20/10 mm Hg Increase in BP*



CV = cardiovascular.

SBP = systolic blood pressure.

DBP = diastolic blood pressure.

*In individuals aged 40 to 69 years (10-year study period), starting at BP 115/75 mm Hg.

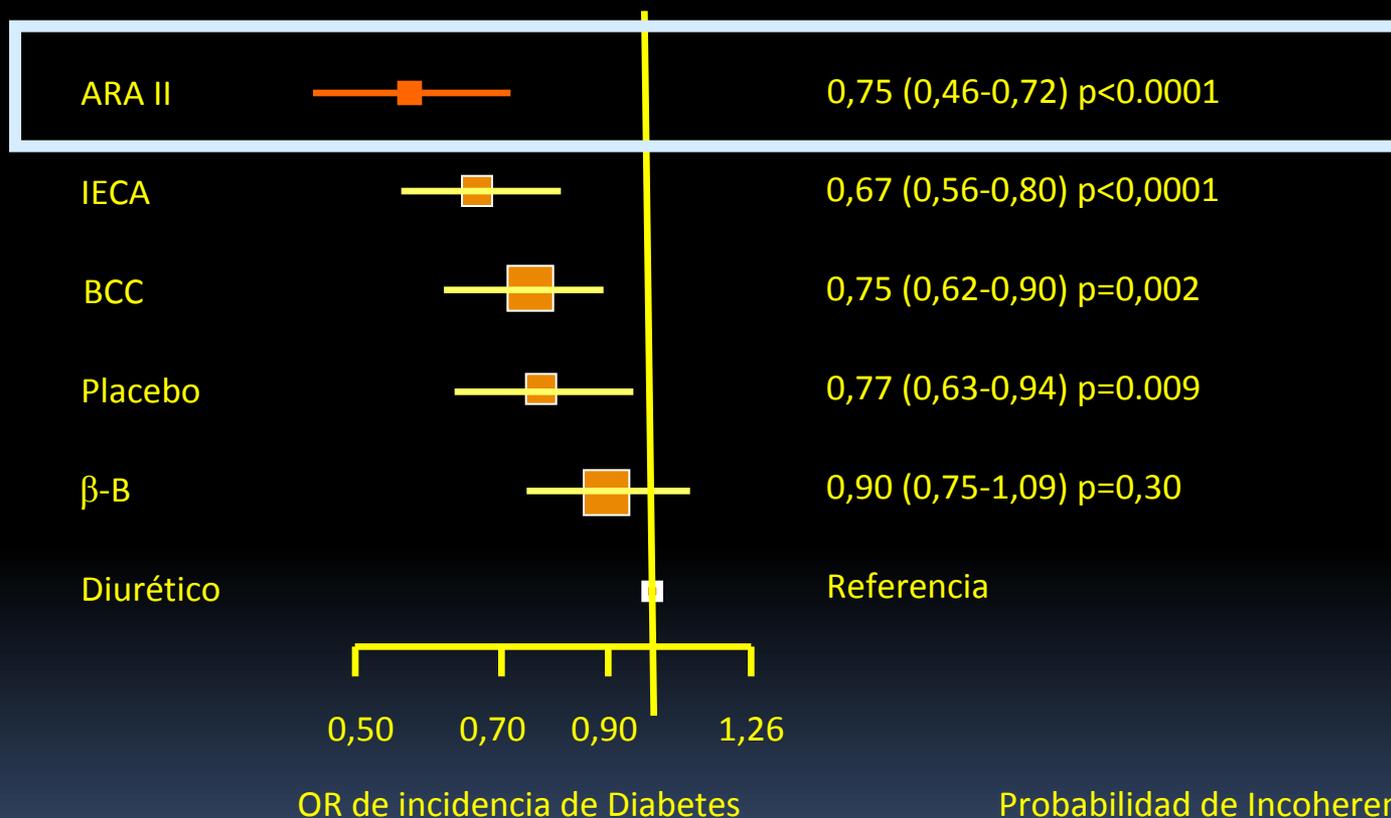
Lewington S, et al. *Lancet*. 2002;360:1903-1913.

