Manejo del paciente diabético con riesgo cardiovascular

Paciente: Pilar

- 65 años.
- Hipertensión arterial conocida desde hace 15 años. En tratamiento con enalapril 10 mg/dia
- DM2 conocida desde hace 12 años en tratamiento con metformina 850 mg/12 h y glicazida de liberación retardada 120 mg/dia.
- Dislipemia en tratamiento dietético.
- No fumadora
- Sedentaria.
- Otros: síndrome ansioso-depresivo en tratamiento con fluoxetina, artrosis y osteoporosis en tratamiento con Ca/vitD y bifosfonatos.

- No síntomas de claudicación intermitente, angor de esfuerzo o reposo ni polineuropatía

Exploración:

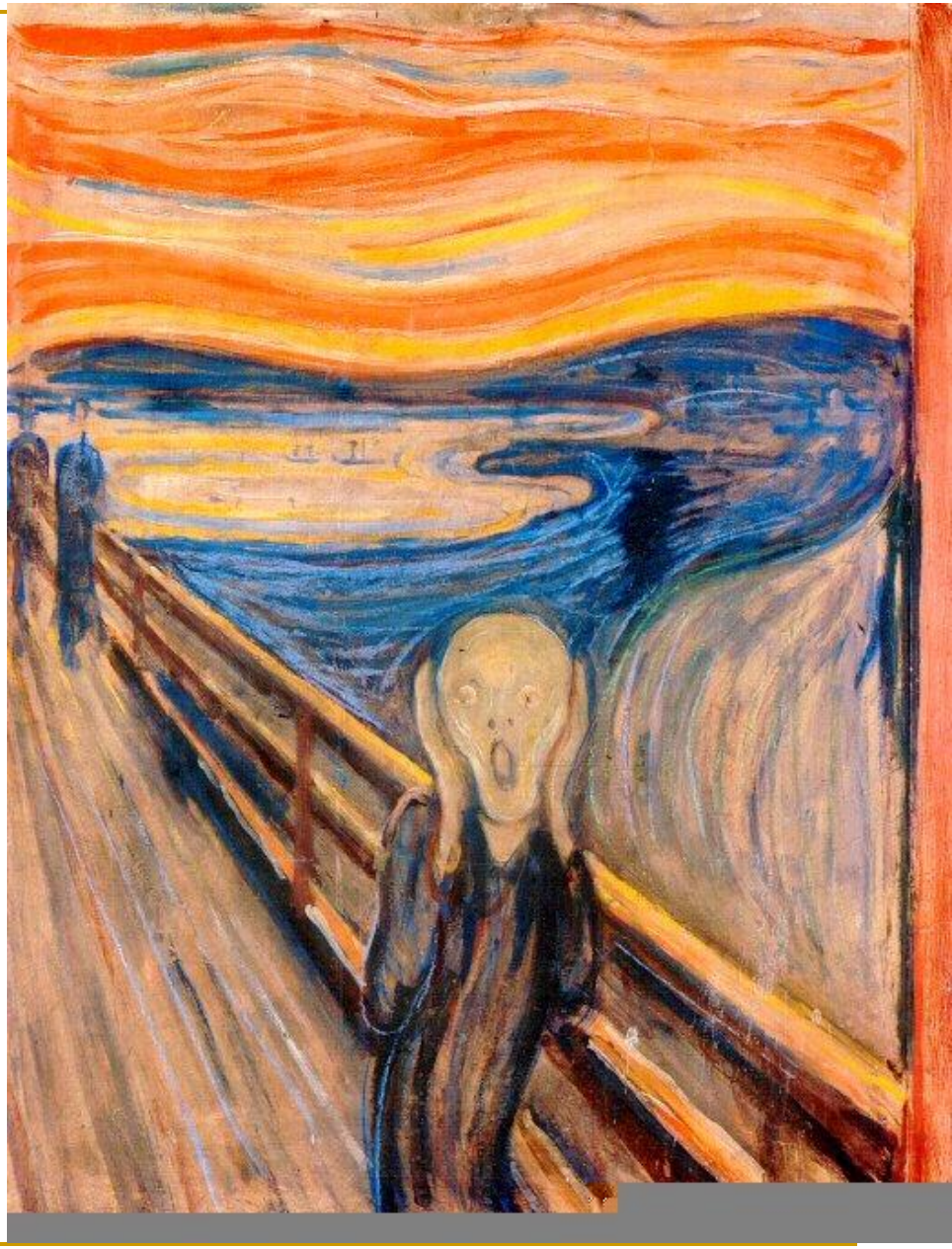
- Peso: 67,3 Kg, Talla 1,55 m, **IMC 28 Kg/m²**. Perimetro cintura **94** cm.
- Presión arterial en las 3 últimas visitas:

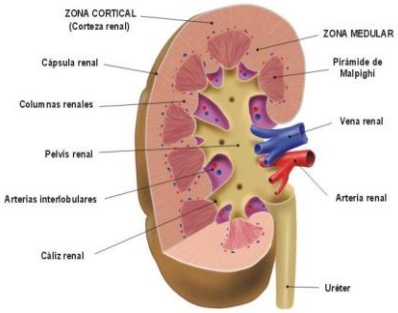
Fecha	TA sistólica	TA diastólica
09/09/2010	**146**	**94**
12/11/2010	**156**	**92**
25/01/2011	**153**	**95**

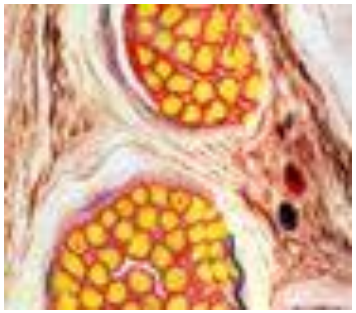
- Pulsos periféricos normales. No alteraciones sensibilidad ni al monofilamento.
- FO (09/2010): **retinopatia diabética leve**.
- ECG: sin alteraciones.

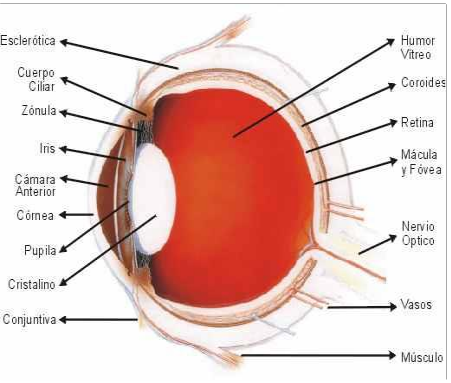
Analítica:

- HbA1C **8,1**%
- Glicemia basal 116 mg/dl
- Colesterol total 222 mg/dl
  - LDL **137** mg/dl
  - HDL 50 mg/dl
  - Triglicéridos **180** mg/dl
- Creatinina 0,9 mg/dl/FG estimado >60 ml/min
- Indice albúmina/creatinina **80** mg/dl







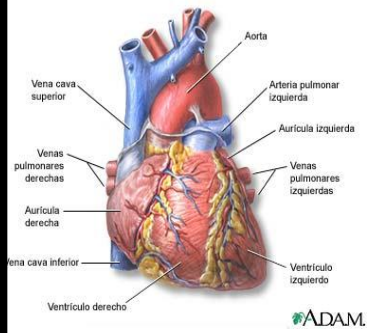


ENFERMEDAD MICROVASCULAR[4,5,6]:

