Česká diabetologická společnost
ČLS JEP z.s.

1. LÉKAŘSKÁ FAKULTA
Univerzita Karlova

VŠEOBECNÁ FAKULTNÍ NEMOCNICE V PRAZE

Neglykemická vaskulární protektivita antidiabetické léčby

Prof. MUDr. Martin Prázný, CSc., Ph.D.

3. Interní klinika 1. LF UK a VFN v Praze

Komorbidity u pacientů s DM – dle věku

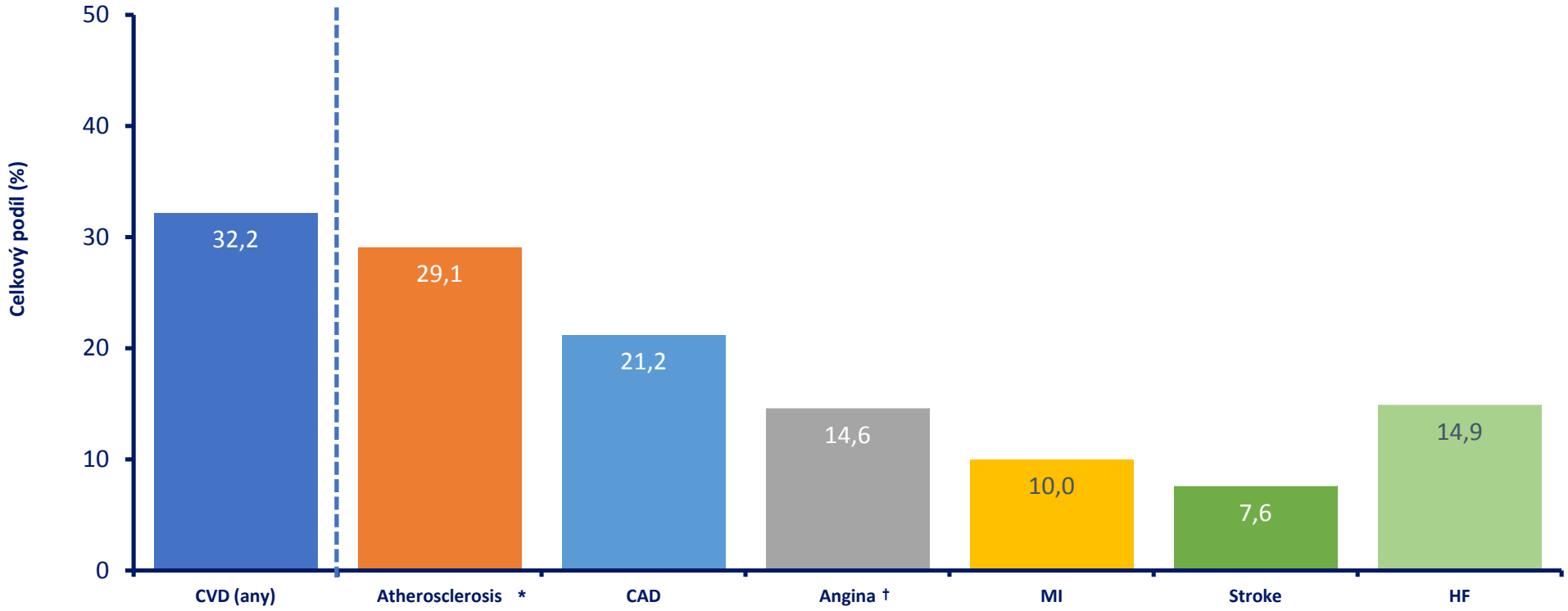
Zdroj: NRHZS 2010–2021

Relativní četnost výskytu komorbidit u pacientů, kteří byli v roce 2021 léčení antidiabetiky (ATC skupina A10):

	Celkem	< 40 let	40–49 let	50–59 let	60–69 let	70–79 let	80+ let
Počet pacientů (2021)	813 873	27 054	50 319	114 391	223 549	282 426	116 134
Poruchy metabolismu lipoproteinů	73,0 %	21,6 %	55,3 %	69,2 %	77,5 %	79,8 %	71,0 %
Hypertenze	64,0 %	14,0 %	42,2 %	55,2 %	64,7 %	71,8 %	73,5 %
Ischemická choroba srdeční	21,8 %	1,5 %	5,8 %	11,1 %	18,0 %	27,1 %	38,5 %
Srdeční selhání	8,4 %	0,6 %	1,9 %	3,3 %	5,8 %	10,1 %	19,1 %
Chronické onemocnění ledvin	7,1 %	2,7 %	2,9 %	3,6 %	5,1 %	8,8 %	13,3 %

Globální prevalence KV onemocnění u diabetiků 2. typu

Systematický přehled odborné literatury: 2007–2017



Rates weighted by inverse variance; Data included from various global studies as available
**Atherosclerosis data reported from China, Korea, and Netherlands only; †Angina data reported from Sweden and USA only*
CAD, coronary artery disease; CVD, cardiovascular disease (includes all complications); HF, heart failure; MI, myocardial infarction
Einarson TR et al. Cardiovasc Diabetol. 2018;17:83. doi: 10.1186/s12933-018-0728-6

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Risk Factors, Mortality, and Cardiovascular Outcomes in Patients with Type 2 Diabetes

Aidin Rawshani, M.D., Araz Rawshani, M.D., Ph.D., Stefan Franzén, Ph.D., Naveed Sattar, M.D., Ph.D., Björn Eliasson, M.D., Ph.D., Ann-Marie Svensson, Ph.D., Björn Zethelius, M.D., Ph.D., Mervete Miftaraj, M.Sc., Darren K. McGuire, M.D., M.H.Sc., Annika Rosengren, M.D., Ph.D., and Soffia Gudbjörnsdottir, M.D., Ph.D.

N ENGL J MED 379;7 NEJM.ORG AUGUST 16, 2018

Rawshani, A., Rawshani, A., Franzén, S., Sattar, N., Eliasson, B., Svensson, A.-M., Zethelius, B., Miftaraj, M., Mcguire, D.K., Rosengren, A., Gudbjörnsdottir, S., 2018. Risk Factors, Mortality, and Cardiovascular Outcomes in Patients with Type 2 Diabetes. New England Journal of Medicine 379, 633–644.. https://doi.org/10.1056/nejmoa1800256

Glukocentrický přístup

1% reduction in HbA1c was associated with the following reductions in risk for microvascular complications[1]*

-43%	-37%	-14%	-12%
Amputation or death from PVD	Microvascular endpoints	Myocardial infarction	Stroke

