Ctrl L + Ctrl G + Ctrl T

CONTROL 3

El poder de controlar los resultados

sanofi

Actualización Guías ADA 2022

Dr. Oscar Badilla Barboza

Especialista en Endocrinología

Costa Rica

Conflictos de interés

- *He participado como conferencista y/o asesor de: Abbott, Asofarma, Aspen, Astra Zeneca, Europharma, Grünenthal, Gutis, Lilly, Luminova, Medix, Merck Serono, MSD, Novartis, Novo Nordisk, Pfizer, Raven, Sandoz, Sanofi, Stein y Unipharm.*
- *Esta actividad cuenta con el patrocinio de Sanofi.*

Las personas con diabetes tienen un riesgo ***2 a 4 veces*** *mayor de desarrollar* ***enfermedad cardiovascular*** *comparado con personas sin diabetes*

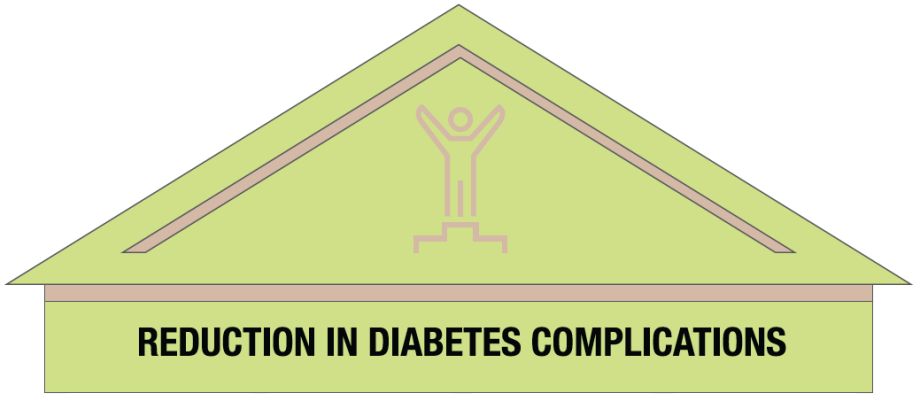
American College of Cardiology. Heart disease is the leading cause of death among adults with diabetes. https://www.cardiosmart.org/DiabetesandHeartDisease. Accessed 26 September 2019.

SUPPLEMENT 1

AMERICAN DIABETES ASSOCIATION

STANDARDS OF MEDICAL CARE IN DIABETES—2022

ADA 2022



Diabetes Care Volume 45, Supplement 1, January 2022



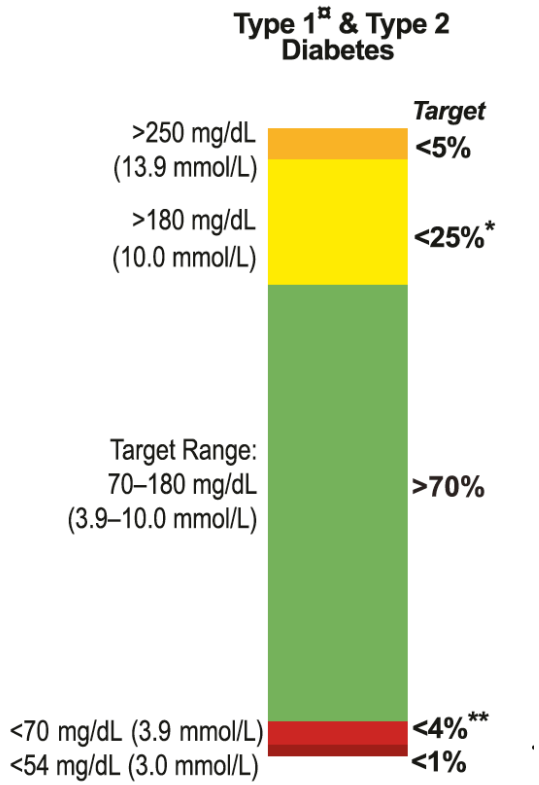
Manejo glicémico

HbA1C ADA 2022

- <7% sin hipoglicemia.
- Es aceptable que sea menor si no hay riesgo de hipoglicemia o efectos secundarios de los medicamentos.
- <8% en pacientes cuyo control intensivo es más riesgoso que beneficioso.

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Tiempo en el rango



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ADA 2022

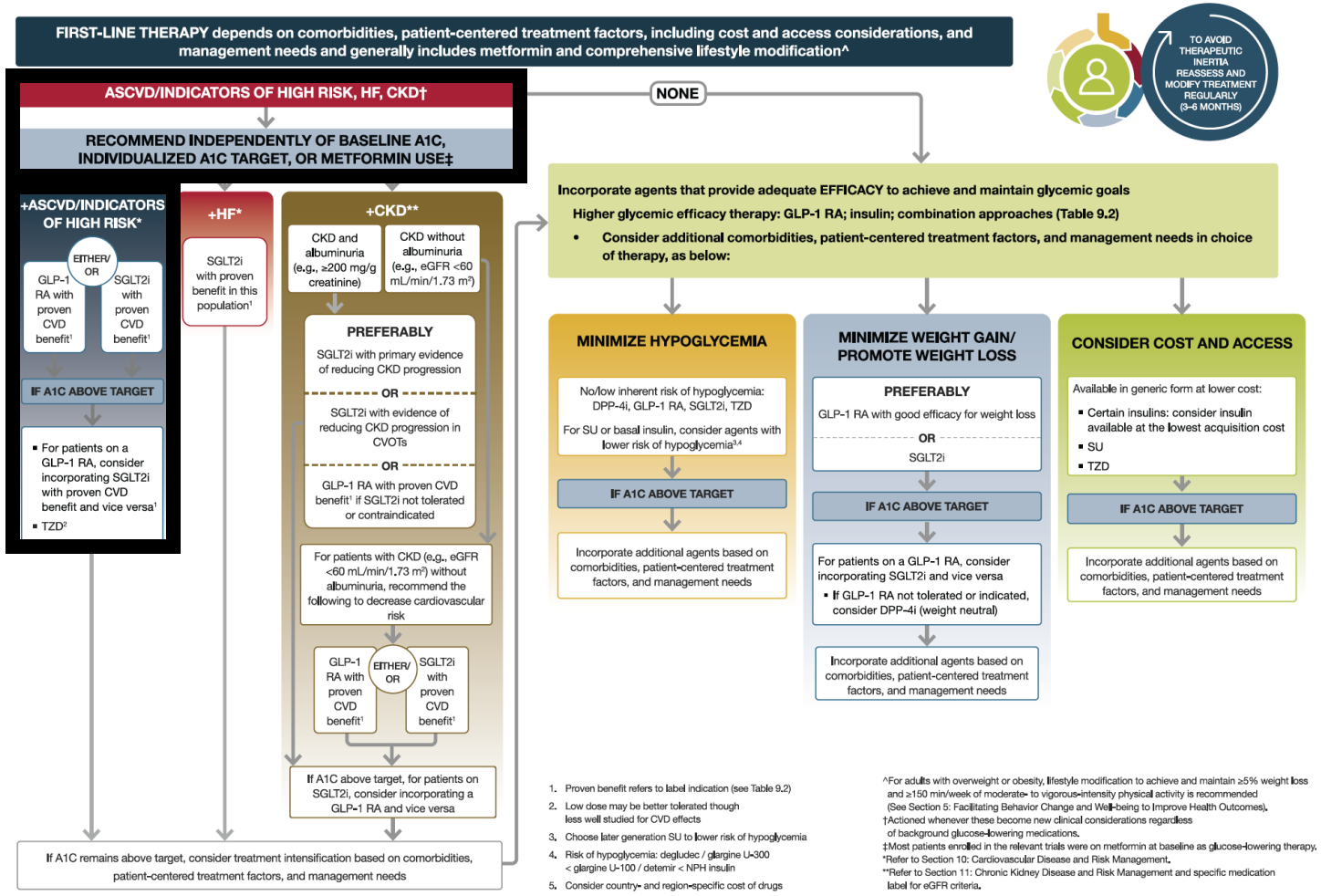
Table 9.2—Drug-specific and patient factors to consider when selecting antihyperglycemic treatment in adults with type 2 diabetes

	Efficacy (60)	Hypoglycemia	Weight change (109)	CV effects		Cost	Oral/SQ	Renal effects		Additional considerations
				ASCVD	HF			Progression of DKD	Dosing/use considerations*	
Metformin	High	No	Neutral (potential for modest loss)	Potential benefit	Neutral	Low	Oral	Neutral	▪ Contraindicated with eGFR <30 mL/min/1.73 m^2	▪ Gastrointestinal side effects common (diarrhea, nausea) ▪ Potential for B12 deficiency
SGLT2 inhibitors	Intermediate	No	Loss	Benefit: empagliflozin†, canagliflozin†	Benefit: empagliflozin‡, canagliflozin, dapagliflozin‡, ertugliflozin	High	Oral	Benefit: canagliflozin§, empagliflozin, dapagliflozin§	▪ See labels for renal dose considerations of individual agents ▪ Glucose-lowering effect is lower for SGLT2 inhibitors at lower eGFR	▪ Should be discontinued before any scheduled surgery to avoid potential risk for DKA ▪ DKA risk (all agents, rare in T2D) ▪ Risk of bone fractures (canagliflozin) ▪ Genitourinary infections ▪ Risk of volume depletion, hypotension ▪ ↑LDL cholesterol ▪ Risk of Fournier's gangrene
GLP-1 RAs	High	No	Loss	Benefit: dulaglutide†, liraglutide†, semaglutide (SQ)† Neutral: exenatide once weekly, lixisenatide	Neutral	High	SQ; oral (semaglutide)	Benefit on renal end points in CVOTs, driven by albuminuria outcomes: liraglutide, semaglutide (SQ), dulaglutide	▪ See labels for renal dose considerations of individual agents ▪ No dose adjustment for dulaglutide, liraglutide, semaglutide ▪ Caution when initiating or increasing dose due to potential risk of nausea, vomiting, diarrhea, or dehydration. Monitor renal function in patients reporting severe adverse GI reactions when initiating or increasing dose of therapy.	▪ **FDA Black Box:** Risk of thyroid C-cell tumors in rodents; human relevance not determined **(liraglutide, dulaglutide, exenatide extended release, semaglutide)** ▪ GI side effects common (nausea, vomiting, diarrhea) ▪ Injection site reactions ▪ Pancreatitis has been reported in clinical trials but causality has not been established. Discontinue if pancreatitis is suspected.
DPP-4 inhibitors	Intermediate	No	Neutral	Neutral	Potential risk: saxagliptin	High	Oral	Neutral	▪ Renal dose adjustment required (sitagliptin, saxagliptin, alogliptin); can be used in renal impairment ▪ No dose adjustment required for linagliptin	▪ Pancreatitis has been reported in clinical trials but causality has not been established. Discontinue if pancreatitis is suspected. ▪ Joint pain
Thiazolidinediones	High	No	Gain	Potential benefit: pioglitazone	Increased risk	Low	Oral	Neutral	▪ No dose adjustment required ▪ Generally not recommended in renal impairment due to potential for fluid retention	▪ **FDA Black Box:** Congestive heart failure **(pioglitazone, rosiglitazone)** ▪ Fluid retention (edema; heart failure) ▪ Benefit in NASH ▪ Risk of bone fractures ▪ Bladder cancer (pioglitazone) ▪ ↑LDL cholesterol (rosiglitazone)
Sulfonylureas (2nd generation)	High	Yes	Gain	Neutral	Neutral	Low	Oral	Neutral	▪ Glyburide: generally not recommended in chronic kidney disease ▪ Glipizide and glimepiride: initiate conservatively to avoid hypoglycemia	▪ FDA Special Warning on increased risk of cardiovascular mortality based on studies of an older sulfonylurea (tolbutamide)
Insulin — Human insulin	High	Yes	Gain	Neutral	Neutral	Low (SQ)	SQ; inhaled	Neutral	▪ Lower insulin doses required with a decrease in eGFR; titrate per clinical response	▪ Injection site reactions ▪ Higher risk of hypoglycemia with human insulin (NPH or premixed formulations) vs. analogs
Insulin — Analogs						High	SQ			

ASCVD, atherosclerotic cardiovascular disease; CV, cardiovascular; CVOT, cardiovascular outcomes trial; DPP-4, dipeptidyl peptidase 4; DKA, diabetic ketoacidosis; DKD, diabetic kidney disease; eGFR, estimated glomerular filtration rate; GI, gastrointestinal; GLP-1 RAs, glucagon-like peptide 1 receptor agonists; HF, heart failure; NASH, nonalcoholic steatohepatitis; SGLT2, sodium–glucose cotransporter 2; SQ, subcutaneous; T2D, type 2 diabetes. *For agent-specific dosing recommendations, please refer to the manufacturers' prescribing information. †FDA-approved for cardiovascular disease benefit. ‡FDA-approved for heart failure indication. §FDA-approved for chronic kidney disease indication.

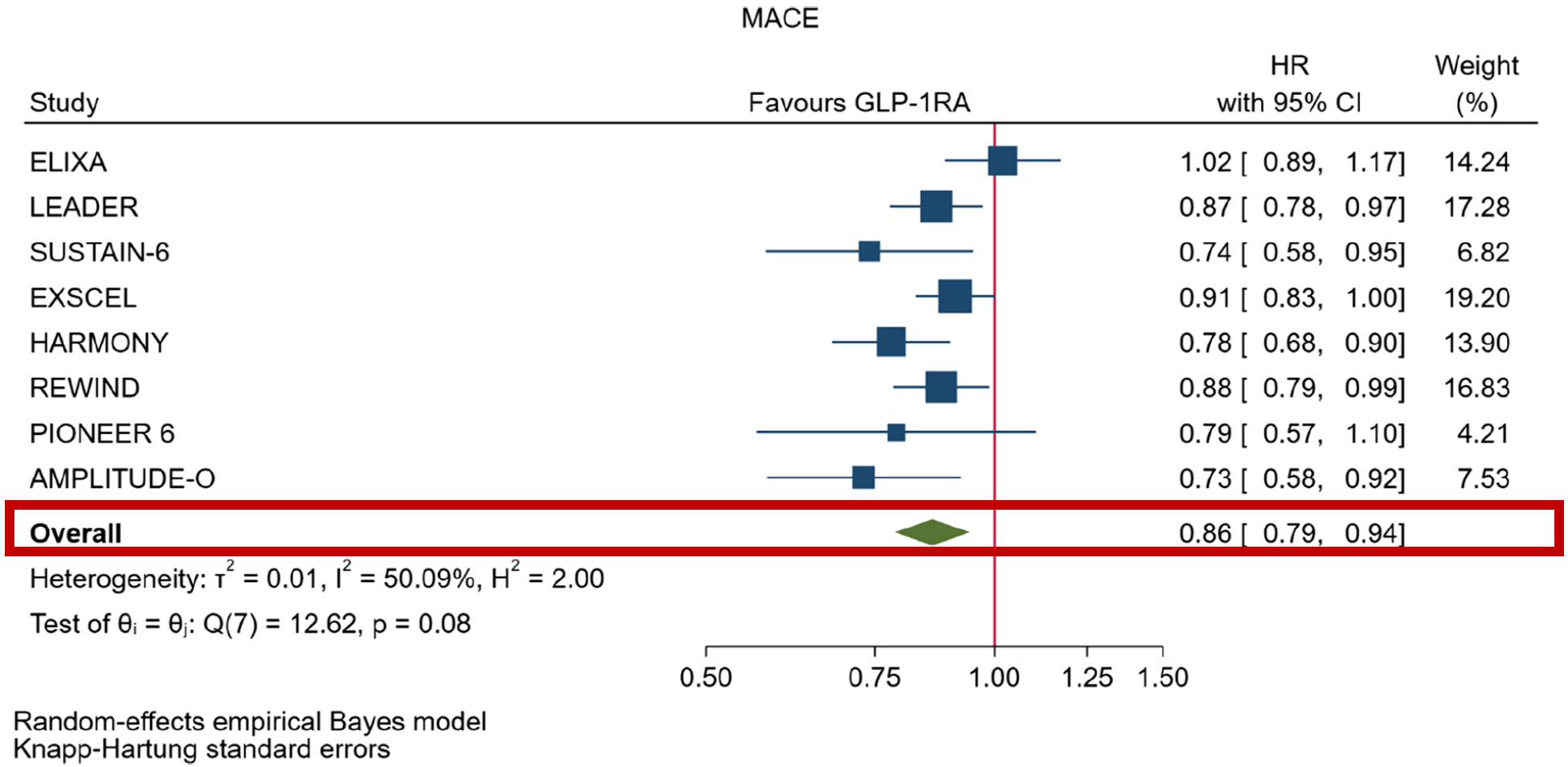
Diabetes Care Volume 45, Supplement 1, January 2022