Áreas Claves de Control en Pacientes Diabéticos

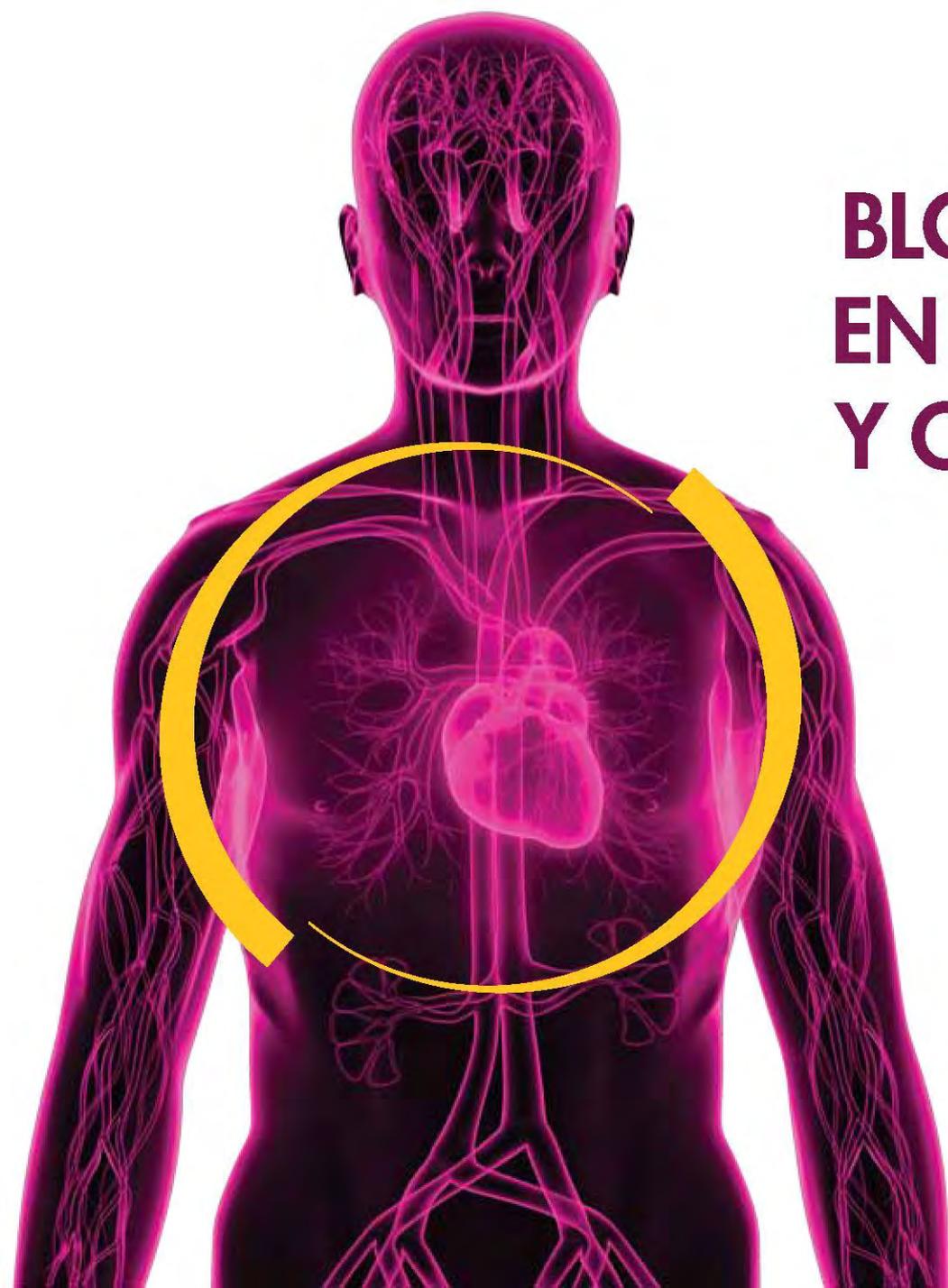
	Control Hipertensión	Protección Vascular	Protección Renal
I ECA	√	√	√
BRAT	√	√	√
Alfa Bloqueadores	√	NO	NO
Beta Bloqueadores	√	√	NO
Calcio Antagonistas	√	√	NO
Diuréticos	√	NO	NO
Inhibidores Directos de Renina	√	¿?	√

Incidencia de DM y tratamiento antihipertensivo

Meta análisis de 22 ensayos clínicos



BLOQUEO DEL SRAA EN HTA: RELEVANCIA Y CARACTERIZACIÓN DE LOS ARA II



Estructuras Químicas de los ARA II más ampliamente utilizados.