-Nefropatía diabética: 1ª causa de IRT

ENFERMEDAD MACROVASCULAR[1,2,3]:

-Riesgo de muerte por causa cardiovascular en

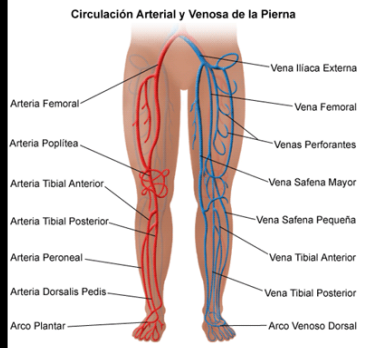


Por cada 1% incremento HbA1c [7,8,9]:

+18% riesgo de eventos cardiovasculares

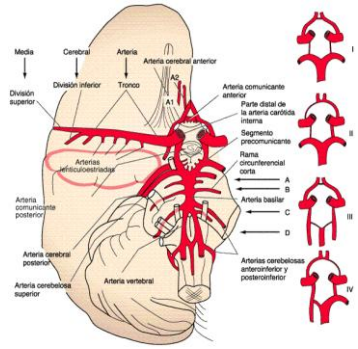
+12-14% riesgo de muerte

+37% retinopatia o fallo renal



-Neuropatía diabética: 1ª causa de amputación no traumática de EEII.

-8/10 individuos con DM2 mueren por enfermedad cardiovascular



(1)Kannel WB, McGee DL. Diabetes and cardiovascular disease: The Framingham Study.JAMA 1979;241:2035. (2)Gu K. Cowie CC, Harris MI. Diabetes and decline in heart disease mortality in US adults.JAMA 1999. (3)Gray RP ¬Yudkin JS. Cardiovascular disease in Diabetes Mellitus. Textbook of diabetes 2nd Edition, 1997. Blackwell Sciencies(4).UK Prospective diabetes study group. Diabetes Res 1990;13:1-11, (5)Fong DS et al., Diabetes Care 2003;26 (Suppl.1):S94-S98.(6)The hypertension in Diabetes Study group.J Hypertens 1993; 11:309-317. (7) Selvin E, Marianopoulus S, Berkenblit et al. Meta-analysis: glycosilated hemoglobin and cardiovascular disease in diabetes mellitus. Ann Intern Med. 2004;141:421-31 (8) Gerstein HC, Pogue J, Mann JF et al. The relationship between dysglycaemia and cardiovascular and renal risk in diabetic and non-diabetic participants in HOPE study a prospective epidemiological analysis. Diabetologia 2005. (9) Stratton IM, Adler AI, Neil HA, et al. Association ofglycaemia with macrovascular and microvascular complications of type2 diabetes (UKPDS 35): prospective observational study. BMJ 2000;321:405-12

Manejo de la hiperglicemia:

- UKPDS 33 N: 3867 DT2 de reciente diagnostico. Seguimiento a 10 años.

AGGREGATE END-POINT	Patients with clinical end-points		Absolute risk events per 1000 patients/year		p	RR for intensive (CI)
Any diabetes r						9-0,99)
Diabetes relate						3-1.11)
All cause morta						0-1.10)
Myocardial infa						1-1.00)
Stroke						L-1.51)
Amputation or death for PVD	29	18	1.1	1.6	0.15	0.65 (0.36-1.18)
Microvascular	225	121	8.6	11.4	0.0099	0.75 (0.60-0.93)

Interpretation Intensive blood-glucose control by either sulphonylureas or insulin substantially decreases the risk of microvascular complications, but not macrovascular disease, in patients with type 2 diabetes. None of the individual drugs had an adverse effect on cardiovascular outcomes. All intensive treatment increased the risk of hypoglycaemia.

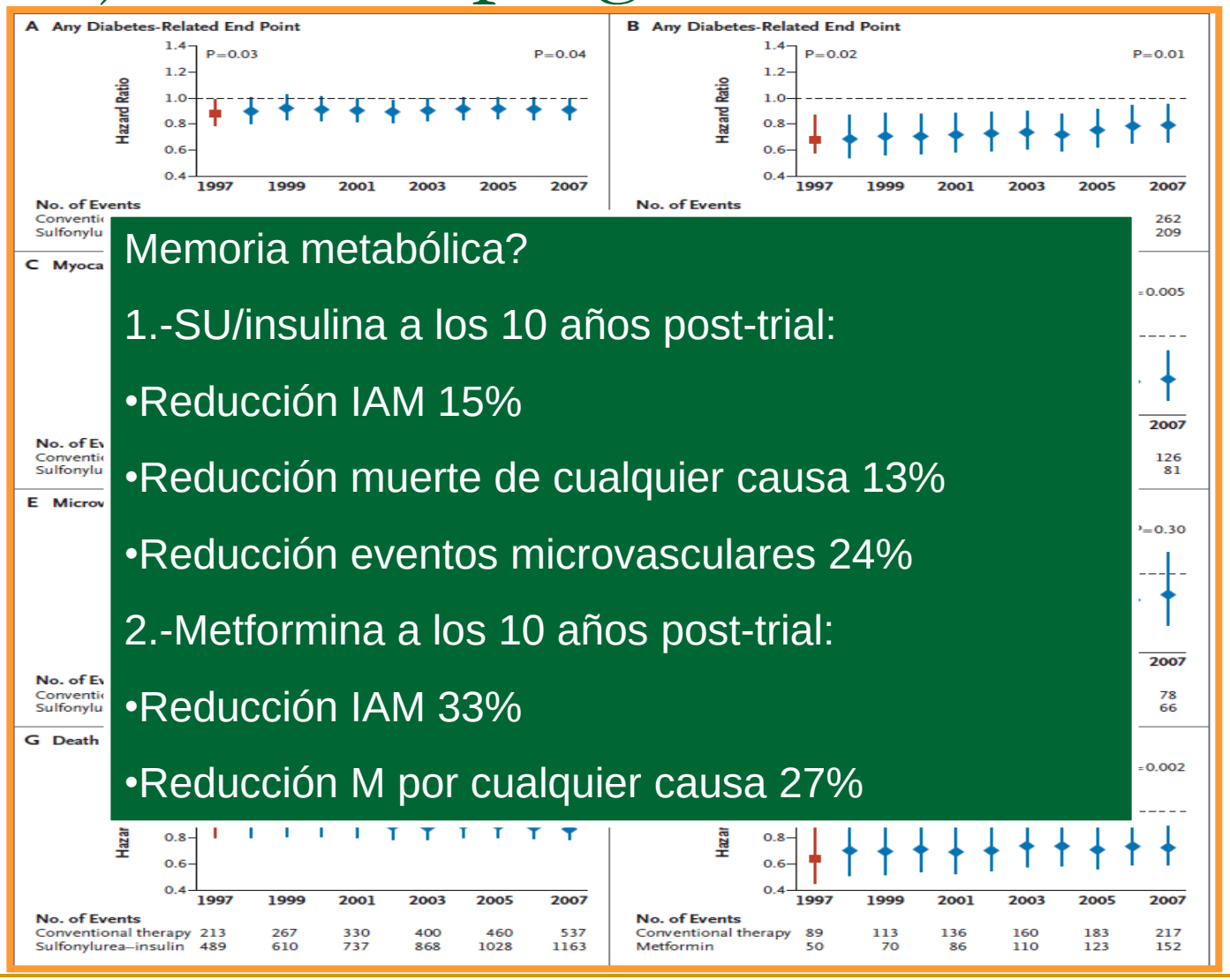
Lancet 1998; **352:** 837–53

UK Prospective study group. *Intensive blood-glucosecontrol with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33).* The Lancet. 1998;352:837-852.

