Diabetes Mellitus 2006.
¿Qué hay de nuevo?

Dr. Juan García Puig,
Unidad Metabólica-Vascular,
Servicio de Medicina Interna,
Hospital Universitario LA PAZ, Madrid.

Hospital Universitario La Paz

Madrid

GRUPO MAPA
(1993 – 2007)

Bastenier MA. EL PAIS, 06 de Abril, 2007.

Matt Damon, a la izquierda, y Robert de Niro, en un fotograma de *El buen pastor*.

2006 Diabetes Mellitus
¿Qué hay de nuevo?

Guión

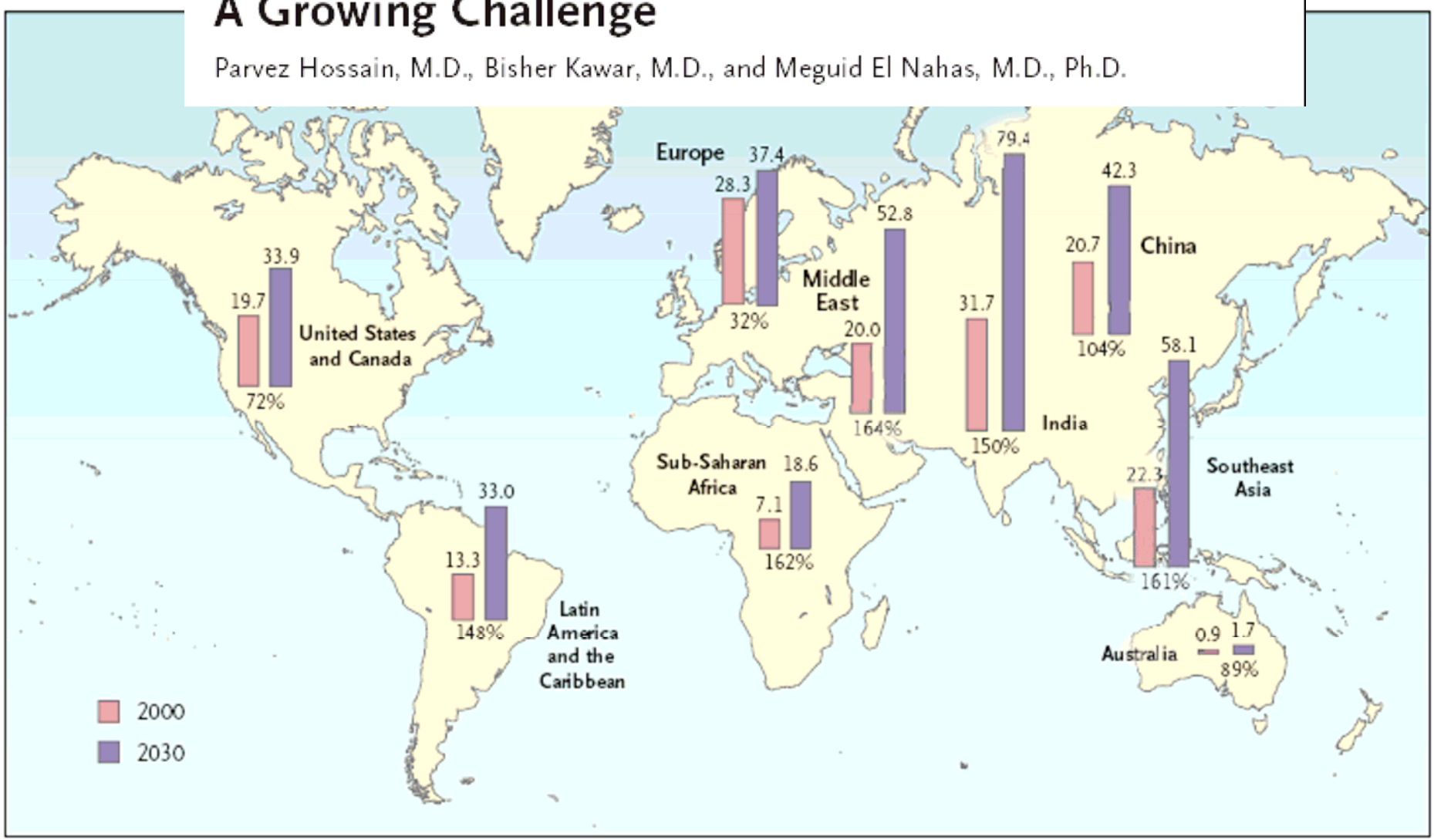
1. Epidemiología.
2. Clínica.
3. Diagnóstico.
4. Tratamiento.

1. Epidemiología.

- Aumento de Obesidad y DM2 en todo el mundo.
- Comunicación de HbA1C en NY (15.01.06).

Obesity and Diabetes in the Developing World — A Growing Challenge

Parvez Hossain, M.D., Bisher Kawar, M.D., and Meguid El Nahas, M.D., Ph.D.



Millions of Cases of Diabetes in 2000 and Projections for 2030, with Projected Percent Changes.

Data are from Wild et al.[3]

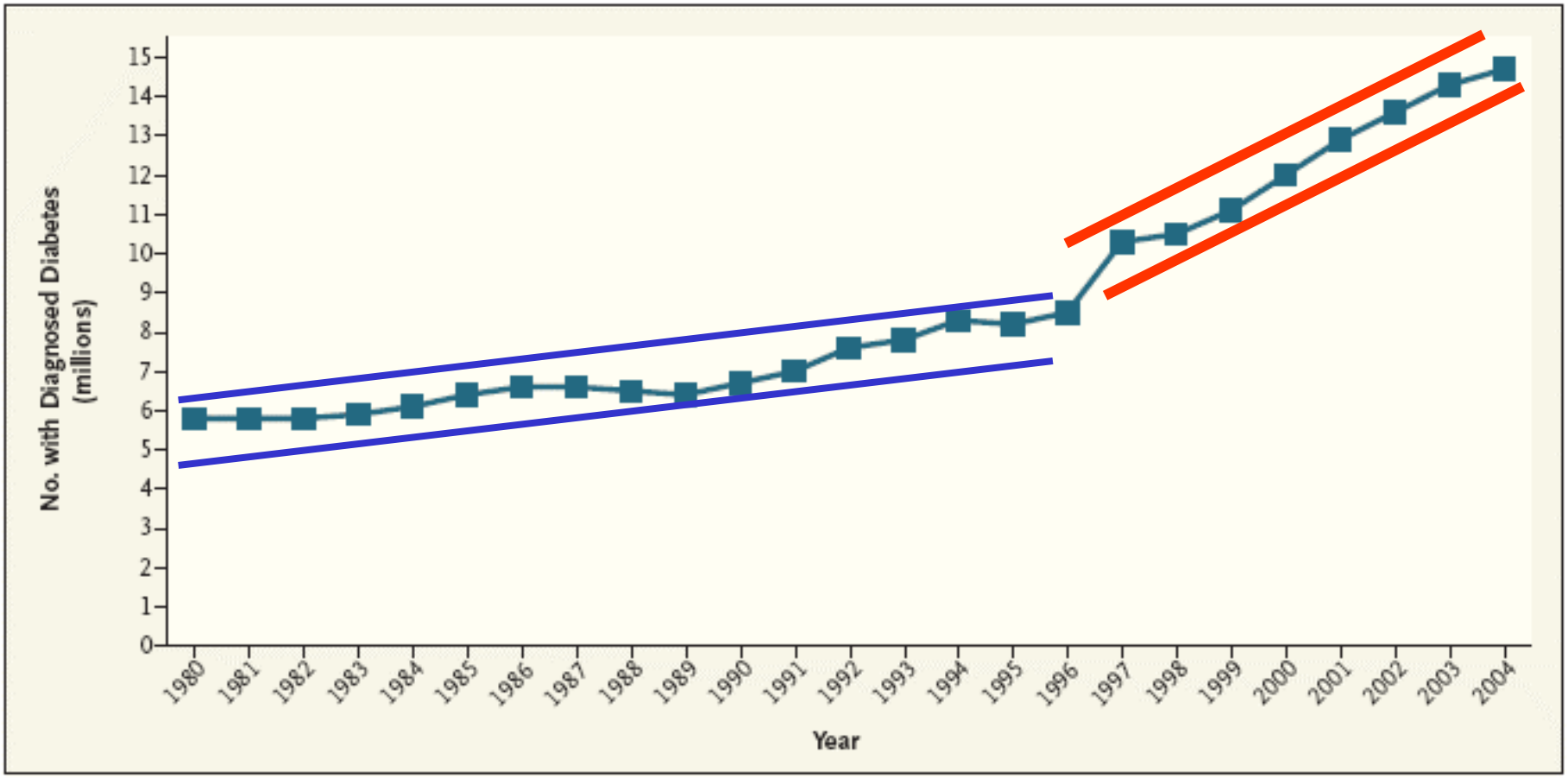
Hossain P, et al. NEJM 2007;356:213-5.

Perspective
FEBRUARY 9, 2006

Facing the Diabetes Epidemic — Mandatory Reporting of Glycosylated Hemoglobin Values in New York City

Robert Steinbrook, M.D.

Steinbrook R. NEJM 2006;354:545-36.



Number of Persons with Diagnosed Diabetes in the United States, 1980–2004.

Data are from the Centers for Disease Control and Prevention. The increase in the number of cases between 1996 and 1997 reflects a redesign of the National Health Interview Survey.

Steinbrook R. NEJM 2006;354:545-36.

poor glycemic control over

cording to the Centers for Disease Control and Prevention (see line graph). Older people, blacks, Hispanics, and members of some other ethnic groups are disproportionately affected.

Diabetes is the sixth most common cause of death in the United States and was the fifth most common cause in New York City in 2004. In December 2005, the New York City Board of Health approved a novel response to the diabetes epidemic: mandatory electronic reporting of glycosylated hemoglobin values by laboratories to the city's Department of Health and Mental Hygiene. The requirement, which took effect on January 15, 2006, was promulgated under the

The endeavor has aroused concern about patients' privacy and raised questions about the role of health departments. However, Thomas Frieden, the city's health commissioner, said the aim is to respond to an epidemic of a chronic disease with the type of surveillance and other tools that health departments routinely use to prevent and control communicable diseases. As he explained in an interview, "We have to get a better handle on what is really the only major health problem in the United States that is getting worse, and getting worse rapidly."

There are an estimated 530,000 adults in New York City with diagnosed diabetes. About 9 percent of adults report having received a diagnosis of diabetes; in the

Steinbrook R. NEJM 2006;354:545-36.

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1. Epidemiología.

