I Escuela de Residentes de la SADEMI

16-17 de Octubre de 2015

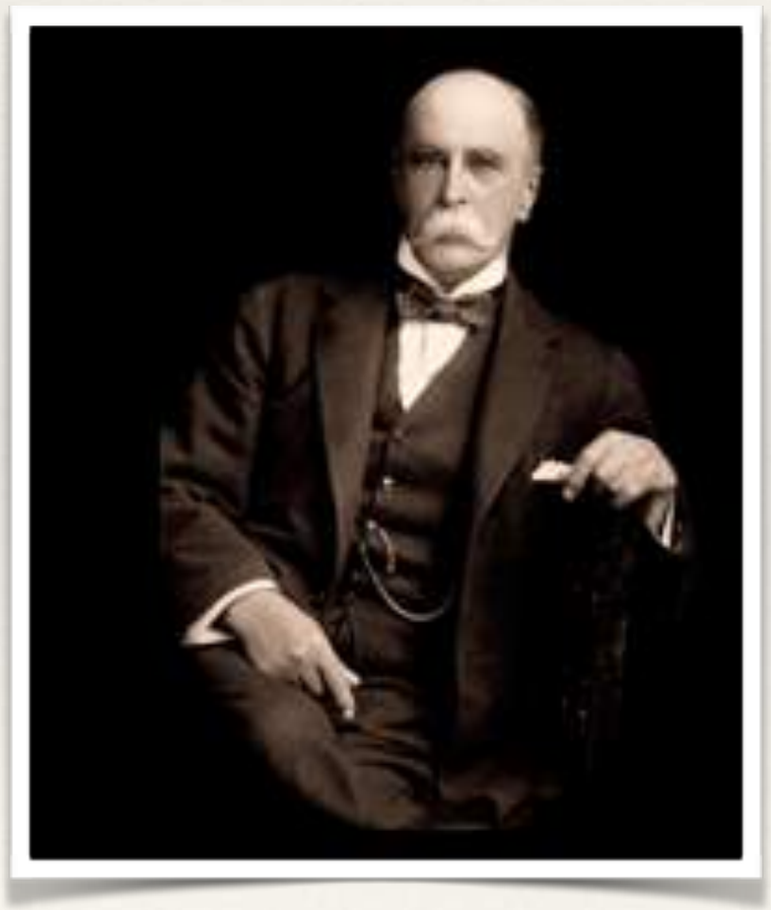
I Escuela de Residentes de Medicina Interna

Diabetes Mellitus:

Poniendo Orden en el Tratamiento

Dr. Javier Carrasco
Medicina Interna
Complejo Hospitalario
Universitario de Huelva

“The good physician treats the disease; the great physician treats the patients who has the disease”

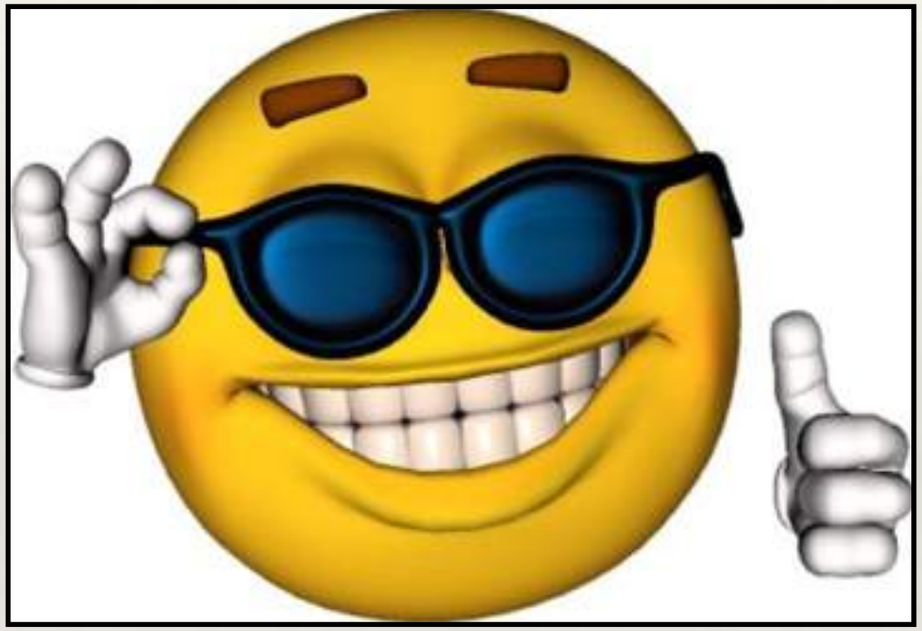


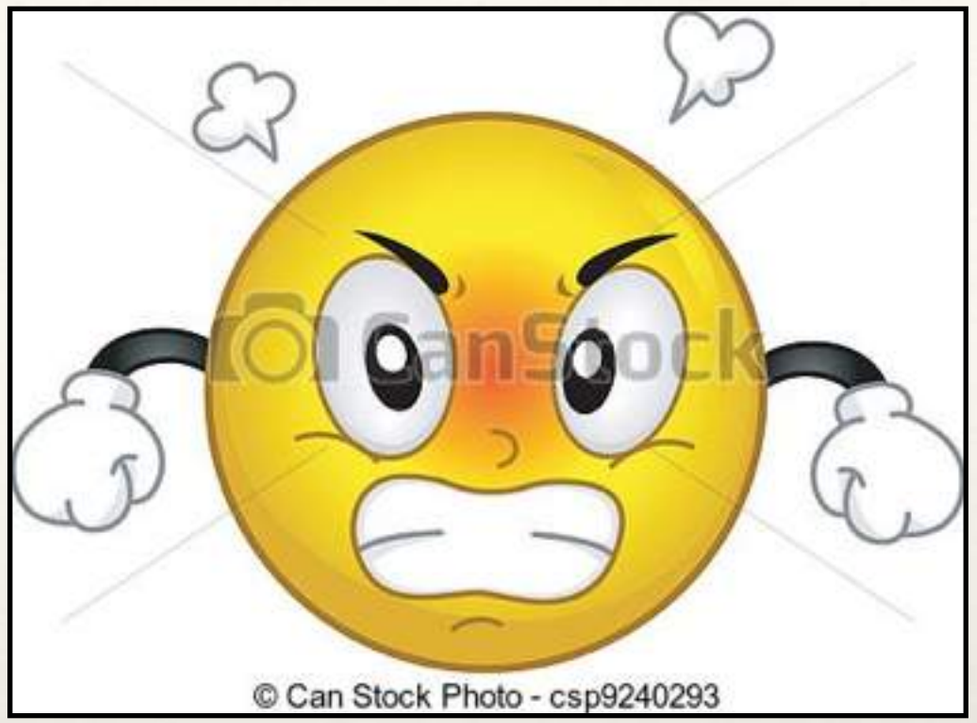
– William Osler


KEEP
CALM
AND
ACCEPT
THE CHALLENGE

Qué quiere realmente saber un MIR-MI sobre el tratamiento de la Diabetes

Tres Posibilidades

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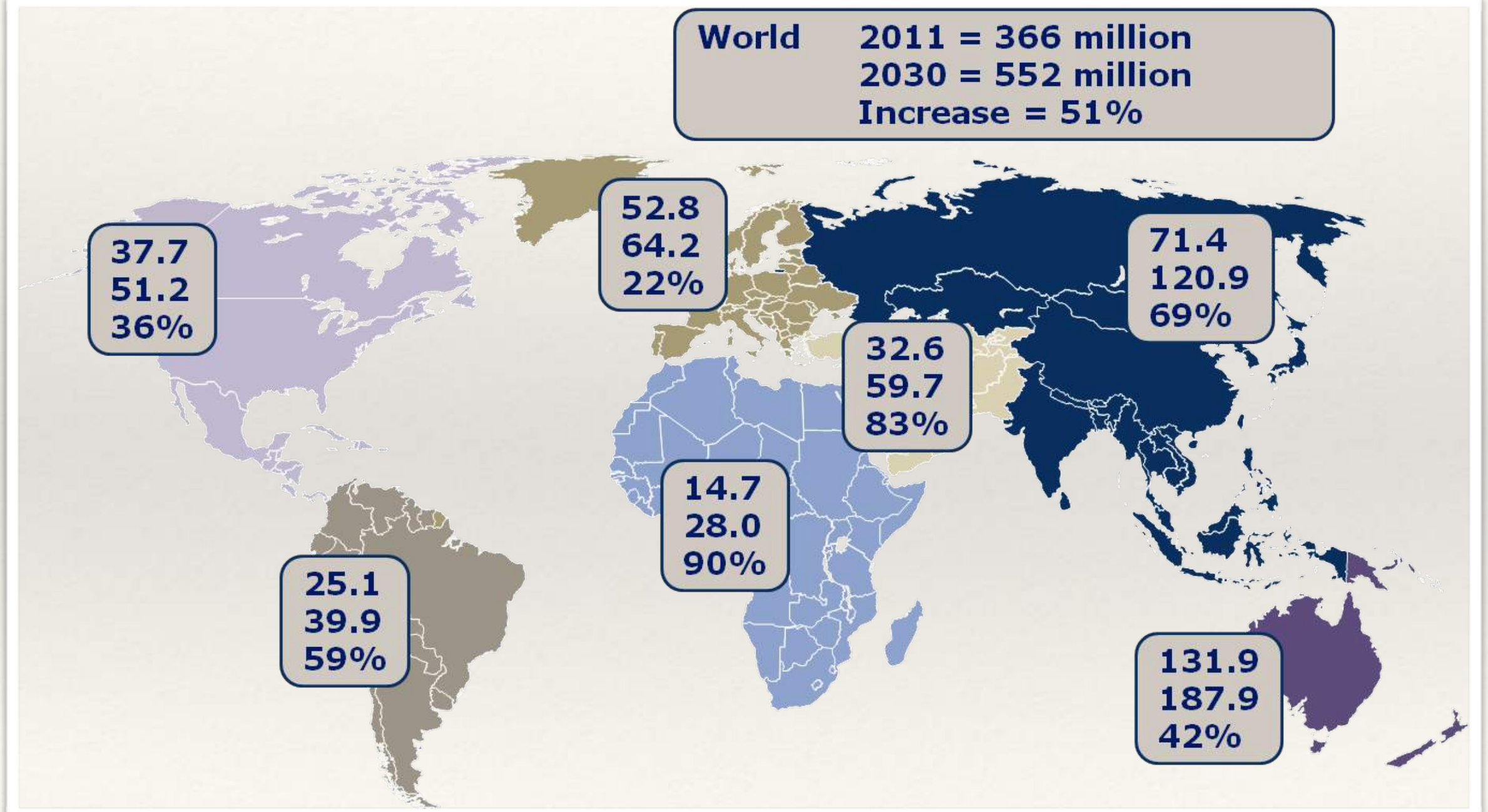
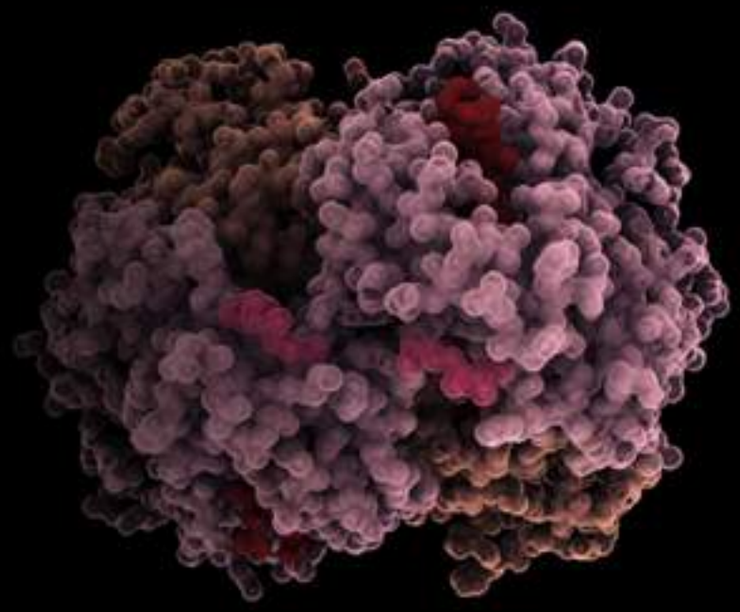
¿Por Qué ?


World 2011 = 366 million
2030 = 552 million
Increase = 51%
37.7
51.2
36%
52.8
64.2
22%
71.4
120.9
69%
32.6
59.7
83%
14.7
28.0
90%
25.1
39.9
59%
131.9
187.9
42%

¿Por Qué es Difícil el Tratamiento de la Diabetes?


Download from

Hemoglobin A1c (HbA1c)



Know Your A1c!