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Estudios de seguridad cardiovascular aGLP-1



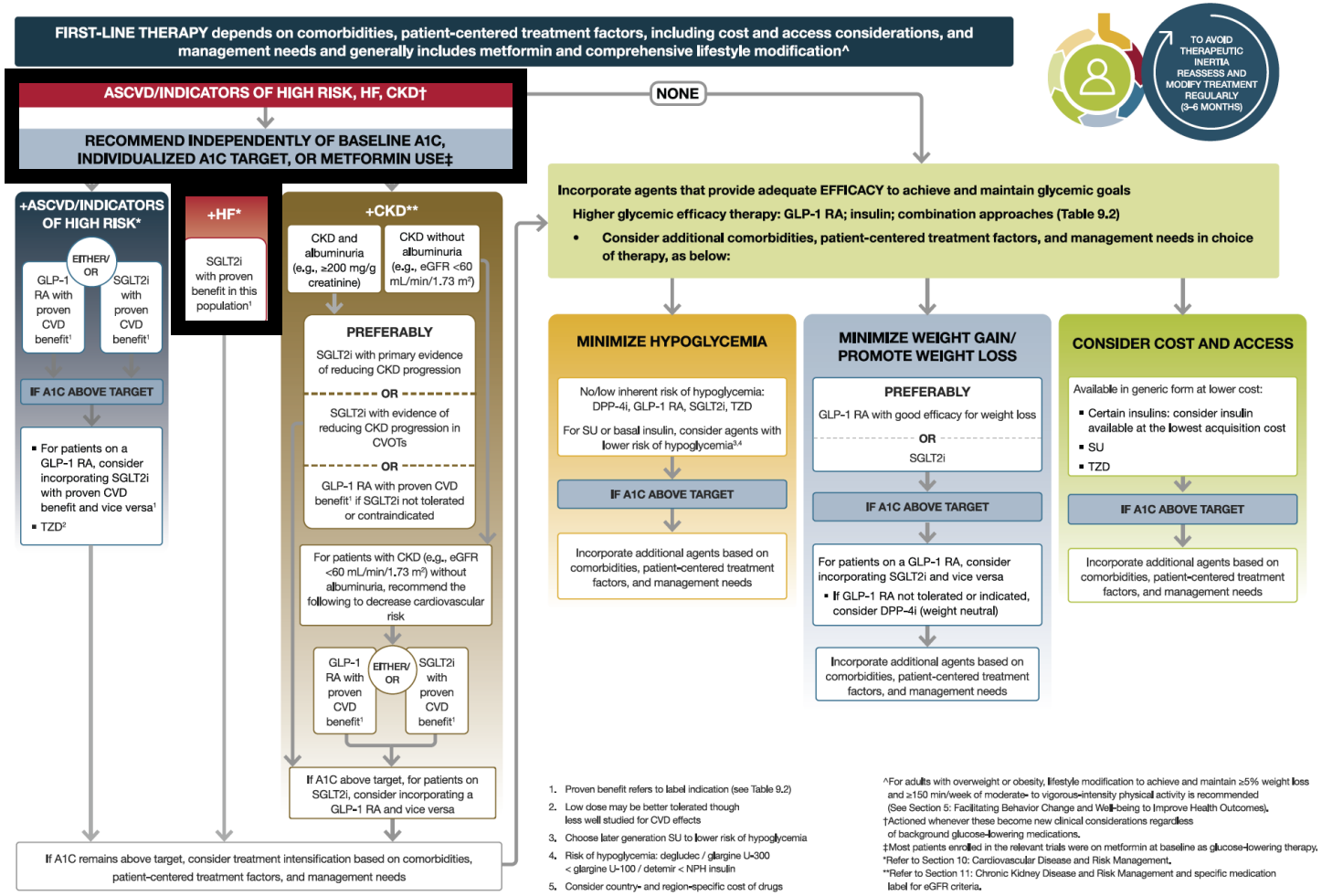
Giugliano et al. Cardiovasc Diabetol (2021) 20:189

iSGLT-2 beneficios cardiovasculares vrs placebo y aGLP-1

Desenlace cardiovascular	Hussein y colaboradores, 2019 (aGLP-1)	Hussein y colaboradores, 2019 (cuidado estándar)
MACE	HR: 1,02 (IC 95 %: 0,83 a 1,23)	0,86 (IC 95 %: 0,74 a 1,01)
ACV no fatal	HR: 0,86 (IC 95 %: 0,55 a 1,30)	1,03 (IC 95 %: 0,74 a 1,43)
IAM no fatal	HR: 1,08 (0,82 a 1,37)	0,87 (IC 95 %: 0,72 a 1,07)
Mortalidad cardiovascular	HR: 1,18 (0,86 a 1,59)	0,77 (IC 95 %: 0,61 a 0,99)
Mortalidad todas las causas	HR: 1,13 (0,92 a 1,39)	0,80 (IC 95 %: 0,68 a 0,95)
Ingreso hospitalario por insuficiencia cardíaca	HR: 0,71 (IC 95 %: 0,53 a 0,93)	0,67 (IC 95 %: 0,53 a 0,85)

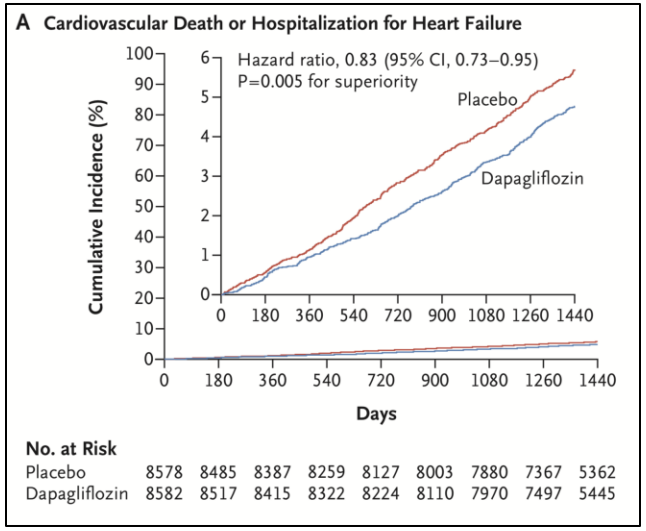
Diabet Med. 2019;36(4):444-452.

ADA 2022

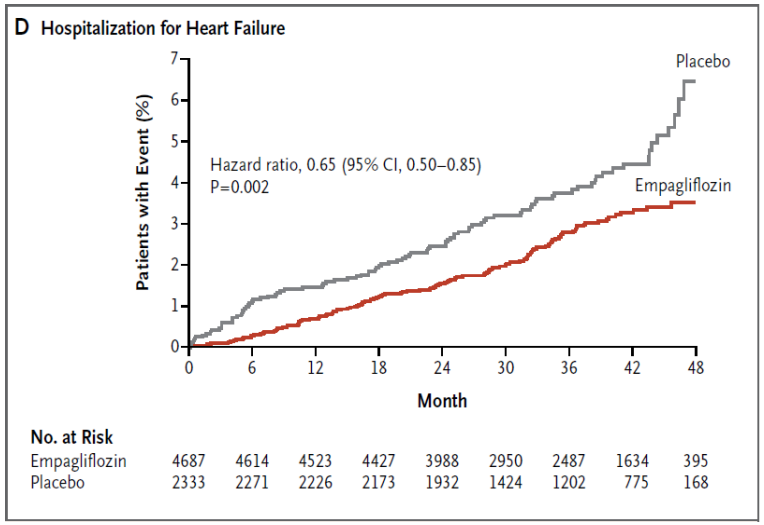


Diabetes Care Volume 45, Supplement 1, January 2022

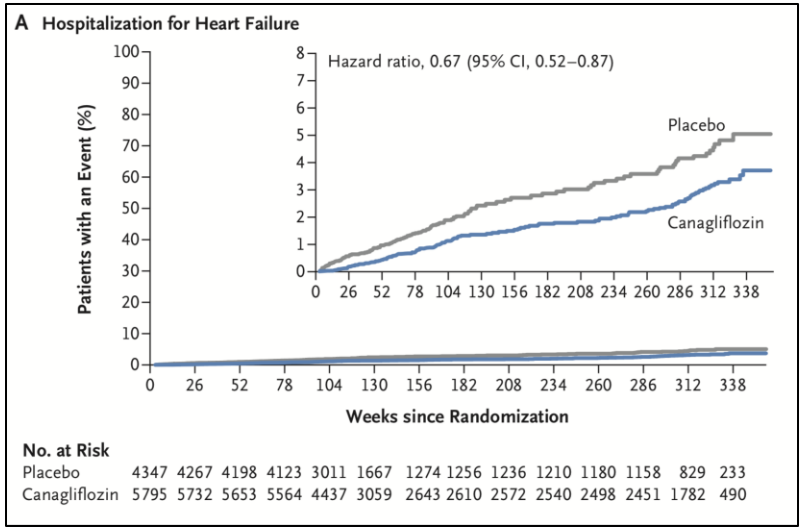
iSGLT-2 insuficiencia cardiaca



DECLARE



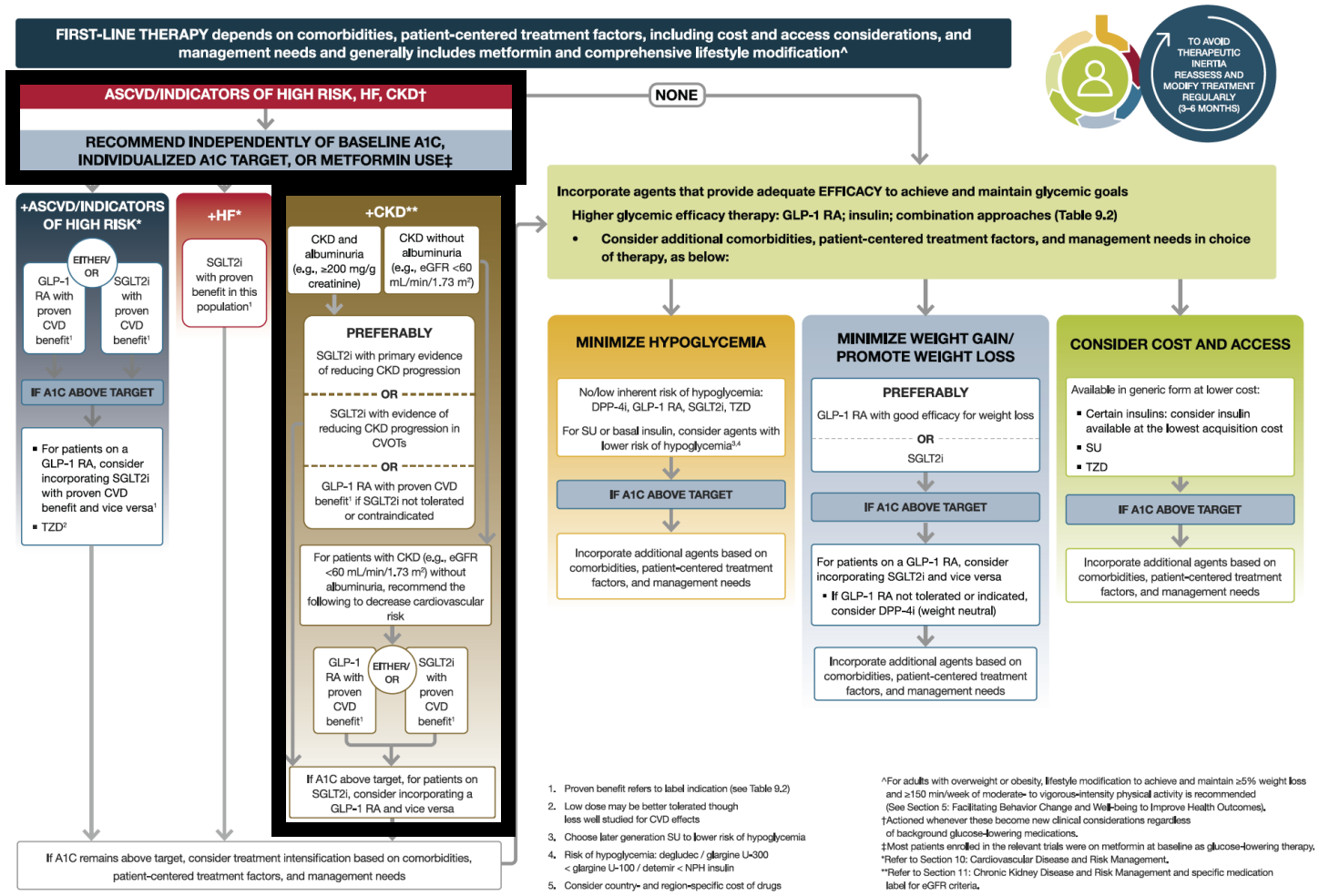
EMPA-REG



CANVAS

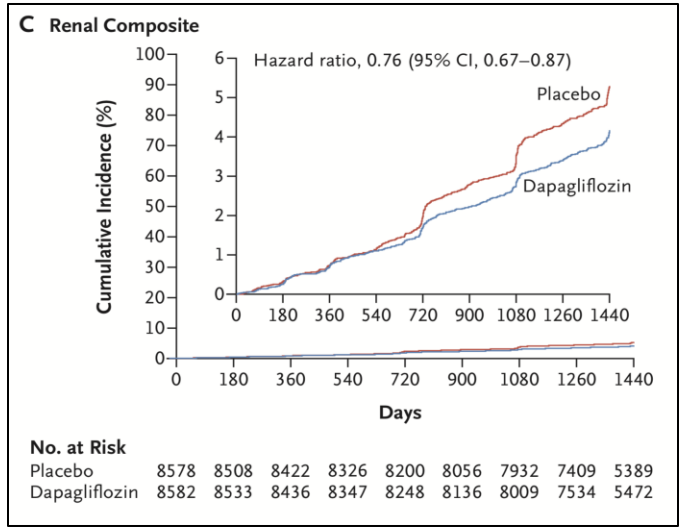
N Engl J Med 2015;373:2117-28. N Engl J Med 2017;377:644-57. N Engl J Med 2019;380:347-57.