Manejo hiperglicemia: ADA guidelines

•Lowering A1C to **below or around 7%** has been shown to **reduce microvascular and neuropathic complications of type 1 and type 2 diabetes**. Therefore, for microvascular disease prevention, the A1C goal for nonpregnant adults in general is <7%.

Manejo de la hiperglicemia:



Memoria metabólica?

1.-SU/insulina a los 10 años post-trial:

- Reducción IAM 15%
- Reducción muerte de cualquier causa 13%
- Reducción eventos microvasculares 24%

2.-Metformina a los 10 años post-trial:

- Reducción IAM 33%
- Reducción M por cualquier causa 27%

Rury H, Sanjoy P, Bethel M, et al. *10 years follow-up of intensive glucose control in type 2 diabetes*. NEJM. 2008; 359(15): 1577-89

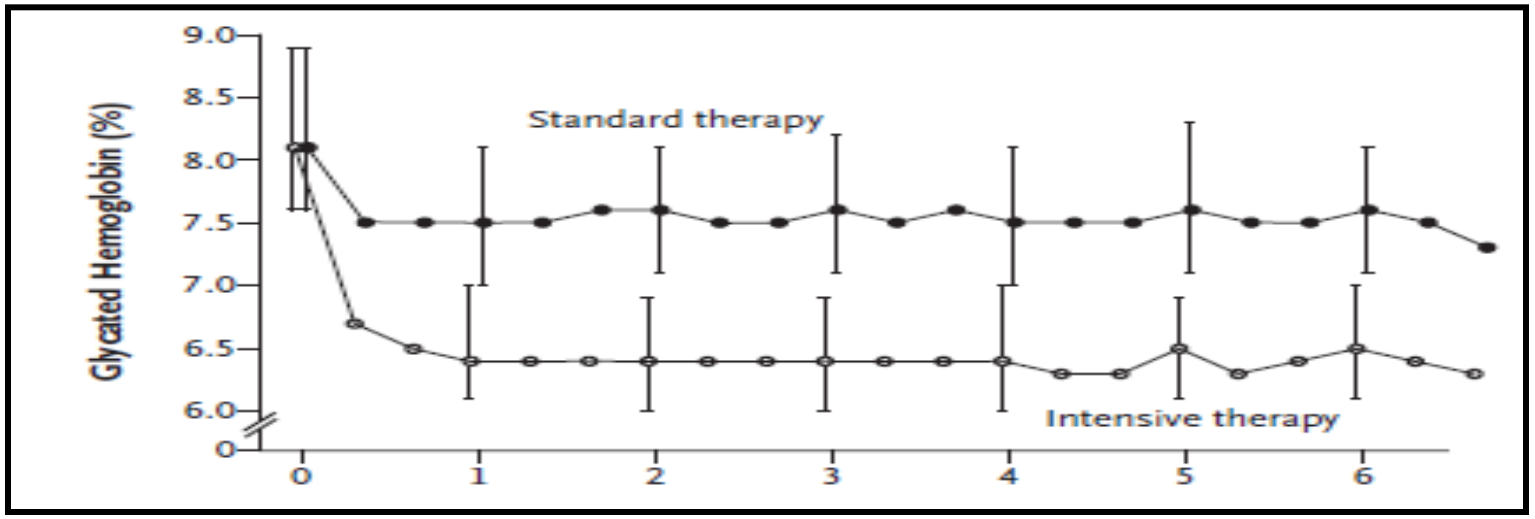
Manejo hiperglicemia: ADA guidelines

•In type 1 and type 2 diabetes, randomized controlled trials of intensive versus standard glycemic control have not shown a significant reduction in CVD outcomes during the randomized portion of the trials. **Long-term follow-up of DCCT and UKPDS cohorts suggest that treatment to A1C targets below 7% in the years soon after the diagnosis of diabetes is associated with long-term reduction in risk of macrovascular disease**. Until more evidence becomes available, the general goal of <7% appears reasonable for many adults for macrovascular risk reduction (B).

Manejo de la hiperglicemia: <7%?

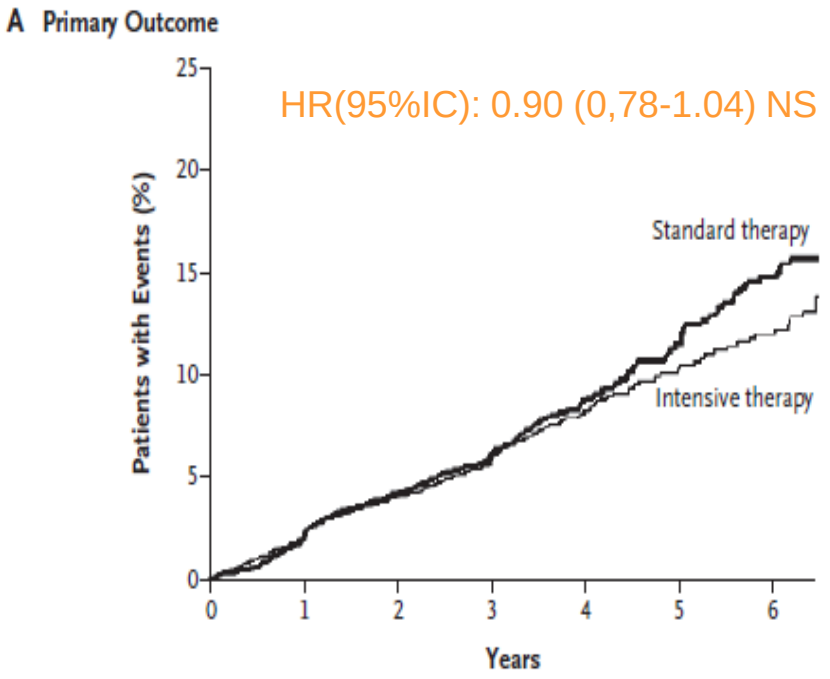
- ACCORD: n=10.251. 3,5 años de seguimiento.

