Diabesity treatments in 2024: the endpoints surgeons need to know

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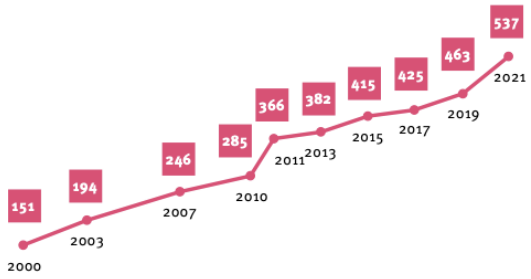
Disclosure

- I don’t have any disclosure for this presentation

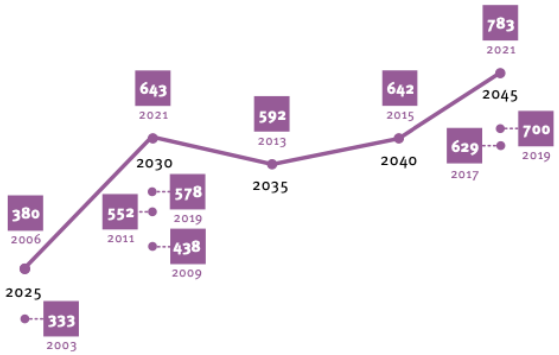
The 10th edition confirms that diabetes is one of the fastest growing global health emergencies of the 21st century

Map 1 Number of people with diabetes worldwide and per IDF Region in 2021–2045 (20–79 years)

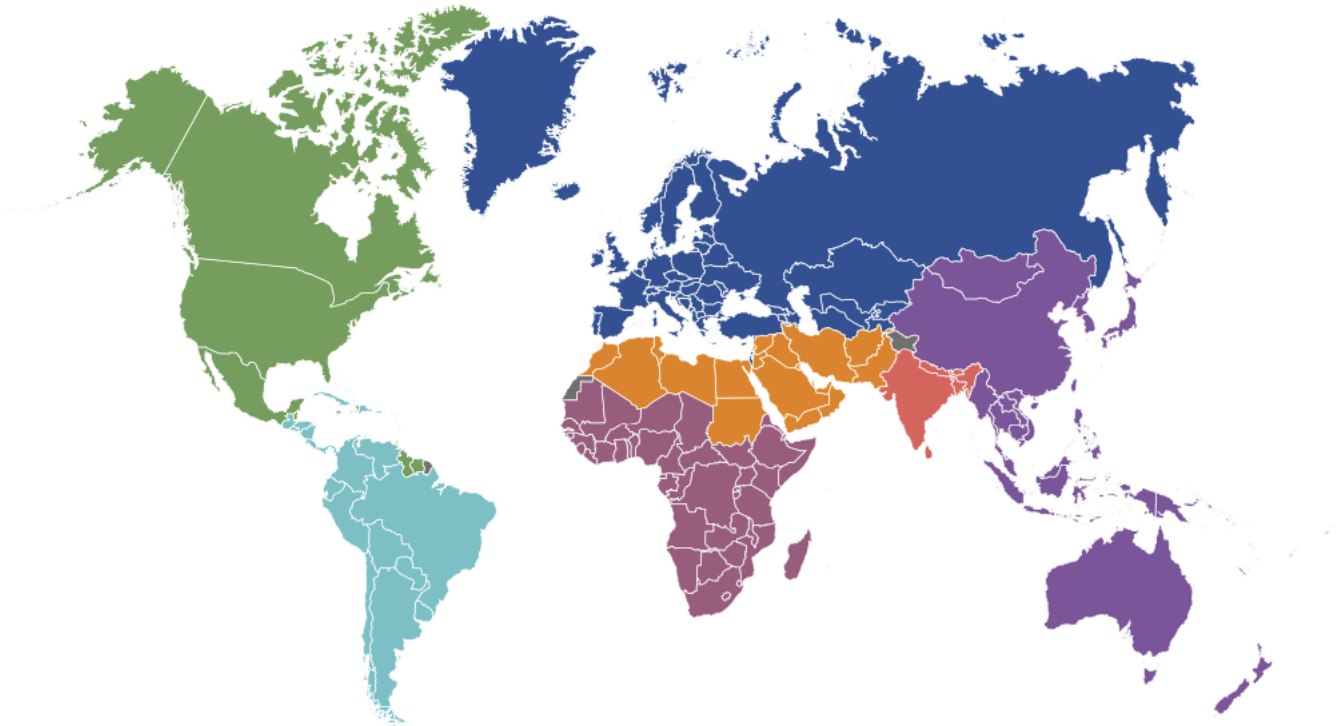
World		North America & Caribbean (NAC)		Europe (EUR)		Western Pacific (WP)	
2045	783 million	2045	63 million	2045	69 million	2045	260 million
2030	643 million	2030	57 million	2030	67 million	2030	238 million
2021	537 million	2021	51 million	2021	61 million	2021	206 million
↑ 46% increase		↑ 24% increase		↑ 13% increase		↑ 27% increase	



Key
151 Number of people with diabetes in millions



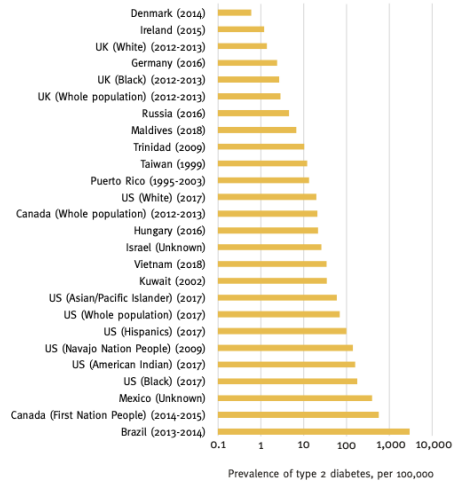
Key
333 Projection in millions
2003 Year projection made



South & Central America (SACA)		Africa (AFR)		Middle East & North Africa (MENA)		South-East Asia (SEA)	
2045	49 million	2045	55 million	2045	136 million	2045	152 million
2030	40 million	2030	33 million	2030	95 million	2030	113 million
2021	32 million	2021	24 million	2021	73 million	2021	90 million
↑ 50% increase		↑ 134% increase		↑ 87% increase		↑ 68% increase	

Type 2 diabetes is the most common type of diabetes, accounting for over 90% of all diabetes worldwide

Figure 3.8 Reported prevalence of type 2 diabetes in youth ranked by region and ethnicity

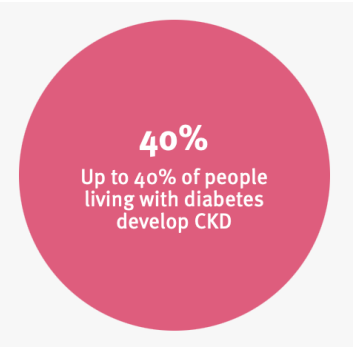


IDF Diabetes Atlas 2021 – 10th edition

Diabetes Complications

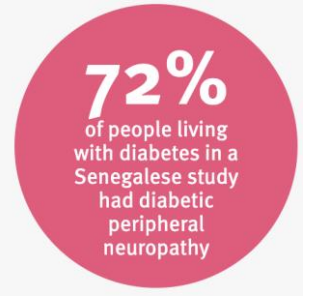
- Retinopathy
- Nefropathy

CKD due to type 2 diabetes increased worldwide by about 74% between 1990 and 2017.