ADA 2022

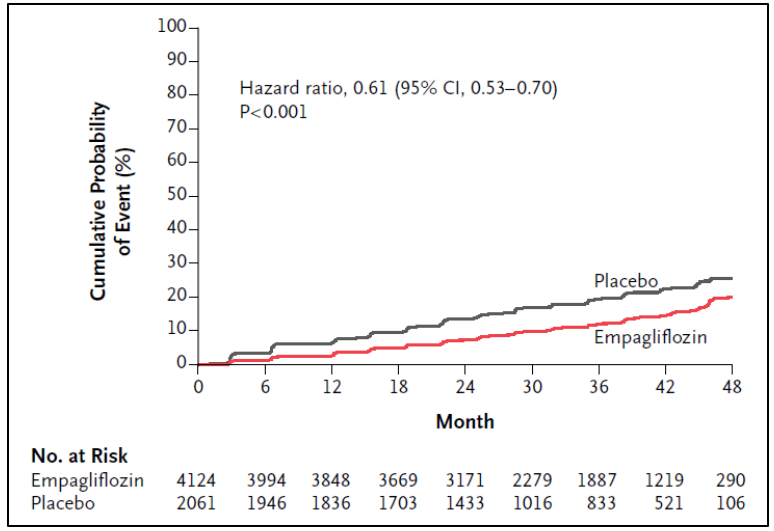


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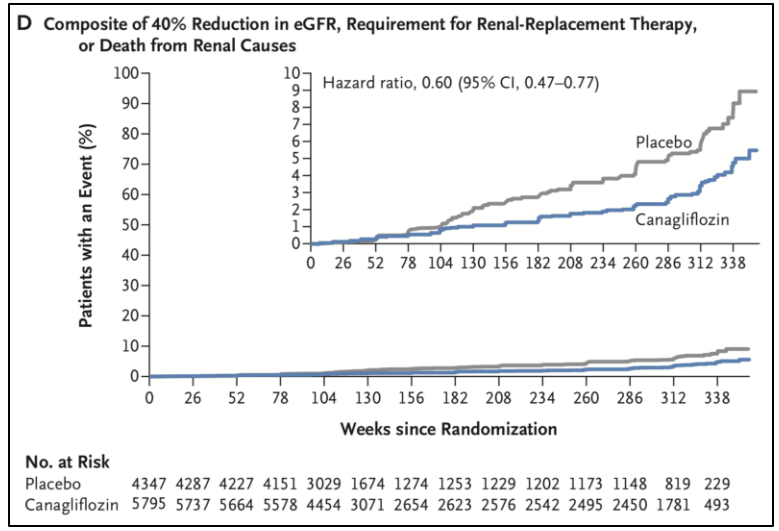
iSGLT-2 compuesto renal



DECLARE



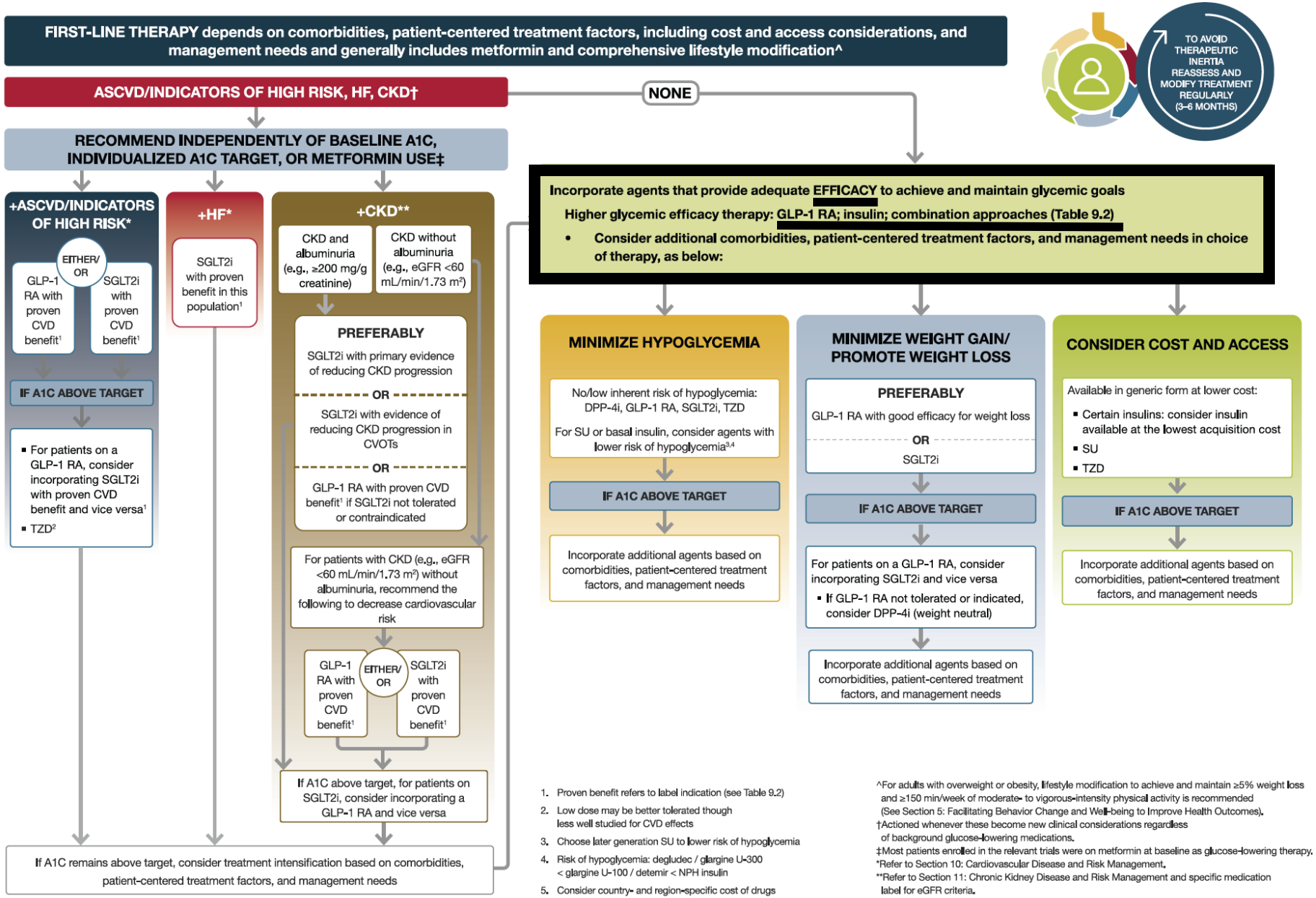
EMPA-REG



CANVAS

N Engl J Med 2015;373:2117-28. N Engl J Med 2017;377:644-57. N Engl J Med 2019;380:347-57.

ADA 2022

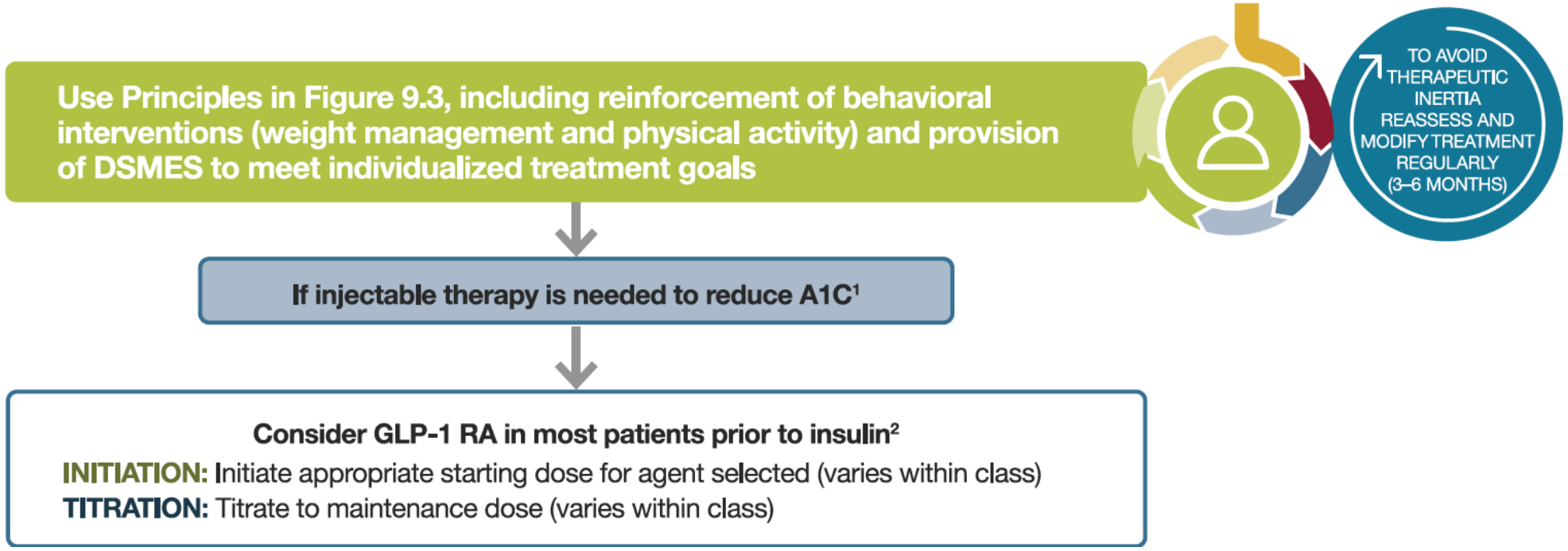


1. Proven benefit refers to label indication (see Table 9.2)
2. Low dose may be better tolerated though less well studied for CVD effects
3. Choose later generation SU to lower risk of hypoglycemia
4. Risk of hypoglycemia: degludec / glargine U-300 < glargine U-100 / detemir < NPH insulin
5. Consider country- and region-specific cost of drugs

^For adults with overweight or obesity, lifestyle modification to achieve and maintain ≥5% weight loss and ≥150 min/week of moderate- to vigorous-intensity physical activity is recommended (See Section 5: Facilitating Behavior Change and Well-being to Improve Health Outcomes).
†Actioned whenever these become new clinical considerations regardless of background glucose-lowering medications.
‡Most patients enrolled in the relevant trials were on metformin at baseline as glucose-lowering therapy.
*Refer to Section 10: Cardiovascular Disease and Risk Management.
**Refer to Section 11: Chronic Kidney Disease and Risk Management and specific medication label for eGFR criteria.

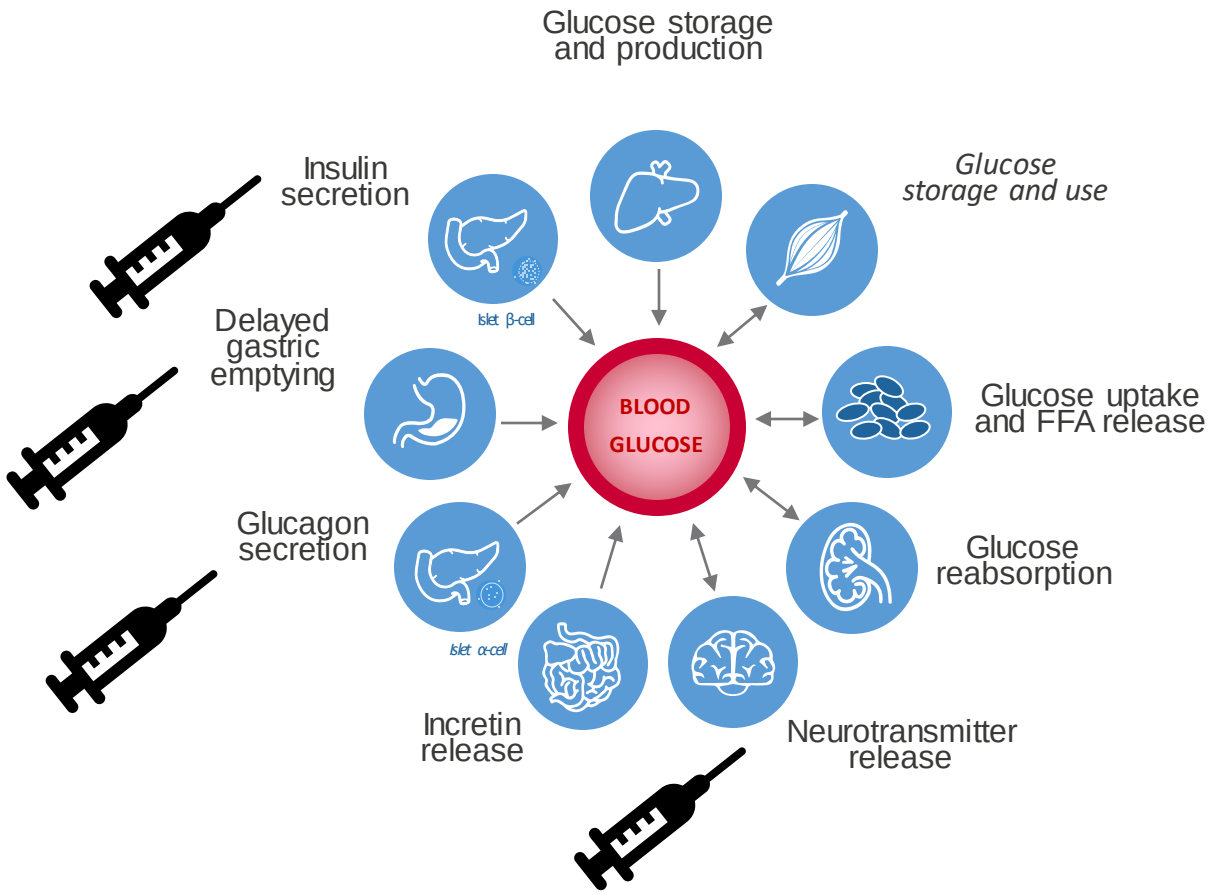
Diabetes Care Volume 45, Supplement 1, January 2022

ADA 2022 terapia inyectable



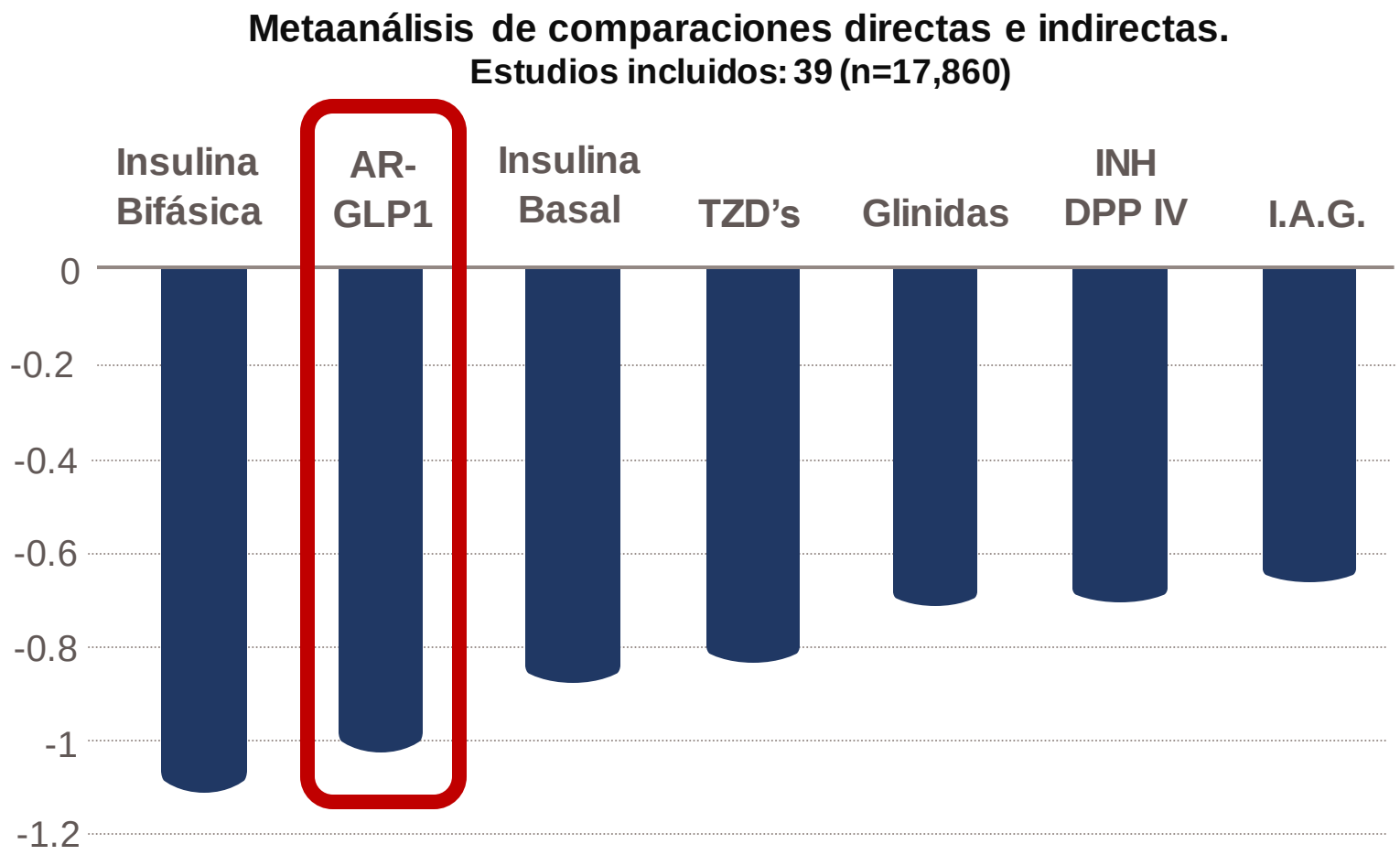
Diabetes Care Volume 45, Supplement 1, January 2022