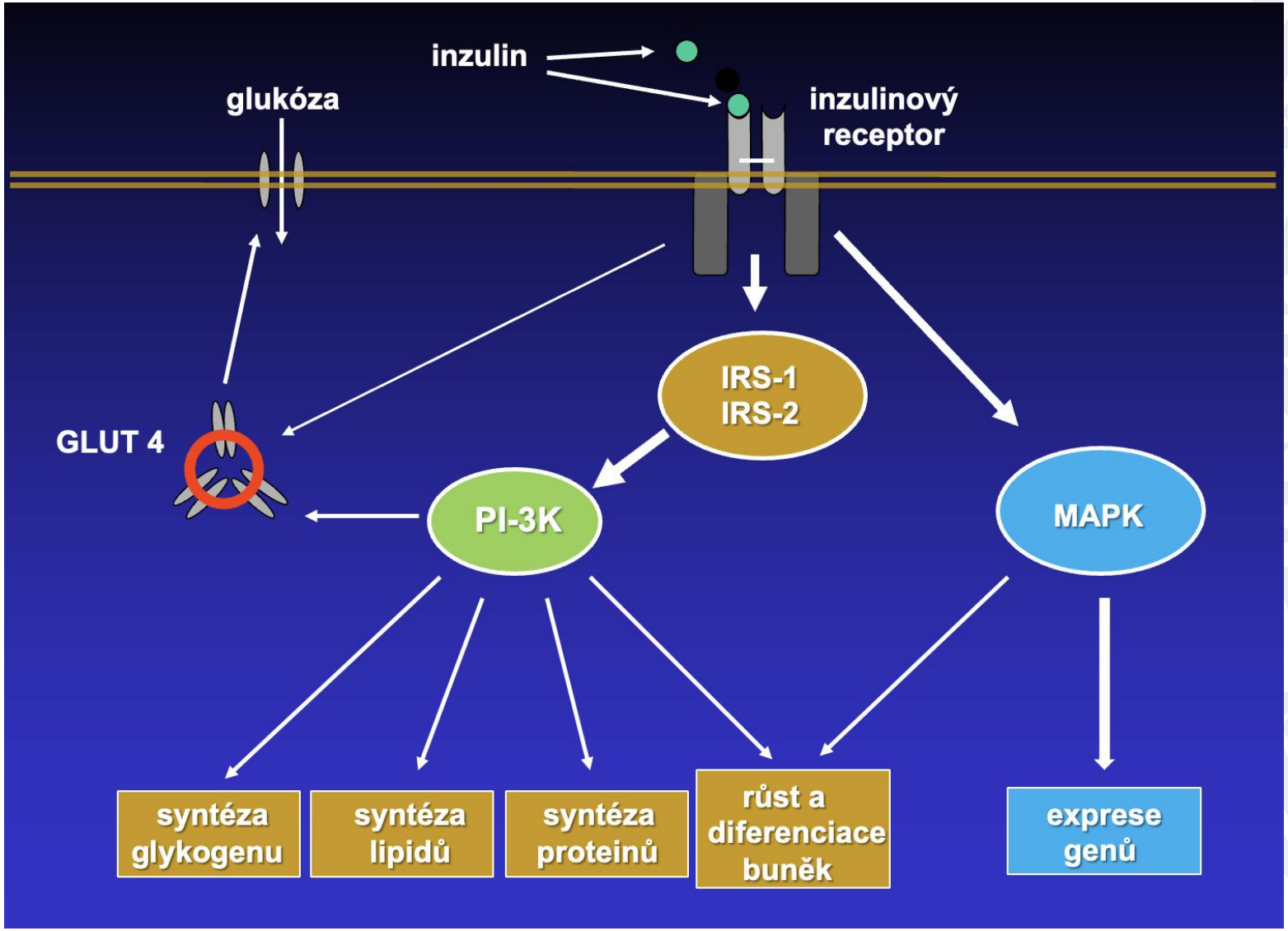
A separate US-based analysis found that every 1% HbA1c reduction was associated with a 7% reduction in T2D-related costs[2†]

PVD=peripheral vascular disease.

*UK Prospective Diabetes Study (UKPDS): prospective observational study in 3642 people with T2D at 23 UK hospital-based clinics randomized to conventional or intensive glycemic control; data are risk-reduction calculated from proportional Cox hazards regression models.

†Two large US claims databases were utilized to examine the relationship between HbA1c and 1-year, post-period, diabetes-related costs in patients identified with T2D from January 2014 to January 2017 who had at least 1 HbA1c laboratory test during that time period and at least 1 additional HbA1c laboratory test 1-year post-period.

Inzulínová rezistence a deficit: vazokonstrikce



JOURNAL ARTICLE GUIDELINES

2023 ESC Guidelines for the management of cardiovascular disease in patients with diabetes: Developed by the task force on the management of cardiovascular disease in patients with diabetes of the European Society of Cardiology (ESC) FREE

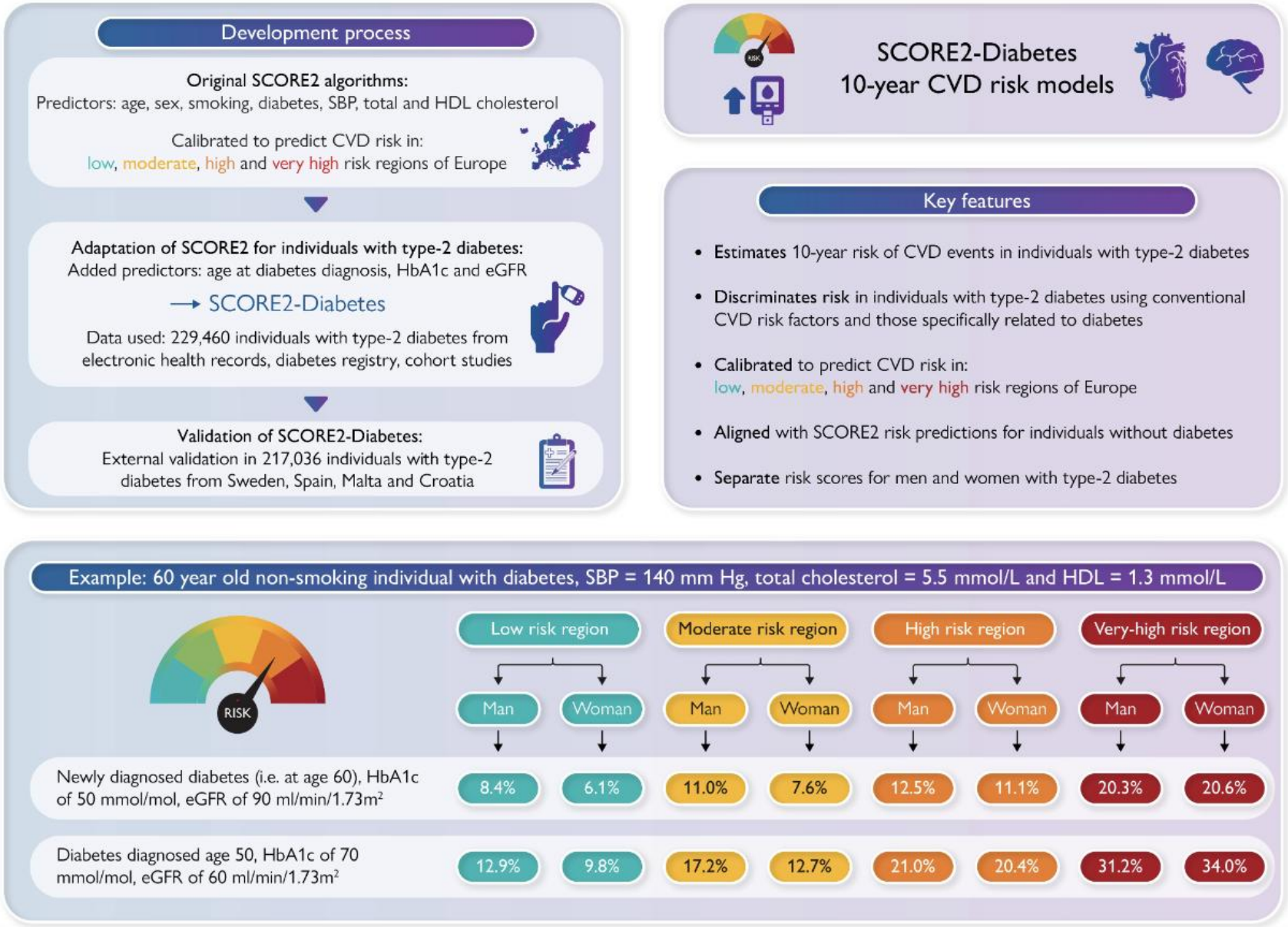
Nikolaus Marx ✉, Massimo Federici ✉, Katharina Schütt, Dirk Müller-Wieland, Ramzi A Ajjan, Manuel J Antunes, Ruxandra M Christodorescu, Carolyn Crawford, Emanuele Di Angelantonio, Björn Eliasson, Christine Espinola-Klein, Laurent Fauchier, Martin Halle, William G Herrington, Alexandra Kautzky-Willer, Ekaterini Lambrinou, Maciej Lesiak, Maddalena Lettino, Darren K McGuire, Wilfried Mullens, Bianca Rocca, Naveed Sattar, ESC Scientific Document Group

Author Notes

European Heart Journal, Volume 44, Issue 39, 14 October 2023, Pages 4043–4140,
https://doi.org/10.1093/eurheartj/ehad192

Published: 25 August 2023

Structured Graphical Abstract SCORE2-Diabetes 10-year CVD risk models: development process, key features and illustrative example.