The blood test with a memory

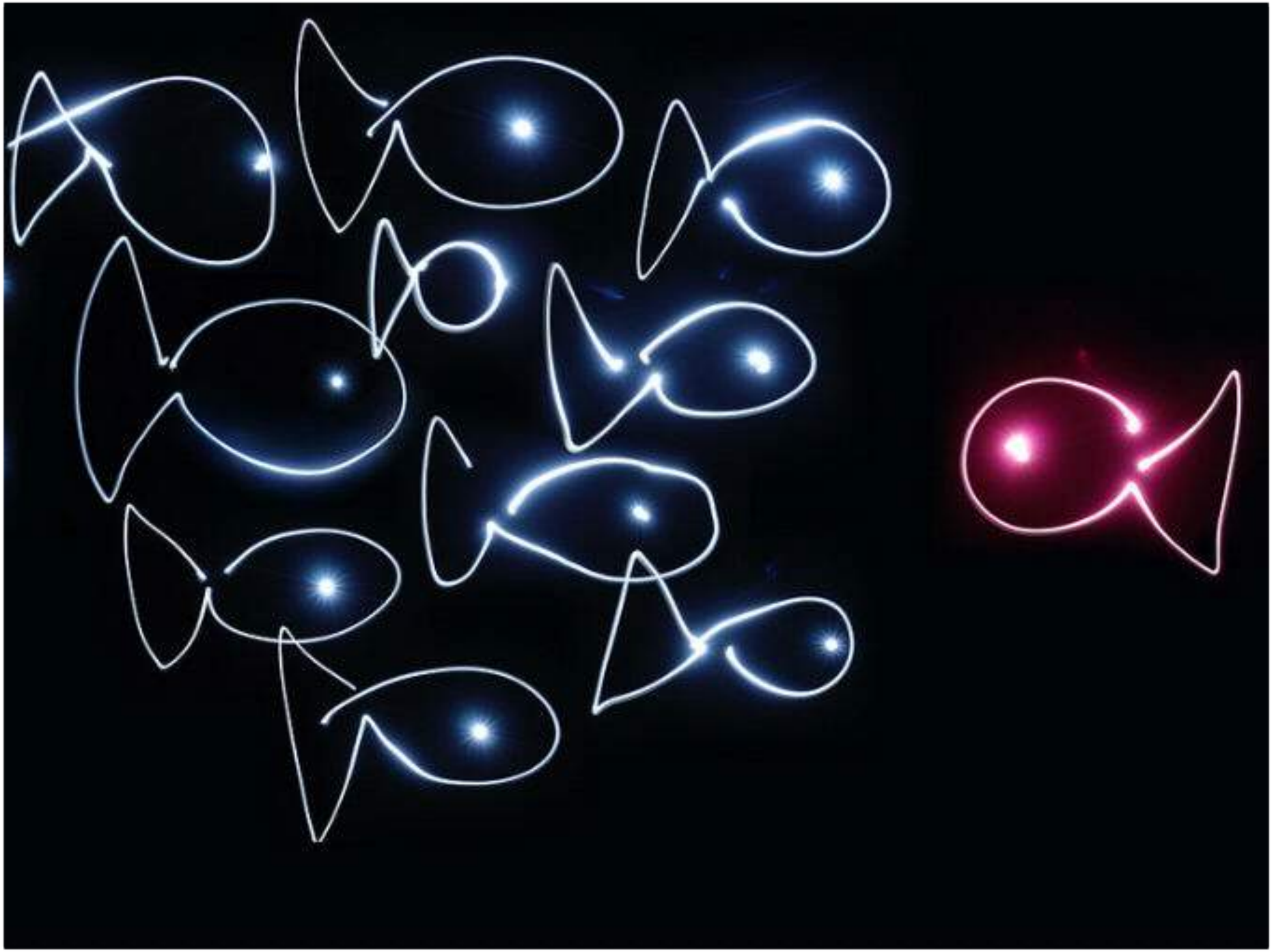
poor control — more than 8

be careful — more than 7

good control — less than 7

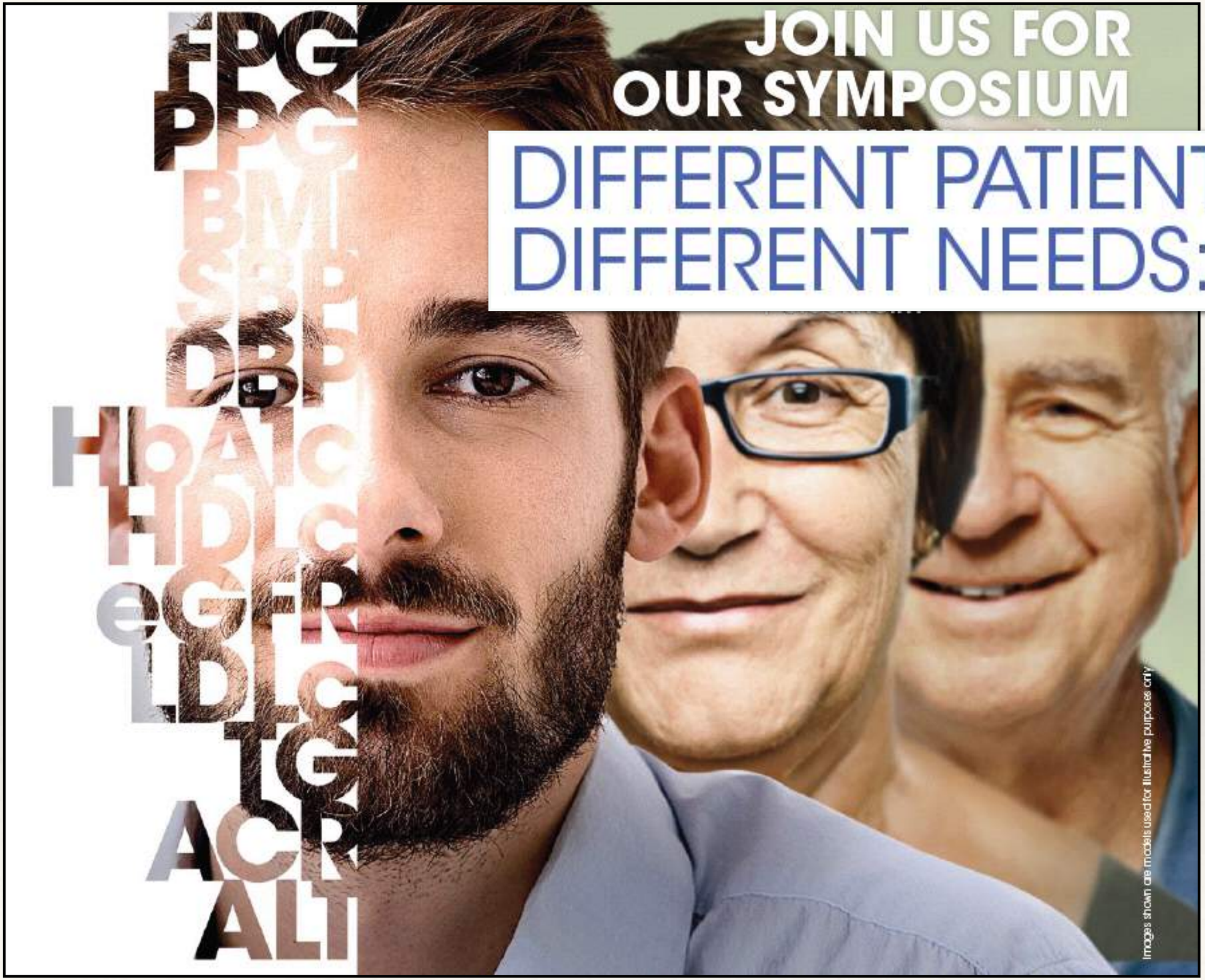

4:17
1-10
211
mg/dL
ONETOUCH
UltraEasy


12:14PM
95
8-25
mg/dL
M



¿Como Trato a mis Pacientes?


metformina cinfa 850 mg
comprimidos EFG
forxiga
dapagliflozin
10mg
Minodiab® 5 mg
glipizida
Comprimidos
5 mg
glipizida
Pharmacia &Upjohn
actos
pioglitazona
15
Amaryl
Glimepirida
1mg
Glucobay® 100
DIAMICRON MR
AVANDIA
4 mg
competact
competact
Euglucon®
Glibenclamida
5 mg
30 Tabletas
Roche
MEDICAMENTO ESENCIAL
Lyxumia 10
Lyxumia 20
SANOFI
VICTOZA
LIRAGLUTIDA
Victoza®
Liraglutida
Humalog Pen
Humalog Mix50 Pen
Humalog Mix25 Pen
Humalog NPL Pen
Apidra SoloSTAR
NovoRapid® FlexPen®
NovoMix® 30
Levemir® FlexPen®
LANTUS SoloSTAR


JOIN US FOR
OUR SYMPOSIUM
DIFFERENT PATIENTS
DIFFERENT NEEDS:
FPG
PPG
BMI
SBP
DBP
HbA1c
HDL
eGFR
LDL
TG
ACR
ALT
Images shown are models used for illustrative purposes only


ALZHEIMER









6. Glycemic Targets

Diabetes Care 2015;38(Suppl. 1):S33–S40 | DOI: 10.2337/dc15-S009

American Diabetes Association®

Table 6.2—Summary of glycemic recommendations for nonpregnant adults with diabetes

A1C	<7.0%*
Preprandial capillary plasma glucose	80–130 mg/dL* (4.4–7.2 mmol/L)
Peak postprandial capillary plasma glucose†	<180 mg/dL* (<10.0 mmol/L)

*More or less stringent glycemic goals may be appropriate for individual patients. Goals should be individualized based on duration of diabetes, age/life expectancy, comorbid conditions, known CVD or advanced microvascular complications, hypoglycemia unawareness, and individual patient considerations.

†Postprandial glucose may be targeted if A1C goals are not met despite reaching preprandial glucose goals. Postprandial glucose measurements should be made 1–2 h after the beginning of the meal, generally peak levels in patients with diabetes.

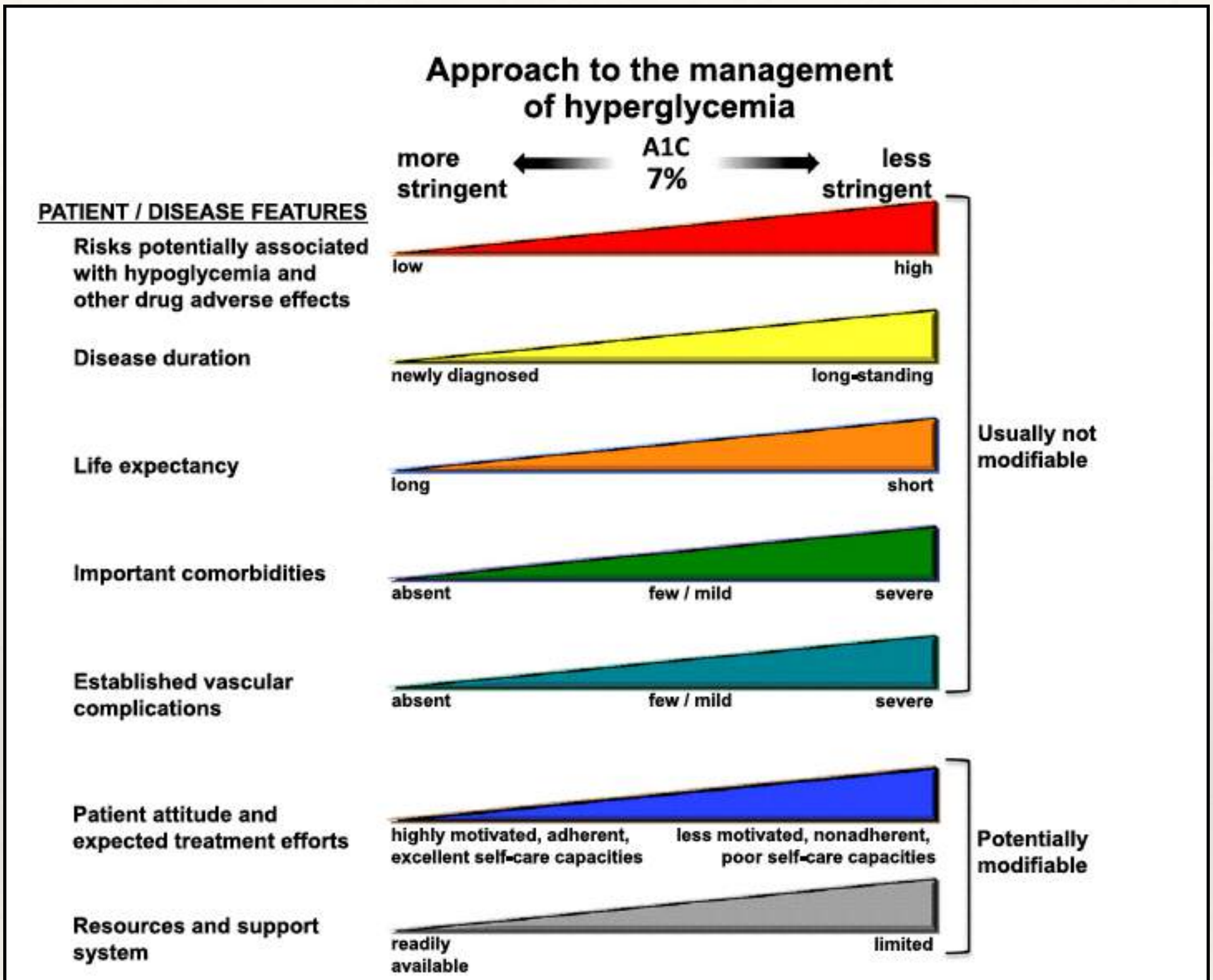


Figure 6.1—Depicted are patient and disease factors used to determine optimal A1C targets. Characteristics and predicaments toward the left justify more stringent efforts to lower A1C; those toward the right suggest less stringent efforts. Adapted with permission from Inzucchi et al. (45).

Diabetes Care 2015;38(Suppl. 1):S33–S40 | DOI: 10.2337/dc15-S009

AACE/ACE COMPREHENSIVE DIABETES MANAGEMENT ALGORITHM

2015

TASK FORCE

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Joshua I. Barzilay, MD, FACE
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Zachary T. Bloomgarden, MD, MACE
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Guillermo Umpierrez, MD, FACP, FACE
Michael H. Davidson, MD, *Advisor*

GOALS FOR GLYCEMIC CONTROL

INDIVIDUALIZE GOALS

A1c ≤ 6.5%

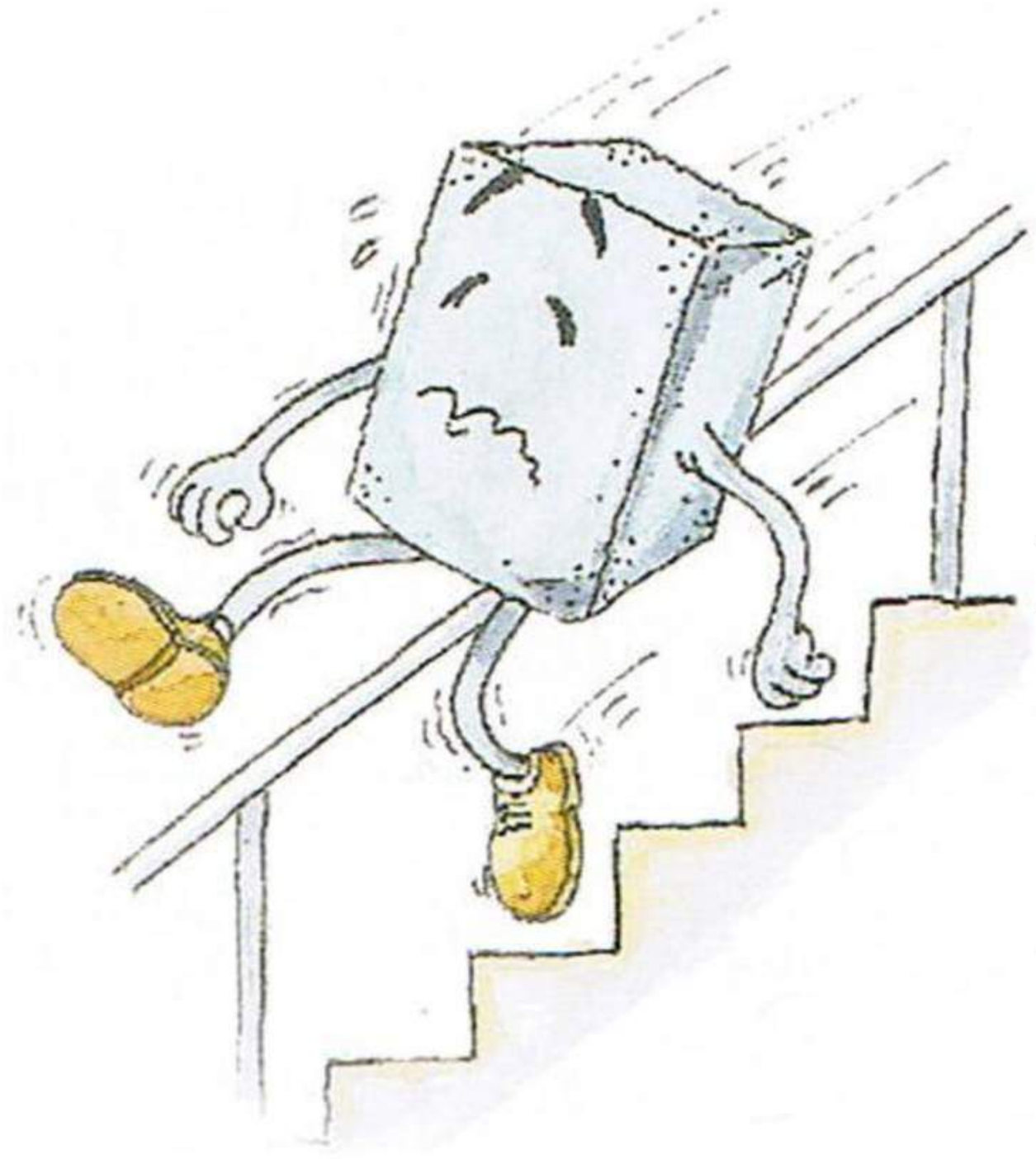
For patients without concurrent serious illness and at low hypoglycemic risk

A1c > 6.5%

For patients with concurrent serious illness and at risk for hypoglycemia

¿Cuales son mis Objetivos?