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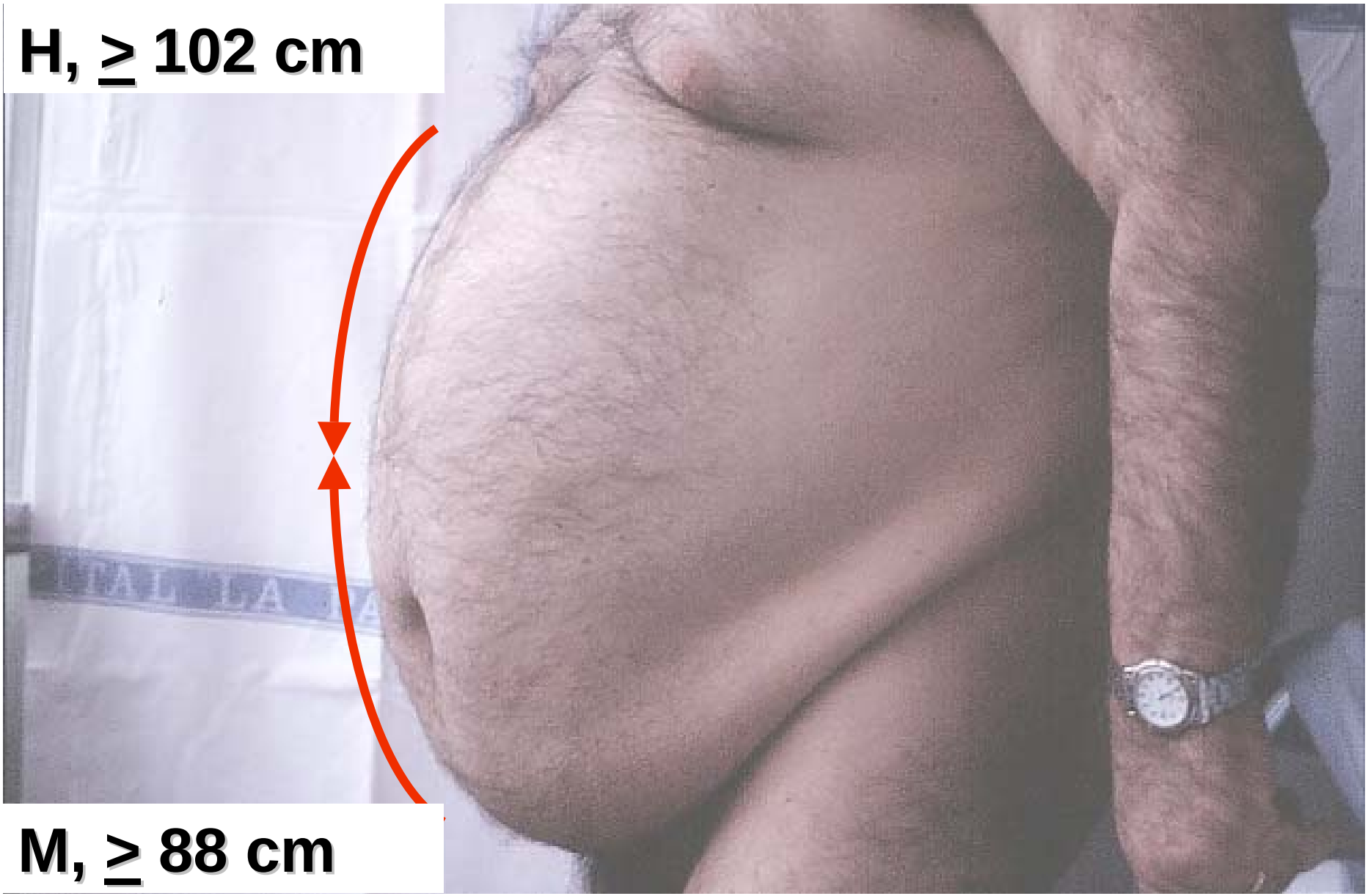
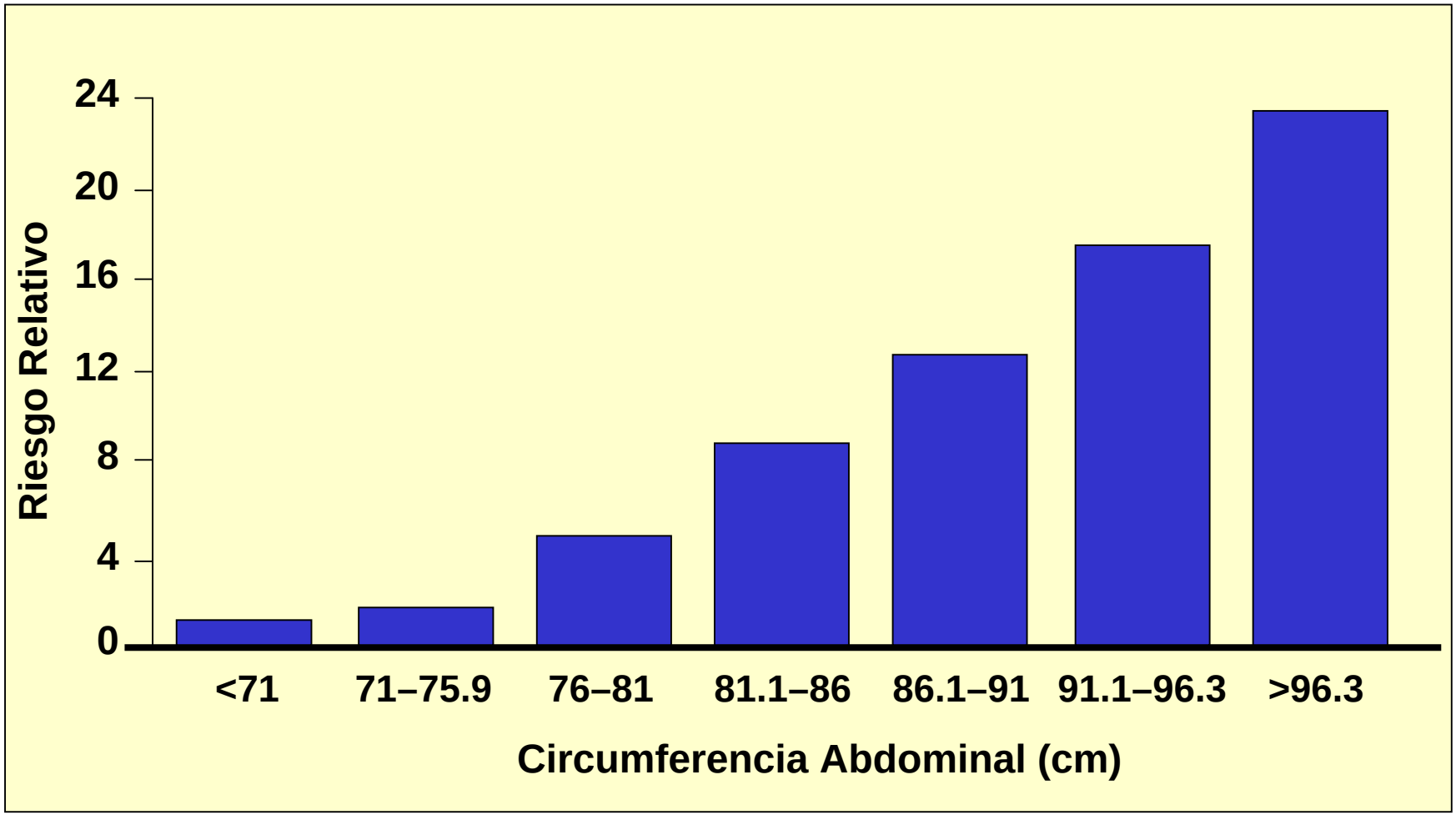
- **Adiposidad abdominal = resistencia insulina.**
- **HTA esencial = resistencia insulina.**