LOSARTÁN



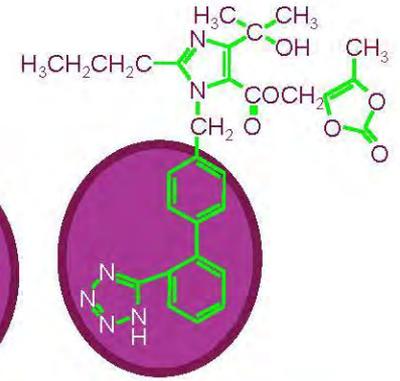
VALSARTÁN



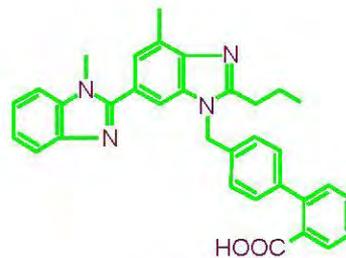
IRBESARTÁN



CANDESARTÁN
CILEXETILO

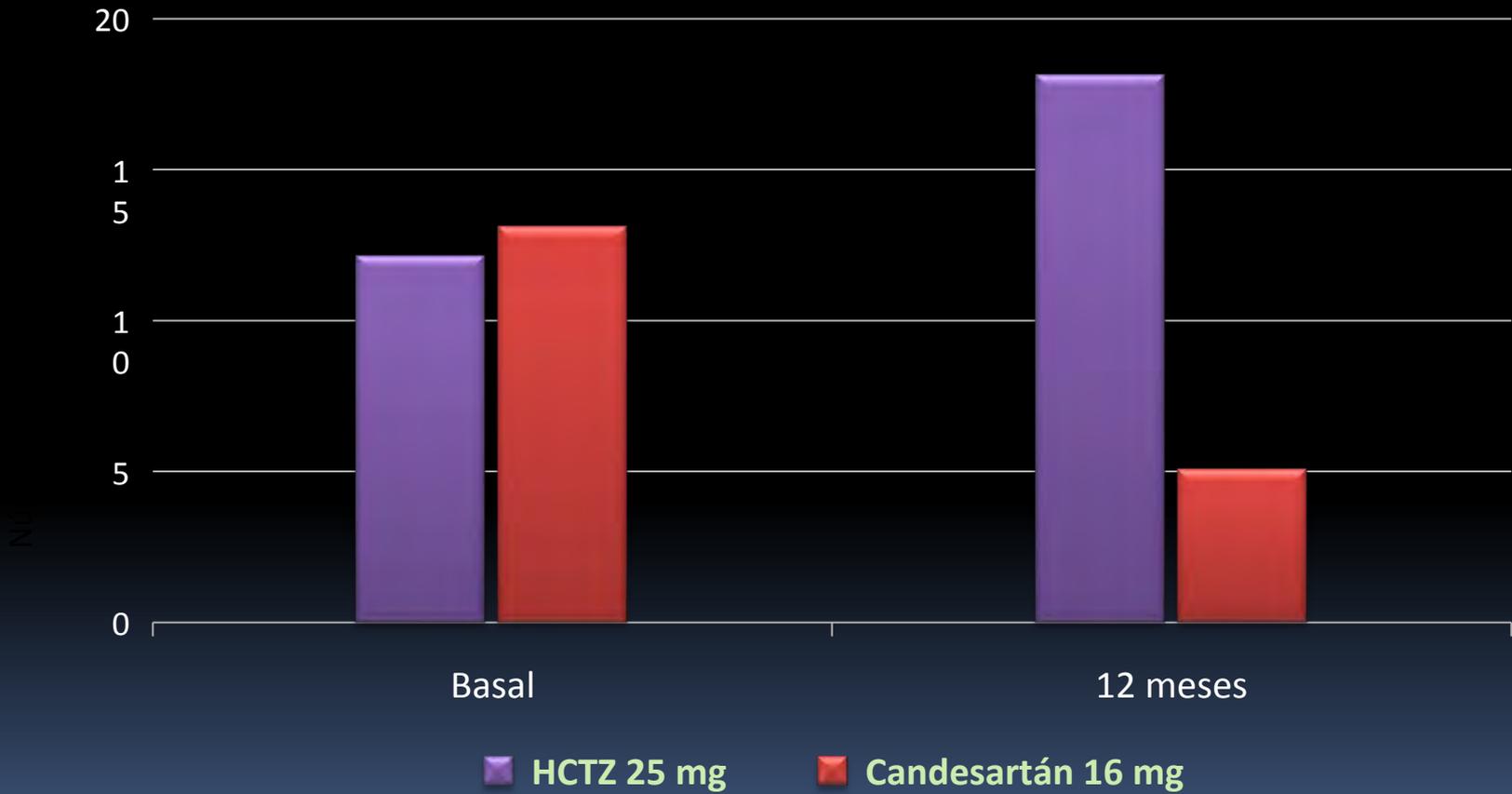


OLMESARTÁN
MEDOXOMILO