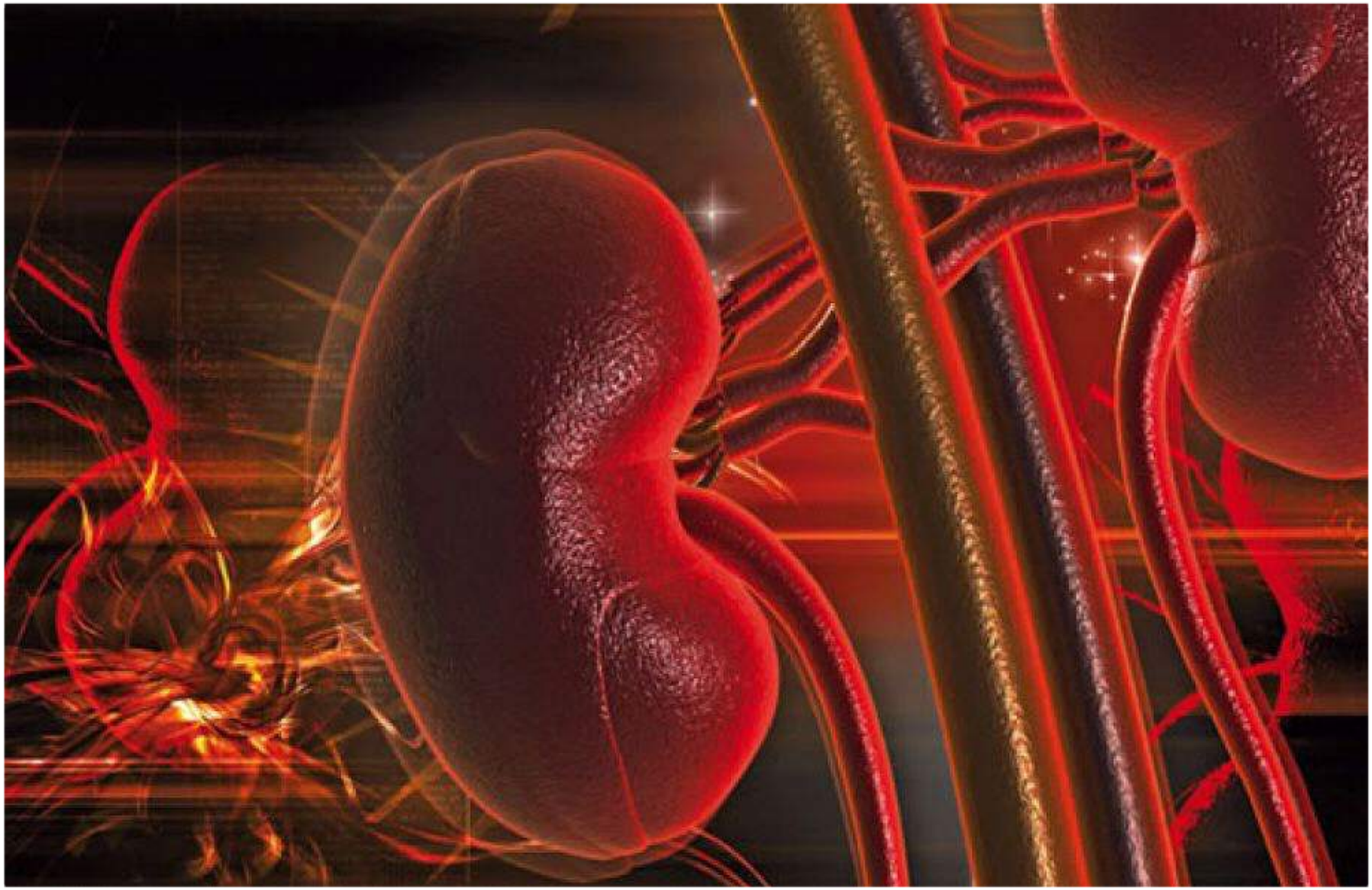
Hb A1c

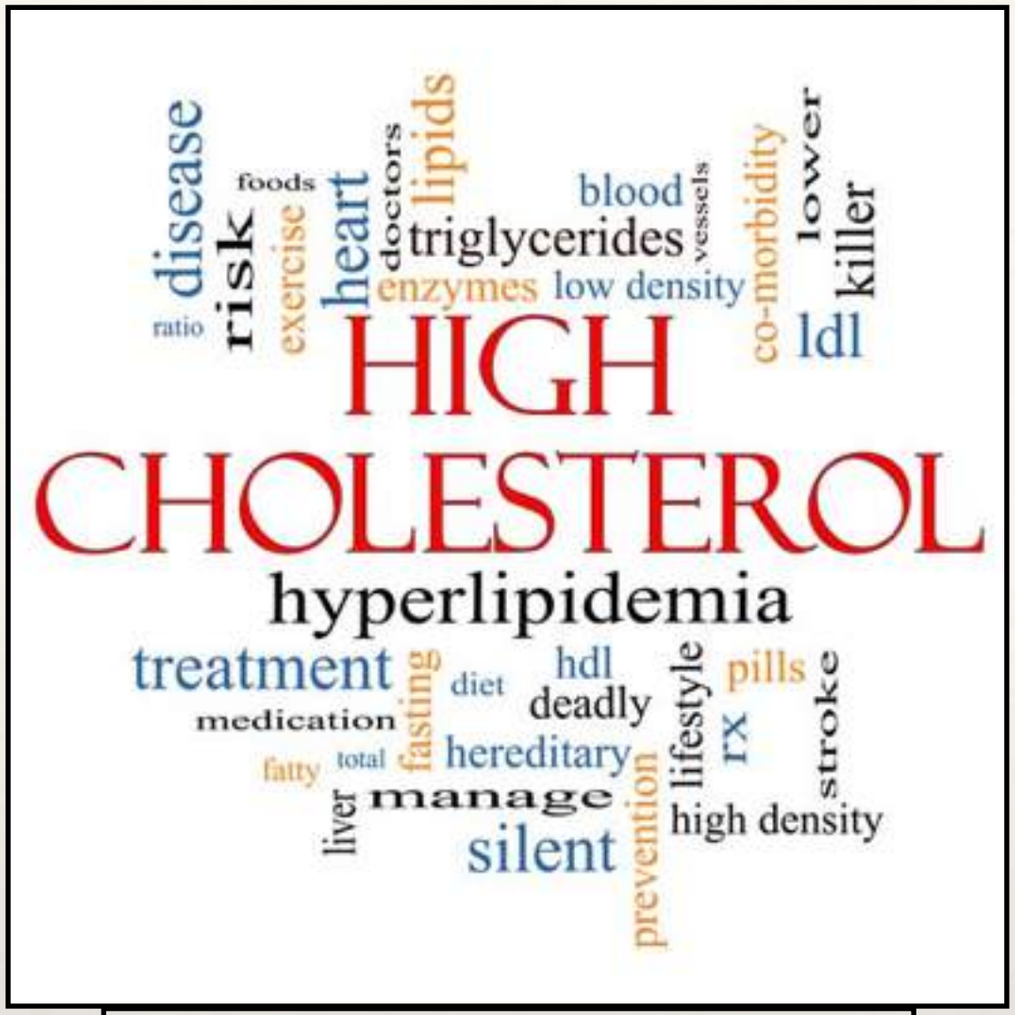


DIABETES E HIPOGLUCEMIA

Side Effects

Riesgo Cardiovascular




disease
risk
foods
exercise
heart
doctors
lipids
blood
vessels
triglycerides
enzymes
low density
co-morbidity
lower
killer
ratio
ldl
HIGH
CHOLESTEROL
hyperlipidemia
treatment
diet
hdl
deadly
pills
medication
fasting
lifestyle
rx
stroke
fatty
total
hereditary
liver
manage
prevention
high density
silent


Heart
Disease


Día Mundial de la
EPOC
Enfermedad Pulmonar Obstructiva Crónica


ALZHEIMER


Hipertensión

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Glucose Levels and Risk of Dementia

Paul K. Crane, M.D., M.P.H., Rod Walker, M.S., Rebecca A. Hubbard, Ph.D.,
Ge Li, M.D., Ph.D., David M. Nathan, M.D., Hui Zheng, Ph.D.,
Sebastien Haneuse, Ph.D., Suzanne Craft, Ph.D., Thomas J. Montine, M.D., Ph.D.,
Steven E. Kahn, M.B., Ch.B., Wayne McCormick, M.D., M.P.H.,
Susan M. McCurry, Ph.D., James D. Bowen, M.D., and Eric B. Larson, M.D., M.P.H.

N Engl J Med 2013;369:540-8.
DOI: 10.1056/NEJMoa1215740

CONCLUSIONS

Our results suggest that higher glucose levels may be a risk factor for dementia, even among persons without diabetes. (Funded by the National Institutes of Health.)

Healthy eating, weight control, increased physical activity, and diabetes education

Monotherapy

Metformin

Efficacy*	high
Hypo risk	low risk
Weight	neutral / loss
Side effects	GI / lactic acidosis
Costs*	low

If A1C target not achieved after ~3 months of monotherapy, proceed to 2-drug combination (order not meant to denote any specific preference—choice dependent on a variety of patient- and disease-specific factors):

Dual therapy†

	Metformin + Sulfonylurea	Metformin + Thiazolidinedione	Metformin + DPP-4 inhibitor	Metformin + SGLT2 inhibitor	Metformin + GLP-1 receptor agonist	Metformin + Insulin (basal)
Efficacy*	high	high	intermediate	intermediate	high	highest
Hypo risk	moderate risk	low risk	low risk	low risk	low risk	high risk
Weight	gain	gain	neutral	loss	loss	gain
Side effects	hypoglycemia	edema, HF, fxs	rare	GU, dehydration	GI	hypoglycemia
Costs*	low	low	high	high	high	variable

If A1C target not achieved after ~3 months of dual therapy, proceed to 3-drug combination (order not meant to denote any specific preference—choice dependent on a variety of patient- and disease-specific factors):

Triple therapy

	Metformin + Sulfonylurea +	Metformin + Thiazolidinedione +	Metformin + DPP-4 inhibitor +	Metformin + SGLT2 inhibitor +	Metformin + GLP-1 receptor agonist +	Metformin + Insulin (basal) +
	TZD	SU	SU	SU	SU	TZD
or	DPP-4-i	DPP-4-i	TZD	TZD	TZD	DPP-4-i
or	SGLT2-i	SGLT2-i	SGLT2-i	DPP-4-i	Insulin§	SGLT2-i
or	GLP-1-RA	GLP-1-RA	Insulin§	Insulin§		GLP-1-RA
or	Insulin§	Insulin§				

If A1C target not achieved after ~3 months of triple therapy and patient (1) on oral combination, move to injectables; (2) on GLP-1-RA, add basal insulin; or (3) on optimally titrated basal insulin, add GLP-1-RA or mealtime insulin. In refractory patients consider adding TZD or SGLT2-i:

Combination injectable

Metformin +

Basal insulin + Mealtime insulin or GLP-1-RA

Glycemic Control Algorithm

LIFESTYLE MODIFICATION
(Including Medically Assisted Weight Loss)

Entry A1c < 7.5%

MONOTHERAPY*
- ✓ Metformin
- ✓ GLP-1 RA
- ✓ SGLT-2i
- ✓ DPP-4i
- ✓ AGi
- ⚠ TZD
- ⚠ SU/GLN

If not at goal in 3 months proceed to Double Therapy

Entry A1c ≥ 7.5%

DUAL THERAPY*
MET or other 1st-line agent +
- ✓ GLP-1 RA
- ✓ SGLT-2i
- ✓ DPP-4i
- ⚠ TZD
- ⚠ Basal Insulin
- ✓ Colesevelam
- ✓ Bromocriptine QR
- ✓ AGi
- ⚠ SU/GLN

If not at goal in 3 months proceed to Triple Therapy

TRIPLE THERAPY*
MET or other 1st-line agent + 2nd-line agent +
- ✓ GLP-1 RA
- ✓ SGLT-2i
- ⚠ TZD
- ⚠ Basal insulin
- ✓ DPP-4i
- ✓ Colesevelam
- ✓ Bromocriptine QR
- ✓ AGi
- ⚠ SU/GLN

If not at goal in 3 months proceed to or intensify insulin therapy

Entry A1c > 9.0%

SYMPTOMS

NO	YES
DUAL Therapy OR TRIPLE Therapy	INSULIN ± Other Agents

ADD OR INTENSIFY INSULIN
Refer to Insulin Algorithm

LEGEND
- ✓ Few adverse events or possible benefits
- ⚠ Use with caution

* Order of medications listed represents a suggested hierarchy of usage

PROGRESSION OF DISEASE

Basal insulin

(usually with metformin +/- other noninsulin agent)

- **Start:** 10 U/day *or* 0.1–0.2 U/kg/day
- **Adjust:** 10–15% or 2–4 U once-twice weekly to reach FBG target.
- **For hypo:** Determine and address cause; ↓ dose by 4 U or 10–20%.

If not controlled after FBG target is reached (or if dose >0.5 U/kg/day), treat PPG excursions with mealtime insulin. **(Consider initial GLP-1-RA trial.)**

Add 1 rapid insulin injection before largest meal

- **Start:** 4 U, 0.1 U/kg, or 10% basal dose. If A1C <8%, consider ↓ basal by same amount.
- **Adjust:** ↑ dose by 1–2 U or 10–15% once-twice weekly until SMBG target reached.
- **For hypo:** Determine and address cause; ↓ corresponding dose by 2–4 U or 10–20%.

If not controlled, consider basal-bolus.

Change to premixed insulin twice daily

- **Start:** Divide current basal dose into 2/3 AM, 1/3 PM or 1/2 AM, 1/2 PM.
- **Adjust:** ↑ dose by 1–2 U or 10–15% once-twice weekly until SMBG target reached.
- **For hypo:** Determine and address cause; ↓ corresponding dose by 2–4 U or 10–20%.