Sitios de acción de aGLP-1



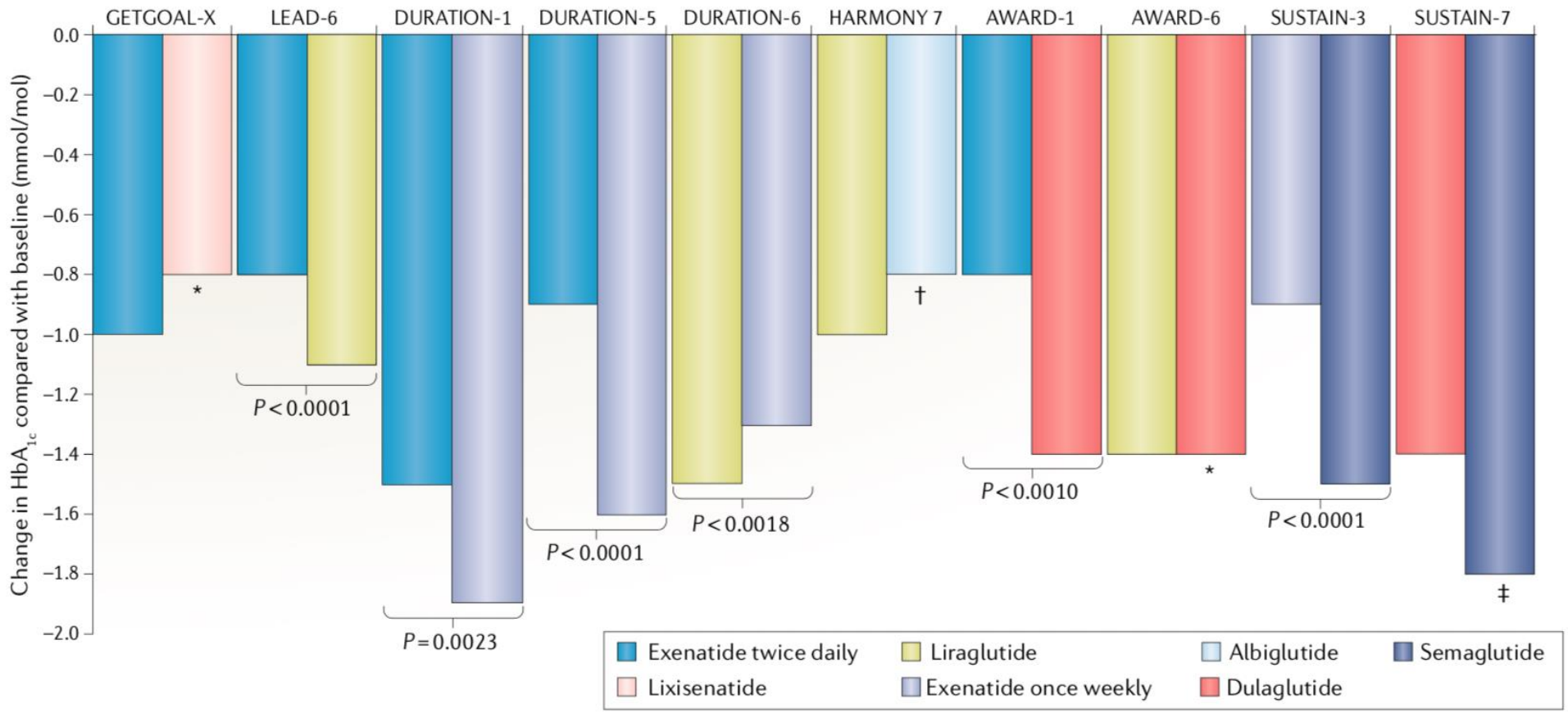
Bailey CJ, et al. Clin Pharmacol Therapeutics 2015;98:170–84
DeFronzo RA, et al. Diabetes 2009;58:773–95

Reducción HbA1C en diabéticos no controlados (HbA1c 7.5 - <10%)



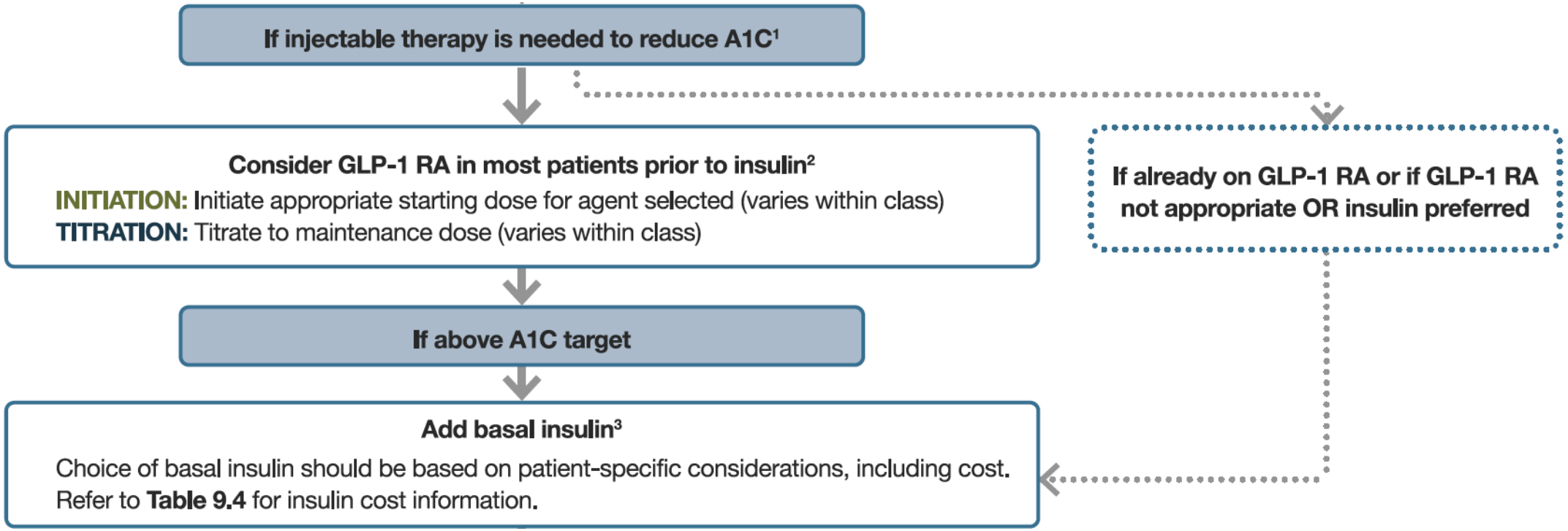
Liu SC ***Diabetes Obes Metab*** 2012: 14: 810–820

aGLP-1 HbA1C



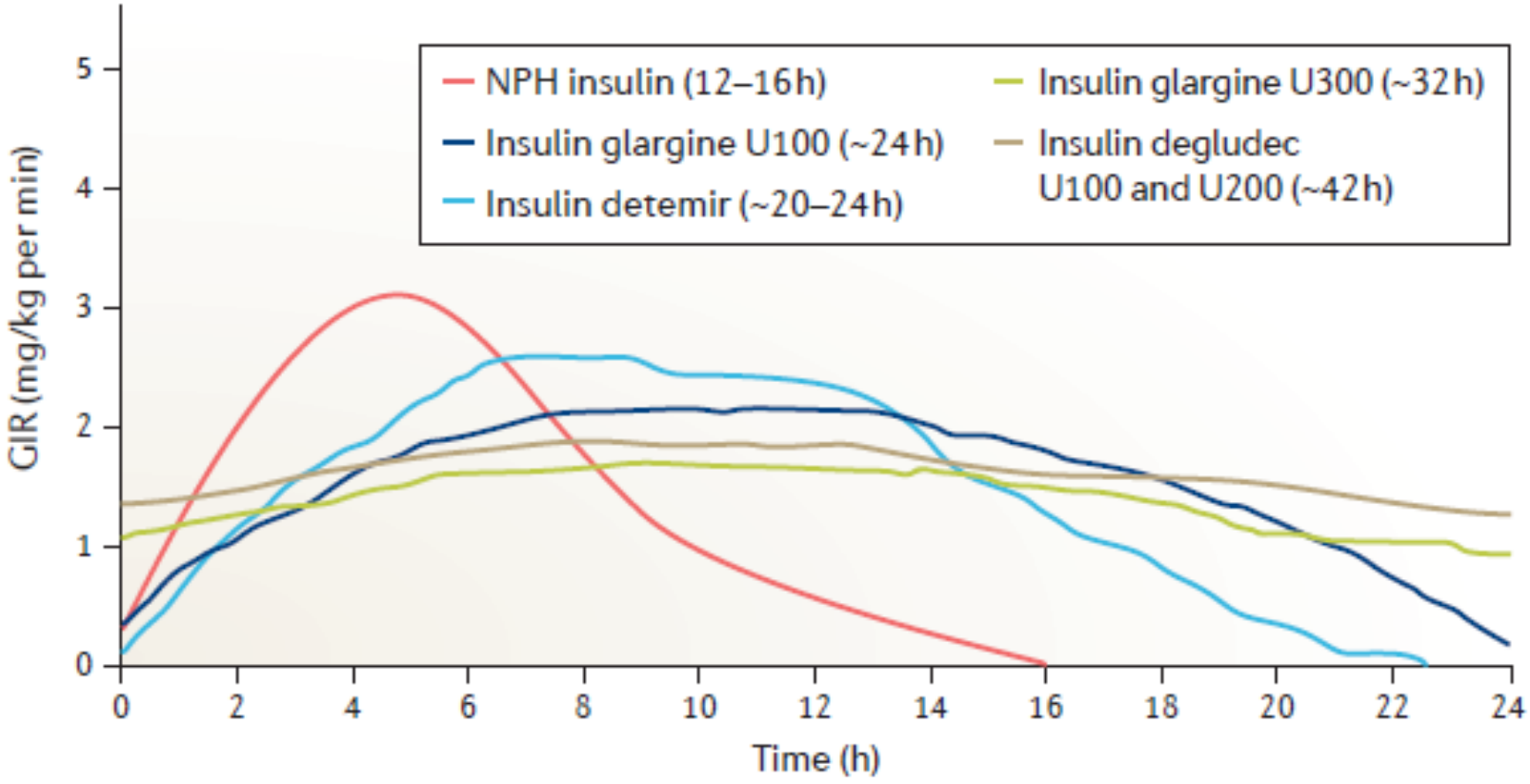
*Nature Reviews Endocrinology***volume 14**, pages390–403 (2018)

ADA 2022 terapia inyectable



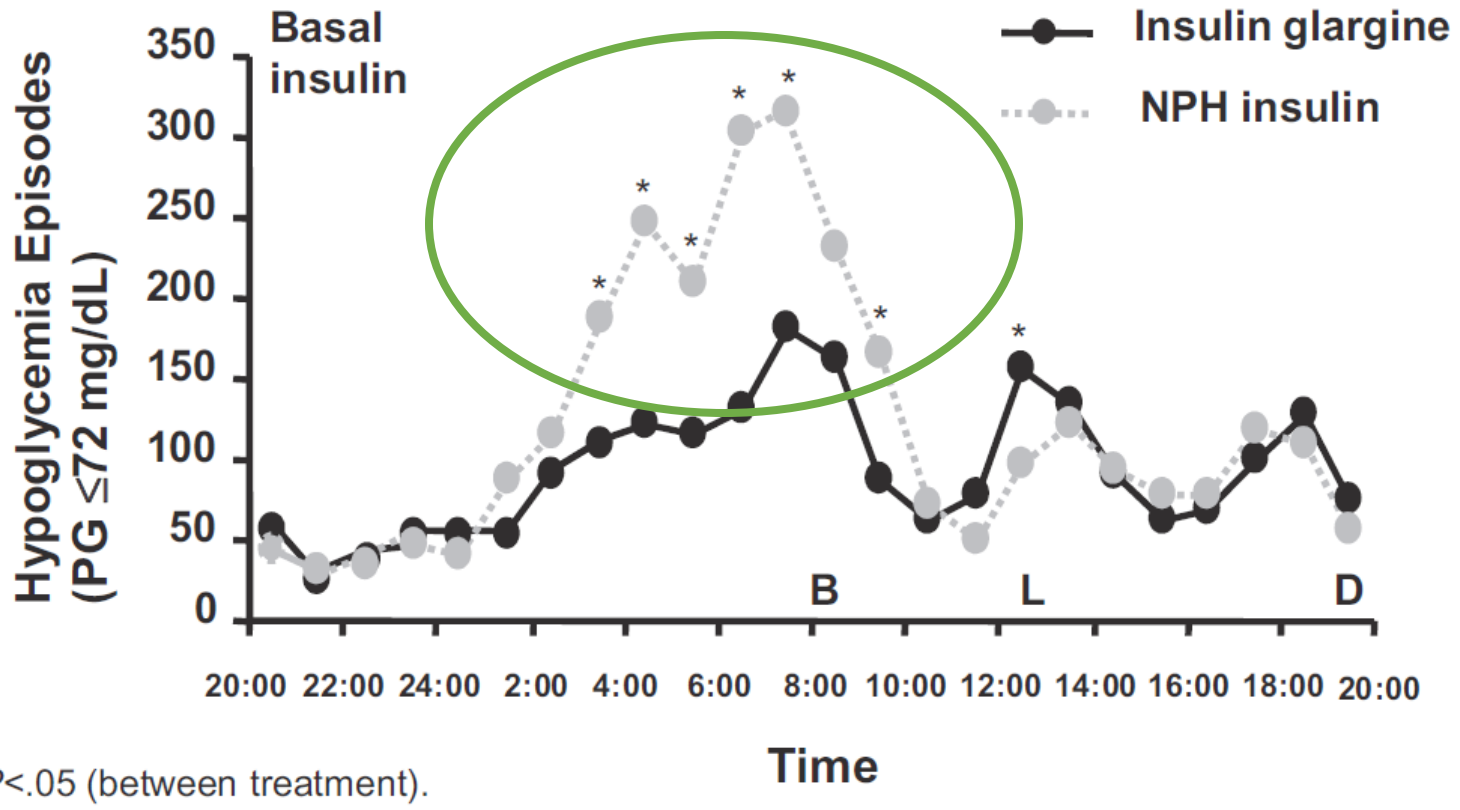
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Insulinas basales



Mathieu C, et al . Nature Reviews Endocrinology 13, 385–399 (2017)

Estudio Treat-to-Target

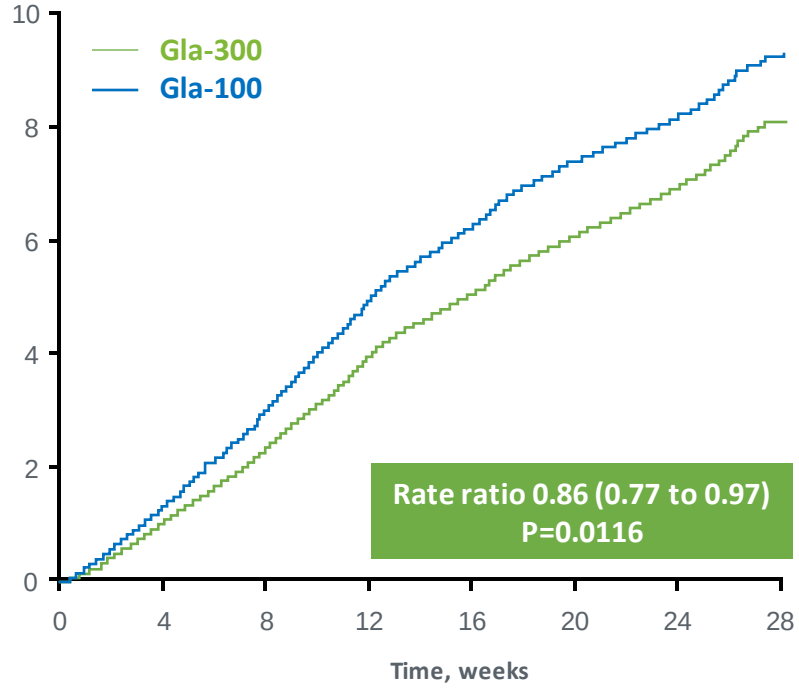


*P<.05 (between treatment).

