



Guías para el manejo de DM-2: actualización y recomendaciones

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Conflictos de interés

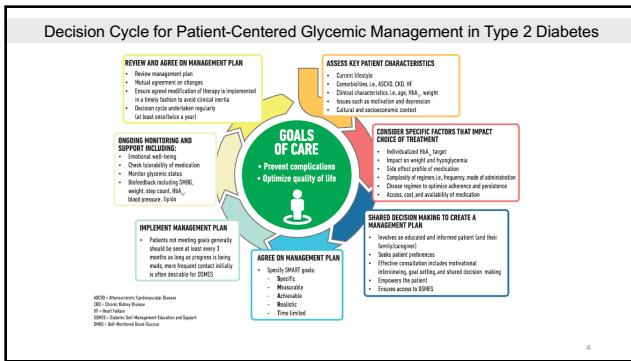
- Conferencista: Astra Zeneca, Abbott Nutrición, Novartis Oncology, Novo Nordisk, Merck Sharp & Dohme, Roche, Glaxo SmithKline, Sanofi Aventis, Bayer, Pfizer, Novartis
- Advisory Board: Novartis Oncology, Sanofi Aventis, Astra Zeneca, Novo Nordisk, Stendhal, Pfizer
- Investigación clínica: Astra Zeneca, Novartis Pharma Logistics Inc., Merck Sharp & Dohme, Glaxo SmithKline, Organon, Boehringer Ingelheim, Roche, Novo Nordisk

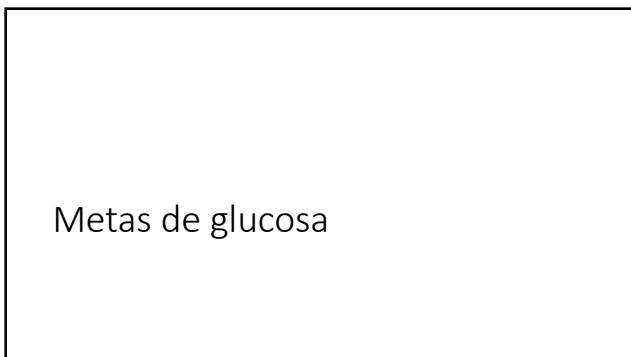
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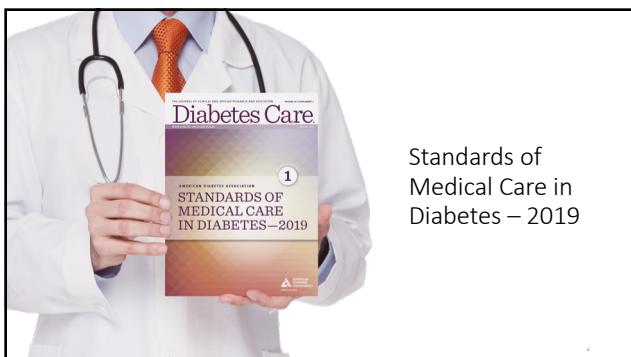
Agenda

- Comparar guías: ADA, AACE, ALAD, ESC
- Recomendaciones en manejo de glucosa, presión arterial y lípidos
- Intérprete personal de guías

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ADA: A1C Goals (1).

- 6.4** A reasonable A1C goal for many nonpregnant adults is <7% (53 mmol/mol) **A**
- 6.5** Providers might reasonably suggest more stringent A1C goals (such as <6.5% [48 mmol/mol]) for selected individual patients if this can be achieved without significant hypoglycemia or other adverse effects of treatment (i.e., polypharmacy). Appropriate patients might include those with short duration of diabetes, type 2 diabetes treated with lifestyle or metformin only, long life expectancy, or no significant cardiovascular disease **C**

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ADA: A1C Goals (2).

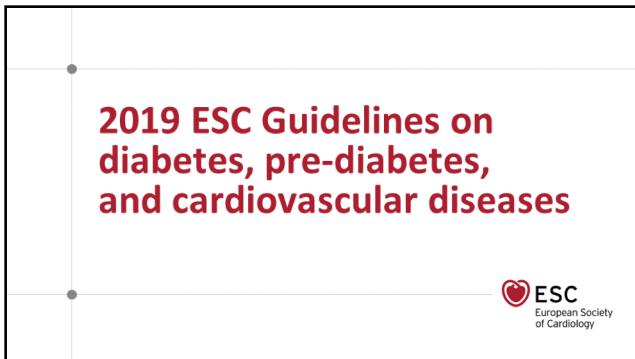
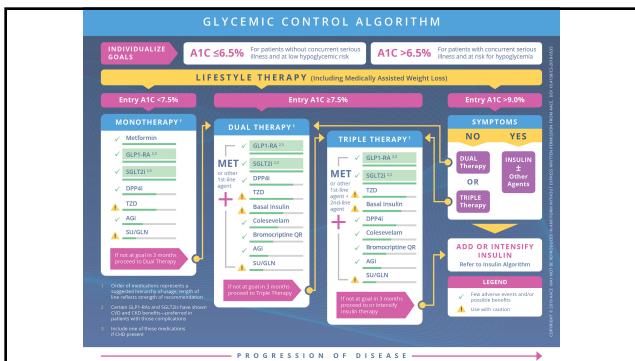
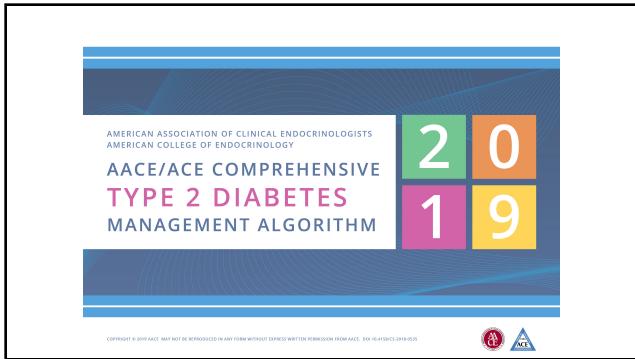
- 6.6** Less stringent A1C goals (such as <8% [64 mmol/mol]) may be appropriate for patients with a history of severe hypoglycemia, limited life expectancy, advanced microvascular or macrovascular complications, extensive comorbid conditions, or long-standing diabetes in whom the goal is difficult to achieve despite diabetes self-management education, appropriate glucose monitoring, and effective doses of multiple glucose-lowering agents including insulin **B**
- 6.7** Reassess glycemic targets over time based on the criteria in Fig. 6.1 or, in older adults, **Table 12.1 E**

