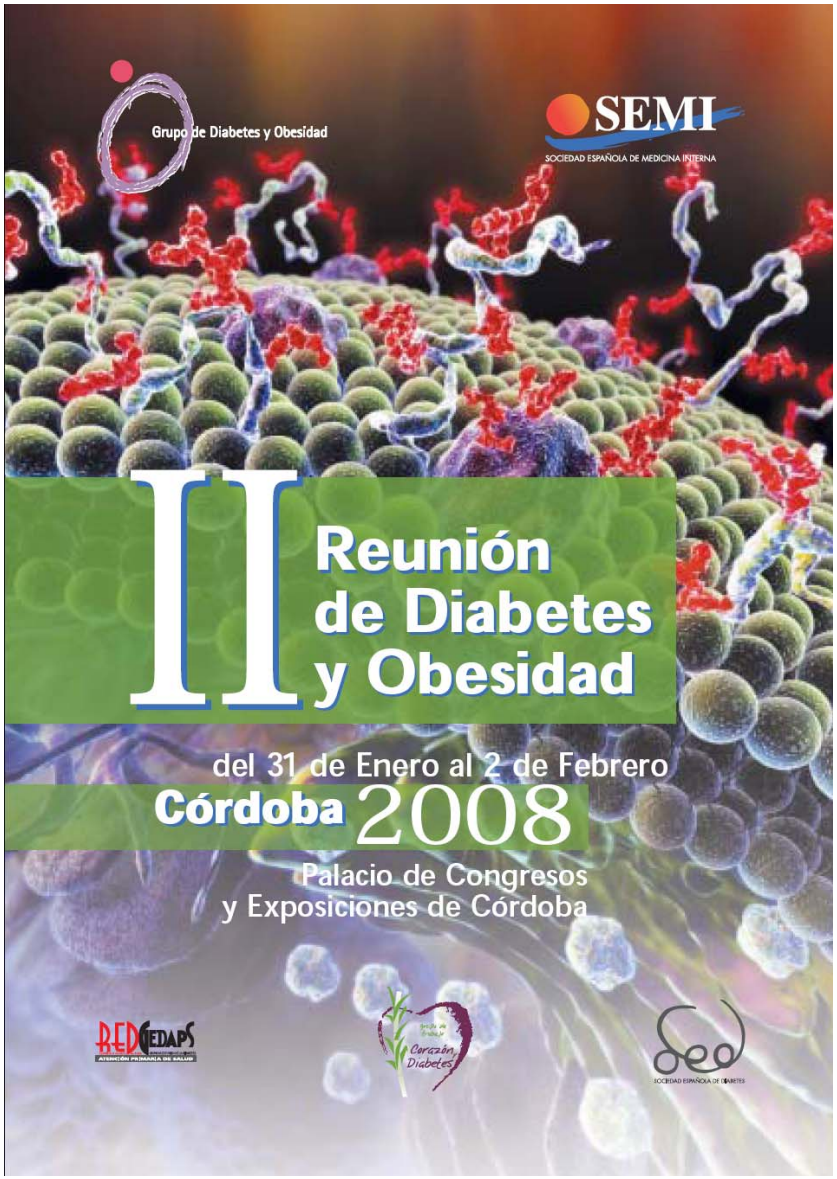

Estrategias terapéuticas de la HTA en la DM tipo 2

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Unidad de HTA. Servicio de Nefrología
Hospital Universitario 12 Octubre. Madrid

Guidelines

2007 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)

Authors/Task Force Members: Giuseppe Mancia, Co-Chairperson (Italy), Guy De Backer, Co-Chairperson (Belgium), Anna Dominiczak (UK), Renata Cifkova (Czech Republic), Robert Fagard (Belgium), Giuseppe Germano (Italy), Guido Grassi (Italy), Anthony M. Heagerty (UK), Sverre E. Kjeldsen (Norway), Stephane Laurent (France), Krzysztof Narkiewicz (Poland), Luis Ruilope (Spain), Andrzej Rynkiewicz (Poland), Roland E. Schmieder (Germany), Harry A.J. Struijker Boudier (Netherlands), Alberto Zanchetti (Italy)

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Journal of Hypertension 2007, **25**:1105–1187

Estratificación del riesgo

Otros FRCV, LOD o Enfermedad	**Normal** PAS 120-129 ó DBP 80-84	**Normal-alta** PAS 130-139 ó PAD 85-89	**HTA Grado 1** PAS 140-159 ó PAD 90-99	**HTA Grado 2** PAS 160-179 ó PAD 100-109	**HTA Grado 3** PAS≥ 180 ó PAD≥ 110
No otros FRCV	Sin riesgo añadido	Sin riesgo añadido	Riesgo añadido bajo	Riesgo añadido moderado	Riesgo añadido elevado
1-2 FRCV	Riesgo añadido bajo	Riesgo añadido bajo	Riesgo añadido moderado	Riesgo añadido moderado	Riesgo añadido muy elevado
3 ó más FRCV, SM, LOD o DM	Riesgo añadido moderado	Riesgo añadido elevado	Riesgo añadido elevado	Riesgo añadido elevado	Riesgo añadido muy elevado
Enfermedad CV o renal establecida	Riesgo añadido muy elevado	Riesgo añadido muy elevado	Riesgo añadido muy elevado	Riesgo añadido muy elevado	Riesgo añadido muy elevado

Equivalentes: Framingham: <15%; 15-20%, 20-30%, >30%; SCORE: <4%; 4-5%, 5-8%, >8%

Inicio del tratamiento antihipertensivo

Other CVRF. OD or Disease	**Normal** SBP 120-129 or DBP 80-84	**High Normal** SBP 130-139 or DBP 85-89	**Grade 1 HT** SBP 140-159 or DBP 90-99	**Grade 2 HT** SBP 160-179 or DBP 100-109	**Grade 3 HT** SBP≥ 180 or DBP≥ 110
No other CVRF	No BP intervention	No BP intervention	Lifestyle changes for several months then drug treatment if BP uncontrolled	Lifestyle changes for several weeks then drug treatment if BP uncontrolled	Lifestyle changes + Immediate drug treatment
1-2 CVRF	Lifestyle changes	Lifestyle changes	Lifestyle changes for several weeks then drug treatment if BP uncontrolled	Lifestyle changes for several weeks then drug treatment if BP uncontrolled	Lifestyle changes + Immediate drug treatment
3 or more CVRF, MS or OD	Lifestyle changes	Lifestyle changes and consider drug treatment	Lifestyle changes + Drug treatment	Lifestyle changes + Drug treatment	Lifestyle changes + Immediate drug treatment
Diabetes	Lifestyle changes	Lifestyle changes + Drug treatment			
Established CV or renal disease	Lifestyle changes + Immediate drug treatment	Lifestyle changes + Immediate drug treatment	Lifestyle changes + Immediate drug treatment	Lifestyle changes + Immediate drug treatment	Lifestyle changes + Immediate drug treatment

Se debe fomentar las **medidas no farmacológicas intensas** en todos los pacientes diabéticos, con especial atención a la reducción de peso y a la disminución del consumo de sal en la diabetes tipo 2

Journal of Hypertension 2007, **25**:1105–1187

Impact of Intensive Lifestyle and Metformin Therapy on Cardiovascular Disease Risk Factors in the Diabetes Prevention Proaram