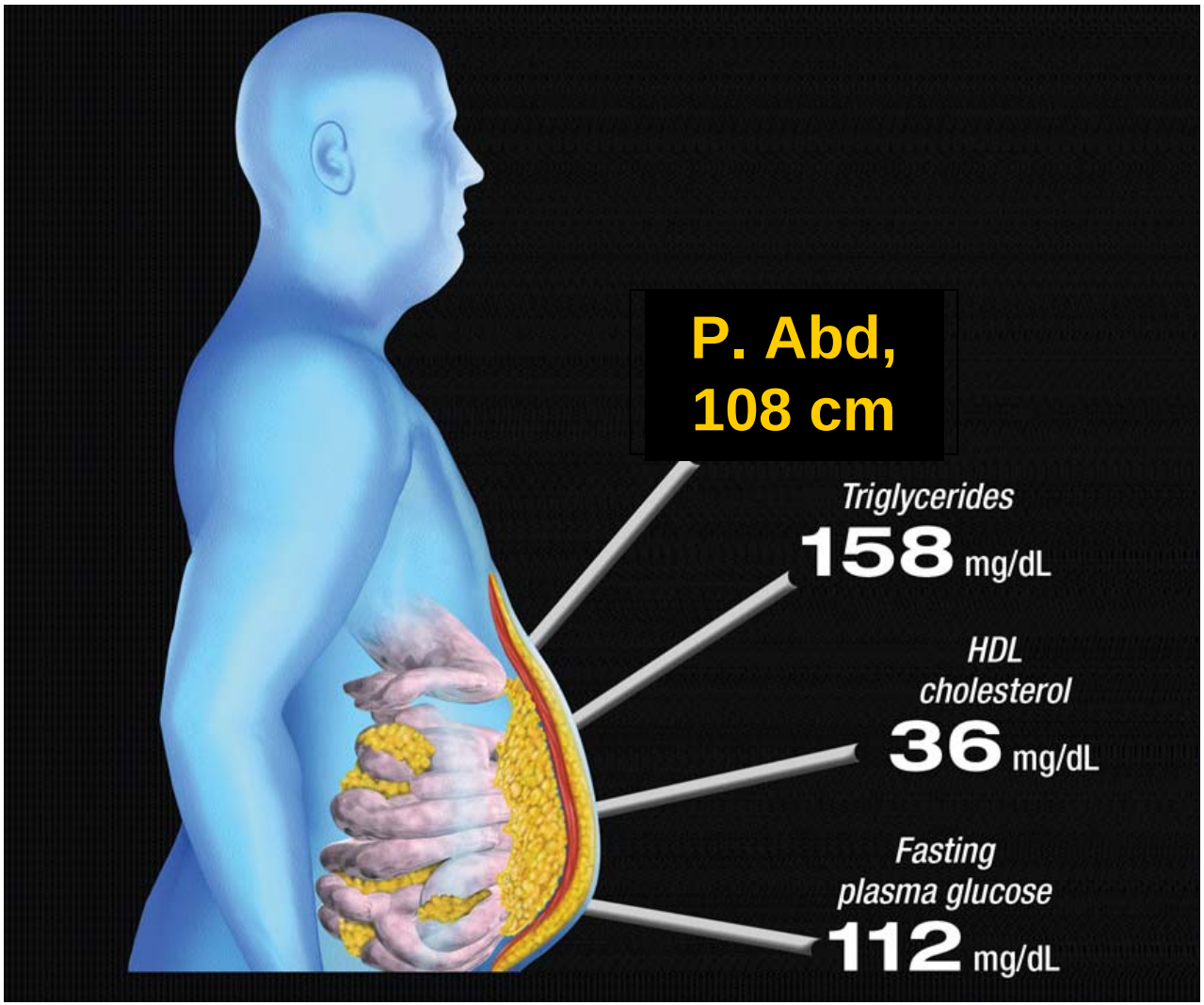

H, ≥ 102 cm
M, ≥ 88 cm

Obesidad Abdominal y Riesgo de DM2



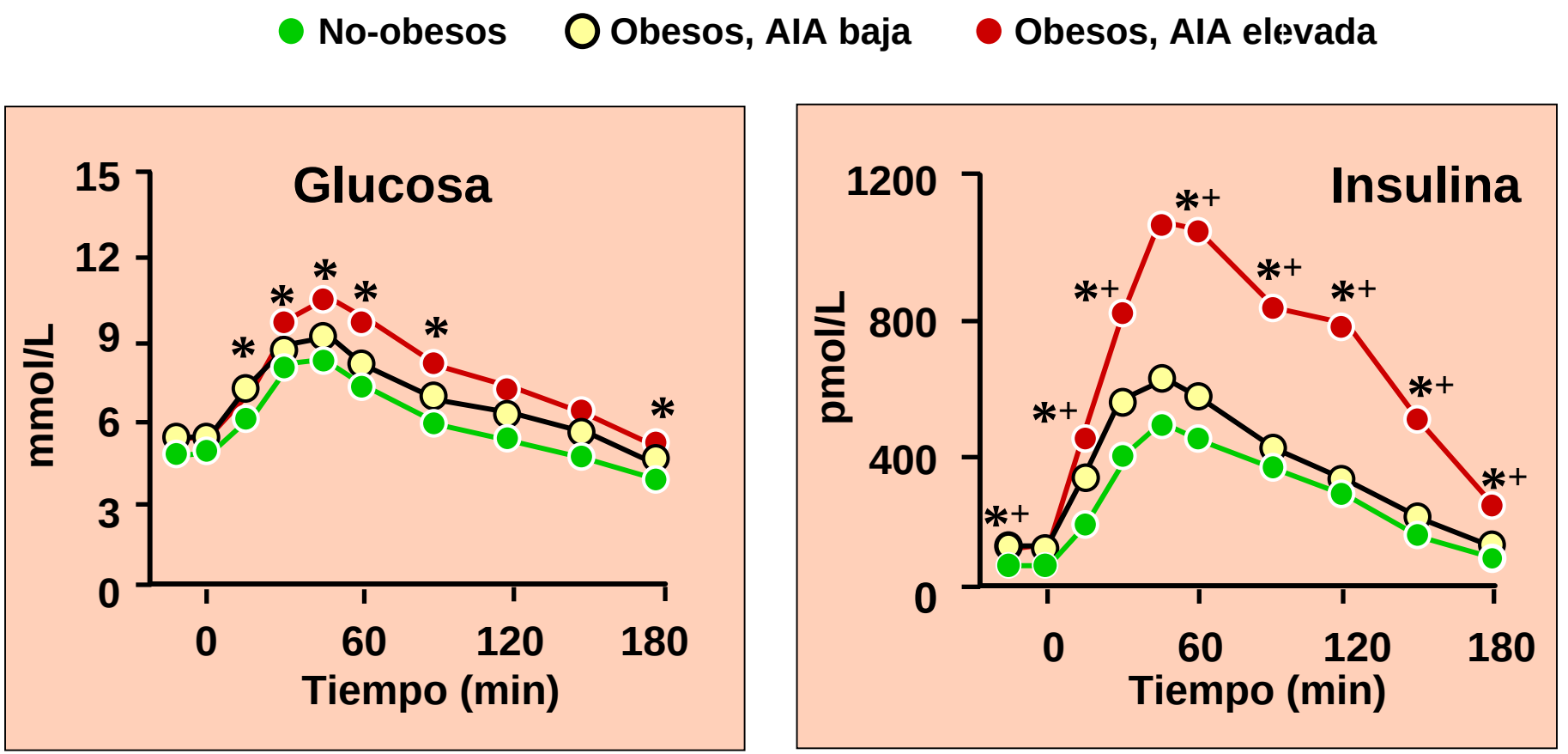
Carey et al 1997

Obesidad Abdominal y Alt. Metabólicas.



Los pacientes con OBESIDAD abdominal presentan, con frecuencia, otras alteraciones metabólicas (FRCV).

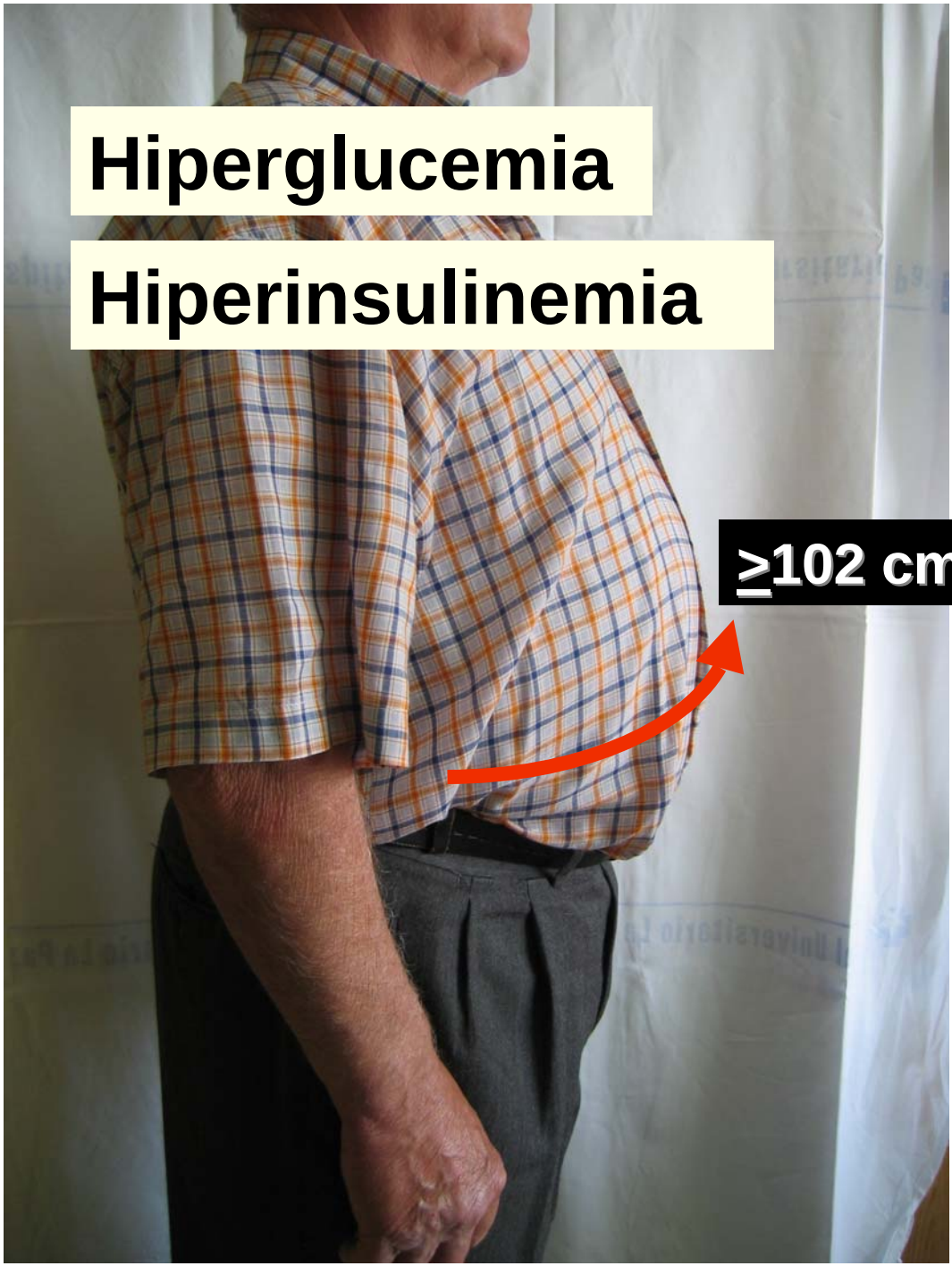
Adiposidad intraabdominal y Metabolismo de glucosa.



AIA: Adiposidad intraabdominal

*p<0.05 vs. no obesos; $^{+}$p<0.05 vs. obesos con AIA baja.

Pouliot et al 1992


Hiperglucemia
Hiperinsulinemia
≥102 cm

The American Journal of Medicine (2006) 119, 318-326

ELSEVIER

THE AMERICAN JOURNAL of MEDICINE®

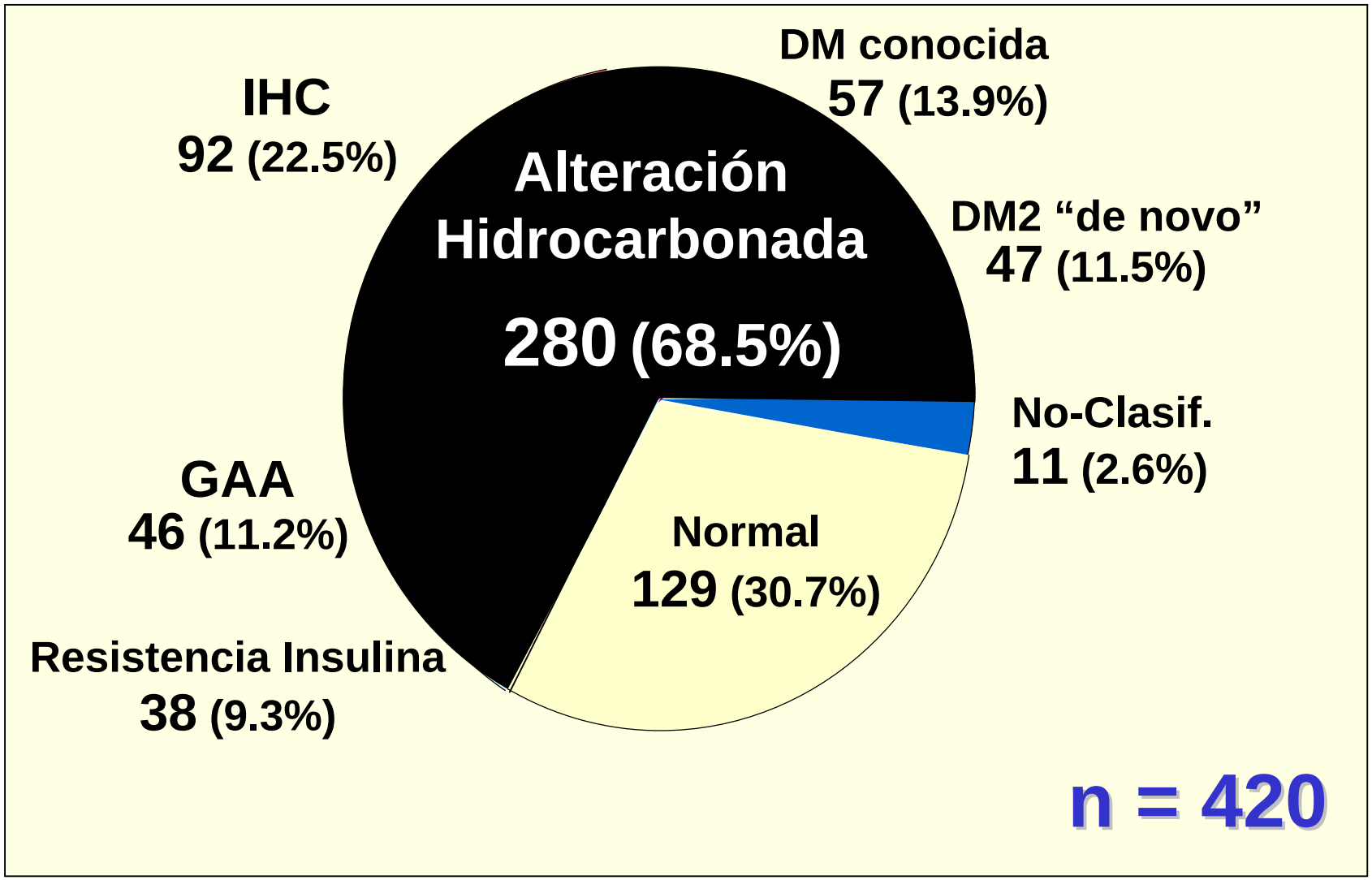
CLINICAL RESEARCH STUDY

Glucose Metabolism in Patients with Essential Hypertension

Juan García-Puig, MD, PhD,[a] Luis M. Ruilope, MD, PhD,[b] Manuel Luque, MD, PhD,[c] Jaime Fernández, MD,[d] Rafael Ortega, MD,[d] Rafael Dal-Ré, MD,[d] on behalf the AVANT Study Group Investigators (see Acknowledgments)

[a]Division of Internal Medicine at Hospital Universitario "La Paz," [b]Hypertension Units at Hospital Universitario 12 de Octubre, [c]Hospital Clínico Universitario, [d]Medical Department, GlaxoSmithKline, Madrid, Spain.

AVANT: Resultados metabolismo HC.



Puig JG, et al. Am J Med 2006;119:318-26.