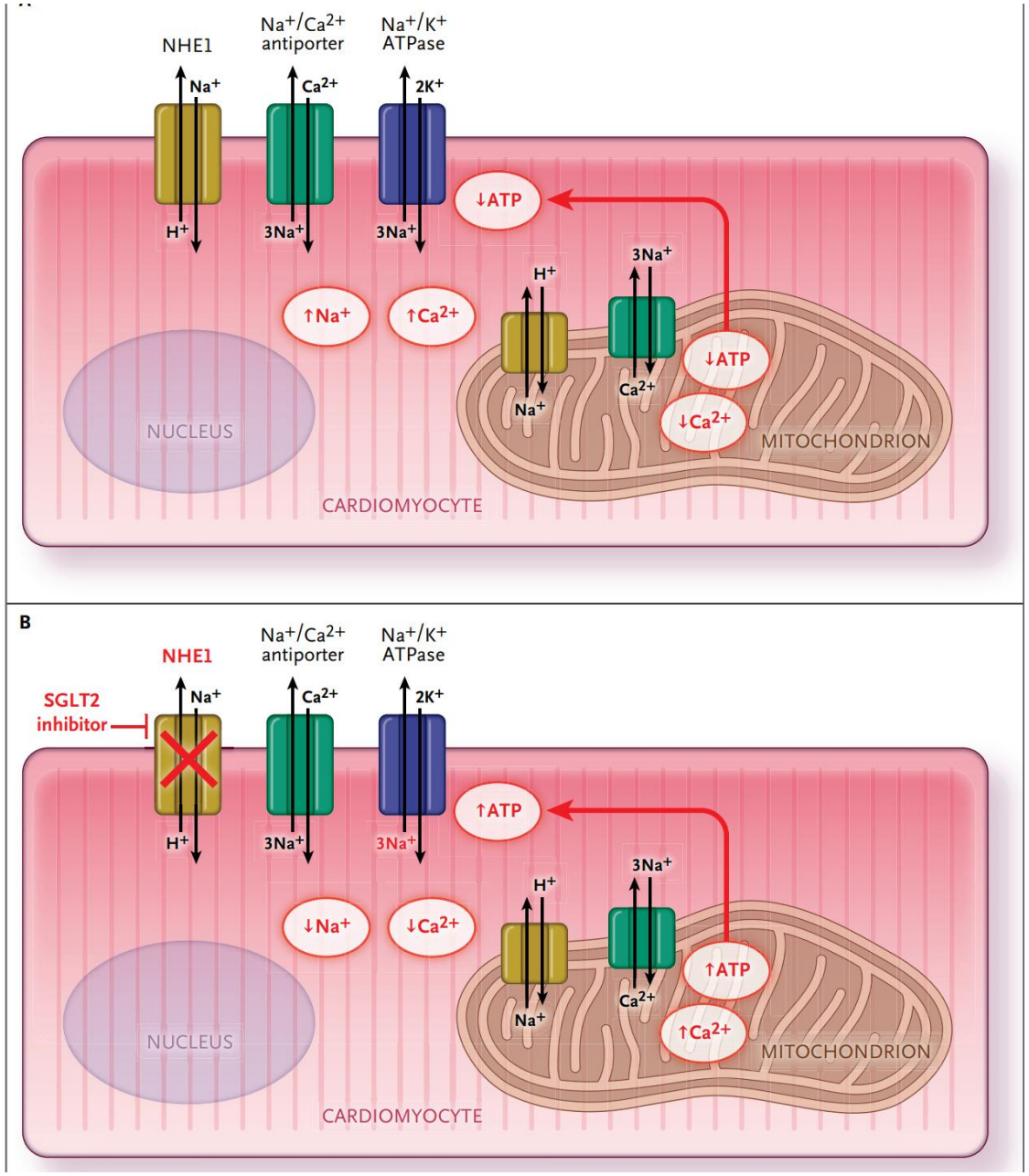
Eur Heart J, Volume 44, Issue 28, 21 July 2023, Pages 2544–2556, https://doi.org/10.1093/eurheartj/ehad260

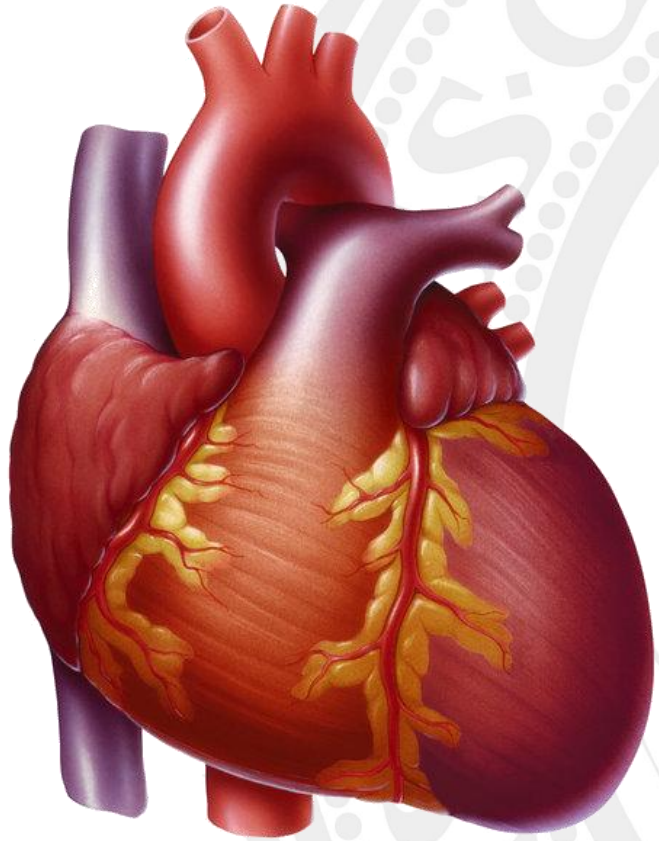
Recommendations	Class[a]	Level[b]
Cardiovascular risk assessment in diabetes—*Section 4*		
In patients with T2DM without symptomatic ASCVD or severe TOD, it is recommended to estimate 10-year CVD risk via SCORE2-Diabetes.	I	B
Weight reduction in patients with diabetes—*Section 5.1.1*		
It is recommended that individuals living with overweight or obesity aim to reduce weight and increase physical exercise to improve metabolic control and overall CVD risk profile.	I	A
Glucose-lowering medications with effects on weight loss (e.g. GLP-1 RAs) should be considered in patients with overweight or obesity to reduce weight.	IIa	B
Bariatric surgery should be considered for high and very high risk patients with BMI ≥35 kg/m^2 (≥Class II) when repetitive and structured efforts of lifestyle changes combined with weight-reducing medications do not result in maintained weight loss.	IIa	B

Table 7 Cardiovascular risk categories in type 2 diabetes

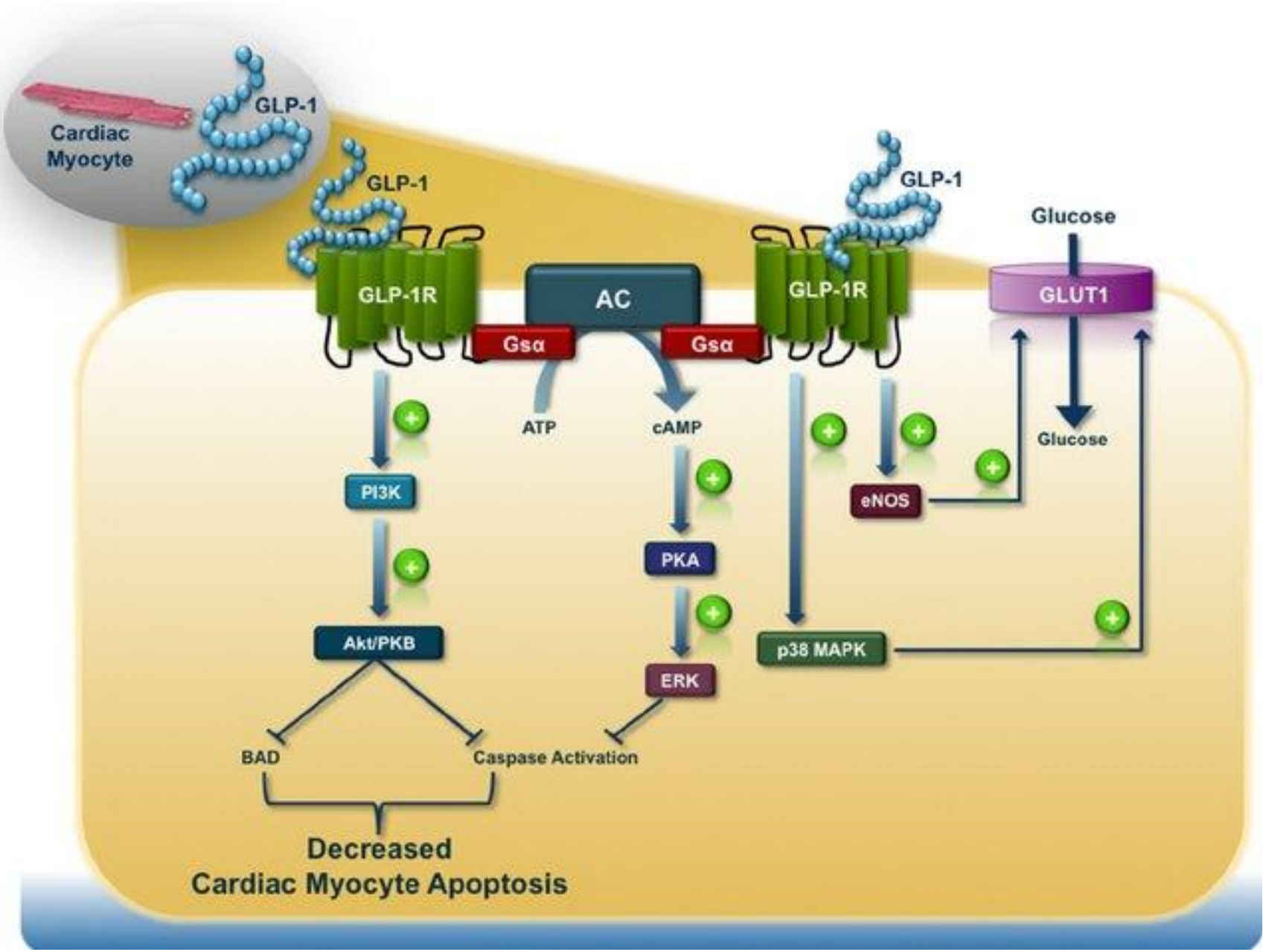
Very high CV risk	Patients with T2DM with: • Clinically established ASCVD or • Severe TOD or • 10-year CVD risk ≥20% using SCORE2-Diabetes
High CV risk	Patients with T2DM not fulfilling the very high-risk criteria and a: • 10-year CVD risk 10 to <20% using SCORE2-Diabetes
Moderate CV risk	Patients with T2DM not fulfilling the very high-risk criteria and a: • 10-year CVD risk 5 to <10% using SCORE2-Diabetes
Low CV risk	Patients with T2DM not fulfilling the very high-risk criteria and a: • 10-year CVD risk <5% using SCORE2-Diabetes