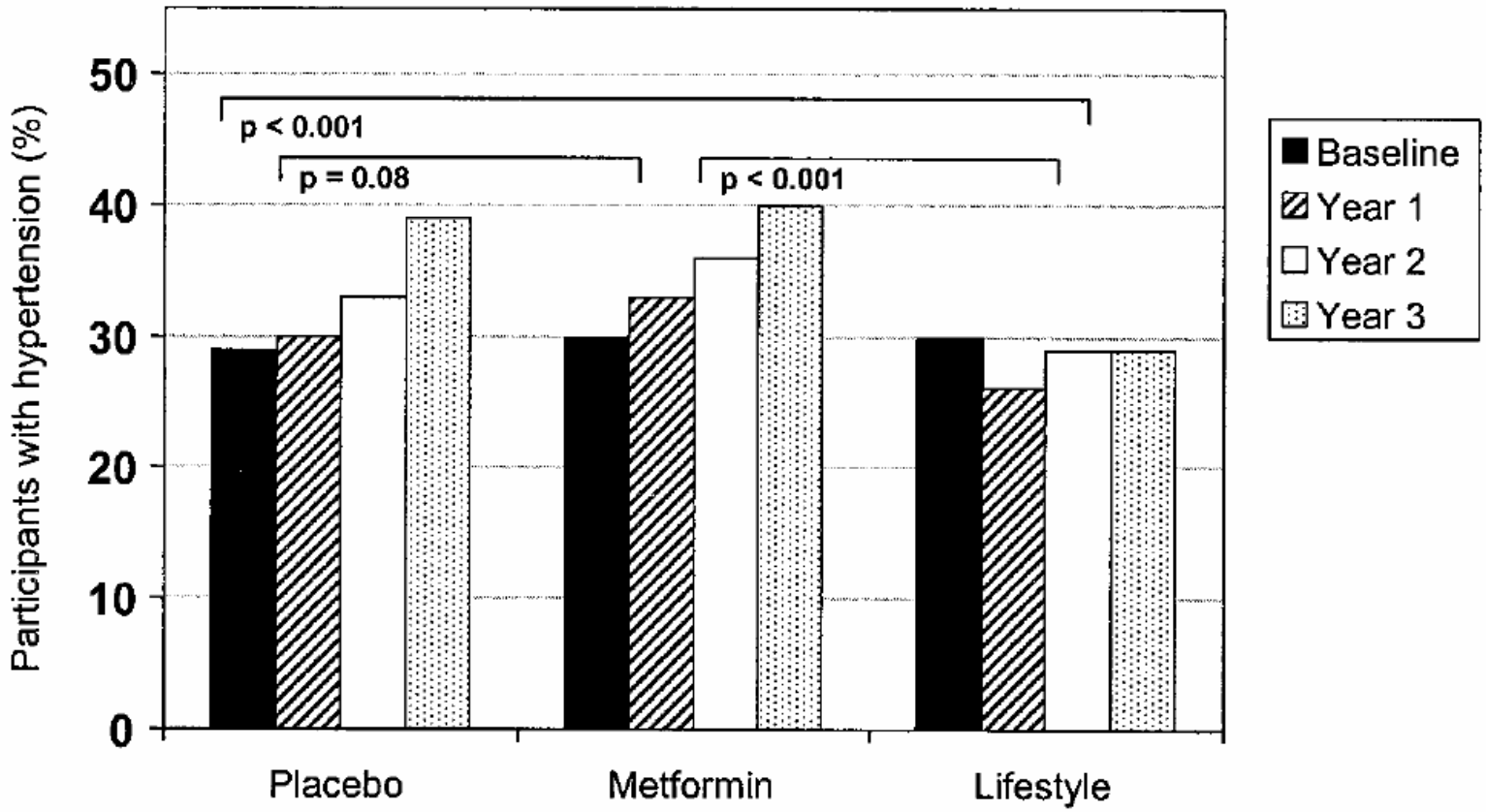

Figure 1—*Categorical changes in hypertension over time by treatment assignment. P represents the pairwise comparison from generalized estimating equation models.*

TECHNICAL REVIEW

Evidence-Based Nutrition Principles and Recommendations for the Treatment and Prevention of Diabetes and Related Complications

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El objetivo de presión arterial (PA) debe ser **< 130/80 mmHg** y el tratamiento con fármacos antihipertensivos puede iniciarse ya cuando la PA esté en **valores normales altos**

Journal of Hypertension 2007, **25**:1105–1187

Tight blood pressure control and risk of macrovascular and microvascular complications in type 2 diabetes: UKPDS 38

UK Prospective Diabetes Study Group

Clinical end point	Patients with aggregate end points: Tight control (n=758)	Patients with aggregate end points: Less tight control (n=390)	Absolute risk (events per 1000 patient years): Tight control	Absolute risk (events per 1000 patient years): Less tight control	P value	Relative risk for tight control (95% CI)
Any diabetes related end point	259	170	50.9	67.4	0.0046	0.76 (0.62 to 0.92)
Deaths related to diabetes	82	62	13.7	20.3	0.019	0.68 (0.49 to 0.94)
All cause mortality	134	83	22.4	27.2	0.17	0.82 (0.63 to 1.08)
Myocardial infarction	107	69	18.6	23.5	0.13	0.79 (0.59 to 1.07)
Stroke	38	34	6.5	11.6	0.013	0.56 (0.35 to 0.89)
Peripheral vascular disease	8	8	1.4	2.7	0.17	0.51 (0.19 to 1.37)
Microvascular disease	68	54	12.0	19.2	0.0092	0.63 (0.44 to 0.89)

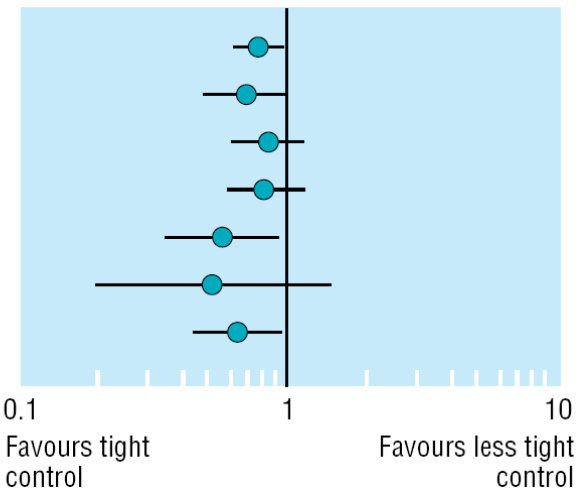


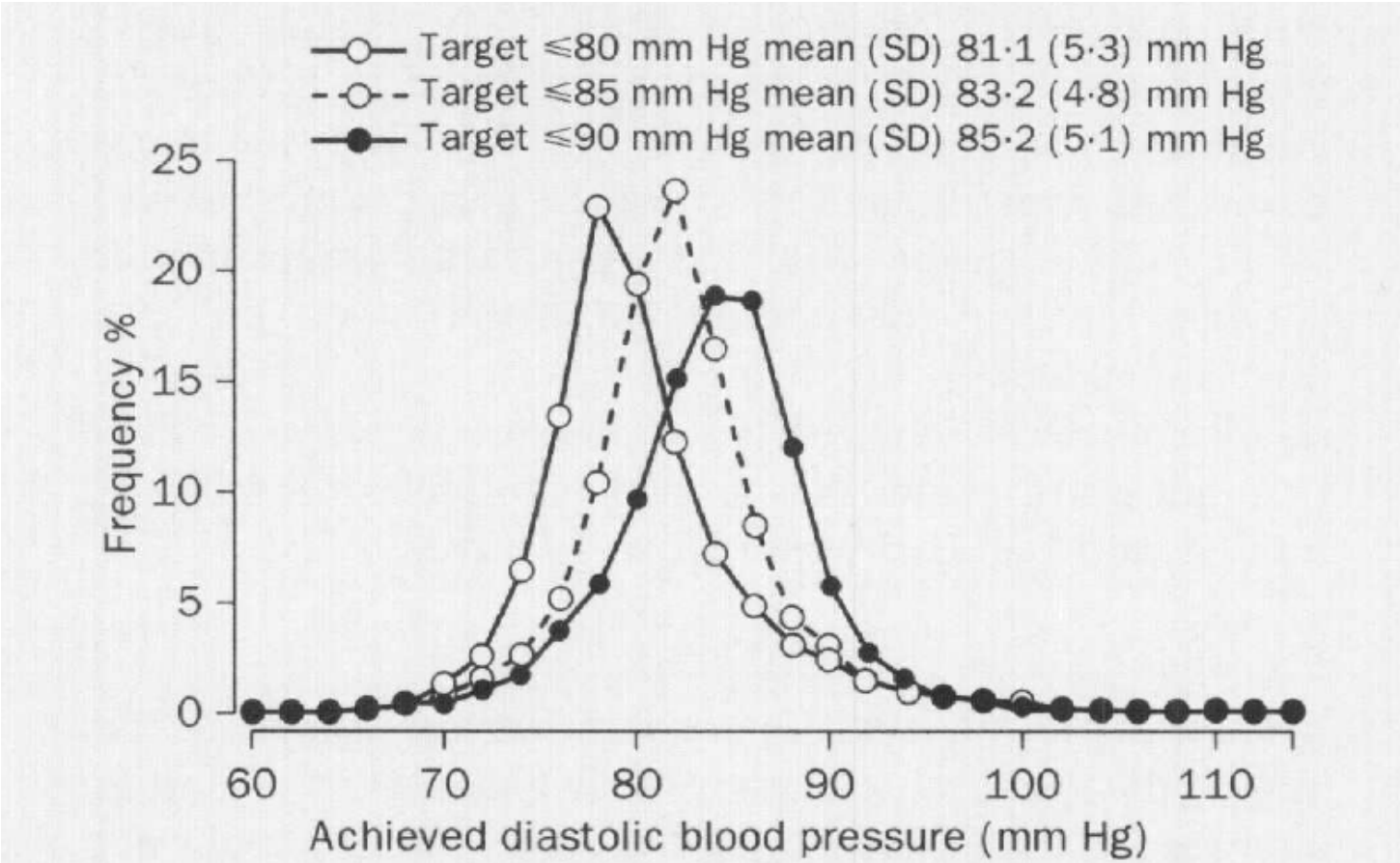
Fig 4 Numbers of patients who attained one or more clinical end points in aggregates representing specific types of clinical complications, with relative risks comparing tight control of blood pressure with less tight control

Mean blood pressure during follow up was significantly reduced in the group assigned tight blood pressure control (144/82 mm Hg) compared with the group assigned to less tight control (154/87 mm Hg) ($P < 0.0001$)

BMJ 1998;317;703-713

Effects of intensive blood-pressure lowering and low-dose aspirin in patients with hypertension: principal results of the Hypertension Optimal Treatment (HOT) randomised trial

*Lennart Hansson, Alberto Zanchetti, S George Carruthers, Björn Dahlöf, Dag Elmfeldt, Stevo Julius, Joël Ménard, Karl Heinz Rahn, Hans Wedel, Sten Westerling for the HOT Study Group**