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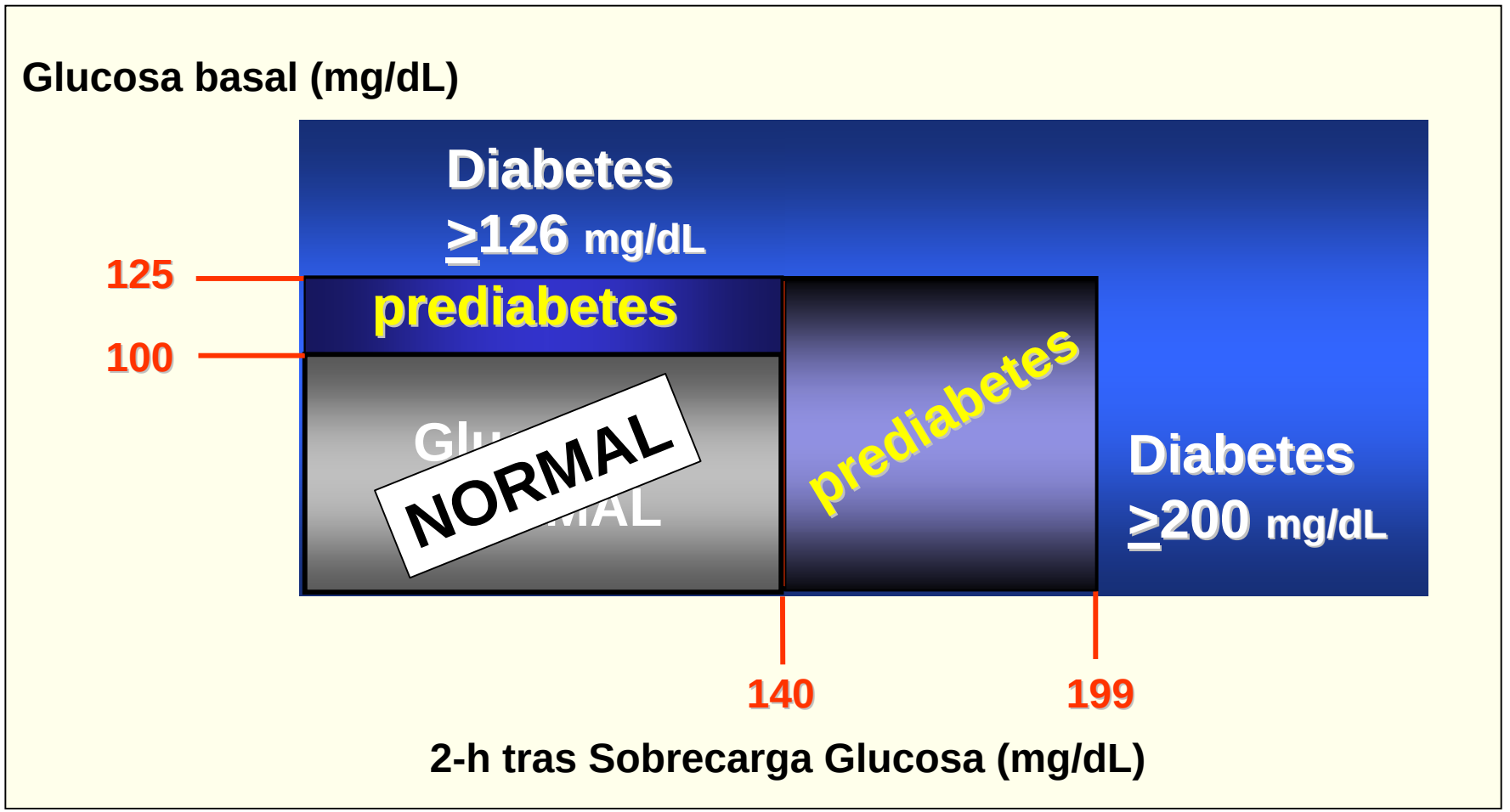
- **GAA e ITG = estados *"prediabéticos" (solo?)***
- **HTA + GAA = 27% DM2.**

Dx alt. metab. hidrocarbonado
(normal, GAA, IHC, DM2)



GAA, glucosa anómala en ayunas; IHC, intolerancia hidrocarbonada; DM2, diabetes mellitus tipo 2.

American Diabetes Association. *Diabetes Care*. 2003;26(suppl 1):S5-S20.

Table 1. Six-Year Cumulative Incidence of Diabetes According to WHO-1985 and ADA Diagnostic Criteria*

Baseline Category	Cutoff Values, FPG/2hPG, mg/dL	No.	Diabetes at Follow-up, No. (%)‡
WHO-1985			
NGT	<126/<140†	1231	46 (3.7)
IGT = ITG	<126/140-200†	111	36 (32.4)
Total		**1342**	**82** (6.1)
ADA			
NFG	<110§	1205	60 (5.0)
IFG = GAA	110-126§	137	52 (38.0)
Total		**1342**	**112** (8.3)

*WHO indicates World Health Organization; ADA, American Diabetes Association; FPG, fasting plasma glucose; 2hPG, 2-hour postload glucose; NGT, normal glucose tolerance; IGT, impaired glucose tolerance; NFG, normal fasting glucose; IFG, impaired fasting glucose. To convert mg/dL to mmol/L, multiply mg/dL by 0.05551.

†Cutoff level for FPG is 126 mg/dL, because all analyses were carried out in the 1342 subjects who did not have diabetes according to any of the diagnostic criteria at baseline.

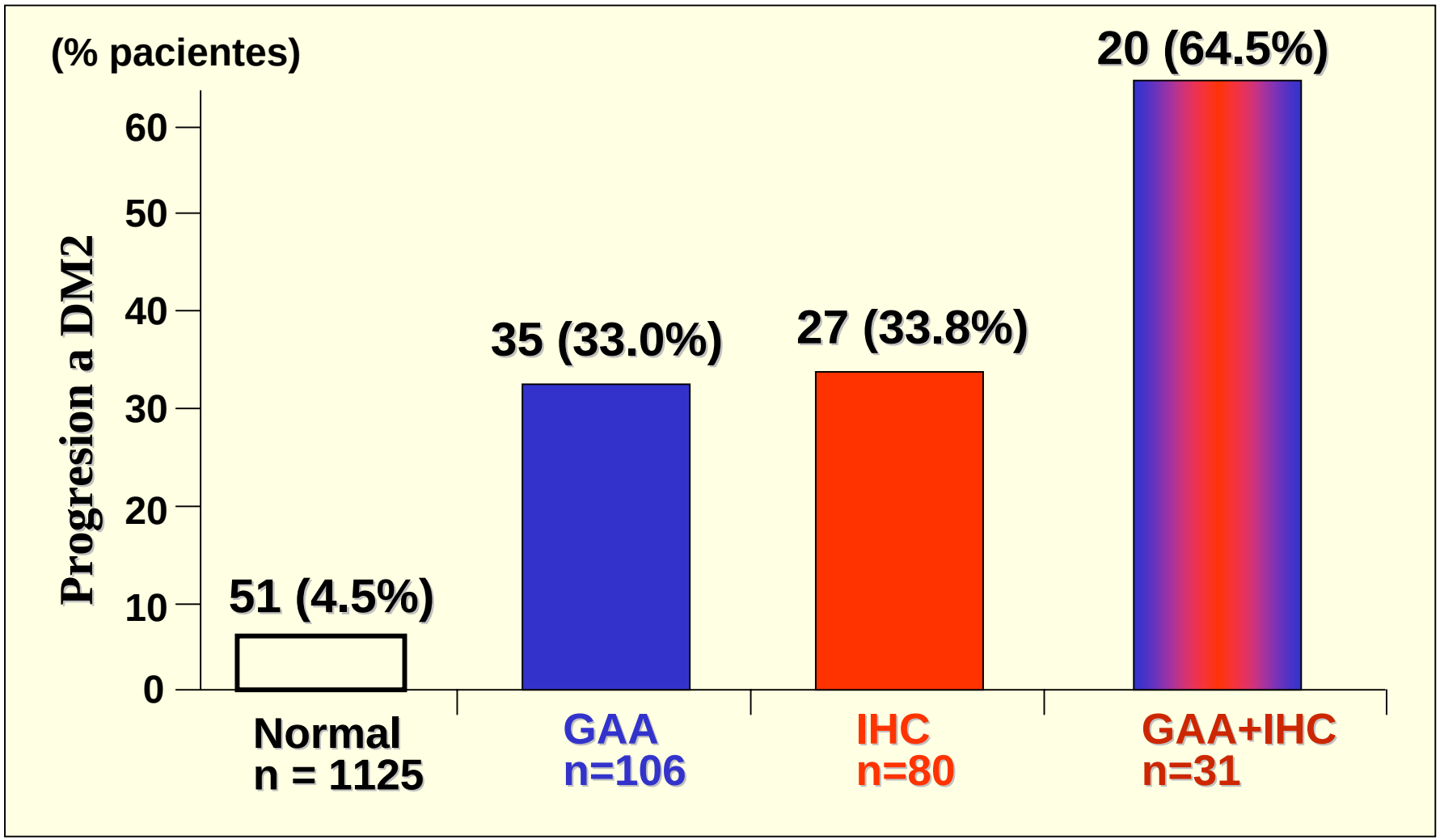
‡Cutoff values for WHO-1985 are FPG ≥140 mg/dL or 2hPG ≥200 mg/dL; for ADA, FPG ≥126 mg/dL.

§Cutoff levels for FPG only.

Diabetes Care 1999;22:399-402.

Incidencia de DM2: Hoorn study.

1342 sujetos de Hoorn (50 a 75 a), 6.4 años.



Vegt F, et al. JAMA 2001;285:2109-13.

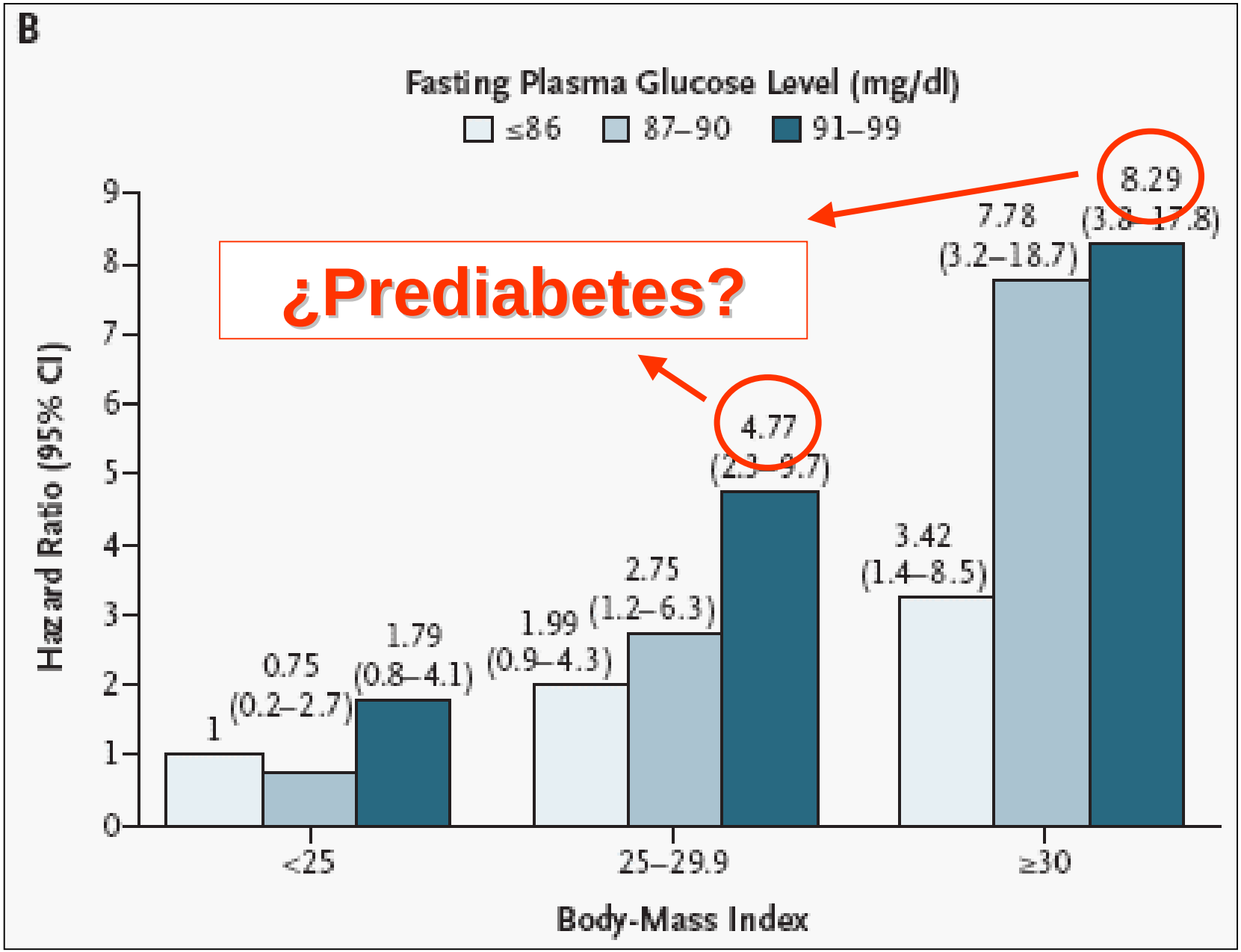
Tirosh A, et al. NEJM 2005;353:1454-62.