TELMISARTÁN

Estudio ALPINE: Desarrollo de Síndrome Metabólico

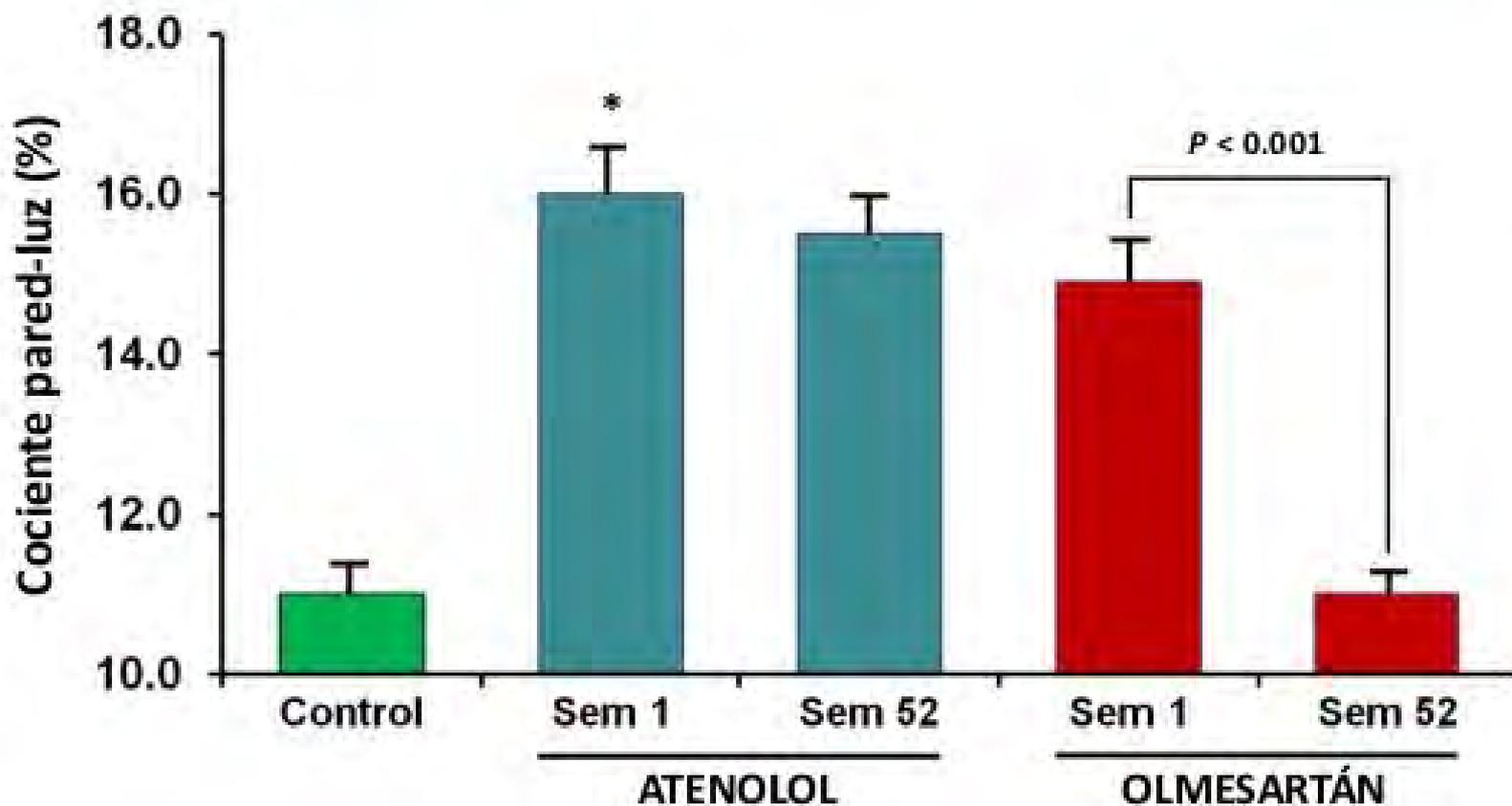


Antihypertensive Treatment and Lipid Profile in a North of Sweden Efficacy Evaluation (**ALPINE study**)