Lancet 1998; **351:** 1755–62

Event	Number of events	Events/ 1000 patient-years	p for trend	Comparison	Relative risk (95% CI)
Major cardiovascular events					
≤90 mm Hg	45	24·4		90 *vs* 85	1·32 (0·84–2·06)
≤85 mm Hg	34	18·6		85 *vs* 80	1·56 (0·91–2·67)
≤80 mm Hg	22	11·9	0·005	90 *vs* 80	2·06 (1·24–3·44)
Major cardiovascular events, including silent myocardial infarction					
≤90 mm Hg	48	26·2		90 *vs* 85	1·13 (0·75–1·71)
≤85 mm Hg	42	23·3		85 *vs* 80	1·42 (0·89–2·26)
≤80 mm Hg	30	16·4	0·045	90 *vs* 80	1·60 (1·02–2·53)
All myocardial infarction					
≤90 mm Hg	14	7·5		90 *vs* 85	1·75 (0·73–4·17)
≤85 mm Hg	8	4·3		85 *vs* 80	1·14 (0·41–3·15)
≤80 mm Hg	7	3·7	0·11	90 *vs* 80	2·01 (0·81–4·97)
All myocardial infarction, including silent cases					
≤90 mm Hg	18	9·7		90 *vs* 85	1·12 (0·57–2·19)
≤85 mm Hg	16	8·7		85 *vs* 80	1·07 (0·53–2·16)
≤80 mm Hg	15	8·1	0·61	90 *vs* 80	1·20 (0·60–2·38)
All stroke					
≤90 mm Hg	17	9·1		90 *vs* 85	1·30 (0·63–2·67)
≤85 mm Hg	13	7·0		85 *vs* 80	1·10 (0·50–2·40)
≤80 mm Hg	12	6·4	0·34	90 *vs* 80	1·43 (0·68–2·99)
Cardiovascular mortality					
≤90 mm Hg	21	11·1		90 *vs* 85	0·99 (0·54–1·82)
≤85 mm Hg	21	11·2		85 *vs* 80	3·0 (1·29–7·13)
≤80 mm Hg	7	3·7	0·016	90 *vs* 80	3·0 (1·28–7·08)
Total mortality					
≤90 mm Hg	30	15·9		90 *vs* 85	1·03 (0·62–1·71)
≤85 mm Hg	29	15·5		85 *vs* 80	1·72 (0·95–3·14)
≤80 mm Hg	17	9·0	0·068	90 *vs* 80	1·77 (0·98–3·21)

Table 5: **Events in patients with diabetes mellitus at baseline in relation to target blood pressure groups (n=501, 501, and 499 in the target groups ≤90 mm Hg, ≤85 mm Hg, and ≤80 mm Hg, respectively)**

Effects of aggressive blood pressure control in normotensive type 2 diabetic patients on albuminuria, retinopathy and strokes

ROBERT W. SCHRIER, RAYMOND O. ESTACIO, ANNE ESLER, and PHILIP MEHLER

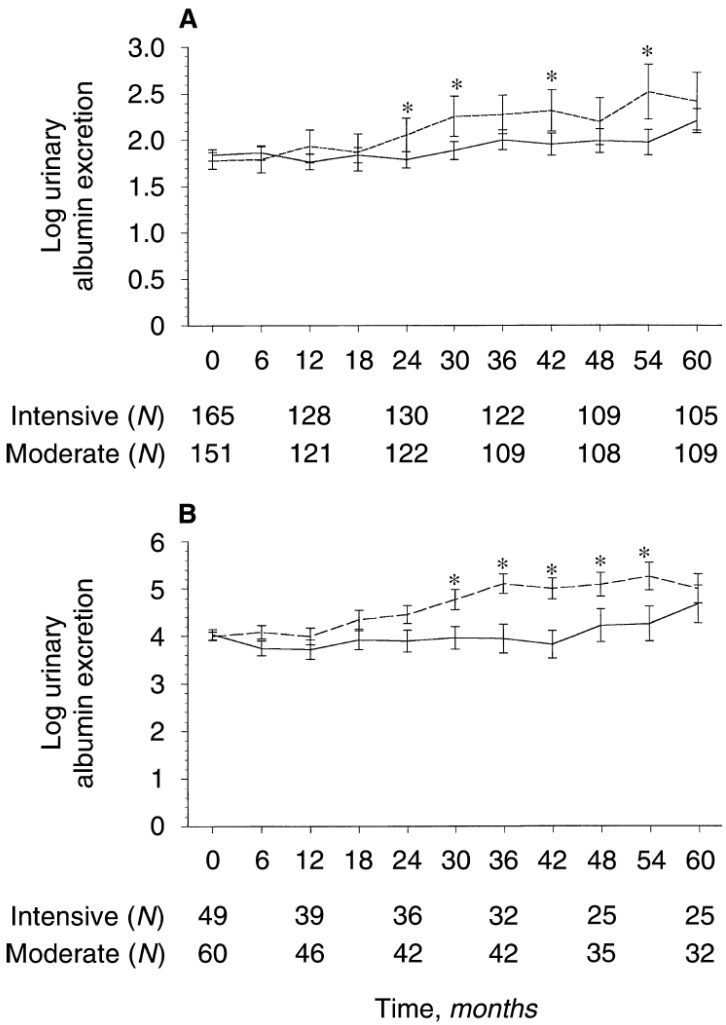


Fig. 6. Log urinary albumin excretion (UAE) for intensive (solid line) and moderate (dashed line) blood pressure control groups: *(A)* normoalbuminuria at baseline; *(B)* microalbuminuria at baseline. *T test performed at various time intervals revealed a P value <0.05.

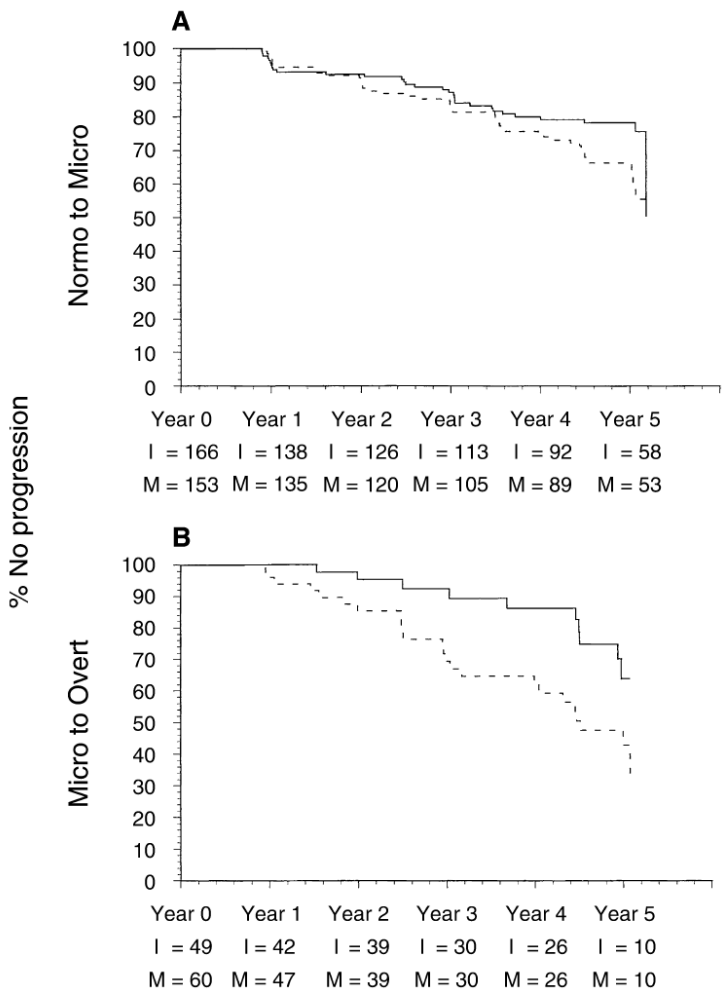


Fig. 7. Kaplan-Meier curves demonstrating progression from normoalbuminuria to microalbuminuria *(A; $P = 0.04$)* and from microalbuminuria to overt albuminuria *(B; $P = 0.02$)* in patients on (solid line) intensive versus (dashed line) moderate therapy.

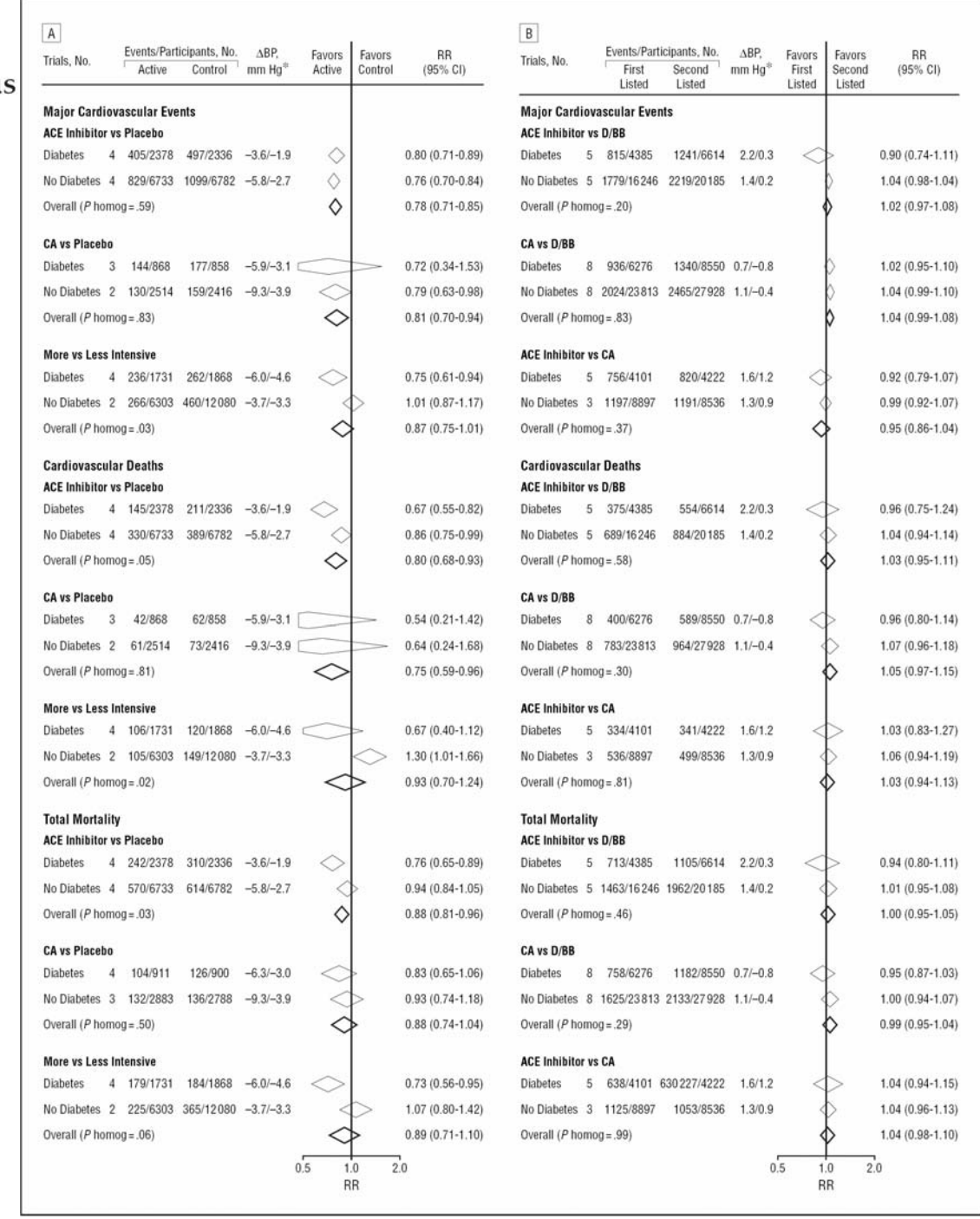
Para la reducción de la PA, pueden utilizarse todos los fármacos que sean efectivos y bien tolerados. A menudo, es necesaria una **combinación de 2 o más fármacos**