ORIGINAL ARTICLE

Normal Fasting Plasma Glucose Levels and Type 2 Diabetes in Young Men

Amir Tirosh, M.D., Ph.D., Iris Shai, R.D., Ph.D., Dorit Tekes-Manova, M.D., Eran Israeli, M.D., David Pereg, M.D., Tzippora Shochat, M.Sc., Ilan Kochba, M.D., and Assaf Rudich, M.D., Ph.D., for the Israeli Diabetes Research Group

- **13.163 militares (1994-2002),** → **208 DM2**


B
Fasting Plasma Glucose Level (mg/dl)
≤86
87–90
91–99
¿Prediabetes?
Hazard Ratio (95% CI)
0
1
2
3
4
5
6
7
8
9
1
0.75 (0.2–2.7)
1.79 (0.8–4.1)
1.99 (0.9–4.3)
2.75 (1.2–6.3)
4.77 (2.3–9.7)
3.42 (1.4–8.5)
7.78 (3.2–18.7)
8.29 (3.8–17.8)
<25
25–29.9
≥30
Body-Mass Index

(1993 – 2007)

FIS, 99/0056-00-14

HTA, NO DM **2050**

↓

Glucemia basal, 110-125 **437 (21.0%)**

↓

2ª analítica, "LA PAZ"

↓

110-125 (GAA) **290 (14.0%)**

(IC 95%, 13-15%)

↓

SOG

Bernardino JI. Datos en archivo.

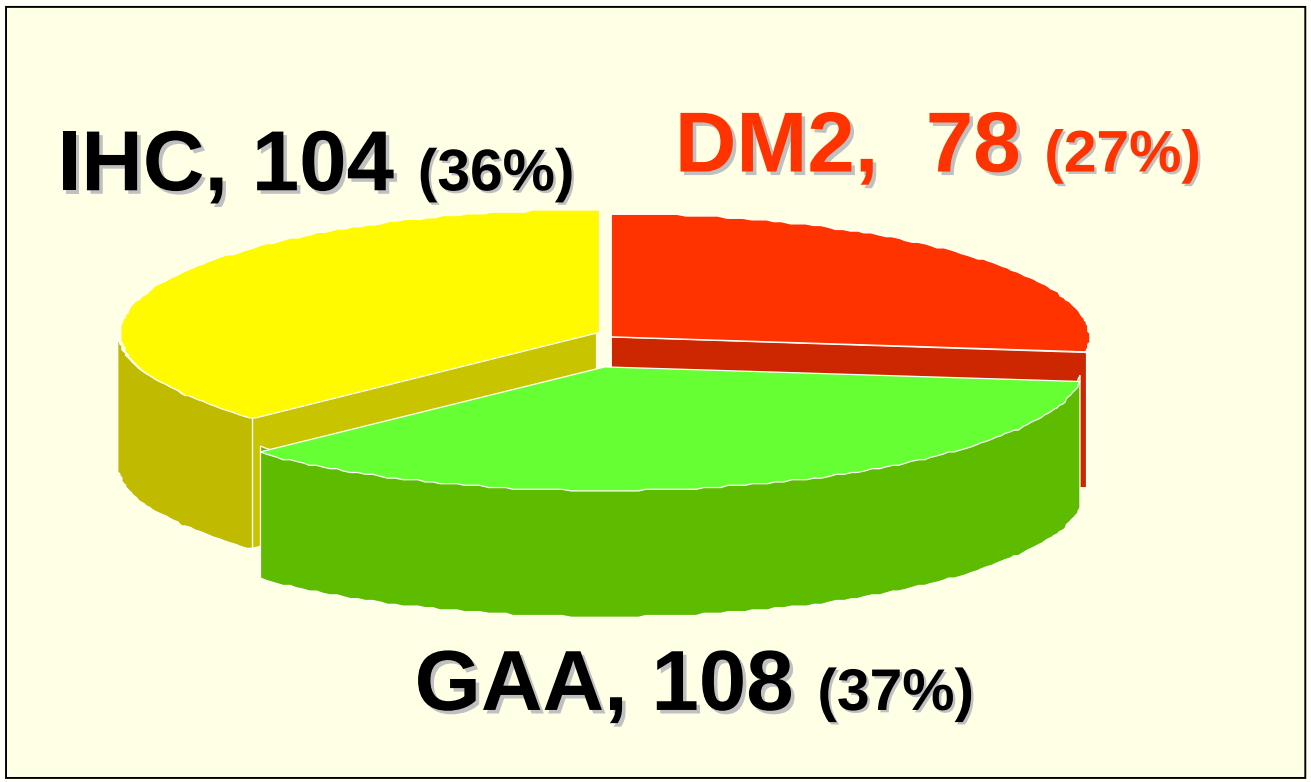
GRUPO MAPA
(1993 – 2007)

110-125 (GAA)

↓

SOG

290 (14.0%)
(IC 95%, 13-15%)



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- HTA + GAA = 27% DM2.

4. Tratamiento.

- **HTA en DM2: ¿diuréticos?**
- **Ttos HIPOGLUCEMIANTES.**

Objetivos

- PA, < 130 / 80 mmHg
- HbA1C, < 7.0%

Objetivos

- **PA, < 130 / 80 mmHg**
- **HbA1C, < 7.0%**


VB

Objetivo Tratamiento HTA en DM2: <130/80 mmHg

Terapia No Farmacológica:

- Reducción de Peso
- Ejercicio Aeróbico
- Restricción consumo de sal
- Cese Hábito Tabáquico
- Restricción consumo de alcohol
- Aumentar consumo de Fibra, Potasio y Calcio

↓

PA ≥ 130/80 mmHg

↓

Inicio Tto. Farmacológico con Diurético Tiazídico +
Continuar Terapia No Farmacológica

↓

PA ≥ 130/80 mmHg

↓

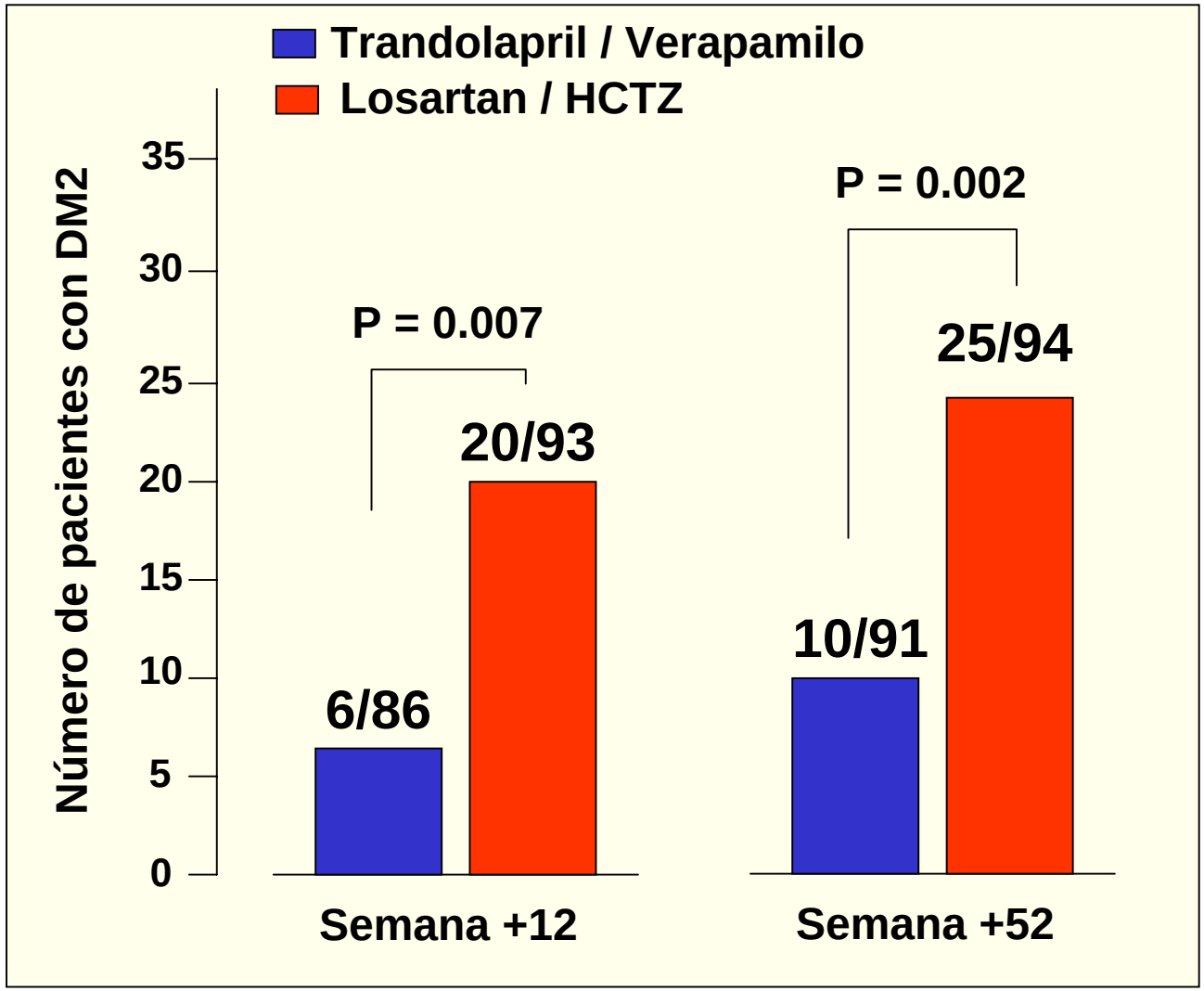
Segundo Fármaco (orden alfabético):
ACEI/ARBs / B-bloqueante/ Antagonistas del calcio

↓

Incrementar la dosis | Añadir otro fármaco

Frohlich ED, Sowers JR. Curr Hypertens Rep 2003;5:309-15.

STAR: Incidencia de DM2 en HTA esencial con SM (n=240) tratados con Trandol./Verap. *vs*. Losart/HCTZ.



Bakris G, et al. Diabetes Care 2006;29:2592-7.

Reviews/Commentaries/ADA Statements
CONSENSUS STATEMENT

Management of Hyperglycemia in Type 2 Diabetes: A Consensus Algorithm for the Initiation and Adjustment of Therapy

A consensus statement from the American Diabetes Association and the European Association for the Study of Diabetes

David M. Nathan, MD[1]
John B. Buse, MD, PHD[2]
Mayer B. Davidson, MD[3]
Robert J. Heine, MD[4]
Rury R. Holman, FRCP[5]
Robert Sherwin, MD[6]
Bernard Zinman, MD[7]

Nathan DM, et al. Diabetes Care 2006;29:1963-72.