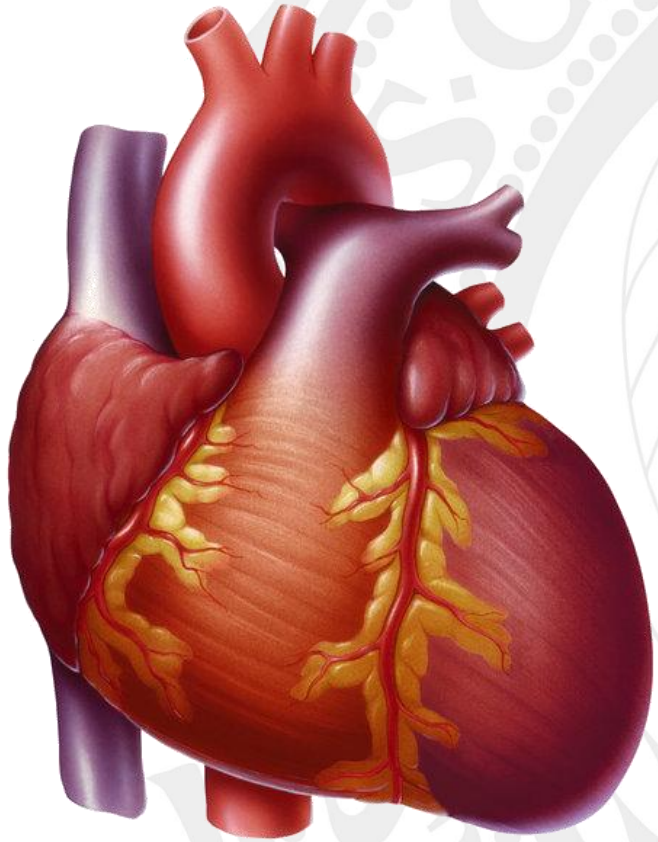
Nikolaus Marx et al. ESC Scientific Document Group , 2023 ESC Guidelines for the management of cardiovascular disease in patients with diabetes: Developed by the task force on the management of cardiovascular disease in patients with diabetes of the European Society of Cardiology (ESC), *European Heart Journal*, Volume 44, Issue 39, 14 October 2023, Pages 4043–4140, https://doi.org/10.1093/eurheartj/ehad192