Journal of Hypertension 2007, **25**:1105–1187

Effects of Different Blood Pressure–Lowering Regimens on Major Cardiovascular Events in Individuals With and Without Diabetes Mellitus

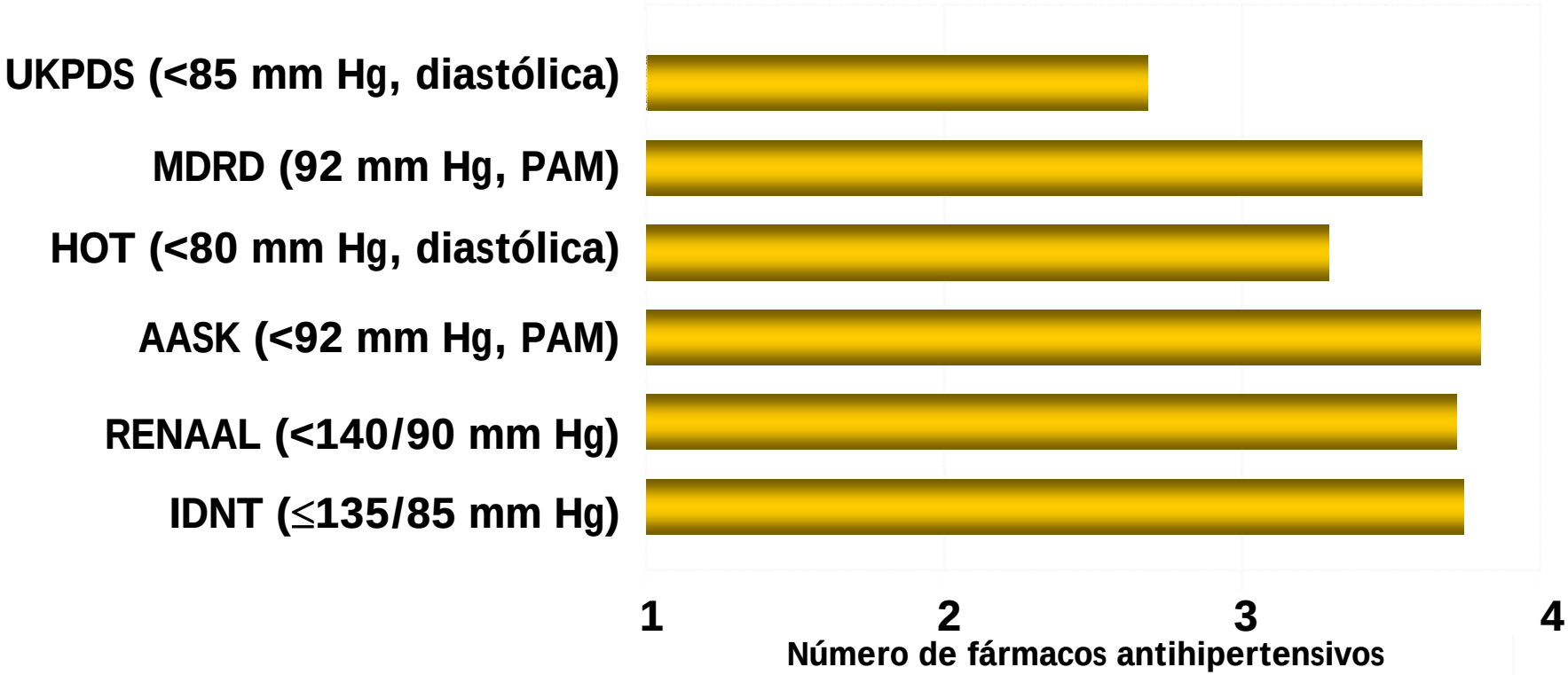
Results of Prospectively Designed Overviews of Randomized Trials

*Blood Pressure Lowering Treatment Trialists' Collaboration**



Arch Intern Med. 2005;165:1410-1419

PACIENTES HIPERTENSOS DE ALTO RIESGO: NÚMERO DE FÁRMACOS NECESARIOS PARA ALCANZAR LOS OBJETIVOS DE CONTROL



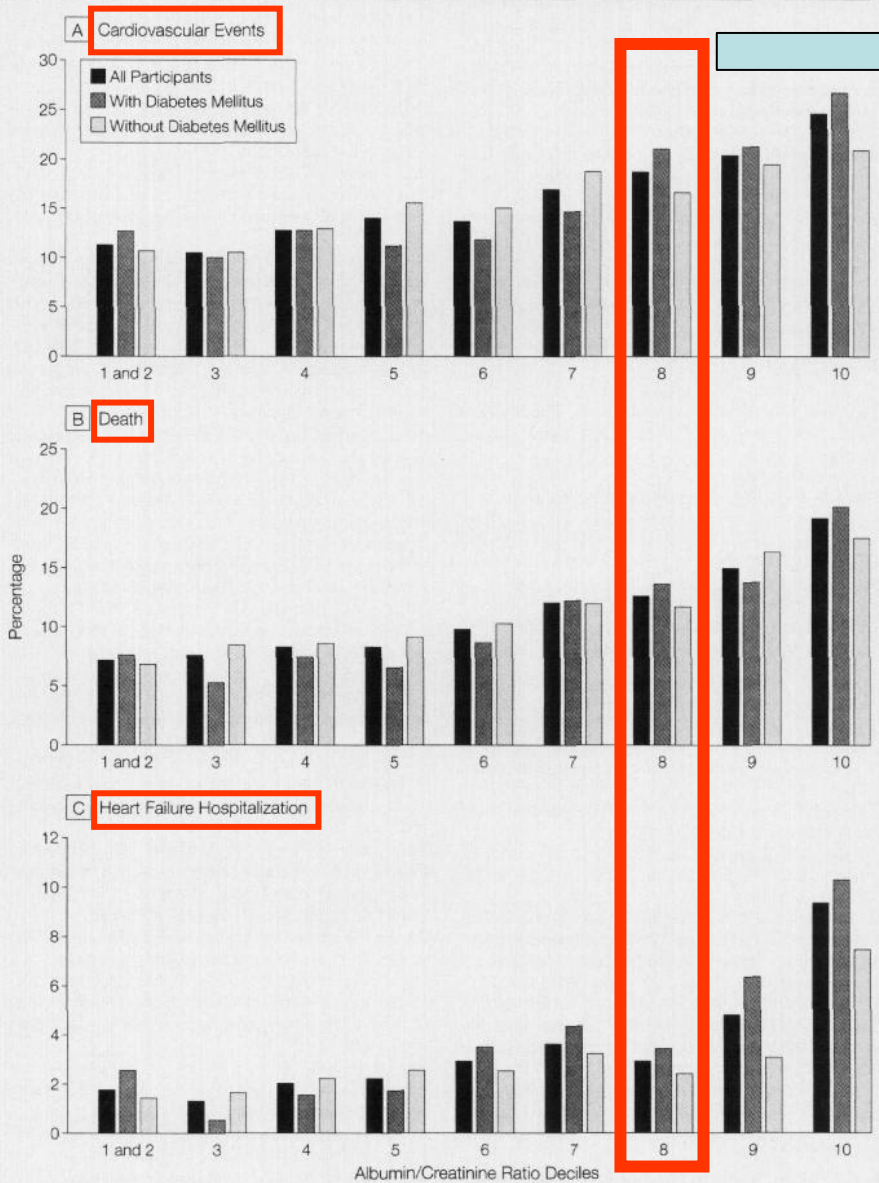
UKPDS=United Kingdom Prospective Diabetes Study; MDRD=Modification of Diet in Renal Disease; HOT=Hypertension Optimal Treatment; AASK=African American Study of Kidney Disease; RENAAL=Reduction of Endpoints in NIDDM with the Angiotensin II Antagonist Losartan; IDNT=Irbesartan Diabetic Nephropathy Trial; MAP=mean arterial pressure.

Bakris et al. Am J Kidney Dis. 2000;36:646-661; Brenner et al. N Engl J Med. 2001;345:861-869; Lewis et al. N Engl J Med. 2001;345:851-860.