Management of hyperglycemia in type 2 diabetes

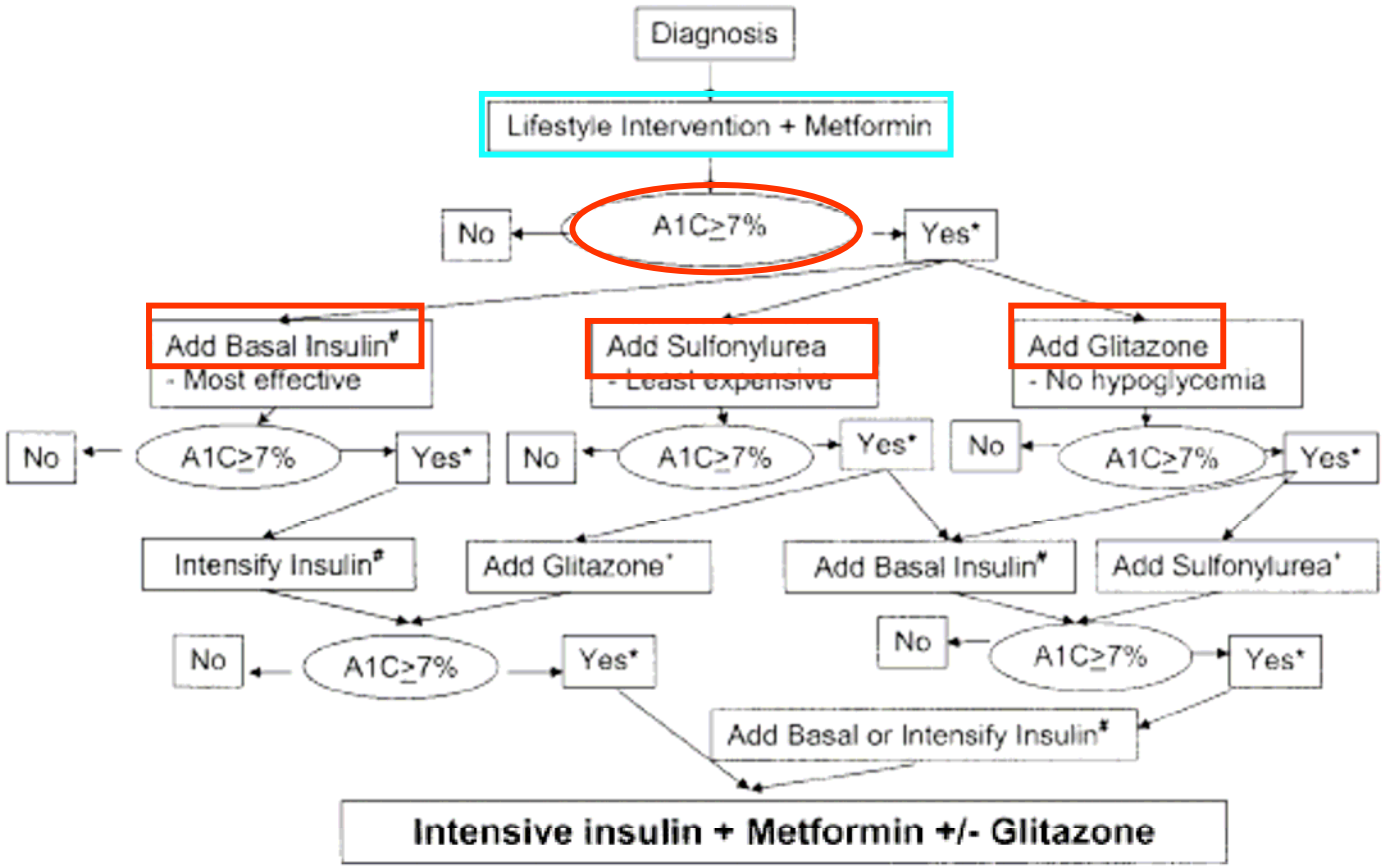


Figure 2—*Algorithm for the metabolic management of type 2 diabetes. Reinforce lifestyle intervention at every visit. *Check A1C every 3 months until <7% and then at least every 6 months. +Although three oral agents can be used, initiation and intensification of insulin therapy is preferred based on effectiveness and expense. #See Fig. 1 for initiation and adjustment of insulin.*

Nathan DM, et al. Diabetes Care 2006;29:1963-72.

Insulinas HUMANAS y análogos

Preparaciones	Comienzo	Pico (h)	Duración (h)
Humana regular	30 – 60 min	2 - 4	6 - 10
Humana NPH / Lenta	1 – 2 h	4 - 8	10 - 20
Humana ultralenta	2 – 4 h	10 - 16	16 - 24
Lispro / aspart	5 – 15 min	1 - 2	4 - 6
Glargina	1 – 2 h	Estable	24
Detemir	2 – 3 h	4 - 8	10 - 20
Insulina inhalada			

Aragón Alonso A, et al. Inf Terapéut SNS 2004;28:41-9.

Approved Antidiabetes Medications in the United States.

Medication*	Route of Administration	Year of Introduction or FDA Approval	Efficacy as Monotherapy, Measured as a Reduction in the Glycated Hemoglobin Concentration
			percentage points
1 Insulin	Parenteral	1921	≥2.5
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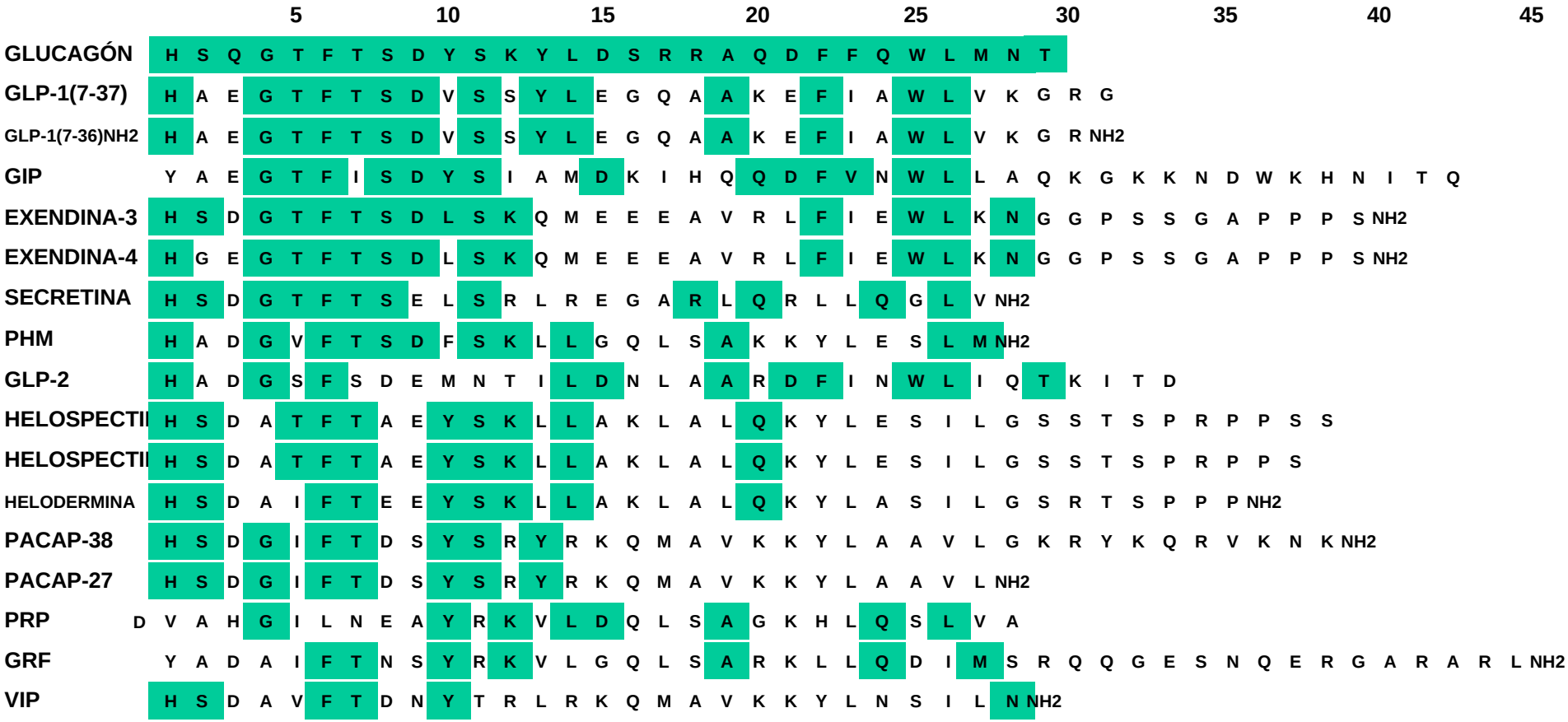
Biguanides	Oral	1957	
3 Metformin†	Oral	1995	1.5
4 Alpha-glycosidase inhibitors	Oral	1995	0.5–0.8
5 Thiazolidinediones	Oral		0.8–1.0
Troglitazone‡	Oral	1997	
Rosiglitazone	Oral	1999	
Pioglitazone	Oral	1999	
6 Glinides	Oral	1997	1.0–1.5
7 GLP analogues	Parenteral	2005	0.6
8 Amylin analogues	Parenteral	2005	0.6
9 DPP-IV inhibitors	Oral	2006	0.5–0.9

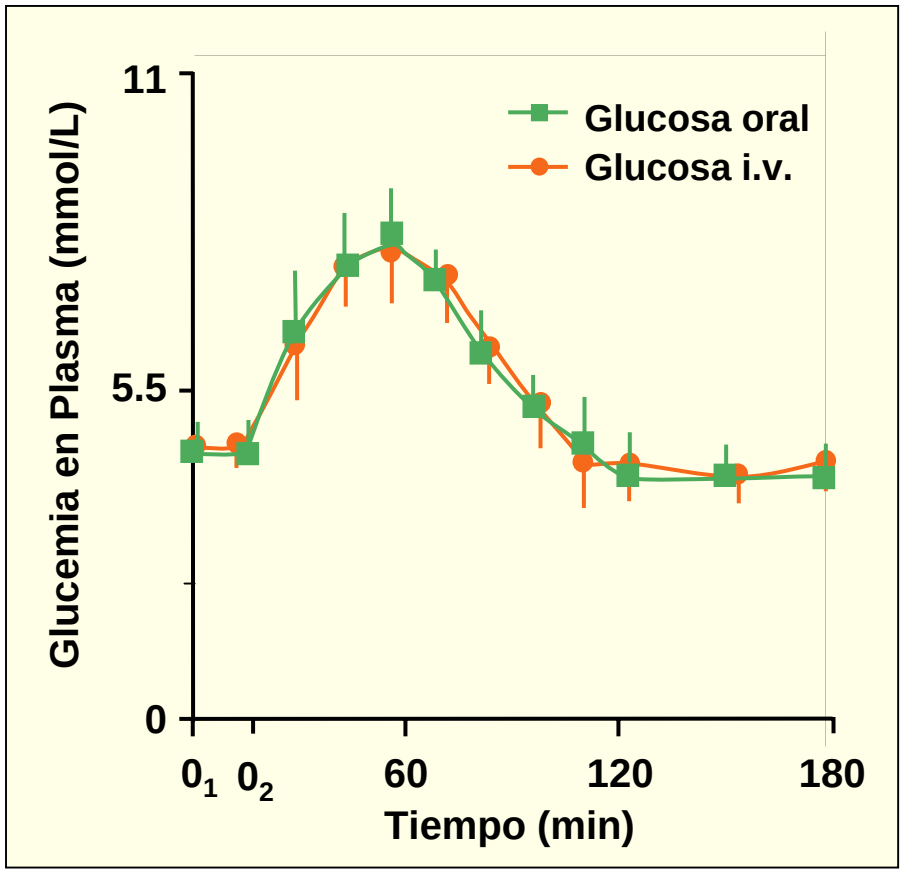
* GLP denotes glucagon-like peptide, and DPP-IV dipeptidyl peptidase IV.
† Metformin has been available in other countries since 1957 but was approved in the United States in 1995.
‡ Troglitazone was approved in 1997 but was withdrawn from the market in 2000 because of hepatotoxicity.