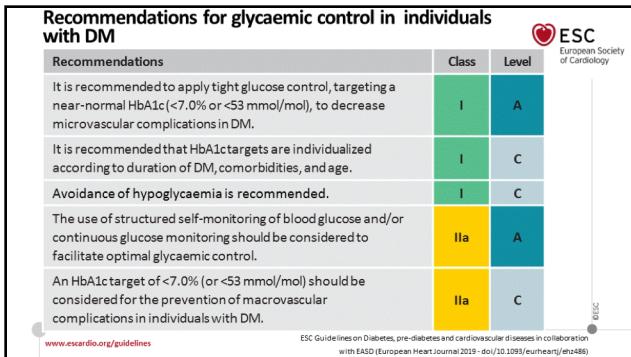
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Table 12.2—Considerations for treatment regimen simplification and deintensification/deprescribing in older adults with diabetes (39,95)

Patient characteristics/ health status	Reasonable A1C/ treatment goal	Rationale/considerations	When may regimen simplification be required?	When may treatment deintensification/ deprescribing be required?
Healthy, well-functioning, no chronic illnesses, intact cognitive and functional status)	A1C <7.5% (58 mmol/mol)	<ul style="list-style-type: none"> • Patients can generally perform complex tasks to maintain good glycemic control when health is stable • During acute illness, patients may be more at risk for administration or dosing errors that can result in hypoglycemia, falls, fractures, etc. 	<ul style="list-style-type: none"> • If severe or recurrent hypoglycemia occurs in patients on insulin therapy (even if A1C is appropriate) • If wide glucose excursions are observed • If cognitive or functional decline occurs following acute illness 	<ul style="list-style-type: none"> • If severe or recurrent hypoglycemia occurs in patients on noninsulin therapies with high risk of hypoglycemia (even if A1C is appropriate) • If wide glucose excursions are observed • In the presence of polypharmacy
Complex/intermediate (multiple coexisting chronic illnesses or 2+ instrumental ADL impairments or mild-to- moderate cognitive impairment)	A1C <8.0% (64 mmol/mol)	<ul style="list-style-type: none"> • Comorbidities may affect self-management abilities and increase risk to avoid hypoglycemia • Long-acting medications formulations may decrease pill burden and complexity of medication regimen 	<ul style="list-style-type: none"> • If severe or recurrent hypoglycemia occurs in patients on insulin therapy (even if A1C is appropriate) • If unable to manage complexity of an insulin regimen • If there is a significant change in social circumstances, such as loss of caregiver, change in living situation, or financial difficulties 	<ul style="list-style-type: none"> • If severe or recurrent hypoglycemia occurs in patients on noninsulin therapies with high risk of hypoglycemia (even if A1C is appropriate) • If wide glucose excursions are observed • In the presence of polypharmacy

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5.3 ¿CUÁL DEBE SER LA META DE CONTROL GLUCÉMICO EN PACIENTES CON DM2?

5.3.1 La meta general de A1c en pacientes con diabetes tipo 2 debe ser menos de 7.0%.
Recomendación A

5.3.2 En pacientes de menos de 60 años de edad, reciente diagnóstico y sin comorbilidades importantes, se puede considerar una meta de 6.5%.
Recomendación de consenso

5.3.3 En el adulto mayor con deterioro funcional importante y/o comorbilidades que limitan la expectativa de vida, se puede considerar una meta de A1c hasta 8.0%.
Recomendación C

Comentarios...

