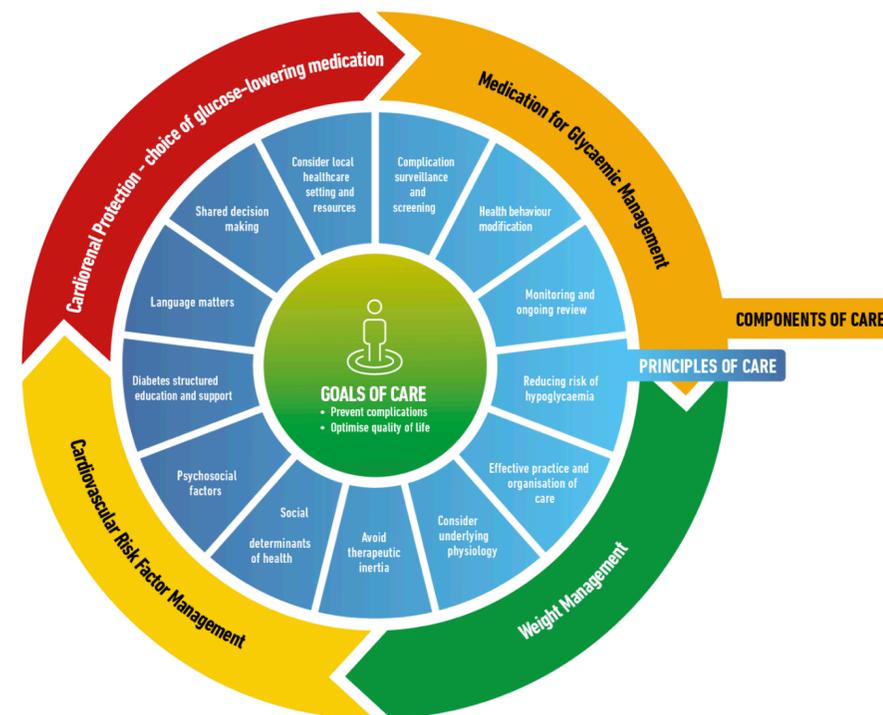


# Prise en charge multi-cible du patient diabétique: de la théorie à la pratique



**Docteur Marie STRIVAY**  
**Cheffe du service d'Endocrino-Diabétologie**  
**Hôpital de la Citadelle**  
**Jeudi 15 juin 2023**

2020



# Diabète

## 6.3%

Prévalence du diabète

## 1/3

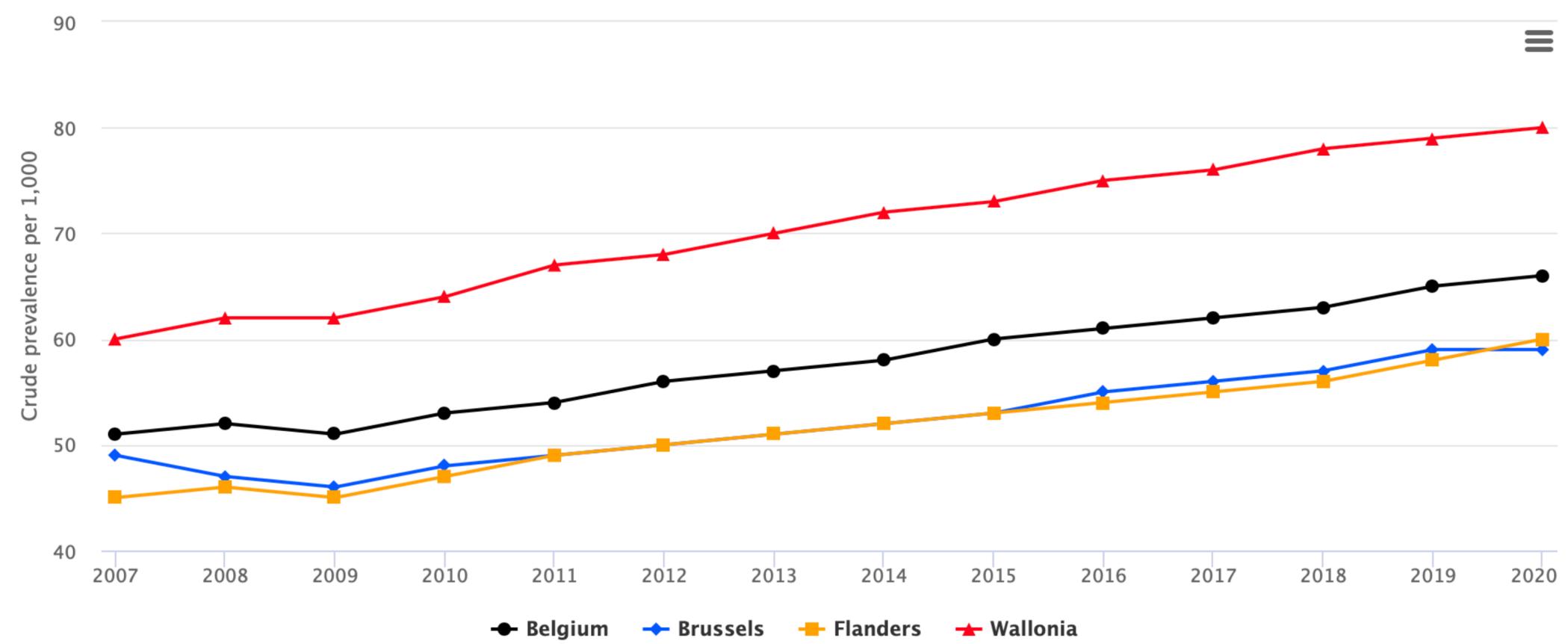
1 personne diabétique sur 3 se méconnaît

## 10%

La réelle prévalence estimée du diabète

### Crude prevalence of diagnosed diabetes in Belgium and its regions, 2007-2020

Source: [IMA-AIM Atlas \[1\]](#).



2018

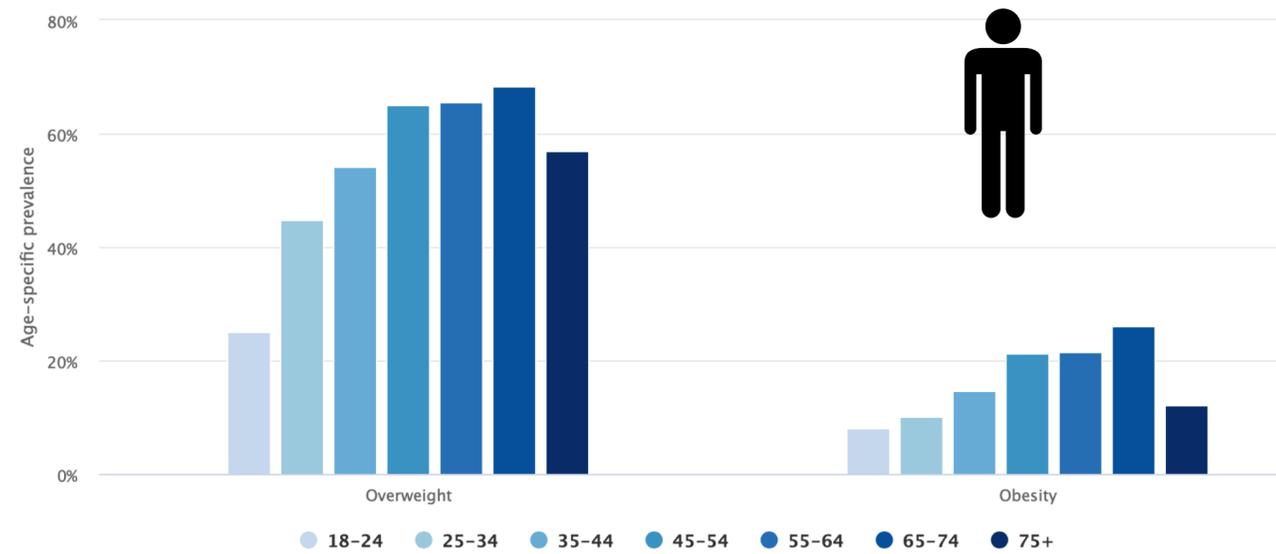


BMI>25: 49%  
BMI>30: 16%

### Excès de poids et obésité

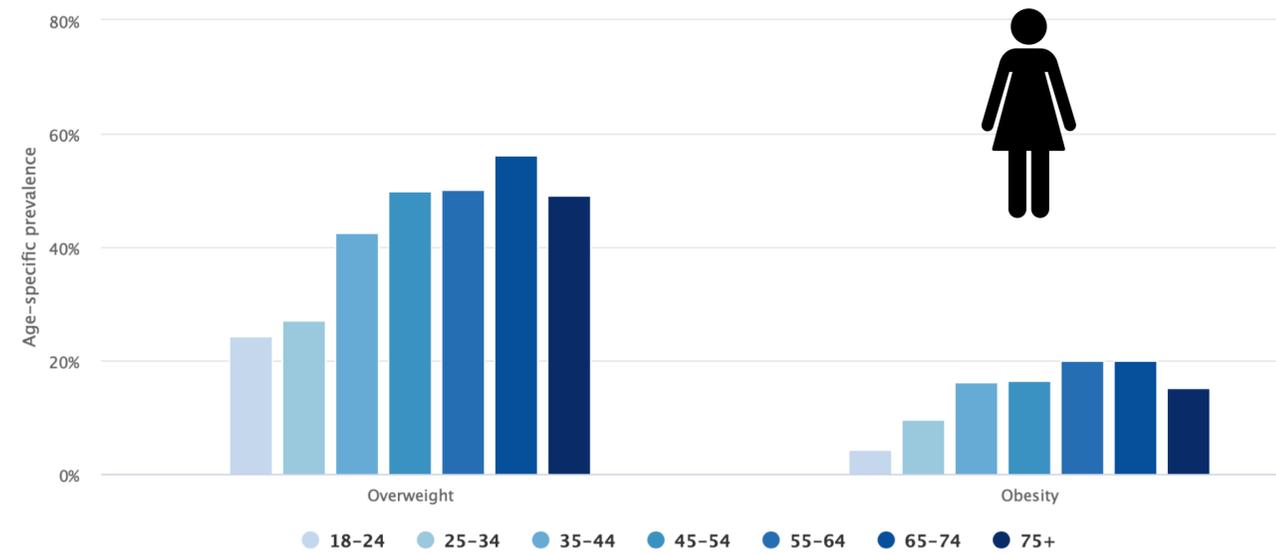
Self-reported prevalence of overweight and obesity among men by age group, Belgium, 2018

Source: [Health Interview Survey, Sciensano \[2\]](#)

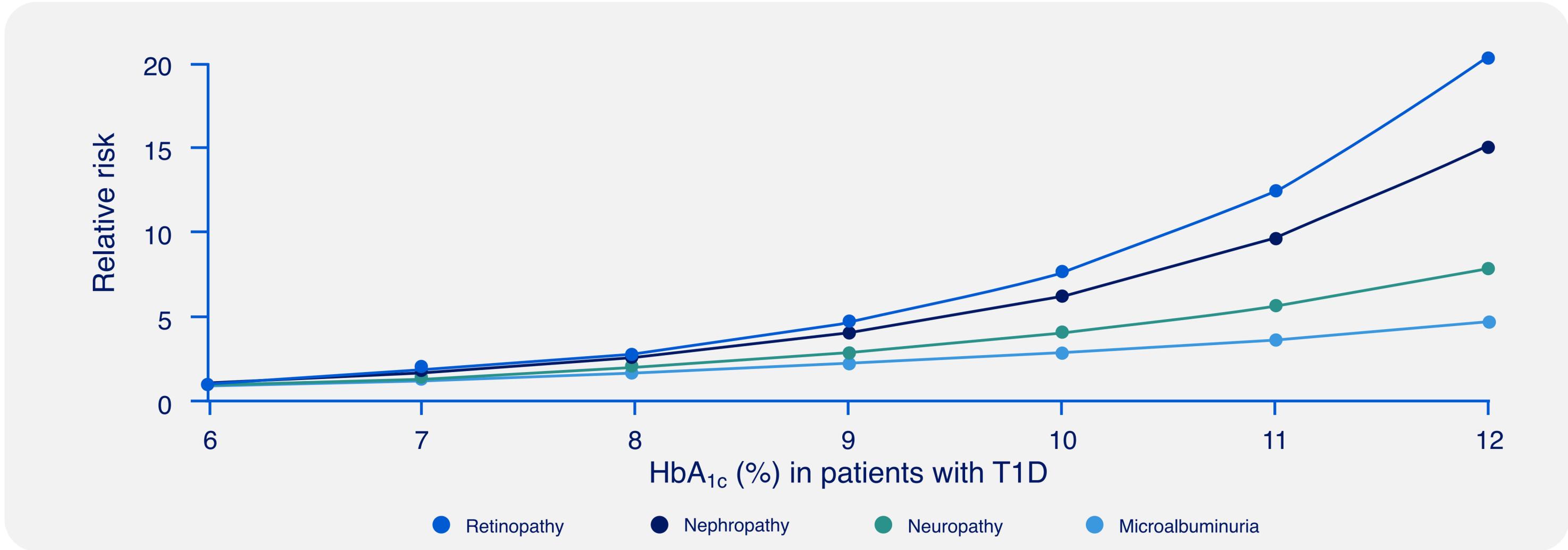


Self-reported prevalence of overweight and obesity among women by age group, Belgium, 2018

Source: [Health Interview Survey, Sciensano \[2\]](#)

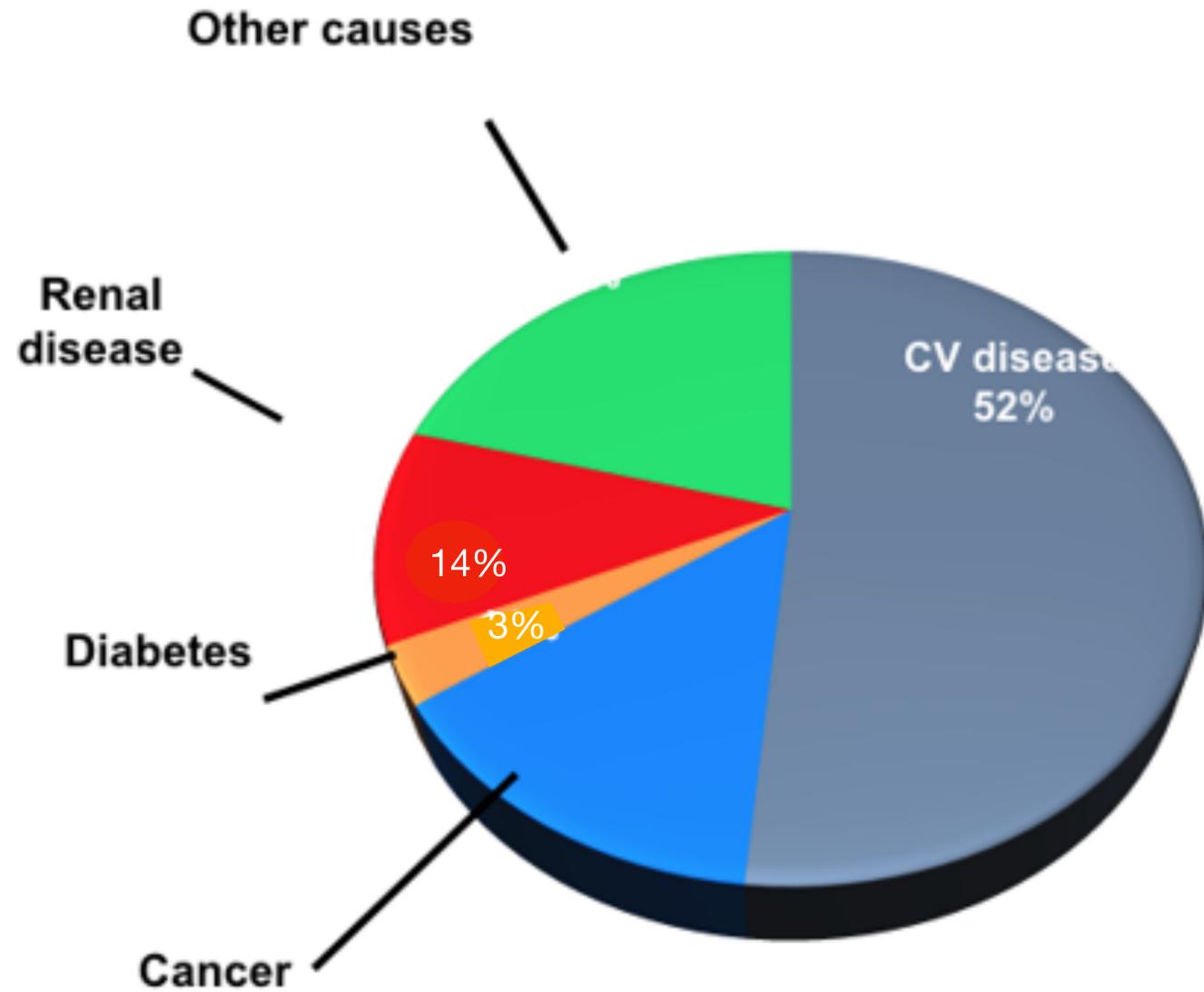


# HbA<sub>1c</sub> level is associated with microvascular long-term diabetes complications



DCCT, The Diabetes Control and Complications Trial.  
 Skyler JS et al. *Endocrinol Metab Clin North Am.* 1996;25:243–54;  
 The Diabetes Control and Complications Trial (DCCT) Research Group. *N Engl J Med.* 1993;329:977–86.