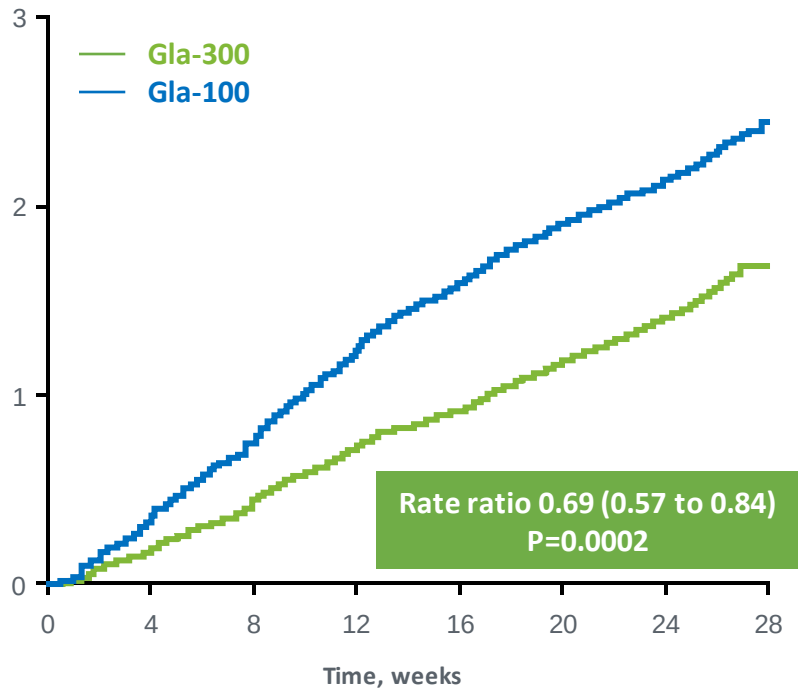
Diabetes Care 2003;26(11) 3080-6.

Hipoglicemia confirmada o severa

At any time of day (24 h)
Cumulative mean numbers of confirmed (≤70 mg/dL [≤3.9 mmol/L]) or severe events



Nocturnal (00:00–05:59 h)
Cumulative mean numbers of confirmed (≤70 mg/dL [≤3.9 mmol/L]) or severe events



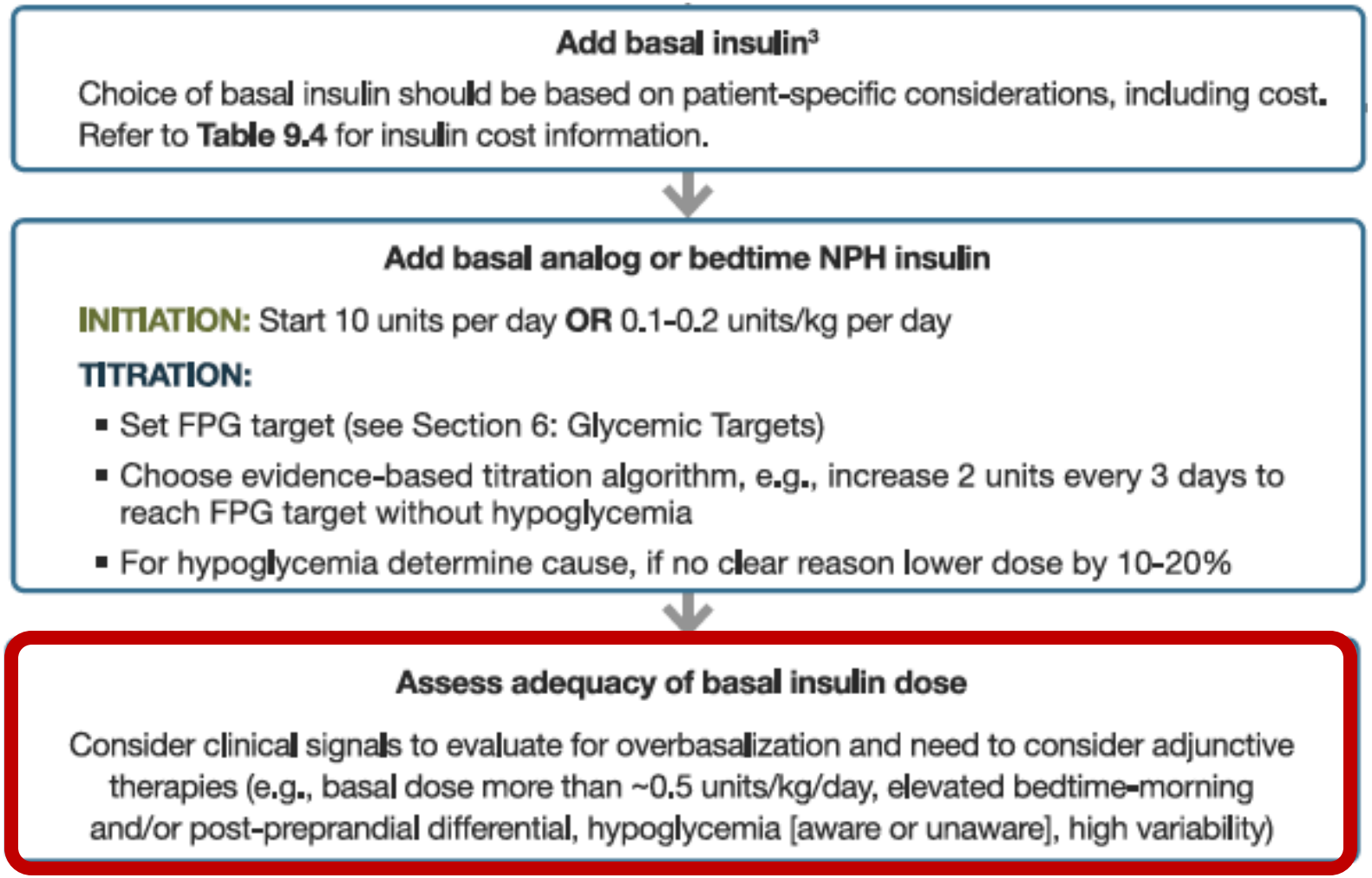
Adapted from Ritzel R et al. Diabetes Obes Metab. 2015;17:859-67

Hipoglicemia insulina basal

- Limitante
- Definir causa y corregir
- Sin causa evidente reducir dosis 10-20%

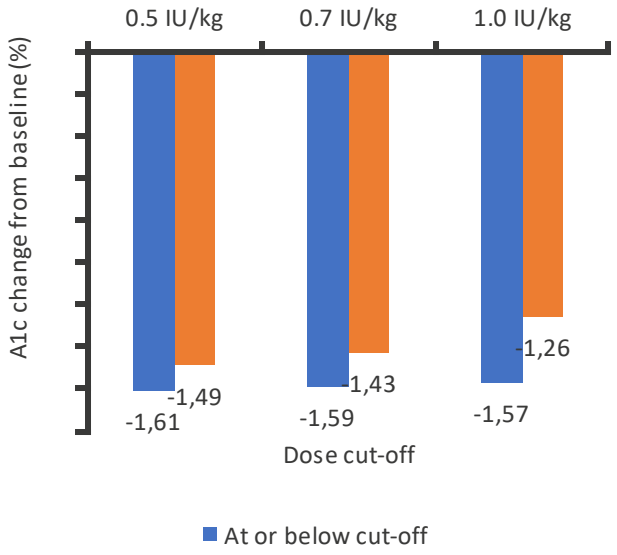
Diabetes Care Volume 45, Supplement 1, January 2022

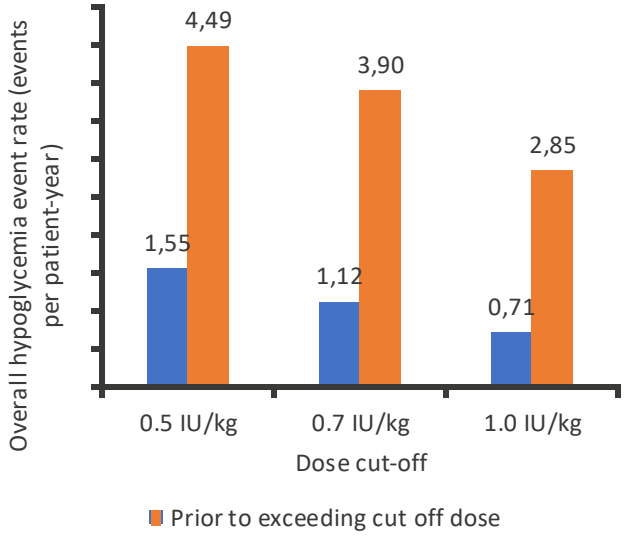
ADA 2022 terapia inyectable



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Sobrebasalización





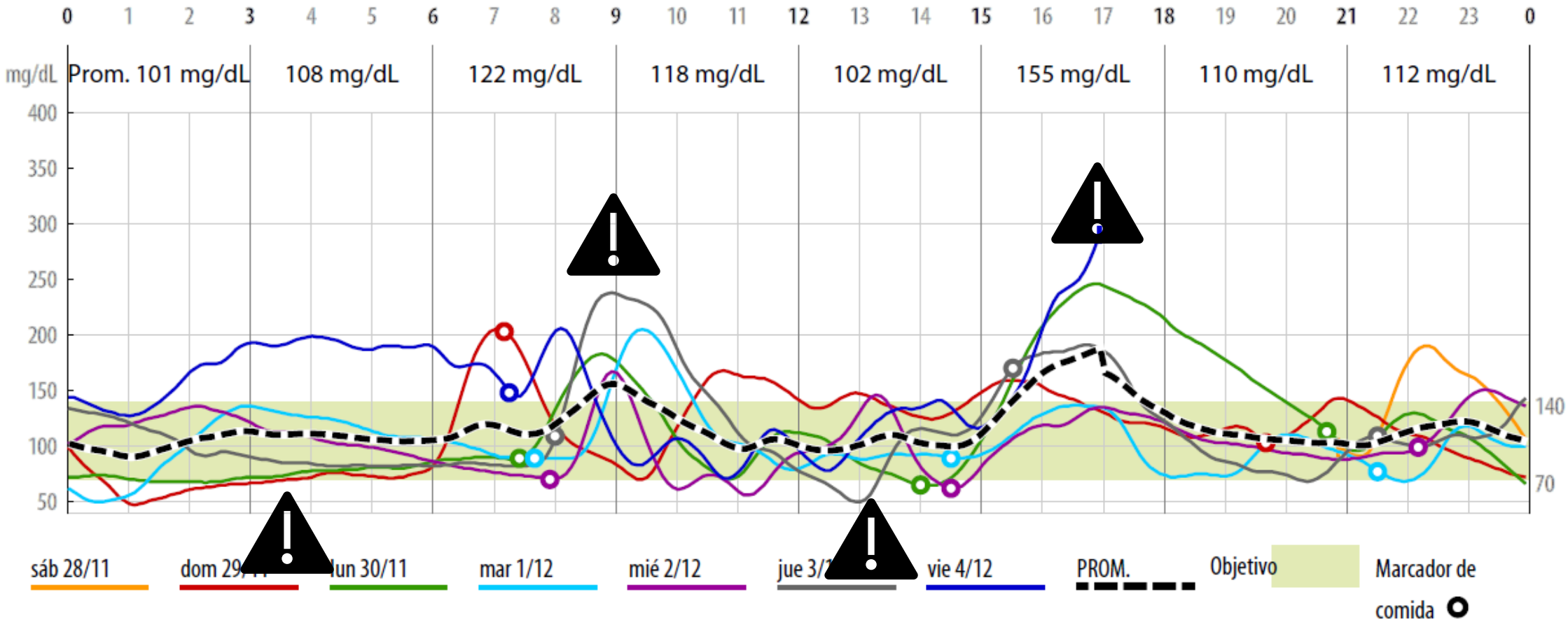
Análisis agrupado de perfiles de glucemia de 15 estudios treat-to-target en los que pacientes con DMT2 fueron tratados con insulina glargina y ADOs por ≥24 semanas (N=2837)

Reid T, et al. Int J Clin Pract 2016;70:56–65

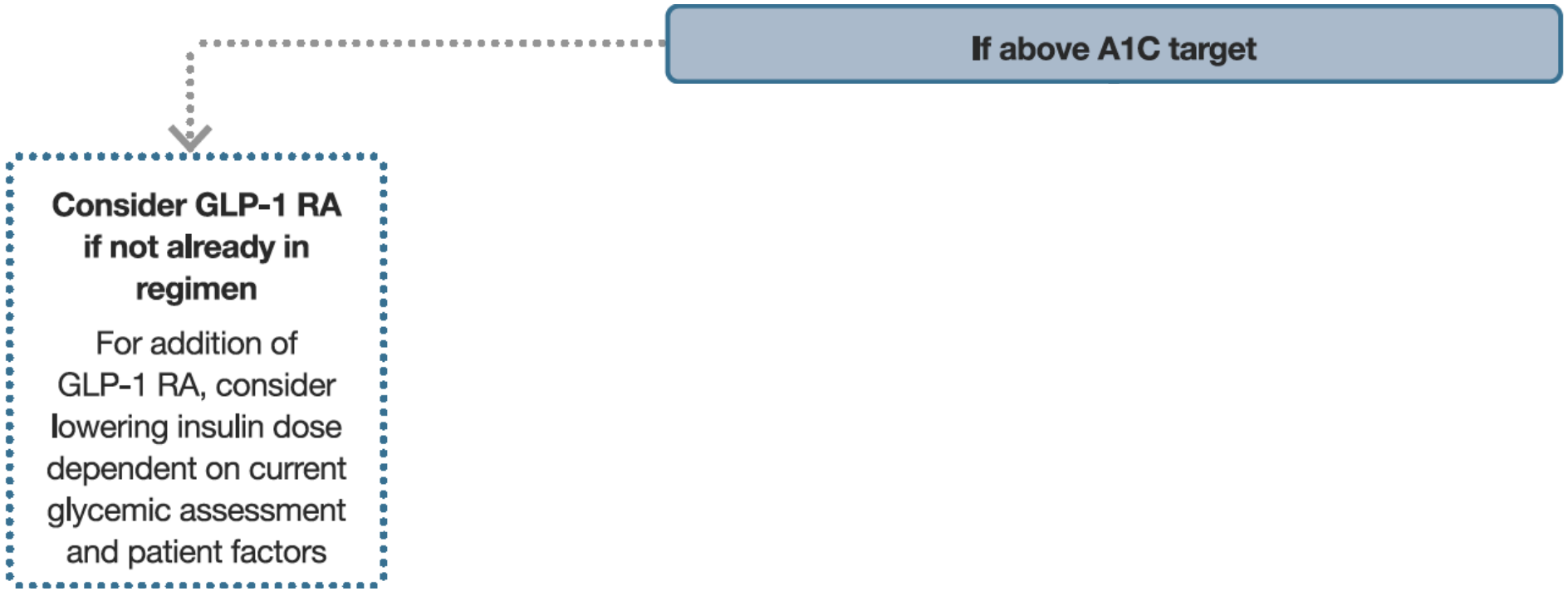
Sobrebasalización

- **Dosis basal > 0,5 U/kg/día**
- Hiperglicemia ayunas
- Hiperglicemia al acostarse
- Hipoglicemias
- Alta variabilidad glicémica

Sobrebasalización



ADA 2022 intensificación



Diabetes Care Volume 45, Supplement 1, January 2022

Mecanismos complementarios insulina basal y arGLP-1

Insulina Basal
Disminución de la producción hepática de glucosa al disminuir la gluconeogénesis y glucogenólisis.