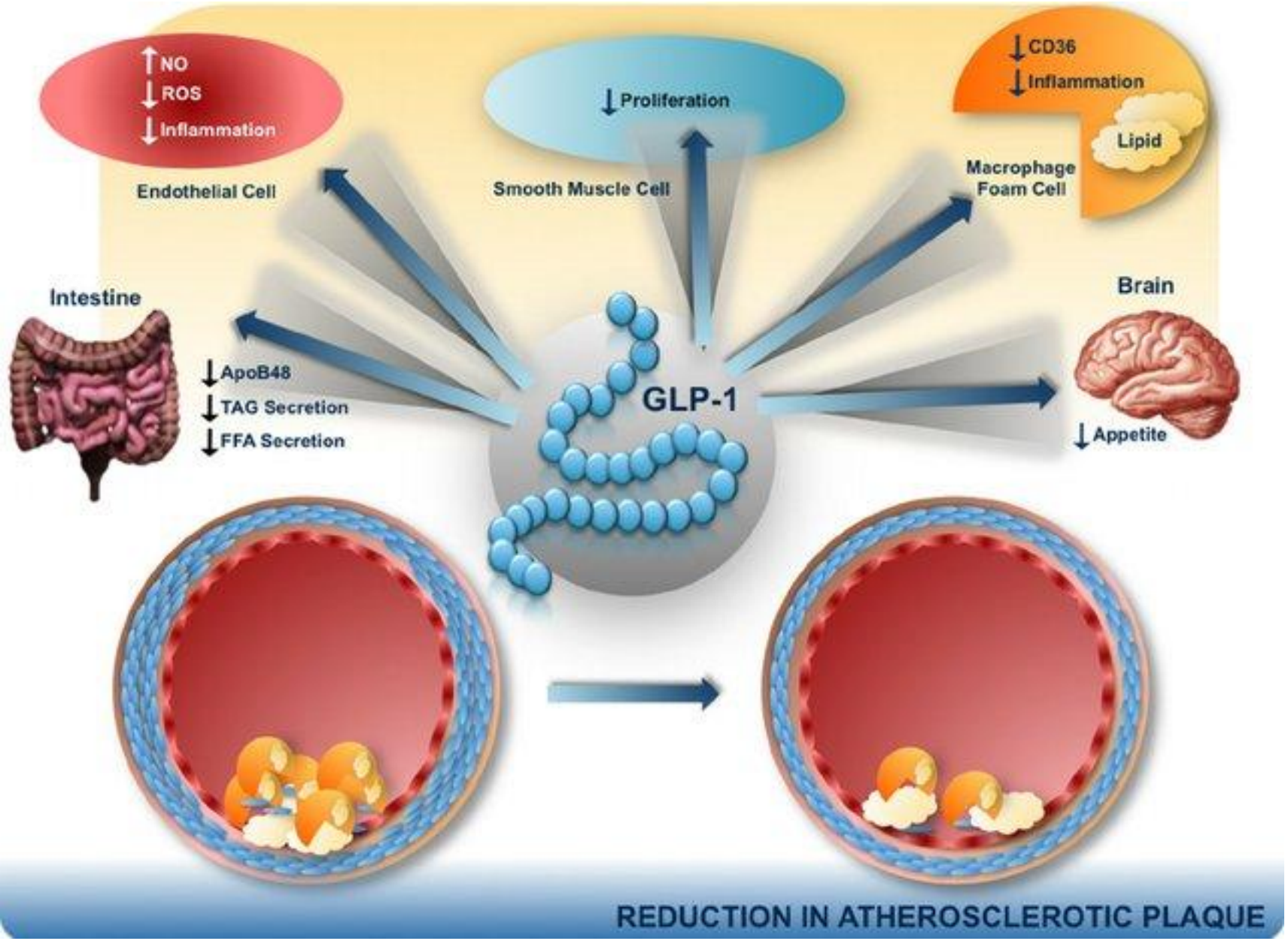


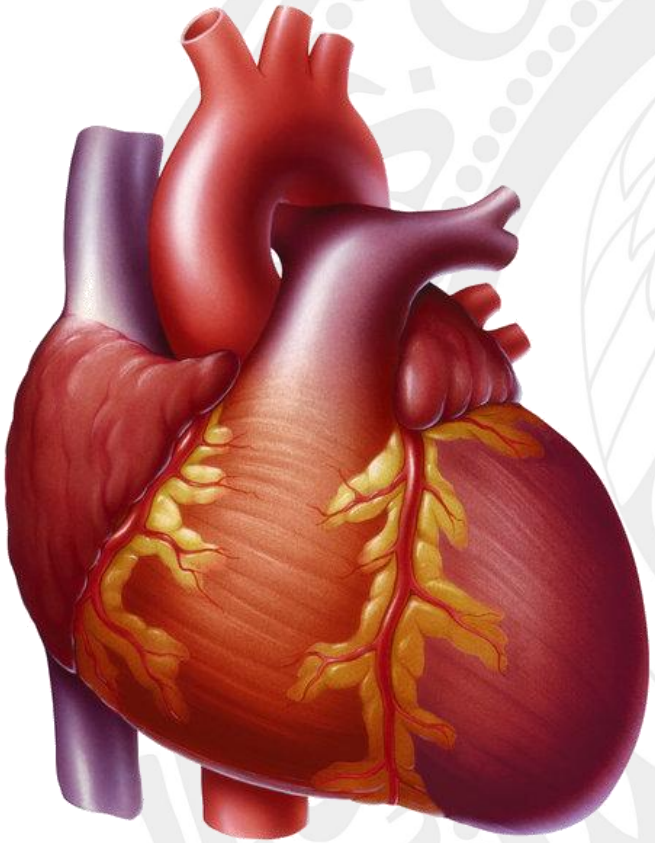
N Engl J Med 2022;386:2024-34. DOI: 10.1056/NEJMra2115011





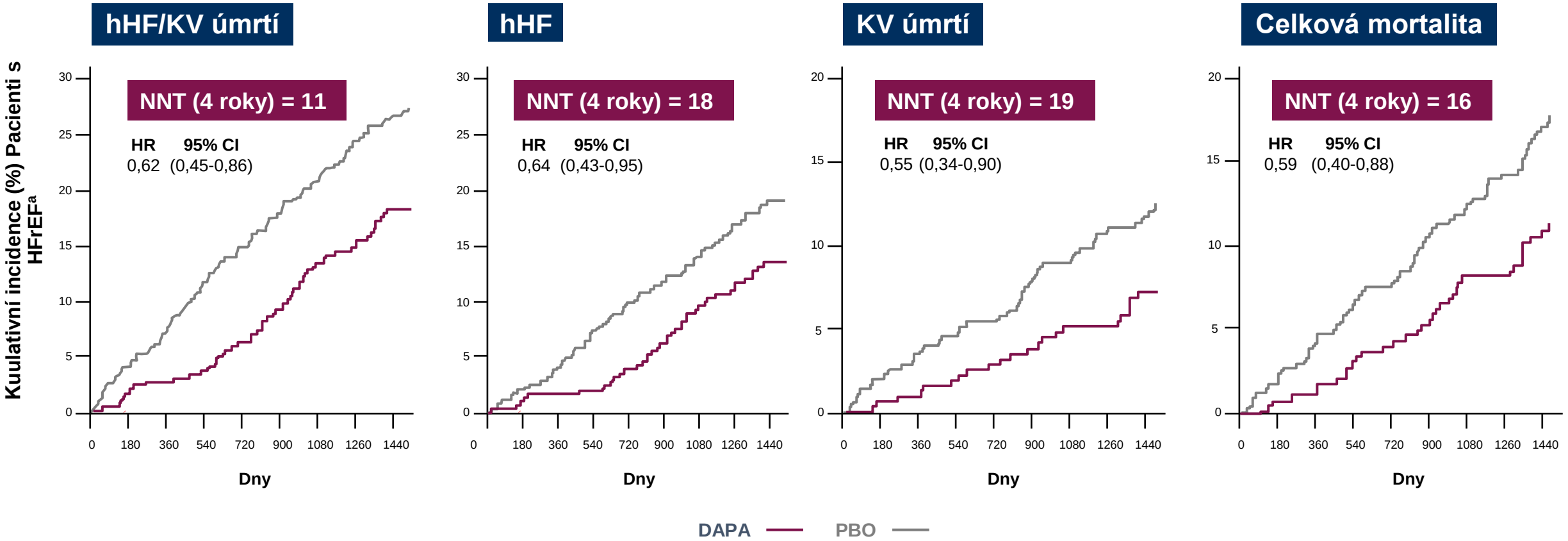
Ussher et al. Endocrine Reviews, April 2012, 33(2):187–215





Ussher et al. Endocrine Reviews, April 2012, 33(2):187–215

KV benefit dapagliflozinu u pacientů s T2D a HFrEF se objevuje brzy[a]



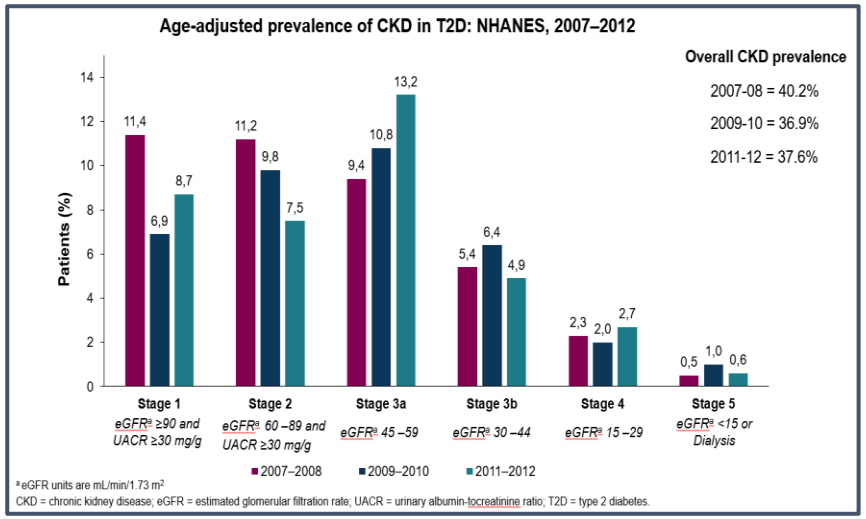
[a]Definováno jako EF <45% či závažná/střední systolická dysfunkce LK s, nebo bez historie srdečního selhání. KV = kardiovaskulární; DAPA = dapagliflozin; EF =ejection fraction; HFrEF = heart failure with reduced ejection fraction, HF s redukovanou ejekční frakcí; hHF = hospitalization for heart failure, hospitalizace pro HF; HR = hazard ratio; LV = left ventricular; NNT = number needed to treat; PBO = placebo; T2D = type 2 diabetes, diabetes 2. typu; yrs = years; HF = heart failure, srdeční selhání

Přejato a upraveno dle:

KATO, Eri T., Michael G. SILVERMAN, Ofri MOSENZON, et al. Effect of Dapagliflozin on Heart Failure and Mortality in Type 2 Diabetes Mellitus. *Circulation* [online]. 2019; **139**(22), 2528-2536 [cit. 2019-09-30]. DOI: 10.1161/CIRCULATIONAHA.119.040130. ISSN 0009-7322. Dostupné z: https://www.ahajournals.org/doi/10.1161/CIRCULATIONAHA.119.040130

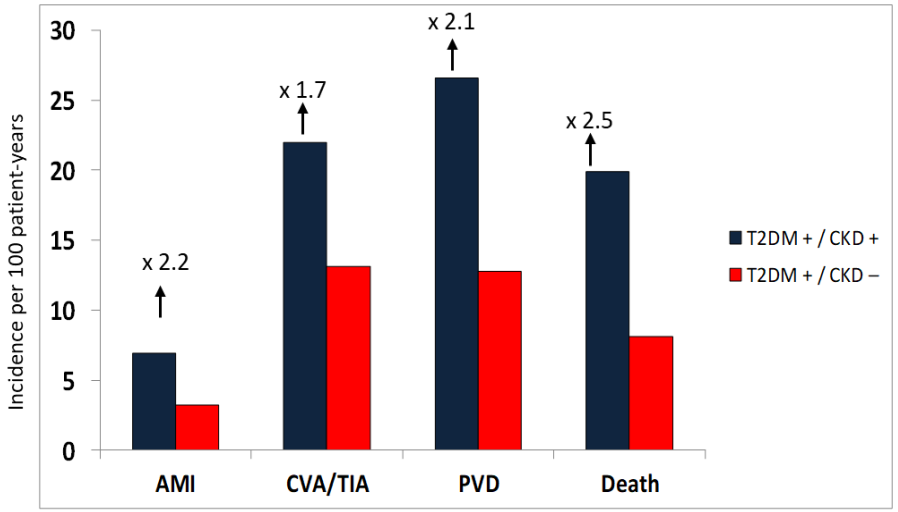
Asi 40% pacientů s DM2 má CKD[1]