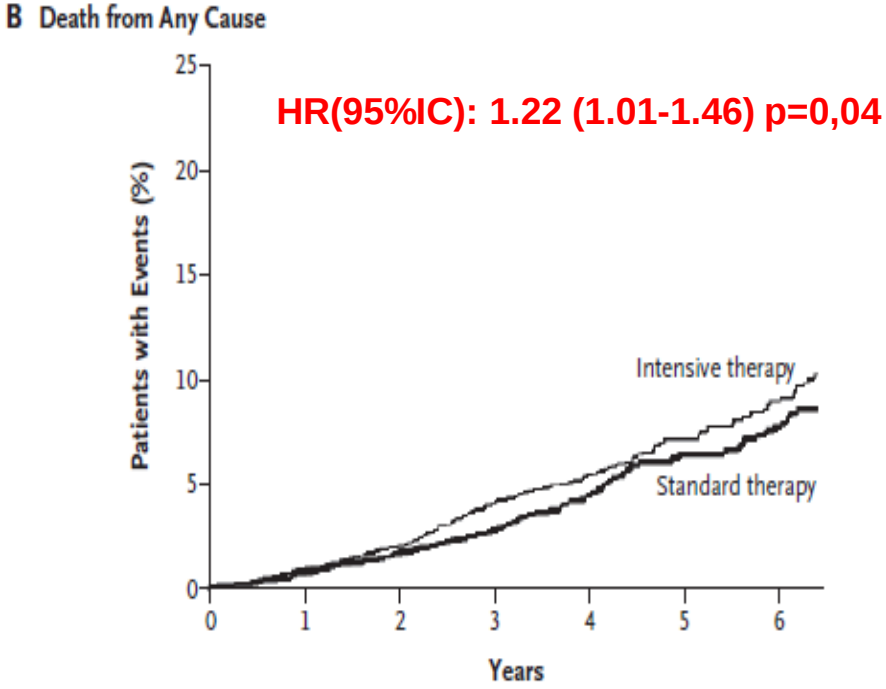
Variable	Intensive (5128)	Standard (5123)
Age (yr)	62.2 6.8	62.2 6.8
Median duration of diabetes (yr)	10	10
Previous cardiovascular event (%)	35.6	34.8
HbA1c (%)	8,3 1.1	8,3 1.1
Fasting Plasmatic glucose	174.9 56.0	175.7 56.5



Manejo de la hiperglicemia: <7%?

- ACCORD:

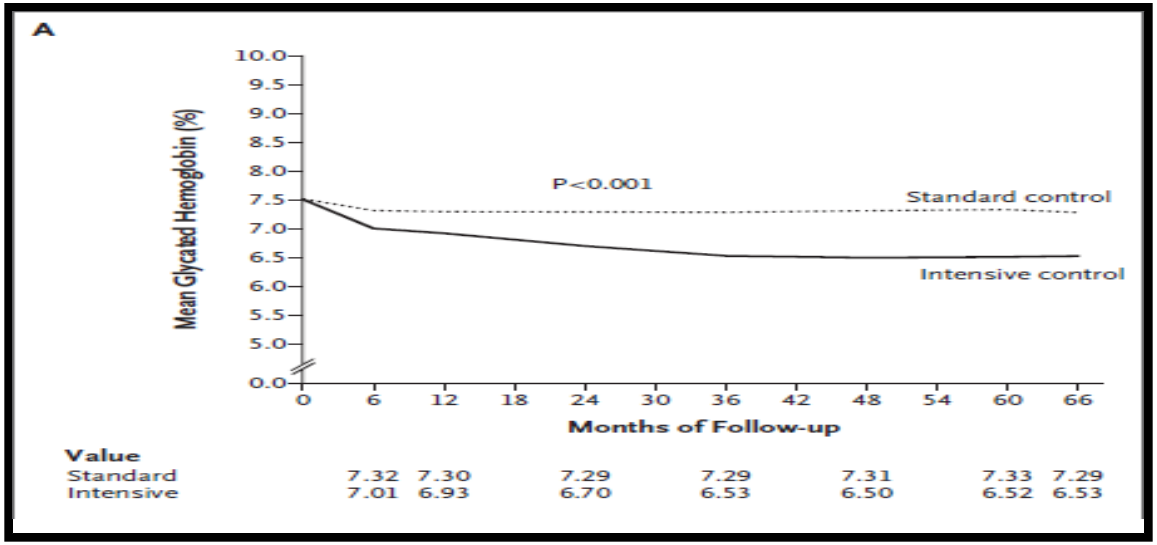




Manejo de la hiperglicemia: <7%?

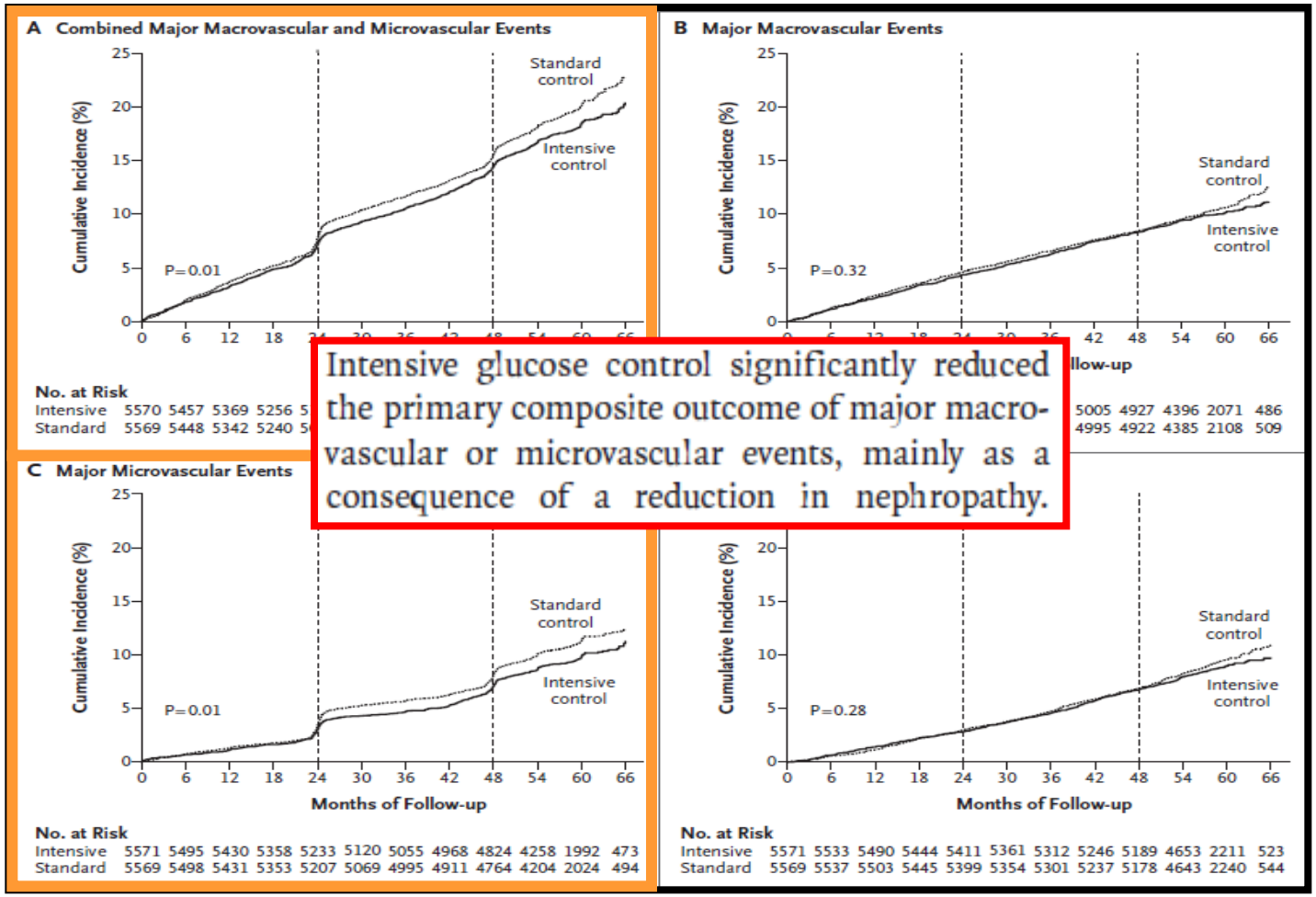
- ADVANCE:

Variable	Intensive (5571)	Standard (5569)
Age (yr)	66 6	66 6
Median duration of diabetes (yr)	7.9 6.3	8.0 6.4
Previous cardiovascular event (%)	32.2	32.3
HbA1c (%)	7.48 1.65	7.48 1.63
Fasting Plasmatic glucose	153.2 50.0	152.6 49.7



Manejo de la hiperglicemia: <7%?

- ADVANCE:

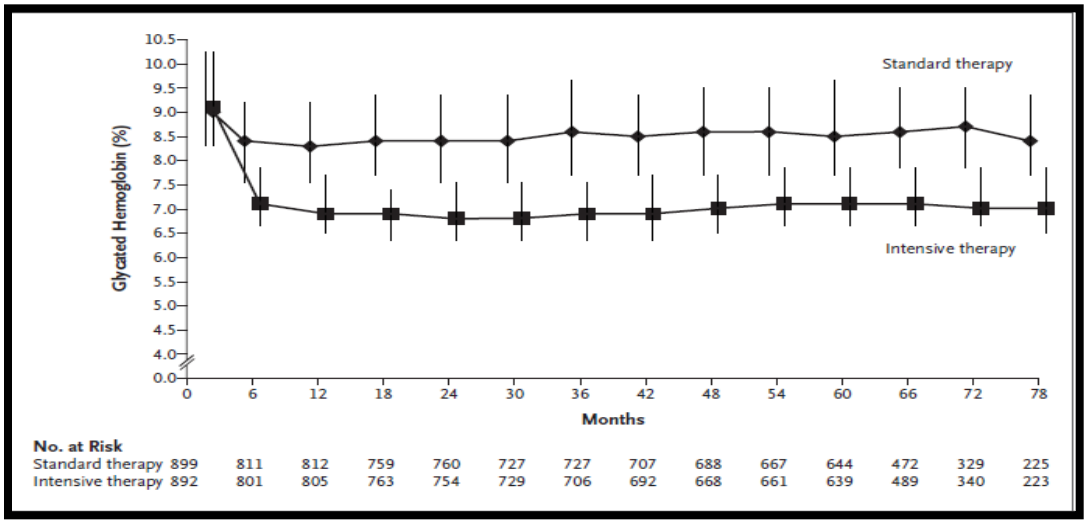


Intensive glucose control significantly reduced the primary composite outcome of major macrovascular or microvascular events, mainly as a consequence of a reduction in nephropathy.

Manejo de la hiperglicemia: <7%?

- VADT: n=1791, 5,6 años de seguimiento.

Variable	Intensive (5128)	Standard (5123)
Age (yr)	60.5 9.0	60.3 9.0
Median duration of diabetes (yr)	11.5 8.0	11.5 7.0
Previous cardiovascular event (%)	39.8%	40.9%
HbA1c (%)	9.4 2.0	9.4 2.0



Manejo de la hiperglicemia: <7%?

- VADT:

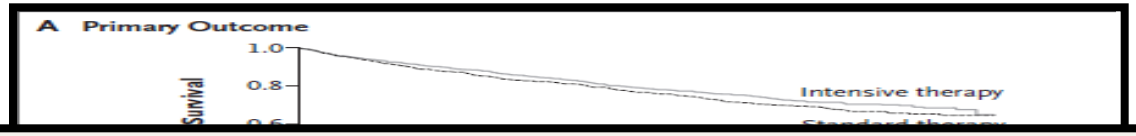


Table 3. Microvascular Outcomes.*

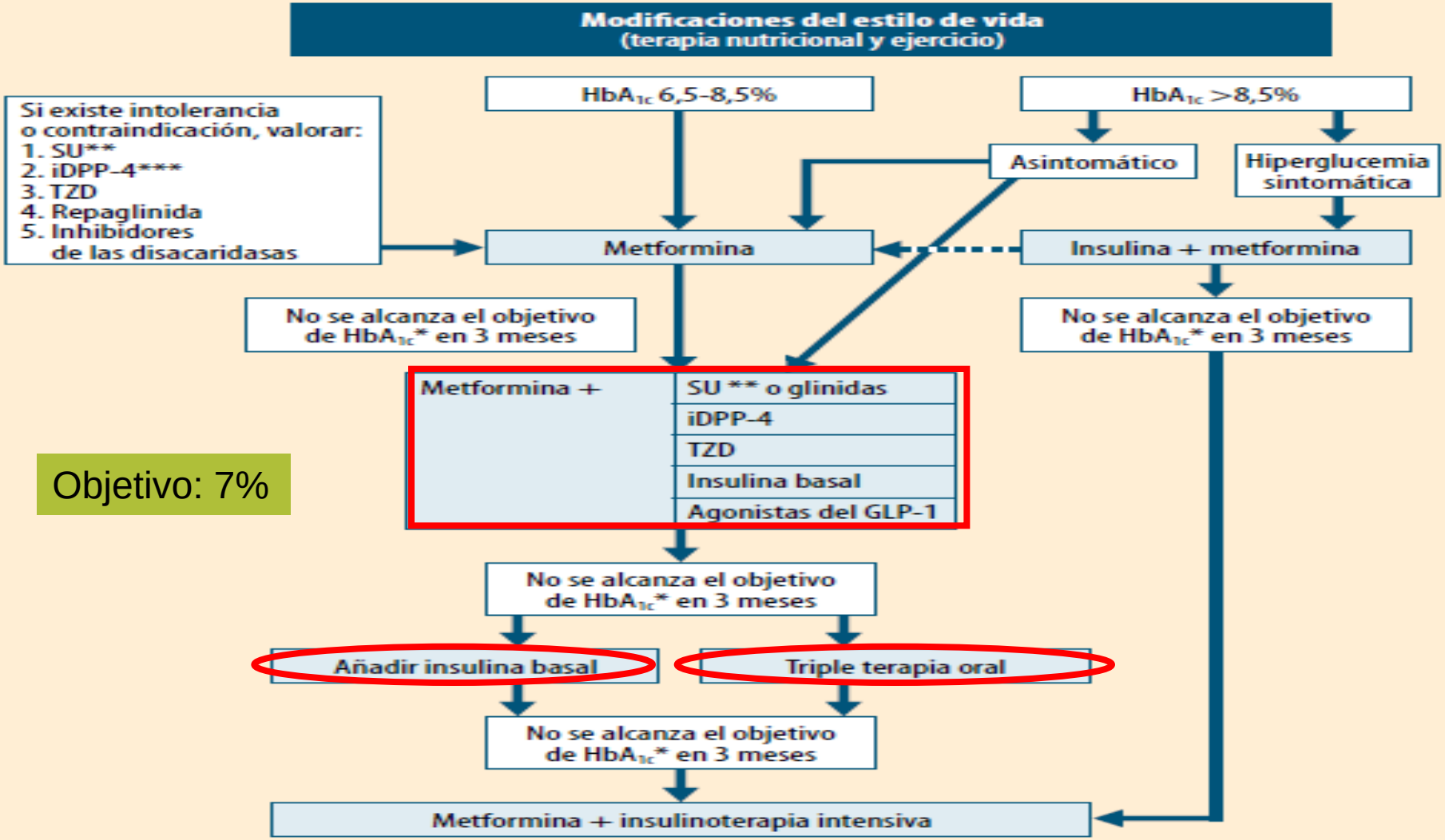
Outcome	Standard Therapy (N=899)	Intensive Therapy (N=892)	P Value†
	no./total no. (%)		
Ophthalmologic disorder			
Cataract surgery			
Any	139/772 (18.0)	144/769 (18.7)	0.71
New	73/719 (10.2)	83/718 (11.6)	0.39
Photocoagulation			
Any	121/772 (15.7)	119/769 (15.5)	0.91
New	66/746 (8.8)	50/719 (7.0)	0.18
Vitrectomy			
Any	34/772 (4.4)	36/769 (4.7)	0.79
New	24/804 (3.0)	26/785 (3.3)	0.71
Retinopathy‡			
Progression to proliferative disease	16/399 (4.0)	23/406 (5.7)	0.27
Progression to clinically significant macular edema	17/361 (4.7)	12/371 (3.2)	0.31
Increase of 2 steps in severity of disease	88/399 (22.1)	69/406 (17.0)	0.07
New onset	66/135 (48.9)	54/128 (42.2)	0.27
Nephropathy			
Serum creatinine			
Doubling of level	78/884 (8.8)	78/882 (8.8)	0.99
>3 mg/dl (265 μmol/liter)	16/884 (1.8)	18/882 (2.0)	0.72
Glomerular filtration rate <15 ml/min	11/884 (1.2)	7/882 (0.8)	0.35
Change in albumin level			
From normal to microalbuminuria	61/463 (13.2)	43/442 (9.7)	0.12
From normal to macroalbuminuria	7/463 (1.5)	1/442 (0.2)	0.07
From microalbuminuria to macroalbuminuria	29/240 (12.1)	19/251 (7.6)	0.10
From normal to microalbuminuria or macroalbuminuria	68/463 (14.7)	44/442 (10.0)	0.03
From normal to microalbuminuria to macroalbuminuria	36/703 (5.1)	20/693 (2.9)	0.04
Any increase in albuminuria	97/703 (13.8)	63/693 (9.1)	0.01
New neuropathy			
Any	218/498 (43.8)	202/464 (43.5)	0.94
Mononeuropathy	20/498 (4.0)	22/464 (4.7)	0.58
Peripheral	199/498 (40.0)	178/464 (38.4)	0.61
Autonomic	26/498 (5.2)	38/464 (8.2)	0.07

Manejo hiperglicemia: ADA guidelines

•Subgroup analysis of clinical trials such as the DCCT and UKPS and evidence for reduced proteinuria in the ADVANCE trial suggest **small but incremental benefit in microvascular outcomes with A1C values closer to normal**. Therefore, **for selected individual** patients, providers might reasonably suggest even **lower A1C goals** than the general goal of <7%, if this can be achieved without significant hypoglycemia or other adverse effects of treatment. Such patients might include **those with short duration of diabetes, long life expectancy, and no significant CVD**.

•Conversely, **less stringent A1C goals than the general goal of <7% may be appropiate for patients with a history of severe hypoglycemia, limited life expectancy, advanced microvascular or macrovascular complications, or extensive comorbid conditions and those with longstanding diabetes** in whom the general goal is difficult to attain despite self-management education, appropiate glucose monitoring and effective doses of multiple glucose lowering agents including insulin.

Manejo hiperglicemia: PILAR



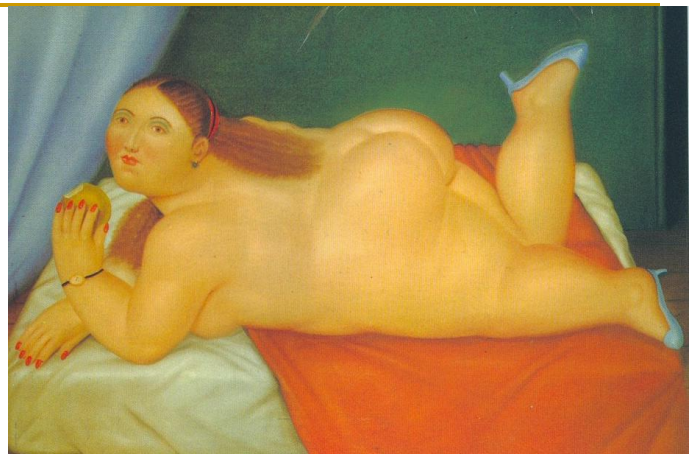
Objetivo: 7%

Tabla 1. Características principales de los antidiabéticos orales

	Riesgo de hipoglucemia	Ventajas	Desventajas	Contraindicaciones
Metformina	No	• Sin aumento de peso • Mejora el perfil lipídico y otros marcadores de riesgo cardiovascular • Disminución de la mortalidad y de las complicaciones macrovasculares en pacientes obesos (UKPDS)	• Efectos adversos digestivos (titular dosis) • Acidosis láctica (muy rara) • Interfiere en la absorción de vitamina B_{12}	• FG <60 mL/min • Insuficiencia cardiaca severa • Insuficiencia hepática • Insuficiencia respiratoria • Alcoholismo • Empleo de contrastes yodados
Sulfonilureas	• Glibenclamida (significativo) • Gliclacida (moderado/mínimo) • Glimepirida (moderado)	• Disminución de las complicaciones microvasculares (UKPDS/ADVANCE)	• Aumento de peso • Duración de la eficacia hipoglucemiante inferior a la de metformina y glitazonas	• Insuficiencia renal grave (FG <30 mL/min) • Insuficiencia hepática grave • Alergia a sulfamidas
Glinidas	• Repaglinida (moderado) • Nateglinida (mínimo)	• No contraindicadas en la insuficiencia renal leve-moderada • Reduce la glucemia posprandial	• Aumento de peso • No asociar repaglinida con gemfibrozilo	• Insuficiencia hepática grave
Tiazolidindionas o glitazonas	No	• No contraindicadas en la insuficiencia renal moderada • Pioglitazona mejora el perfil lipídico y otros marcadores de riesgo cardiovascular • Control glucémico más duradero (frente a metformina o sulfonilureas)	• Aumento de peso • Edemas • Incremento de la incidencia de insuficiencia cardiaca • Aumento de fracturas de extremidades en mujeres • Se necesitan 6-12 semanas para valorar el máximo efecto	• Insuficiencia cardiaca • Insuficiencia hepática • Rosiglitazona: – Cardiopatía isquémica – Enfermedad vascular periférica – Combinada con insulina
Inhibidores de las alfa-glucosidasas	No	• Sin aumento de peso • Reducen la glucemia posprandial • Disminución de la mortalidad y de las complicaciones cardiovasculares	• Efectos adversos GI • Baja eficacia si dieta pobre en HC • La hipoglucemia debe tratarse con glucosa pura	• Miglitol – FG <60 mL/min • Acarbosa – FG <30 mL/min • Insuficiencia hepática grave • Enfermedad intestinal crónica
Inhibidores de la DPP-4	No	• Sin aumento de peso • Reducen sobre todo la glucemia posprandial	• Se han notificado casos de pancreatitis aguda • Beneficios y seguridad a largo plazo desconocidos • Vildagliptina: no indicada con insulina, monoterapia ni triple terapia	• FG <50 mL/min • Vildagliptina: – Insuficiencia hepática o ALT o AST >3 × LSN
Agonistas del GLP-1	No	• Disminución de peso • Disminución de la PA • Mejora de los lípidos • Reducen sobre todo la glucemia posprandial	• Administración subcutánea • Efectos adversos digestivos (náuseas, vómitos, diarrea) • Se han notificado casos de pancreatitis aguda • Beneficios y seguridad a largo plazo desconocidos • No indicados con insulina, ni en monoterapia ni en triple terapia	• FG <30 mL/min • Enfermedad gastrointestinal grave