## Multinational WHO data on causes of mortality in type 2 diabetes mellitus<sup>1</sup>



Of all CVD deaths in type 2 diabetes:<sup>2</sup>

- Ischaemic heart disease=53.6%
- Cerebrovascular disease=26.2%
- Other CVD=20.2%

# « Management of Hyperglycaemia in Type 2 Diabetes »

## Présenté au Congrès de EASD à Stockholm 09/2022



Davies MJ, Aroda VR, Collins BS, Gabbay RA, Green J, Maruthur NM, Rosas SE, Del Prato S, Mathieu C, Mingrone G, Rossing P, Tankova T, Tsapas A, Buse JB

*Diabetes Care* 2022; <https://doi.org/10.2337/dci22-0034>. *Diabetologia* 2022; <https://doi.org/10.1007/s00125-022-05787-2>.

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European Association  
for the Study of Diabetes



**Co-Chair: Melanie J. Davies MB ChB, MD**  
University of Leicester, UK



**Co-Chair: John B. Buse, MD, PhD**  
UNC School of Medicine, USA



### Support Across Groups

**Robert  
Gabbay, MD,  
PhD**  
ADA

**Stefano Del  
Prato, MD**  
EASD



### Project Oversight & Integration with SOC Mindy Saraco & Malaika Hill

ADA



### The Rationale

**Peter Rossing, MD**  
Steno Diabetes Center Copenhagen, Denmark



**Billy Collins, DHSc, PA-C**  
U.S. Public Health Service, USA



### Therapeutic Options

**Vanita Aroda, MD**  
Brigham & Women's Hospital, Boston, USA



**Geltrude Mingrone, MD, PhD**  
Catholic University of the Sacred heart, Rome, Italy



**Tsvetalina Tankova, MD, DSC**  
Medical University, Sofia, Bulgaria



### Personalised Approach

**Apostolos Tsapas, MD, PhD, MSc**  
Aristotle University Thessaloniki, Greece



**Jennifer Green, MD**  
Duke University, Durham, USA



### Strategies for Implementation

**Chantal Mathieu, MD, PhD**  
KU Leuven, Leuven, Belgium



**Nisa Maruthur, MD, MHS**  
Johns Hopkins Medicine, Baltimore, USA



**Sylvia Rosas, MD, MSCE**  
Joslin Diabetes Center, Boston, USA

Davies MJ, Aroda VR, Collins BS, Gabbay RA, Green J, Maruthur NM, Rosas SE, Del Prato S, Mathieu C, Mingrone G, Rossing P, Tankova T, Tsapas A, Buse JB

*Diabetes Care* 2022; <https://doi.org/10.2337/dci22-0034>. *Diabetologia* 2022; <https://doi.org/10.1007/s00125-022-05787-2>.

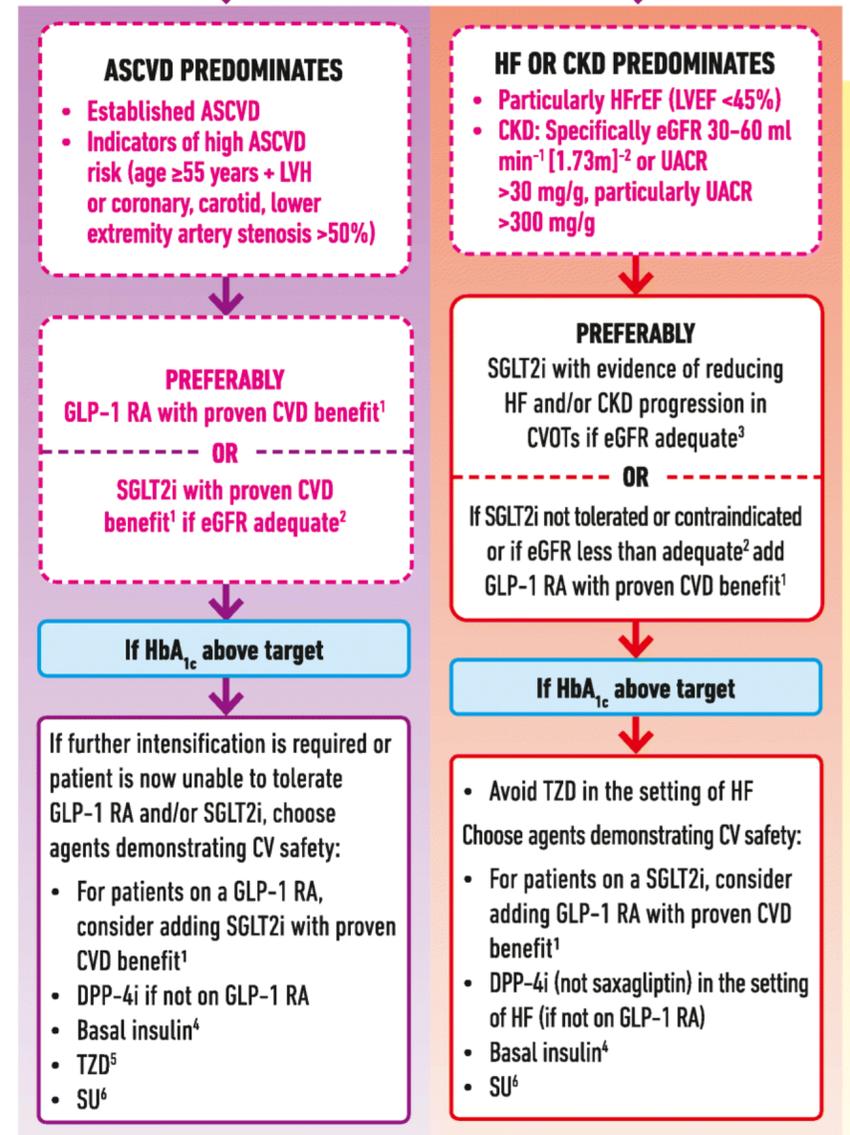
# GLUCOSE-LOWERING MEDICATION IN TYPE 2 DIABETES: OVERALL APPROACH

TO AVOID CLINICAL INERTIA REASSESS AND MODIFY TREATMENT REGULARLY (3-6 MONTHS)

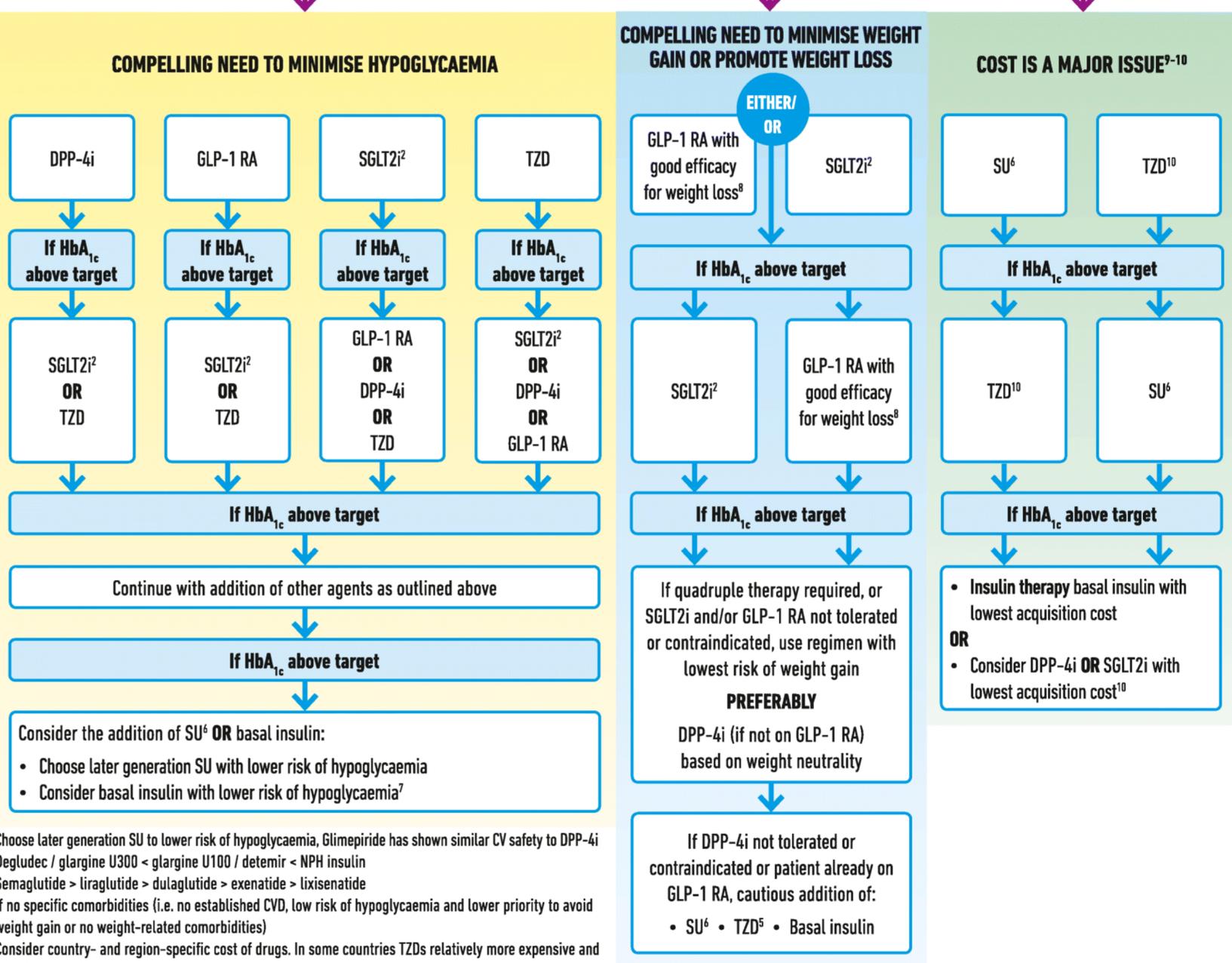
**FIRST-LINE THERAPY IS METFORMIN AND COMPREHENSIVE LIFESTYLE (INCLUDING WEIGHT MANAGEMENT AND PHYSICAL ACTIVITY)**

Independently of HbA1c!!

**INDICATORS OF HIGH-RISK OR ESTABLISHED ASCVD, CKD OR HF†**  
 Consider independently of baseline HbA<sub>1c</sub> or individualised HbA<sub>1c</sub> target



**NO**  
 If HbA<sub>1c</sub> above individualised target proceed as below



1. Proven CVD benefit means it has label indication of reducing CVD events.  
 2. Be aware that SGLT2i labelling varies by region and individual agent with regard to indicated level of eGFR for initiation and continued use  
 3. Empagliflozin, canagliflozin and dapagliflozin have shown reduction in HF and to reduce CKD progression in CVOTs. Canagliflozin has primary renal outcome data from CREDENCE, Dapagliflozin has primary heart failure outcome data from DAPA-HF  
 4. Degludec and U100 glargine have demonstrated CVD safety  
 5. Low dose may be better tolerated though less well studied for CVD effects

6. Choose later generation SU to lower risk of hypoglycaemia, Glimepiride has shown similar CV safety to DPP-4i  
 7. Degludec / glargine U300 < glargine U100 / detemir < NPH insulin  
 8. Semaglutide > liraglutide > dulaglutide > exenatide > lixisenatide  
 9. If no specific comorbidities (i.e. no established CVD, low risk of hypoglycaemia and lower priority to avoid weight gain or no weight-related comorbidities)  
 10. Consider country- and region-specific cost of drugs. In some countries TZDs relatively more expensive and DPP-4i relatively cheaper

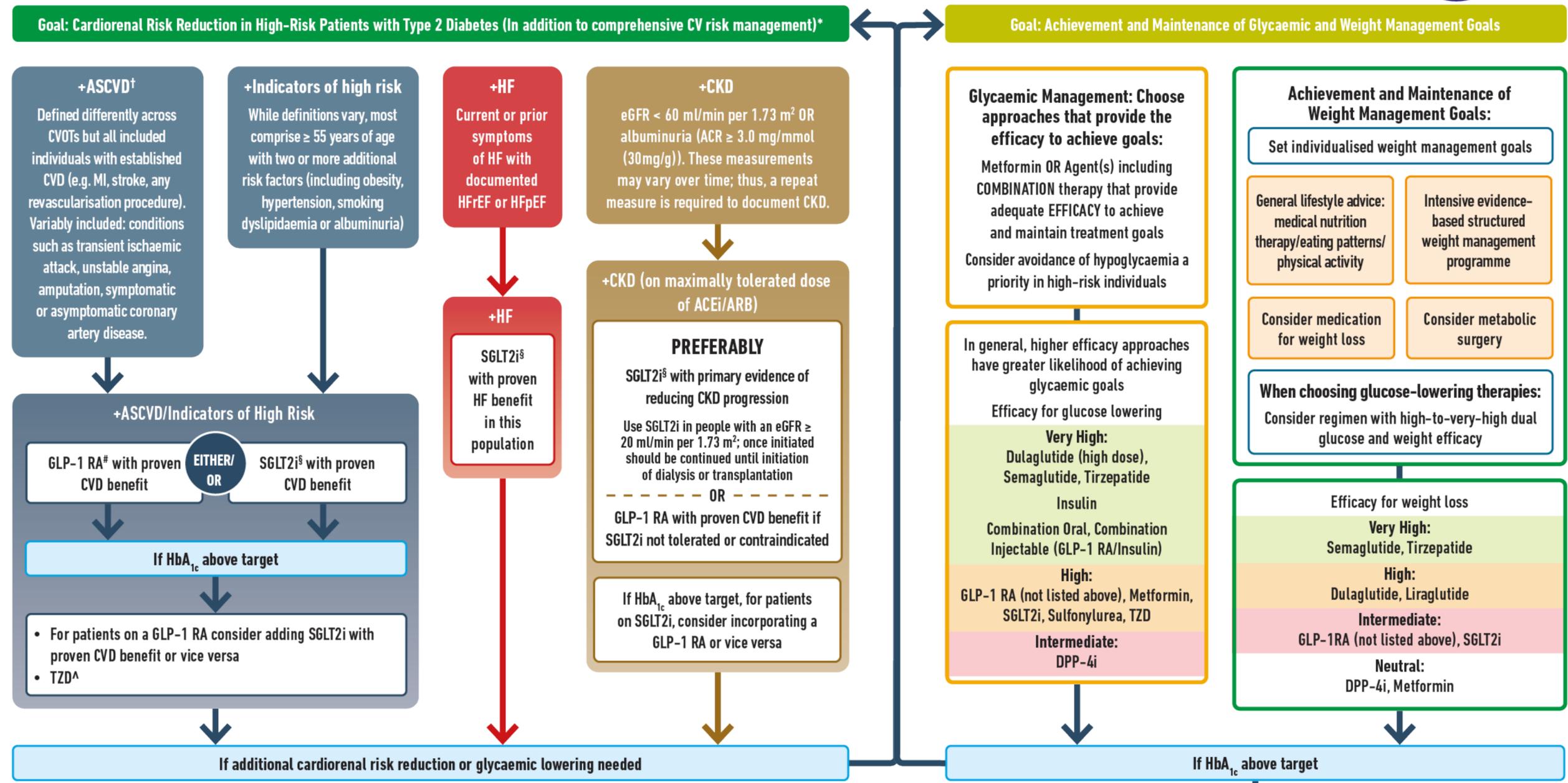
LVH = Left Ventricular Hypertrophy; HFrEF = Heart Failure reduced Ejection Fraction  
 UACR = Urine Albumin-to-Creatinine Ratio; LVEF = Left Ventricular Ejection Fraction

Buse JB et al. 2019 update to: Management of hyperglycaemia in type 2 diabetes, 2018. A consensus report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD) Diabetologia. 2020;63(2):221-228

# FIGURE 3: USE OF GLUCOSE-LOWERING MEDICATIONS IN THE MANAGEMENT OF TYPE 2 DIABETES



HEALTHY LIFESTYLE BEHAVIOURS; DIABETES SELF-MANAGEMENT EDUCATION AND SUPPORT (DSMES); SOCIAL DETERMINANTS OF HEALTH (SDOH)



ACEi, Angiotensin-Converting Enzyme Inhibitor; ACR, Albumin/Creatinine Ratio; ARB, Angiotensin Receptor Blocker; ASCVD, Atherosclerotic Cardiovascular Disease; CGM, Continuous Glucose Monitoring; CKD, Chronic Kidney Disease; CV, Cardiovascular; CVD, Cardiovascular Disease; CVOT, Cardiovascular Outcomes Trial; DPP-4i, Dipeptidyl Peptidase-4 Inhibitor; eGFR, Estimated Glomerular Filtration Rate; GLP-1 RA, Glucagon-Like Peptide-1 Receptor Agonist; HF, Heart Failure; HFpEF, Heart Failure with preserved Ejection Fraction; HFrEF, Heart Failure with reduced Ejection Fraction; HHF, Hospitalisation for Heart Failure; MACE, Major Adverse Cardiovascular Events; MI, Myocardial Infarction; SDOH, Social Determinants of Health; SGLT2i, Sodium-Glucose Cotransporter-2 Inhibitor; T2D, Type 2 Diabetes; TZD, Thiazolidinedione.