Prevalence CKD u DM2 je trvale vysoká[2]



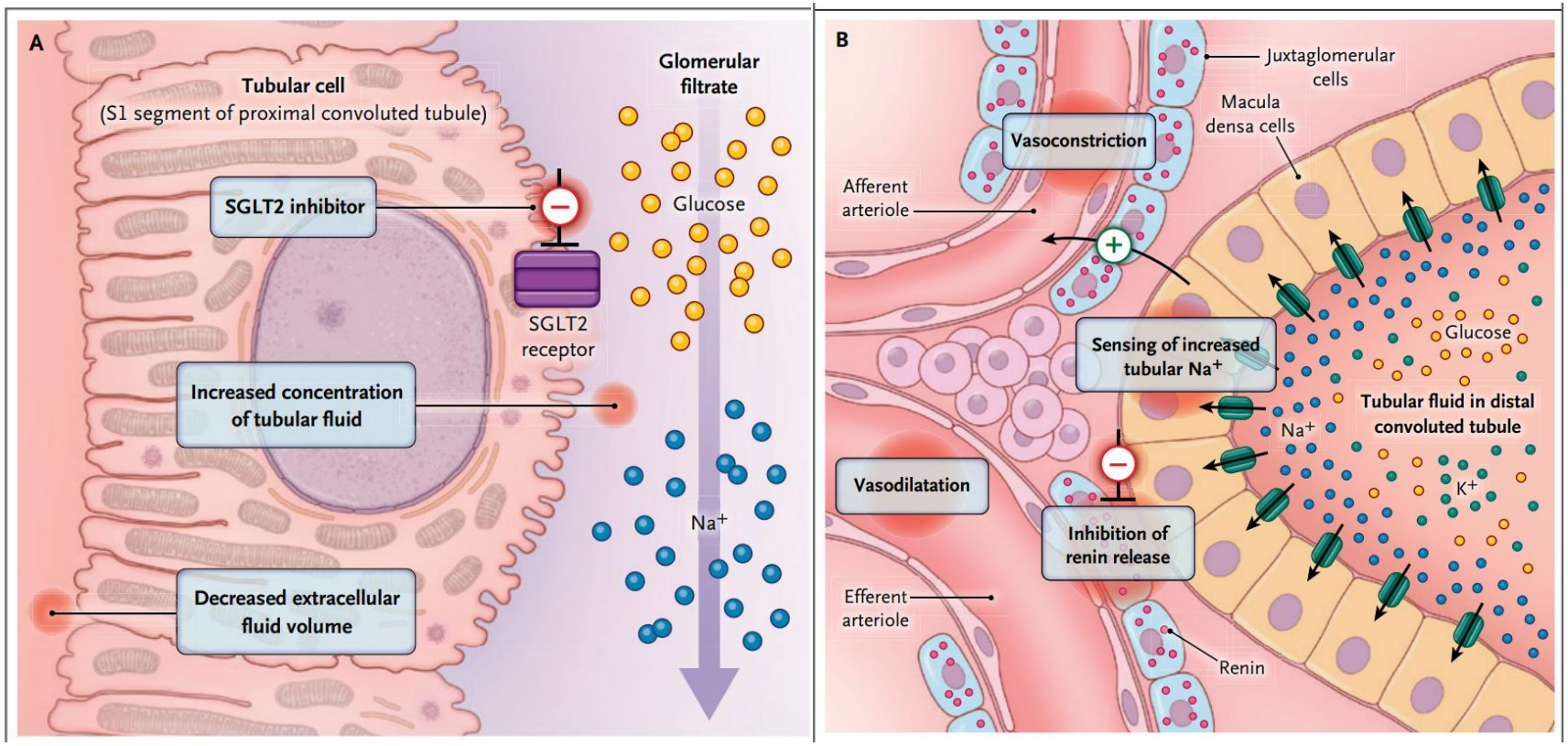
1.Alicic RZ et al.Clin J Am Soc Nephrol. 2017; 12: 2032–2045; 2. Upraveno dle:Wu B, Bell K, Stanford A, et al. Understanding CKD among patients with T2D: prevalence, temporal trends, and treatment patterns-NHANES 2007-2012 [Article and supplementary tables]. *BMJ Open Diabetes Res Care*. 2016. https://dx.doi.org/10.1136/bmjdrc-2015-000154. Accessed February 22, 2019.

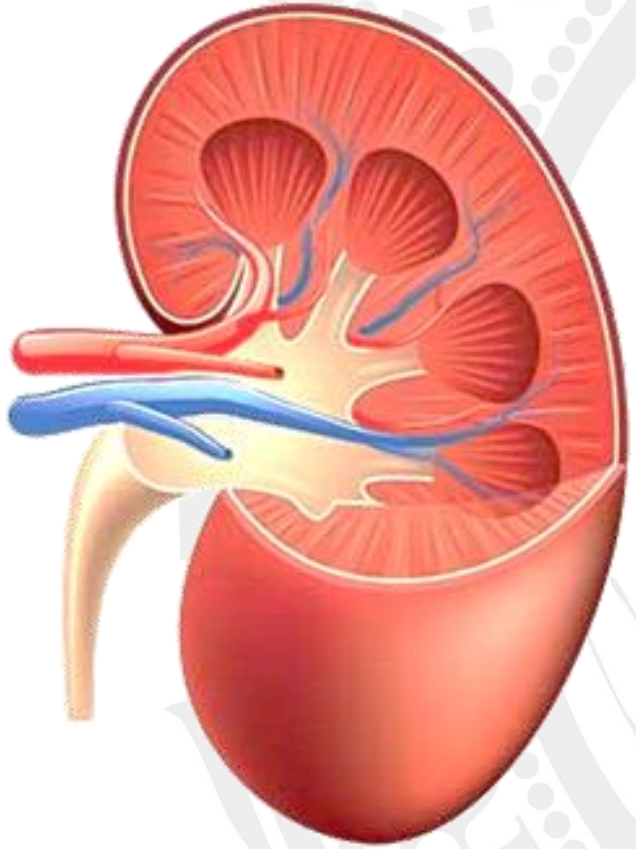
Diabetik s CKD má 2 x vyšší KV riziko než diabetik bez CKD



CKD = chronické onemocnění ledvin; AMI = akutní infarkt myokardu;
CVA/TIA = cerebrovaskulární příhoda/tranzitorní ischemická ataka;
PVD = onemocnění periferních cév; Death = smrt ze všech příčin

Upraveno dle: Foley RN et al. *J Am Soc Nephrol.* 2005;16:489–95.