La **microalbuminuria** debe motivar el tratamiento farmacológico antihipertensivo incluso cuando la PA inicial esté en valores normales altos. Los bloqueadores del sistema renina-angiotensina tienen un intenso efecto antiproteinúrico y deben utilizarse de manera preferente

Journal of Hypertension 2007, **25**:1105–1187

Figure. Incidence of Cardiovascular Outcomes According to Degree of Albuminuria



Panels A, B, and C show the rate of major cardiovascular events (myocardial infarction, stroke, or cardiovascular death), all-cause mortality, and hospitalization for congestive heart failure in each decile of albumin/creatinine ratio (ACR) for all participants, participants with diabetes mellitus, and participants without diabetes mellitus. Decile 1 and 2 are combined because of very low incidence rates in these 2 deciles. The 8th decile includes ACR of 2 mg/mmol, which is the microalbuminuria threshold.

Cociente A/C 30 mg/g
EUA 30 mg/24h

JAMA 2001; 286: 421-427.

La reducción de la PA también tiene **efectos protectores** contra la **aparición** y la **progresión** de una **lesión renal**. Puede obtenerse una cierta protección adicional con el empleo de un fármaco que bloquee el sistema renina-angiotensina (un antagonista de los receptores de la angiotensina o un IECA).

Un bloqueador del sistema renina-angiotensina debe ser un componente habitual del tratamiento combinado y la medicación preferida si basta con una monoterapia

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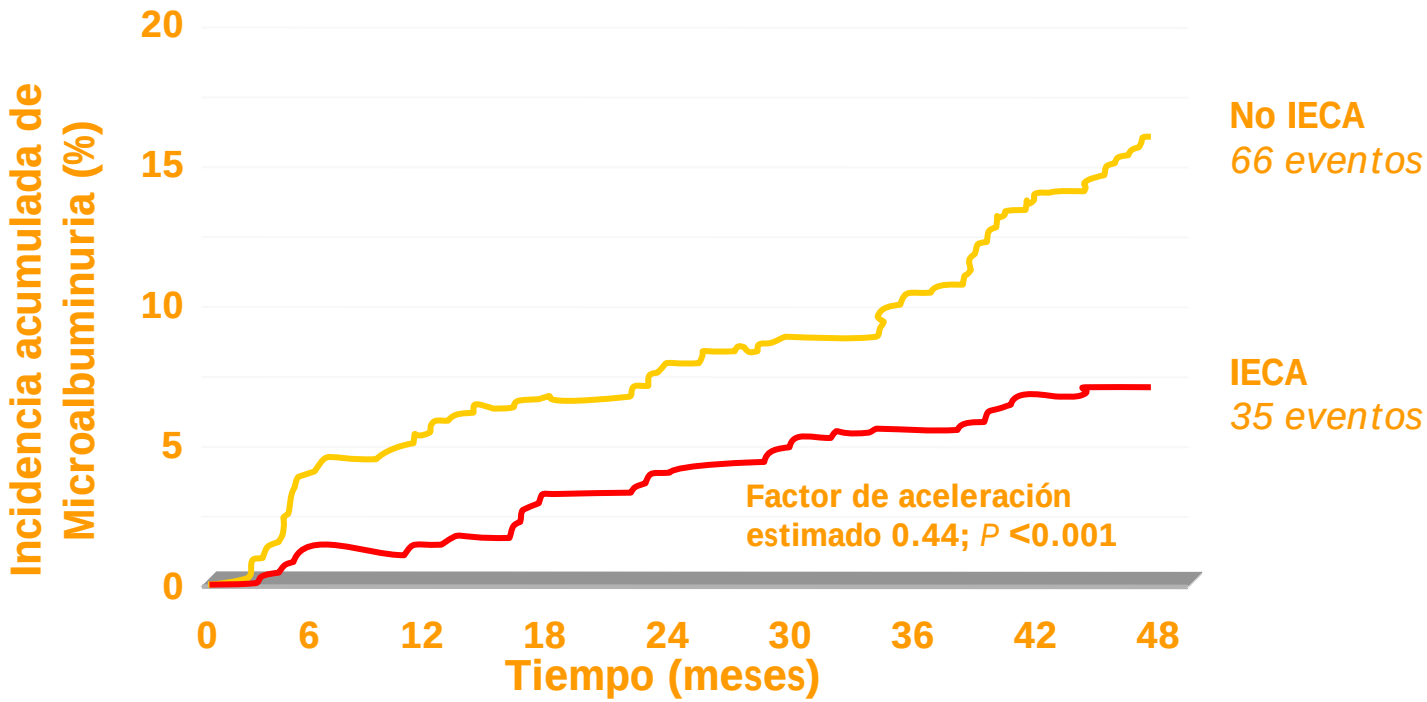
INCIDENCIA DE MICROALBUMINURIA A LO LARGO DEL TIEMPO: IECA VERSUS NO IECA

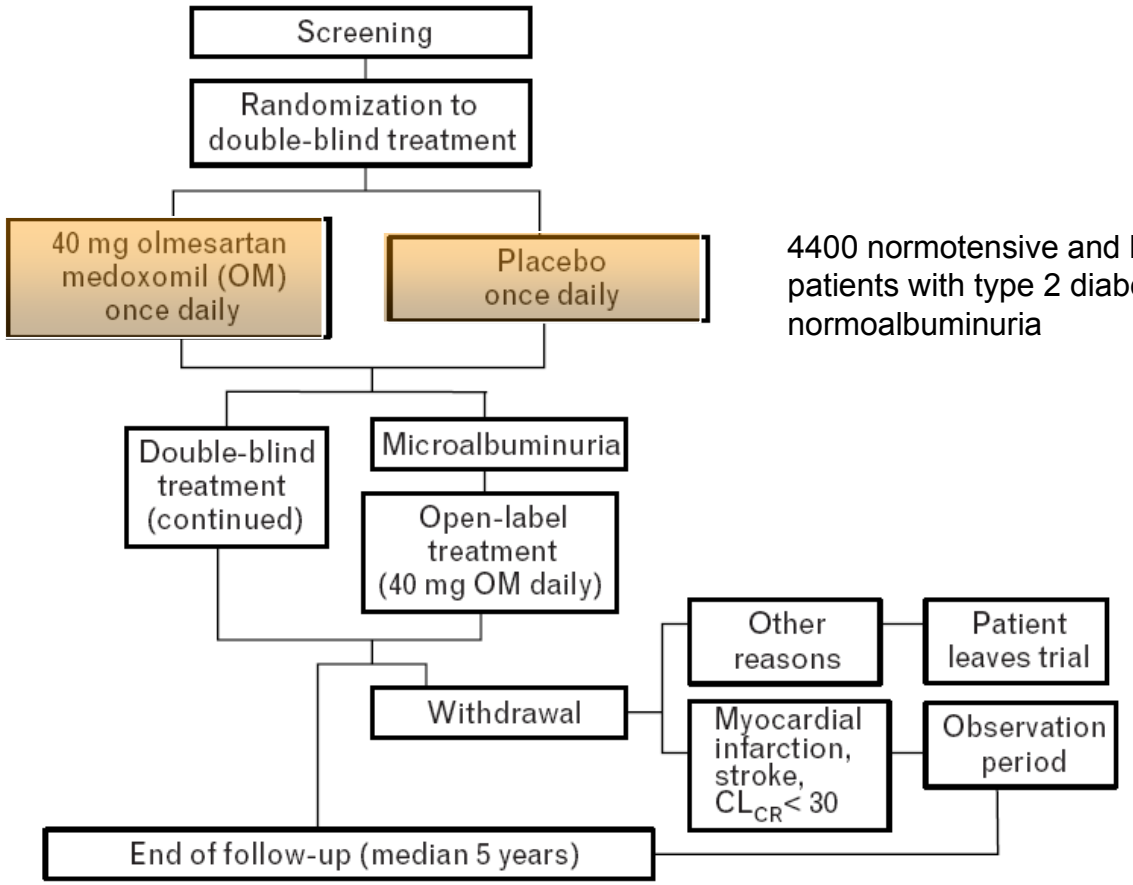


No. al riesgo									
ACE inhibitor	601	503	469	441	417	399	380	311	220
No ACE inhibitor	603	463	424	405	376	357	338	270	188

Ruggenenti P et al. N Engl J Med 2004; 351: 1941-51.

Preventing microalbuminuria in patients with diabetes: rationale and design of the Randomised Olmesartan and Diabetes Microalbuminuria Prevention (ROADMAP) study

Hermann Haller[a], Gian C. Viberti[b], Albert Mimran[c], Giuseppe Remuzzi[d], Antonius J. Rabelink[e], Eberhard Ritz[f], Lars C. Rump[g], Luis M. Ruilope[h], Shigehiro Katayama[i], Sadayoshi Ito[j], Joseph L. Izzo Jr[k] and Andrzej Januszewicz[l]