- Si son los mismos estudios, por qué no nos ponemos de acuerdo entre 6.5 y 7.0%?
- Las metas hay que individualizarlas:
 - Contexto clínico
 - Disponibilidad terapéutica
 - Objetivos terapéuticos

Impact of Intensive Therapy for Diabetes: Summary of Major Clinical Trials

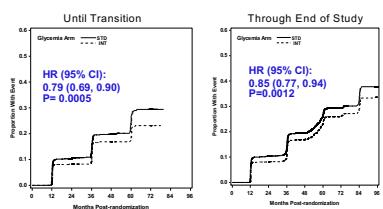
Study	Microvasc	CVD	Mortality
UKPDS	7.0 vs 7.9%	↔	↓
DCCT / EDIC*	7.0 vs 9%	↔	↓
ACCORD	6.4 vs 7.5%	↔	↑
ADVANCE	6.5 vs 7.3%	↔	↔
VADT	6.9 vs 8.4%	↔	↔

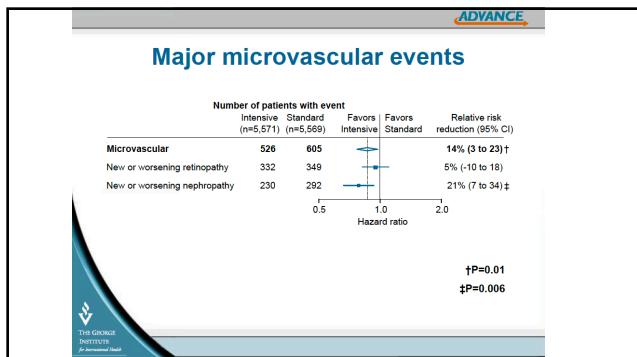
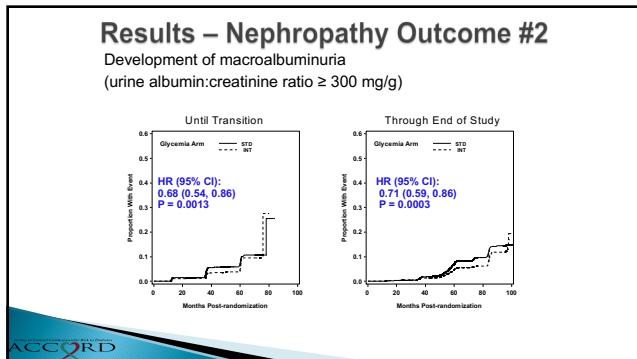
Legend: □ Initial Trial ■ Long Term Follow-up
 * in T1DM

UK Prospective Diabetes Study (UKPDS) Group. *Lancet* 1998;352:834.
 UK Prospective Diabetes Study (UKPDS) Group. *Diabetologia* 1998;41:709-19. *N Engl J Med* 1993;329:977.
 Nathan DM et al. *N Engl J Med* 2005;353:2843. Geelhoed HC et al. *N Engl J Med* 2008;358:2545.
 Patel A et al. *N Engl J Med* 2008;358:2560. Duckworth W et al. *N Engl J Med* 2009;360:1259. (erratum)
 Moeller T. *N Engl J Med* 2009;361:1024)

Results – Nephropathy Outcome #1

Development of microalbuminuria
 (urine albumin:creatinine ratio ≥ 30 mg/g)

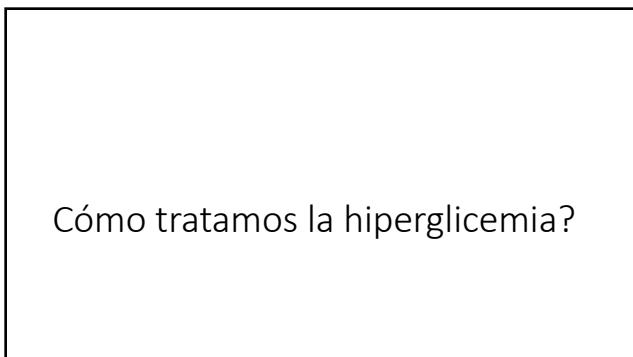


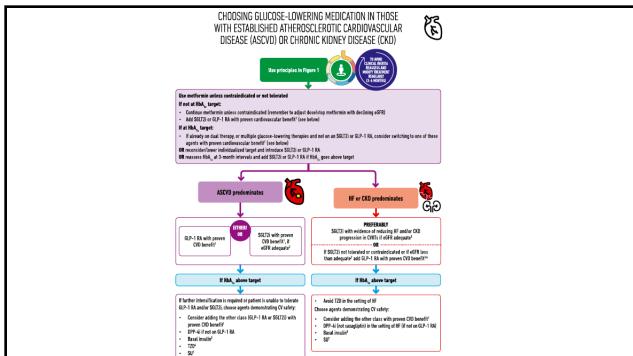


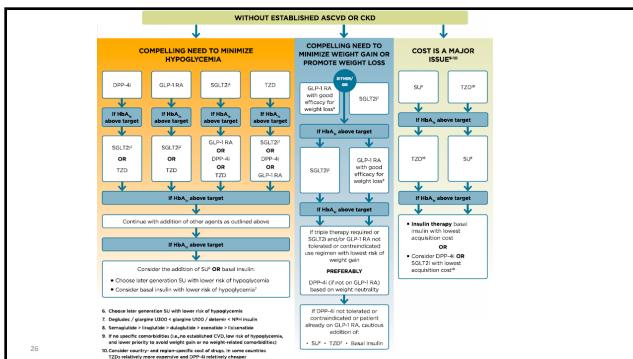
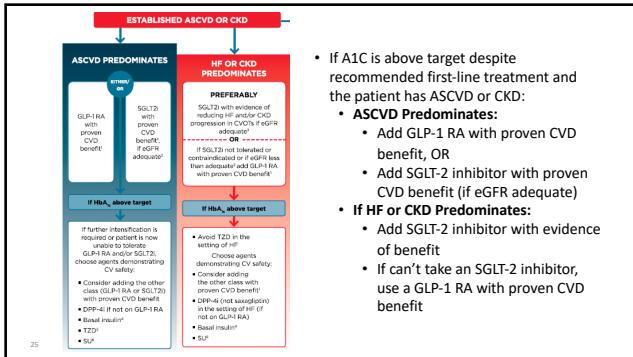
Por lo tanto...