\* In people with HF, CKD, established CVD or multiple risk factors for CVD, the decision to use a GLP-1 RA or SGLT2i with proven benefit should be independent of background use of metformin; † A strong recommendation is warranted for people with CVD and a weaker recommendation for those with indicators of high CV risk. Moreover, a higher absolute risk reduction and thus lower numbers needed to treat are seen at higher levels of baseline risk and should be factored into the shared decision-making process. See text for details; ^ Low-dose TZD may be better tolerated and similarly effective; § For SGLT2i, CV/renal outcomes trials demonstrate their efficacy in reducing the risk of composite MACE, CV death, all-cause mortality, MI, HHF and renal outcomes in individuals with T2D with established/high risk of CVD; # For GLP-1 RA, CVOTs demonstrate their efficacy in reducing composite MACE, CV death, all-cause mortality, MI, stroke and renal endpoints in individuals with T2D with established/high risk of CVD.

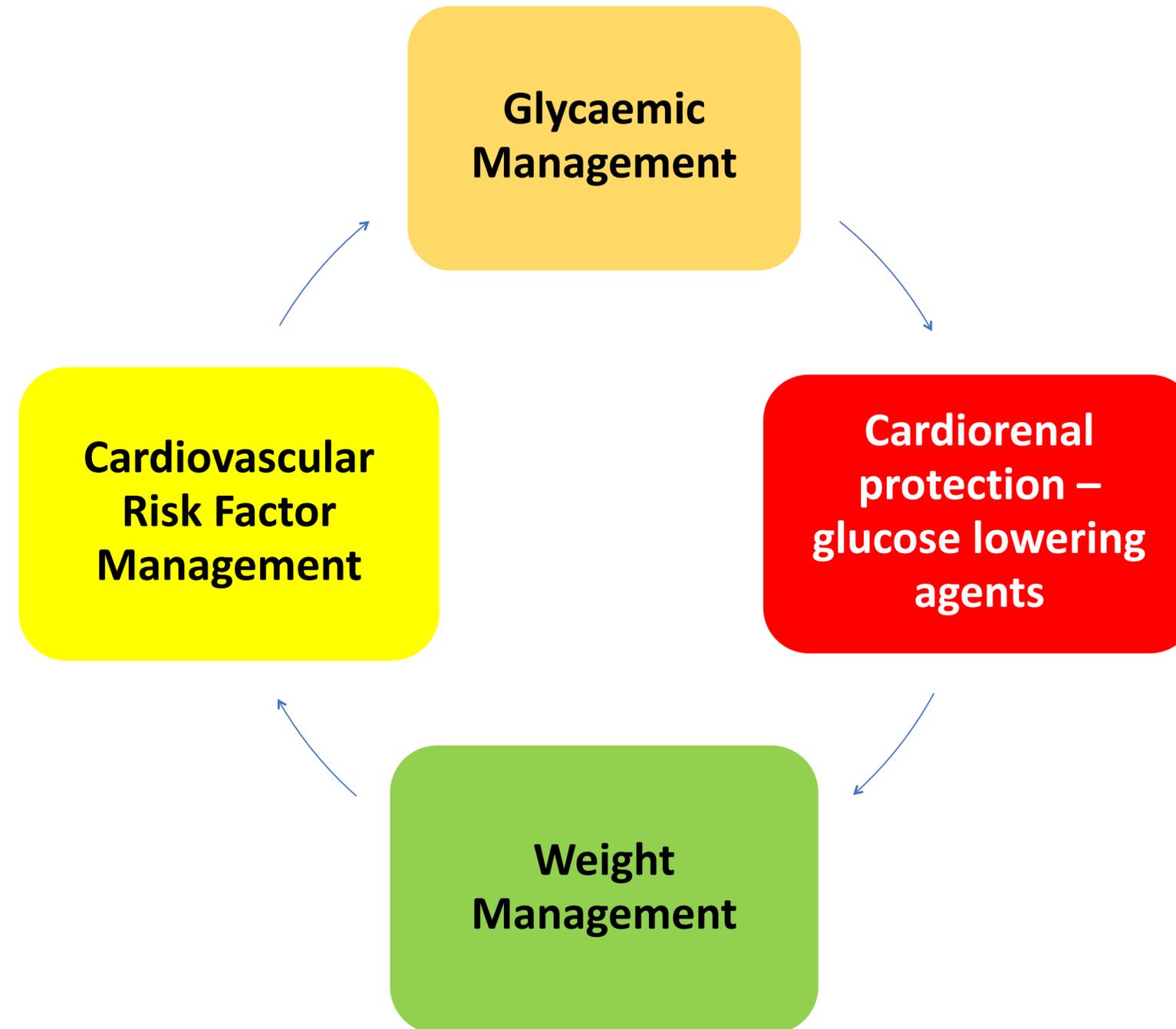
Davies MJ, Aroda VR, Collins BS, Gabbay RA, Green J, Maruthur NM, Rosas SE, Del Prato S, Mathieu C, Mingrone G, Rossing P, Tankova T, Tsapas A, Buse JB

Diabetes Care 2022; <https://doi.org/10.2337/dci22-0034>. Diabetologia 2022; <https://doi.org/10.1007/s00125-022-05787-2>. Copyright ADA/EASD 2022

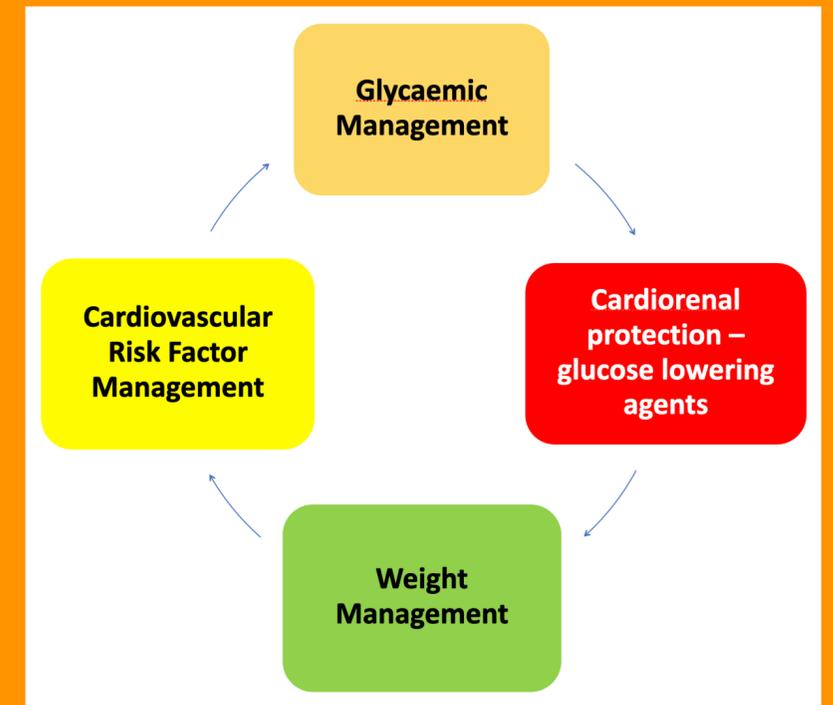


European Association for the Study of Diabetes

# Prise en charge multiscience du patient diabétique de type 2



# Le contrôle glycémique



# OBTENIR LA CIBLE GLYCEMIQUE

1ère ligne: **metformine**

**Après 3 mois** associer si nécessaire/remboursé:

- GLP-1
- SGLT-2
- Sulfonylurée  
(Glitazone)
- DPP-4 (moins puissant)

In general, higher efficacy approaches have greater likelihood of achieving glycaemic goals

Efficacy for glucose lowering

**Very High:**

Dulaglutide (high dose),  
Semaglutide, Tirzepatide

Insulin

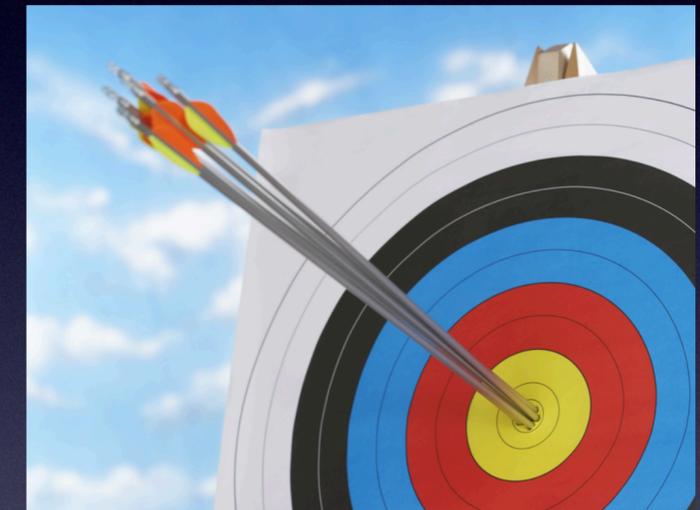
Combination Oral, Combination  
Injectable (GLP-1 RA/Insulin)

**High:**

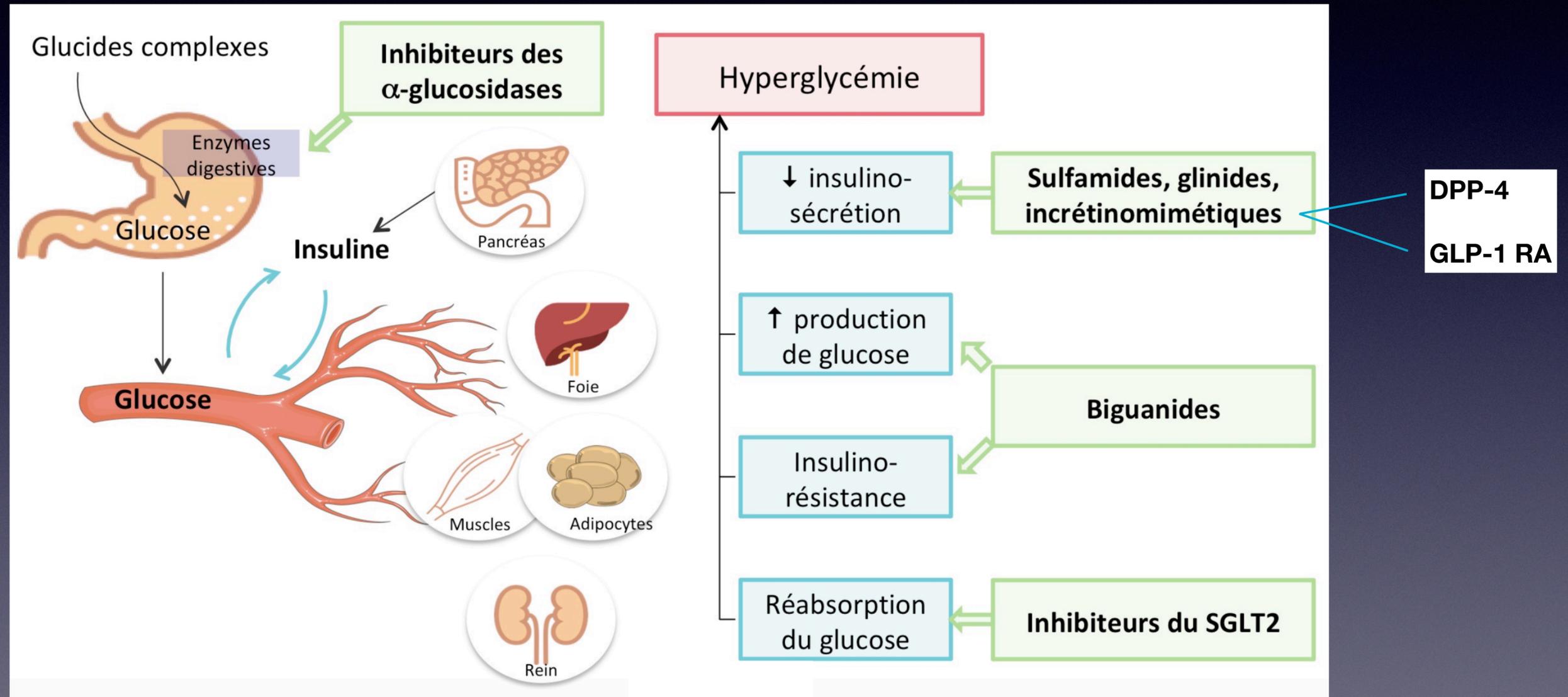
GLP-1 RA (not listed above), Metformin,  
SGLT2i, Sulfonylurea, TZD

**Intermediate:**

DPP-4i

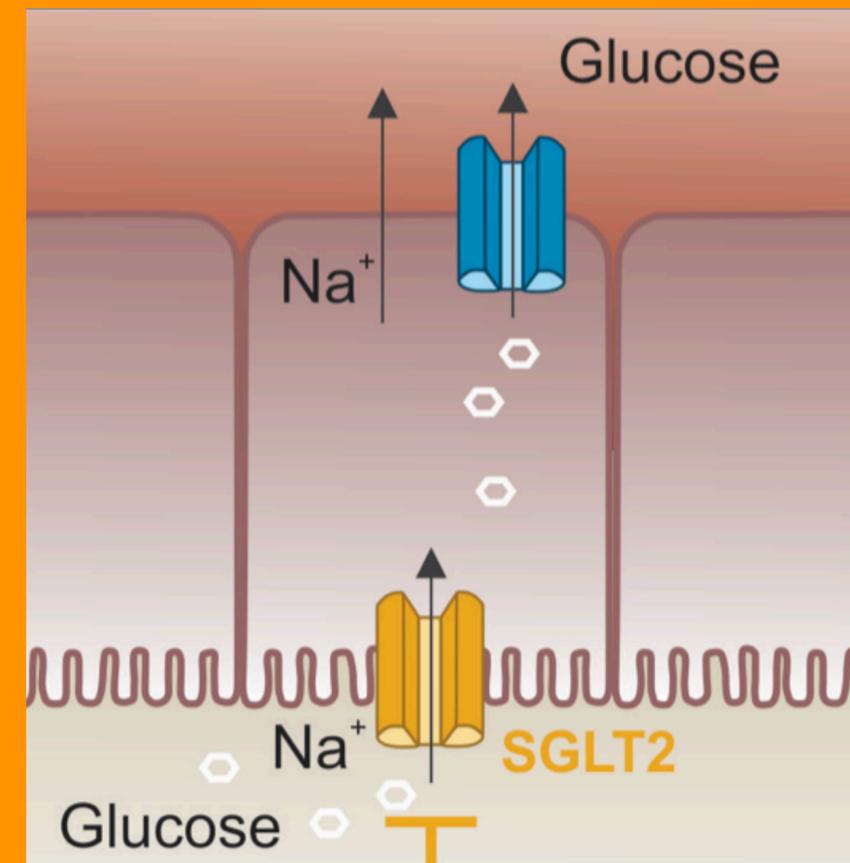
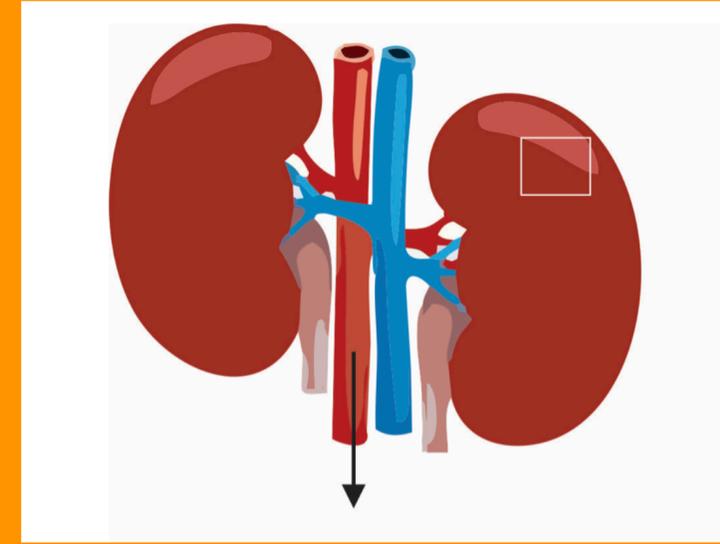