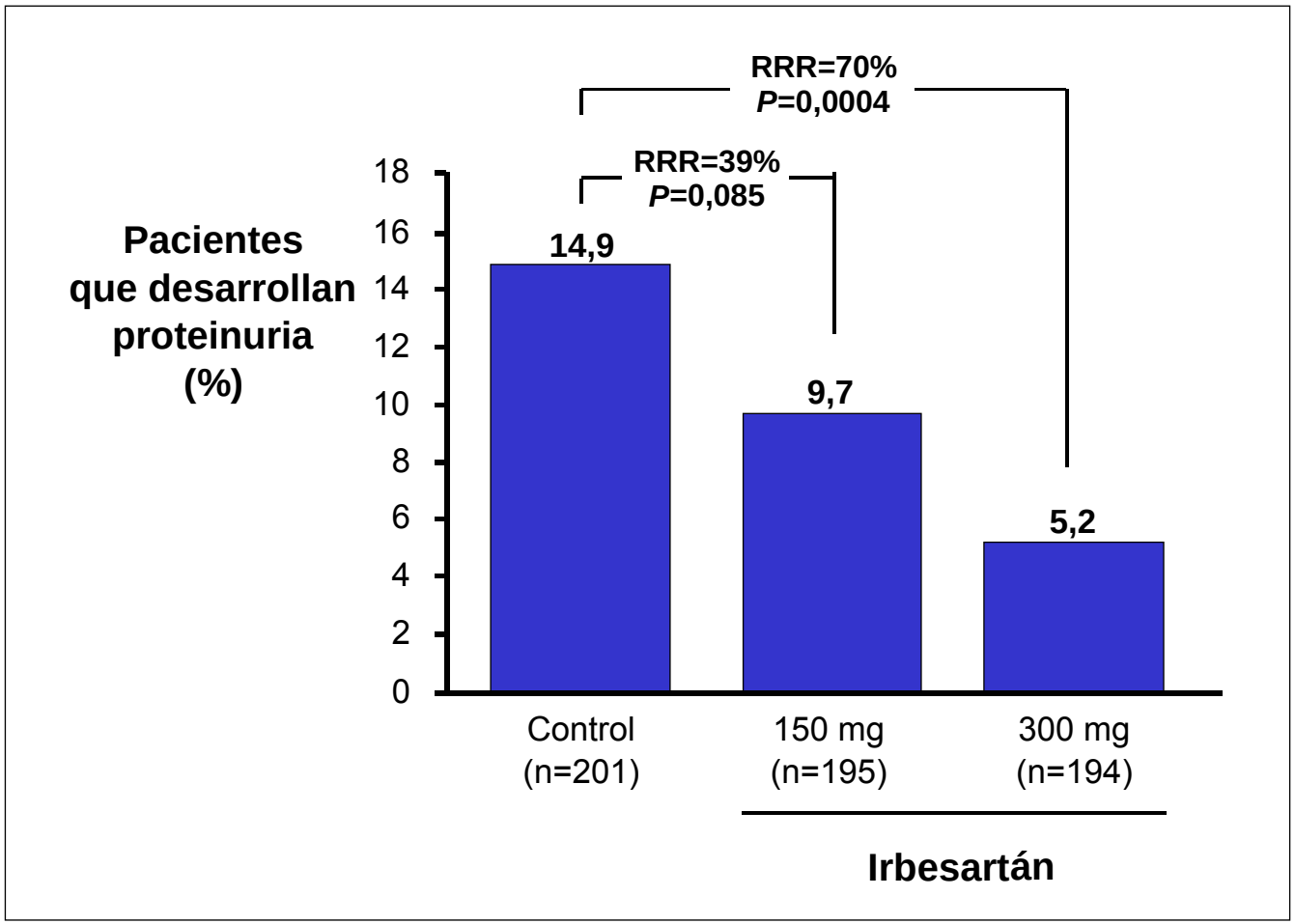


4400 normotensive and hypertensive patients with type 2 diabetes and normoalbuminuria

Journal of Hypertension 2006, 24:403–408

EFECTO DE IRBESARTÁN EN EL DESARROLLO DE NEFROPATÍA EN PACIENTES CON DIABETES TIPO 2

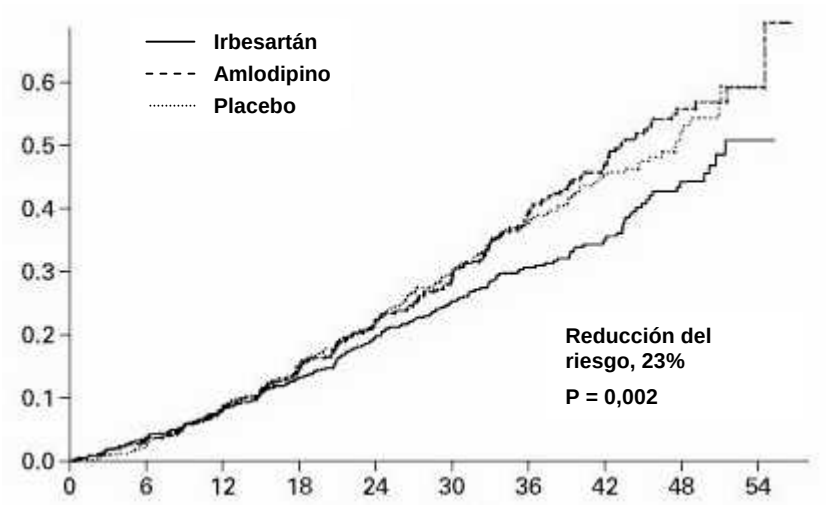
IRMA 2



Parving HH, et al. N Engl J Med 2001;345:870-878.

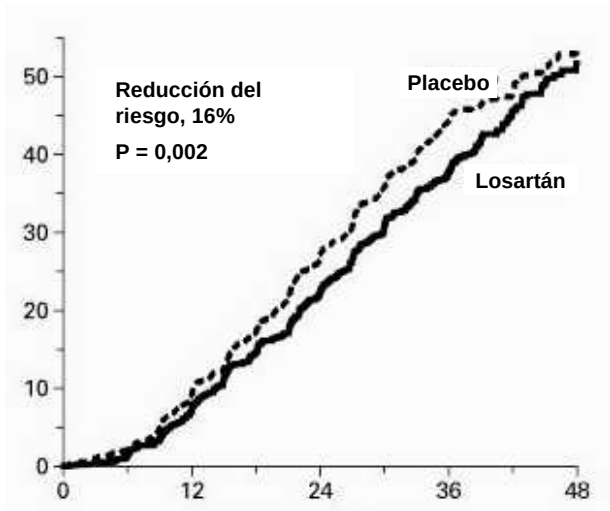
EFECTO DE LOS ARA2 EN LA PROGRESIÓN DE LA NEFROPATÍA ESTABLECIDA ASOCIADA A DIABETES TIPO 2

IDNT



Lewis EJ, et al.
N Engl J Med 2001;345:851-860.

RENAAL

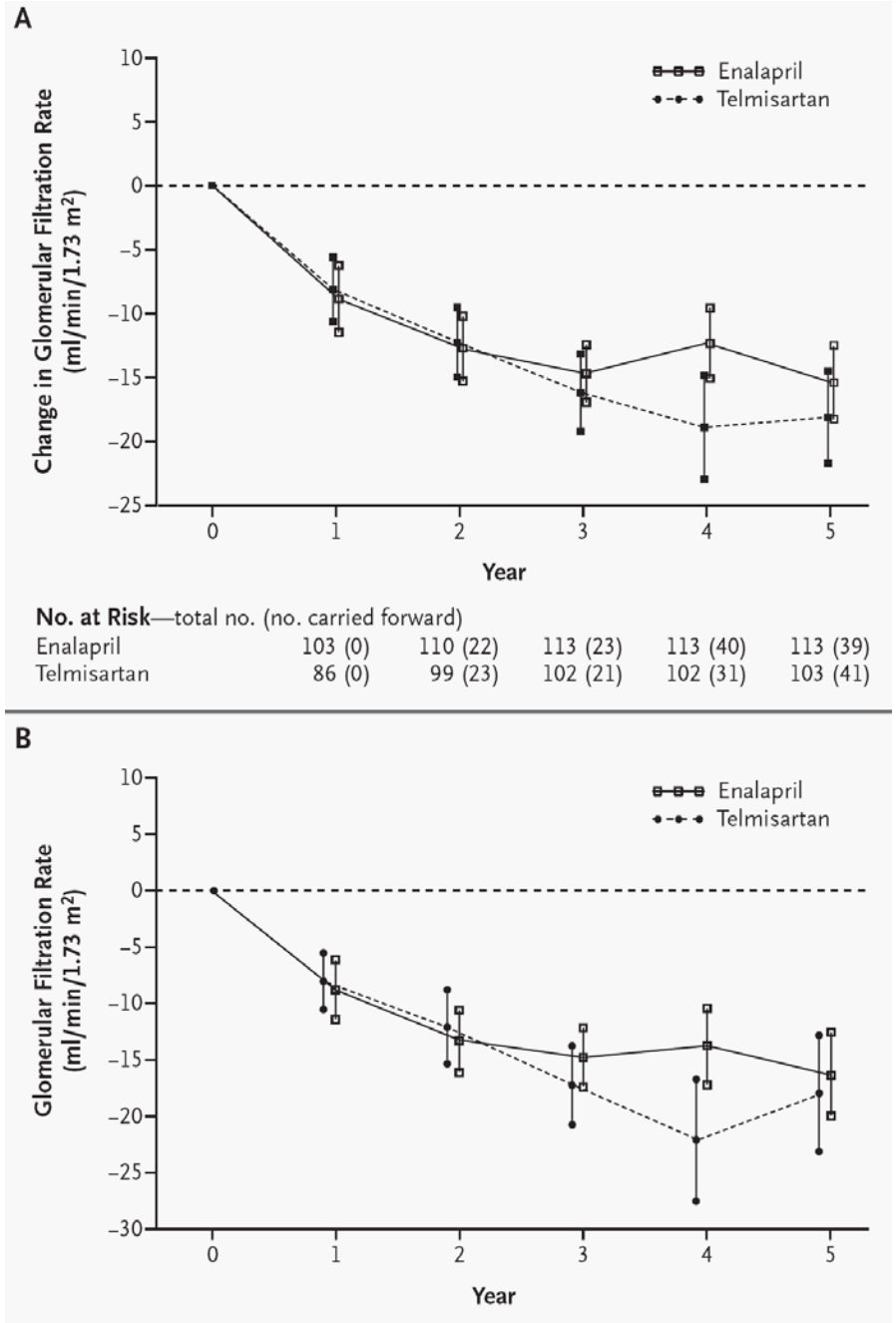


Brenner BM, et al.
N Engl J Med 2001;345:861-869.