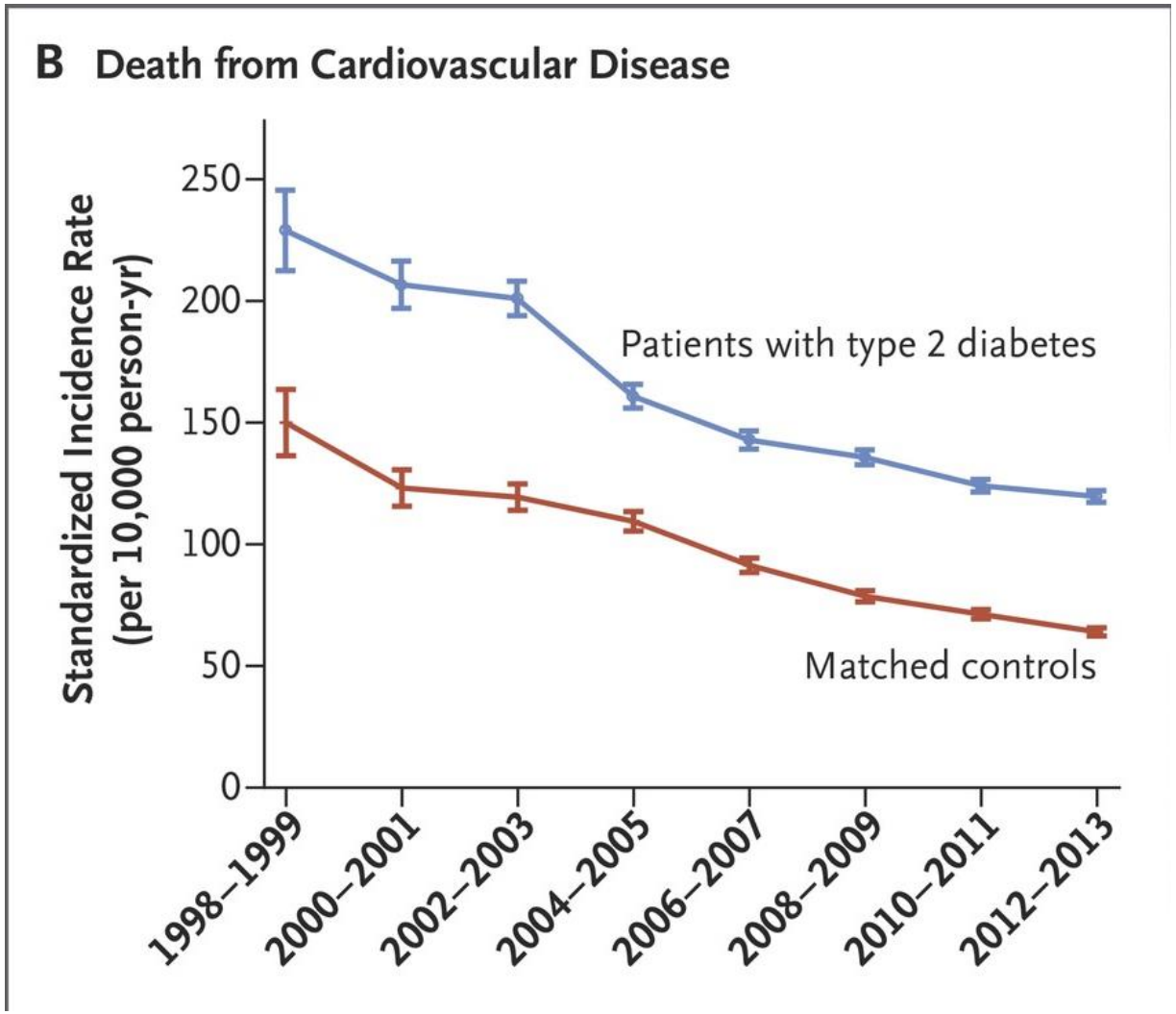
- Neuropathy

In most countries where data are available, the incidence of lower-limb amputation due to diabetes seems to be decreasing.



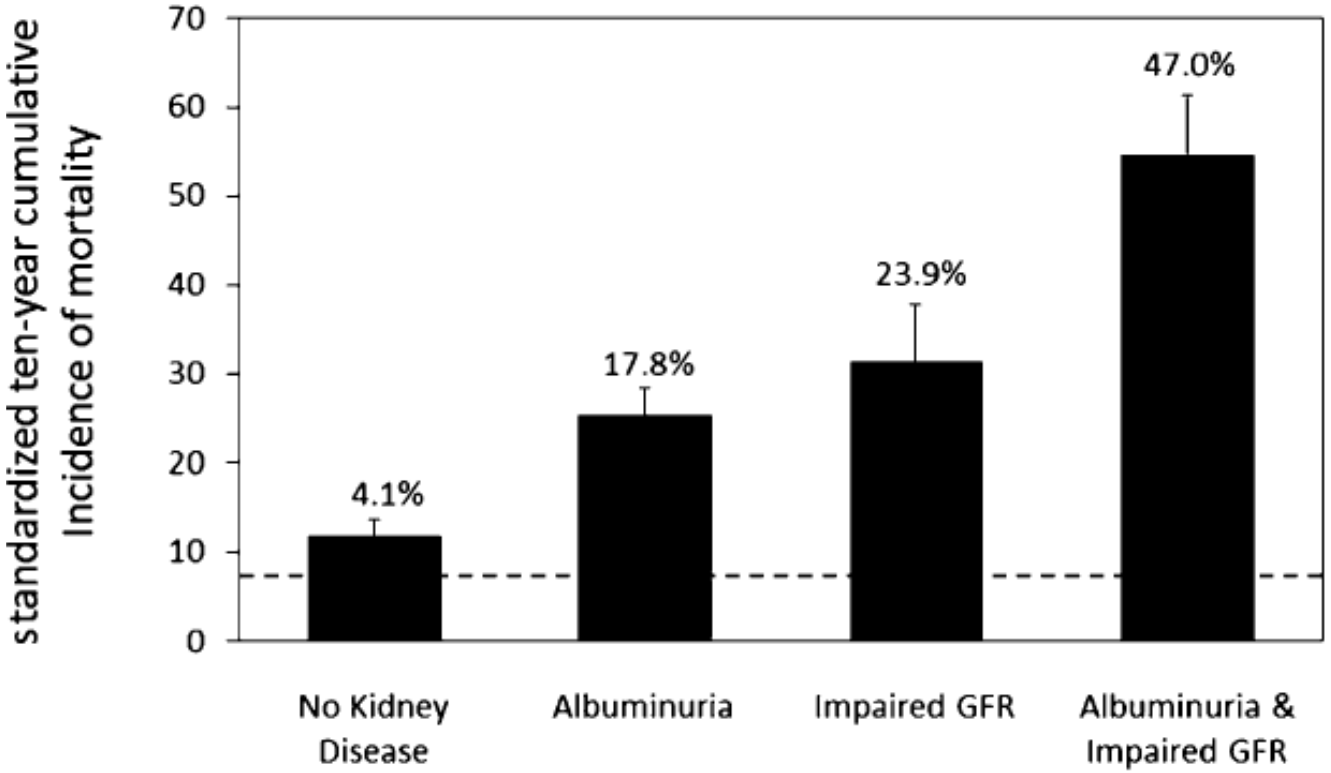
International Diabetes Federation: http://www.idf.org: **IDF Diabetes Atlas report on diabetes foot-related complications** – 2022, **Diabetes and kidney disease** – 2023

Mortality has decreased among patients with type 2 diabetes over time…
…But there is still a gap that needs to be reduced



Rawshan A et al. N Engl J Med 2017

Mortality increases little in the population with uncomplicated diabetes compared to the general population, but…

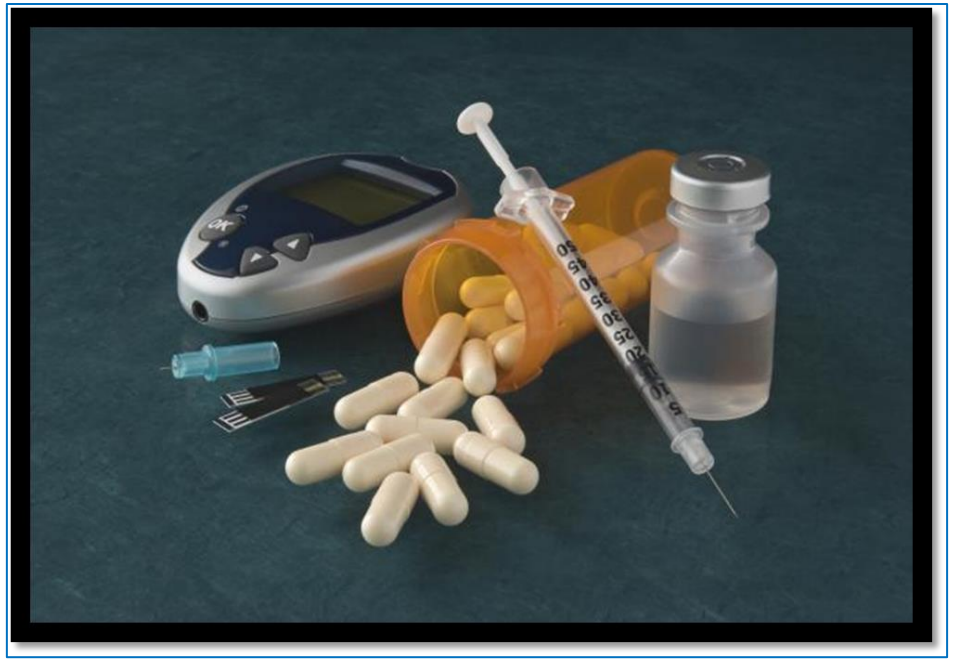


Afkarian M et al. J Am Soc Nephrol 24: 302–308, 2013

Type 2 Diabetes Treatment

PREVIOUSLY

Only glycemic control (A1c)