N Engl J Med 2022;386:2024-34. DOI: 10.1056/NEJMra2115011

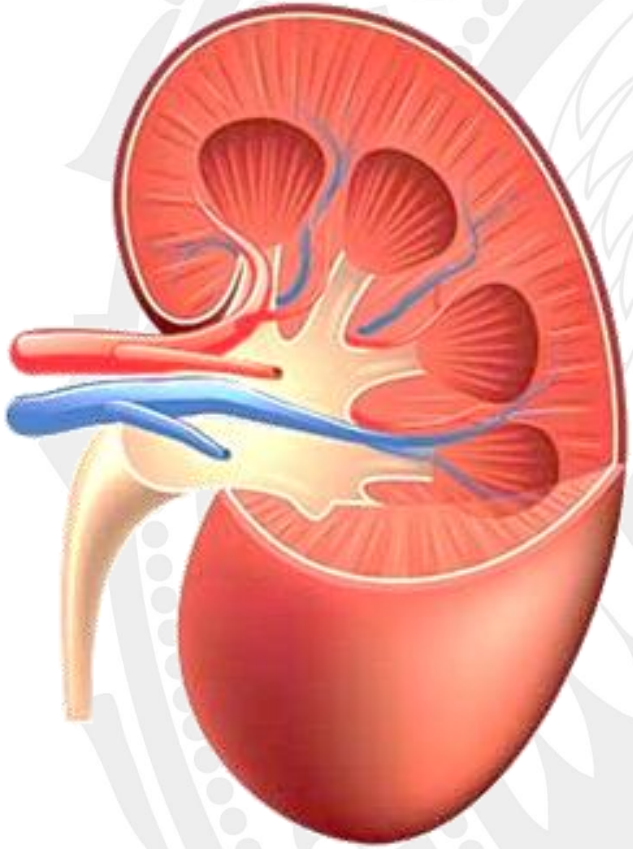
NOVO NORDISK

Company announcement

10:37 10 October 2023

Announcement.pdf

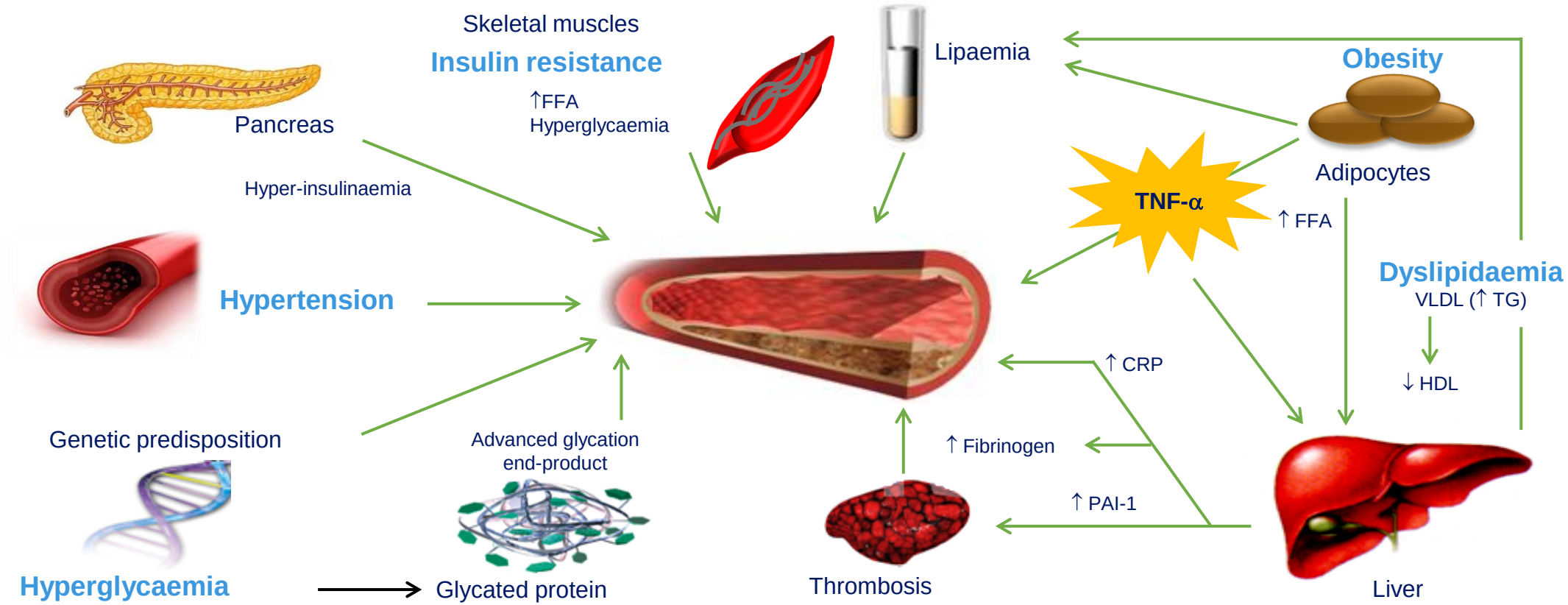
Novo Nordisk will stop the once-weekly injectable semaglutide kidney outcomes trial, FLOW, based on interim analysis



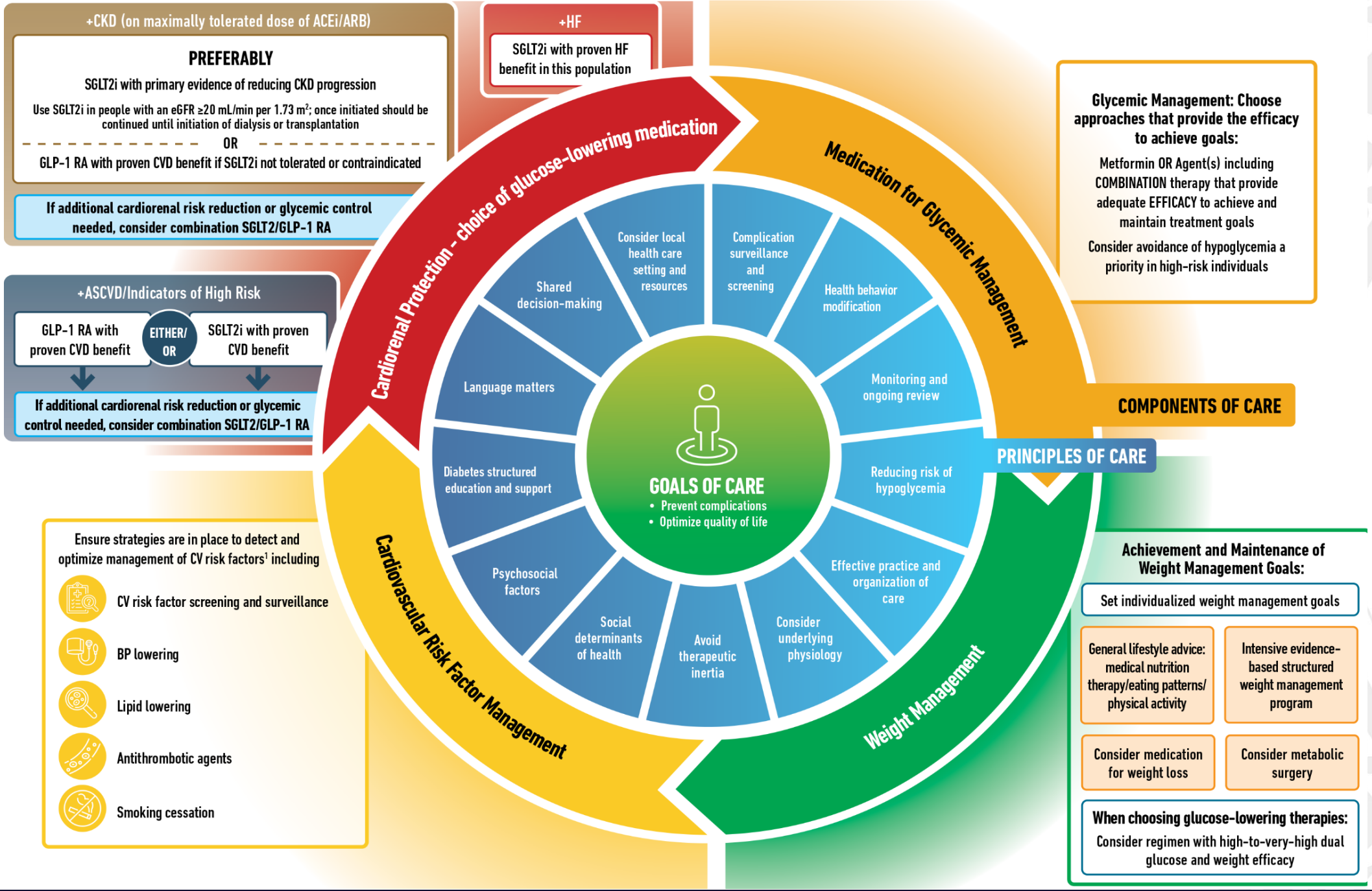
Novo Nordisk will stop the once-weekly injectable semaglutide kidney outcomes trial, FLOW, based on interim analysis

Bagsværd, Denmark, 10 October 2023 – Novo Nordisk today announced the decision to stop the kidney outcomes trial FLOW (Effect of semaglutide versus placebo on the progression of renal impairment in people with type 2 diabetes and chronic kidney disease).

