BETA BLOQUEANTES EN HTA Y PASAN LOS AÑOS…..

HAY LUGAR PARA LOS BB EN HTA?

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Equipo de HTA del ICBA

Presidente Científico del VI WEEKEND HTA

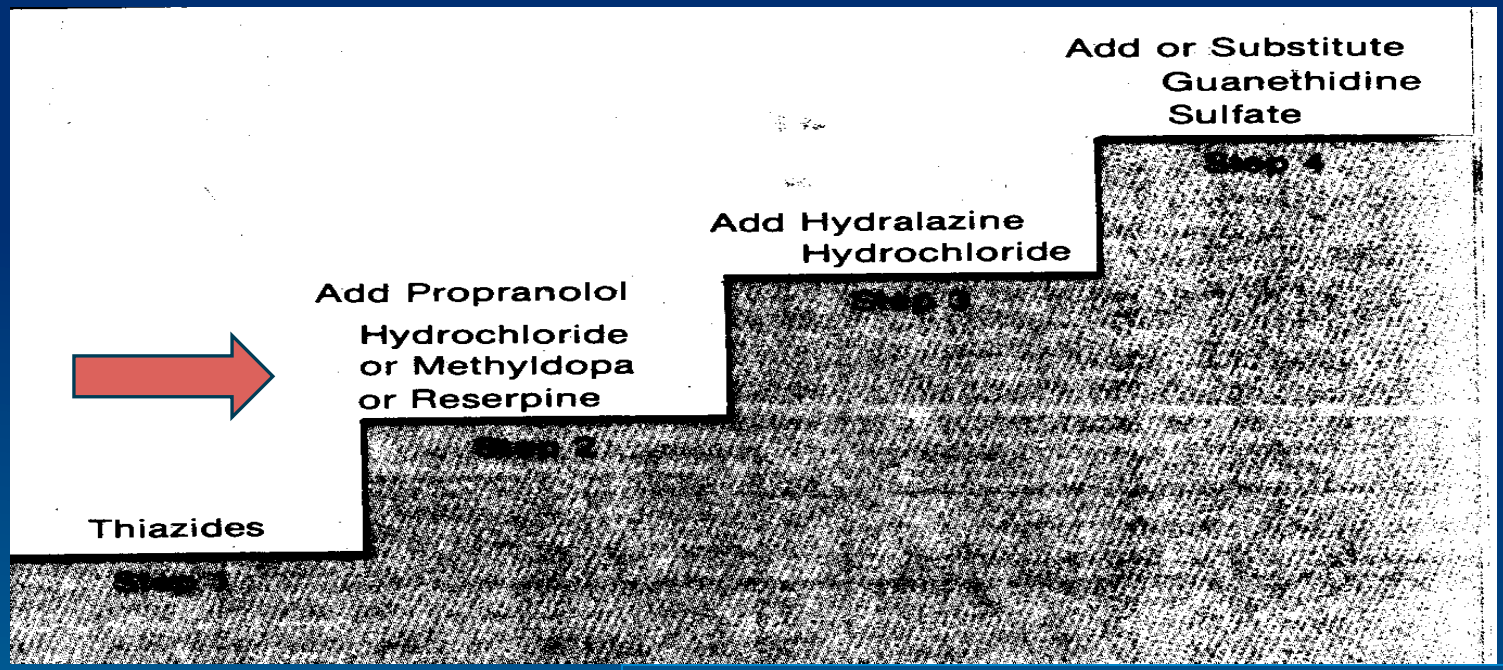
Ex Presidente del Comité de HTA, FAC 2014-2015

JNC 1

Special Communication

Report of the Joint National Committee on Detection, Evaluation, and Treatment of High Blood Pressure

A Cooperative Study



Moser et al. High Blood Pressure. JAMA, jan ,1977;vol 237, Nº 3.
Modificado Dr. Villamil.

JNC 2

Special Report

The 1980 Report of the Joint National Committee on Detection, Evaluation, and Treatment of High Blood Pressure

The Joint National Committee on Detection, Evaluation, and Treatment of High Blood Pressure

Stepped-Care Regimens

Step	Drugs
1	Diuretic*
2	Adrenergic Inhibiting Agents†
	Clonidine hydrochloride
	Methyldopa
	Metoprolol tartrate
	Nadolol
	Prazosin hydrochloride‡
	Propranolol hydrochloride
	Rauwolfia alkaloids
3	Vasodilator§
	Hydralazine hydrochloride
4	Additional Adrenergic Inhibiting Agent
	Guanethidine sulfate‖

Arch Intern Med. High Blood Pressure. Vol 140, Oct 1980
Modificado Dr. Villamil.

JNC 3

The 1984 Report of the Joint National Committee on Detection, Evaluation, and Treatment of High Blood Pressure

The Joint National Committee on Detection, Evaluation, and Treatment of High Blood Pressure

Table 4.—Stepped-Care Approach to Drug Therapy*

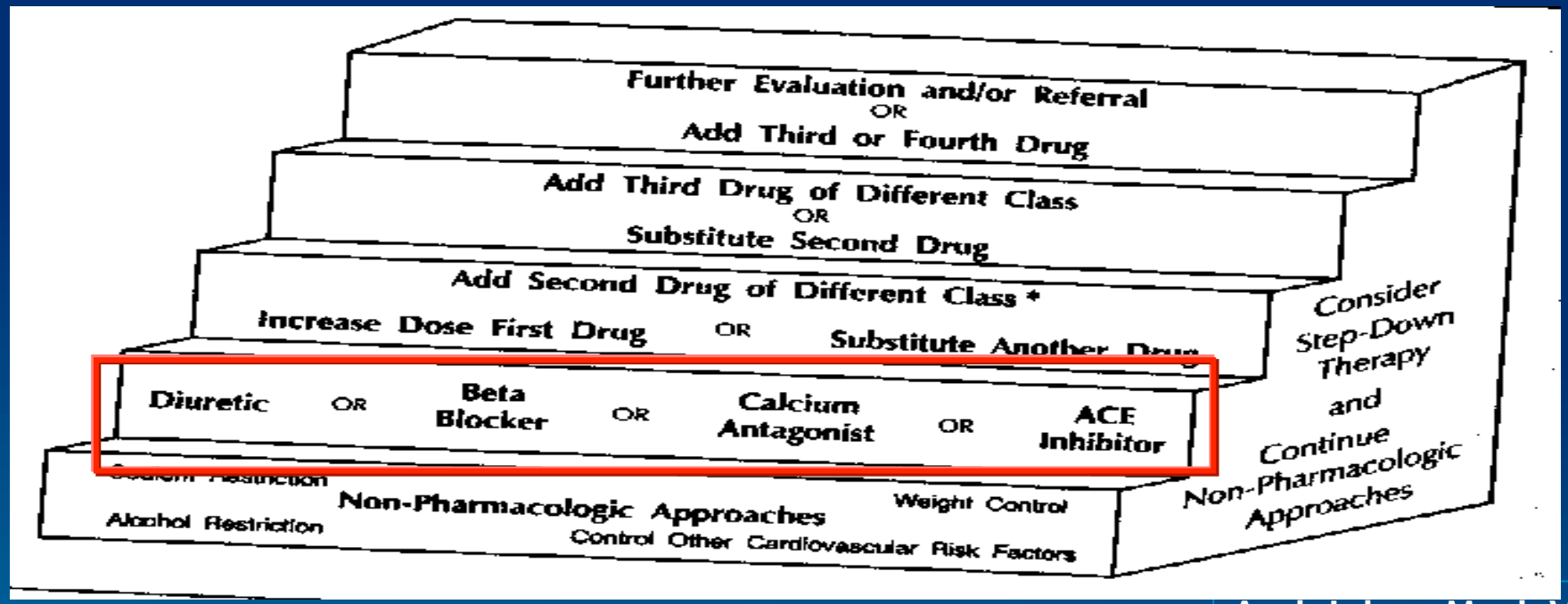
Step	Drug Regimens
1	Begin with less than a full dose of either a thiazide-type diuretic or a β-blocker†; proceed to full dose if necessary and desirable
2	If BP control is not achieved, either add a small dose of an adrenergic-inhibiting agent‡ or a small dose of thiazide-type diuretic; proceed to full dose if necessary and desirable§; additional substitutions may be made at this point‖
3	If BP control is not achieved add a vasodilator, hydralazine hydrochloride, or minoxidil for resistant cases
4	If BP control is not achieved, add guanethidine monosulfate

Arch Intern Med. High BP. Vol 144, May 1984
Modificado Dr. Villamil.