Correlación clínica:
Control de Glucosa plasmática en ayuno (GPA)

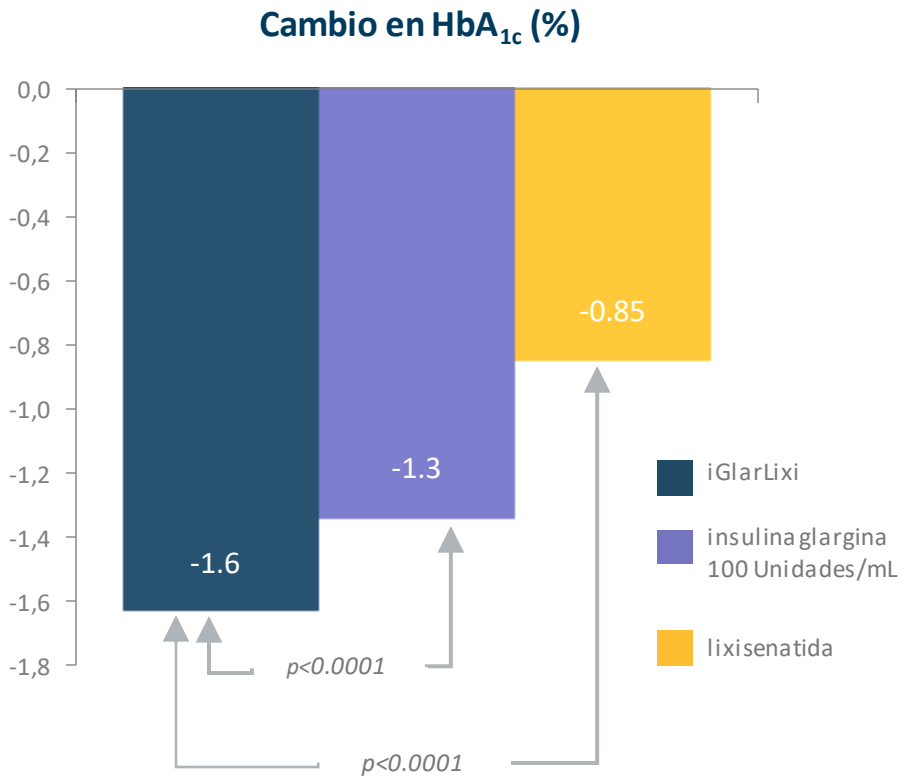
arGLP-1 de acción corta
Actúa en la función de la célula beta y alfa, retraso en el vaciamiento gástrico

Correlación clínica:
Control de Glucosa Postprandial (GPP)

Control glucémico más completo

Wang et al. Diab Care 2010; 33: 1555–60. 2. Baggio and Drucker Gastroenterol 2007; 132: 2131–57. 3. Holst et al. Physiol Rev 2007; 87: 1409–39

LixiLan O cambio HbA1C



Diabetes Care 2016;39:2026–2035

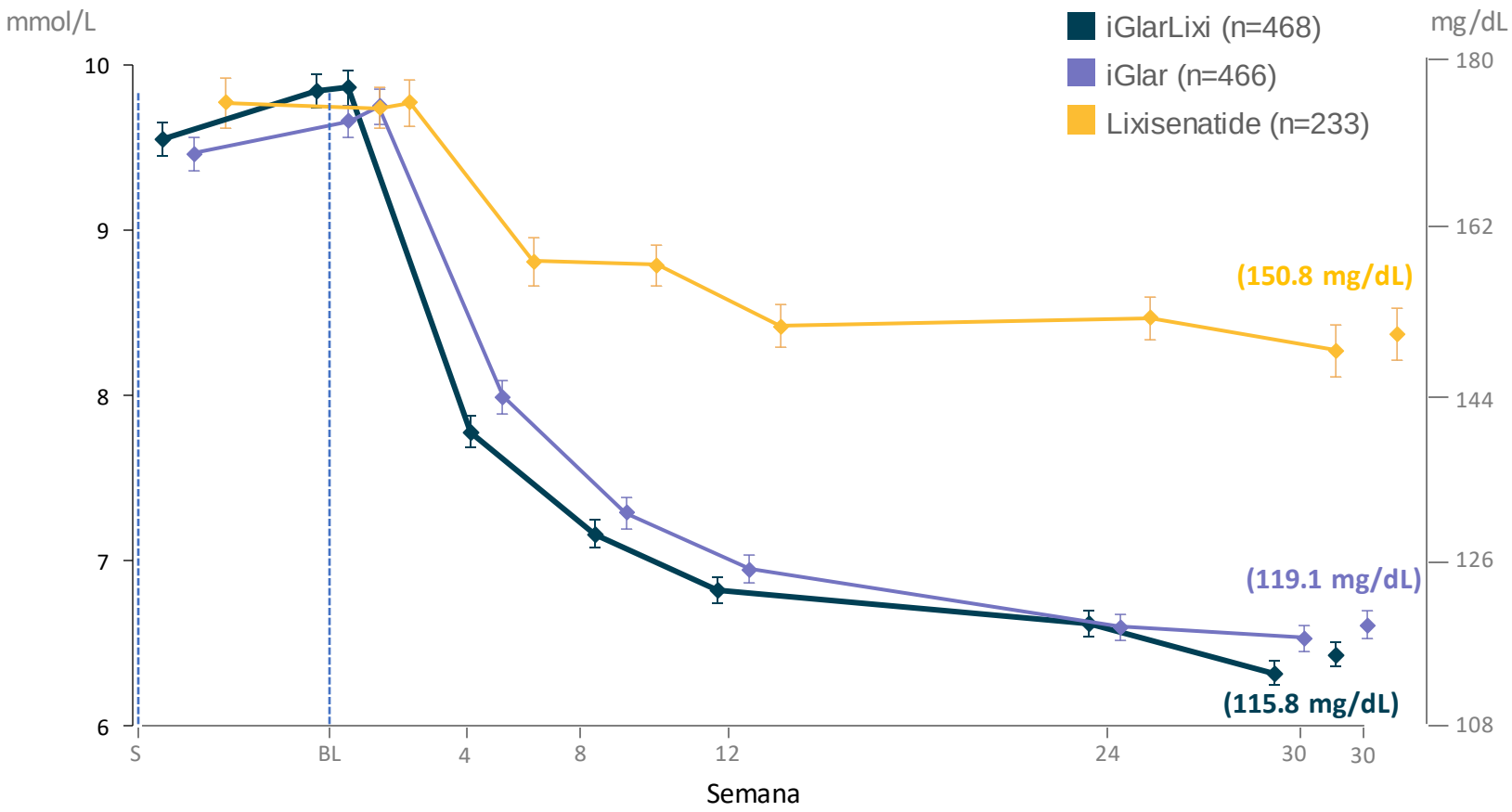
LixiLan O porcentaje d pacientes que logran meta HbA1C