FG: filtrado glomerular; GI: gastrointestinales; HC: hidratos de carbono.

Manejo hiperglicemia



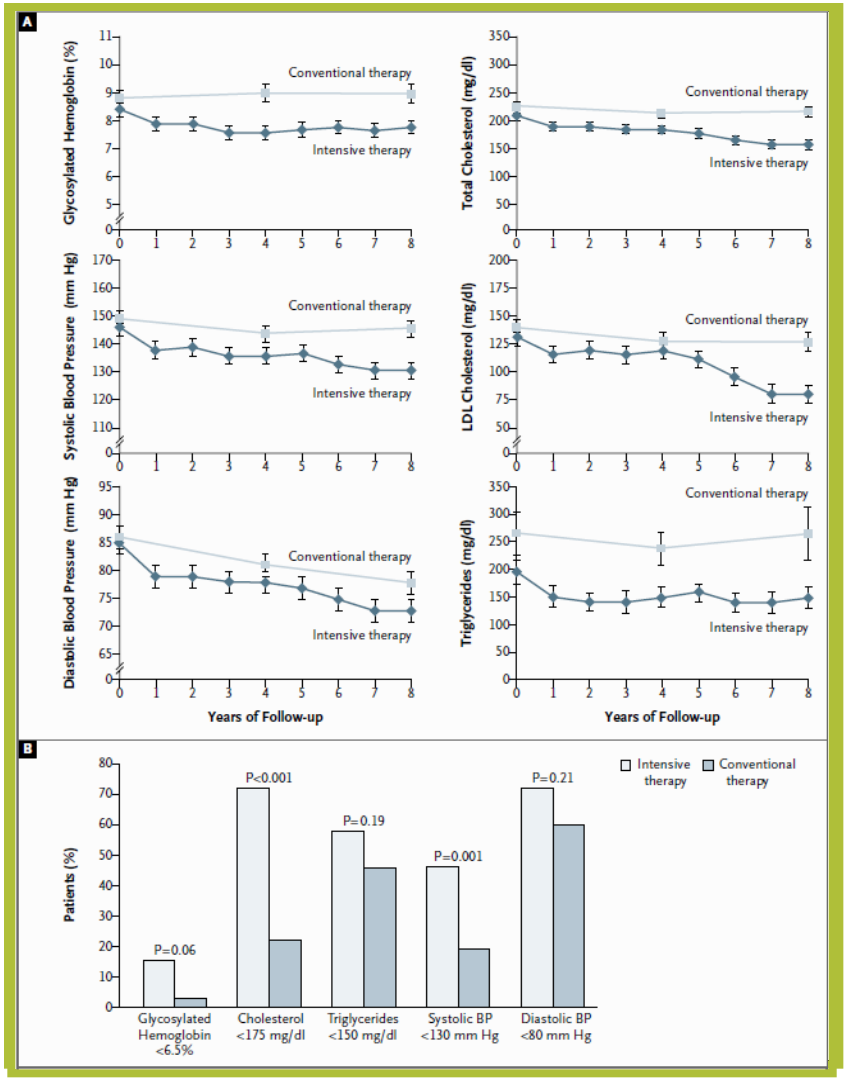
- Función hepática/renal normal.
- **IMC 28.**
- HbA1C **8,1%** asintomática
- **Basales bastante correctas** (120 mg/dl en analítica) (probables picos post-prandiales)
- Poco receptiva a tratamiento con insulina

Inicio de combinación de Metformina (1000 mg)/Sitagliptina (50 mg) (1 comp/12h) manteniendo Glicazida (120 mg/dia). Educación y visitas con enfermeria para reforzar adherencia a dieta y estimular cambios de estilo de vida

Manejo factores de riesgo cardiovasculares: Steno-2

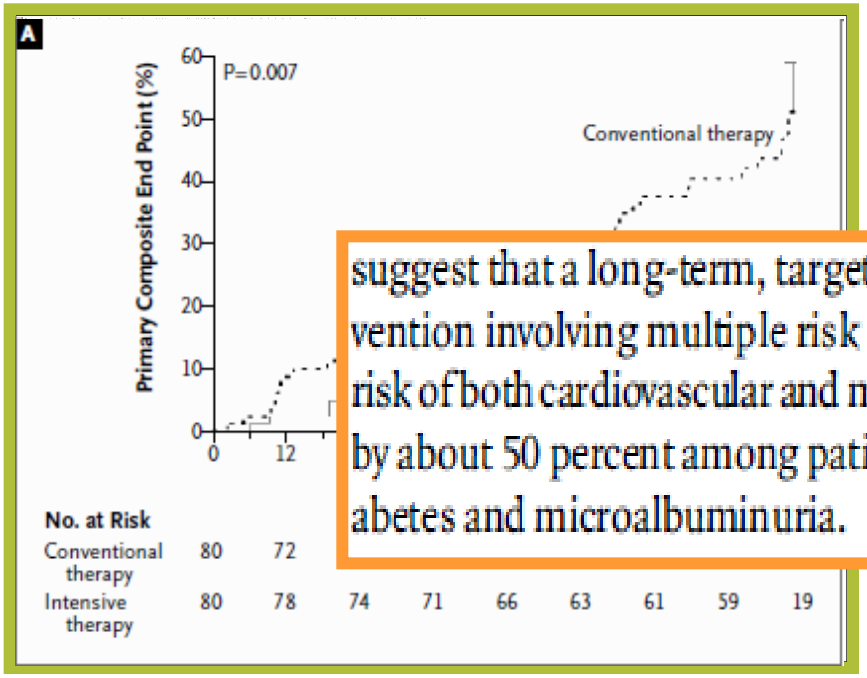
Table 1. Treatment Goals for the Conventional-Therapy Group and the Intensive-Therapy Group.*

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



Gaede P., Vedel P., Larsen N., et al. *Multifactorial Intervention and cardiovascular disease in patients with type 2 diabetes*. NEJM. 2003; 348(5):383-93

Manejo factores de riesgo cardiovasculares: Steno-2



suggest that a long-term, targeted, intensive intervention involving multiple risk factors reduces the risk of both cardiovascular and microvascular events by about 50 percent among patients with type 2 diabetes and microalbuminuria.