If not controlled, consider basal-bolus.

Add ≥2 rapid insulin injections before meals ("basal–bolus")

- **Start:** 4 U, 0.1 U/kg, or 10% basal dose/meal, If A1C <8%, consider ↓ basal by same amount.
- **Adjust:** ↑ dose by 1–2 U or 10–15% once-twice weekly until SMBG target reached.
- **For hypo:** Determine and address cause; ↓ corresponding dose by 2–4 U or 10–20%.

 # Injections: 1 → 2 → 3+

Complexity: low → mod. → high

Flexibility: more flexible → less flexible

ALGORITHM FOR ADDING/INTENSIFYING INSULIN

START BASAL (long-acting insulin)

A1c < 8%

TDD 0.1–0.2 U/kg

A1c > 8%

TDD 0.2–0.3 U/kg

Insulin titration every 2–3 days to reach glycemic goal:

- Fixed regimen: Increase TDD by 2 U
- Adjustable regimen:
  - **FBG** > 180 mg/dL: add 20% of TDD
  - **FBG** 140–180 mg/dL: add 10% of TDD
  - **FBG** 110–139 mg/dL: add 1 Unit
- If hypoglycemia, reduce TDD by:
  - BG < 70 mg/dL: 10% – 20%
  - BG < 40 mg/dL: 20% – 40%

Consider discontinuing or reducing sulfonylurea after basal insulin started (basal analogs preferred to NPH)

****Glycemic Goal:**

- <7% for most patients with T2DM; fasting and premeal BG < 110 mg/dL; absence of hypoglycemia
- A1c and FBG targets may be adjusted based on patient's age, duration of diabetes, presence of comorbidities, diabetic complications, and hypoglycemia risk

Glycemic Control Not at Goal**

INTENSIFY (prandial control)

Add GLP-1 RA

or SGLT-2i
or DPP-4i

Add Prandial Insulin

TDD 0.3–0.5 U/kg

- 50% Basal Analog
- 50% Prandial Analog
- Less desirable: NPH and regular insulin or premixed insulin

Insulin titration every 2–3 days to reach glycemic goal:

- Increase prandial dose by 10% for any meal if the 2-hr postprandial or next premeal glucose is > 180 mg/dL
- Premixed: Increase TDD by 10% if fasting/premeal BG > 180 mg/dL
- If fasting AM hypoglycemia, reduce basal insulin
- If nighttime hypoglycemia, reduce basal and/or pre-supper or pre-evening snack short/rapid-acting insulin
- If between-meal daytime hypoglycemia, reduce previous premeal short/rapid-acting insulin

PROPIEDADES HIPOGLUCEMIANTES

	Advantages	Disadvantages	Cost*
SGLT2 inhibitors	• No hypoglycemia • ↓ Weight • ↓ Blood pressure • Effective at all stages of T2DM	• Genitourinary infections • Polyuria • Volume depletion/hypotension/ dizziness • ↑ LDL-C • ↑ Creatinine (transient)	High
GLP-1 receptor agonists	• No hypoglycemia • ↓ Weight • ↓ Postprandial glucose excursions • ↓ Some cardiovascular risk factors	• Gastrointestinal side effects (nausea/ vomiting/diarrhea) • ↑ Heart rate • ? Acute pancreatitis • C-cell hyperplasia/medullary thyroid tumors in animals • Injectable • Training requirements	High

	Advantages	Disadvantages	Cost*
Biguanides	• Extensive experience • No hypoglycemia • ↓ CVD events (UKPDS)	• Gastrointestinal side effects (diarrhea, abdominal cramping) • Lactic acidosis risk (rare) • Vitamin B_{12} deficiency • Multiple contraindications: CKD, acidosis, hypoxia, dehydration, etc.	Low
Sulfonylureas	• Extensive experience • ↓ Microvascular risk (UKPDS)	• Hypoglycemia • ↑ Weight • ? Blunts myocardial ischemic preconditioning • Low durability	Low
Meglitinides (glinides)	• ↓Postprandial glucose excursions • Dosing flexibility	• Hypoglycemia • ↑ Weight • ? Blunts myocardial ischemic preconditioning • Frequent dosing schedule	Moderate
TZDs	• No hypoglycemia • Durability • ↑ HDL-C • ↓ Triglycerides (pioglitazone) • ? ↓ CVD events (PROactive, pioglitazone)	• ↑ Weight • Edema/heart failure • Bone fractures • ↑ LDL-C (rosiglitazone) • ? ↑ MI (meta-analyses, rosiglitazone)	Low

PROPIEDADES HIPOGLUCEMIANTES

DPP-4 inhibitors	• No hypoglycemia • Well tolerated	• Angioedema/urticaria and other immune-mediated dermatological effects • ? Acute pancreatitis • ? ↑ Heart failure hospitalizations		High
Insulins	• Rapid-acting analogs - Lispro - Aspart - Glulisine • Short-acting - Human Regular • Intermediate-acting - Human NPH • Basal insulin analogs - Glargine - Detemir - Degludec† • Premixed (several types)	• Nearly universal response • Theoretically unlimited efficacy • ↓ Microvascular risk (UKPDS)	• Hypoglycemia • Weight gain • ? Mitogenic effects • Injectable • Patient reluctance • Training requirements	Variable#

PROFILES OF ANTIDIABETIC MEDICATIONS

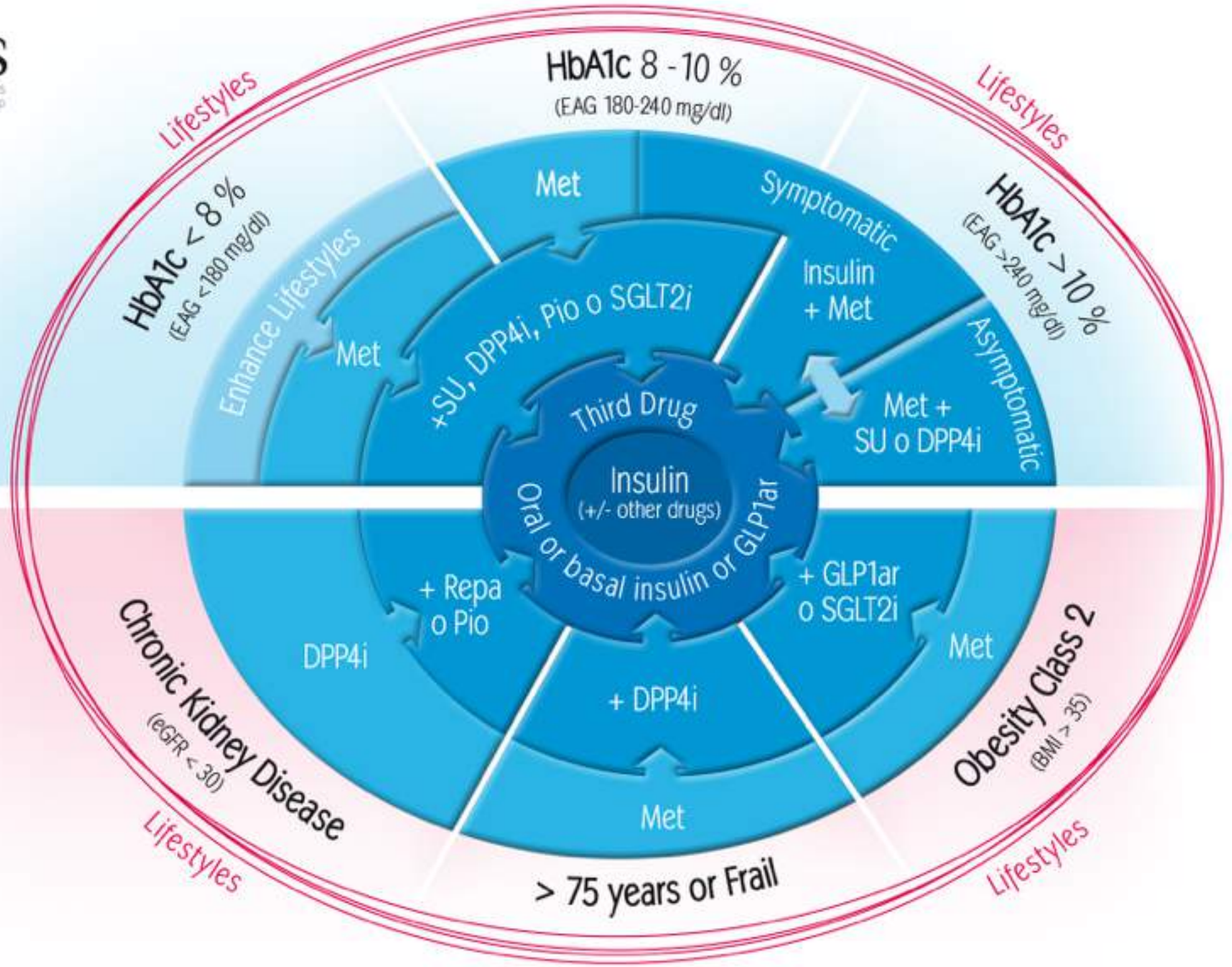
	MET	GLP-1 RA	SGLT-2i	DPP-4i	TZD	SU / GLN	INSULIN
HYPO	Neutral	Neutral	Neutral	Neutral	Neutral	Moderate/Severe / Mild	Moderate to Severe
WEIGHT	Slight Loss	Loss	Loss	Neutral	Gain	Gain	Gain
RENAL/ GU	Contra-indicated CKD Stage 3B,4,5	Exenatide Contra-indicated CrCl < 30	Genital Mycotic Infections	Dose Adjustment May be Necessary (Except Linagliptin))	May Worsen Fluid Retention	More Hypo Risk	More Hypo Risk & Fluid Retention
GI Sx	Moderate	Moderate	Neutral	Neutral	Neutral	Neutral	Neutral
CHF	Neutral	Neutral	Neutral	Neutral	Moderate	Neutral	Neutral
CVD	Benefit		Increased LDL		Neutral	?	
BONE	Neutral	Neutral	Neutral	Neutral	Moderate Bone Loss	Neutral	Neutral

Few adverse events or possible benefits — Use with caution — Likelihood of adverse effects

redGDPS
Red de Grupos de Estudio de la Diabetes
EN ATENCIÓN PRIMARIA DE LA SALUD

DEGREE OF GLYCEMIC CONTROL

SPECIAL CLINICAL CONDITIONS



Aprender Haciendo

Caso Clínico: MARIA

- Mujer de 83 años hipertensa (losartán 50 mg) y diabética desde hace 20 años. TTo: gliclazida 60 mg en desayuno y metformina 850 mg/D-C. Le gusta cuidar a sus nietos
- ERC estadio 3 (eFG 35 ml/min/1,73 m^2) y proteinuria no nefrótica. Cardiopatia hipertensiva con FEVI preservada y FA (atenolol 50 mg y sintrom).
- Varios ingresos por ICC en el ultimo año
- PA: 160/55; FC: 63 x'; IMC: 23 Kg/m^2
- HbA1c 7,5%; creatinina 1,5 mg/dl; colesterol 180; LDL 75 mg/dl
- Tiene episodios ocasionales de hipoglucemia con una caída con traumatismo en la rodilla sin consecuencias.

Caso Clínico: MARIA

- Mujer 83 años
- Edad avanzada
- Hipoglucemias
- Insuficiencia Renal
- Insuficiencia Cardiaca

Caso Clínico: MARIA

- OBJETIVO TERAPEUTICO

- REALIZAMOS CAMBIO DE TRATAMIENTO

- QUE CAMBIOS REALIZARÍAMOS

Caso Clínico: MARIA

- Dejar mismo tratamiento HbA1c correcta
- Suspender Metformina por IR y dejar Gliclazida
- Suspender Gliclazida
- Subir metformina a 850 mg/8h
- Dejar metformina y añadir i-DPP4
- Reducir Metformina y añadir i-DPP4
- Reducir Metformina + Insulina Basal
- Metformina + SGLT2

Caso Clínico: MARIA

- Dejar mismo tratamiento HbA1c correcta
- Suspender Metformina por IR y dejar Gliclazida
- Suspender Gliclazida
- Subir metformina a 850 mg/8h
- Dejar metformina y añadir i-DPP4
- **<u>Reducir Metformina y añadir i-DPP4</u>**
- Reducir Metformina + Insulina Basal
- Metformina + SGLT2

	SITAGLIPTIN	SAXAGLIPTIN	VILDAGLIPTIN	LINAGLIPTIN
DOSIS	100 mg once daily	5 mg once daily	50 mg twice daily	5 mg once daily
Elderly ≥ 65 years	No dose adjustment	No dose adjustment	No dose adjustment	No dose adjustment
≥ 75 years	Limited safety data	Very limited experience	No dose adjustment	Limited clinical experience

	SITAGLIPTIN	SAXAGLIPTIN	VILDAGLIPTIN	LINAGLIPTIN
DOSIS	100 mg once daily	5 mg once daily	50 mg twice daily	5 mg once daily
Mild Renal Impairment (≥ 50 ml/min)	No dose adjustment	No dose adjustment	No dose adjustment	No dose adjustment
Moderate Renal Impairment (49-30 ml/min)	50 mg once daily	2.5 mg once daily	50 mg once daily	No dose adjustment
Severe Renal Impairment (< 30 ml/min)	25 mg once daily	2.5 mg once daily	50 mg once daily	No dose adjustment
End Stage Renal Disease (ESRD) requiring dialysis	25 mg once daily	Not recommended	Limited experience	No dose adjustment

original article

Diabetes, Obesity and Metabolism 13: 55–64, 2011.