- Deberíamos llevar al menos a 7% en la mayoría de los pacientes, a menos que sean pacientes adultos mayores, frágiles o con corta expectativa de vida
- Se puede tratar de llevar a menos de 6.5% en pacientes jóvenes, de recién inicio, especialmente si lo logramos con pocas hipoglicemias y efectos adversos
 - El beneficio es principalmente prevención de aparición de microalbuminuria en alrededor de 20%
 - No es insignificante!

Parámetro	ADA	AACE	ESC	ALAD
HbA1c	<7%	<6.5%	<7%	<7%

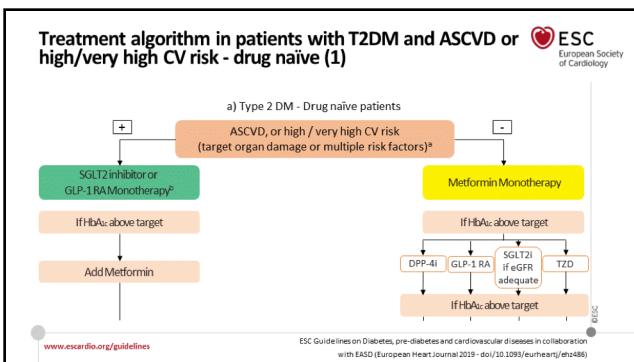
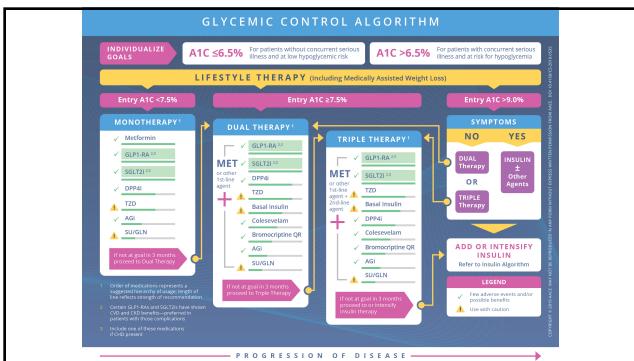
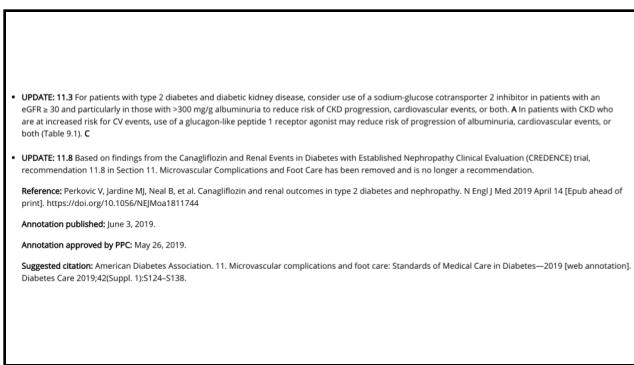


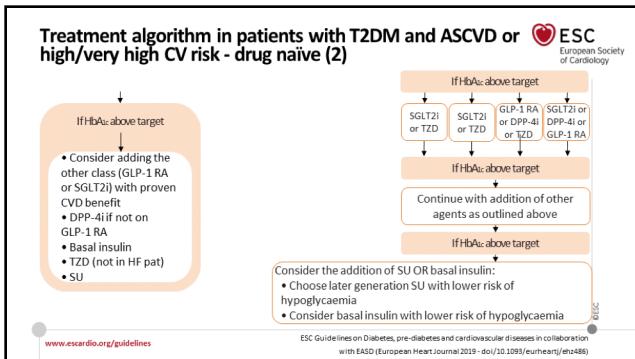




Within many of these trials the benefit of treatment (in terms of MACE endpoints) was less pronounced in subjects with lower risk for ASCVD; however, data from DECLARE-TIMI 58 and REWIND trials indicate that the CV benefits of SGLT2 inhibitors (in terms of reduction in the risk for heart failure hospitalization) and GLP-1 receptor agonists (in terms of lower risk of MACE) may extend to higher-risk type 2 diabetes patients in the primary prevention group. In addition, canagliflozin significantly reduced the risk of MACE events and hospitalization for HF in patients with diabetic kidney disease, regardless of prior ASCVD status. For patients at high risk for cardiovascular events due to established ASCVD or multiple risk factors for ASCVD (which may include diabetic kidney disease), incorporating one of the SGLT2 inhibitors or GLP-1 receptor agonists that have been demonstrated to reduce cardiovascular events is recommended (Table 9.1).

Suggested citation: American Diabetes Association. 9. Pharmacologic Approaches to Glycemic Treatment: Standards of Medical Care in Diabetes—2019 [web annotation]. Diabetes Care 2019;42(Suppl. 1):S90–S102.