JNC 4

The 1988 Report of the Joint National Committee on Detection, Evaluation, and Treatment of High Blood Pressure

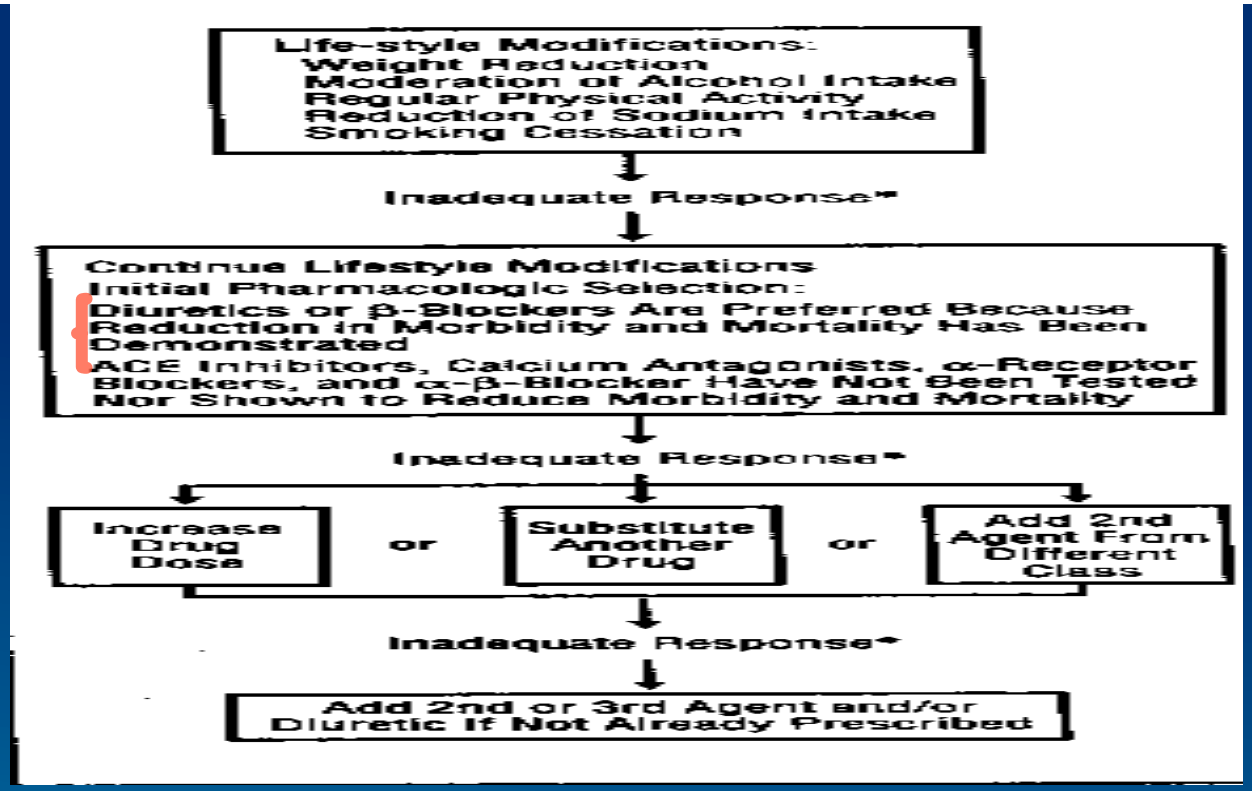
1988 Joint National Committee



Arch Intern Med. Vol 148, May 1988
Modificado Dr. Villamil.

JNC 5

The Fifth Report of the Joint National Committee on Detection, Evaluation, and Treatment of High Blood Pressure (JNC V)



Arch Intern Med. Vol 153, Jan 1993

Modificado Dr. Villamil.

JNC 6

1998

Initial Drug Choices*

Uncomplicated Hypertension†

Diuretics
Beta-blockers

Specific Indications for the Following Drugs (see table 9)

ACE inhibitors
Angiotensin II receptor blockers
Alpha-blockers
Alpha-beta-blockers
Beta-blockers
Calcium antagonists
Diuretics

Compelling Indications†

Diabetes mellitus (type 1) with proteinuria
- ACE inhibitors

Heart failure
- ACE inhibitors
- Diuretics

Isolated systolic hypertension (older persons)
- Diuretics **preferred**
- Long-acting dihydropyridine calcium antagonists

Myocardial infarction
- Beta-blockers (non-ISA)
- ACE inhibitors (with systolic dysfunction)

- Start with a low dose of a long-acting once-daily drug, and **titrate dose**.
- Low-dose combinations may be appropriate.