Clinical experience with vildagliptin in the management of type 2 diabetes in a patient population ≥75 years: a pooled analysis from a database of clinical trials

A. Schweizer[1], S. Dejager[2], J. E. Foley[3], Q. Shao[3] & W. Kothny[3]

Clinical Interventions in Aging

Dovepress

ORIGINAL RESEARCH

Tolerability and efficacy of glycemic control with saxagliptin in older patients (aged ≥ 65 years) with inadequately controlled type 2 diabetes mellitus

This article was published in the following Dove Press journal:
Clinical Interventions in Aging
15 April 2013

Articles

Linagliptin for patients aged 70 years or older with type 2 diabetes inadequately controlled with common antidiabetes treatments: a randomised, double-blind, placebo-controlled trial

Prof Anthony H Barnett, MD, Holger Huisman, MSc, Russell Jones, MSc, Maximilian von Eynatten, MD, Sanjay Patel, MB ChB, Hans-Juergen Woerle, MD

Published Online: 13 August 2013

Altmetric 19

DOI: http://dx.doi.org/10.1016/S0140-6736(13)61500-7 | CrossMark

Original Research Article
Drugs & Aging
June 2015, Volume 32, Issue 6, pp 469-476

First online: 04 June 2015

Efficacy and Tolerability of Sitagliptin Compared with Glimepiride in Elderly Patients with Type 2 Diabetes Mellitus and Inadequate Glycemic Control: A Randomized, Double-Blind, Non-Inferiority Trial

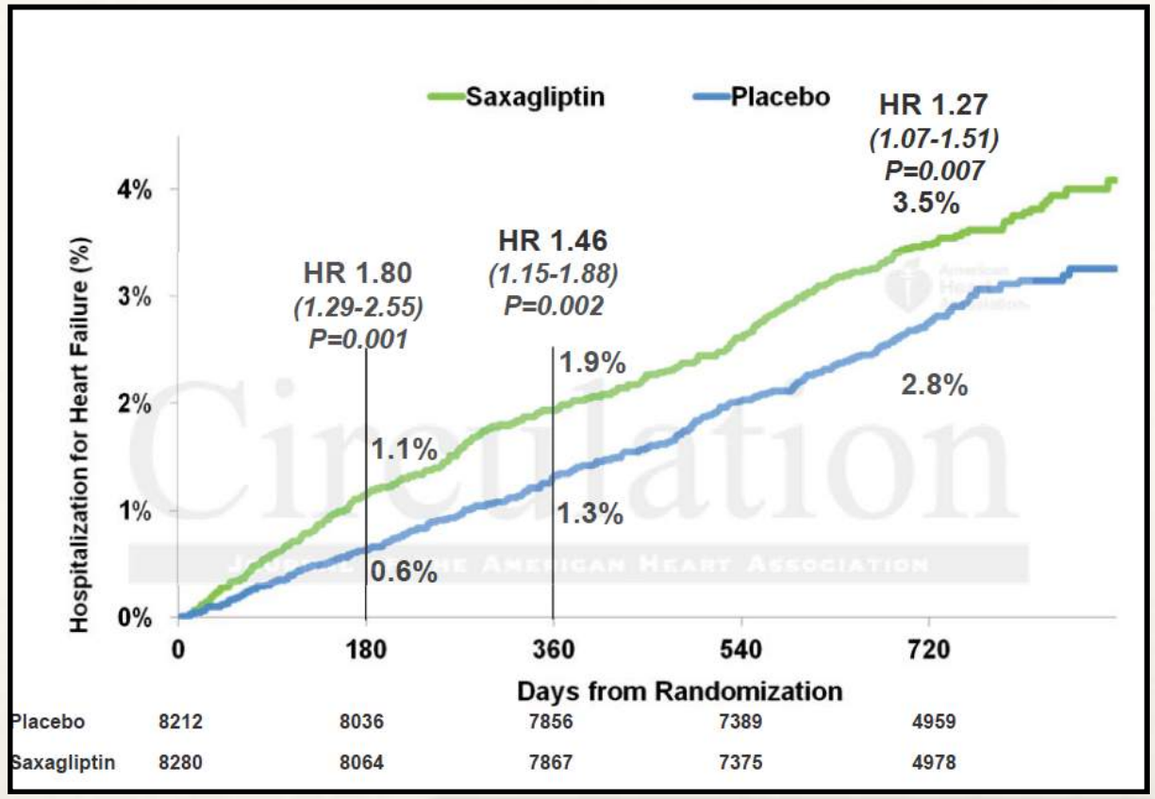
Paul Hartley, Yue Shentu, Patricia Betz-Schiff, Gregory T. Golm, Christine McCrary Sisk, Samuel S. Engel, R. Ravi Shankar

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Saxagliptin and Cardiovascular Outcomes in Patients with Type 2 Diabetes Mellitus

N Engl J Med 2013;369:1317-26.
DOI: 10.1056/NEJMoa1307684



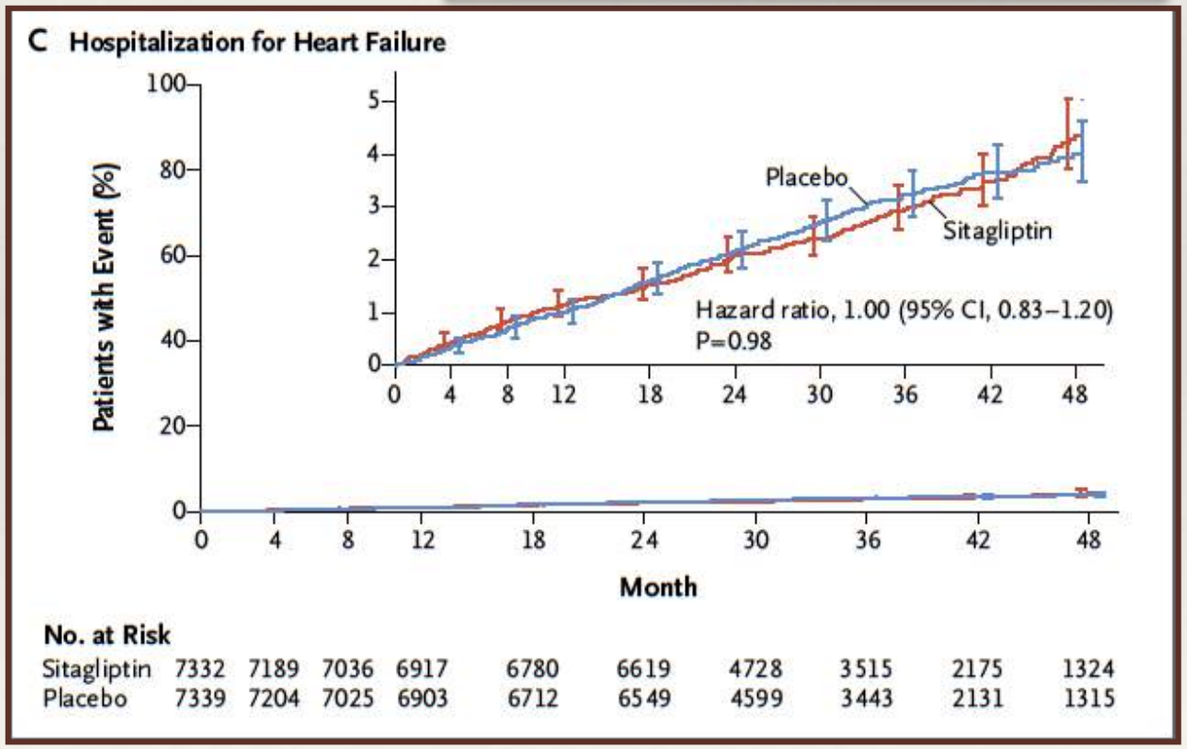
Circulation 2014; 130:1579-1588

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Effect of Sitagliptin on Cardiovascular Outcomes in Type 2 Diabetes

Jennifer B. Green, M.D., M. Angelyn Bethel, M.D., Paul W. Armstrong, M.D., John B. Buse, M.D., Ph.D., Samuel S. Engel, M.D., Jyotsna Garg, M.S., Robert Josse, M.B., B.S., Keith D. Kaufman, M.D., Joerg Koglin, M.D., Scott Korn, M.D., John M. Lachin, Sc.D., Darren K. McGuire, M.D., M.H.Sc., Michael J. Pencina, Ph.D., Eberhard Standl, M.D., Ph.D., Peter P. Stein, M.D., Shailaja Suryawanshi, Ph.D., Frans Van de Werf, M.D., Ph.D., Eric D. Peterson, M.D., M.P.H., and Rury R. Holman, M.B., Ch.B., for the TECOS Study Group*



This article was published on June 8, 2015, at NEJM.org.

DOI: 10.1056/NEJMoa1501352

Rosenstock et al. Cardiovascular Diabetology (2015) 14:57
DOI 10.1186/s12933-015-0215-2

CARDIO VASCULAR DIABETOLOGY

ORIGINAL INVESTIGATION Open Access

Cardiovascular safety of linagliptin in type 2 diabetes: a comprehensive patient-level pooled analysis of prospectively adjudicated cardiovascular events

Julio Rosenstock[1], Nikolaus Marx[2], Dietmar Neubacher[3], Thomas Seck[4], Sanjay Patel[5], Hans-Juergen Woerle[4] and Odd Erik Johansen[6*]

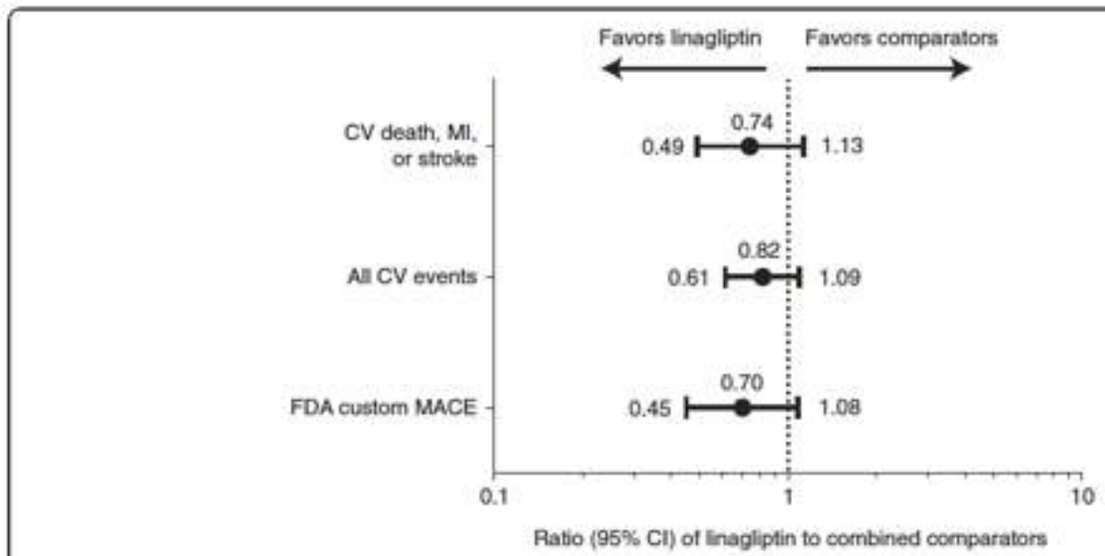


Figure 4 HR estimates for secondary composite CV end points with linagliptin versus total comparators based on Cox hazard model. *CI*, confidence interval; *CV*, cardiovascular; *FDA*, Food and Drug Administration; *HR*, hazard ratio; *MACE*, major adverse CV events; *MI*, myocardial infarction.

Clinical Trial Design

Design and baseline characteristics of the CARdiovascular Outcome Trial of LINAgliptin Versus Glimepiride in Type 2 Diabetes (CAROLINA®)

Diabetes & Vascular Disease Research
2015, Vol. 12(3) 164–174

DOI: 10.1177/1479164115570301
dvr.sagepub.com
SAGE

10. Older Adults

Diabetes Care 2015;38(Suppl. 1):S67–S69 | DOI: 10.2337/dc15-S013

Table 10.1—Framework for considering treatment goals for glycemia, blood pressure, and dyslipidemia in older adults with diabetes

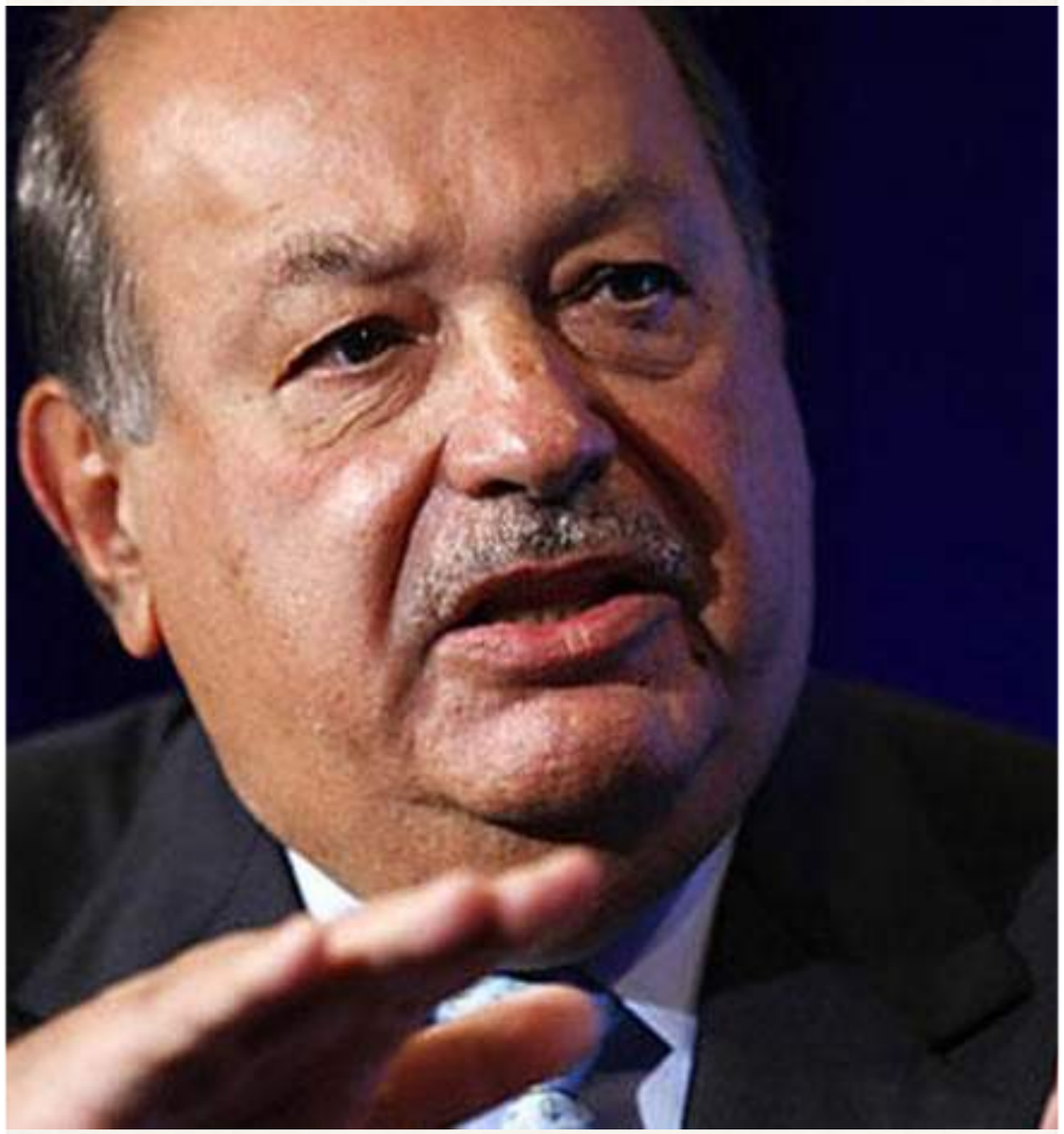
Patient characteristics/ health status	Rationale	Reasonable A1C goal‡	Fasting or preprandial glucose (mg/dL)	Bedtime glucose (mg/dL)	Blood pressure (mmHg)	Lipids
Healthy (few coexisting chronic illnesses, intact cognitive and functional status)	Longer remaining life expectancy	<7.5%	90–130	90–150	<140/90	Statin unless contraindicated or not tolerated
Complex/intermediate (multiple coexisting chronic illnesses* or 2+ instrumental ADL impairments or mild-to-moderate cognitive impairment)	Intermediate remaining life expectancy, high treatment burden, hypoglycemia vulnerability, fall risk	<8.0%	90–150	100–180	<140/90	Statin unless contraindicated or not tolerated
Very complex/poor health (long-term care or end-stage chronic illnesses** or moderate-to-severe cognitive impairment or 2+ ADL dependencies)	Limited remaining life expectancy makes benefit uncertain	<8.5%†	100–180	110–200	<150/90	Consider likelihood of benefit with statin (secondary prevention more so than primary)