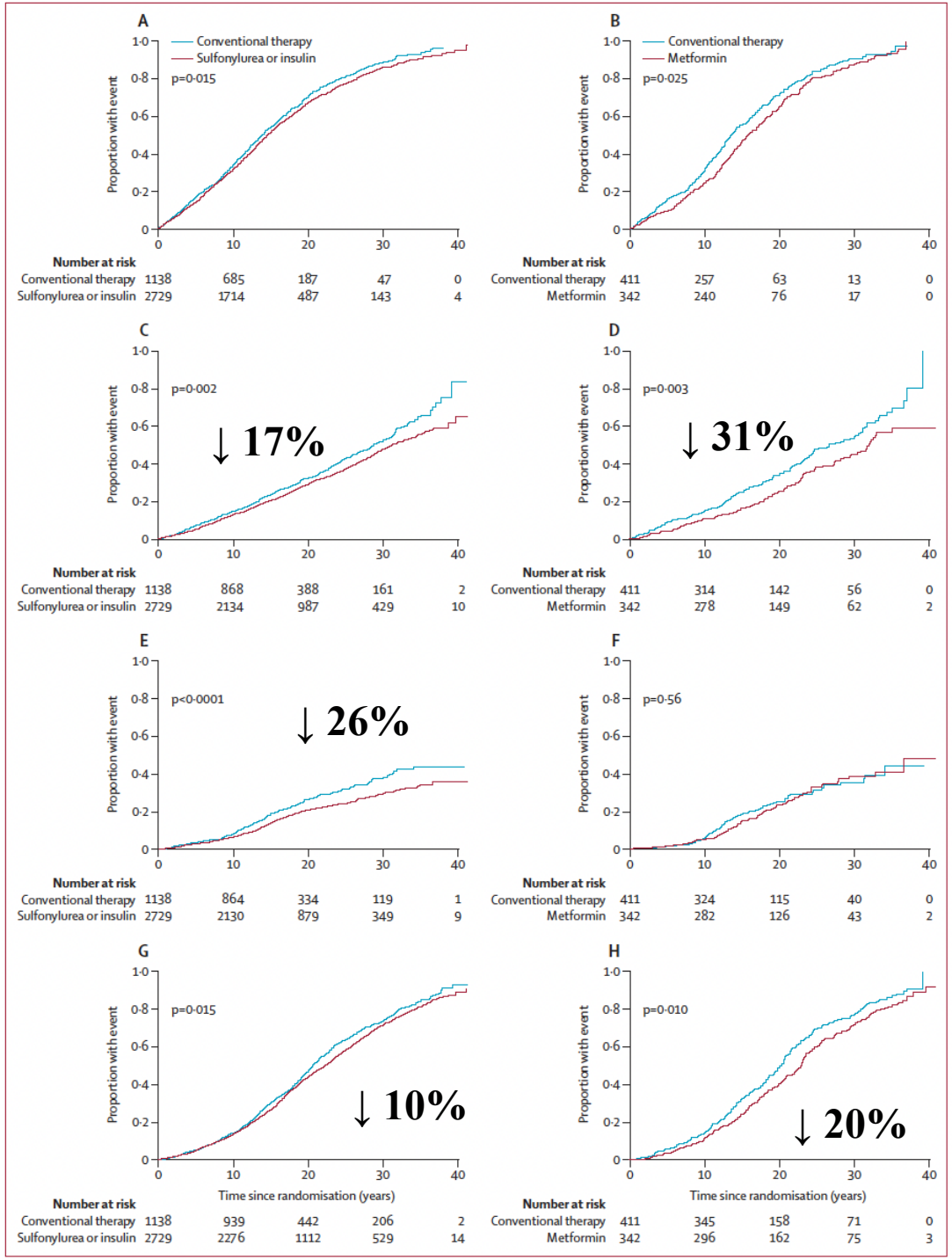
UKPDS

24 years after trial end

1977 - UKPDS randomly allocated people with newly diagnosed type 2 diabetes to an intensive blood glucose control strategy with sulfonylureas, insulin or metformin or to a conventional blood glucose control strategy

Legacy Effect

***Lancet* 2024; 404: 145–55**



any diabetes-related endpoint

myocardial infarction

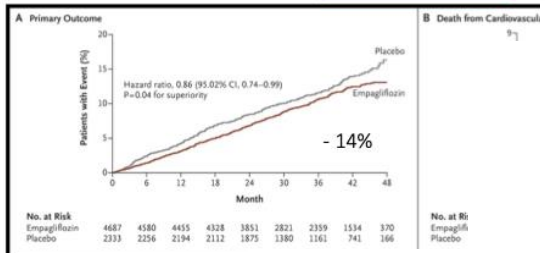
microvascular disease

died from any cause

Since then...

Inibidores da SGLT2

EMPA-REG



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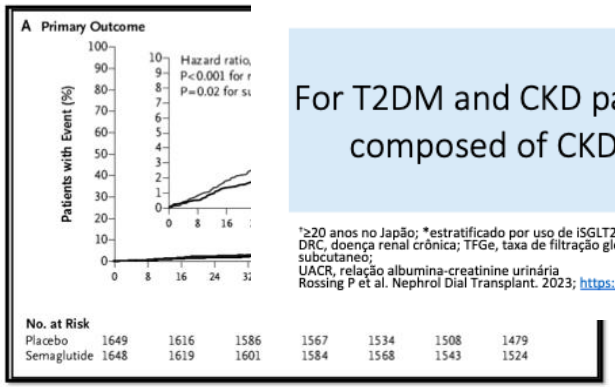
SUSTA



first occurrence of cardiovascular death, nonfatal myocardial infarction, or nonfatal stroke

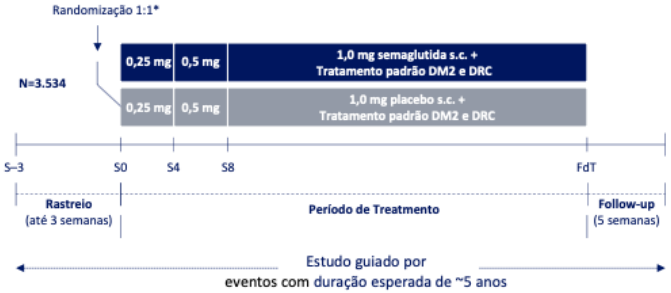
Marso SP et al. N Engl J Med 2016;375:1834-44.

Inibidores da SGLT2

ESTUDO FLOW-SEMAGLUTIDA

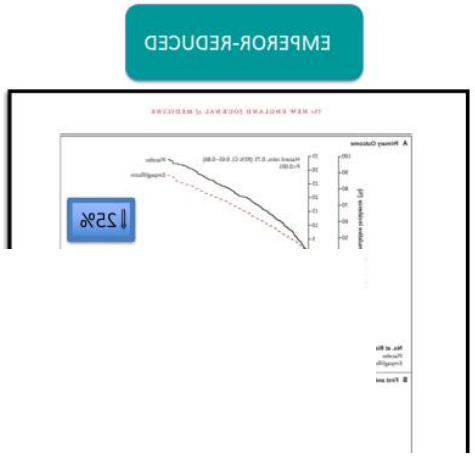
Adultos com DRC e DM2

- Idade ≥18 anos†
- HbA_{1c} ≤10%
- TFGe ≥50 a ≤75 mL/min/1.73 m² e UACR >300 a <5,000 mg/g
  OU
- TFGe ≥25 a <50 mL/min/1.73 m² e UACR >100 a <5,000 mg/g
- Bloqueio SRAA



For T2DM and CKD patients, semaglutide reduced the risk of an outcome composed of CKD progression, CV death, and renal death by 24%.

†≥20 anos no Japão; *estratificado por uso de iSGLT2 (sim/não).
DRC, doença renal crônica; TFGe, taxa de filtração glomerular estimada; FdT, fim do tratamento; N, número de participantes; SRAA, sistema renina-angiotensina-aldosterone; s.c., subcutaneo;
UACR, relação albumina-creatinine urinária
Rossing P et al. Nephrol Dial Transplant. 2023; https://doi.org/10.1093/ndt/gfad009



EMPEROR-REDUCED

Primary outcome: composite of cardiovascular death or hospitalization for worsening heart failure