Beta-adrenoceptor blocking drugs

Non selective

- ISA

Nadolol
Propanolol
Timolol
Sotalol
Tertalolol

+ ISA

Pindolol
Carteolol
Penbutolol
Alprenolol
Oxprenolol

Selective

- ISA

Atenolol
Esmolol
Metroprolol
Bisoprolol
Betaxolol
Bevantolol

+ ISA

Acebutolol
(Practolol)
Celiprolol

With alpha-blocking activity

Nebivolol

Labetalol
Bucindolol
Carvedilol

BETA BLOQUEANTES CLASIFICACIÓN

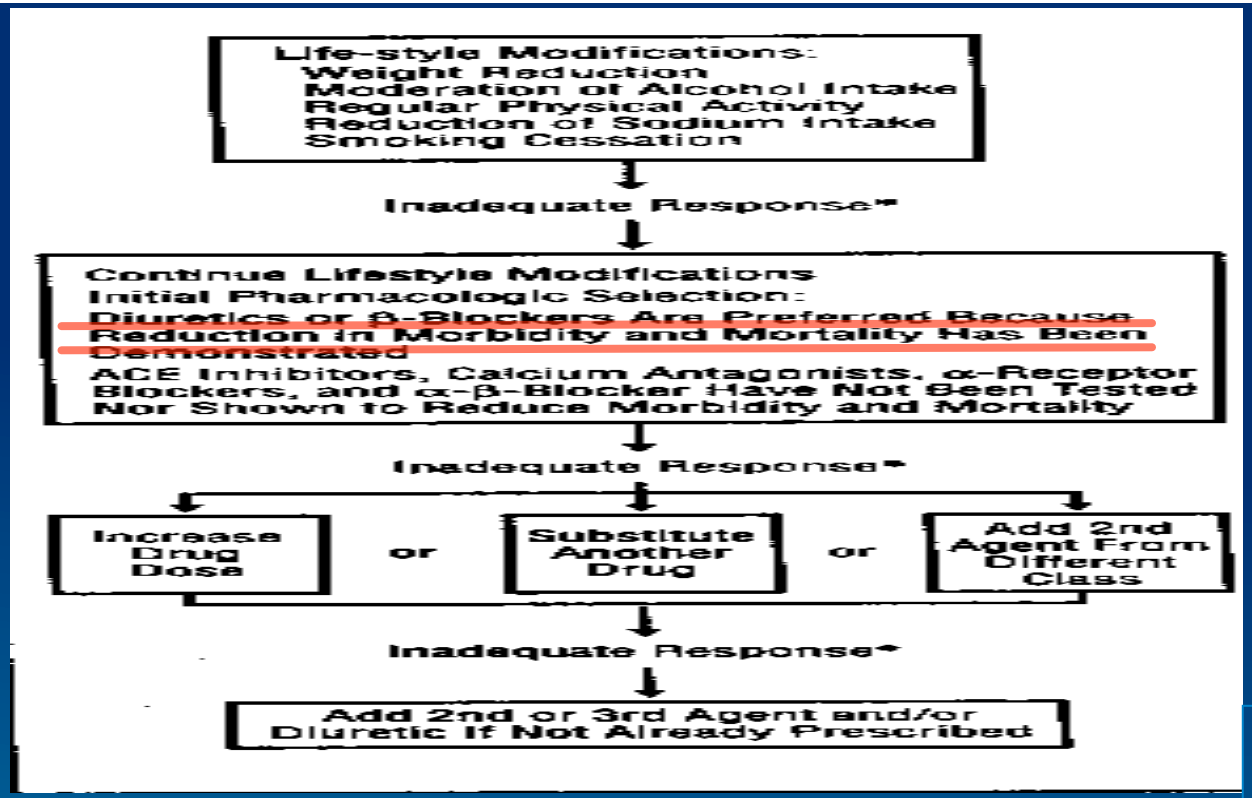
- Liposolubles
- Hidrofílicos
- Lipofílicos
- Hidroliposolubles

FARMACODINAMIA

- ***Bloqueo Beta 1:*** Disminuye la FC
  Disminuye Gasto Cardíaco
  Disminuye la contractilidad
  Disminuye la secreción de renina por estimulación adrenérgica
- ***Bloqueo Alfa Pre-Sináptico:***
  Disminuye la producción de NORA en las terminaciones nerviosas

JNC 5

The Fifth Report of the Joint National Committee on Detection, Evaluation, and Treatment of High Blood Pressure (JNC V)



Arch Intern Med. Vol 153, Jan 1993

Modificado Dra. Calabria

LIFE: STUDY DESIGN

Patients with hypertension (blood pressure 160-200/ 95-115 mm Hg) and left ventricular hypertrophy

Losartan
Angiotensin II antagonist
Dose titrated to BP <140/90 mm Hg

(n=4,605)

Atenolol
Beta-blocker
Dose titrated to BP <140/90 mm Hg

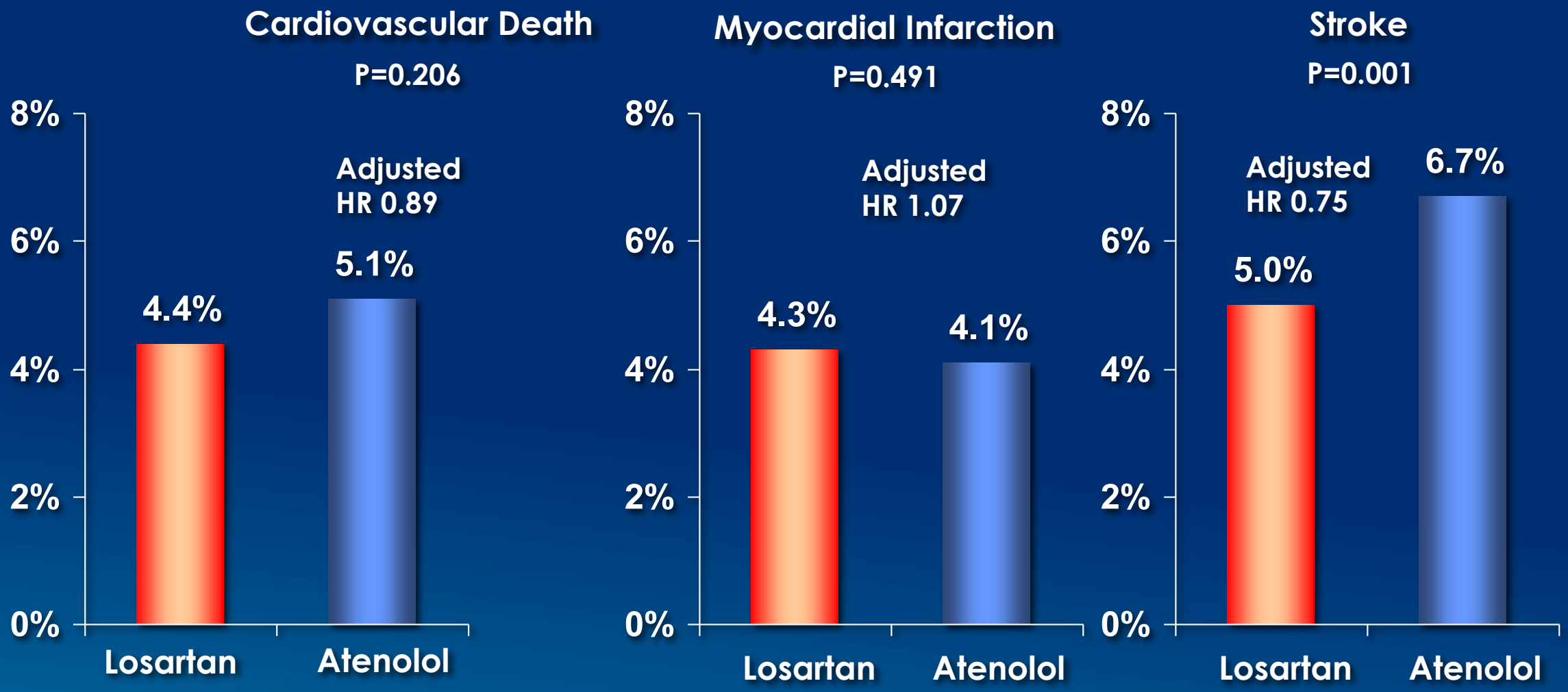
(n=4,588)