Caso Clínico: MANUEL

- Manuel tiene 60 años, diabetes desde hace 9 años, hipertenso, EPOC, SAOS e HTP moderada. Frecuentes agudizaciones respiratorias, precisando esteroides con muy mal control glucemia. TTo: Ramipril 10 mg, Metformina/ Linagliptina 1000/2,5 mg cada 12 horas, atrovent y seretide. Es director de banco
- CPAP Nocturna. Sin oxigeno domiciliario
- IMC: 35 Kg/m^2, TA 180/95, FC 85 x'.
- Glucemia Basales elevadas 225 mg/dl. Hb A1c 8,9%. Pefil lipídico normal. FG: 55 ml/min/1,73 m^2

Caso Clínico: MANUEL

- Hombre 60 años
- Obesidad y Sedentarismo
- Mal control Metabolico
- SAOS
- Hipertensión Arterial



Caso Clínico: MANUEL

- Insulinización Basal para mejorar control glucémico
- Añadir un tercer ADO: SGLT2
- Suspender linagliptina y añadir GLP1 basal (Liraglutide)
- Añadir una SU para mejorar control glucémico
- Suspender Met-Lina y pasar a Estrategia Basal-Bolo

Caso Clínico: MANUEL

- Insulinización Basal para mejorar control glucémico
- Añadir un tercer ADO: SGLT2
- **Suspender linagliptina y añadir GLP1 basal (Liraglutide)**
- Añadir una SU para mejorar control glucémico
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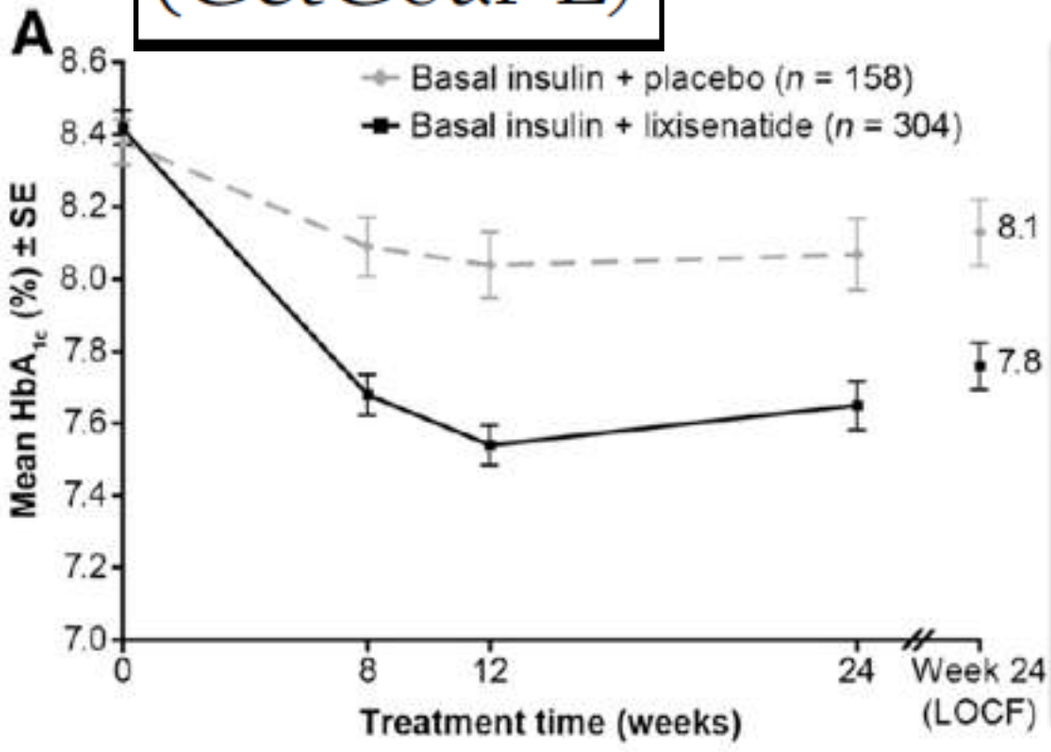
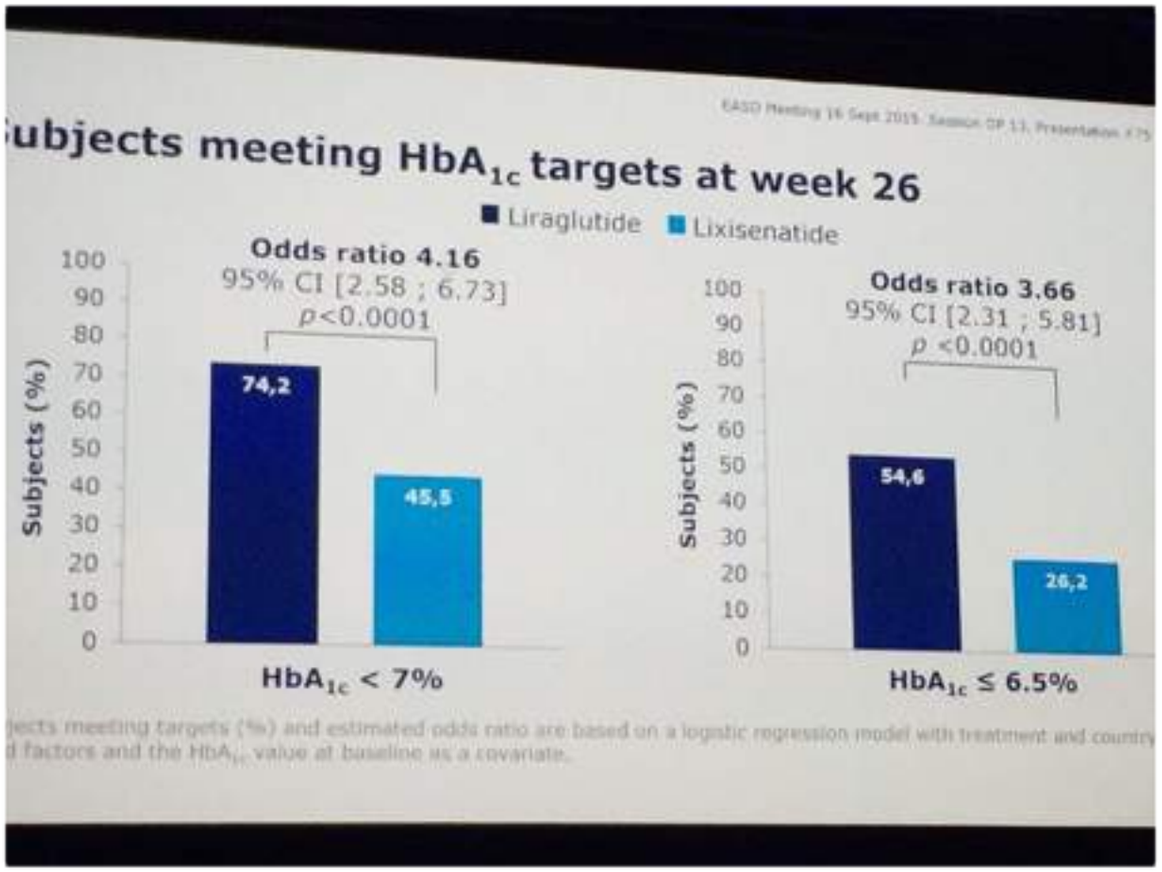
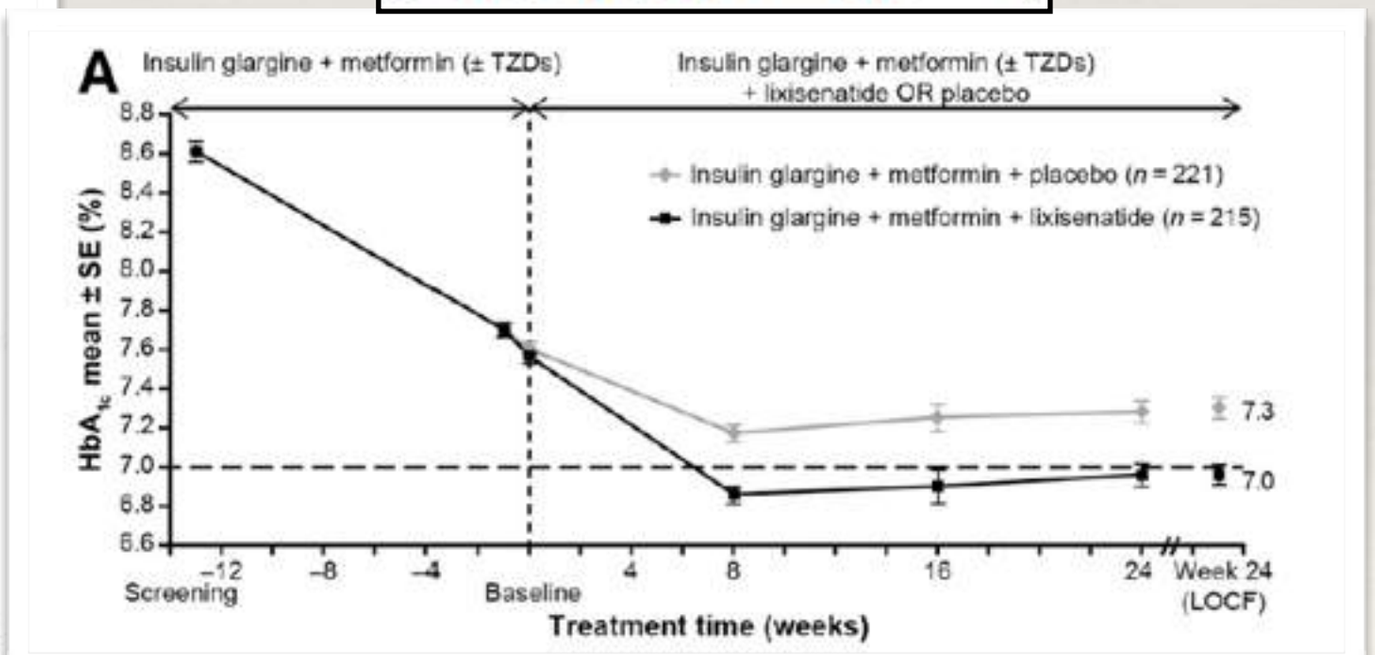
(GetGoal-L)



Diabetes Care 36:2489–2496, 2013



(GetGoal-Duo 1)



Diabetes Care 36:2497–2503, 2013

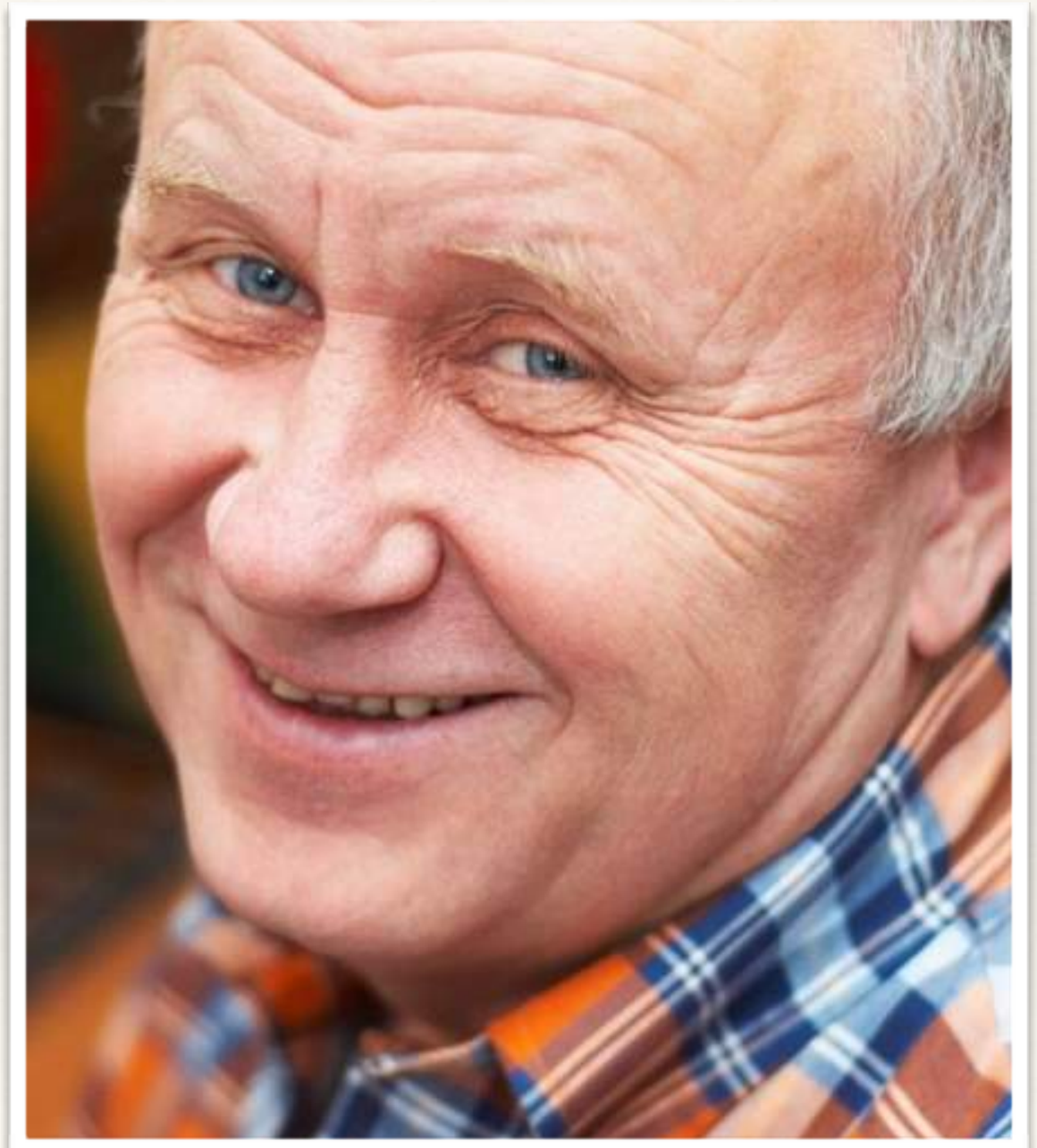

VICTOZA®
liraglutide
(rDNA origin) injection
18 mg/3 mL (6 mg/mL)
Each pen delivers doses of 0.6 mg, 1.2 mg or 1.8 mg
Subcutaneous use only
Discard pen 30 days after first use
REFRIGERATE – DO NOT FREEZE
NDC 0169-4060-13
List 406013
Victoza®
Single patient use only
Rx Only
Contains: 3 Victoza Pens, Product Literature
Dispense the enclosed Medication Guide to each patient
Intended for use with Novo Nordisk disposable needles
3 Pens: 30 doses of 1.8 mg