HR: 0,47 (0,24-0,73)

Gaede P., Vedel P., Larsen N., et al. *Multifactorial Intervention and cardiovascular disease in patients with type 2 diabetes*. NEJM. 2003; 348(5):383-93

Manejo factores de riesgo cardiovasculares: ADA guidelines

HTA mal controlada + Microalbuminuria

Patients with diabetes should be treated to systolic blood pressure <130 mmHg (C).

Patients with diabetes should be treated to diastolic blood pressure <80 mmHg (C).

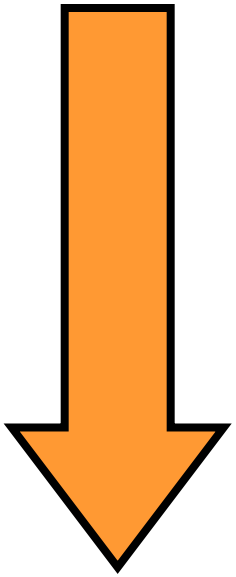
Pharmacologic therapy for patients with diabetes and hypertension should be with a regimen that includes either ACE inhibitor or ARB.

If needed to achieve blood pressure targets, a thiazide diuretic should be added to those with GFR>30 ml/min, and loop diuretic for those with <30 ml/min,

Incrementar dosis de enalapril a 10 mg/12h. Monitorización TA, función renal, kaliemia y excreción urinaria de albumina. Si persiste TA>130/80. Cambiar a combinación Enalapril/HTZ.

Manejo factores de riesgo cardiovasculares: ADA guidelines

LDL 137/HDL50/TAG 180



•In individuals without overt CVD, the primary goal is an LDL cholesterol <100 mg/dl. (A).

•Statin therapy should be added to life-style therapy, regardless of baseline lipid levels, for diabetic patients:

•-with overt CVD (A)

•-without CVD who are over the age of 40 years and have one or more other CVD risk.

Inicio de estatina (p.ej Atorvastatina 20 mg/dia).

Manejo factores de riesgo cardiovasculares: ADA guidelines

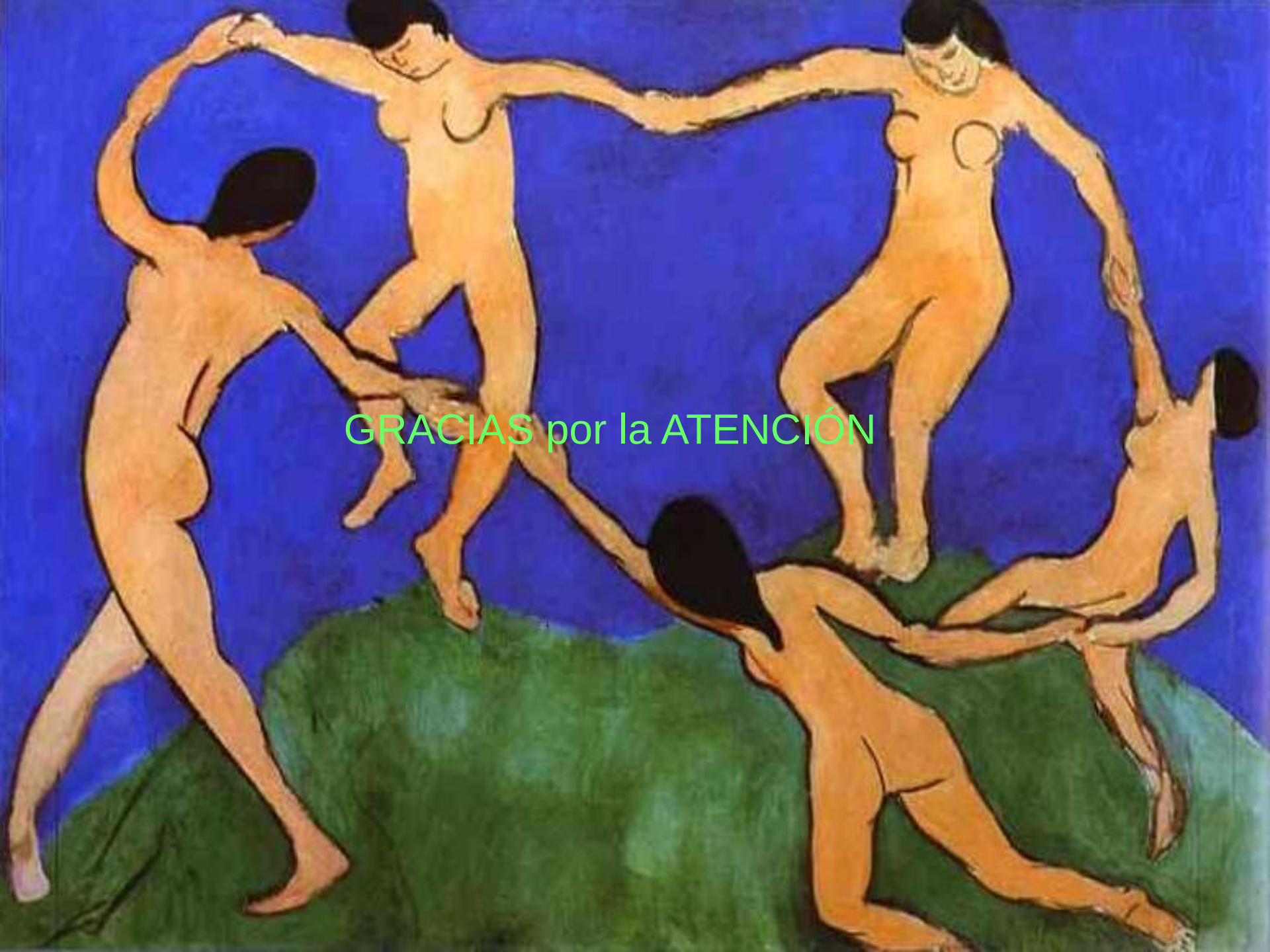
>60 años, DM, HTA y dislipémica

Consider aspirin therapy (75-162mg/day) as a prymary prevention strategy in those with type 1 or type 2 diabetes at increased cardiovascular risk (10 years risk >10%). This includes most men >50 years of age or women >60 years of age who have at least one additional major risk factor (family history of CVD, hypertension, smoking, dyslipidemia, or albuminuria) (C).

Se inician 100 mg/dia de AAS con protección gástrica

Evolución

- A los 3 meses:
  - HbA1c 7,1%
  - LDL 95/HDL 45
  - TAG 125 mg/dl
  - Pérdida de 4 Kg (5,9% peso corporal).
  - TA 125/76.


GRACIAS por la ATENCIÓN