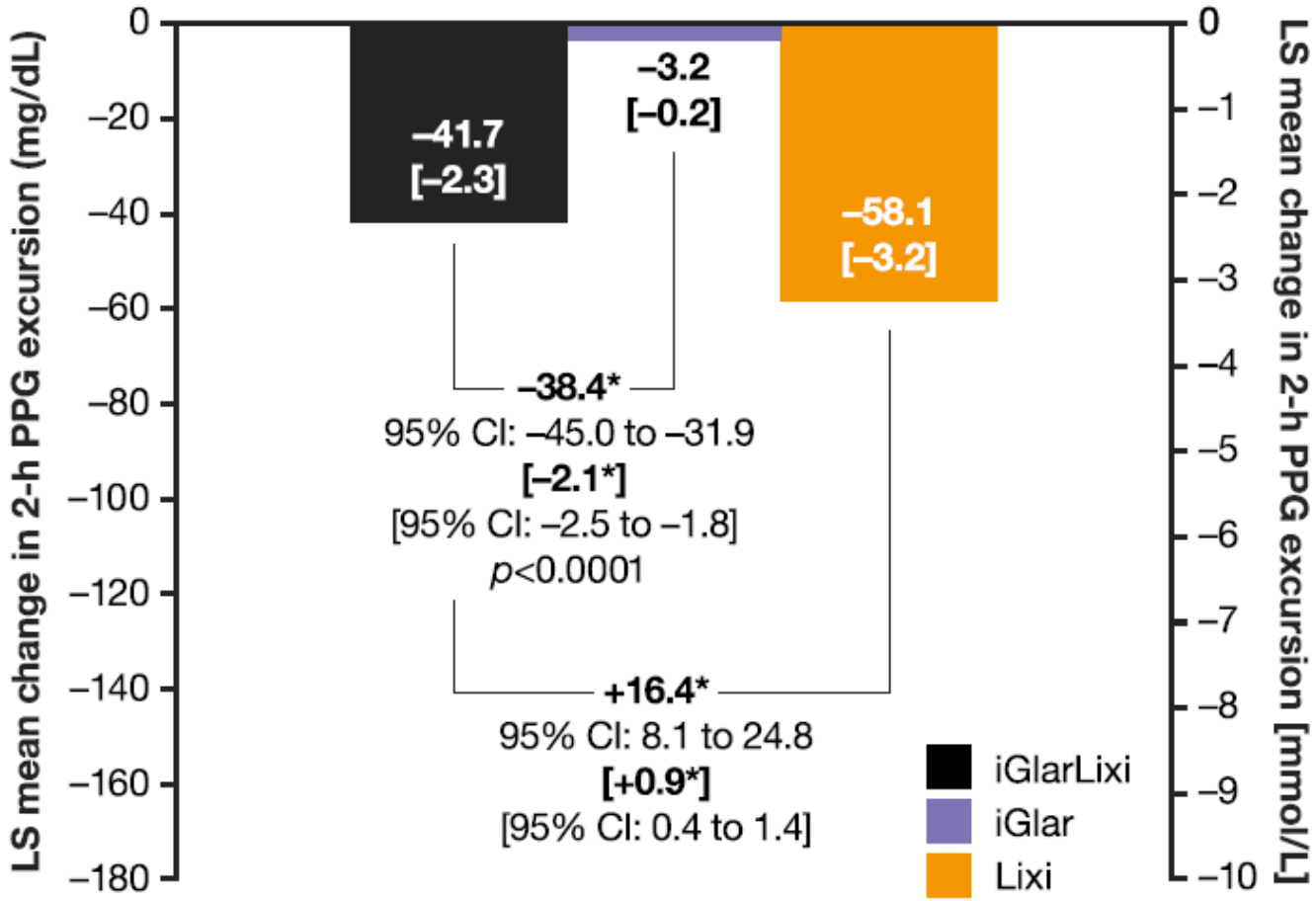
Diabetes Care 2016;39:2026–2035

LixiLan O glicemia ayunas



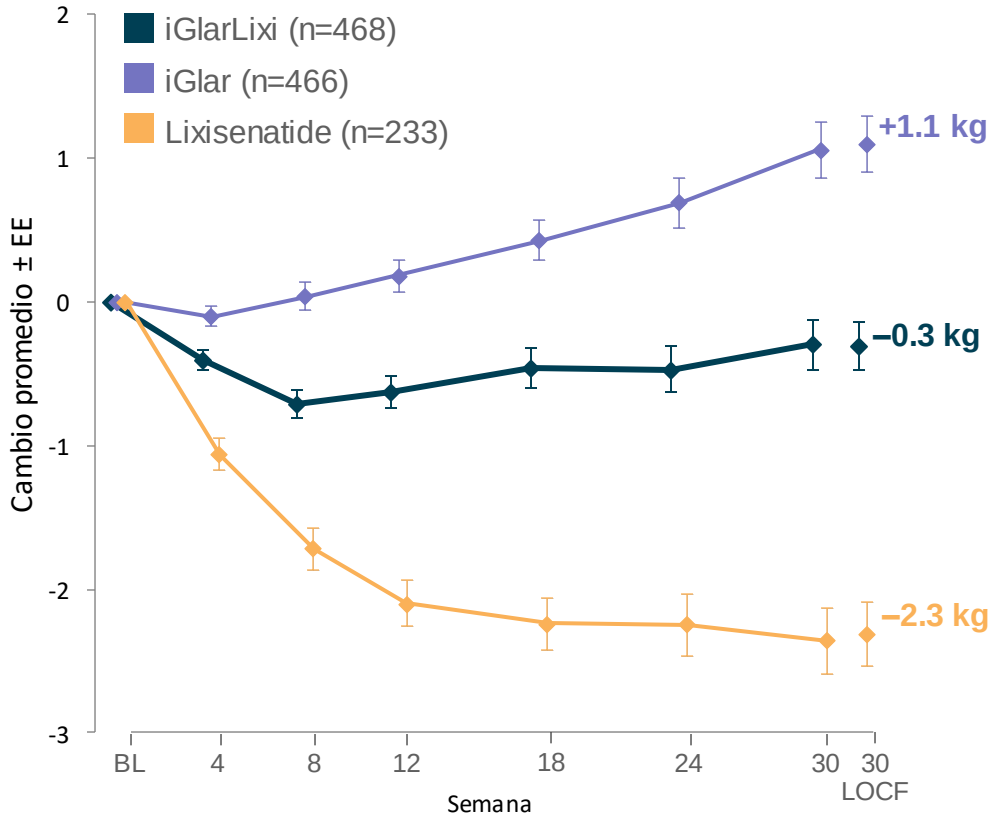
Diabetes Care 2016;39:2026–2035

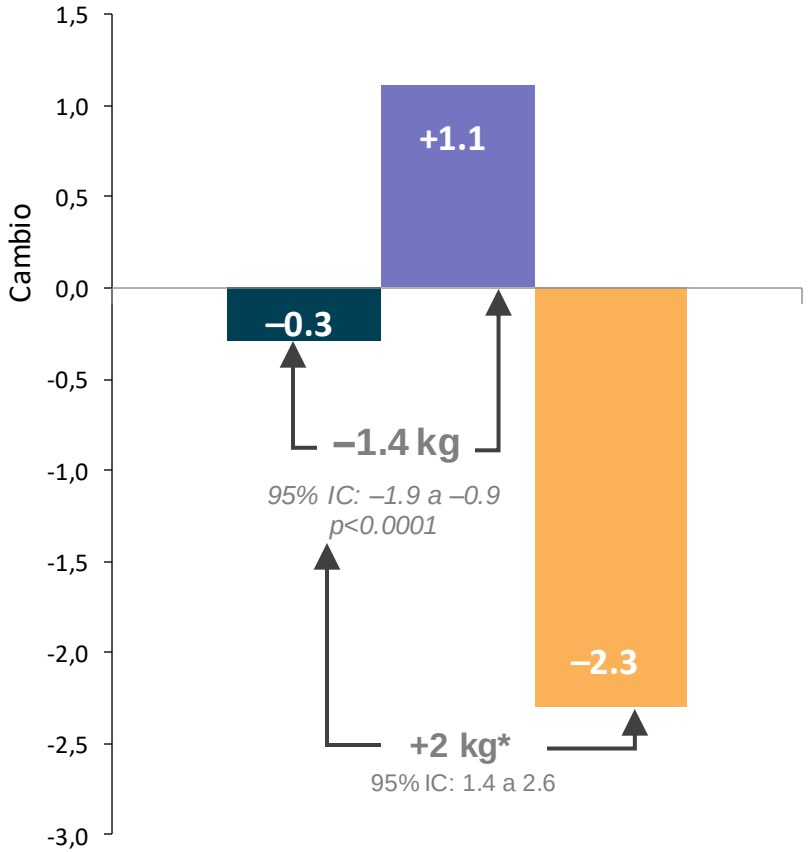
LixiLan O glicemia 2 hpp



Diabetes Care 2016;39:2026–2035

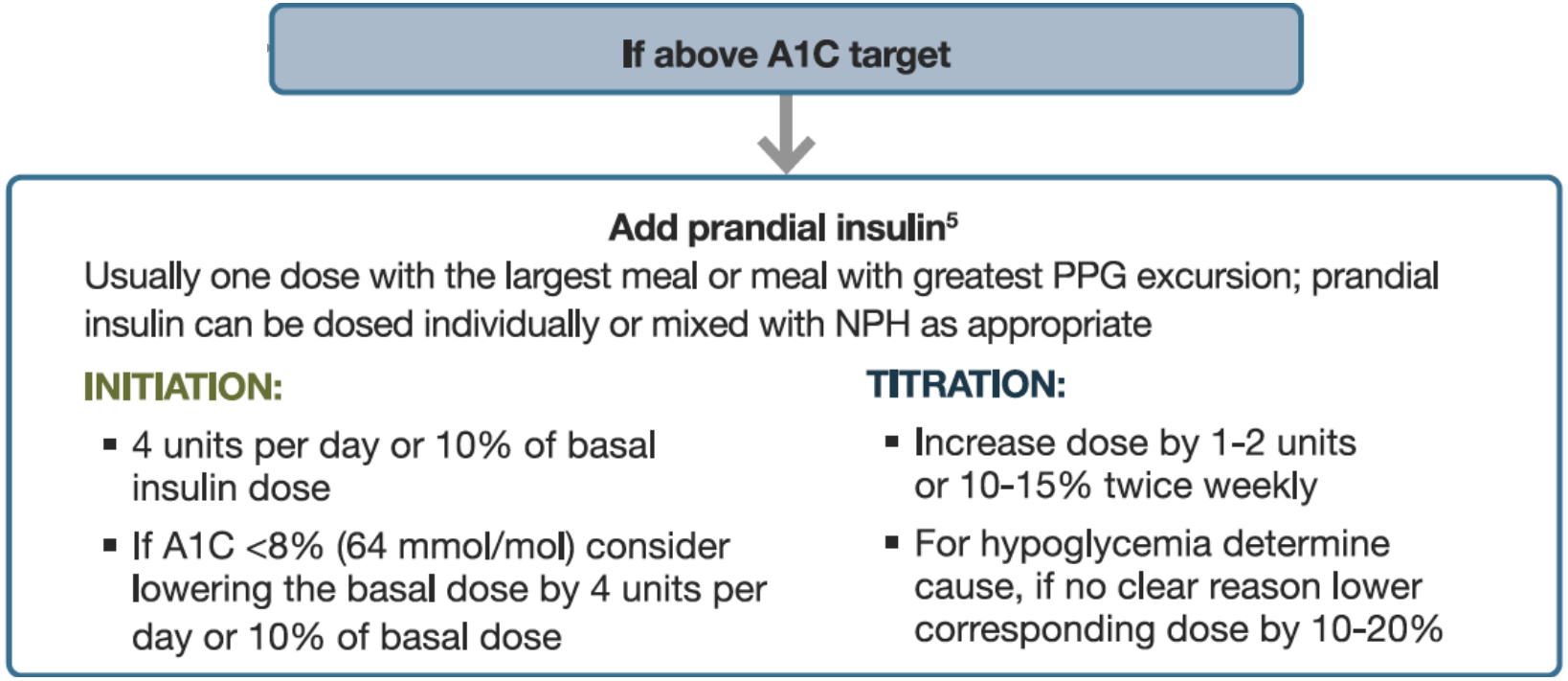
LixiLan O peso





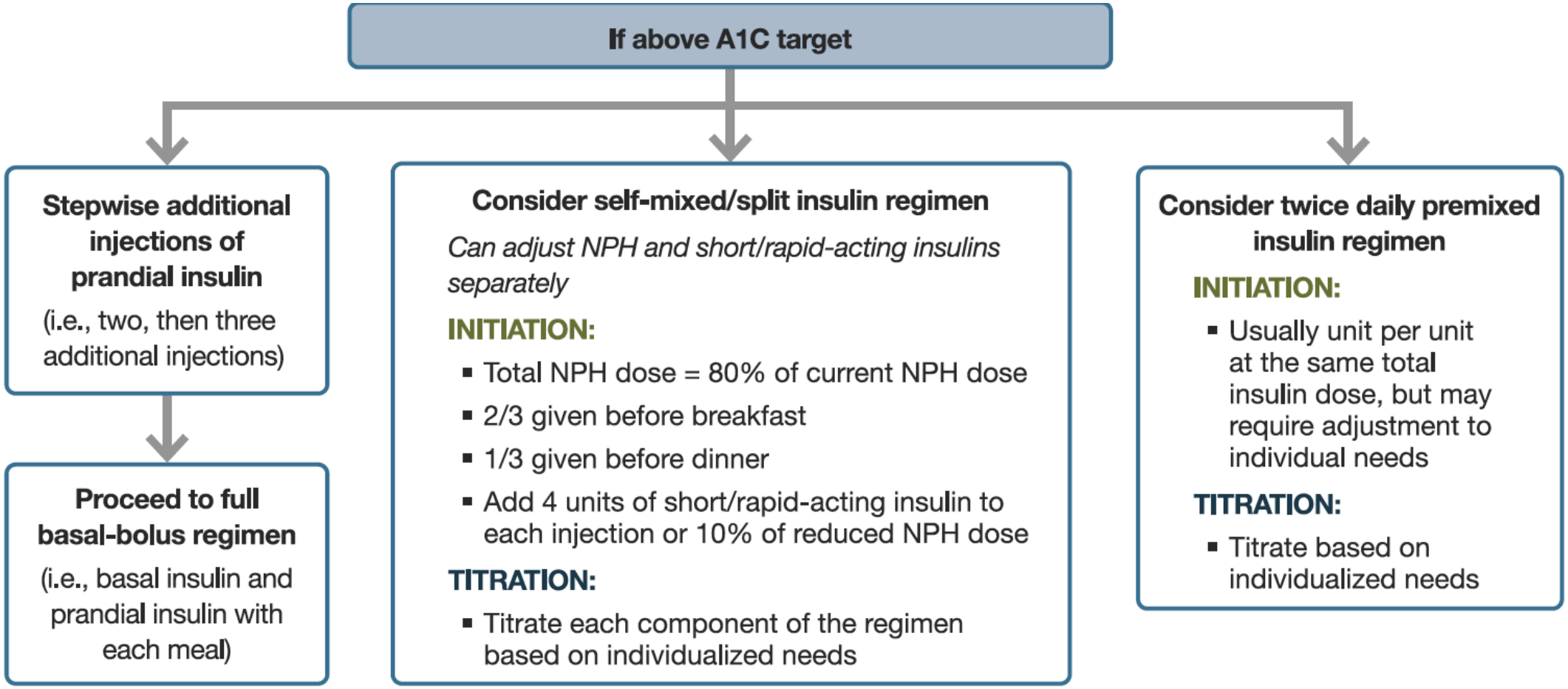
Diabetes Care 2016;39:2026–2035

ADA 2022 intensificación



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ADA 2022 intensificación



Diabetes Care Volume 45, Supplement 1, January 2022



Manejo de la presión arterial

ADA 2022 Presión arterial

- Toma de presión arterial en cada visita
- Debe de individualizarse las metas
- >120/80 mmHg intensificar estilos de vida

Diabetes Care Volume 45, Supplement 1, January 2022

ADA 2022 Presión arterial metas



Alto riesgo cardiovascular

<130/80 mmHg

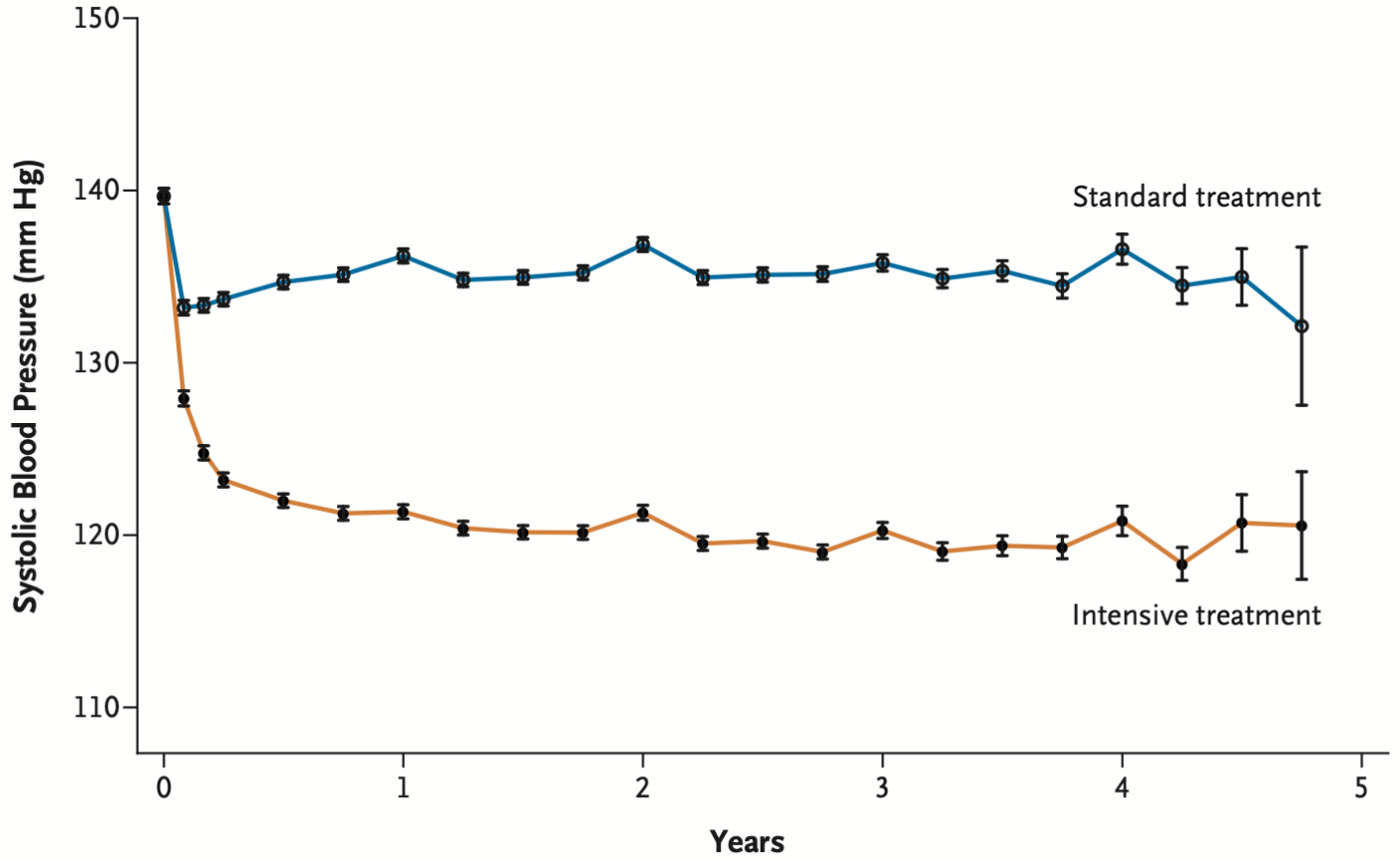


Bajo riesgo cardiovascular

<140/90 mmHg

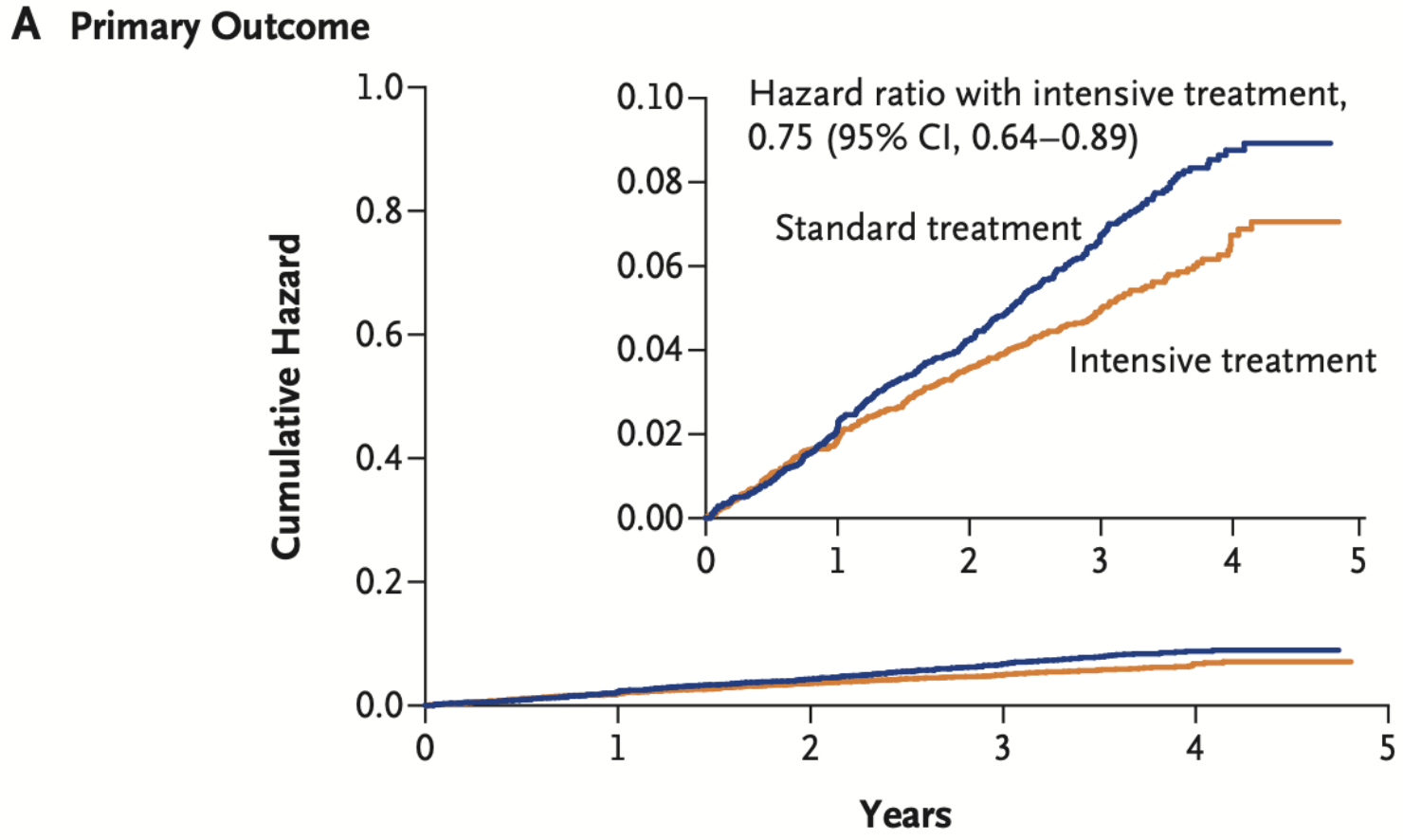
Diabetes Care Volume 45, Supplement 1, January 2022