# Organes cibles des anti-diabétiques

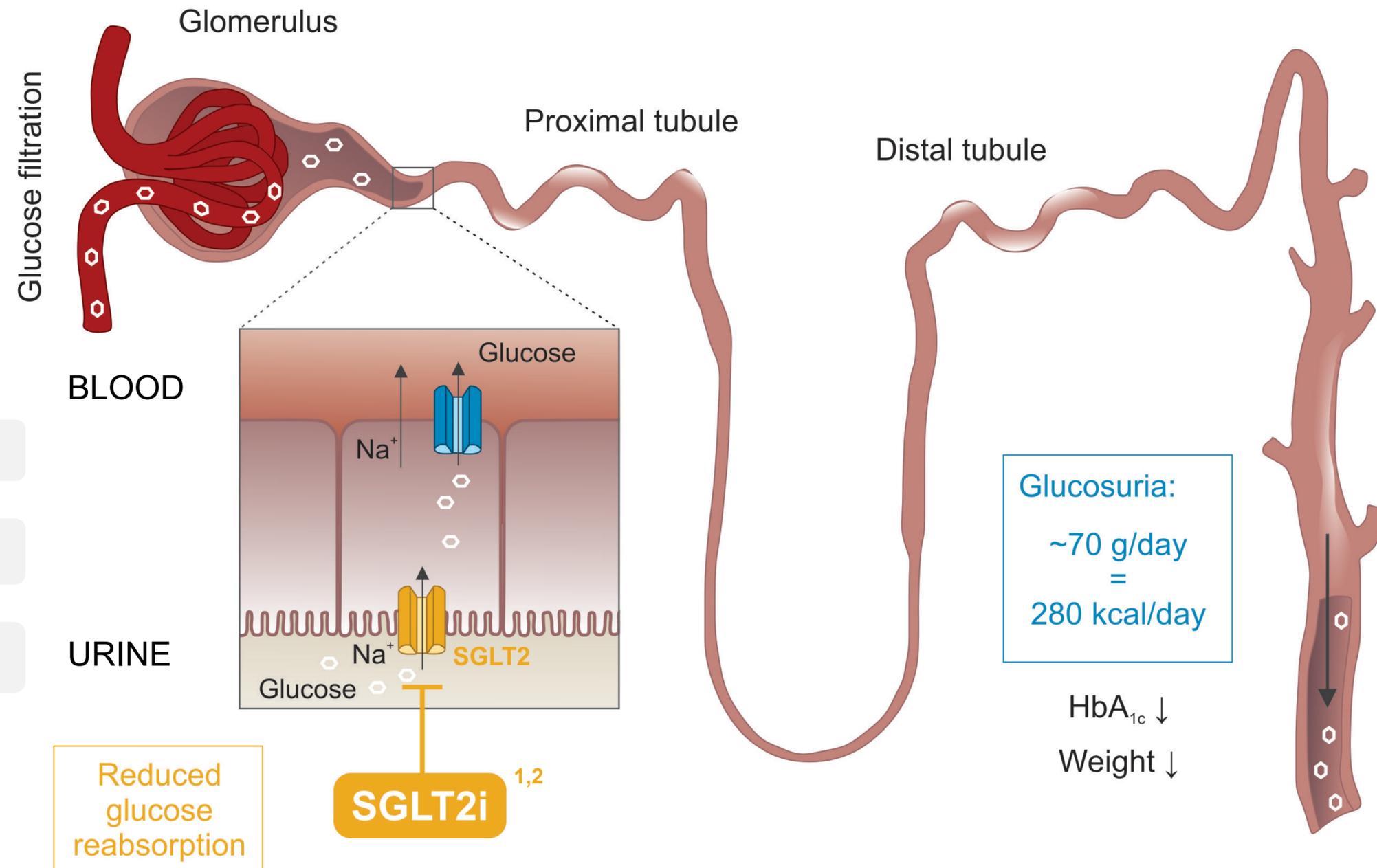
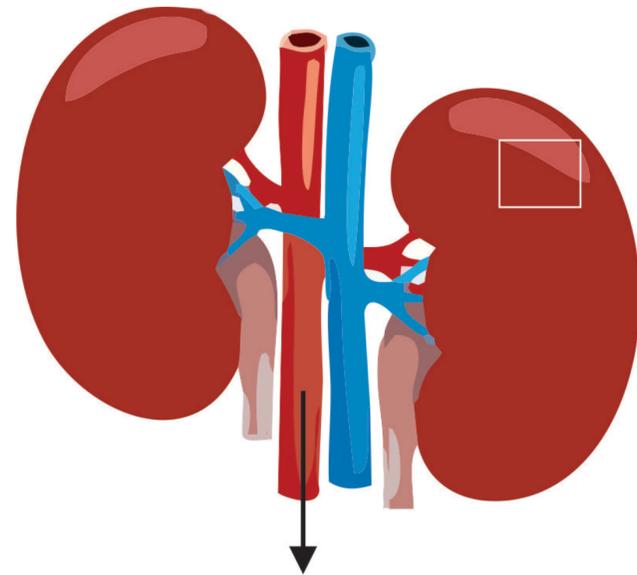


# Les inhibiteurs du SGLT-2

Ou gliflozines



# L'inhibition du récepteur SGLT2 entraîne une augmentation de la glucosurie, de la natriurèse et de la diurèse osmotique



↑ GLUCOSURIA<sup>5</sup>

↑ NATRIURESIS<sup>3,4</sup>

↑ OSMOTIC DIURESIS<sup>3,4</sup>

## Les effets métaboliques

- Etudes de phase 2 et 3 :
  - Réduction de l'HbA1c de 0,5 à 0,9%
  - Perte de poids de 2 à 4 kg en moyenne, au dépend de la masse grasse
  - Diminution de la PAS de 4 mm de Hg et de la PAD de 1,6 mm de Hg
  - Augmentation modérée de LDL-C et plus importante du HDL-c.

CLINICAL TRIAL | VOLUME 85, ISSUE 4, P962-971, APRIL 01, 2014

Long-term study of patients with type 2 diabetes and moderate renal impairment shows that dapagliflozin reduces weight and blood pressure but does not improve glycemic control

Donald E. Kohan   • Paola Fioretto • Weihua Tang • James F. List

L'effet hypoglycémiant des iSGLT-2 diminue en cas d'altération de la fonction rénale.

# Effets secondaires des Gliflozines



## Sodium–Glucose Cotransporter Inhibitors: Effects on Renal and Intestinal Glucose Transport : From Bench to Bedside

Mudaliar S et al. *Diabetes Care* 2015; 38: 2344-2353

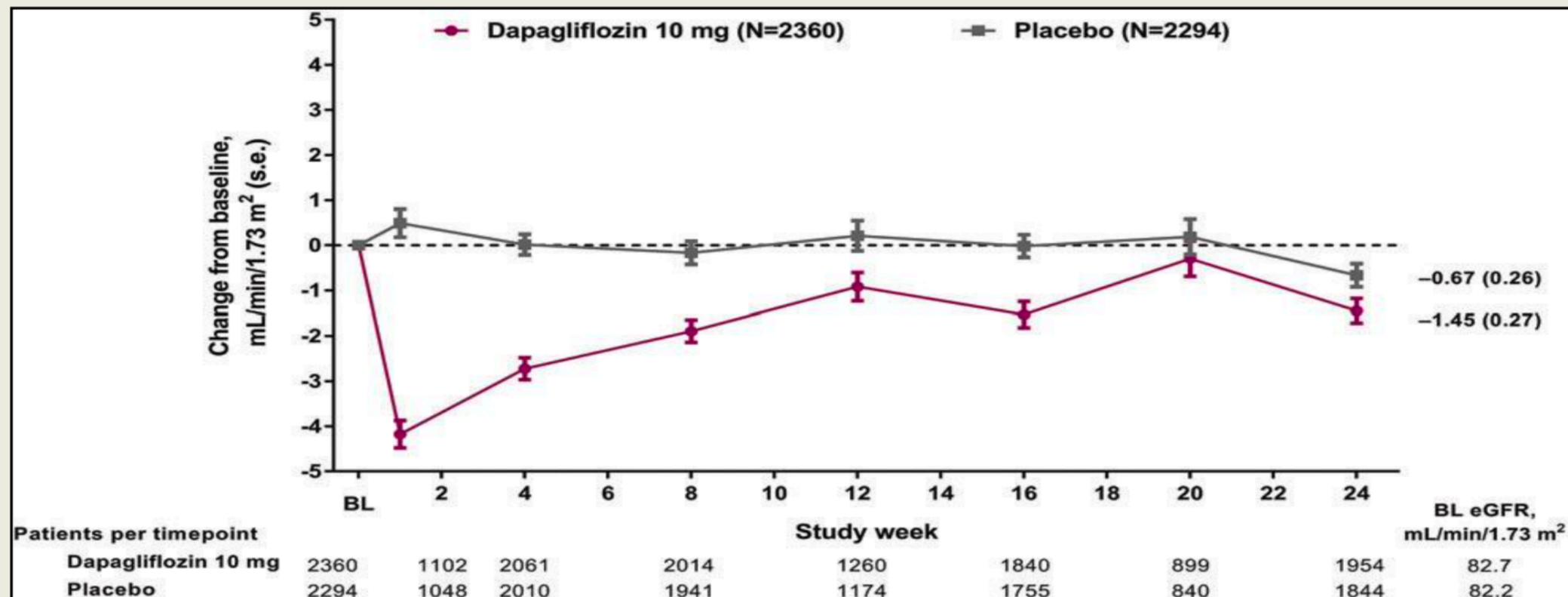
**Infections urinaires (UTI) et génitales (GTI) rapportées dans les études de phase III vs placebo.**

	Canagliflozine (300 mg/j)	Dapagliflozine (10 mg/j)	Empagliflozine (25 mg/j)
<b>UTI</b>	4,3% vs 4,0%	4,3% vs 3,7%	7,7% vs 7,6%
<b>GTI (M)</b>	<b>3,7%</b> vs 0,6%	<b>2,7%</b> vs 0,3%	<b>1,0%</b> vs 0,4%
<b>GTI (F)</b>	<b>11,4%</b> vs 3,2%	<b>4,8%</b> vs 0,9%	<b>6,4%</b> vs 1,5%

Les GTI mycotiques étaient plus fréquentes chez les hommes non-circoncis et chez ceux avec un antécédent de balanite mycotique.

# Autres effets 2aires des Gliflozines

- Polyurie, déshydratation, hypotension (surtout en début de traitement ou si diabète mal équilibré).
- Lié à la diurèse osmotique de la glycosurie et la natriurie



# Rare: **acidocétose euglycémique**

- Risque majoré chez patients insulino-dépendants (type 1 ou type 2 très anciens), indication retirée
- acidocétose avec hyperglycémie MODEREE (glucosurie ++)
- Facteurs de risque: déshydratation, alcool, jeûne prolongé
- **Contre-indiqué dans le diabète de type 1** (et par extension chez les insulino-dépendants au sens large) - en cas de doute: doser C-peptide

Empagliflozin as Adjunctive to  
Insulin Therapy in Type 1 Diabetes:  
The EASE Trials

<https://doi.org/10.2337/dc18-1749>

Julio Rosenstock,<sup>1</sup> Jan Marquard,<sup>2</sup>  
Lori M. Laffel,<sup>3</sup> Dietmar Neubacher,<sup>4</sup>  
Stefan Kaspers,<sup>2</sup> David Z. Cherney,<sup>5</sup>  
Bernard Zinman,<sup>6</sup> Jay S. Skyler,<sup>7</sup>  
Jyothis George,<sup>2</sup> Nima Soleymanlou,<sup>8</sup> and  
Bruce A. Perkins\*

Af

# Critères de remboursement des SGLT-2 dans le diabète de type 2

Pas de formulaire à remplir si TDS

>18 ans

	Jardiance 10 -25	Forxiga 10	Invokana 100 - 300
	<b>1ère demande</b>		
au moins 3 mois avec au moins 1 antidiabétique, dont la metformine		+	
HbA1c entre 7 et 9%		+	
Ne pas associer à incrétine		+	
Ne pas associer ultérieurement DPP4		+	
GFR (ml/min)	10 mg: > 30 25 mg: > 60	> 60 > 45 prolongation	100 mg: 30/45 avec macroA 45-59 300 mg: > 60

+ Formes combinées avec la Metformine: Synjardy, Xigduo

# Autres indications des SGLT-2 - autres critères de remboursement

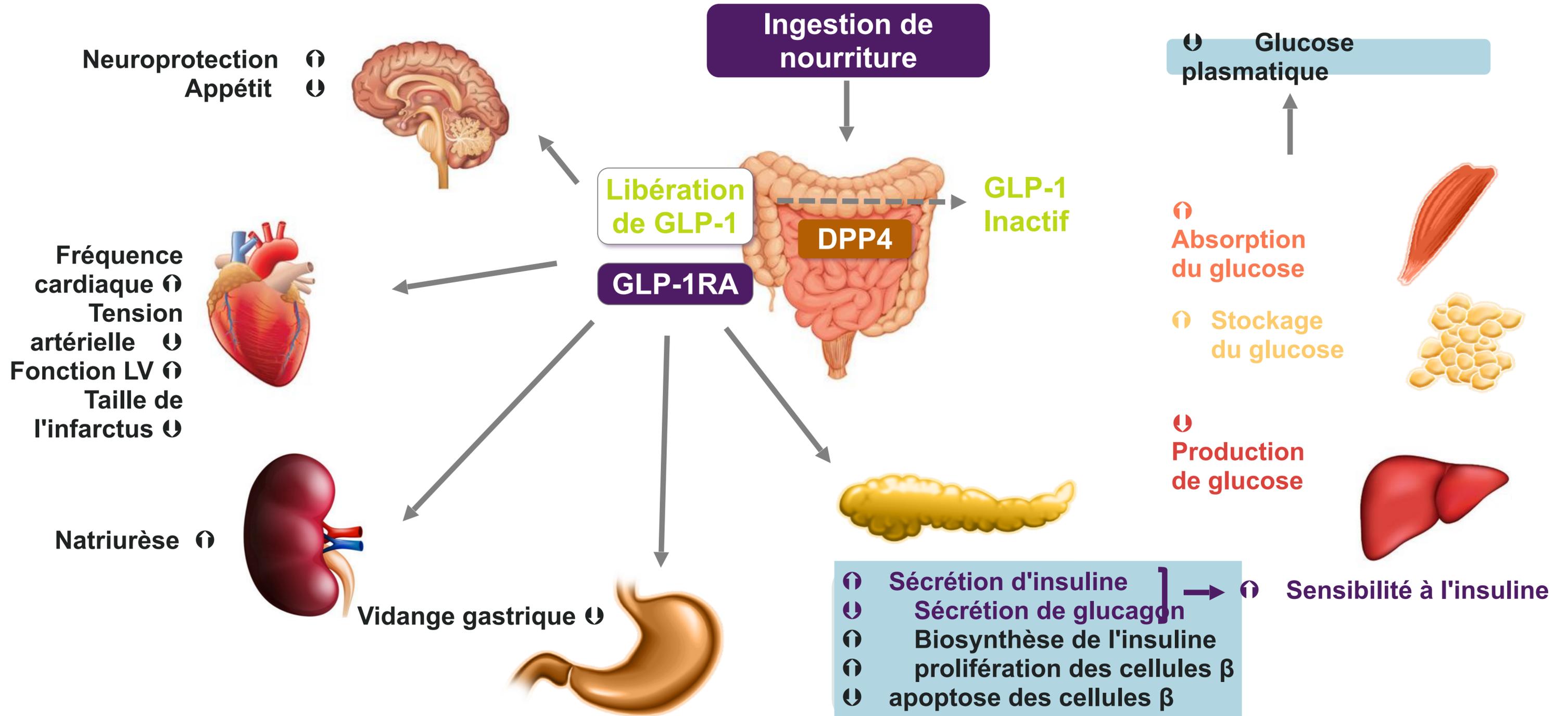
- Insuffisance rénale chronique:
  - **Forxiga** Demande par MG/spécialiste
- Insuffisance cardiaque
  - **Forxiga** Demande par cardiologue
  - **Jardiance**
- Permettent d'associer les GLP-1 et les SGLT-2 chez certains patients diabétiques de type 2 sélectionnés

# Différentes indications/ remboursements des SGLT-2

	<b>INDICATIONS</b>	<b>Remboursements</b>
<b>DIABETE DE TYPE2</b>	TOUS	TOUS
<b>IRC albuminurique</b>	TOUS	FORXIGA
<b>Insuffisance cardiaque</b>	FORXIGA + JARDIANCE	FORXIGA +JARDIANCE



# La stimulation du récepteur GLP1 entraîne une augmentation de la libération d'insuline et une réduction de la réponse à la libération de glucagon



1. Drucker DJ et al. Diabetes. 2015;64:317-326; 2. Campbell JE et al. Cell Metab. 2013;17:819-837; 3. Baggio LL et al. Gastroenterology. 2007;132:2131-2157; 4. Ussher JR et al. Circ Res. 2014;114:1788-1803; 5. Hinnen et al. Diabetes spectrum 2017; 30(3):202-210

# Les agonistes du Récepteur GLP-1

## ▪ Exenatide

- **Byetta®** ( Af, Stylo 5 µg ou 10 µg – s.c. 2x/jour )
- **Bydureon®** ( Af, Stylo 2 mg – s.c. 1x/semaine )

- Courte durée d'action
- Longue durée d'action
- Très longue durée d'action

## ▪ Liraglutide

- **Victoza®** ( Af, Stylo 0.6 mg à 1.8 mg – s.c. 1x/jour )
- **Xultophy®** ( Af, premix avec insuline, 16 à 50U 1x/jour )
- **Saxenda®** ( Af, Stylo 0.6 mg à 3.0 mg – s.c. 1x/jour ) Traitement Obésité

## ▪ Lixisénatide

- **Lyxumia®** ( Af, Stylo 10 µg ou 20 µg – s.c. 1x/jour )