Recommendations for glucose-lowering treatment in DM (1)

Recommendations	Class	Level
SGLT2 Inhibitors		
Empagliflozin, canagliflozin, or dapagliflozin are recommended in patients with T2DM and CVD or at very high/high CV risk to reduce CV events.	I	A
Empagliflozin is recommended in patients with T2DM and CVD to reduce the risk of death.	I	B

www.escardio.org/guidelines

ESC Guidelines on Diabetes, pre-diabetes and cardiovascular diseases in collaboration with EASD (European Heart Journal 2019 - doi:10.1093/euroheartj/ehz488)

Recommendations for glucose-lowering treatment in DM (2)

Recommendations	Class	Level
GLP1-RAs		
Liraglutide, semaglutide or dulaglutide are recommended in patients with T2DM and CVD or at very high/high CV risk to reduce CV events.	I	A
Liraglutide is recommended in patients with T2DM and CVD or at very high/high CV risk to reduce the risk of death.	I	B

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ESC Guidelines on Diabetes, pre-diabetes and cardiovascular diseases in collaboration with EASD (European Heart Journal 2019 - doi:10.1093/euroheartj/ehz488)

Recommendations for glucose-lowering treatment in DM (3)		
Recommendations	Class	Level
Biguanides		
Metformin should be considered in overweight patients with T2DM without CVD and at moderate CV risk.	IIa	C
Insulin		
Insulin-based glycaemic control should be considered in patients with ACS with significant hyperglycaemia (>10 mmol/L or >180 mg/dL), with the target adapted according to comorbidities.	IIa	C

 ESC
European Society of Cardiology

www.escardio.org/guidelines ESC Guidelines on Diabetes, pre-diabetes and cardiovascular diseases in collaboration with EASD (European Heart Journal 2019 - doi:10.1093/euroheart/ehz488)

Recommendations for T2DM treatment to reduce heart failure risk (1)		
Recommendations	Class	Level
SGLT2 inhibitors (empagliflozin, canagliflozin, dapagliflozin) are recommended to lower risk of HF hospitalization in patients with DM.	I	A
Metformin should be considered for DM treatment in patients with HF, if the eGFR is stable and >30 mL/min/1.73 m ² .	IIa	C
GLP1-RAs (lixisenatide, liraglutide, semaglutide, exenatide, dulaglutide) have a neutral effect on the risk of HF hospitalization, and may be considered for DM treatment in patients with HF.	IIb	A

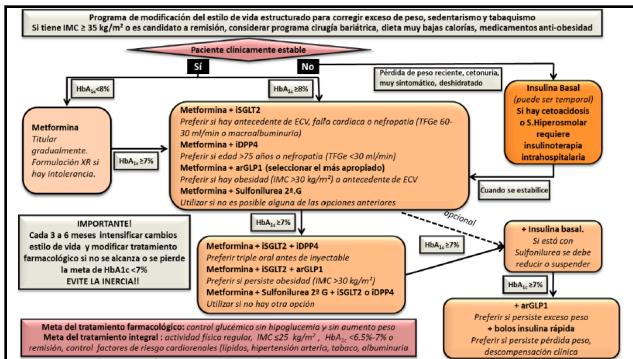
 ESC
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www.escardio.org/guidelines ESC Guidelines on Diabetes, pre-diabetes and cardiovascular diseases in collaboration with EASD (European Heart Journal 2019 - doi:10.1093/euroheart/ehz488)

Recommendations for the prevention and management of CKD in patients with DM (2)		
Recommendations	Class	Level
A RAAS blocker (ACEI or ARB) is recommended for the treatment of hypertension in DM, particularly in the presence of proteinuria, microalbuminuria, or LVH.	I	A
Treatment with a SGLT2 inhibitor (empagliflozin, canagliflozin, dapagliflozin) is associated with a lower risk of renal endpoints and is recommended if eGFR is 30 to <90 mL/min/1.73 m ² .	I	B
Treatment with the GLP1-RAs liraglutide and semaglutide is associated with a lower risk of renal endpoints and should be considered for DM treatment if eGFR is >30 mL/min/1.73m ² .	IIa	B

 ESC
European Society of Cardiology

www.escardio.org/guidelines ESC Guidelines on Diabetes, pre-diabetes and cardiovascular diseases in collaboration with EASD (European Heart Journal 2019 - doi:10.1093/euroheart/ehz488)



13.2.7 El tratamiento con un inhibidor de SGLT-2 (empagliflozina, canagliflozina o dapagliflozina) se asocia a un menor riesgo de deterioro de la función renal.

Recomendación B

13.2.8 El tratamiento con un agonista GLP-1 (liraglutida o semaglutida) se asocia a un menor riesgo de deterioro de la función renal.