Followed for ≥4 years - Mean follow-up 4.8 years

Cardiovascular death, MI, stroke

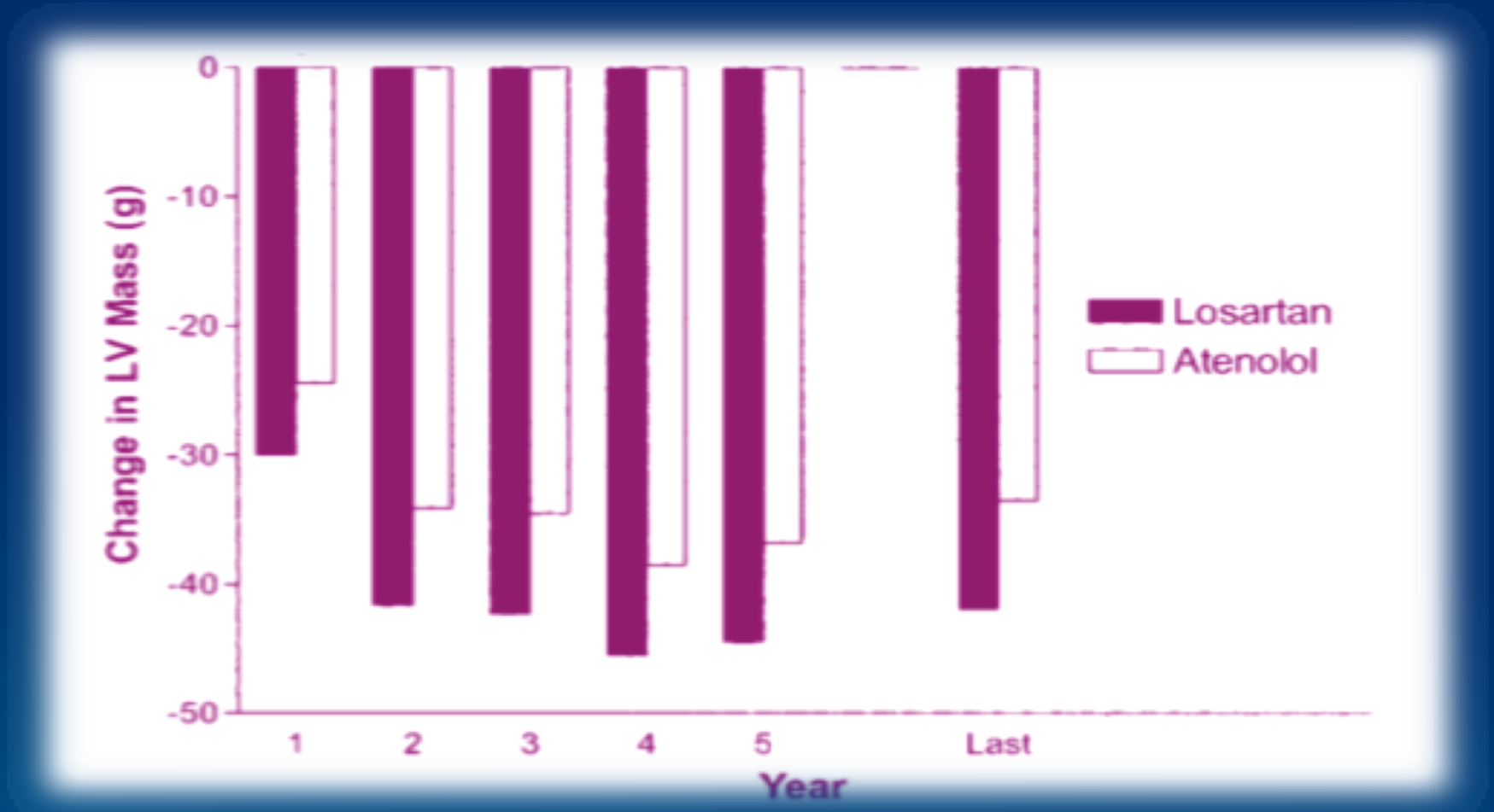
Lancet 2002; 359:995-1003

LIFE: INDIVIDUAL ENDPOINT RESULTS



Lancet 2002; 359:995-1003

LIFE: STUDY DESIGN



Circulation 2004;110:1456-1462

Prevention of cardiovascular events with an antihypertensive regimen of amlodipine adding perindopril as required versus atenolol adding bendroflumethiazide as required, in the Anglo-Scandinavian Cardiac Outcomes Trial-Blood Pressure Lowering Arm (ASCOT-BPLA): a multicentre randomised controlled trial

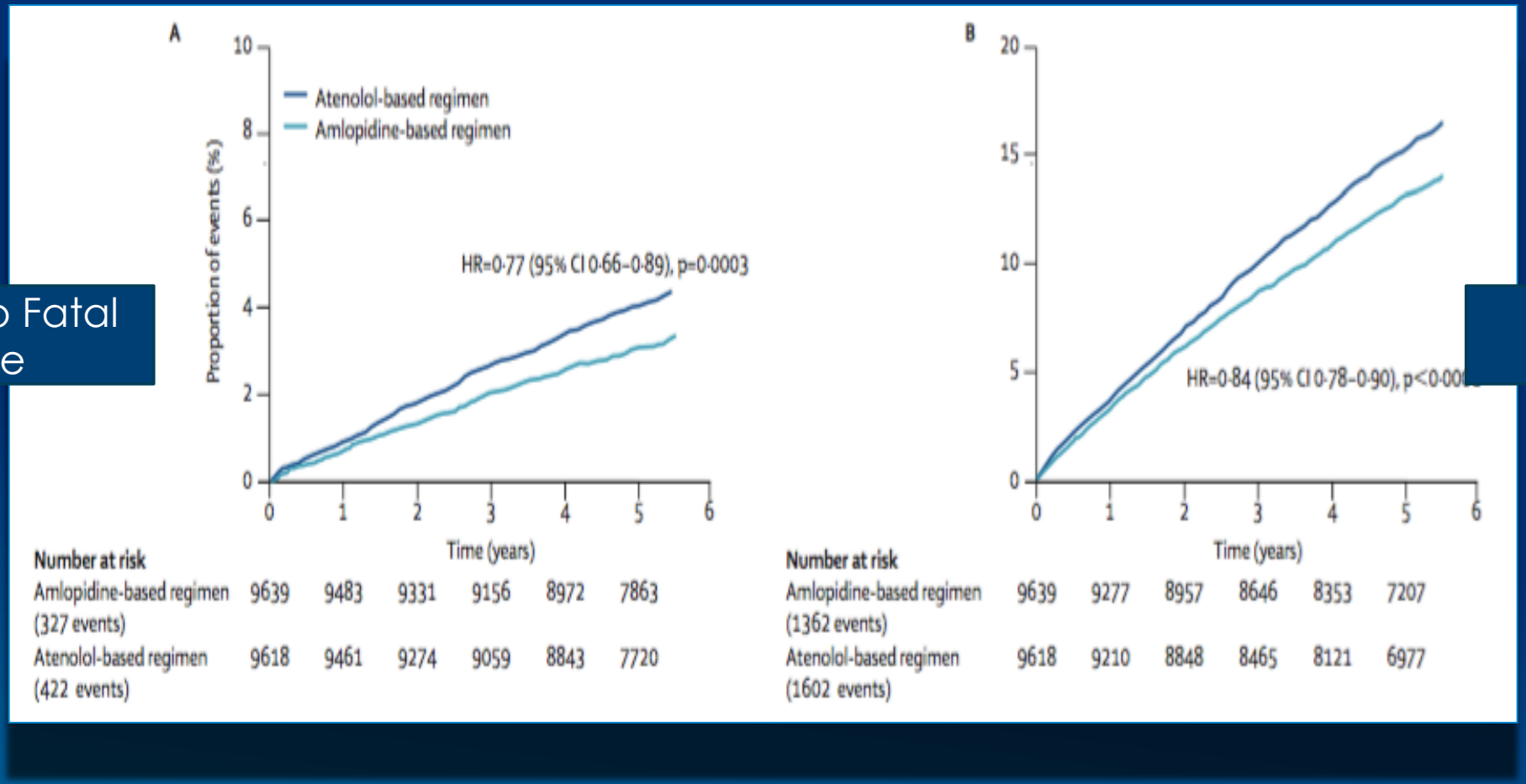
*Björn Dahlöf, Peter S Sever, Neil R Poulter, Hans Wedel, D Gareth Beevers, Mark Caulfield, Rory Collins, Sverre E Kjeldsen, Arni Kristinsson, Gordon T McInnes, Jesper Mehlsen, Markku Nieminen, Eoin O´Brien, Jan Östergren, for the ASCOT investigators**

- Incluyo 19.257 ptes.
- Comparó Amlodipina más Perindopril Vs Atenolol más Bendroflumethiazide
- End Point: IAM y Enfermedad CV
- Duración del estudio 5.5 años.