## ▪ Dulaglutide

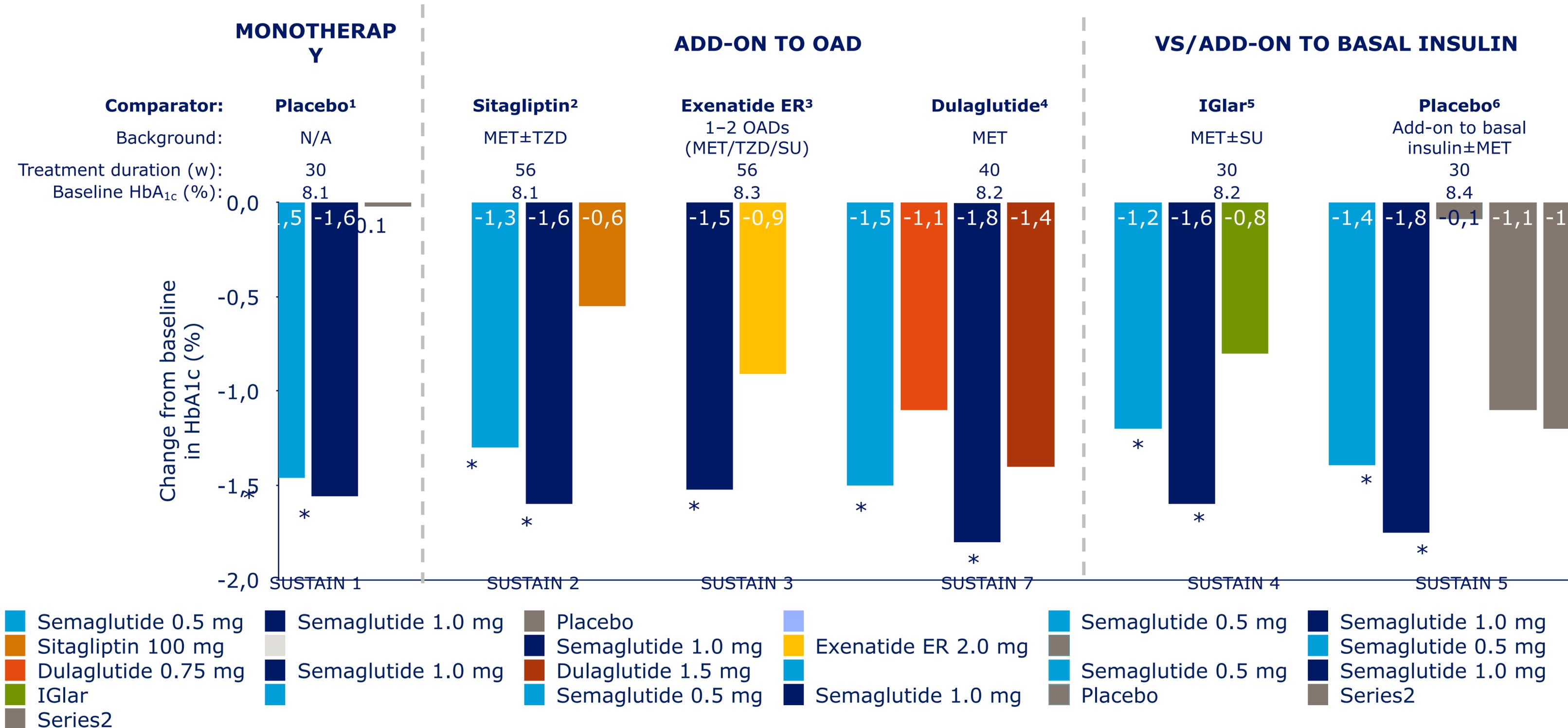
- **Trulicity®** ( Af, Stylo 0,75 mg ou 1,5 mg – s.c. 1x/semaine )

## ▪ Semaglutide

- **Ozempic®** ( Af, Stylo 0,25 mg, 0;50 mg et 1,0 mg – s.c. 1x/semaine )
- **Rybelsus** ( Af cp 3 mg, 7 mg 14 mg, oral 1x/J )

# Change in HbA<sub>1c</sub>

SUSTAIN 1-5 and 7



# Effets secondaires des GLP-1

## Etude REWIND (dulaglutide)

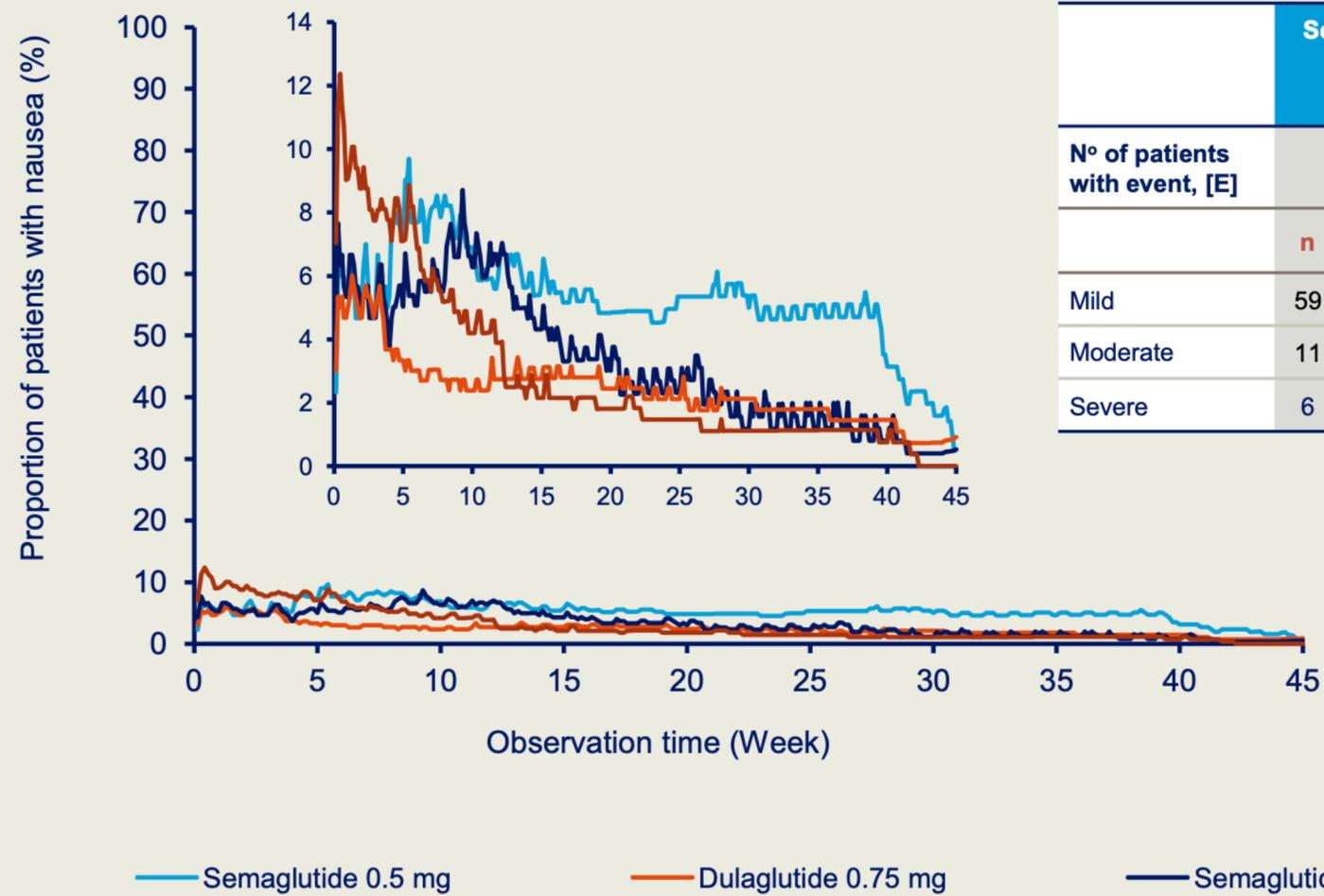
### Adverse Events of Special Interest (cont.)

<b>Adverse Event</b>	<b>Dulaglutide n=4949</b>	<b>Placebo n=4952</b>	<b>P-Value</b>
Serious hepatic event (%)	0.5	0.8	.057
Serious renal/urinary event (%)	1.7	1.9	.46
Immune reactions (%)	0.2	0.4	.022
Serious GI event (%)	2.4	2.4	.87
SVT/CV conduction disorders (%)	4.4	3.9	.26
Severe hypoglycaemia (%)	1.3	1.5	.38
<i>Gastrointestinal disorders*</i> (%)	47.4	34.1	<.0001

\*adverse events that occurred in more than 5% of participants were diarrhea, nausea, constipation, and vomiting

# GLP-1: effets secondaires digestifs

## Nausées



	Semaglutide 0.5 mg (n=301)			Dulaglutide 0.75 mg (n=299)			Semaglutide 1.0 mg (n=300)			Dulaglutide 1.5 mg (n=299)		
N° of patients with event, [E]	68 [145]			39 [66]			63 [192]			60 [108]		
	n	E	(E%)	n	E	(E%)	n	E	(E%)	n	E	(E%)
Mild	59	127	(87.6)	34	60	(90.9)	51	147	(76.6)	48	84	(77.8)
Moderate	11	12	(8.3)	6	6	(9.1)	22	42	(21.9)	16	21	(19.4)
Severe	6	6	(4.1)	0			3	3	(1.6)	3	3	(2.8)

Adapted from Figure S7.

Adverse events include events that had an onset, or increase in severity, shown from first exposure to the planned follow-up visit scheduled 5 weeks (+7-day visit window) after the end of treatment visit at week 40 (on-treatment data). Severity of adverse events was defined as follows: mild (transient symptoms, no interference with patient's daily activities); moderate (marked symptoms, moderate interference with patient's daily activities); severe (considerable interference with patient's daily activities, unacceptable).

E, number of events; E%, proportion of events (mild/moderate/severe); n, number of patients.

# Caractéristiques des analogues GLP-1

- Efficacité élevée (chute HbA1c parfois  $>1,5\%$ ) (=insuline)
- Faible risque d'hypoglycémie
- Perte de poids (2,5 à 6 kg)
- ES: gastro-intestinaux, majoritairement temporaires
- CI: gastroparésie - **rétinopathie (vérifier le FO)**
- Insuffisance rénale: GFR  $> 15$ , sans adaptation de la dose

# SC

# ORAL

5 ou 10 mcg 2x/J



2x/jour

2 mg 1x/sem



0,6 à 1,8 mg 1x/J



1x/jour

0,75-1,5 mg 1x/sem



20 mcg 1x/J



1x/J

0,25-0,5-1 mg 1x/sem



3, 7 ou 14 mg 1x/J



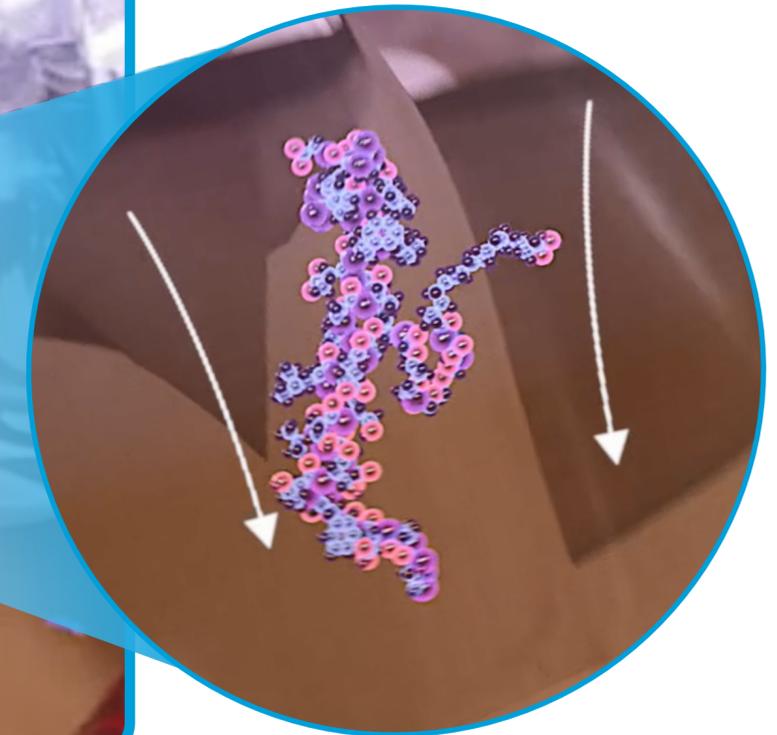
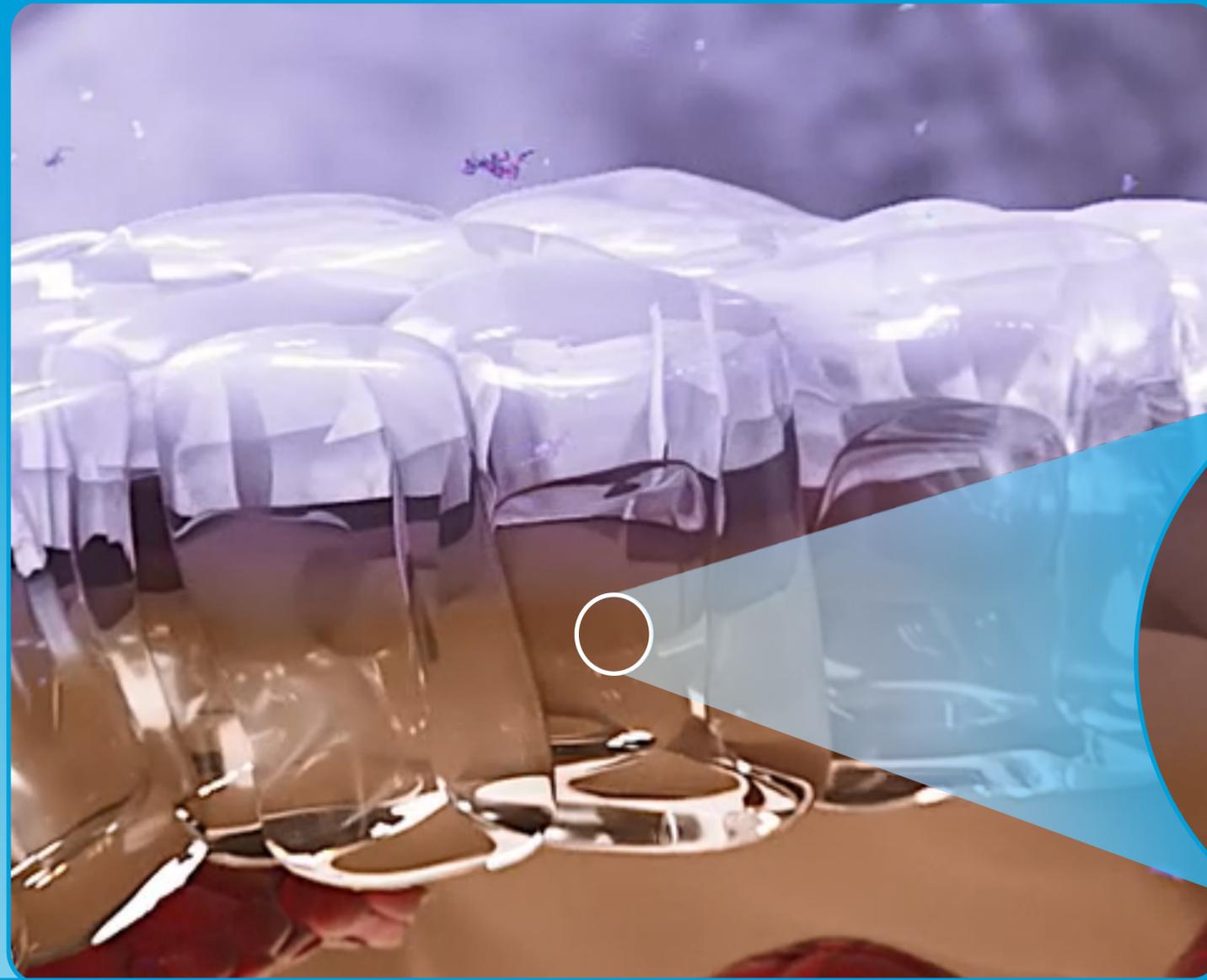
## Absorption challenges of oral peptide-based drugs

- Degradation in the stomach
  - Low pH
  - Proteolytic enzymes
- Limited permeability across the gastrointestinal epithelium
- GLP-1RAs administered alone have very low oral bioavailability (<0.01%)



## Transcellular absorption of semaglutide

- The effect of SNAC is strictly time- and concentration-dependent, and fully reversible
- Approximately 1% of semaglutide is absorbed, the rest is degraded in the GI tract



# Critères de remboursement des GLP-1

- **Au moins un antidiabétique dont la metformine pendant au moins 3 mois.**
- **HbA1c est  $>7,5$  %**
- **IMC égal ou supérieur à  $30 \text{ kg/m}^2$**

Jamais en monothérapie mais en association avec la :

- metformine
- metformine et sulfamidé hypoglycémiant
- metformine et glinide
- metformine et glitazone
- metformine et insuline basale

Pas d'association avec: gliptine, gliflozine ou autre incrétinomimétique.

**Première prolongation:** HbA1c  $< 7,0$  % ou diminution de l'HbA1c  $>$  ou  $= 1,0$  % par rapport à la valeur initiale obtenue.

Pas de formulaire à remplir  
si TDS

# GLP-1 RA Therapeutic Updates

- Higher dose GLP-1 RAs (dulaglutide, semaglutide) with incremental benefits in glucose weight efficacy
- Greater clinical expertise in anticipating and addressing GI effects

## Efficacy and safety of once-weekly semaglutide 2.0 mg versus 1.0 mg in patients with type 2 diabetes (SUSTAIN FORTE): a double-blind, randomised, phase 3B trial



Juan P Frias, Pemille Auerbach, Harpreet S Bajaj, Yasushi Fukushima, Ildiko Lingvay, Stanislava Macura, Anette L Sondergaard, Tsvetelina I Tankova, Nikolaos Tentolouris, John B Buse

### Summary

**Background** Semaglutide is an effective treatment for type 2 diabetes; however, 20–30% of patients given semaglutide 1.0 mg do not reach glycaemic treatment goals. We aimed to investigate the efficacy and safety of once-weekly semaglutide 2.0 mg versus 1.0 mg in adults with inadequately controlled type 2 diabetes on a stable dose of metformin with or without a sulfonylurea.