Caso Clínico: MIGUEL

- **MIGUEL** tiene 53 años y es diabético tipo 2 desde hace 4 años, historia familiar de diabetes. Trabaja en la bolsa de Madrid. No fuma pero es hipertenso y dislipémico.
- Hace 1 mes sufre un IAM inferior (enfermedad monovaso revascularizada).
- IMC: 29 Kg/m^2
- PA: 126/75 mm Hg Colesterol total 168 mg/dl (HDL 32 mg/dl, LDL 91 mg/dl), TG 225 mg/dl. Hb A1c 7.9%
- Tratamiento: Metformina 850 mg (x3), Rosuvastatina 10 mg, AAS 100 mg, prasugrel, irbesartan 150/hidroclorotiazida 12.5 mg

Caso Clínico: MIGUEL

- Hombre 53 años
- Sobrepeso
- Alto riesgo Cardiovascular
- Mal control metabólico



Caso Clínico: MIGUEL

Caso Clínico: MIGUEL

- SULFONILUREA
- INSULINA GLARGINA
- PIOGLITAZONA
- LIRAGLUTIDE
- SGLT2
- SITAGLIPTINA

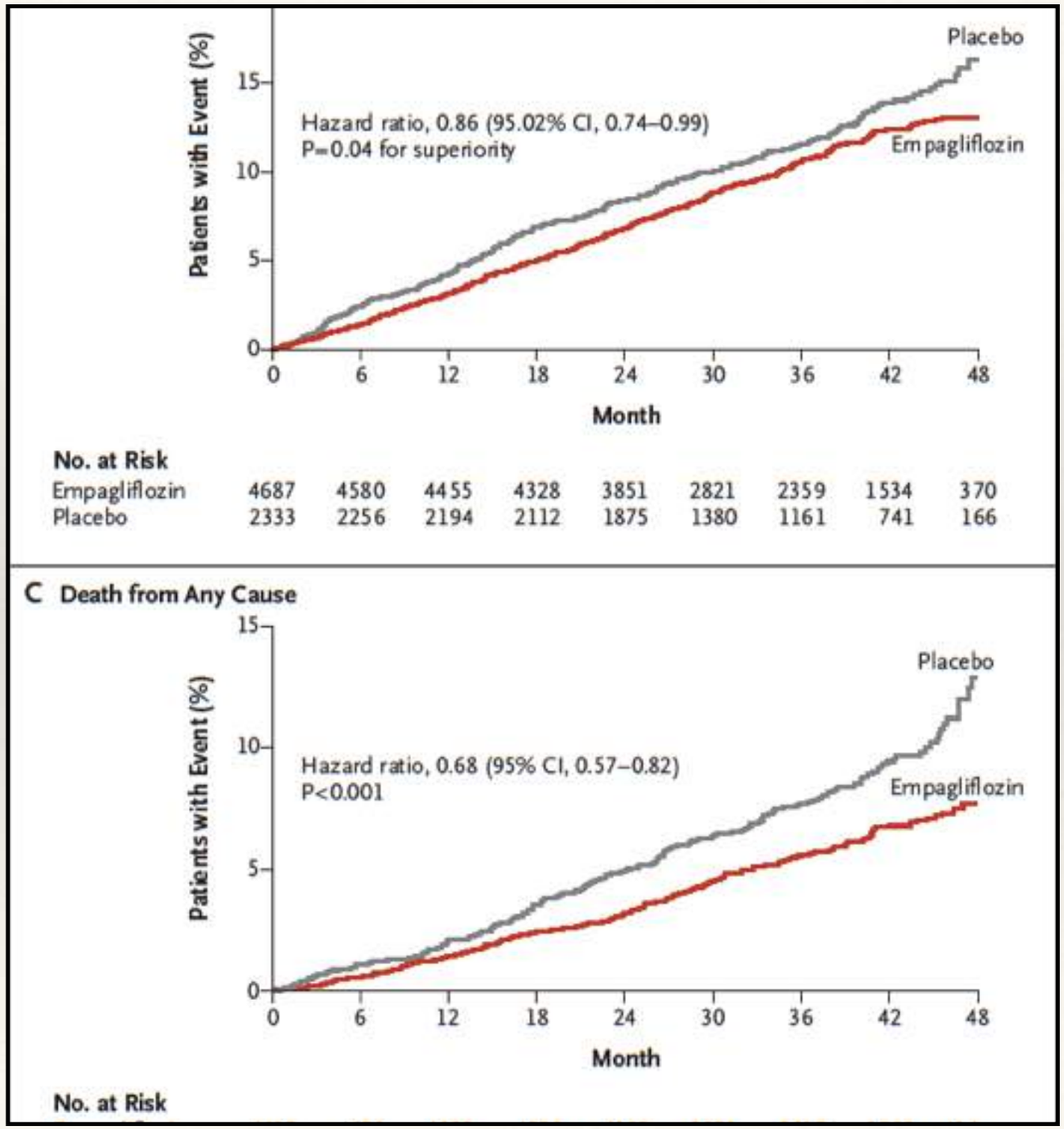
Caso Clínico: MIGUEL

- SULFONILUREA
- INSULINA GLARGINA
- PIOGLITAZONA
- LIRAGLUTIDE
- **SGLT2**
- SITAGLIPTINA

Bloqueantes SGLT-2

Caso Clínico: MIGUEL

- **<u>EMPAGLIFLOZINA 15 mg</u>**
- **OTRAS:**
  - **CANA / DAPA**
  - **LIRAGLUTIDE**
  - **SITAGLIPTINA**



This article was published on September 17, 2015, at NEJM.org.

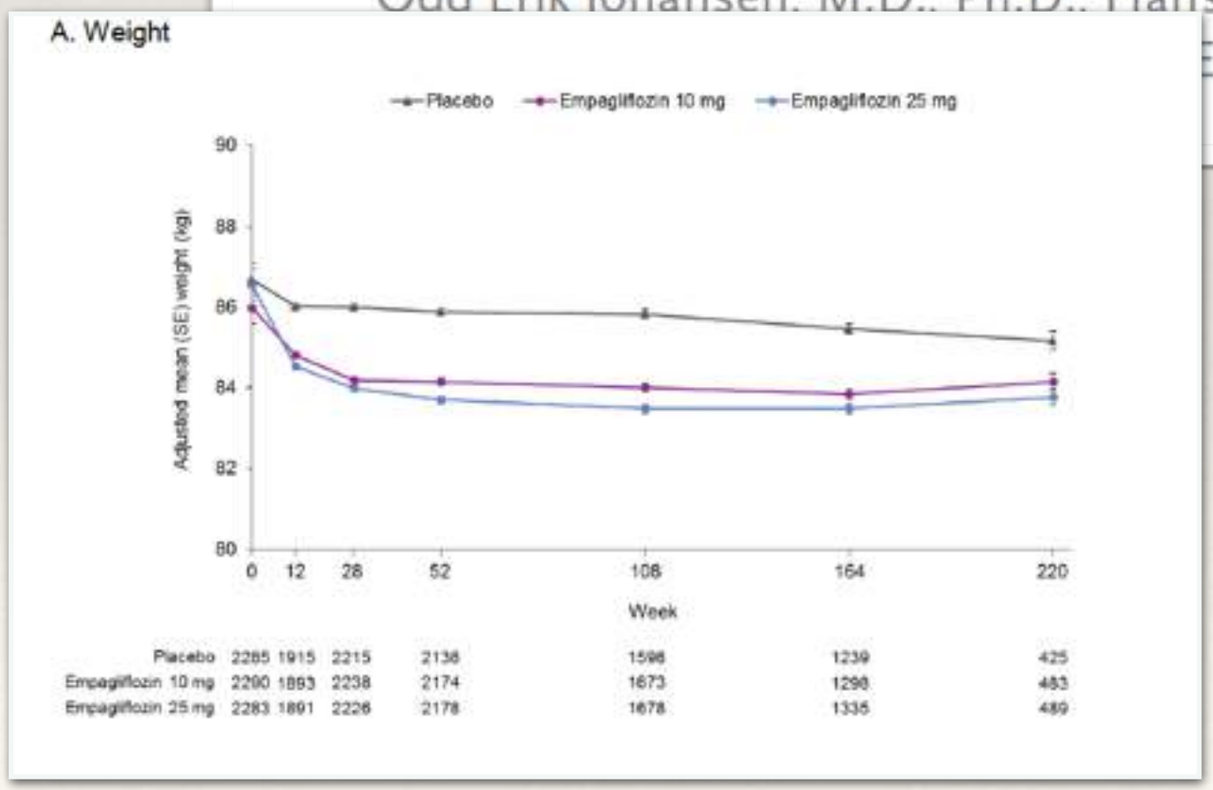
DOI: 10.1056/NEJMoa1504720

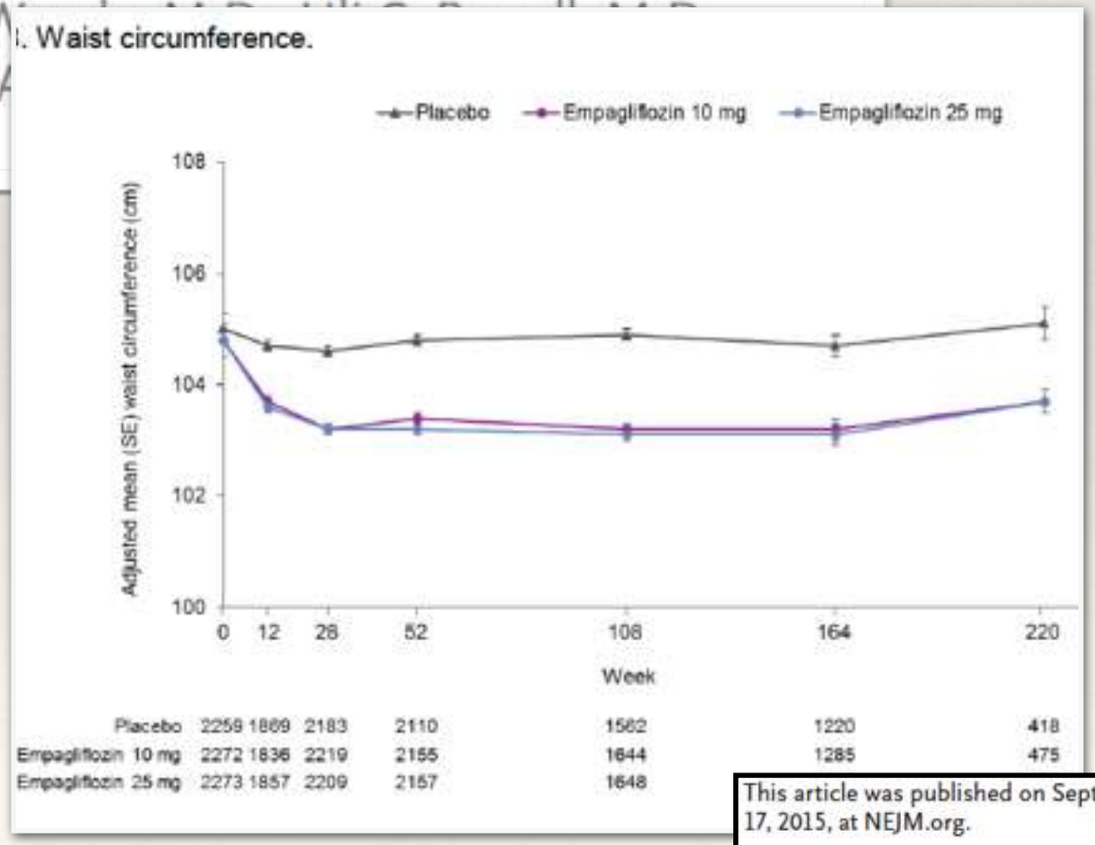
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Empagliflozin, Cardiovascular Outcomes, and Mortality in Type 2 Diabetes

Bernard Zinman, M.D., Christoph Wanner, M.D., John M. Lachin, Sc.D., David Fitchett, M.D., Erich Bluhmki, Ph.D., Stefan Hantel, Ph.D., Michaela Mattheus, Dipl. Biomath., Theresa Devins, Dr.P.H., Odd Erik Johansen, M.D., Ph.D., Hans J. W... EMPA...





This article was published on September 17, 2015, at NEJM.org.

DOI: 10.1056/NEJMoa1504720

Euglycemic Diabetic Ketoacidosis: A Predictable, Detectable, and Preventable Safety Concern With SGLT2 Inhibitors

Julio Rosenstock[1] and Ele Ferrannini[2]

Diabetes Care 2015;38:1638–1642 | DOI: 10.2337/dc15-1380

Caso Clínico:ISABEL

- Mujer de 44 años que ingresa por pielonefritis aguda, tiene dos hijos sin diabetes gestacional. Su madre tiene hipotiroidismo autoinmune y su abuela diabética. No fuma y toma simvastatina 20 mg por hipercolesterolemia.
- En el hospital glucemias de hasta 350 mg/dl precisando tratamiento con basal bolo-corrección. Tiene síntomas cardinales con pérdida de peso en los últimos 2 meses.
- IMC 21 Kg/m^2; TA 135/65; FC 72 x'
- HbA1c 12%; colesterol 256 mg/dl, HDL 36, LDL 145, TA 135

Caso Clínico: ISABEL

- Mujer 47 años
- Debut Diabético
- Síntomas Cardinales
- Muy mal control metabólico