Lancet 2005;vol 366

ASCOT Study

Fatal y No Fatal Stroke



Eventos CV

Lancet 2005;vol 366

Hypertension

Differential Impact of Blood Pressure–Lowering Drugs on Central Aortic Pressure and Clinical Outcomes

Principal Results of the Conduit Artery Function Evaluation (CAFE) Study

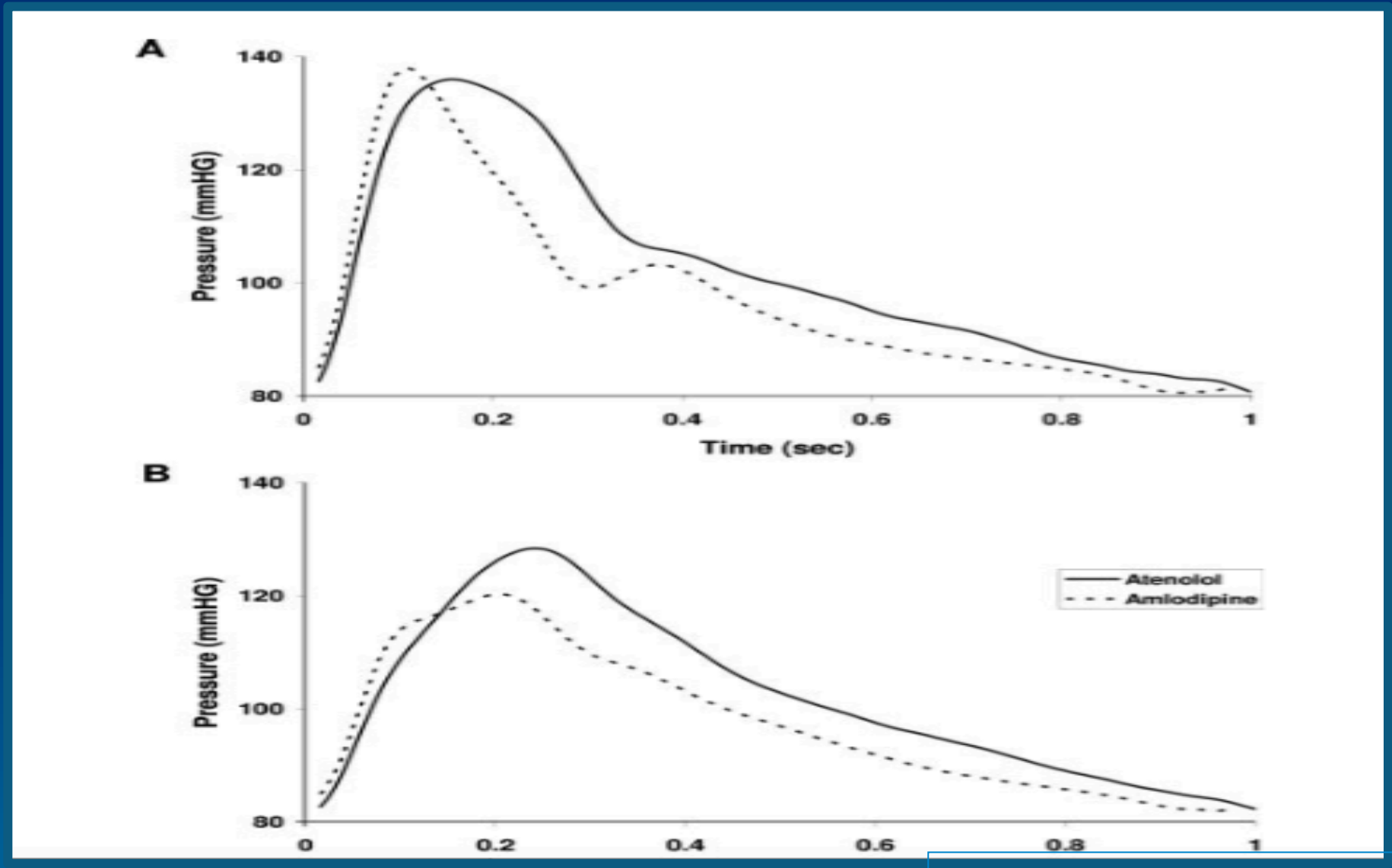
The CAFE Investigators, for the Anglo-Scandinavian Cardiac Outcomes Trial (ASCOT) Investigators

CAFE Steering Committee and Writing Committee: Bryan Williams, MD, FRCP; Peter S. Lacy, PhD; Simon M. Thom, MD, FRCP; Kennedy Cruickshank, MD; Alice Stanton, MB, PhD, FRCPI; David Collier, MBBS, PhD; Alun D. Hughes, MBBS, PhD; H. Thurston, MD, FRCP