ɔmes in type 2 diabetes
d placebo-controlled trial

Prem Pais 6, Jeffrey Probstfield 7, Jeffrey S Riesmeyer 5, Matthew 10, Purnima Rao-Melacini 10, Gloria Wong 10, Alvaro Avezum 11, icolae Hancu 17, Markolf Hanefeld 18, Shaun Holt 19, Petr Jansky sto German Cardona Munoz 25, Valdis Pirags 26, Nana Pogosova 0, Theodora Temelkova-Kurktschiev 31;

oi: 10.1016/S0140-6736(19)31149-3. Epub 2019

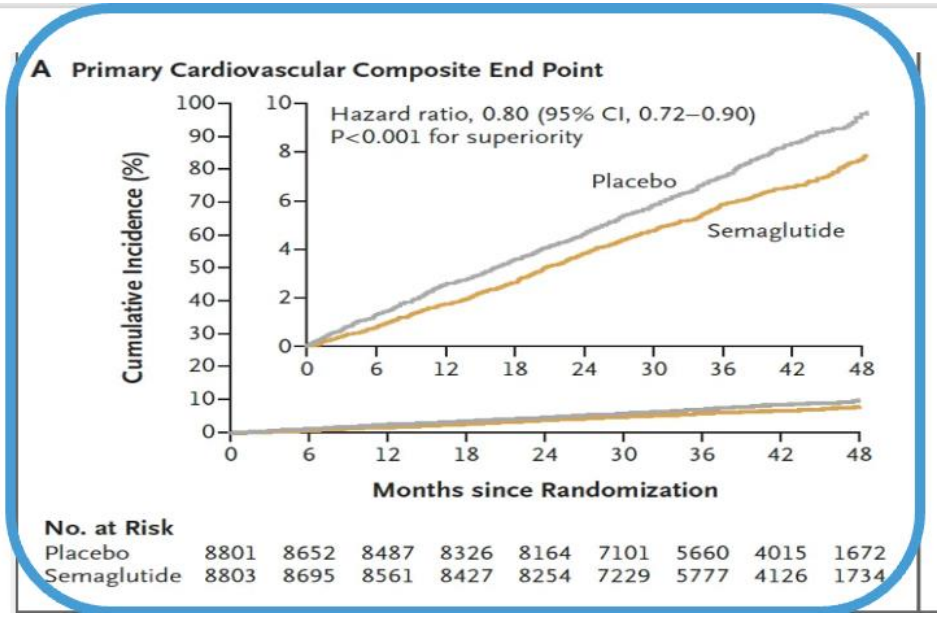
Redução de 12% do desfecho primário (principalmente AVC)
70% DM2 sem DCV prévia : prevenção primária

ORIGINAL ARTICLE

Semaglutide and Cardiovascular Outcomes in Obesity without Diabetes

A. Michael Lincoff, M.D., Kirstine Brown-Frandsen, M.D., Helen M. Colhoun, M.D., John Deanfield, M.D., Scott S. Emerson, M.D., Ph.D., Sille Esbjerg, M.Sc., Søren Hardt-Lindberg, M.D., Ph.D., G. Kees Hovingh, M.D., Ph.D., Steven E. Kahn, M.B., Ch.B., Robert F. Kushner, M.D., Ildiko Lingvay, M.D., M.P.H., Tugce K. Oral, M.D., Marie M. Michelsen, M.D., Ph.D., Jorge Plutzky, M.D., Christoffer W. Tornøe, Ph.D., and Donna H. Ryan, M.D., for the SELECT Trial Investigators*

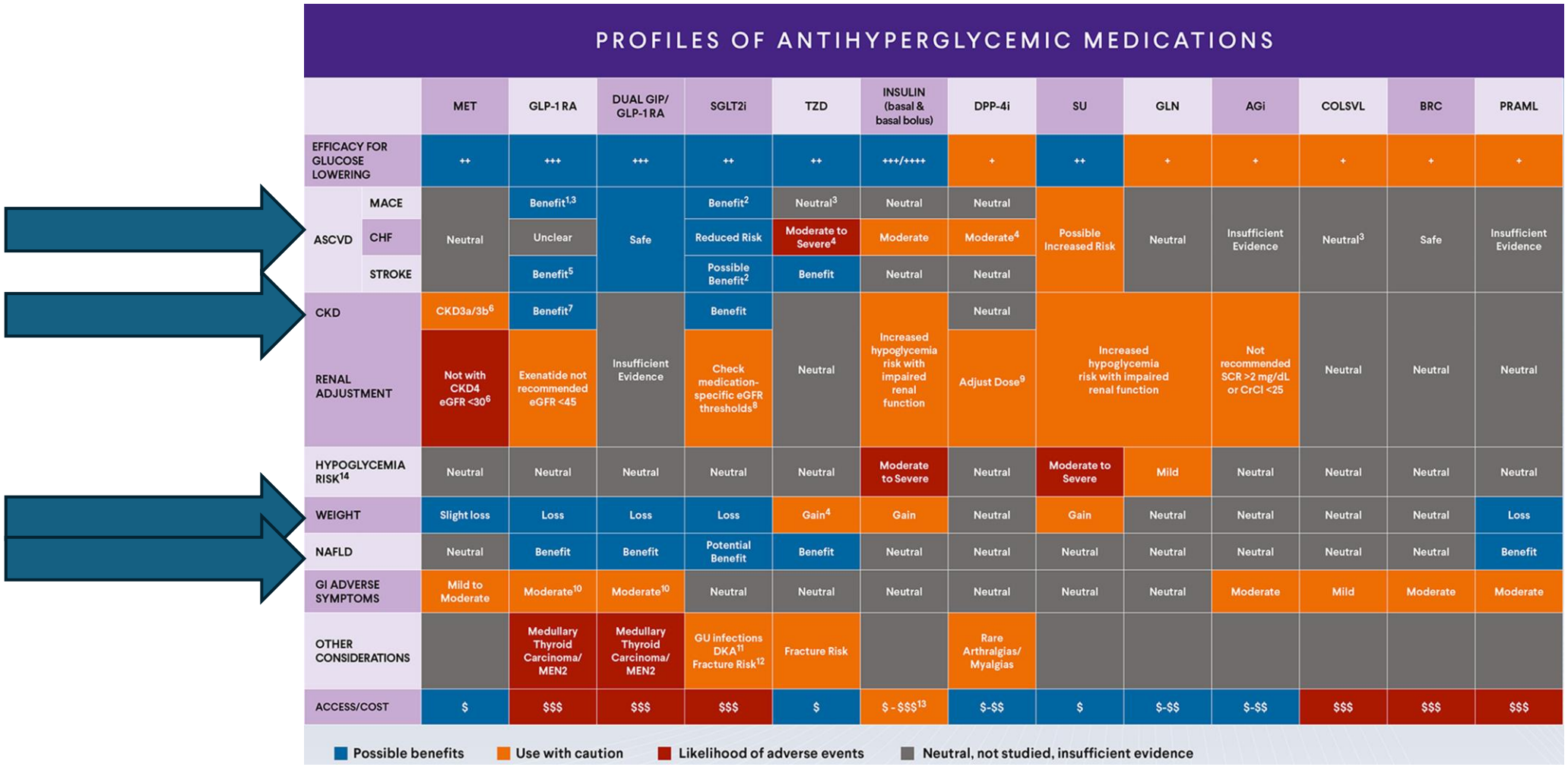
Select RCT



20% CV events

NEJM, Nov 2023

AACE 2023



PROFILES OF ANTIHYPERGLYCEMIC MEDICATIONS

		MET	GLP-1 RA	DUAL GIP/ GLP-1 RA	SGLT2i	TZD	INSULIN (basal & basal bolus)	DPP-4i	SU	GLN	AGi	COLSVL	BRC	PRAML
EFFICACY FOR GLUCOSE LOWERING		++	+++	+++	++	++	+++/++++	+	++	+	+	+	+	+
ASCVD	MACE	Neutral	Benefit[1,3]	Safe	Benefit[2]	Neutral[3]	Neutral	Neutral	Possible Increased Risk	Neutral	Insufficient Evidence	Neutral[3]	Safe	Insufficient Evidence
	CHF		Unclear		Reduced Risk	Moderate to Severe[4]	Moderate	Moderate[4]						
	STROKE		Benefit[5]		Possible Benefit[2]	Benefit	Neutral	Neutral						
CKD		CKD3a/3b[6]	Benefit[7]	Insufficient Evidence	Benefit	Neutral	Increased hypoglycemia risk with impaired renal function	Neutral	Increased hypoglycemia risk with impaired renal function		Not recommended SCR >2 mg/dL or CrCl <25	Neutral	Neutral	Neutral
RENAL ADJUSTMENT		Not with CKD4 eGFR <30[6]	Exenatide not recommended eGFR <45		Check medication-specific eGFR thresholds[8]			Adjust Dose[9]						
HYPOGLYCEMIA RISK[14]		Neutral	Neutral	Neutral	Neutral	Neutral	Moderate to Severe	Neutral	Moderate to Severe	Mild	Neutral	Neutral	Neutral	Neutral
WEIGHT		Slight loss	Loss	Loss	Loss	Gain[4]	Gain	Neutral	Gain	Neutral	Neutral	Neutral	Neutral	Loss
NAFLD		Neutral	Benefit	Benefit	Potential Benefit	Benefit	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Benefit
GI ADVERSE SYMPTOMS		Mild to Moderate	Moderate[10]	Moderate[10]	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Moderate	Mild	Moderate	Moderate
OTHER CONSIDERATIONS			Medullary Thyroid Carcinoma/ MEN2	Medullary Thyroid Carcinoma/ MEN2	GU infections DKA[11] Fracture Risk[12]	Fracture Risk		Rare Arthralgias/ Myalgias						
ACCESS/COST		$	$$$	$$$	$$$	$	$ - $$$[13]	$-$$	$	$-$$	$-$$	$$$	$$$	$$$