Recomendación B

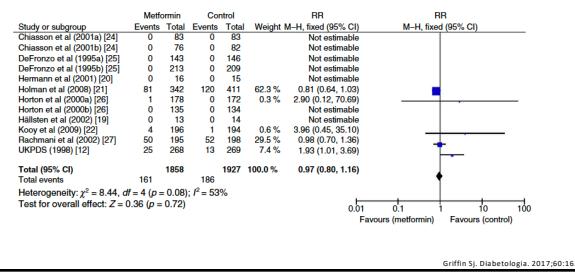
14.6.4 En pacientes con elevado riesgo cardiovascular o enfermedad cardiovascular documentada, el tratamiento con el inhibidor del cotransportador de sodio-glucosa tipo 2 (SGLT-2) los inhibidores de SGLT disminuyen el riesgo de hospitalización por insuficiencia y de muerte cardiovascular

14.6.5 El tratamiento farmacológico para la insuficiencia cardíaca sistólica en pacientes con diabetes incluye tres tipos de antagonistas neurohormonales: los inhibidores de la enzima convertidora de angiotensina (IECA) o bloqueadores del receptor de angiotensina 2 (ARA2), los beta-bloqueadores (BB) metoprolol, bisoprolol y carvedilol, y los antagonistas del receptor de mineralocorticoides espironolactona e eplerenona.

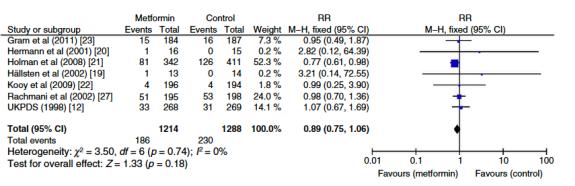
Reflexiones...

- Tenemos suficiente evidencia para quitar de primera línea a metformin en pacientes con enfermedad cardiovascular?
 - UKPDS no es la mejor evidencia científica para los estándares de hoy
 - Es la referencia más citada pero no es la única

Metanálisis: metformin y mortalidad cardiovascular



Metanálisis: metformin e IAM



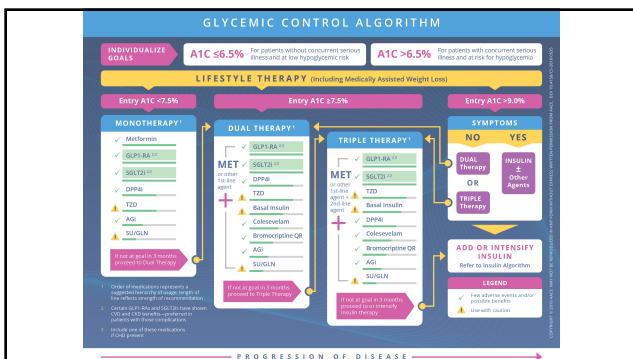
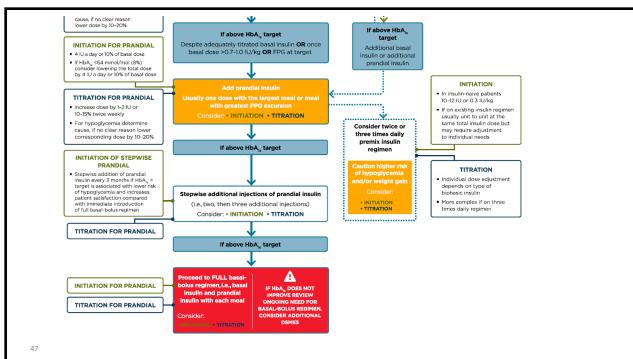
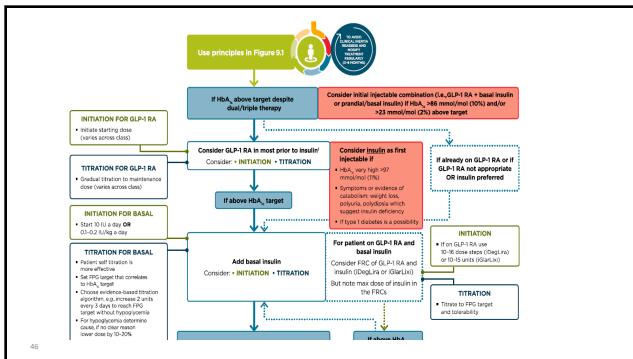
Reflexiones...

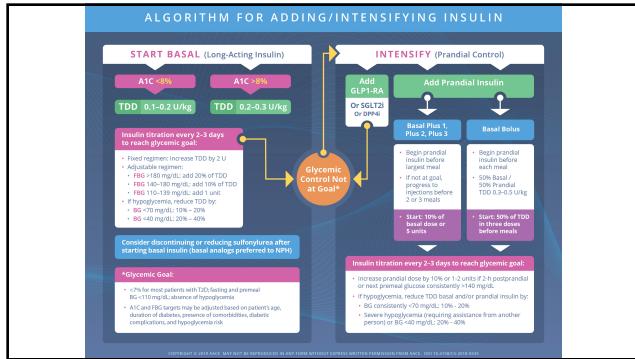
- Tenemos suficiente evidencia para quitar de primera línea a metformin en pacientes con enfermedad cardiovascular?
 - UKPDS no es la mejor evidencia científica para los estándares de hoy
 - Es la referencia más citada pero no es la única
- Es una droga barata, segura, disponible en la mayoría de los lugares del mundo
- Depende de la rigurosidad con la que se quiere interpretar los ensayos clínicos
- No hay interés comercial en hacer un estudio comparativo directo entre metformin y alguno de los agentes nuevos en desenlaces CV

Reflexiones

- En todos los demás, más o menos de acuerdo:
 - Alto riesgo CV o prevención secundaria: iSGLT2 ó arGLP-1
 - Nefropatía: iSGLT2 (mayor evidencia) ó arGLP-1 (menor evidencia)
 - Falla cardíaca: iSGLT2

Cómo iniciar inyectables?