Lindholm LH. J Hypertens 2003; 21:1563-1574

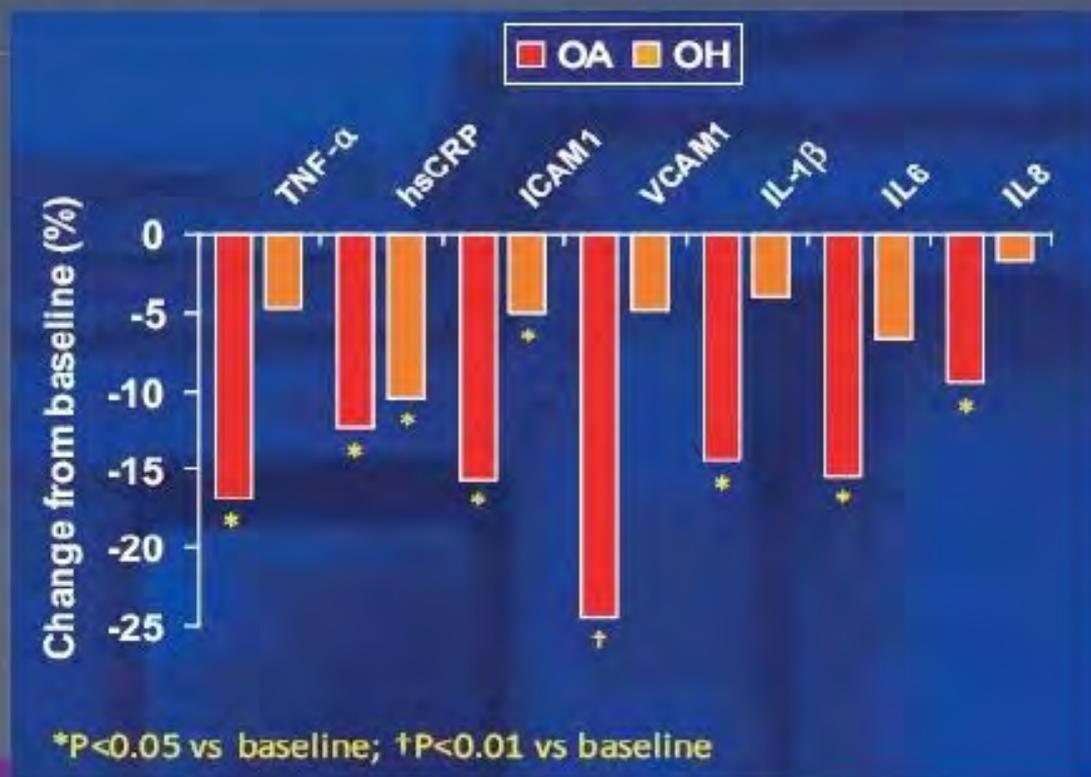
VIOS

Olmesartán revierte la hipertrofia vascular



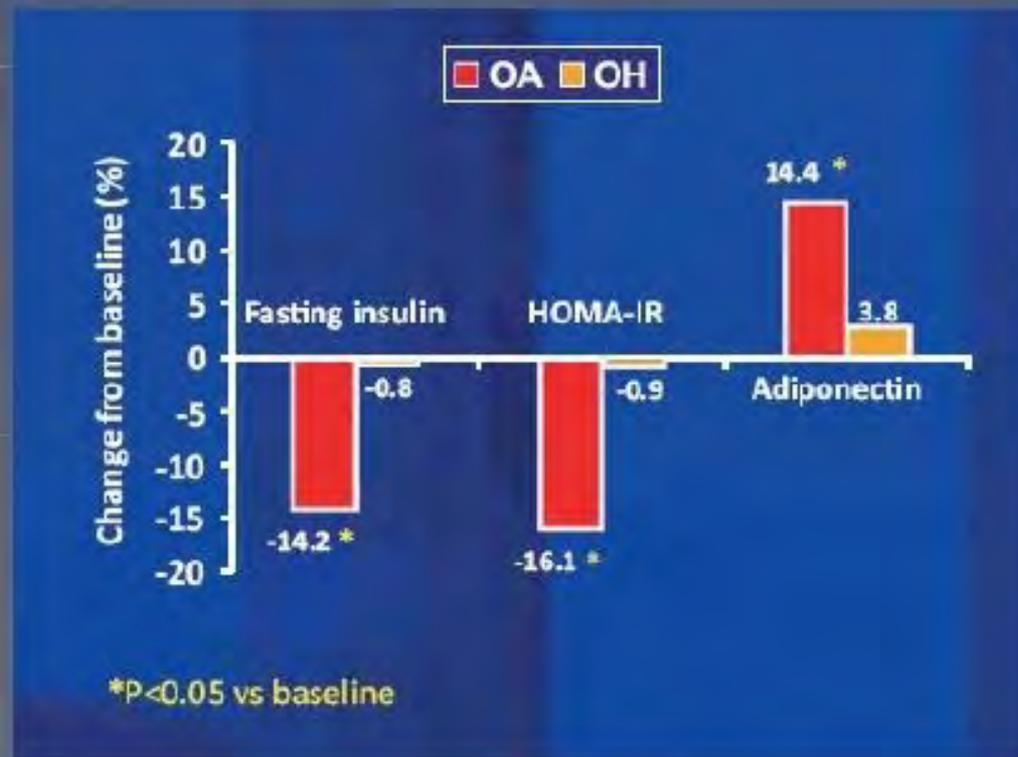
Efecto de Olmesartán/amlodipino sobre la inflamación