Possible benefits | Use with caution | Likelihood of adverse events | Neutral, not studied, insufficient evidence

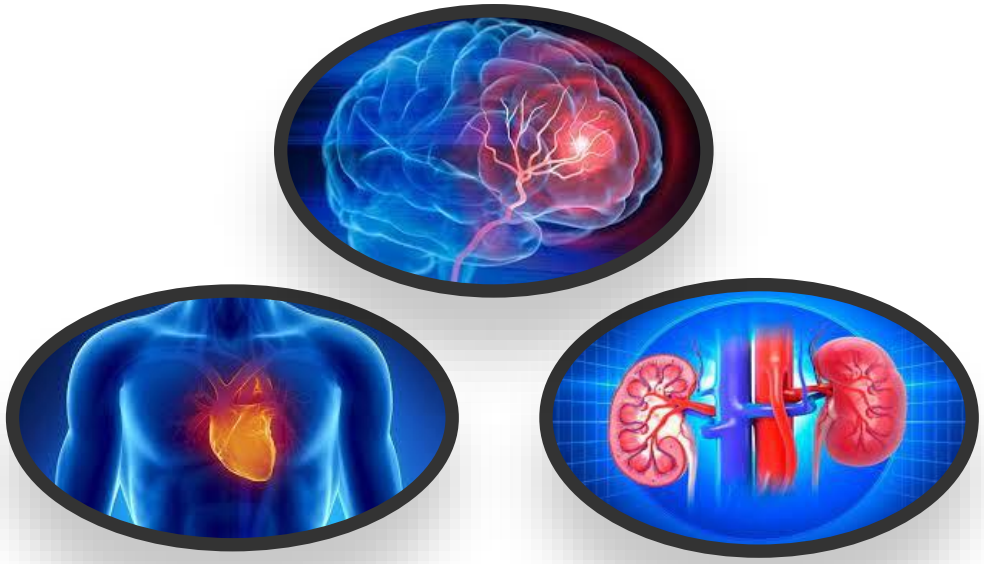
Endocrine Practice 29 (2023) 305e340

Type 2 Diabetes Treatment

Currently

Guidelines recommend Reduction of hard endpoints (cardio-renal)

Pathologies related to Mortality or Complications that impact life expectancy



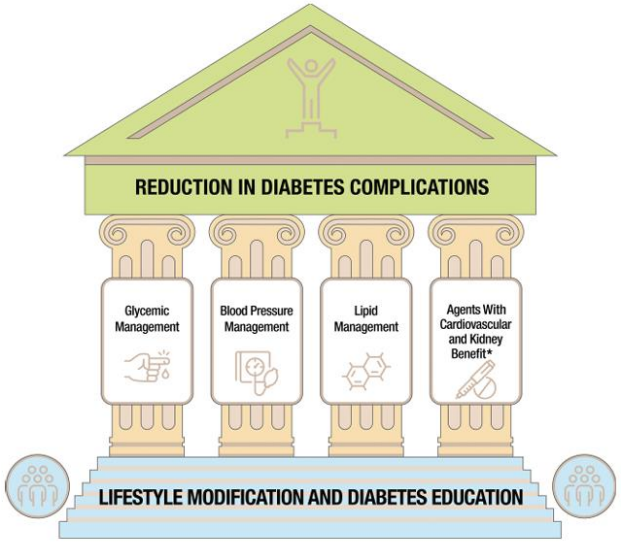
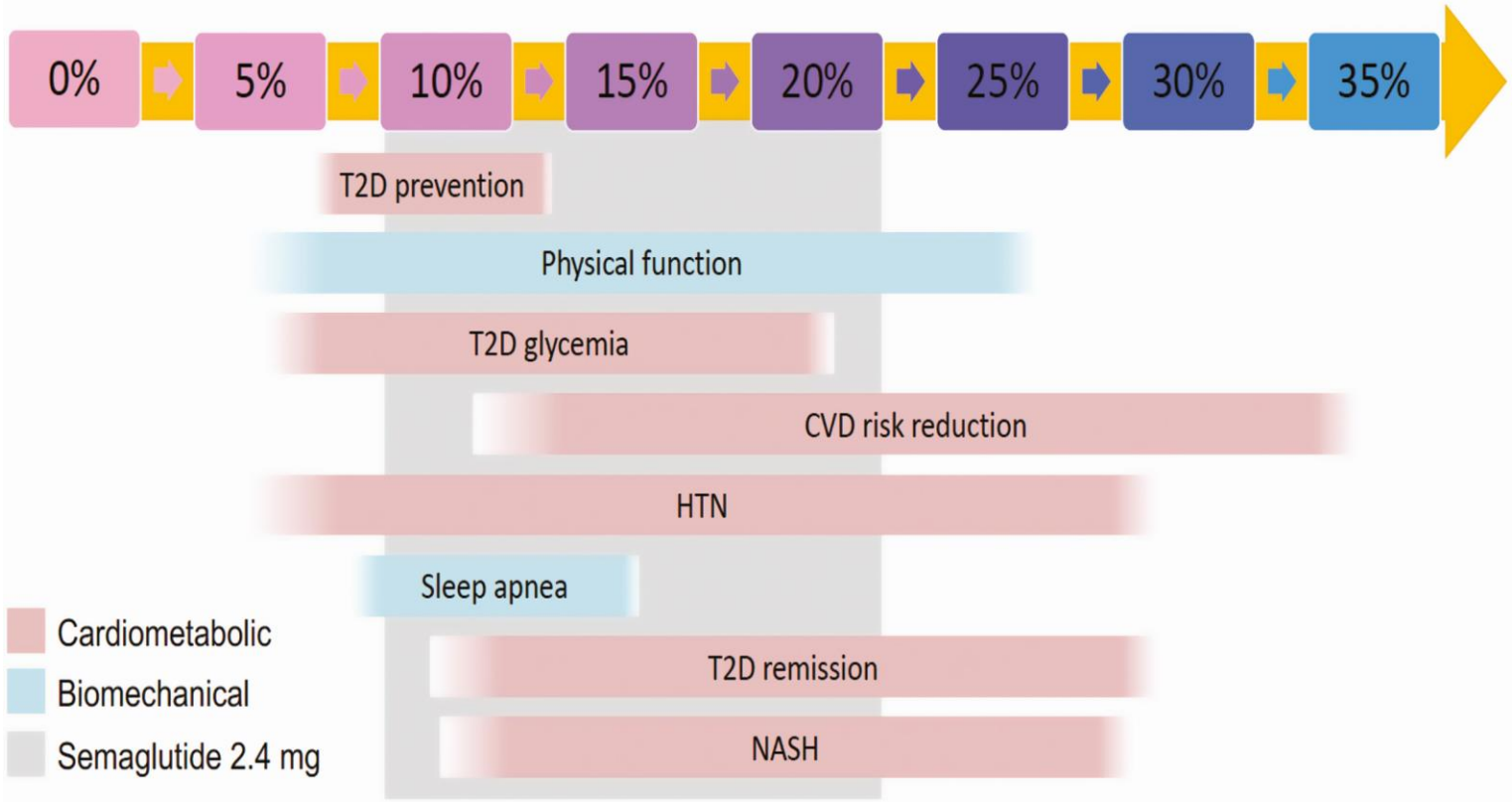


Figure 10.1—Multifactorial approach to reduction in risk of diabetes complications. *Risk reduction interventions to be applied as individually appropriate.

Furthermore, we have evidence that weight loss is essential to improve these outcomes

Treating ABCD/obesity to target for prevention and treatment of complications.