SPRINT



N Engl J Med 2015;373:2103-16

SPRINT

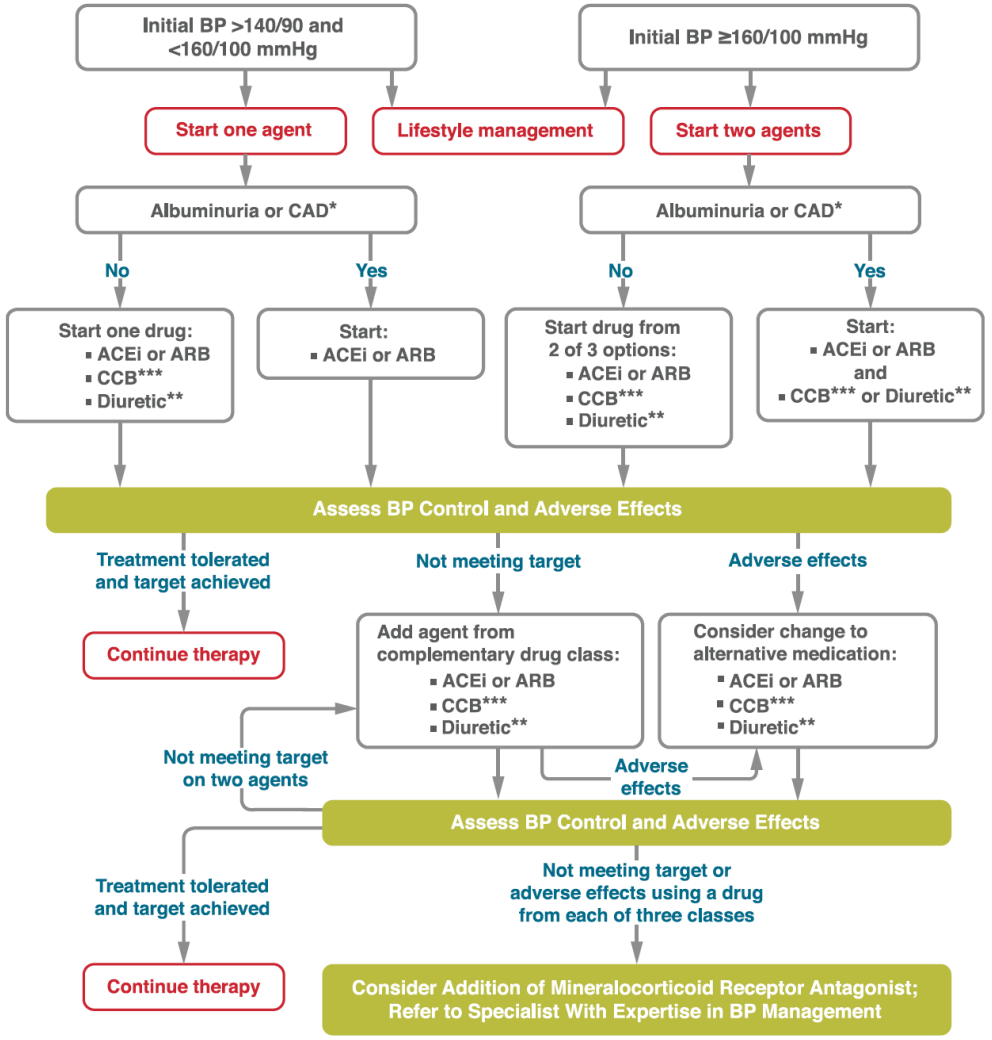


N Engl J Med 2015;373:2103-16

ADA 2022 Presión arterial fármacos

- Evidencia de reducción eventos cardiovasculares
- IECAS
- ARA II
- Calcio-antagonistas
- Diuréticos tiazídicos

Control de presión arterial



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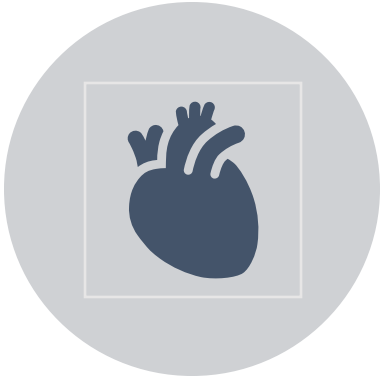
Manejo de lípidos

ADA 2022 prevención primaria



40 A 75 AÑOS

ESTATINA MODERADA INTENSIDAD



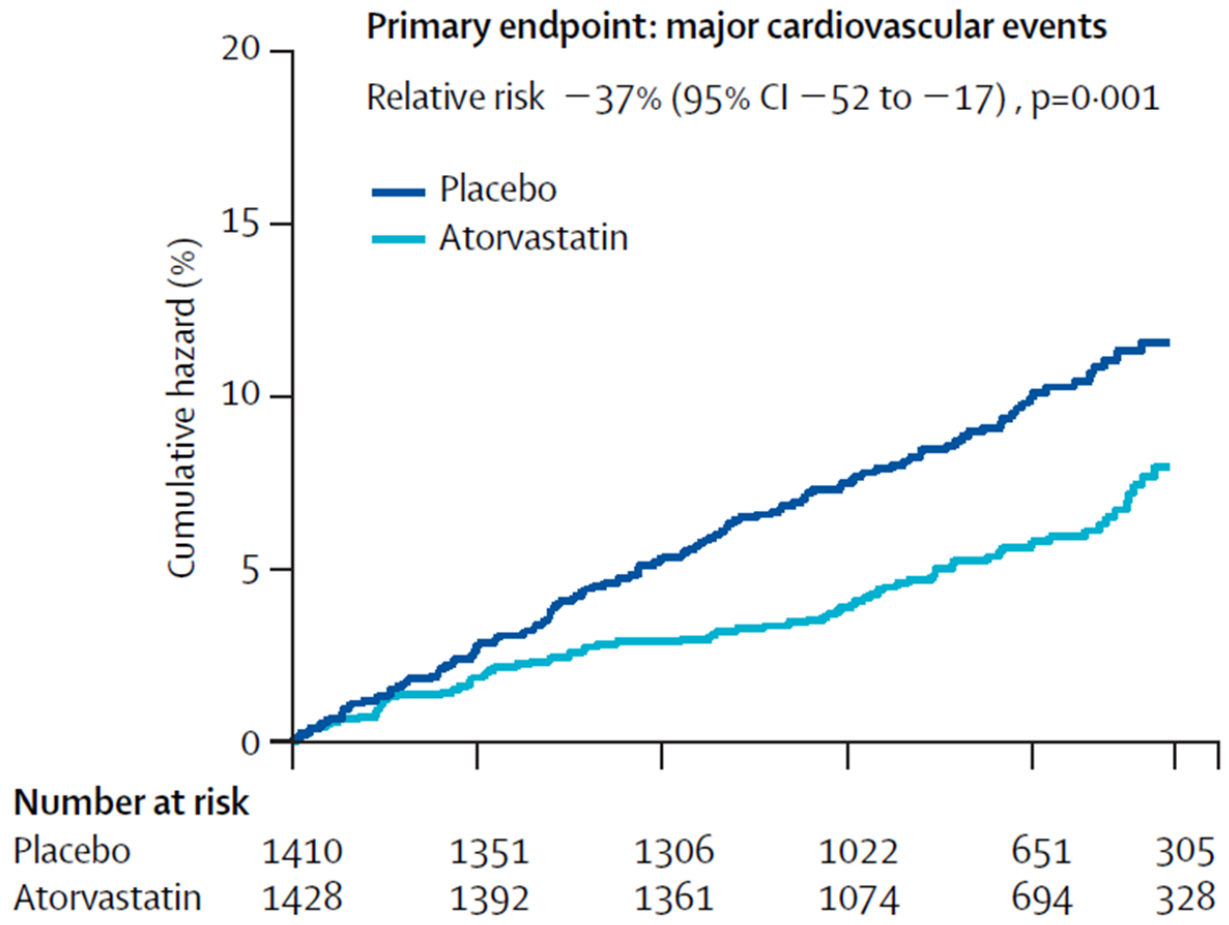
20 A 39 AÑOS CON FACTORES DE RIESGO CARDIOVASCULARES ADICIONALES USAR ESTATINA



50 A 70 AÑOS MÚLTIPLES FACTORES DE RIESGO CARDIOVASCULARES ESTATINA DE INTENSIDAD ALTA

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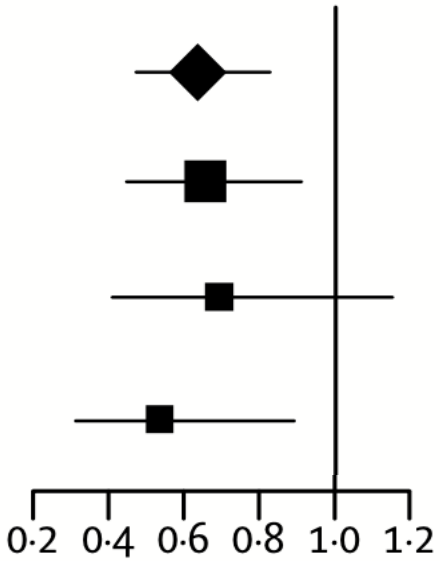
CARDS MACE



Lancet 2004; 364: 685–96

CARDS MACE

	Number of patients with an event (%)			
	Placebo	Atorvastatin 10 mg	Hazard ratio (95% CI)	p
Primary endpoint	127 (9·0%)	83 (5·8%)	0·63 (0·48–0·83)	0·001
Acute coronary events	77 (5·5%)	51 (3·6%)	0·64 (0·45–0·91)	
Coronary revascularisation	34 (2·4%)	24 (1·7%)	0·69 (0·41–1·16)	
Stroke	39 (2·8%)	21 (1·5%)	0·52 (0·31–0·89)	



Lancet 2004; 364: 685–96

Intensidad estatinas

Table 10.2—High-intensity and moderate-intensity statin therapy*

High-intensity statin therapy (lowers LDL cholesterol by ≥50%)	Moderate-intensity statin therapy (lowers LDL cholesterol by 30–49%)
Atorvastatin 40–80 mg	Atorvastatin 10–20 mg
Rosuvastatin 20–40 mg	Rosuvastatin 5–10 mg
	Simvastatin 20–40 mg
	Pravastatin 40–80 mg
	Lovastatin 40 mg
	Fluvastatin XL 80 mg
	Pitavastatin 1–4 mg

*Once-daily dosing. XL, extended release.

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ADA 2020 prevención secundaria



ESTATINAS ALTA INTENSIDAD



NO METAS
ADICIONAR EZETIMIBE O PCSK9



NO TOLERANCIA ESTATINAS
INTENSIFIACADAS USAR DOSIS
MÁXIMA TOLERADA

Diabetes Care Volume 43, Supplement 1, January 2020

ADA 2020 triglicéridos



≥ 500 TRATAMIENTO FÁRMACOLÓGICO



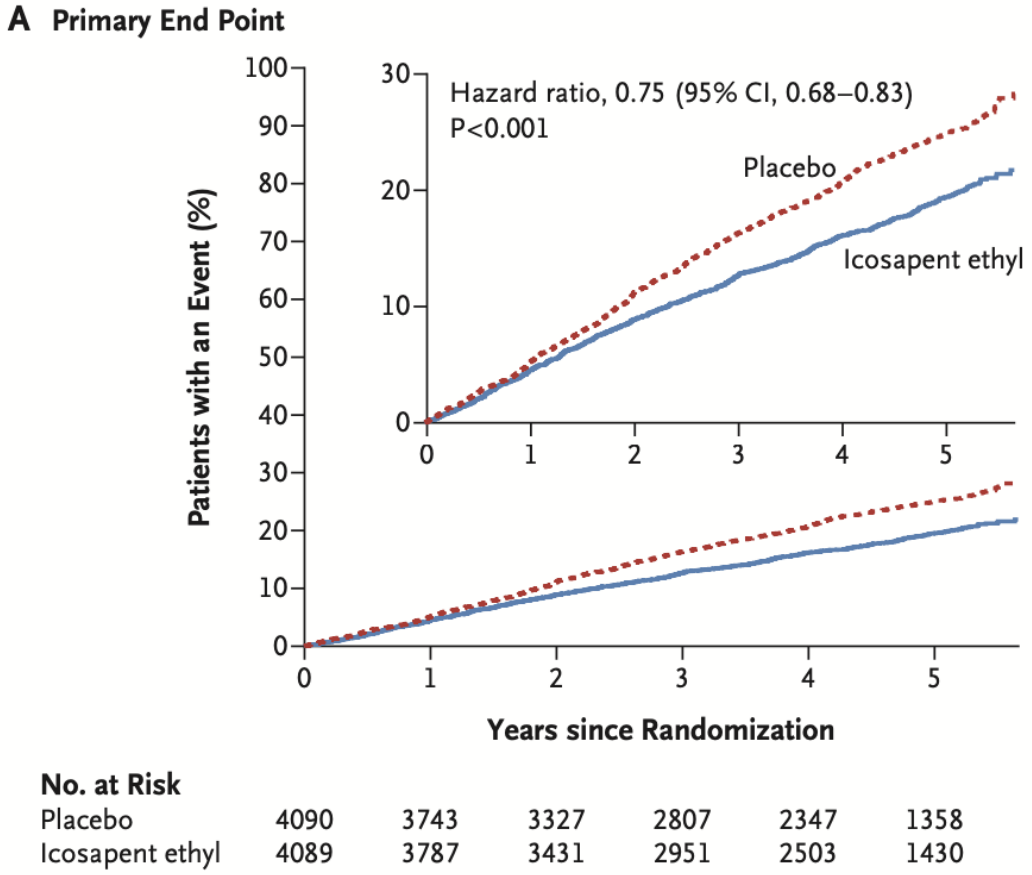
175-499 REFORZAR ESTILOS DE VIDA, CONTROL GLICÉMICO Y BUSCAR CAUSAS ADICIONALES



135-499 CON ECV O FACTORES DE RIESGO CARDIOVASCULAR CONSIDERAR FÁRMACOS

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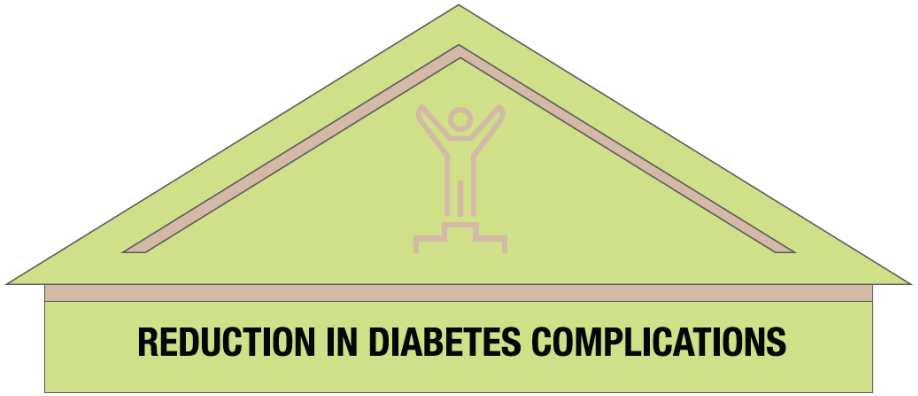
REDUCE-IT MACE



N Engl J Med 2019;380:11-22

Conclusiones

Conclusiones



¡Muchas gracias!

El poder de controlar los resultados

sanofi

“La información contenida en esta presentación está dirigida al profesional de la salud con la intención de brindar información científica de interés y refleja las consideraciones del autor y no las de SANOFI. Cualquier indicación OFF LABEL mencionada será con el único objetivo de intercambio científico y no representa una promoción. SANOFI no recomienda indicaciones que no estén contenidas en la información para prescribir aprobada de sus productos en la Entidad Regulatoria de cada país.” MAT-AW-2200067-1.0-(05/2022)