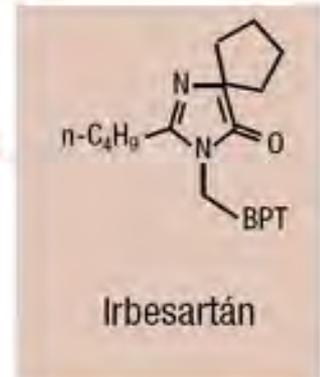
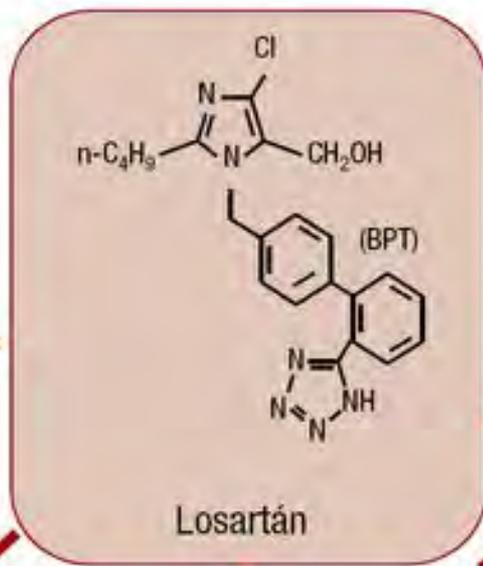
Estudio OLAS; N=120 pacientes con síndrome metabólico, entre 28 y 75a
Aleatorizados a Olmesartán/amlodipino (OA 20/5) u Olmesartán/HCTZ
(OH 20/12,5) 24 semanas



Efecto de Olmesartán/amlodipino sobre la resistencia a la insulina

Estudio OLAS; N=120 pacientes con síndrome metabólico, entre 28 y 75a
Aleatorizados a Olmesartán/amlodipino (OA 20/5) o Olmesartán/HCTZ
(OH 20/12,5) 24 semanas





**2014 Guideline for the
Management of High Blood
Pressure (Eighth Joint National
Committee): Take-Home Messages**



Table 2

Three suggested strategies to dose the blood pressure (BP) medications

Strategy A Maximize first medication before adding second and third from the list (thiazide, calcium channel blocker [CCB], angiotensin-converting enzyme inhibitor [ACEI], or angiotensin receptor blocker [ARB]). Avoid both ACEI and ARB together. Titrate each drug to maximum recommended dose to achieve goal BP before adding another medication.

Table 3
Strategies to dose and titrate antihypertensive drugs

A	B	C
Maximize first medication before adding second.	Add second medication before reaching maximum dose of first medication.	Start with 2 medication classes separately or as fixed-dose combinations.

If goal BP not achieved

- Reinforce compliance with medication and lifestyle.
- For strategies A and B, add and titrate thiazide-type diuretic or angiotensin-converting enzyme inhibitor (ACEI) or angiotensin receptor blocker (ARB) or calcium channel blocker (CCB) (use medication class not previously selected and avoid combined use of ACEI and ARB).
- For strategy C, titrate doses of initial medications to maximum.