J Clin Endocrinol Metab, Volume 107, Issue 4, April 2022, Pages e1339–e1347, https://doi.org/10.1210/clinem/dgab848

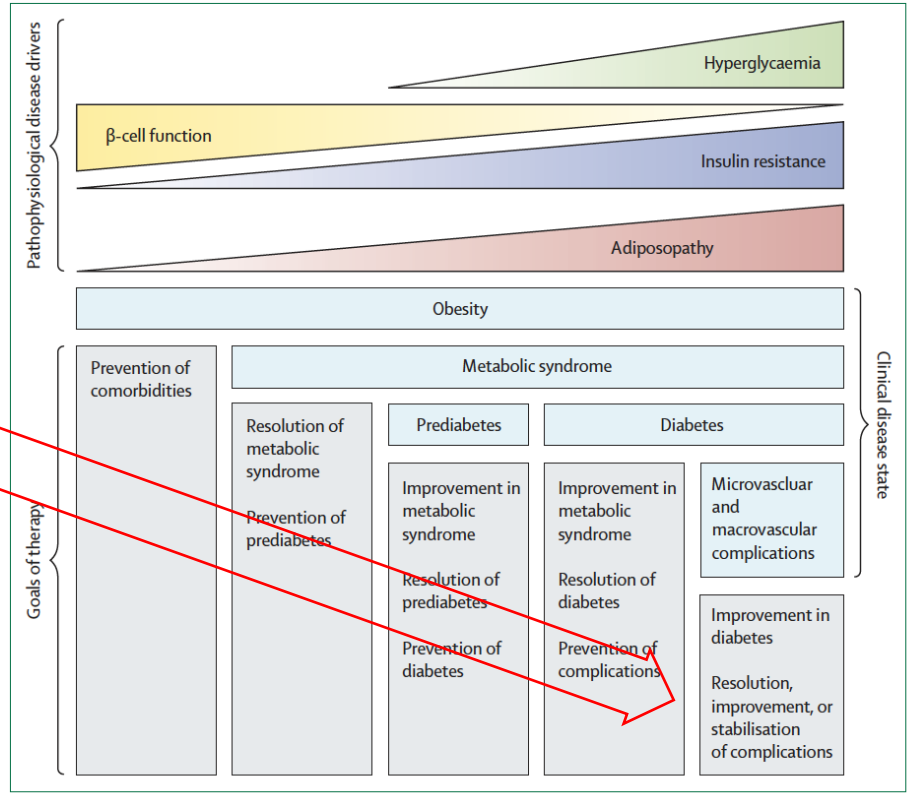
Obesity management as a primary treatment goal for type 2 diabetes: time to reframe the conversation

Ildiko Lingvay, Priya Sumithran, Ricardo V Cohen, Carel W le Roux

The Lancet 2022

> 15%TBWL

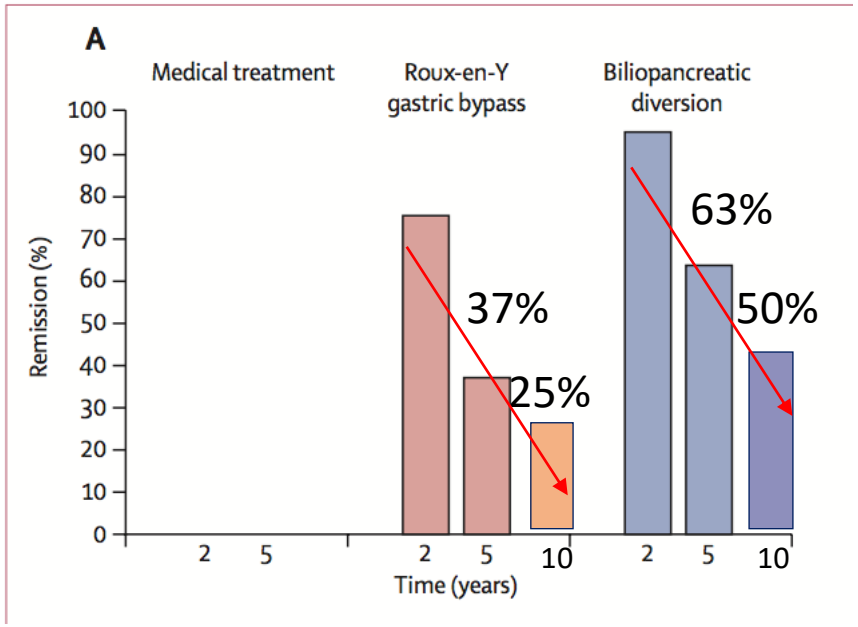
Disruption of the disease continuum

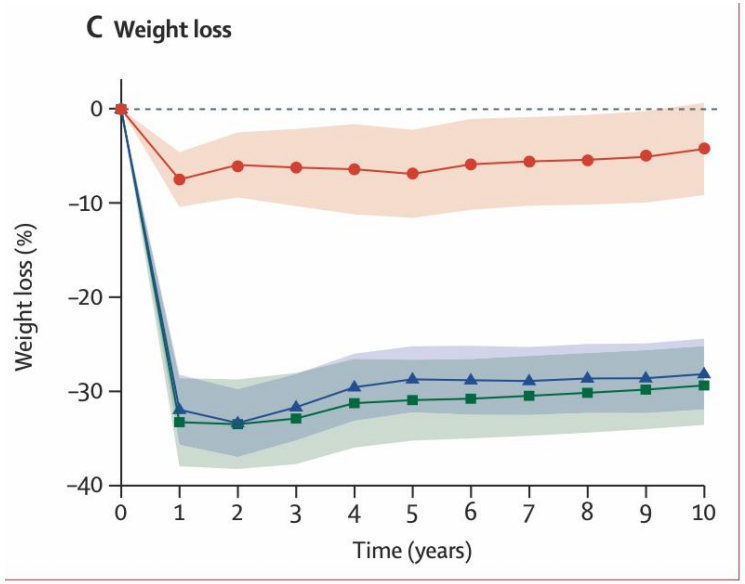


Metabolic surgery versus conventional medical therapy in patients with type 2 diabetes: 10-year follow-up of an open-label, single-centre, randomised controlled trial

Geltrude Mingrone, Simona Panunzi, Andrea De Gaetano, Caterina Guidone, Amerigo Iaconelli, Esmeralda Capristo, Ghassan Chamseddine, Stefan R Bornstein, Francesco Rubino

- RCT with 10 years follow up, Med Tx x RYGB x BPD
- 60 pts randomized
- Complete remission: A1c < 6.5% and fasting blood glucose < 100 mg/dl with no medication



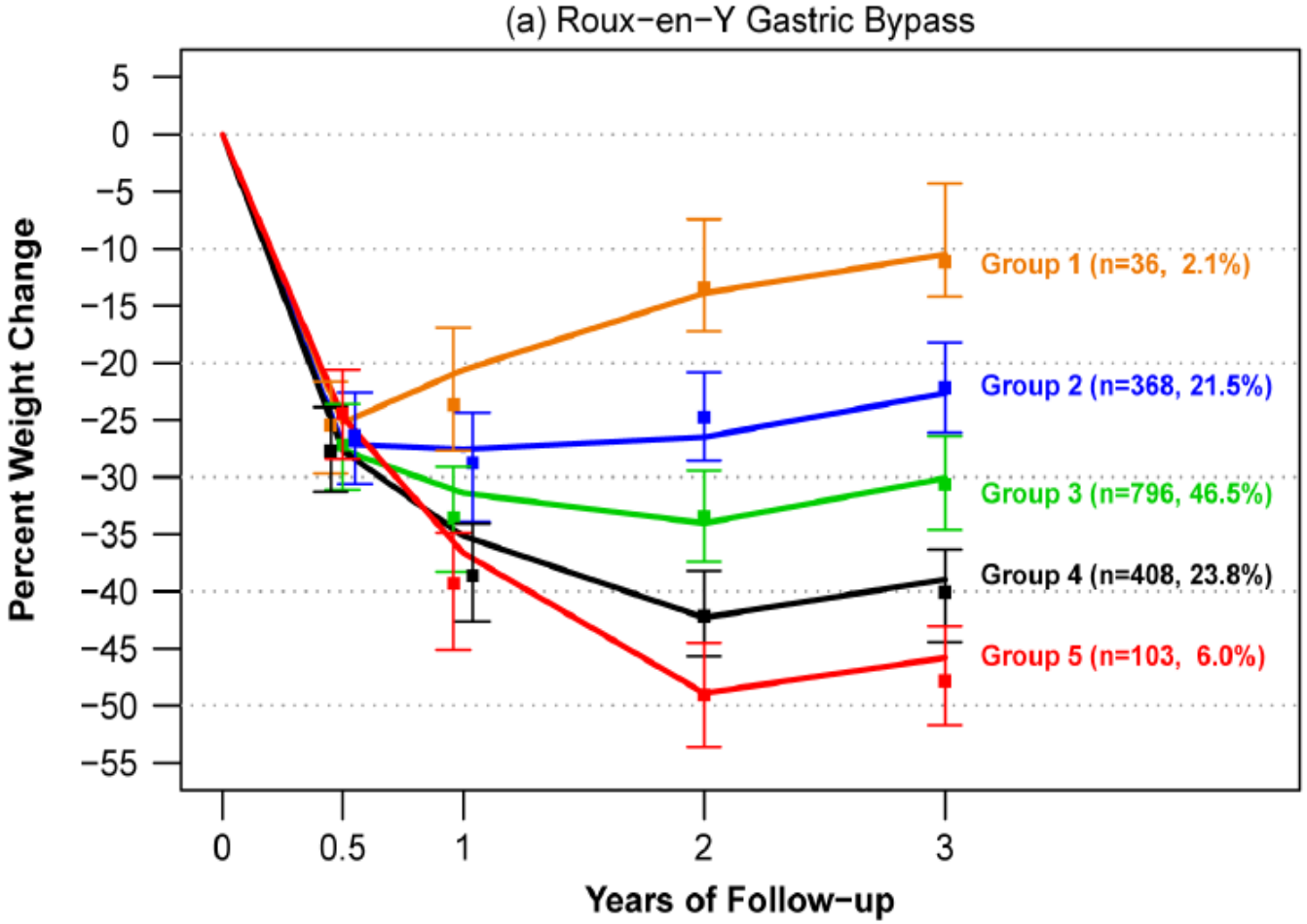


LABS 2 STUDY

Original Investigation

Weight Change and Health Outcomes at 3 Years After Bariatric Surgery Among Individuals With Severe Obesity

n=2458
1738: RYGB
610: LAGB



JAMA. 2013 December 11; 310(22): 2416–2425. doi:10.1001/jama.2013.280928.