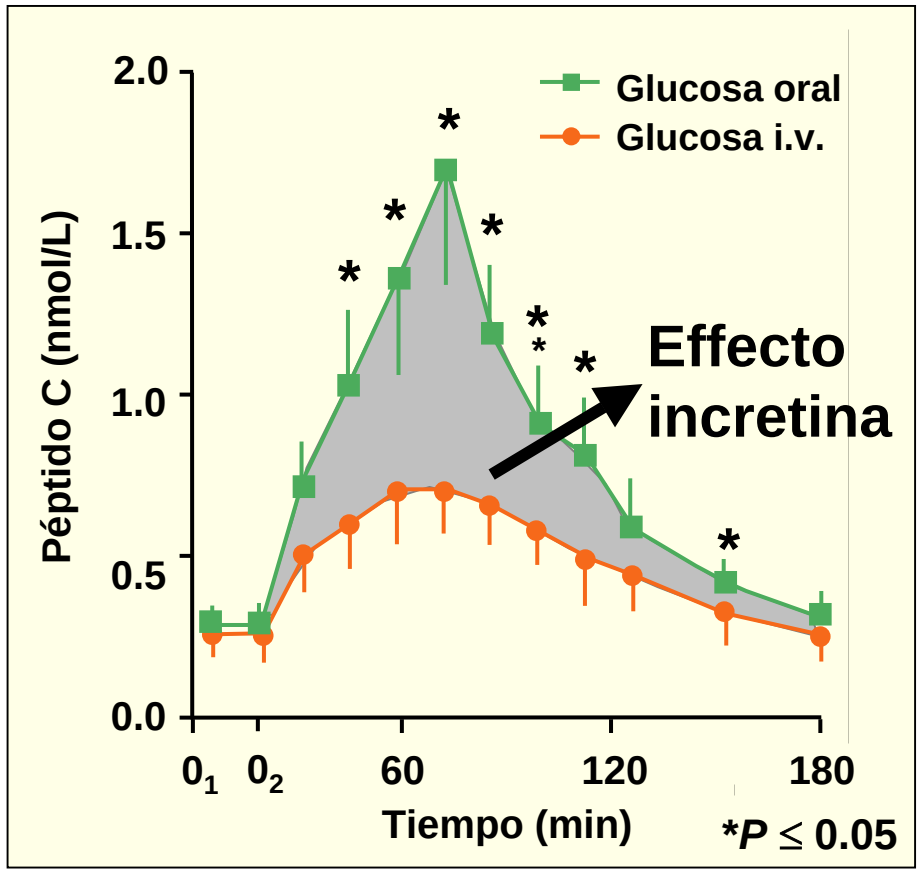
INCRETINAS

Las incretinas son péptidos relacionados con el glucagón



Efecto incretina





Zunz, LaBarre, 1929.
Nauck MA, et al. J Clin Endocrinol Metab. 1986;63:492-8.

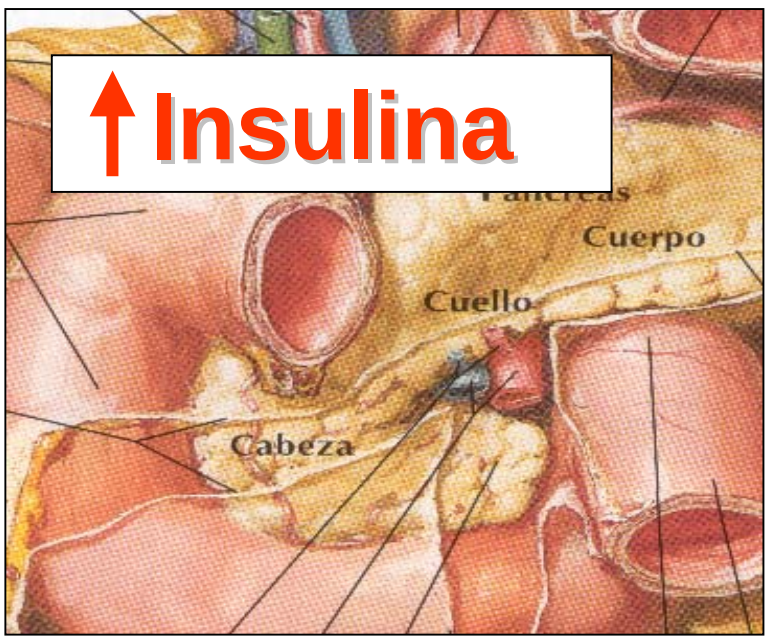
↑Glucemia

Cel. L

GLP-1

DPP-IV

↑Insulina



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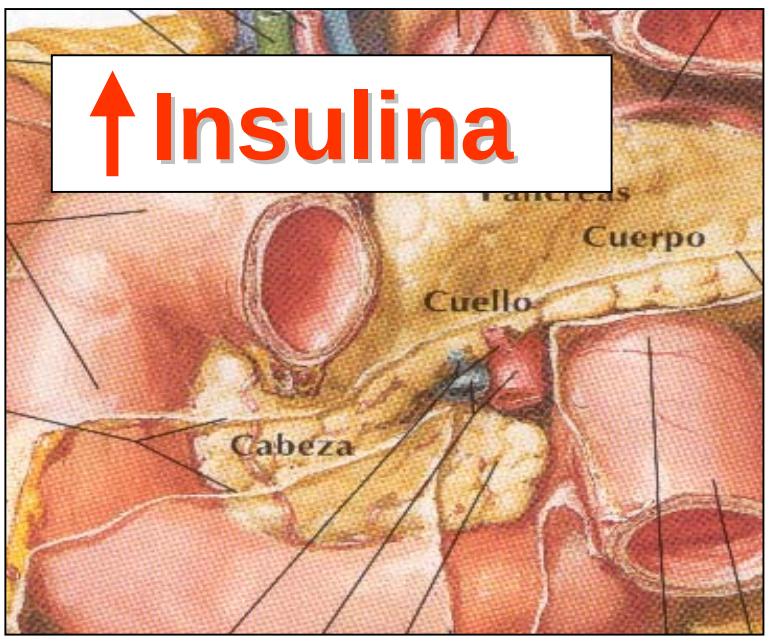


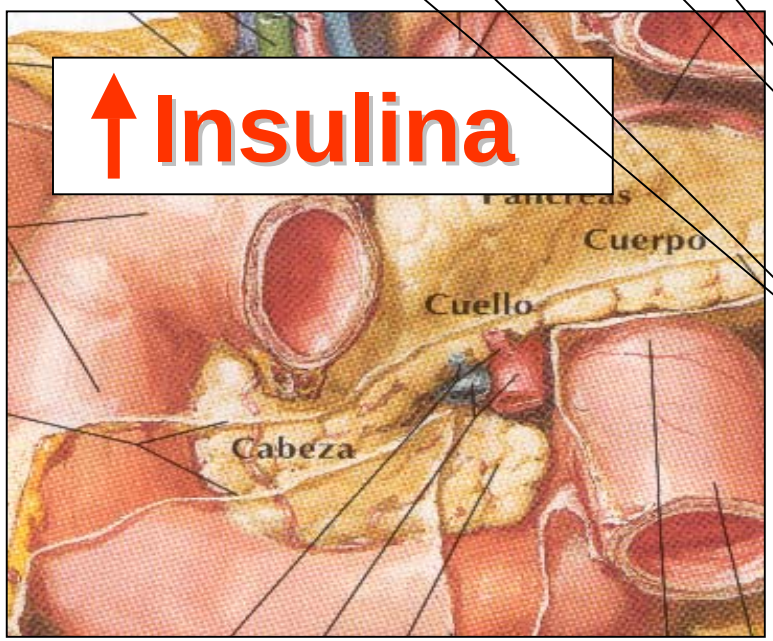
DPP-IV

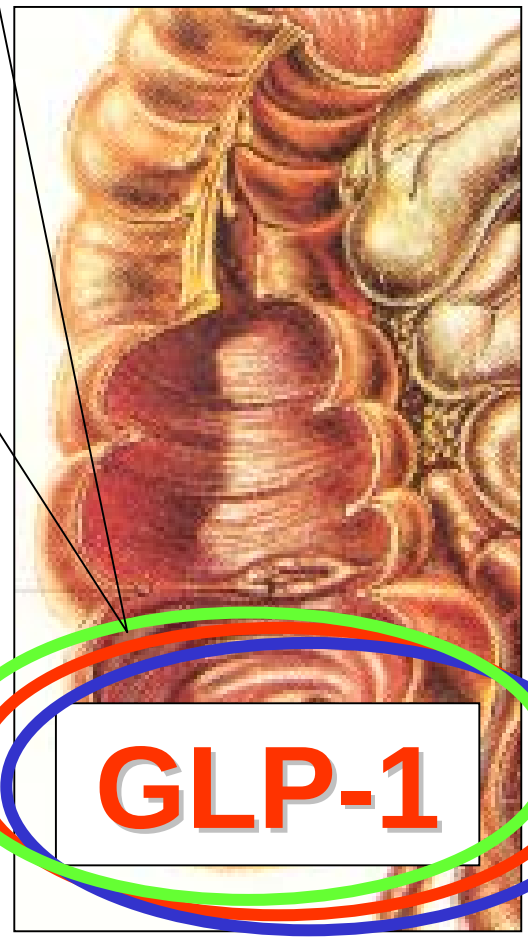
GLP-1

Exenatide, s.c. 10 mcg/12 h (Januvia)

Sitagliptina

Vildagliptina





GLP-1

DPP-IV

Perspective
FEBRUARY 1, 2007

Finding New Treatments for Diabetes — How Many, How Fast . . . How Good?

David M. Nathan, M.D. **NEJM 2007;356:437-9.**

What is surprising is that despite the paucity of published data from long-term clinical trials, sitagliptin was approved by the FDA.

The failure of clinicians and their patients with diabetes to implement currently available interventions aggressively and effectively is, I suspect, the major barrier to good care. This problem will not be fixed by making more medications available. Ensuring the effective and cost-effective use of the medications that have already been established by high-quality clinical trials to control glycemia or prevent diabetes should be a higher priority than flooding the market with ever more medications.