Study Advisor: Michael O'Rourke, MD, FRACP

Circulation 2006;113:1213-1225

CAFE Study



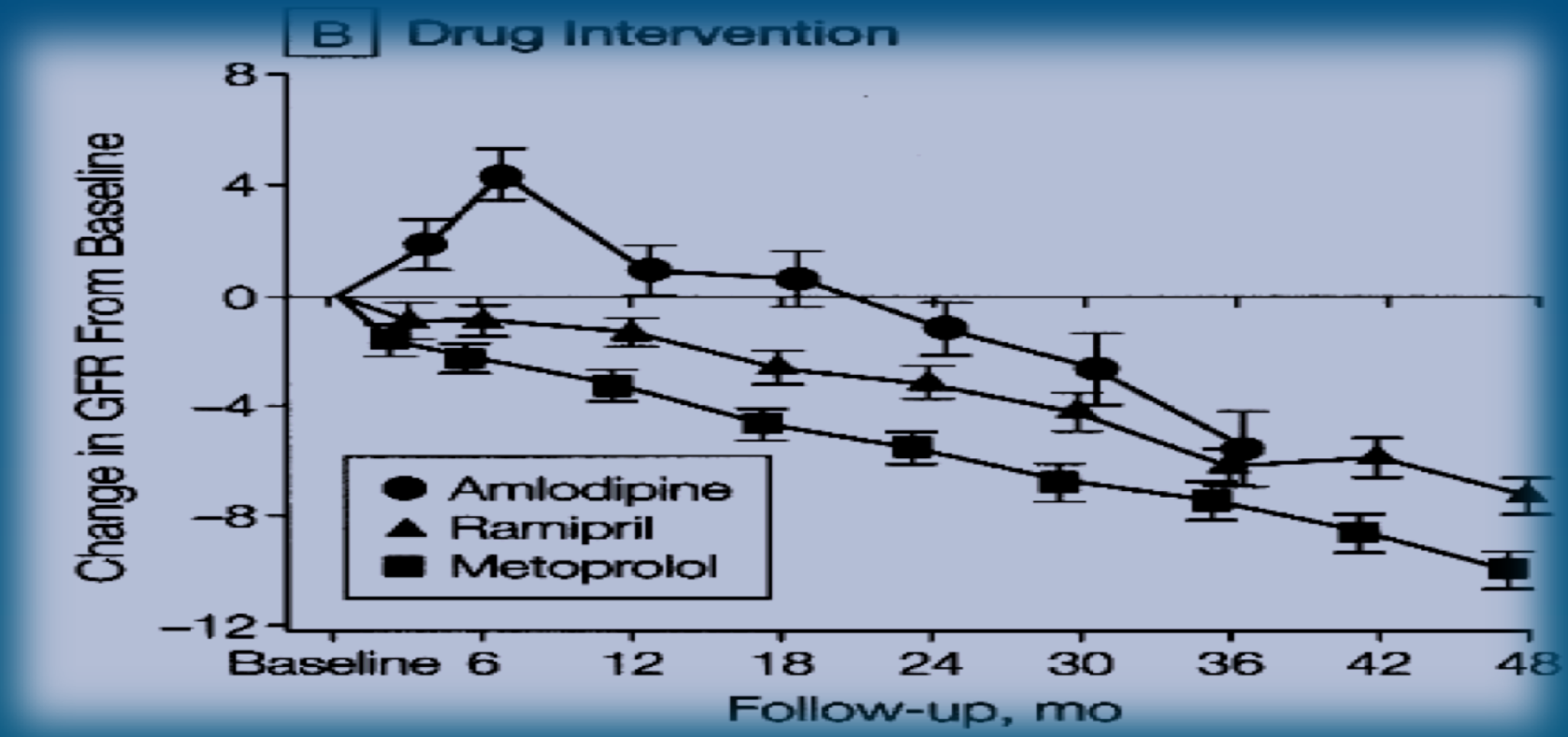
Circulation 2006;113:1213-1225

AASK Study

Current Concepts of Pharmacotherapy in Hypertension
Domenic A. Sica, MD, Section Editor

The African American Study of Kidney Disease and Hypertension (AASK) Trial: What More Have We Learned?

Domenic A. Sica, MD



Circulation 2006;113:1213-1225

Tanto en el Estudio LIFE, ASCOTT y CAFÉ los
Beta Bloqueantes

Propanolol

Atenolol

Bisoprolol

Metoprolol

SELECTIVOS Y NO SELECTIVOS

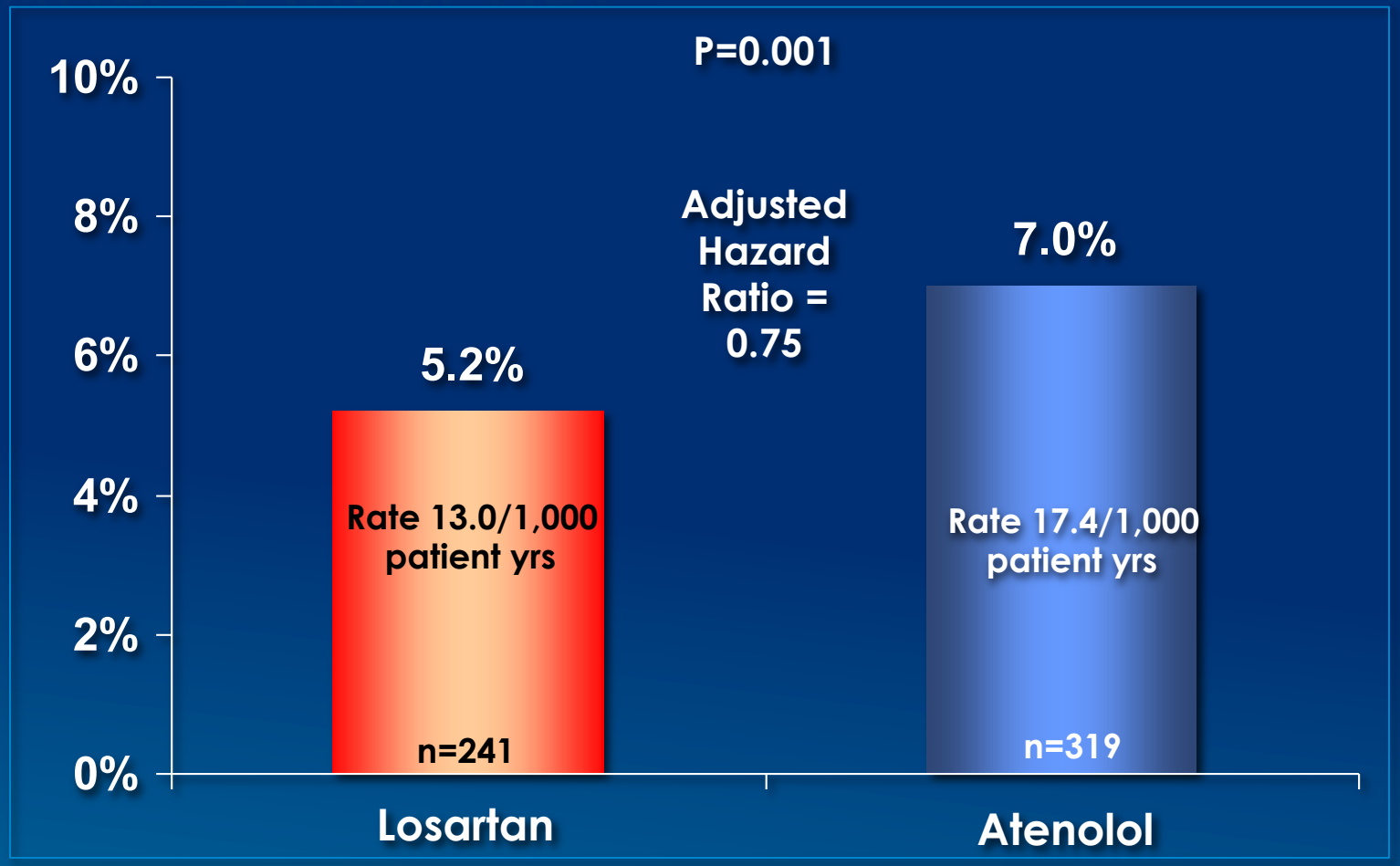
No demostraron en HTA

- Prevenir la ECV
- Prevenir el Desarrollo de HVI
- No mejora la PAC, VOP
- No tiene acción de Nefroprotección
- A nivel Cerebrovascular no hay evidencias de prevención de ACV ni deterioro Cognitivo