Obesity Surgery
https://doi.org/10.1007/s11695-020-04934-1

BRIEF COMMUNICATION

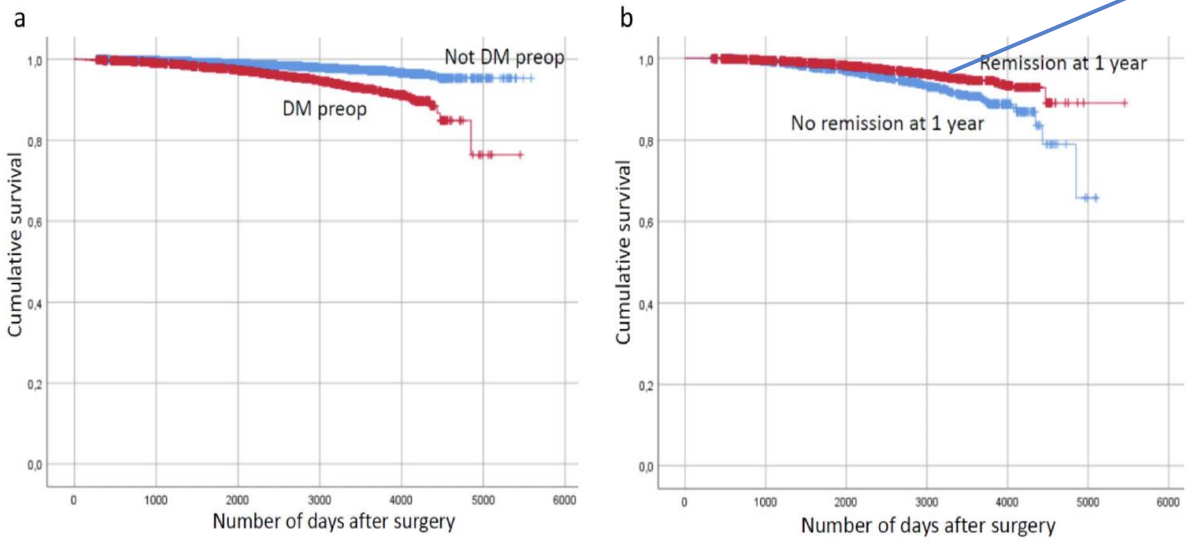
Bariatric Surgery: There Is a Room for Improvement to Reduce Mortality in Patients with Type 2 Diabetes

Carel W. le Roux[1] · Johan Ottosson[2,3] · Erik Näslund[2,4] · Ricardo V. Cohen[5] · Erik Stenberg[2,3] · Magnus Sundbom[2,6] · Ingmar Näslund[2,3]

Received: 6 July 2020 / Revised: 13 August 2020 / Accepted: 14 August 2020

SoReg, Scandinavian Obesity Surgery Registry
65,345 patients with more than 10 years of follow-up

Pharmacotherapy?

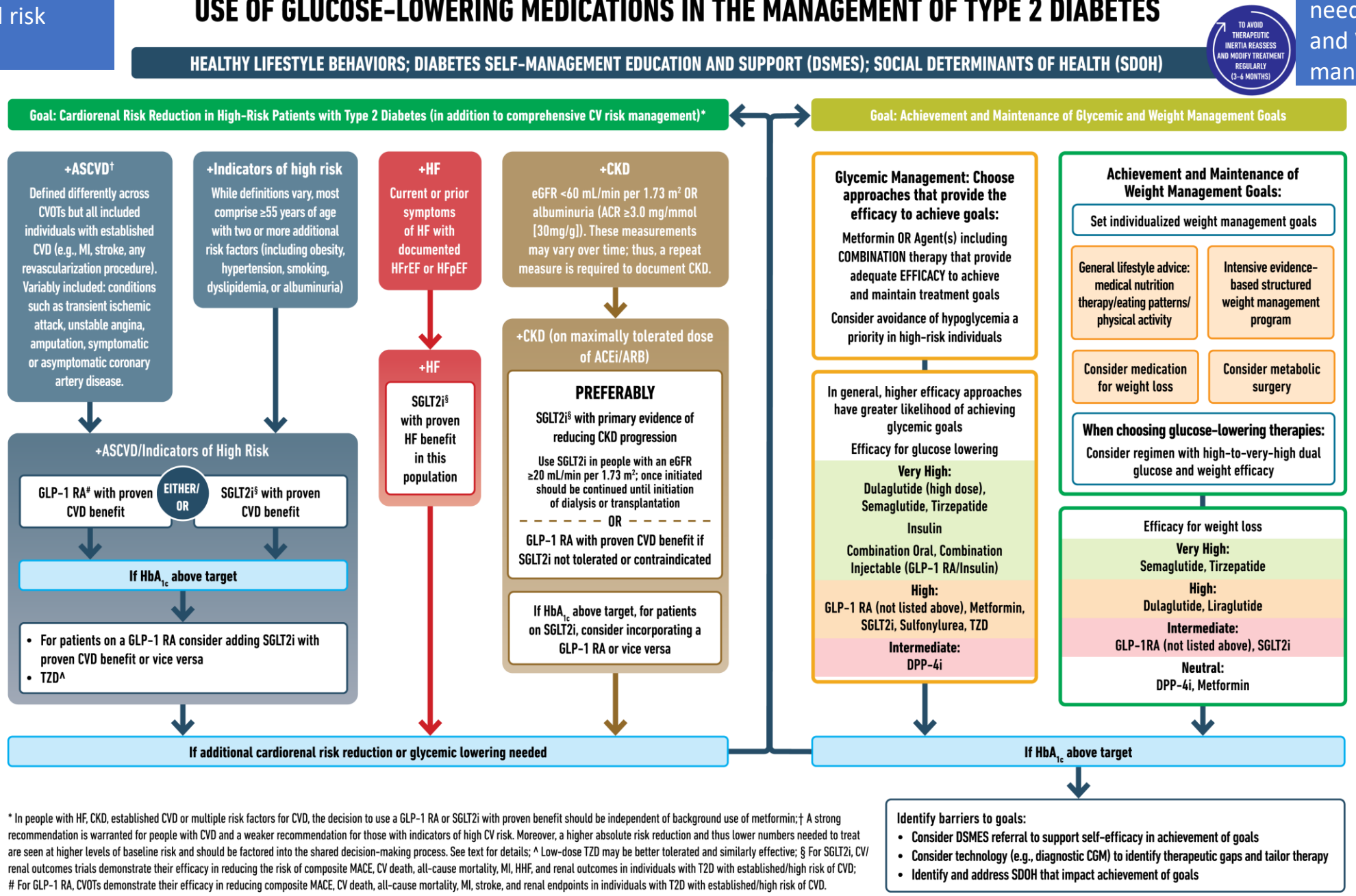


Patients with T2D who achieved remission in the first year post-op had lower mortality than those who did not