Reflexiones

- arGLP-1 debería ser el primer inyectable
- ... limitante es el costo!
- Es una alternativa para intensificación
- Facilidad de usar un único dispositivo

Metas de presión arterial

Hypertension/Blood Pressure Control:
Treatment Goals (1).

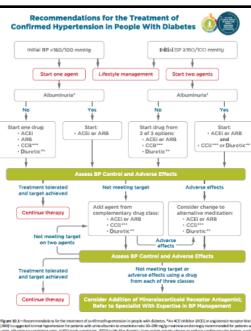
- 10.3** For patients with diabetes and hypertension, blood pressure targets should be individualized through a shared decision-making process that addresses cardiovascular risk, potential adverse effects of antihypertensive medications, and patient preferences **C**
- 10.4** For individuals with diabetes and hypertension at high cardiovascular risk (existing atherosclerotic cardiovascular disease or 10-year atherosclerotic cardiovascular disease risk >15%), a blood pressure target of <130/80 mmHg may be appropriate, if it can be safely attained **C**

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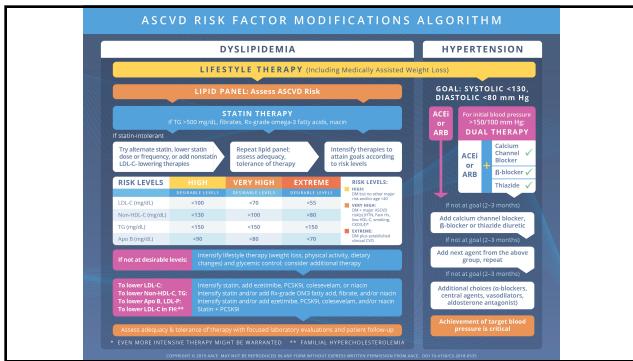
Hypertension/Blood Pressure Control:
Treatment Goals (2).

- 10.5** For individuals with diabetes and hypertension at lower risk for cardiovascular disease (10-year atherosclerotic cardiovascular disease risk <15%), treat to a blood pressure target <140/90 mmHg **A**
- 10.6** In pregnant patients with diabetes and preexisting hypertension who are treated with antihypertensive therapy, blood pressure targets of 120-160/80-105 mmHg are suggested in the interest of optimizing long-term maternal health and minimizing impaired fetal growth **E**

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Recommendations for the management of BP in patients with DM and pre-DM (1)		
Recommendations	Class	Level
Treatment targets		
Antihypertensive drug treatment is recommended for people with DM when office BP is >140/90 mmHg.	I	A
It is recommended that patients with hypertension and DM are treated in an individualized manner. The BP goal is to target SBP to 130 mmHg and <130 mmHg if tolerated, but not <120 mmHg. In older people (aged >65 years), the SBP goal is to a range of 130 - 139 mmHg.	I	A
It is recommended to target DBP <80 mmHg, but not >70 mmHg.	I	C
An on-treatment SBP of <130 mmHg may be considered in patients at particularly high risk of a cerebrovascular event, such as those with a history of stroke.	IIb	C

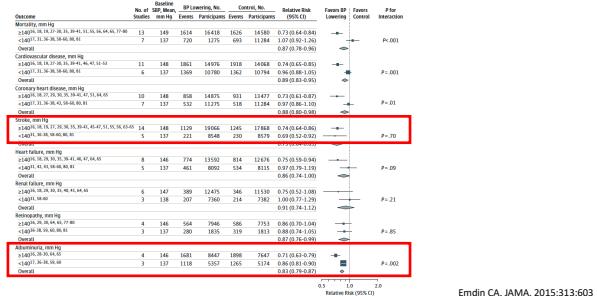
www.escardio.org/guidelines
ESC Guidelines on Diabetes, pre-diabetes and cardiovascular diseases in collaboration with EASD [European Heart Journal 2019; doi:10.1093/euroheartj/ehz486]

11.1 ¿CUÁL DEBE SER LA META DE PRESIÓN ARTERIAL EN UN PACIENTE CON DM2?

11.1.1 Se debe alcanzar una meta entre 130 mmHg y 140 mmHg para la presión arterial sistólica (PAS), y menor o igual a 80 mmHg para la presión arterial diastólica (PAD). En mayores de 65 años, la meta para la sistólica es 130-139

Recomendación B

Reducción de eventos según PA inicial



Reflexiones

- De dónde vienen entonces las metas más estrictas (<130 mm Hg de PAS)?
- Son extrapolaciones del SPRINT, que no incluyó pacientes diabéticos!
- Si hay evidencia que metas más estrictas pueden ser beneficiosos para el riñón e ictus, pero no tenemos datos suficientes para el corazón
- Por lo tanto... al menos <140 mm Hg PAS y si se puede llevar a <130 mm Hg sin efectos adversos (ortostatismo)

Parámetro	ADA	AACE	ESC	ALAD
HbA1c	<7%	<6.5%	<7%	<7%
Presión sistólica	<130 mm Hg (alto riesgo) <140 mm Hg (riesgo intermedio)	<130 mm Hg	120-130 mm Hg	<140 mm Hg
Presión diastólica	<80 mm Hg (alto riesgo) <90 mm Hg (riesgo intermedio)	<80 mm Hg	70-80 mm Hg	<80 mm Hg