Caso Clínico: ISABEL

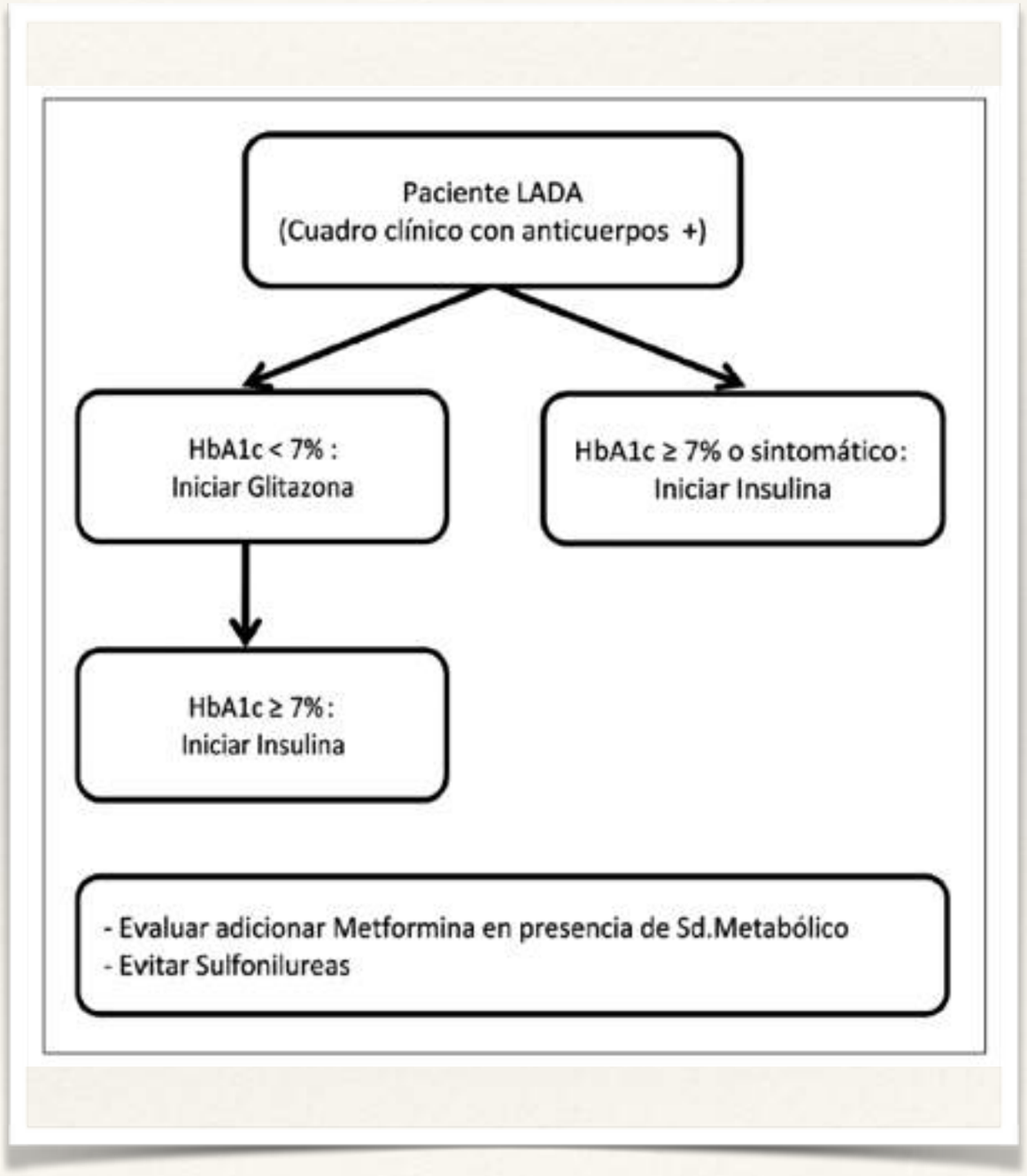
- METFORMINA MONOTERAPIA
- METFORMINA + SGLT2
- METFORMINA + PIOGLITAZONA
- METFORMINA + INSULINA BASAL
- BASAL - BOLO -CORRECCIÓN
- TRIPLE TERAPIA

Caso Clínico: ISABEL

- METFORMINA MONOTERAPIA
- METFORMINA + SGLT2
- METFORMINA + PIOGLITAZONA
- METFORMINA + INSULINA BASAL
- **BASAL - BOLO -CORRECCIÓN**
- TRIPLE TERAPIA

Caso Clínico: ISABEL

- PLANTEAR DIABETES TIPO LADA (Latent Autoimmune Diabetes in Adults)
- MAYORES 35 AÑOS
- ANTI-GAD (antidescarboxilasa del ácido glutámico).
- Insulina tratamiento elección



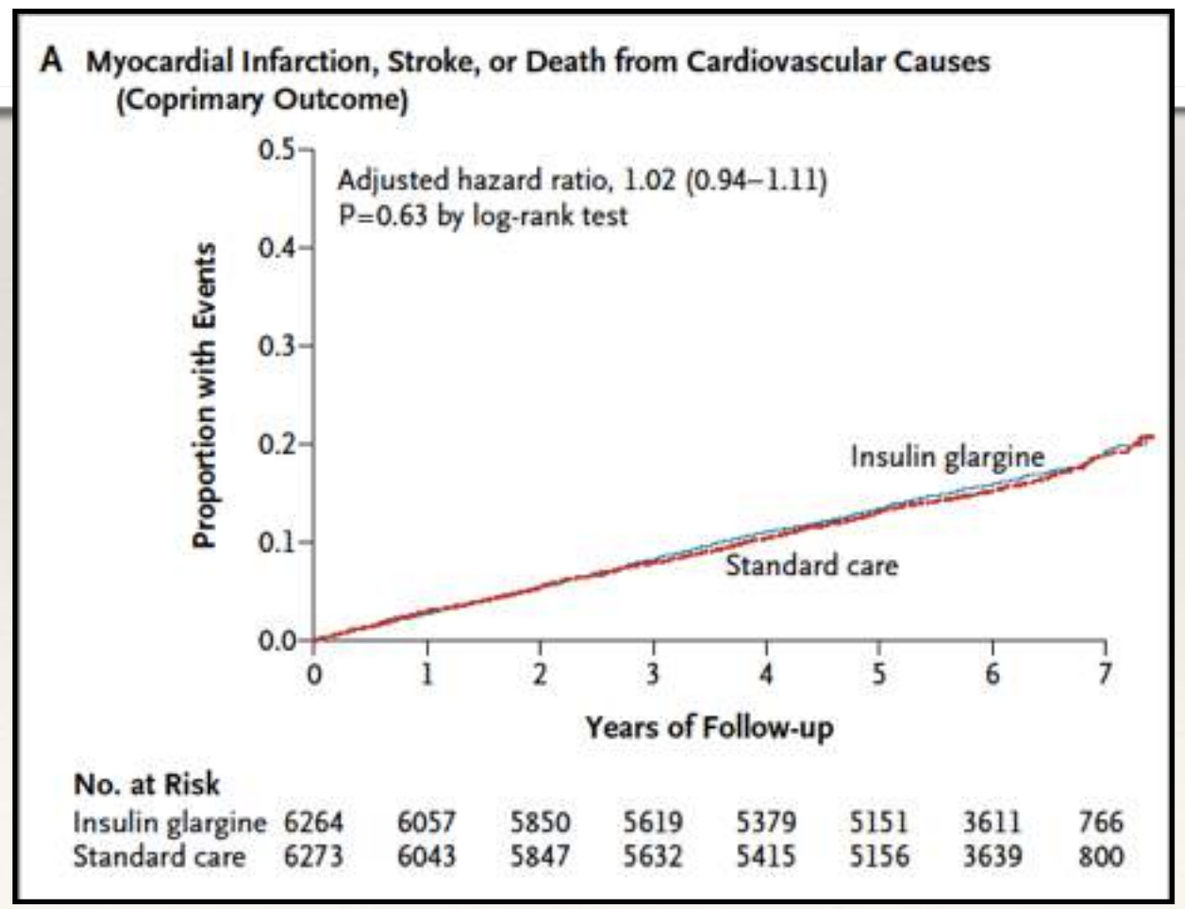
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Basal Insulin and Cardiovascular and Other Outcomes in Dysglycemia

The ORIGIN Trial Investigators*

N Engl J Med 2012;367:319-28.
DOI: 10.1056/NEJMoa1203858



Caso Clínico: JOSEFA

- Josefa tiene 67 años y es diabética desde hace 15 años. Controlada con Metformina correctamente añadió a su tratamiento Vildagliptina hace 2 años con buen control metabólico. No es hipertensa ni dislipémica. Monorrena por una pielonefritis crónica desde hace 3 años. En los últimos meses regular control metabólico.
- Enfermedad Renal Crónica estadio 3 con FG 45 ml/min
- Ingresa por Neumonía de la Comunidad que evoluciona bien con ceftriaxona y levofloxacino.
- Mal control glucémico durante la hospitalización precisando dosis altas de insulina en régimen basal-bolo

Caso Clínico: JOSEFA

- IMC 22 Kg/m^2; TA 167/87; FC 78 x'
- HbA1c 8.4 %; Colesterol 234; HDL 35; LDL 123
- Creatinina 2,4 mg/dl; FG 21 ml/min; Proteinuria no nefrótica
- Se inicia tratamiento con losartan 50 mg/d y atorvastatina 40 mg/d

Caso Clínico: JOSEFA

- Mujer 67 años
- Insuficiencia Renal Severa
- Mal Control Metabolico
- No otras comorbilidades

Caso Clinico: JOSEFA

- Insulinización Basal - Bolo - Corrección

- **<u>Insulina Basal + Linagliptina</u>**

- Insulina Basal + Repaglinida

- Linagliptina + Metformina a dosis ajustadas

- Pioglitazona + Linagliptina

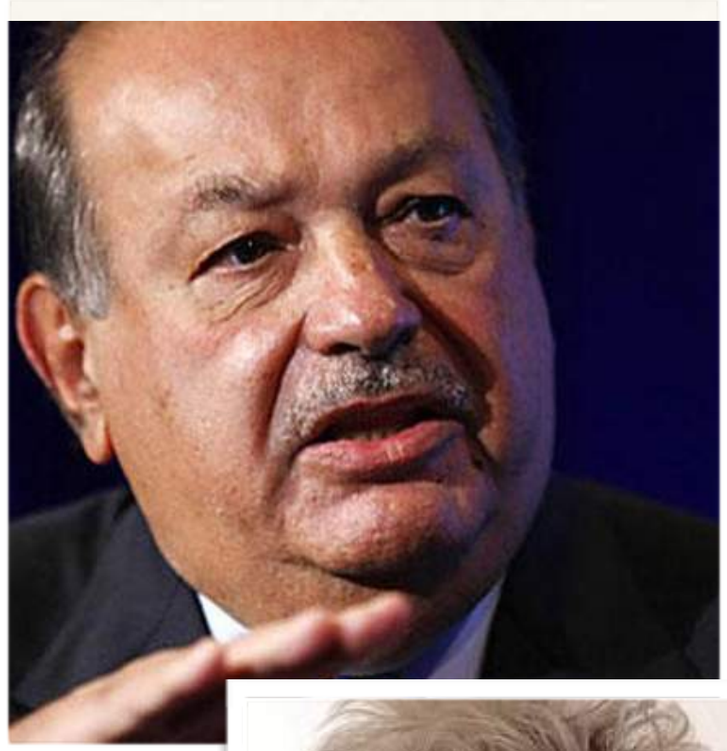
TITULAR LA INSULINA BASAL

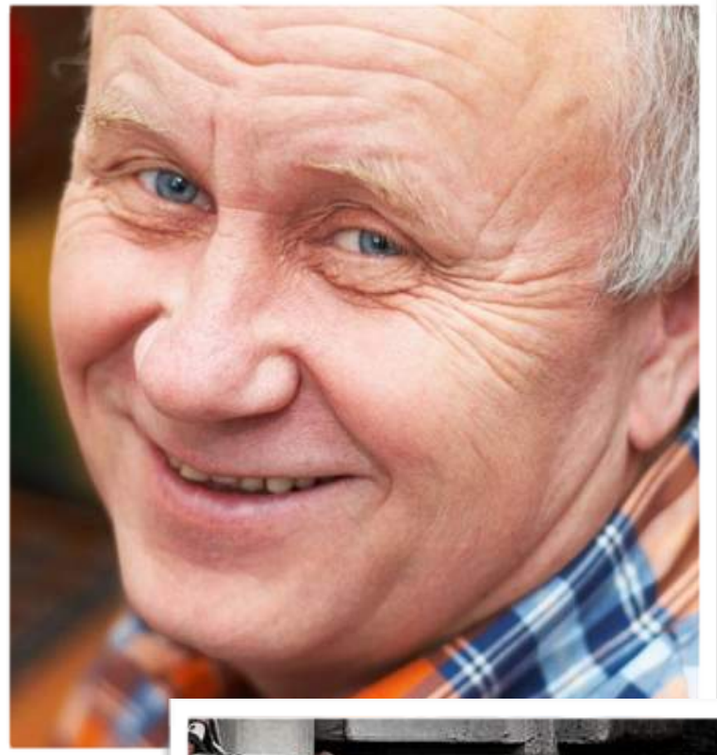
- Subir 2 ui de Insulina si cada 3 días la glucemia es mayor de 140 mg/dl

Caso Clinico: Mario

- Metformina
- Metformina + Glicazida
- ¿?

DIFERENTES PACIENTES
DIFERENTES NECESIDADES

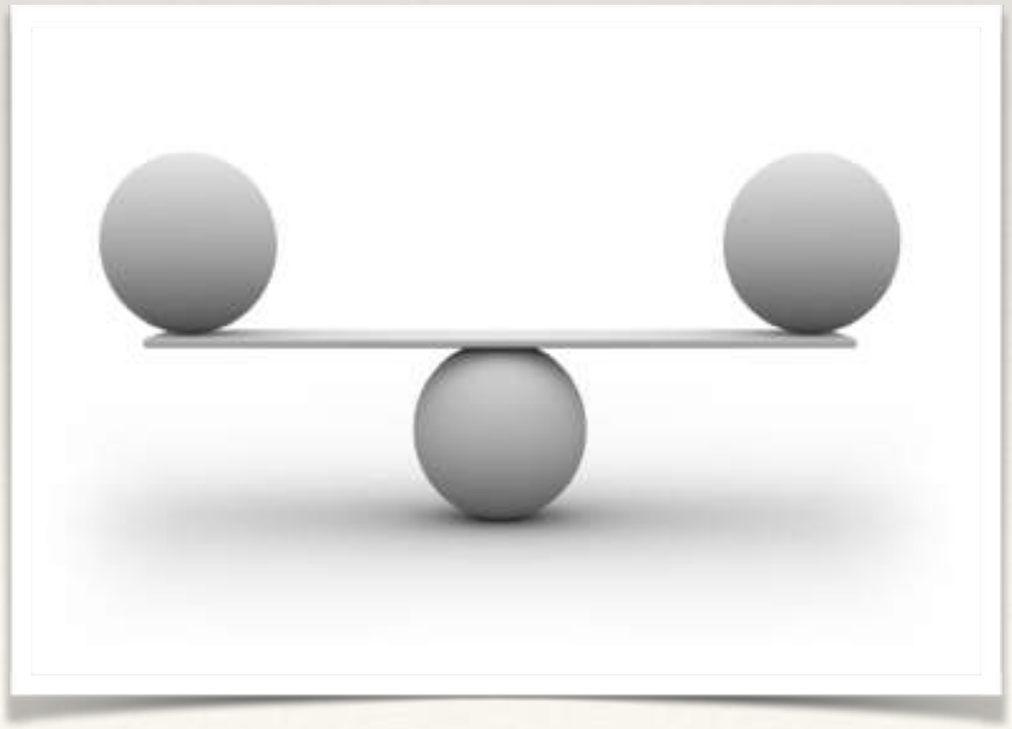




Evitar

Excesivos tratamientos en un paciente en el cual el pronóstico ya no depende de la progresión de la diabetes

Insuficiente tratamiento en pacientes con larga esperanza de vida y alto riesgo de desarrollar complicaciones micro y macroangiopáticas



Lorem Ipsum Dolor

No Inercia Terapeutica
No Retraso Tratamiento

INFORME DE ALTA

Tratamiento de la diabetes como venía realizando

HbA1c = 10.5%

"You should not try to add years to your life,
but rather add life to yours years"

– Oscar Wilde

Mensajes Para Recordar