If goal BP not achieved

- Reinforce compliance with medication and lifestyle.
- Add and titrate thiazide-type diuretic or ACEI or ARB or CCB (use medication class not previously selected and avoid combined use of ACEI and ARB).

If goal BP not achieved

- Reinforce compliance with medication and lifestyle.
- Add additional medication class (eg, β -blocker, aldosterone antagonist, or others) and/or refer to physician with expertise in hypertension management.

Table 4
Summary recommendations from JNC 8

Patient Subgroup	Target SBP (mm Hg)	Target DBP (mm Hg)
Age \geq 60 y	<150	<90
Age <60 y	<140	<90
Age >18 y with CKD	<140	<90
Age >18 y with diabetes	<140	<90

General population (nonblack)

- Thiazides, CCB, ACEI, or ARB initially

General population (black)

- Thiazides or CCB initially

Chronic kidney disease

- Treatment should include ACEI or ARB

Adjust therapy after 1 month if BP goal not achieved.

Do not use ACEI or ARB together.

If patients need >3 drugs, refer to hypertension specialist.

Hipertension es Factor de Riesgo para:

- Enfermedad Cerebrovascular
- Enfermedad Arteria Coronaria
- Insuficiencia Cardiaca Congestiva
- Insuficiencia Renal
- Enfermedad Vascular Peripheral
- Dementia
- Fibrilacion Atrial
- Disfuncion Erectil

Metas de Tratamiento

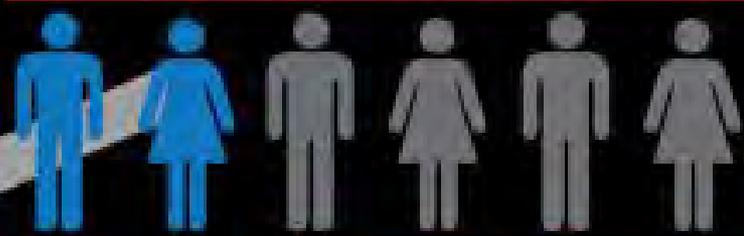
VALORES DE PRESION ARTERIAL EN PACIENTES

CONDICION	META
Hipertension Sistolica Aislada	<140
Hipertension Sistolo/Diastolica	
• Sistolica	<140
• Diastolica	<90
Diabetes o Enfermedad Renal	
• Sistolica	<130
• Diastolica	<80

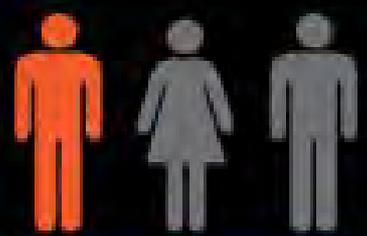
1



1 de cada 3 adultos sufre de hipertensión



1 de cada 3 adultos con hipertensión desconoce su enfermedad



1 de cada 3 adultos que se está tratando por hipertensión no logra mantener su presión bajo 140/90

3

Muchas Gracias



Projected Average Cost-Effectiveness of Full Implementation of the 2014 Guidelines for Hypertension Treatment in Patients without Cardiovascular Disease, According to Sex, Age, Hypertension Stage, and Status with Respect to Diabetes and Chronic Kidney Disease.

Groups without Prior Cardiovascular Disease	<div style="display: flex; justify-content: space-around; font-size: small;"> ■ Cost-saving ■ Cost-effective (ICER <\$50,000) ■ Intermediate value (ICER ≥\$50,000 and <\$150,000) ■ Low value (ICER ≥\$150,000) </div>					
	Men			Women		
	Stage 2 hypertension	Stage 1 hypertension, diabetes or CKD	Stage 1 hypertension, no diabetes or CKD	Stage 2 hypertension	Stage 1 hypertension, diabetes or CKD	Stage 1 hypertension, no diabetes or CKD
33–44 Yr	Cost-saving	\$13,000	\$40,000	\$26,000	\$125,000	\$181,000
45–59 Yr	Cost-saving	Cost-saving	Cost-saving	Cost-saving	\$16,000	\$22,000
60–74 Yr	Cost-saving	Cost-saving	Cost-saving	Cost-saving	\$3,000	\$7,000

Coronary Microvascular Dysfunction, Microvascular Angina, and Treatment Strategies