*Lancet Diabetes Endocrinol* 2021; 9:563-74  
Published Online July 19, 2021  
[https://doi.org/10.1016/S2213-8587\(21\)00174-1](https://doi.org/10.1016/S2213-8587(21)00174-1)

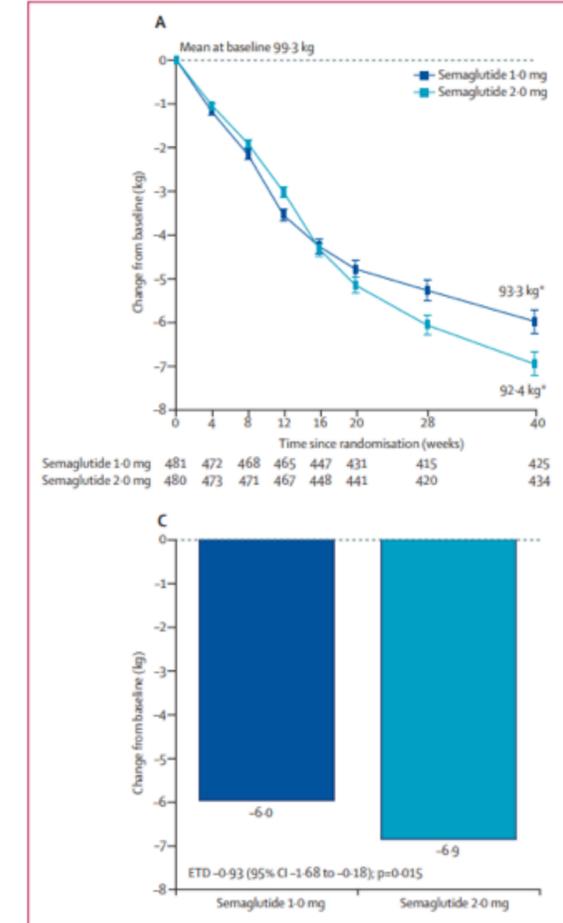
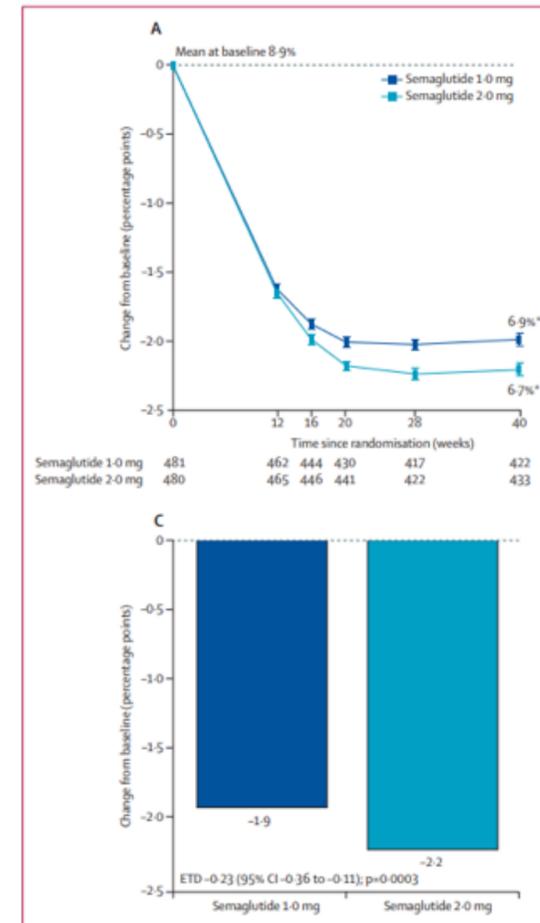
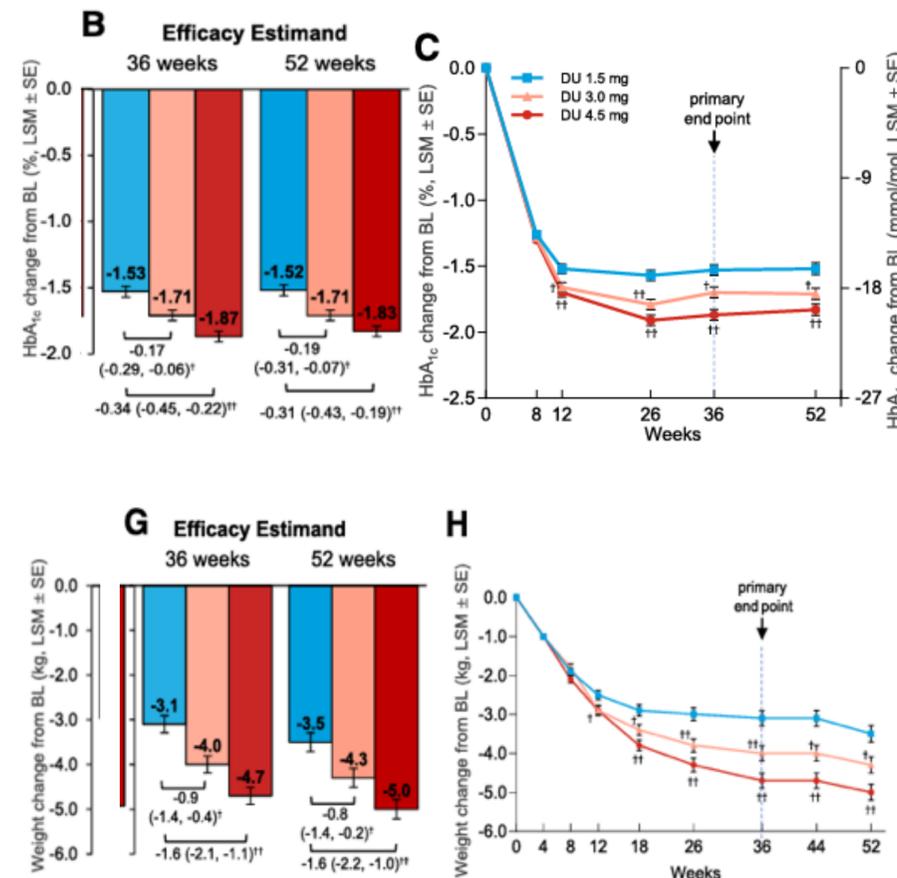
Diabetes Care Volume 44, March 2021 765



### Efficacy and Safety of Dulaglutide 3.0 mg and 4.5 mg Versus Dulaglutide 1.5 mg in Metformin-Treated Patients With Type 2 Diabetes in a Randomized Controlled Trial (AWARD-11)

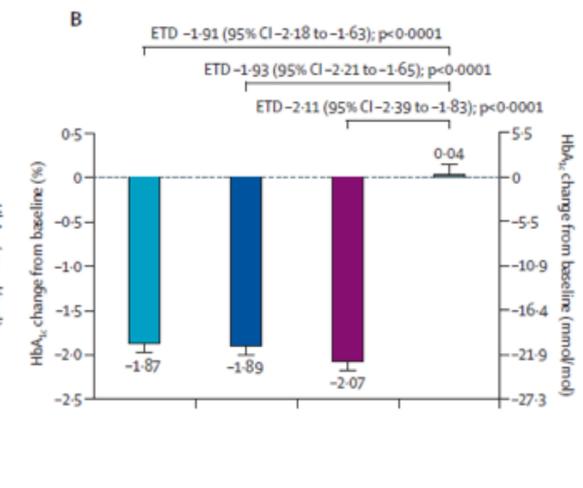
Juan P. Frias,<sup>1</sup> Enzo Bonora,<sup>2</sup> Luis Nevarez Ruiz,<sup>3</sup> Ying G. Li,<sup>4</sup> Zhuoxin Yu,<sup>4</sup> Zvonko Milicevic,<sup>4</sup> Raleigh Malik,<sup>4</sup> M. Angelyn Bethel,<sup>4</sup> and David A. Cox<sup>4</sup>

*Diabetes Care* 2021;44:765–773 | <https://doi.org/10.2337/dc20-1473>

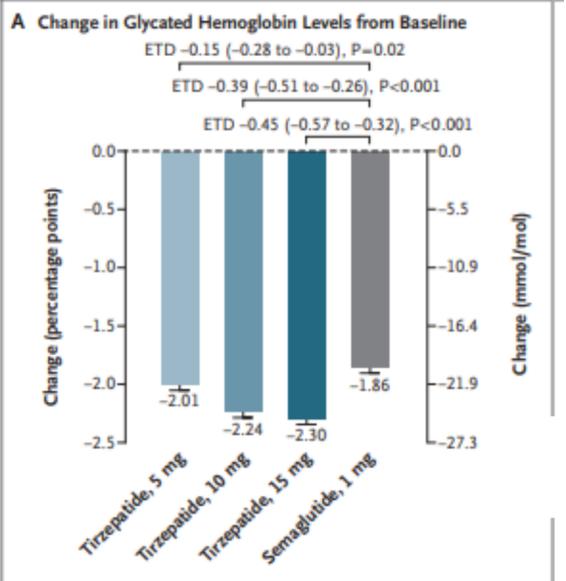


# Glucose-dependent insulinotropic polypeptide (GIP) receptor and GLP-1 receptor agonist (tirzepatide)

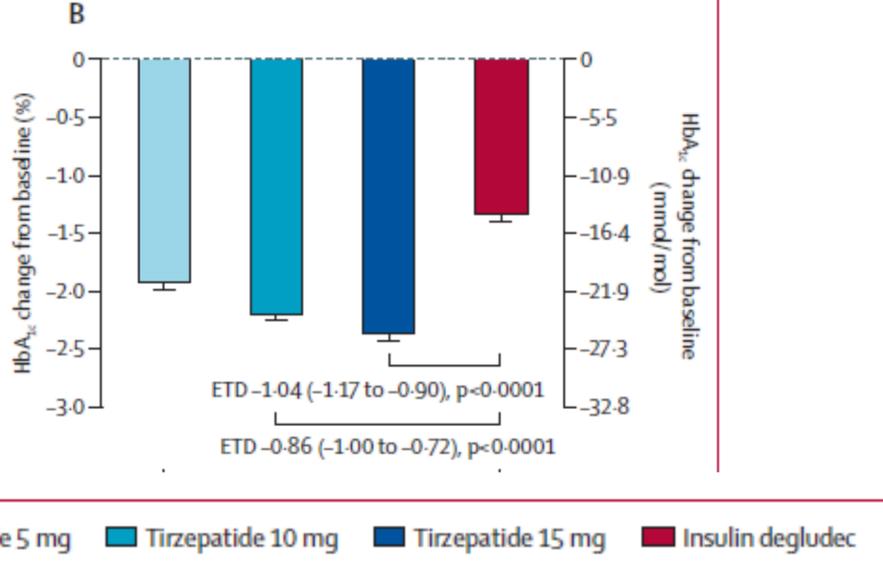
**SURPASS-1**



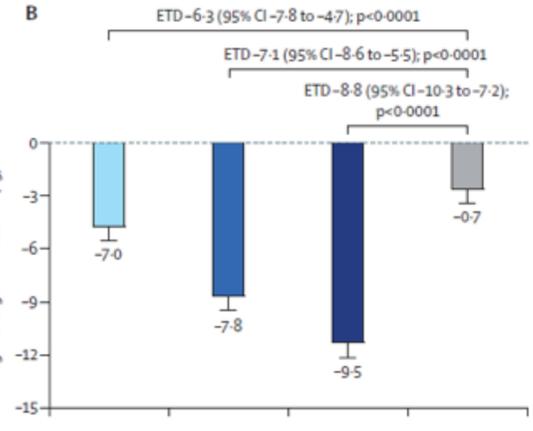
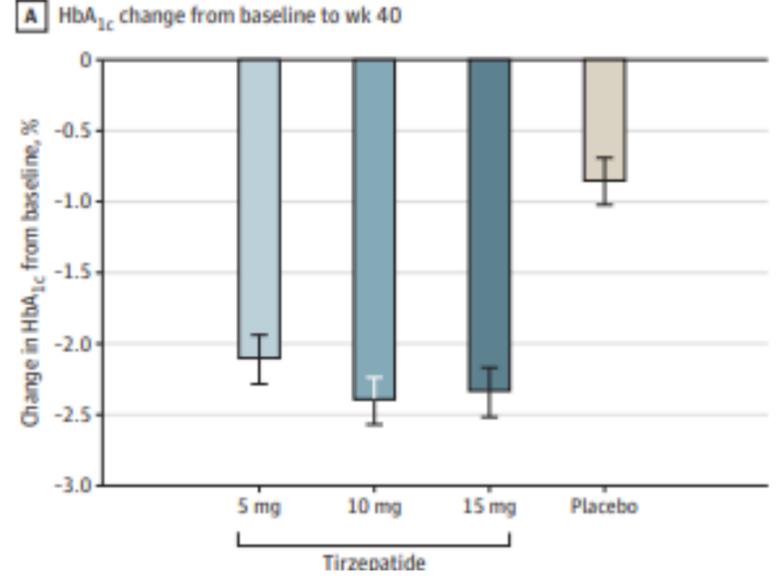
**SURPASS-2**



**SURPASS-3**



**SURPASS-5**



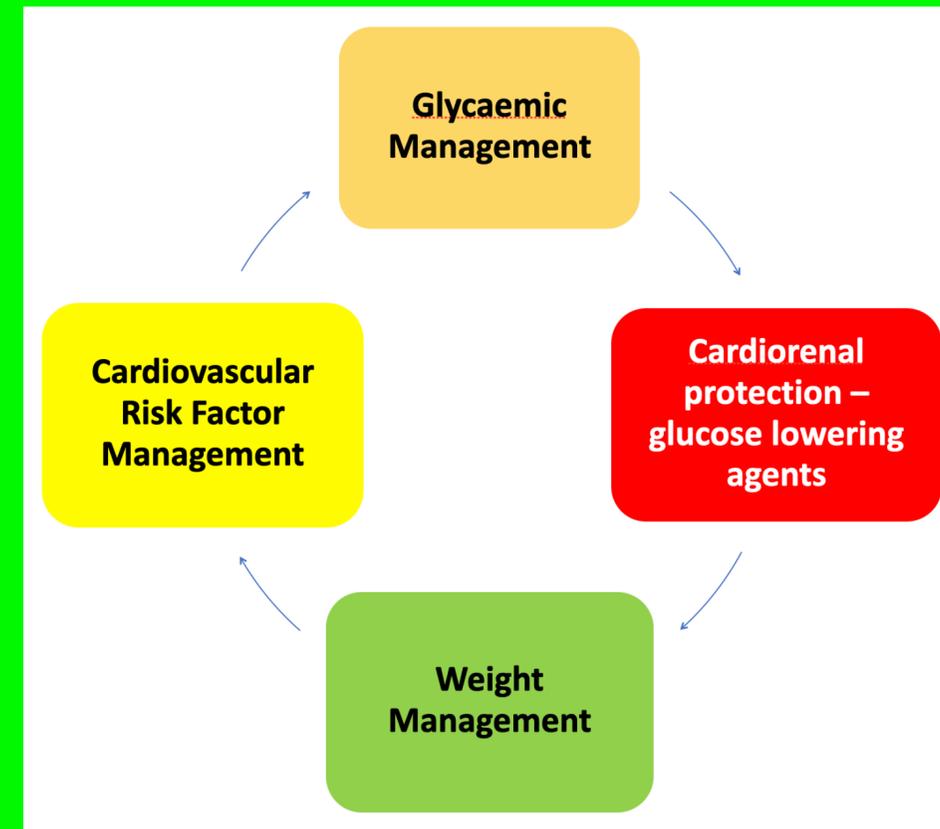
	Tirzepatide 5 mg (n=326)	Tirzepatide 10 mg (n=321)	Tirzepatide 15 mg (n=334)	Insulin glargine (n=978)
<b>HbA<sub>1c</sub> %</b>				
Baseline	8.52 (0.049)	8.60 (0.049)	8.52 (0.048)	8.51 (0.028)
At week 52	6.29 (0.054)	6.09 (0.054)	5.95 (0.054)	7.09 (0.031)
Change from baseline at week 52*†	-2.24 (0.053)	-2.43 (0.053)	-2.58 (0.053)	-1.44 (0.030)
ETD vs insulin glargine	-0.80 (-0.92 to -0.68), p<0.0001‡	-0.99 (-1.11 to -0.87), p<0.0001‡	-1.14 (-1.26 to -1.02), p<0.0001‡	..