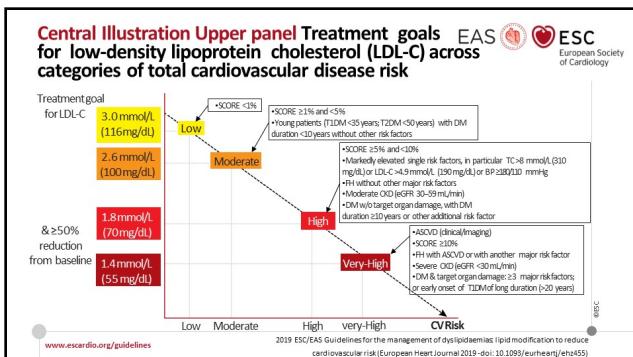
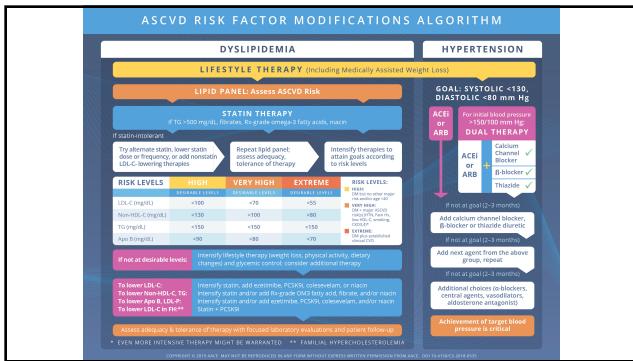
Manejo de dislipidemia

Lipid Management: Statin Treatment (1).

- 10.19** For patients of all ages with diabetes and atherosclerotic cardiovascular disease or 10-year atherosclerotic cardiovascular disease risk >20%, high-intensity statin therapy should be added to lifestyle therapy **A**
- 10.20** For patients <40 years with additional atherosclerotic cardiovascular disease risk factors, the patient and provider should consider using moderate-intensity statin in addition to lifestyle therapy **C**
- 10.21** For patients with diabetes aged 40-75 years **A** and >75 years **B** without atherosclerotic cardiovascular disease, use moderate-intensity statin in addition to lifestyle therapy.

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• Section 10.8 is updated based on the outcome of Reduction of Cardiovascular Events with Icosapent Ethyl-Intervention Trial (REDUCE-IT), which determined the addition of icosapent ethyl to statin therapy for patients with high triglyceride levels reduced cardiovascular events. The Standards of Care now include a recommendation that icosapent ethyl be considered for patients with diabetes and atherosclerotic cardiovascular disease (ASCVD) or other cardiac risk factors on a statin with controlled LDL-C, but with elevated triglycerides (135-499) to reduce cardiovascular risk.



12.1 ¿CUÁLES SON LAS METAS DE PERFIL LÍPIDICO EN EL PACIENTE CON DM2?

12.1.1 El nivel de colesterol de LDL (cLDL) recomendado para las personas con diabetes sin enfermedad cardiovascular (ECV) es < 100 mg/dL. El nivel correspondiente para los casos en preventión secundaria es < 70 mg/dL. Valores aún menores (< 55 mg/dL) aplican para casos con muy alto riesgo (CHD o con complicaciones crónicas). **Recomendación A**

12.1.2 Es deseable mantener un nivel de triglicéridos < 150 mg/dL y un nivel de colesterol HDL > 40 mg/dL. **Recomendación C**

Comentarios

- Las metas de LDL se derivan del promedio de LDL alcanzado en los ensayos de estatinas
- No hay ensayos clínicos diseñados con metas de LDL
- Sin embargo, hasta el momento los estudios que han comparado una nueva intervención y bajar más el LDL ha sido efectivo en reducir MACE, al menos ezetimibe e inhibidores de PCSK9
- Los 2 ensayos realizados en prevención primaria en DM (CARDS y HPS-DM) han sido en pacientes >40 años con factores de riesgo adicionales (retinopatía, microalbuminuria, tabaquismo)

Parámetro	ADA	AACE	ESC	ALAD
Hba1c	<7%	<6.5%	<7%	<7%
Presión sistólica	<130 mm Hg (alto riesgo) <140 mm Hg (riesgo intermedio)	<130 mm Hg	120-130 mm Hg	<140 mm Hg
Presión diastólica	<80 mm Hg (alto riesgo) <90 mm Hg (riesgo intermedio)	<80 mm Hg	70-80 mm Hg	<80 mm Hg
LDL	Alto riesgo estatinas alta intensidad 40-70 años sin ECV estatinas de intensidad moderada	<55 mg/dl riesgo extremo <70 mg/dl altísimo riesgo <100 mg/dl alto riesgo	<55 mg/dl muy alto riesgo <70 mg/dl alto riesgo <100 mg/dl riesgo moderado	<55 mg/dl muy alto riesgo <70 mg/dl prevención secundaria <100 mg/dl sin ECV

Conclusiones

- Metformin sigue siendo primera línea en mayoría de guías
- Segundo agente va a depender de la presencia de enfermedad cardiovascular, enfermedad renal crónica o falla cardíaca
- Primer inyectable debería ser arGLP1
- Post insulina basal una forma de intensificar es con arGLP1

Preguntas...

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Puede descargar la
presentación en:



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