ADEMÁS……

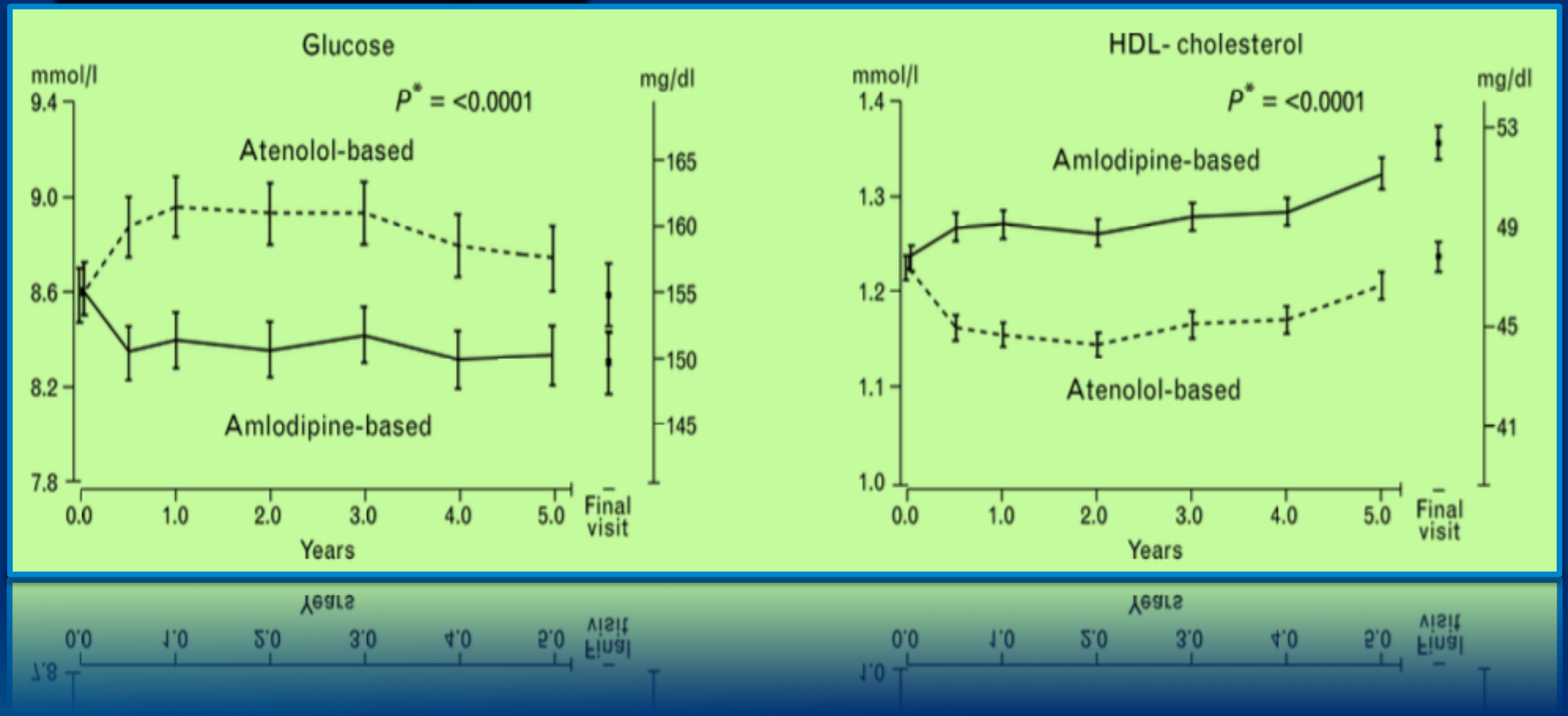
- *No son Drogas Metabolicamente NEUTRAS*