**SURPASS-4**

Rosenstock J *et al*; *Lancet* 2021; 398: 143-55  
 Frias JP *et al*; *NEJM* 2021;385:503-  
 Ludvik B *et al*; *Lancet* 2021; 398: 583-98  
 Del Prato S Kahn SE *et al*; *Lancet* 2021; 398:1811-1824  
 Dahl D *et al*; *JAMA*. 2022;327(6):534-545



# La prise en charge de l'excès pondéral

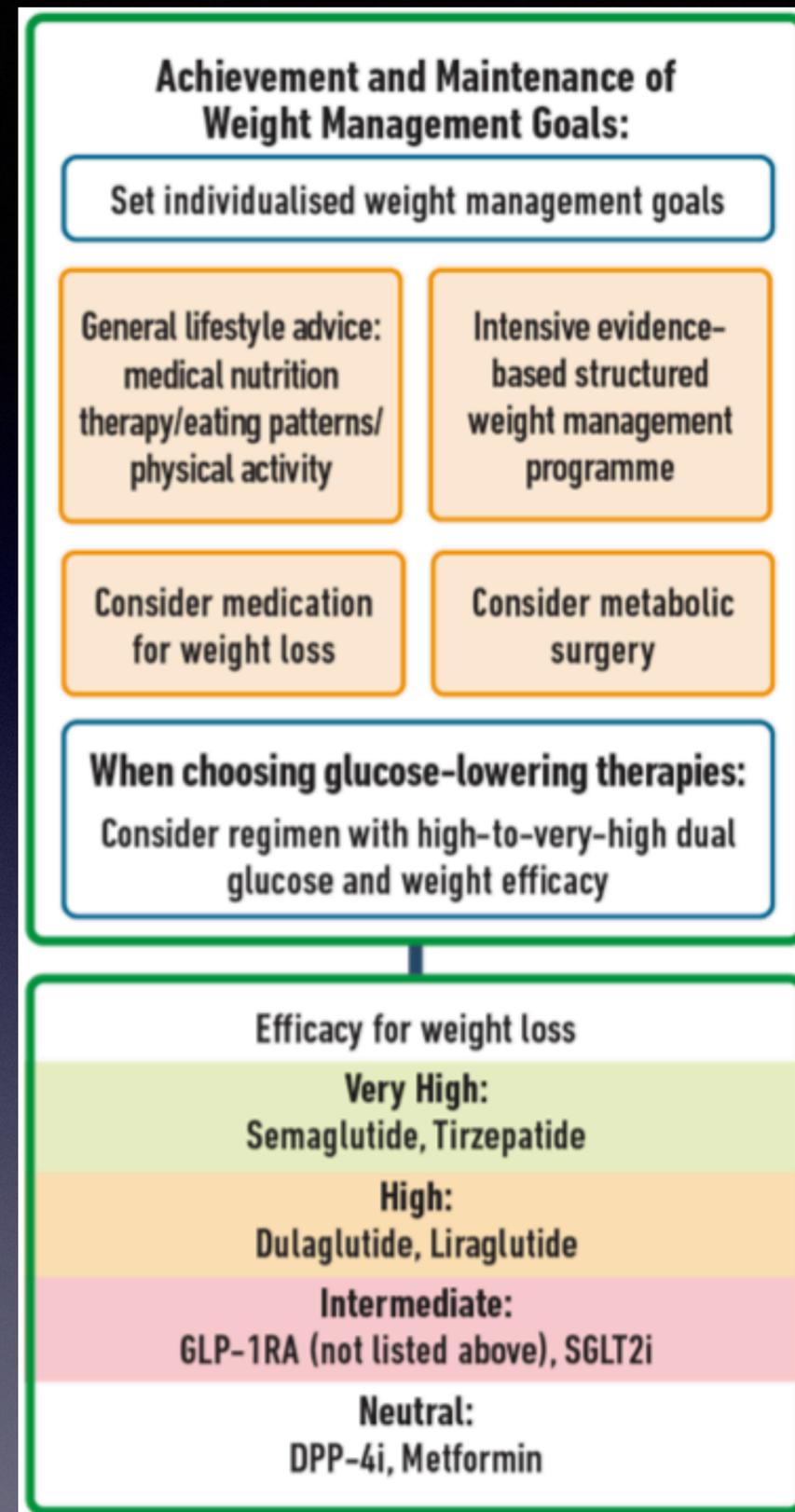


Mesures diététiques

Activité physique

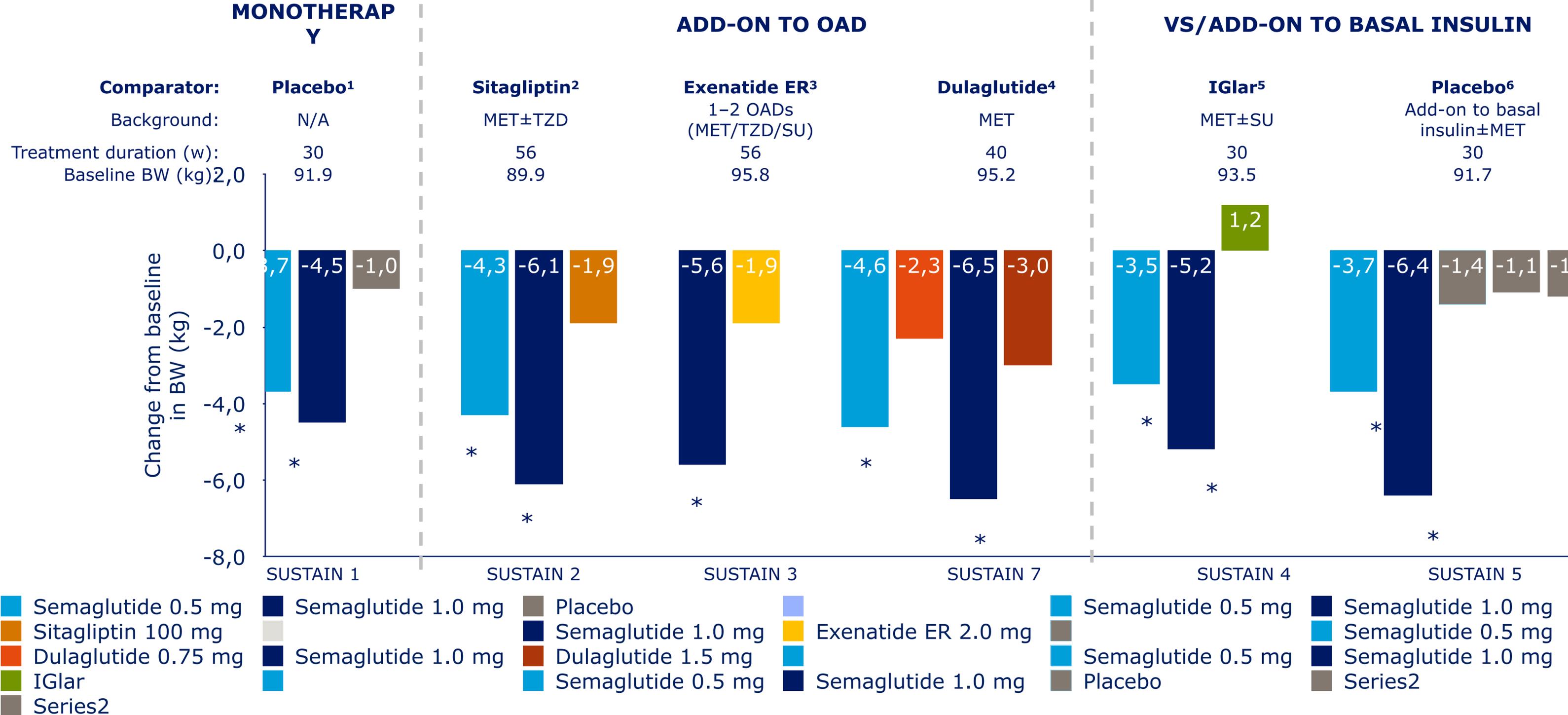
Envisager  
médicament

Considérer la  
chirurgie



# Change in body weight - OZEMPIC

SUSTAIN 1-5 and 7



# Weight Management in Type 2 Diabetes

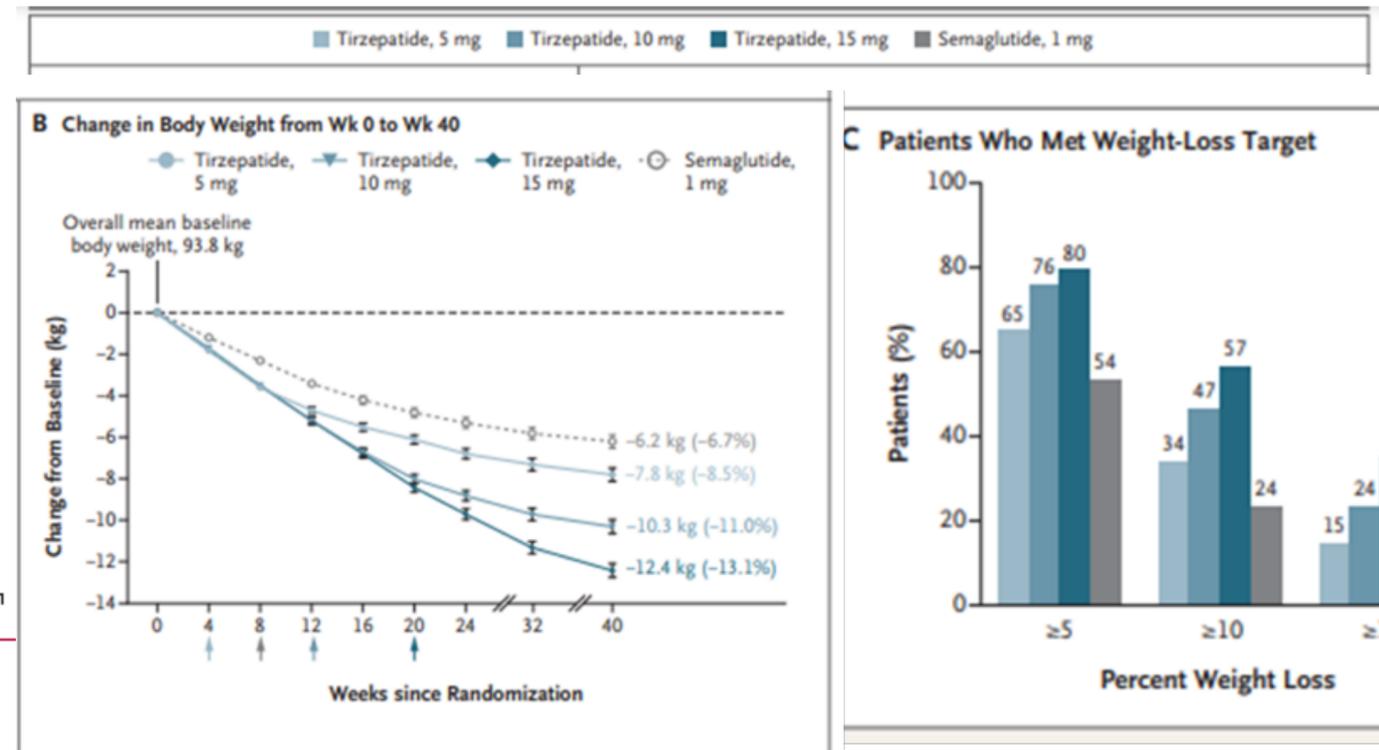
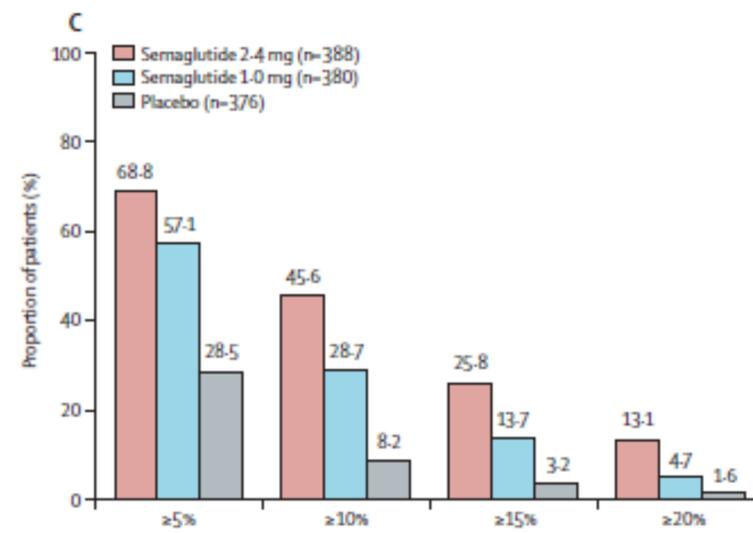
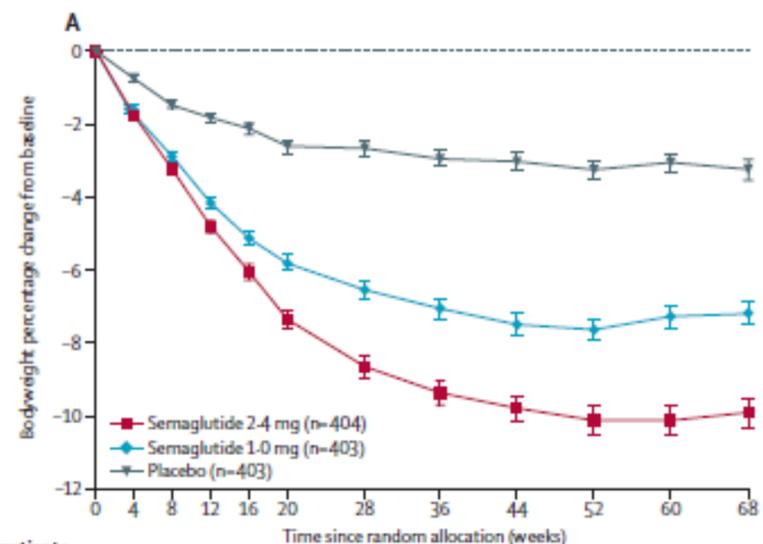
## Tirzepatide versus Semaglutide Once Weekly in Patients with Type 2 Diabetes

Juan P. Frías, M.D., Melanie J. Davies, M.D., Julio Rosenstock, M.D., Federico C. Pérez Manghi, M.D., Laura Fernández Landó, M.D., Brandon K. Bergman, Pharm.D., Bing Liu, Ph.D., Xuwei Cui, Ph.D., and Katelyn Brown, Pharm.D., for the SURPASS-2 Investigators\*

Semaglutide 2.4 mg once a week in adults with overweight or obesity, and type 2 diabetes (STEP 2): a randomised, double-blind, double-dummy, placebo-controlled, phase 3 trial



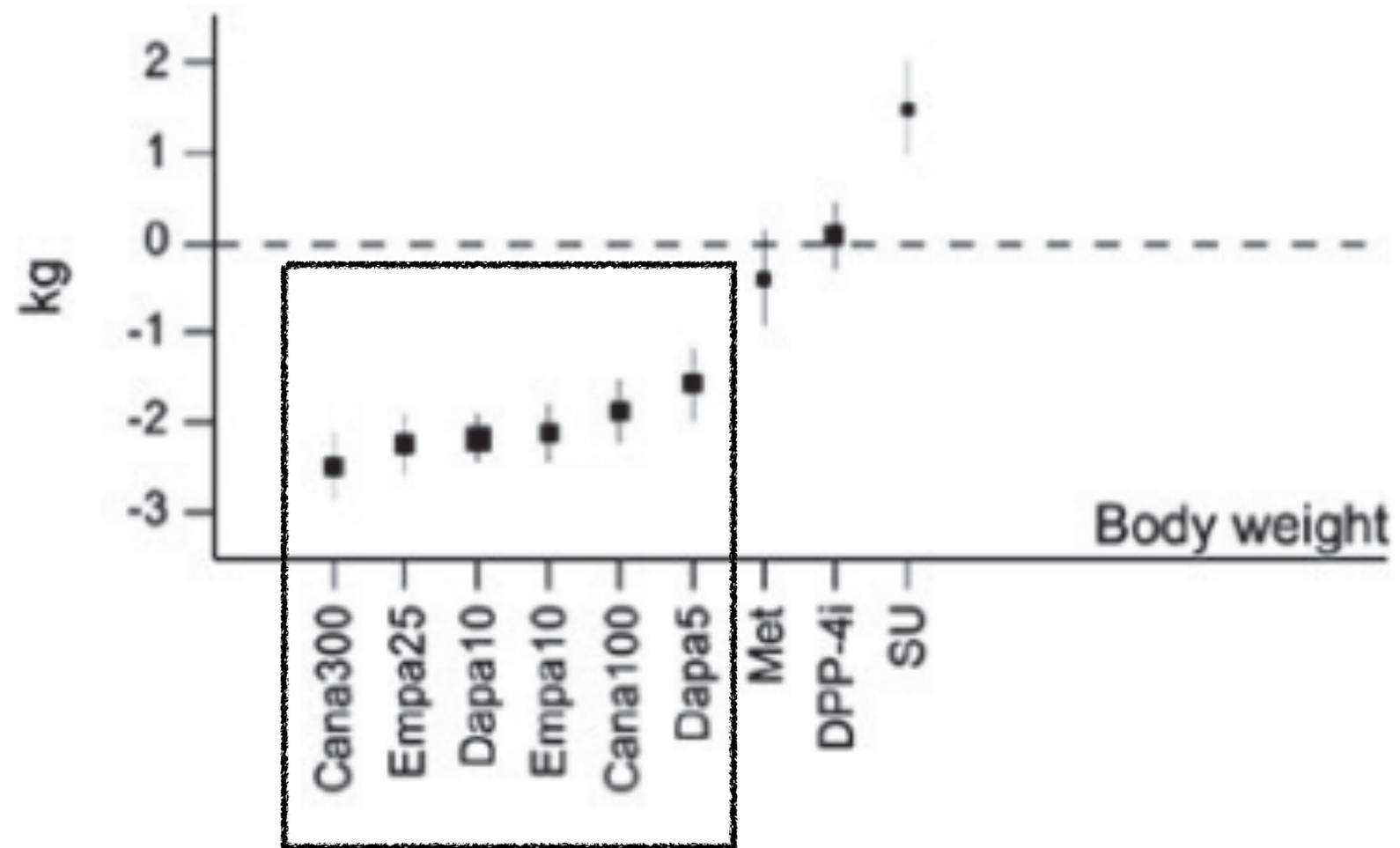
Melanie Davies, Louise Færch, Ole K. Jeppesen, Arash Pakseresh, Sue D. Pedersen, Leigh Perreault, Julio Rosenstock, Ichiro Shimomura, Adie Viljoen, Thomas A. Wadden, Ildiko Lingway, for the STEP 2 Study Group\*