Patients who need Cardiorenal risk reduction

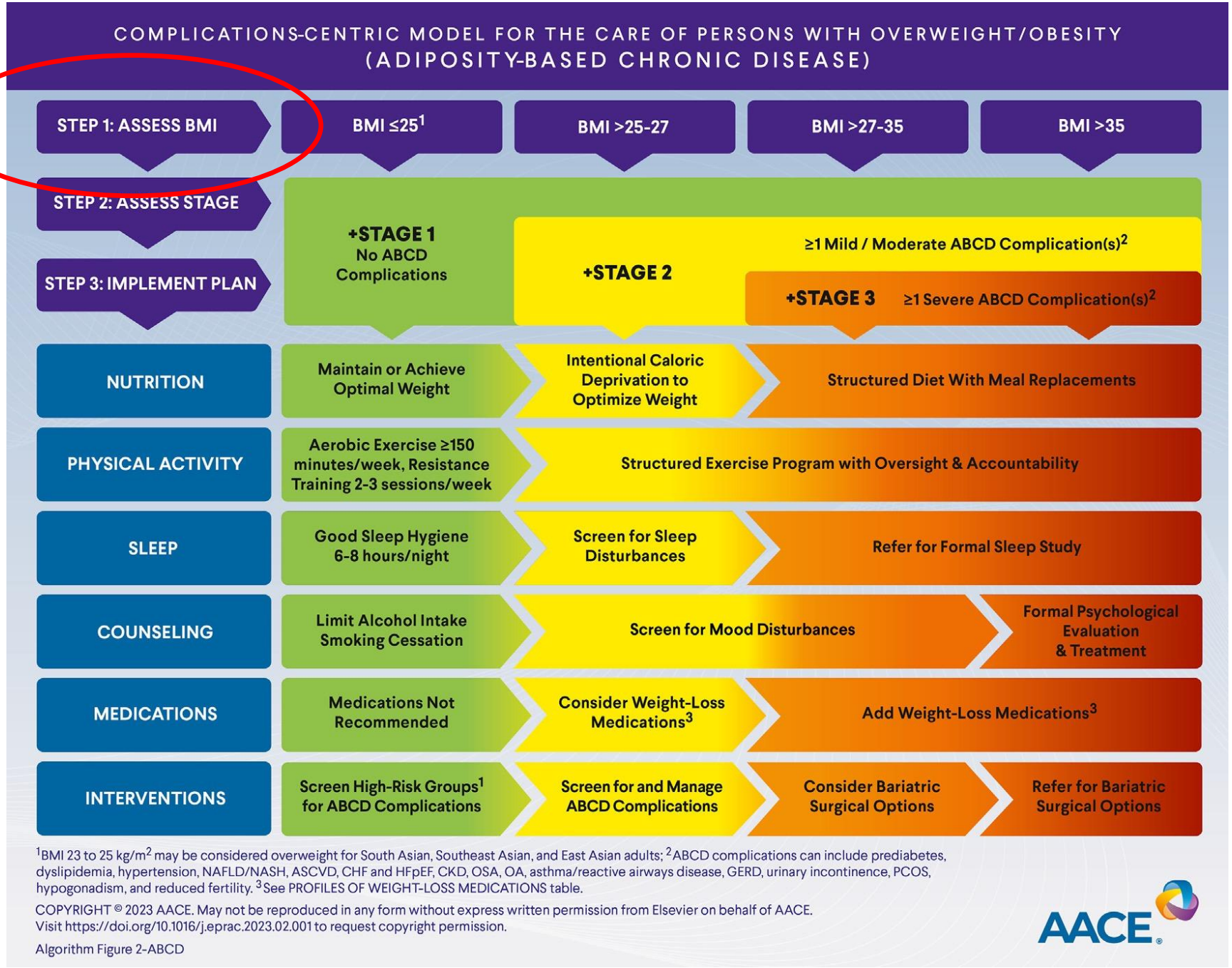
USE OF GLUCOSE-LOWERING MEDICATIONS IN THE MANAGEMENT OF TYPE 2 DIABETES

Patients who need Glycemic and Weight management



* 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.

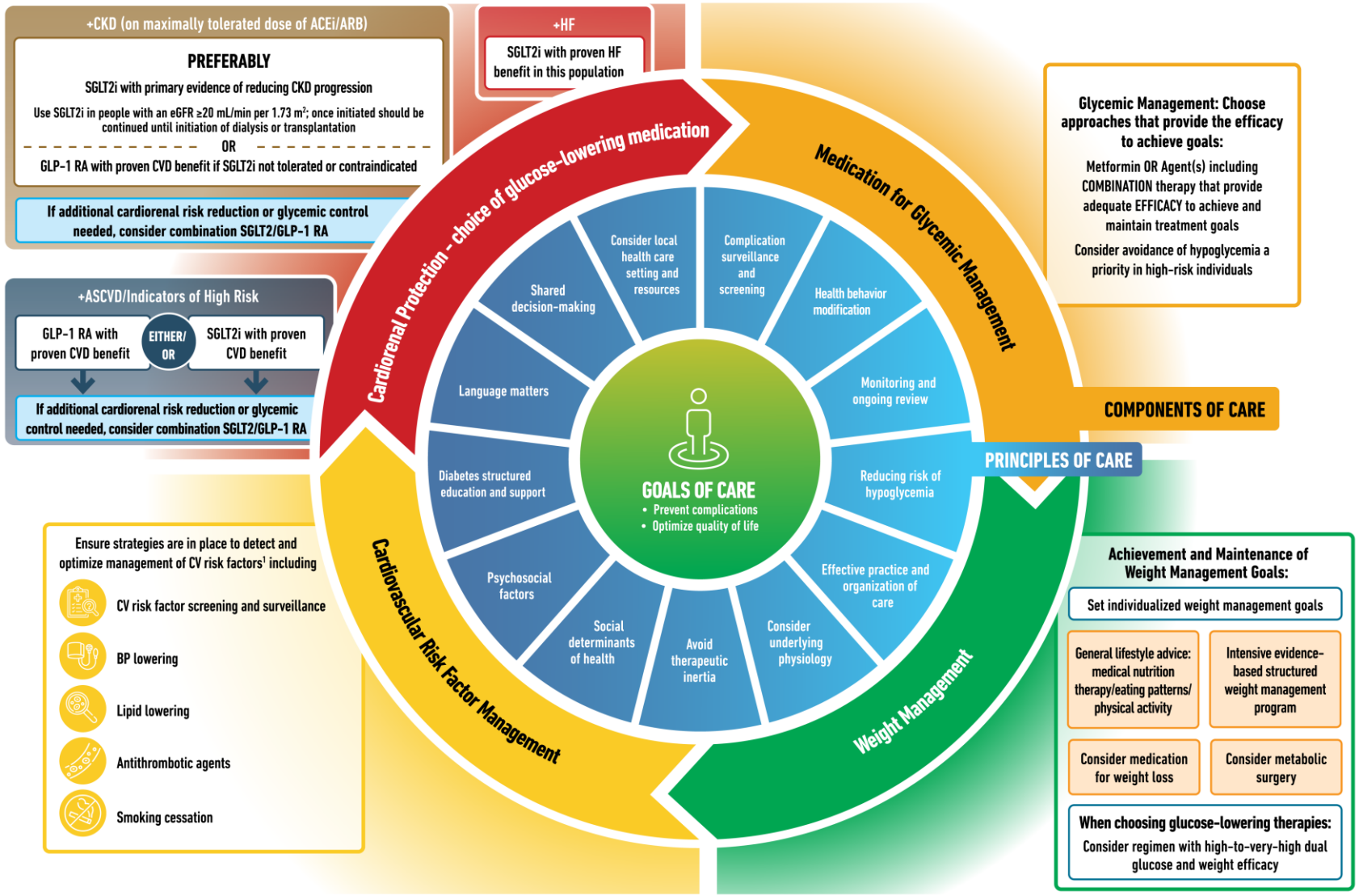
Diabetes Care Volume 47, Supplement 1, January 2024



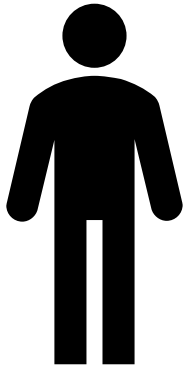
[1]BMI 23 to 25 kg/m^2 may be considered overweight for South Asian, Southeast Asian, and East Asian adults; [2]ABCD complications can include prediabetes, dyslipidemia, hypertension, NAFLD/NASH, ASCVD, CHF and HFpEF, CKD, OSA, OA, asthma/reactive airways disease, GERD, urinary incontinence, PCOS, hypogonadism, and reduced fertility. [3]See PROFILES OF WEIGHT-LOSS MEDICATIONS table.

Algorithm Figure 2-ABCD

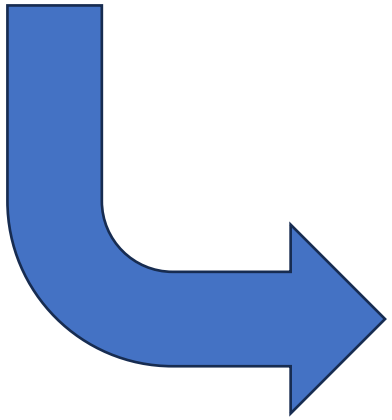
HOLISTIC PERSON-CENTERED APPROACH TO T2DM MANAGEMENT



American Diabetes Association Professional Practice Committee. 10. Cardiovascular Disease and Risk Management: Standards of Medical Care in Diabetes-2022. Diabetes Care. 2022 Jan 1;45 (Suppl 1)S144-74.



- Male
- BMI: 40
- A1c: 8.0%
- Chronic Kidney disease
- Heart attack 2 years ago



After 2 years of Metabolic Surgery

- BMI: 27
- A1c: 6.5%
- Chronic Kidney disease
- Heart attack 4 years ago

Should we keep this patient without medication?

Thank you

tpetry@haoc.com.br

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