Angiotensin-Receptor Blockade versus Converting–Enzyme Inhibition in Type 2 Diabetes and Nephropathy

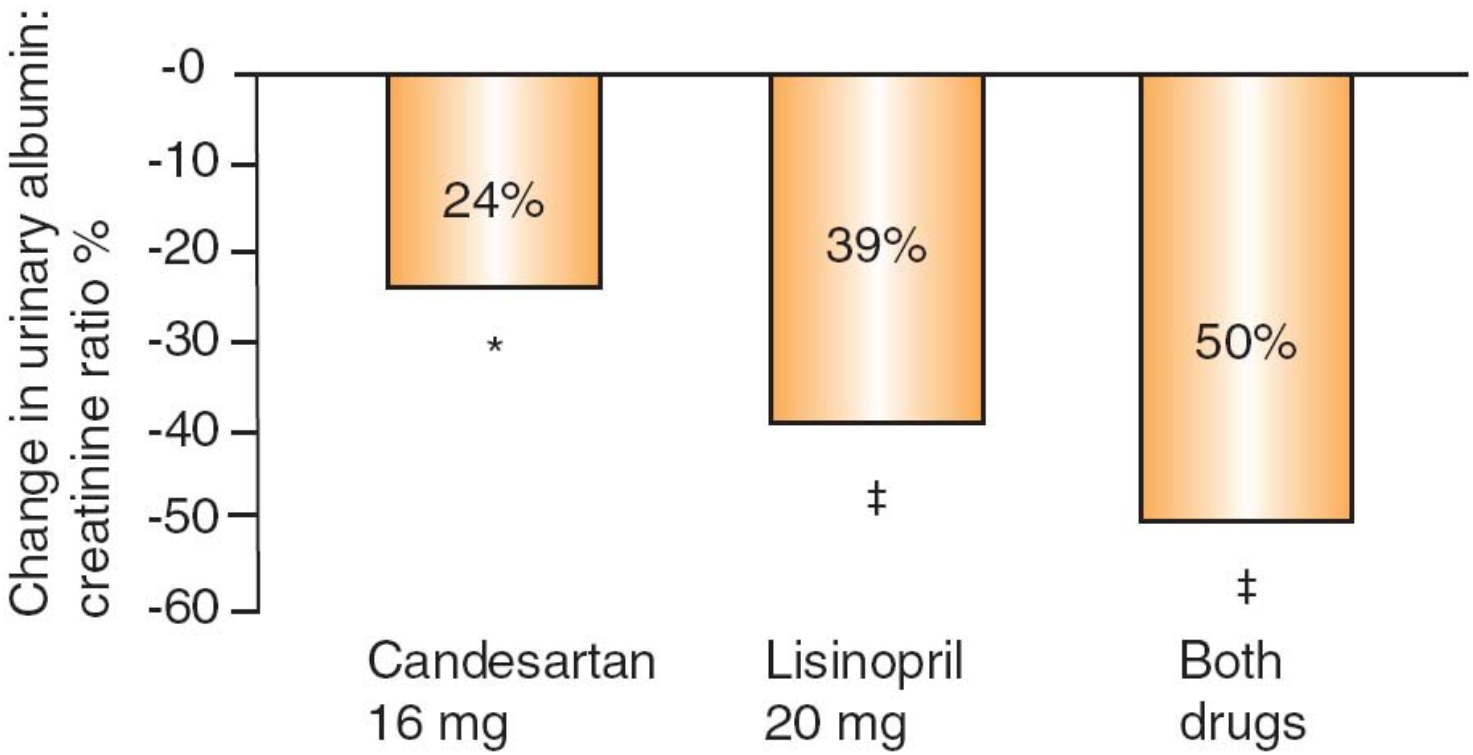
Anthony H. Barnett, M.D., Stephen C. Bain, M.D., Paul Bouter, Ph.D., Bengt Karlberg, M.D., Sten Madsbad, M.D., Jak Jervell, Ph.D., and Jukka Mustonen, Ph.D., for the Diabetics Exposed to Telmisartan and Enalapril Study Group*

250 subjects with type 2 diabetes and early nephropathy to receive either the angiotensin II–receptor blocker telmisartan (80 mg daily, in 120 subjects) or the ACE inhibitor enalapril (20 mg daily, in 130 subjects). The primary end point was the change in the glomerular filtration rate (determined by measuring the plasma clearance of iohexol)



N Engl J Med 2004;351:1952-61.

Estudio CALM
Candesartán y lisinopril en DM tipo 2



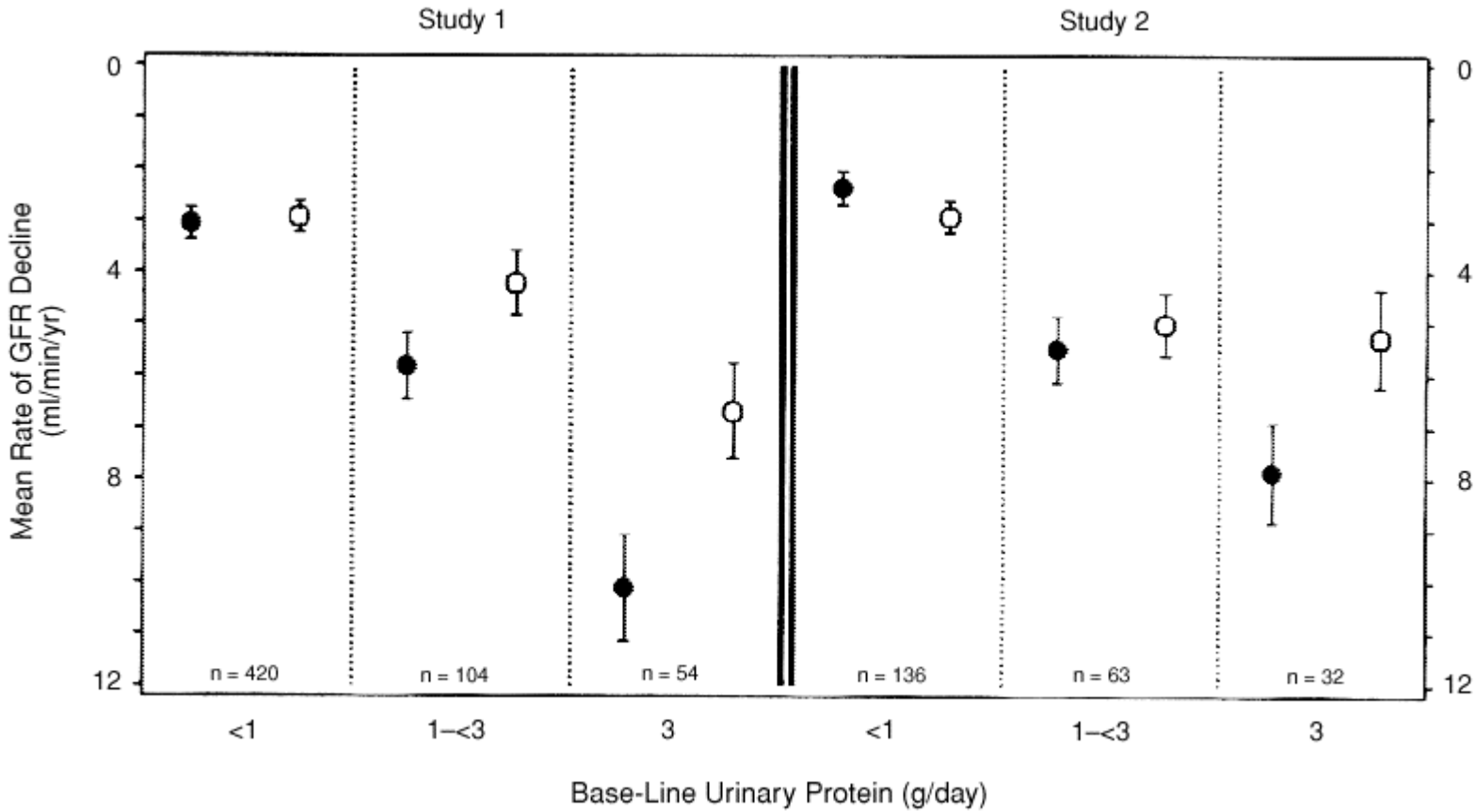
CE Mogensen et al. BMJ 2000;321:1440-1444.

La protección contra la progresión de la disfunción renal tiene dos exigencias básicas: a) un control estricto de la presión arterial (< 130/80 mmHg o incluso inferior si la proteinuria es > 1 g/día), y b) una reducción de la proteinuria a valores lo más próximos posibles al normal

Journal of Hypertension 2007, **25**:1105–1187

The Effects of Dietary Protein Restriction and Blood-Pressure Control on the Progression of Chronic Renal Disease

Saulo Klahr, Andrew S. Levey, Gerald J. Beck, Arlene W. Caggiula, Lawrence Hunsicker, John W. Kusek, Gary Striker, for The Modification of Diet in Renal Disease Study Group



● Usual BP control for 18-60 yr old at entry was 140/90 mmHg or 160/90 mmHg for patients older than 61 yr.

○ Low BP control for patients 18-60 yr old at entry was 125/75 mmHg or 145/75 mmHg for patients older than 61 yr.

N Engl J Med 1994; 330:877-884

Las estrategias de tratamiento deben considerar una intervención dirigida a **todos** los factores de riesgo cardiovascular

Con frecuencia es preciso considerar una **intervención terapéutica integral** (antihipertensivo, estatina y tratamiento antiagregante plaquetario) en los pacientes con lesión renal, ya que en esas circunstancias el riesgo cardiovascular es extremadamente alto

Journal of Hypertension 2007, **25**:1105–1187

Multifactorial Intervention and Cardiovascular Disease in Patients with Type 2 Diabetes

Peter Gæde, M.D., Pernille Vedel, M.D., Ph.D., Nicolai Larsen, M.D., Ph.D., Gunnar V.H. Jensen, M.D., Ph.D., Hans-Henrik Parving, M.D., D.M.Sc., and Oluf Pedersen, M.D., D.M.Sc.