Number of patients	0	4	8	12	16	20	28	36	44	52	60	68
Semaglutide 2.4 mg	404	395	397	390	388	392	386	383	381	381	378	388
Semaglutide 1.0 mg	403	394	392	385	383	383	378	377	373	370	374	380
Placebo	403	398	394	389	387	383	381	377	371	367	366	376

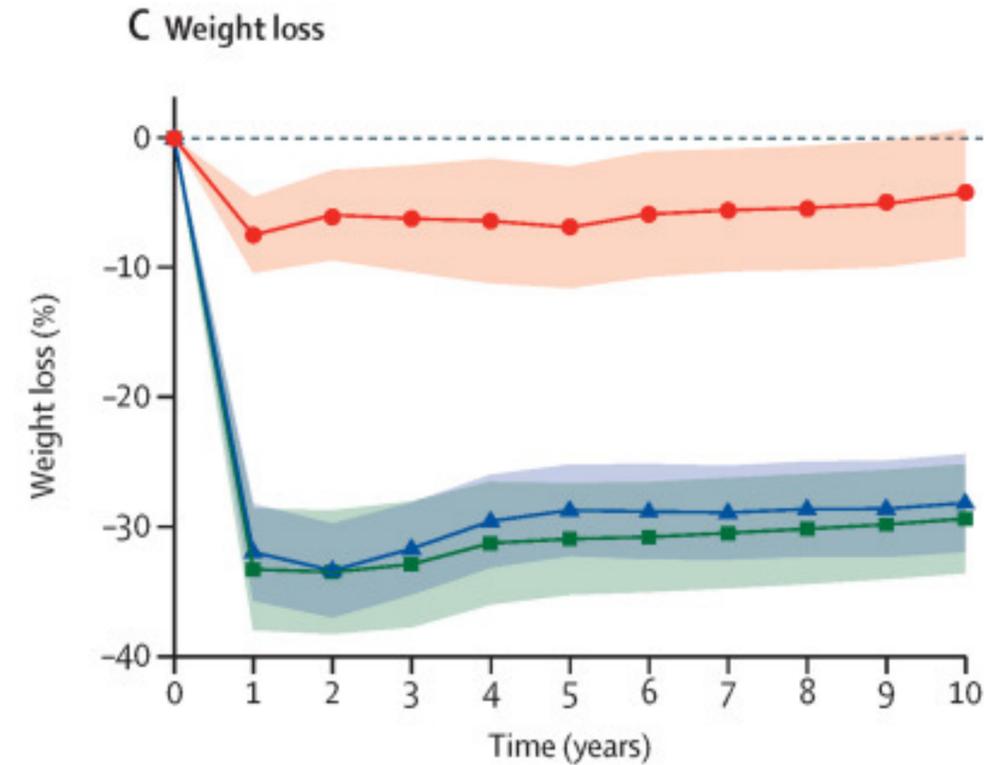
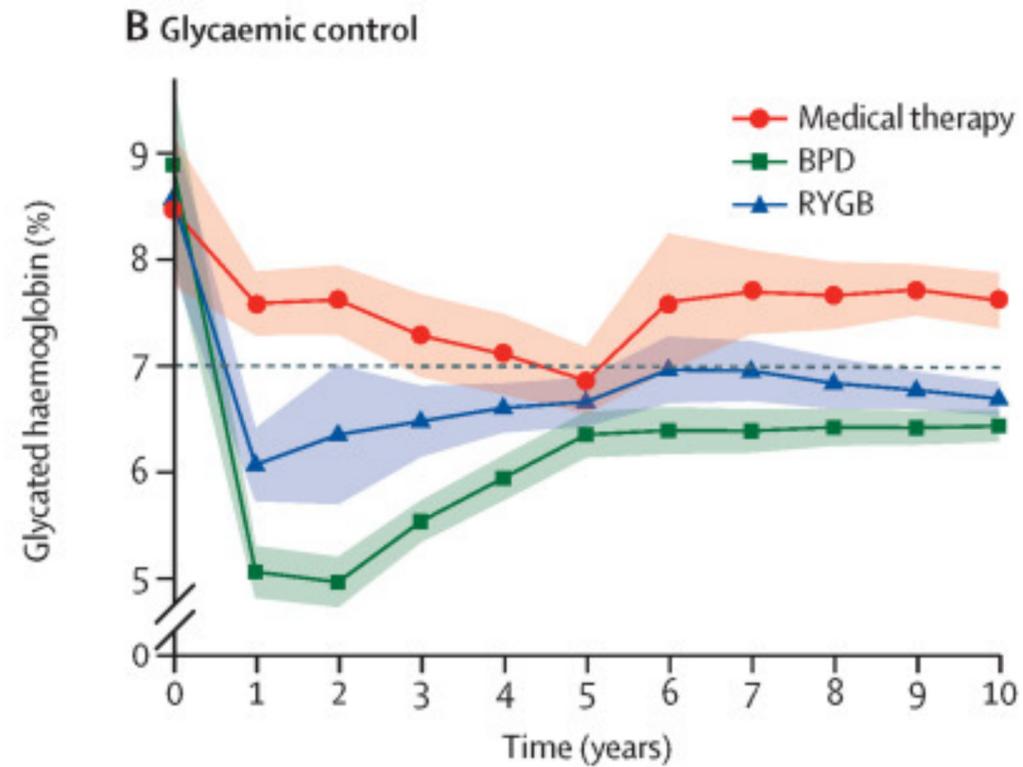
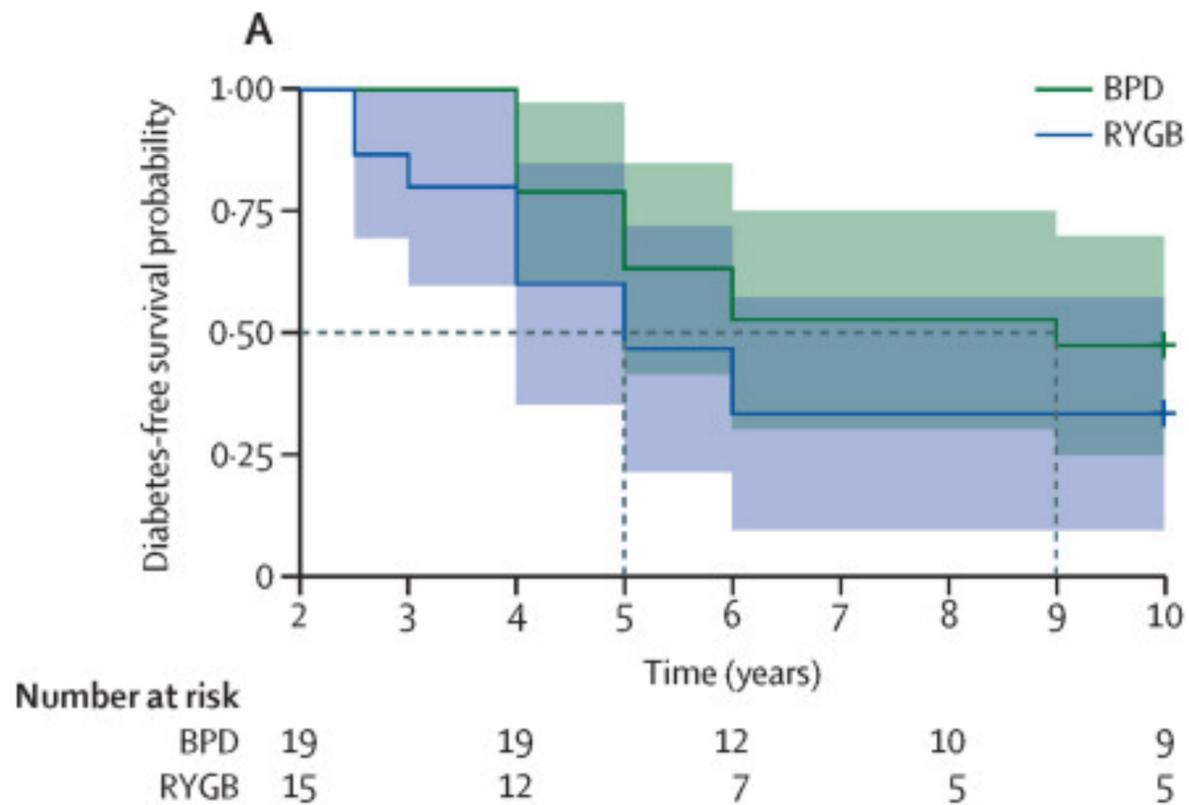
Davies M *et al*; *Lancet* 2021; 397: 971-84  
Frías JP *et al*. *N Engl J Med* 2021;385:503-515

# Impact pondéral des antidiabétiques oraux



SGLT-2

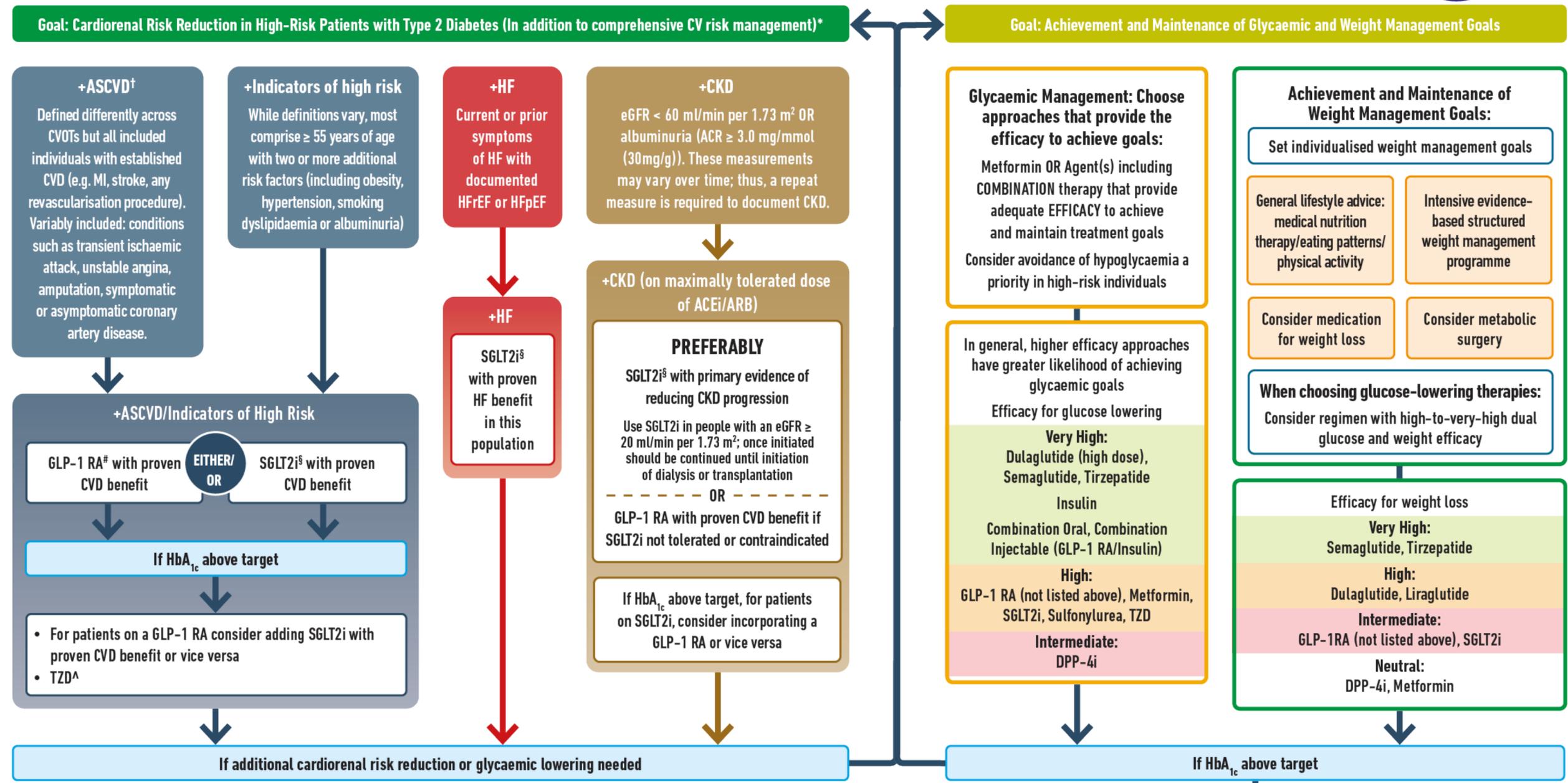
# Gestion pondérale: Chirurgie métabolique



# FIGURE 3: USE OF GLUCOSE-LOWERING MEDICATIONS IN THE MANAGEMENT OF TYPE 2 DIABETES



HEALTHY LIFESTYLE BEHAVIOURS; DIABETES SELF-MANAGEMENT EDUCATION AND SUPPORT (DSMES); SOCIAL DETERMINANTS OF HEALTH (SDOH)



ACEi, Angiotensin-Converting Enzyme Inhibitor; ACR, Albumin/Creatinine Ratio; ARB, Angiotensin Receptor Blocker; ASCVD, Atherosclerotic Cardiovascular Disease; CGM, Continuous Glucose Monitoring; CKD, Chronic Kidney Disease; CV, Cardiovascular; CVD, Cardiovascular Disease; CVOT, Cardiovascular Outcomes Trial; DPP-4i, Dipeptidyl Peptidase-4 Inhibitor; eGFR, Estimated Glomerular Filtration Rate; GLP-1 RA, Glucagon-Like Peptide-1 Receptor Agonist; HF, Heart Failure; HFpEF, Heart Failure with preserved Ejection Fraction; HFrEF, Heart Failure with reduced Ejection Fraction; HHF, Hospitalisation for Heart Failure; MACE, Major Adverse Cardiovascular Events; MI, Myocardial Infarction; SDOH, Social Determinants of Health; SGLT2i, Sodium-Glucose Cotransporter-2 Inhibitor; T2D, Type 2 Diabetes; TZD, Thiazolidinedione.

\* In people with HF, CKD, established CVD or multiple risk factors for CVD, the decision to use a GLP-1 RA or SGLT2i with proven benefit should be independent of background use of metformin; † A strong recommendation is warranted for people with CVD and a weaker recommendation for those with indicators of high CV risk. Moreover, a higher absolute risk reduction and thus lower numbers needed to treat are seen at higher levels of baseline risk and should be factored into the shared decision-making process. See text for details; ^ Low-dose TZD may be better tolerated and similarly effective; § For SGLT2i, CV/renal outcomes trials demonstrate their efficacy in reducing the risk of composite MACE, CV death, all-cause mortality, MI, HHF and renal outcomes in individuals with T2D with established/high risk of CVD; # For GLP-1 RA, CVOTs demonstrate their efficacy in reducing composite MACE, CV death, all-cause mortality, MI, stroke and renal endpoints in individuals with T2D with established/high risk of CVD.

**Identify barriers to goals:**

- Consider DSMES referral to support self-efficacy in achievement of goals
- Consider technology (e.g. diagnostic CGM) to identify therapeutic gaps and tailor therapy
- Identify and address SDOH that impact on achievement of goals

Davies MJ, Aroda VR, Collins BS, Gabbay RA, Green J, Maruthur NM, Rosas SE, Del Prato S, Mathieu C, Mingrone G, Rossing P, Tankova T, Tsapas A, Buse JB



European Association for the Study of Diabetes

# En pratique

- Instaurer un traitement dès HbA1c > 7%: Metformine (si >10% surtout si symptomatique: insuline?)
- **Bio à 3 mois:**
  - HbA1c >7,5% et IMC >30:  
**GLP-1**
- **Sauf si:**
  - **Gastroparésie**
  - **Nausées persistantes**
  - **MDRD < 15**
  - **Rétinopathie prolifération non stabilisée**
  - **Grossesse ou allaitement**

# En pratique

- **Bio à 3 mois:**

- HbA1c > 7% (et < 9%) et IMC < 30: **SGLT-2**

- **GFR < 60: Jardiance 10 (Invokana 100)**

- **GFR > 60: Jardiance 10 ou 25, Forxiga 10, Invokana 100 ou 300**

- **SAUF SI:**

- **IR trop sévère (< 30 ml/min)**
- **Candidoses génitales à répétition**
- **ATCD d'acidocétose diabétique**
- **Projet de grossesse ou allaitement en cours**
- **Si actif d'amputation ou de fracture: éviter Invokana (étude Canvas)**

# En pratique

## Combiner les indications si possible

- Si néphropathie diabétique: intérêt **SGLT-2 +++**
  - **Metformine (dose adaptée) et GLP-1 (si obèse) = traitement AD**
  - **Forxiga 10mg (insuffisance rénale chronique)**
- Si insuffisance cardiaque: intérêt **SGLT-2 +++**
  - **Metformine et GLP-1 (si obèse) = traitement AD**
  - ***Forxiga ou Jardiance***

# Prise en charge multiscience du patient diabétique de type 2