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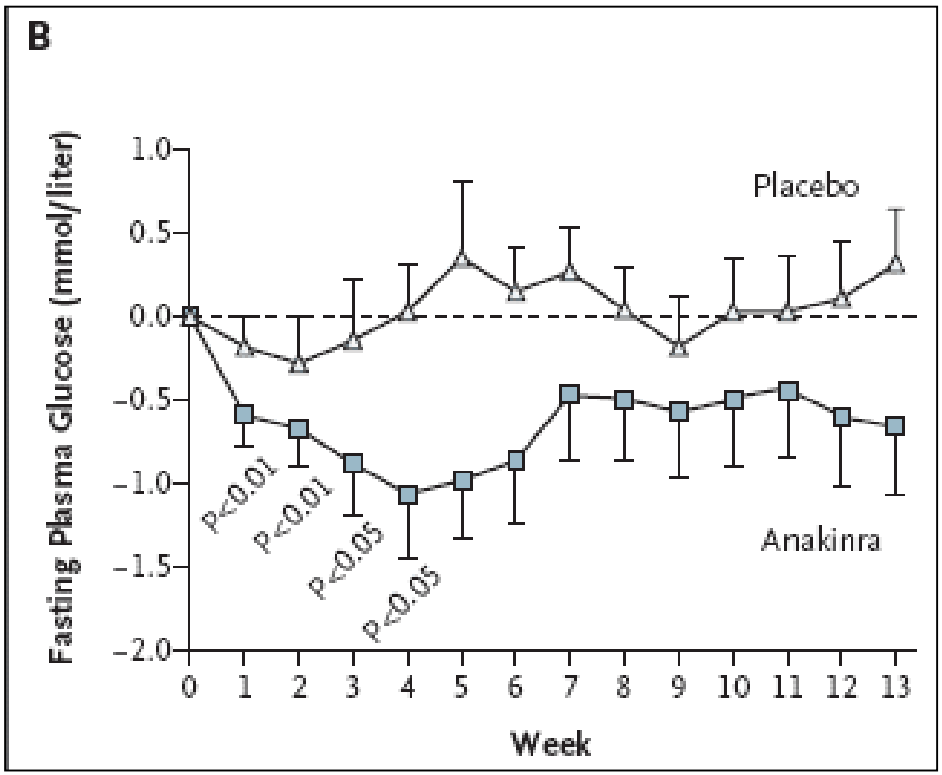
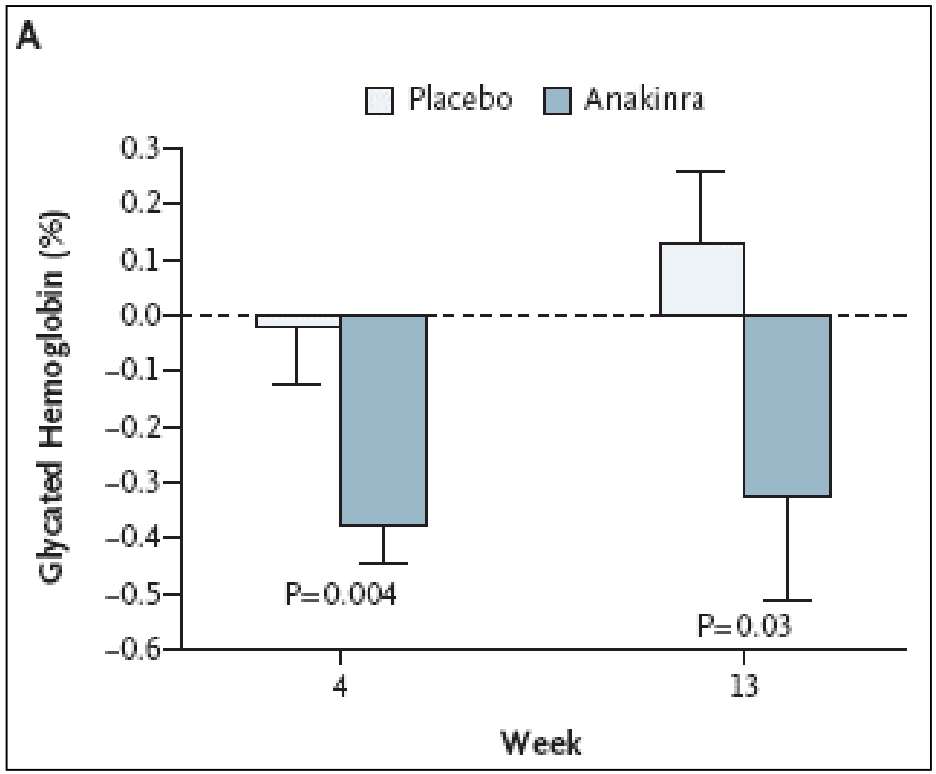
10 **PPAR α/γ, tesaglitazar, muraglitazar**

11 **ANAKINRA: Inhibidor de IL-1**

Nathan DM. NEJM 2007;356:437-9.

ANAKINRA: Inhibidor de la IL-1 en DM2





Larsen CM, et al. NEJM 2007;356:1517-26.

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PPAR α/γ, tesaglitazar, muraglitazar

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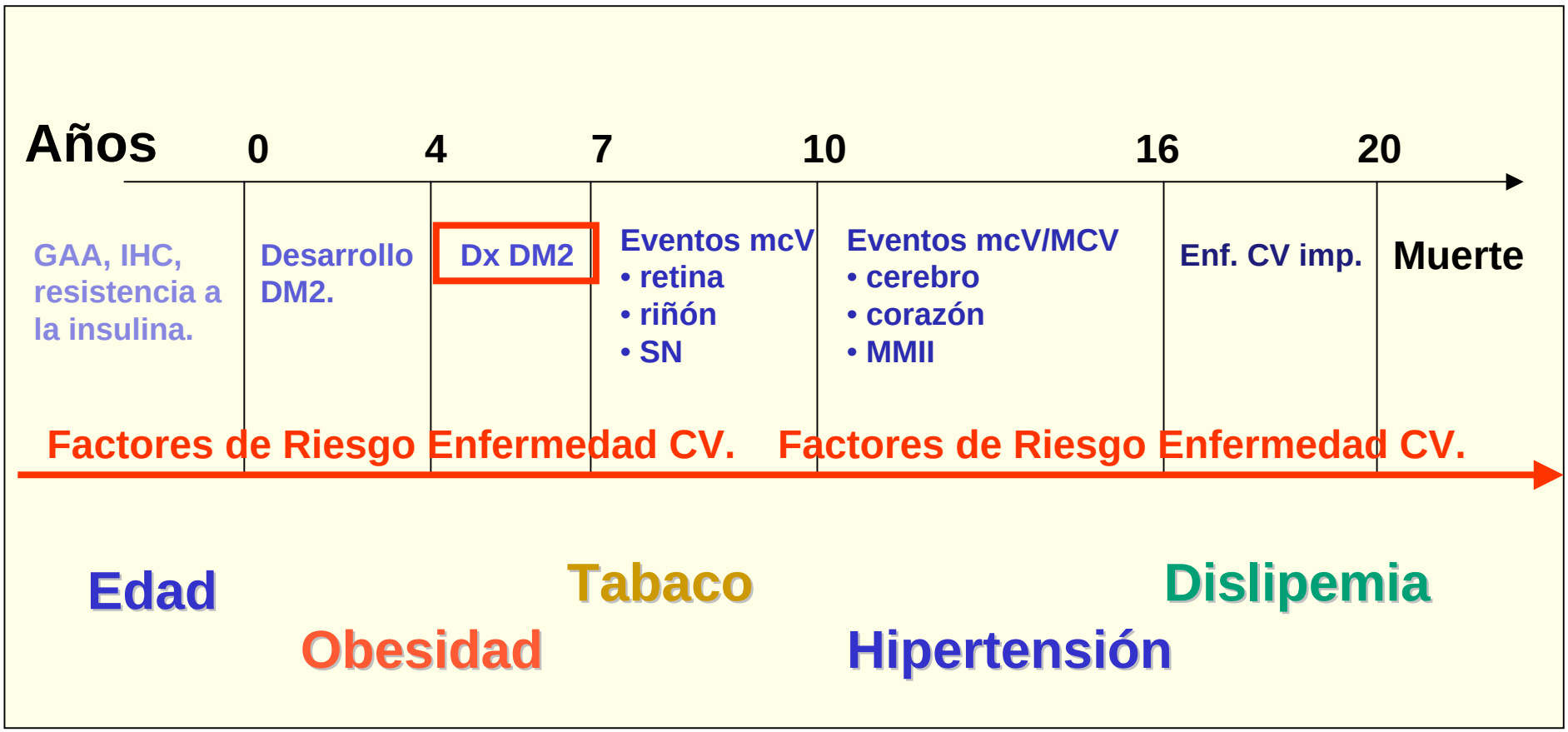
Nathan DM. NEJM 2007;356:437-9.

Evolución Natural de la DM2

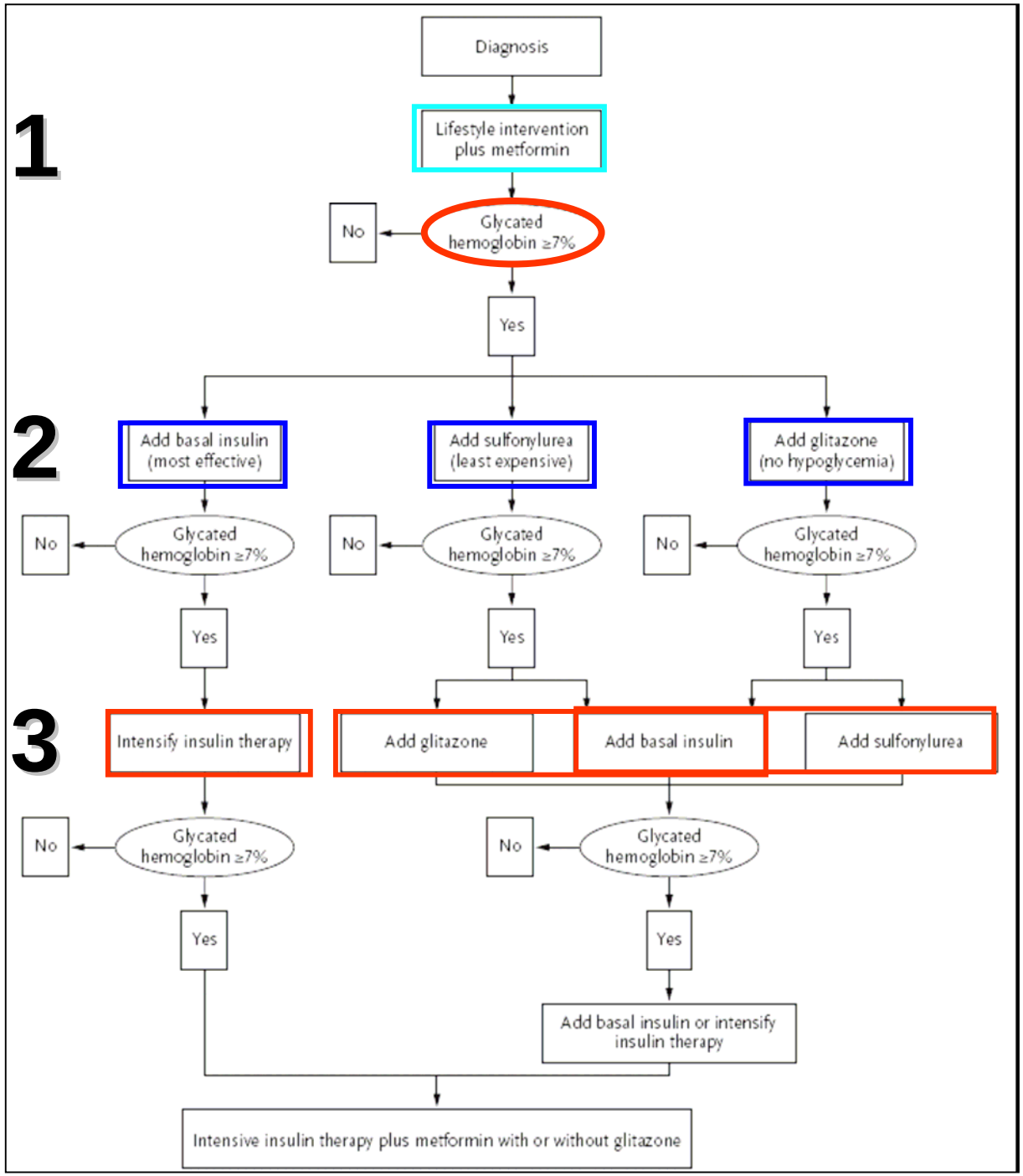
Curso Clínico habitual



Nathan DM. N Engl J Med 2003;347:1342-9.


HE TENIDO UNA PESADILLA HORRIBLE: ME PERDÍAN EL EQUIPAJE LOS DE IBERIA Y YO LO TENÍA QUE BUSCAR UTILIZANDO EL SERVICIO DE ATENCIÓN AL CLIENTE DE TELEFÓNICA
OREMÍA DE LA MOR HERMOSO

… 2007



Nathan DM, et al. NEJM 2006;355:2477-80.

Diabetes Mellitus … 2006

1. Epidemiología.

- Aumento de Obesidad y DM2 en todo el mundo.
- Comunicación de HbA1C en NY (15.01.06).

2. Clínica.

- Adiposidad abdominal = resistencia insulina.
- HTA esencial = resistencia insulina.

3. Diagnóstico.

- GAA e ITG = estados *"prediabéticos" (?)*
- HTA + GAA = 27% DM2.

4. Tratamiento.

- HTA en DM2: ¿diuréticos?
- Ttos HIPOGLUCEMIANTES.

Diabetes Mellitus 2006.
¿Qué hay de nuevo?

Resumen

- **HTA = resistencia insulina.**
- **GAA (100-125 mg/dL)** $\xrightarrow[33\%]{\text{6 a.}}$ **DM2**

Grupo MAPA-MADRID (1993-2006). 27 February 2006.

Hospital Universitario La Paz

Madrid

Unidad Metabólico – Vascular. Servicio Medicina Interna. HULP.