LIFE: New –Onset DBT



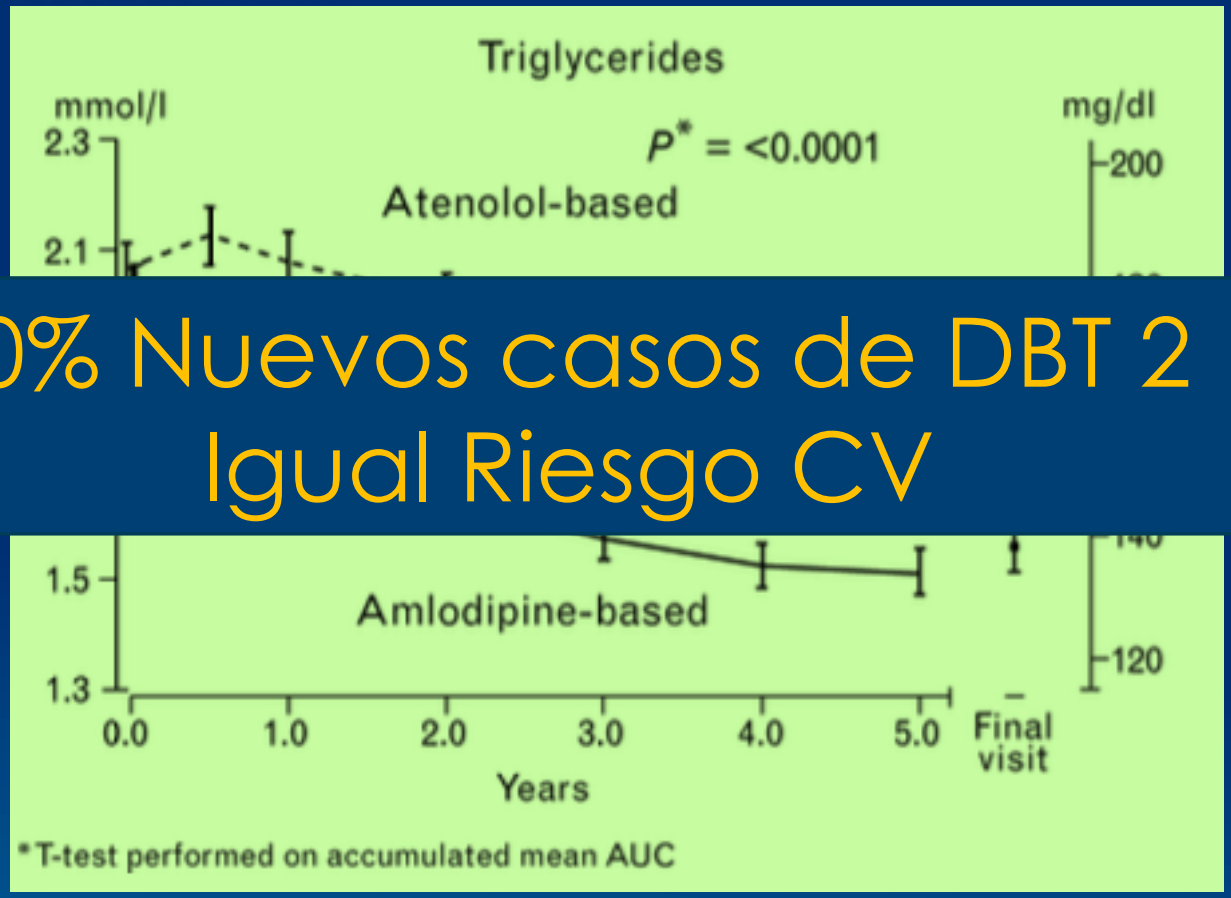
Lancet 2002; 359:995-1003

ASCOT Study



J of Hyp 2008;26:2103-2111

ASCOT Study



30% Nuevos casos de DBT 2
Igual Riesgo CV

J of Hyp 2008;26:2103-2111

JNC 7/8

Table 1. Comparison of Current Recommendations With JNC 7 Guidelines

Topic	JNC 7	2014 Hypertension Guideline
Methodology	Nonsystematic literature review by expert committee including a range of study designs Recommendations based on consensus	Critical questions and review criteria defined by expert panel with input from methodology team Initial systematic review by methodologists restricted to RCT evidence Subsequent review of RCT evidence and recommendations by the panel according to a standardized protocol
Definitions	Defined hypertension and prehypertension	Definitions of hypertension and prehypertension not addressed, but thresholds for pharmacologic treatment were defined
Treatment goals	Separate treatment goals defined for "uncomplicated" hypertension and for subsets with various comorbid conditions (diabetes and CKD)	Similar treatment goals defined for all hypertensive populations except when evidence review supports different goals for a particular subpopulation
Lifestyle recommendations	Recommended lifestyle modifications based on literature review and expert opinion	Lifestyle modifications recommended by endorsing the evidence-based Recommendations of the Lifestyle Work Group
Drug therapy	Recommended 5 classes to be considered as initial therapy but recommended thiazide-type diuretics as initial therapy for most patients without compelling indication for another class Specified particular antihypertensive medication classes for patients with compelling indications, ie, diabetes, CKD, heart failure, myocardial infarction, stroke, and high CVD risk Included a comprehensive table of oral antihypertensive drugs including names and usual dose ranges	Recommended selection among 4 specific medication classes (ACEI or ARB, CCB or diuretics) and doses based on RCT evidence Recommended specific medication classes based on evidence review for racial, CKD, and diabetic subgroups Panel created a table of drugs and doses used in the outcome trials
Scope of topics	Addressed multiple issues (blood pressure measurement methods, patient evaluation components, secondary hypertension, adherence to regimens, resistant hypertension, and hypertension in special populations) based on literature review and expert opinion	Evidence review of RCTs addressed a limited number of questions, those judged by the panel to be of highest priority.
Review process prior to publication	Reviewed by the National High Blood Pressure Education Program Coordinating Committee, a coalition of 39 major professional, public, and voluntary organizations and 7 federal agencies	Reviewed by experts including those affiliated with professional and public organizations and federal agencies; no official sponsorship by any organization should be inferred

Rev Esp Cardiol. 2003;56:843-7 - Vol. 56 Núm.09

Jama 2013, dic. 18

NUEVOS BETA BLOQUEANTES

- Bloqueo Alfa 1
  - Labetalol
  - *Carvedilol*
- Agonista Parcial B_2
  - Celiprolol
  - *Pindolol*
- Por Liberación ON
  - Nebivolol

ACCIONES PLEITRÓPICAS

Carvedilol:

- Actúa en la regulación citosólica y mitocondrial del calcio durante el stress oxidativo de la apoptosis de las fibras del miocardio.
- Inhibe la agregación plaquetaria por su acción sobre la adenosina diphosphate

Nebivolol:

- Facilita los procesos de reparación tisular y angiogénesis por su acción sobre la transcriptasa inversa en la rta. inmune.
- Inhibe la expresión de Metalloproteinasas y proteinasas involucradas en procesos inflamatorios y remodelación vascular.
- Down regulation en genes inflamatorios e involucrados en el stress oxidativo.

NUEVOS BETA BLOQUEANTES

- Mejoran la función endotelial
- Mejora la insulino resistencia
- Son metabolicamente neutros

NEBIVOLOL - CARVEDILOL

- Mejoran la Tolerancia al Ejercicio en Enfermedad Coronaria
- Mejoran el indice cardíaco en Insuficiencia Cardíaca
- Inhiben la agregación plaquetaria
- No interfieren en el metabolismo de los Lípidos e Hidratos de Carbono
- Menor Impotencia sexual
- Menos astenia

JAAC 2009;vol 54:1491-99

INDICACIÓN DE LOS BB EN HTA
CUÁNDO UTILIZARLOS?

GUIAS DE LA SOCIEDAD ARGENTINA DE HIPERTENSION PARA EL DIAGNOSTICO, ESTUDIO, TRATAMIENTO Y SEGUIMIENTO DE LA HIPERTENSION ARTERIAL

Grupo principal	Subgrupo	Indicaciones (*)	Contraindicaciones Absolutas	Contraindicaciones Relativas
Betabloqueantes		HTA asociada con CI HTA asociada con IC o disfunción VI HTA gestacional HTA asociada con hiperdinamia HTA en pacientes con jaqueca HTA asociada con temblor esencial HTA e hipertiroidismo	Bloqueo AV de 2do o 3er grado Bradicardia sinusal extrema (< 50 lpm)	Enfermedad vascular periférica, intolerancia a la glucosa, EPOC, asma bronquial, atletas o pacientes con actividad física intensa

Toma Posición de la SAHA
Rol Actual de los BB en HTA
2016

Guías de la Sociedad Arg de HTA en:
htpp://saha.org.ar/1pdf/
GUIA_SAHA_VERSION_COMPLETA.pdf

Canadian Journal of Cardiology 29 (2013) 528–542

Guidelines

The 2013 Canadian Hypertension Education Program Recommendations for Blood Pressure Measurement, Diagnosis, Assessment of Risk, Prevention, and Treatment of Hypertension

	Initial therapy	Second-line therapy	Notes and/or cautions
Hypertension without other compelling indications			
Diastolic hypertension with or without systolic hypertension (target BP < 140/90 mm Hg)	Thiazide diuretics, β-blockers, ACE inhibitors, ARBs, or long-acting CCBs (consider ASA and statins in selected patients). Consider initiating therapy with a combination of first-line drugs if the BP is ≥ 20 mm Hg systolic or ≥ 10 mm Hg diastolic above target	Combinations of first-line drugs	Not recommended for monotherapy: α-blockers, β-blockers in those ≥ 60 years of age, ACE inhibitors in black individuals. Hypokalemia should be avoided in those prescribed diuretic monotherapy. ACE inhibitors, ARBs, and direct renin inhibitors are potential teratogens, and caution is required if prescribing to women of child-bearing potential. Combination of an ACE inhibitor with an ARB is not recommended
Isolated systolic hypertension without other compelling indications (target BP for age < 80 is < 140/90 mm Hg; for age ≥, the target SBP is < 150 mm Hg)	Thiazide diuretics, ARBs or long-acting dihydropyridine CCBs	Combinations of first-line drugs	Same as diastolic hypertension with or without systolic hypertension

2013 ESH/ESC Guidelines for the management of arterial hypertension

The Task Force for the management of arterial hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC)

above analyses [403]. Some of the limitations of traditional beta-blockers do not appear to be shared by some of the vasodilating beta-blockers, such as celiprolol, carvedilol and nebivolol—more widely used today—which reduce central pulse pressure and aortic stiffness better than atenolol or metoprolol [404–406] and affect insulin sensitivity less than metoprolol [407,408]. Nebivolol has recently been shown not to worsen glucose tolerance compared with placebo and when added to hydrochlorothiazide [409]. Both carvedilol and nebivolol have been favourably tested in RCTs, although in heart failure rather than arterial hypertension [410]. Finally, beta-blockers have recently been

Special Communication

2014 Evidence-Based Guideline for the Management of High Blood Pressure in Adults

Report From the Panel Members Appointed to the Eighth Joint National Committee (JNC 8)

Recommended selection among 4 specific medication classes (ACEI or ARB, CCB or diuretics) and doses based on RCT evidence

Recommended specific medication classes based on evidence review for racial, CKD, and diabetic subgroups

Panel created a table of drugs and doses used in the outcome trials

Jama 2013, dic. 18

EN CONCLUSIÓN…..

QUEDA LUGAR PARA LOS BETA BLOQUEANTES EN EL TRATAMIENTO DE LA HTA?

- Las guías hay que aplicarlas acorde a la práctica diaria y al paciente.
- De Primera o Segunda indicación los **BB** siguen siendo una indicación válida en HTA
- Siguen siendo de Primera Elección en HTA Asociada con Enfermedad Coronaria, Insuficiencia Cardíaca, Hiperdinamia, Hipertiroidismo entre otras.

Muchas Gracias!!!!!

Los Beta Bloqueantes no están Muertos

Los Beta Bloqueantes con acción Vasodilatares siguen siendo una indicación en HTA.