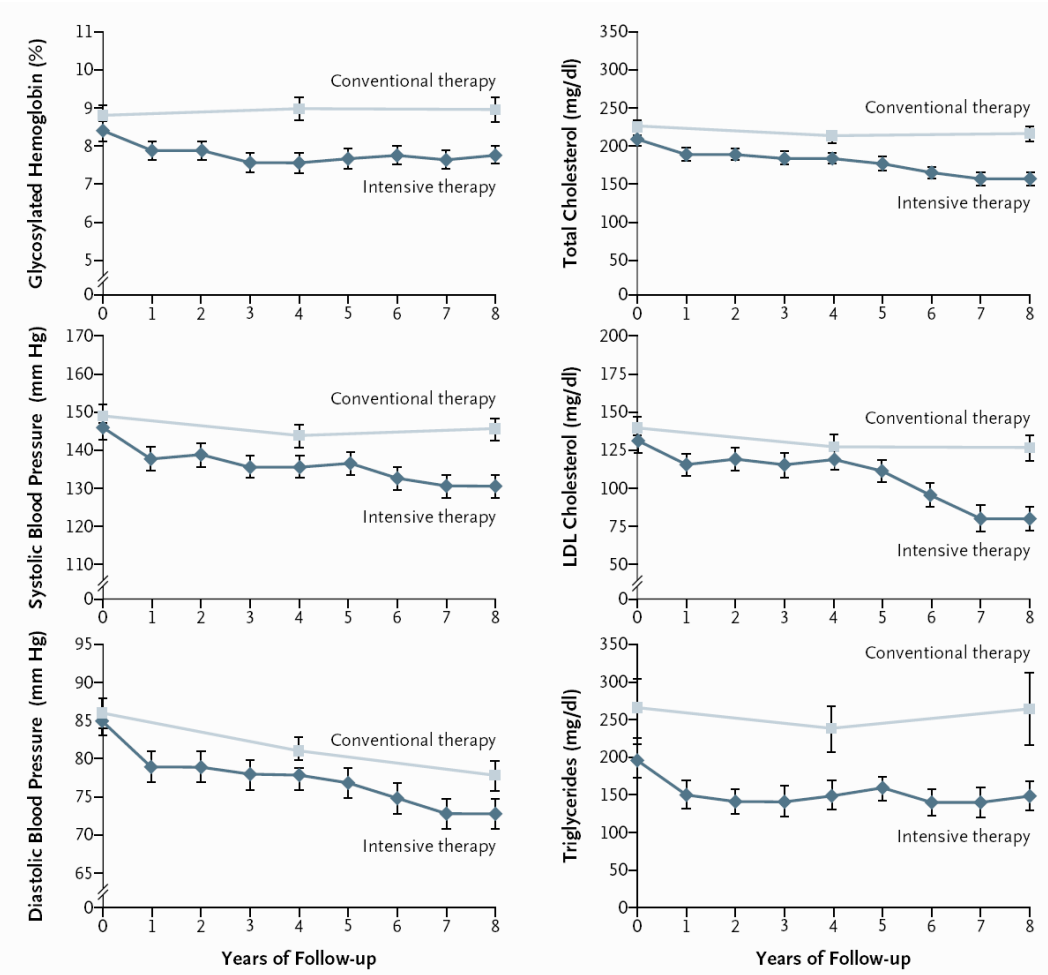
Table 1. Treatment Goals for the Conventional-Therapy Group and the Intensive-Therapy Group.*

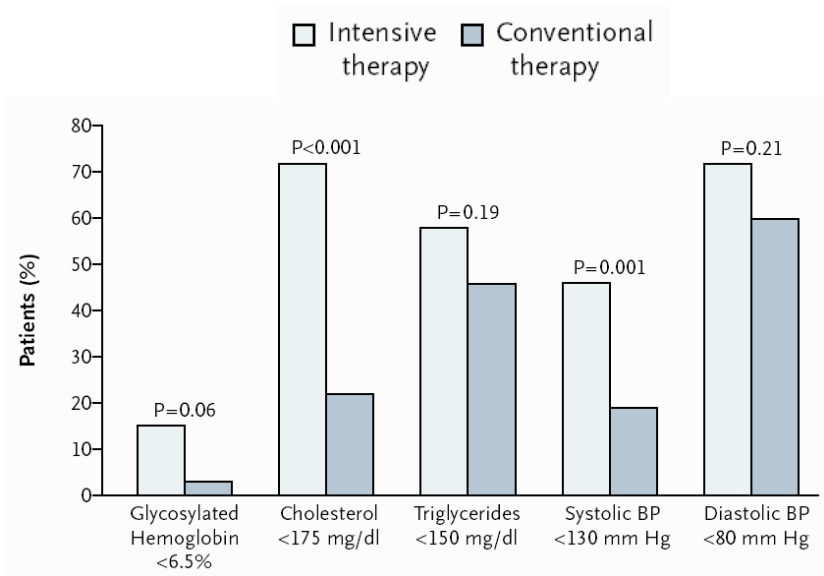
Variable	Conventional Therapy		Intensive Therapy	
	1993–1999	2000–2001	1993–1999	2000–2001
Systolic blood pressure (mm Hg)	<160	<135	<140	<130
Diastolic blood pressure (mm Hg)	<95	<85	<85	<80
Glycosylated hemoglobin (%)	<7.5	<6.5	<6.5	<6.5
Fasting serum total cholesterol (mg/dl)	<250	<190	<190	<175
Fasting serum triglycerides (mg/dl)	<195	<180	<150	<150
Treatment with ACE inhibitor irrespective of blood pressure	No	Yes	Yes	Yes
Aspirin therapy				
For patients with known ischemia	Yes	Yes	Yes	Yes
For patients with peripheral vascular disease	No	No	Yes	Yes
For patients without coronary heart disease or peripheral vascular disease	No	No	No	Yes

N Engl J Med 2003;348:383-93.

Multifactorial Intervention and Cardiovascular Disease in Patients with Type 2 Diabetes

Peter Gæde, M.D., Pernille Vedel, M.D., Ph.D., Nicolai Larsen, M.D., Ph.D., Gunnar V.H. Jensen, M.D., Ph.D., Hans-Henrik Parving, M.D., D.M.Sc., and Oluf Pedersen, M.D., D.M.Sc.





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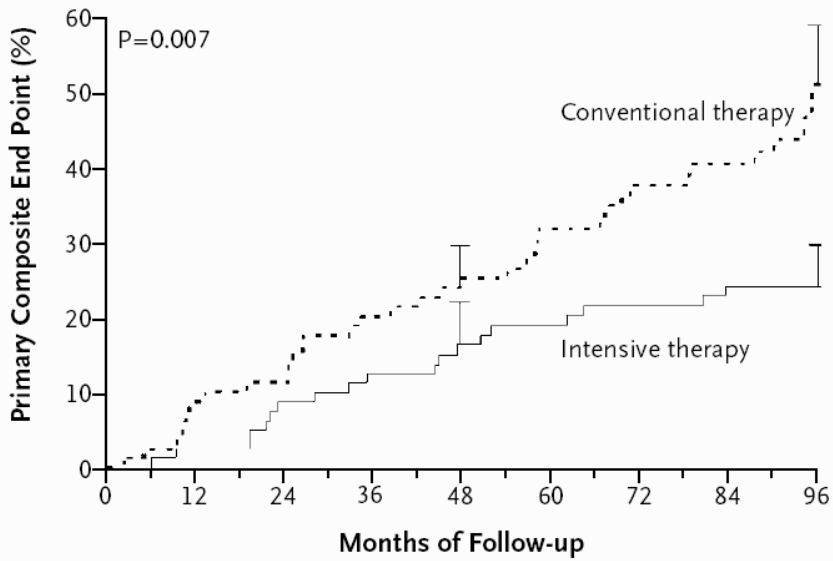
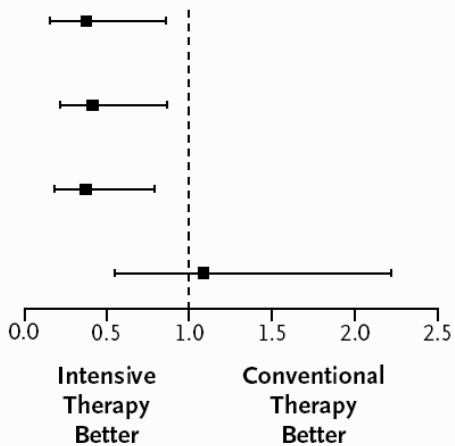


No. at Risk									
Conventional therapy	80	72	70	63	59	50	44	41	13
Intensive therapy	80	78	74	71	66	63	61	59	19

Kaplan–Meier Estimates of the Composite End Point of Death from Cardiovascular Causes, Nonfatal Myocardial Infarction, Coronary-Artery Bypass Grafting, Percutaneous Coronary Intervention, Nonfatal Stroke, Amputation, or Surgery for Peripheral Atherosclerotic Artery Disease in the Conventional-Therapy Group and the Intensive-Therapy Group

B

Variable	Relative Risk (95% CI)	P Value
Nephropathy	0.39 (0.17–0.87)	0.003
Retinopathy	0.42 (0.21–0.86)	0.02
Autonomic neuropathy	0.37 (0.18–0.79)	0.002
Peripheral neuropathy	1.09 (0.54–2.22)	0.66



Relative Risk of the Development or Progression of Nephropathy, Retinopathy, and Autonomic and Peripheral Neuropathy during the Average Followup of 7.8 Years

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Evolution in understanding of cardiovascular risk factors management

Traditional