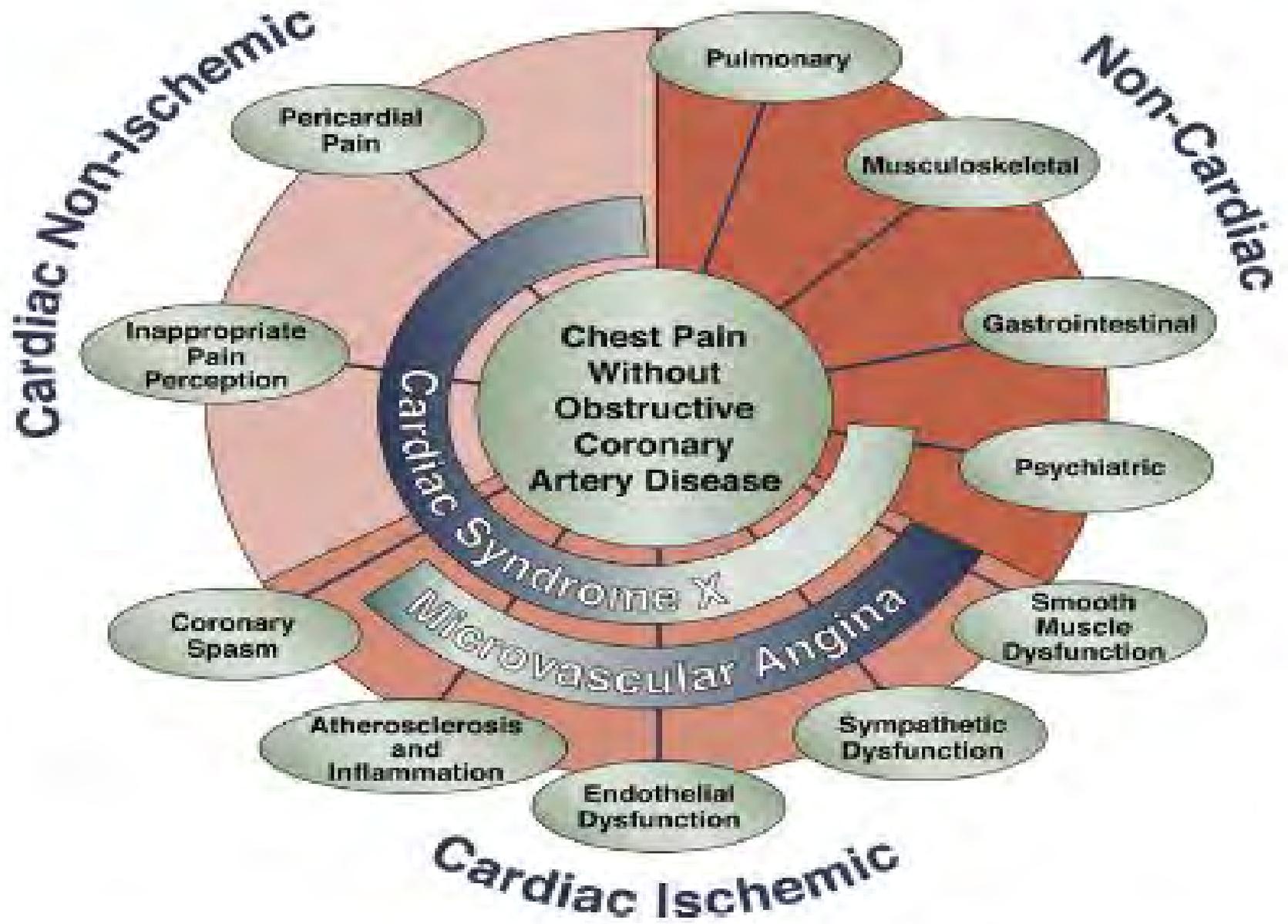


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JACC: CARDIOVASCULAR IMAGING CME

Angina without coronary artery disease (CAD) has substantial morbidity and is present in 10% to 30% of patients undergoing angiography. Coronary microvascular dysfunction (CMD) is present in 50% to 65% of these patients. The optimal treatment of this cohort is undefined. We performed a systematic review to evaluate treatment strategies for objectively-defined CMD in the absence of CAD. We included studies assessing therapy in human subjects with angina and coronary flow

FIGURE 1 Etiologies of Chest Pain Without Obstructive CAD



FACTORES DE RIESGO



Historia familiar



Sedentarismo



Dieta no saludable



Sobrepeso

346 millones

En el mundo hay más de 346 millones de personas con diabetes.

80%

Más del 80% de las muertes por diabetes se registran en países de ingresos bajos y medios.

2030

Las muertes por diabetes podrían multiplicarse por dos entre 2005 y 2030.