DIABETES NENÍ JEN HYPERGLYKÉMIE: k rozvoji vaskulárních komplikací u DM2 vede více cest



CRP, C-reactive protein; CV, cardiovascular; FFA, free fatty acid; HDL, high-density lipoprotein; IGT, impaired glucose tolerance; LDL, low-density lipoprotein; PAI-1, plasminogen activator inhibitor-1; T2D, type 2 diabetes; TG, triglyceride; TNF-α, tumour necrosis factor-alpha; VLDL, very low-density lipoprotein
Libby P, Plutzky J. Circulation 2002;106:2760–2763


+CKD (on maximally tolerated dose of ACEi/ARB)
PREFERABLY
SGLT2i with primary evidence of reducing CKD progression
Use SGLT2i in people with an eGFR ≥20 mL/min per 1.73 m²; once initiated should be continued until initiation of dialysis or transplantation
OR
GLP-1 RA with proven CVD benefit if SGLT2i not tolerated or contraindicated
If additional cardiorenal risk reduction or glycemic control needed, consider combination SGLT2/GLP-1 RA
+HF
SGLT2i with proven HF benefit in this population
+ASCVD/Indicators of High Risk
GLP-1 RA with proven CVD benefit
EITHER/ OR
SGLT2i with proven CVD benefit
If additional cardiorenal risk reduction or glycemic control needed, consider combination SGLT2/GLP-1 RA
Cardiorenal Protection - choice of glucose-lowering medication
Medication for Glycemic Management
Glycemic Management: Choose approaches that provide the efficacy to achieve goals:
Metformin OR Agent(s) including COMBINATION therapy that provide adequate EFFICACY to achieve and maintain treatment goals
Consider avoidance of hypoglycemia a priority in high-risk individuals
COMPONENTS OF CARE
PRINCIPLES OF CARE
Consider local health care setting and resources
Complication surveillance and screening
Health behavior modification
Monitoring and ongoing review
Reducing risk of hypoglycemia
Effective practice and organization of care
Consider underlying physiology
Avoid therapeutic inertia
Social determinants of health
Psychosocial factors
Diabetes structured education and support
Language matters
Shared decision-making
GOALS OF CARE
• Prevent complications
• Optimize quality of life
Cardiovascular Risk Factor Management
Weight Management
Ensure strategies are in place to detect and optimize management of CV risk factors[1] including
CV risk factor screening and surveillance
BP lowering
Lipid lowering
Antithrombotic agents
Smoking cessation
Achievement and Maintenance of Weight Management Goals:
Set individualized weight management goals
General lifestyle advice: medical nutrition therapy/eating patterns/ physical activity
Intensive evidence-based structured weight management program
Consider medication for weight loss
Consider metabolic surgery
When choosing glucose-lowering therapies:
Consider regimen with high-to-very-high dual glucose and weight efficacy

Holistický přístup

According to *ADA Standards of Medical Care in Diabetes—2022*,

sustained weight loss of

10% -15 %

can maximize outcomes[1]

The EASD-ADA Consensus Report recommends considering the impact on weight when choosing a glucose-lowering agent[2]

5%-10%
Weight loss

Up to 1% reduction in HbA1c

9 kg -13 kg
Weight loss

25% decreased mortality rate

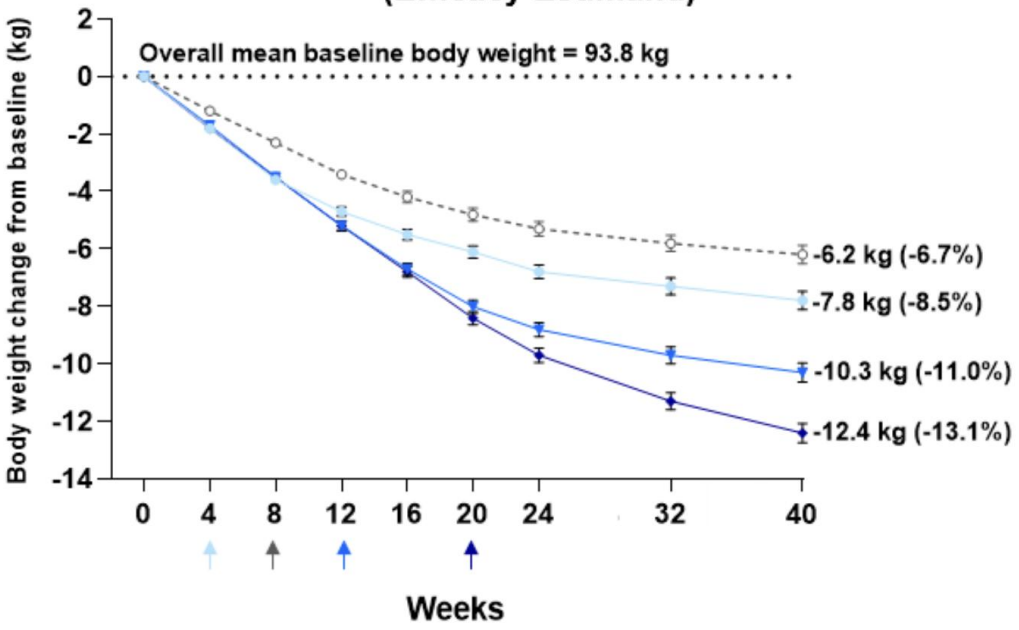
According to the AHA/ACC/TOS guideline, for adults with T2D and overweight or obesity1*

ADA=American Diabetes Association; EASD=European Association for the Study of Diabetes.

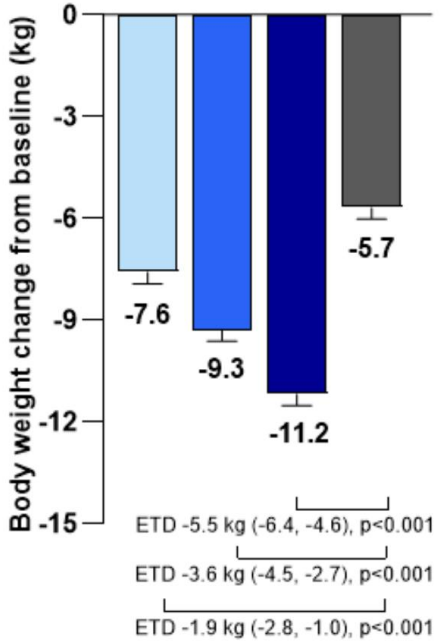
References: 1. American Diabetes Association Professional Practice Committee. *Diabetes Care*. 2022;45(suppl 1):S60-S82. **2.** Buse JB, et al. *Diabetologia*. 2020;63(2):221-228. doi:10.1007/s00125-019-05039-w

Tirzepatide versus Semaglutide Once Weekly in Patients with Type 2 Diabetes

A. Change from Baseline in Body Weight Over Time at 40 Weeks (Efficacy Estimand)



B. Change from baseline in body weight at 40 weeks (Treatment-Regimen Estimand)



Tirzepatide 5 mg Tirzepatide 10 mg Tirzepatide 15 mg Semaglutide 1 mg

Note: Data are LSM (SE), unless otherwise noted. Estimated treatment differences are LSM (95% confidence interval) at 40 weeks, mITT population. mITT (efficacy estimand) ANCOVA analysis (week 0) and MMRM analysis (week 40). Arrows indicate when the maintenance dose of Tirzepatide 5 mg, 10 mg and 15 mg and Semaglutide 1 mg are achieved. (A) Change from baseline in body weight over time from MMRM analysis (efficacy estimand). Percent change from baseline values at 40 weeks are in parentheses. (B) Change from baseline in body weight at 40 weeks from ANCOVA with multiple imputation by treatment for missing weight at 40 weeks (treatment-regimen estimand). Estimated treatment difference (95% CI) of Tirzepatide vs Semaglutide was: i) 5 mg -1.7** (-2.6, -0.7), ii) 10 mg -4.1** (-5.0, -3.2), and iii) 15 mg -6.2** (-7.1, -5.3). *p<0.05 and **p<0.001 vs. Semaglutide 1 mg at 40 weeks
ANCOVA=Analysis of Covariance; LSM=Least Squares Mean; mITT=Modified Intent-to-Treat; MMRM=Mixed Model Repeated Measures; SE=Standard Error.
Frias JP, et al. *N Engl J Med*. 2021; doi: 10.1056/NEJMoa2107519 (Ahead of Print).

The NEW ENGLAND JOURNAL of MEDICINE

RESEARCH SUMMARY

Semaglutide and Cardiovascular Outcomes in Obesity without Diabetes

Lincoff AM et al. DOI: 10.1056/NEJMoa2307563

CLINICAL PROBLEM

Glucagon-like peptide-1 (GLP-1) receptor agonists can reduce the risk of adverse cardiovascular events in patients with diabetes. Whether the GLP-1 receptor agonist semaglutide can also reduce cardiovascular risk in patients with overweight or obesity but without diabetes is unknown.

CLINICAL TRIAL

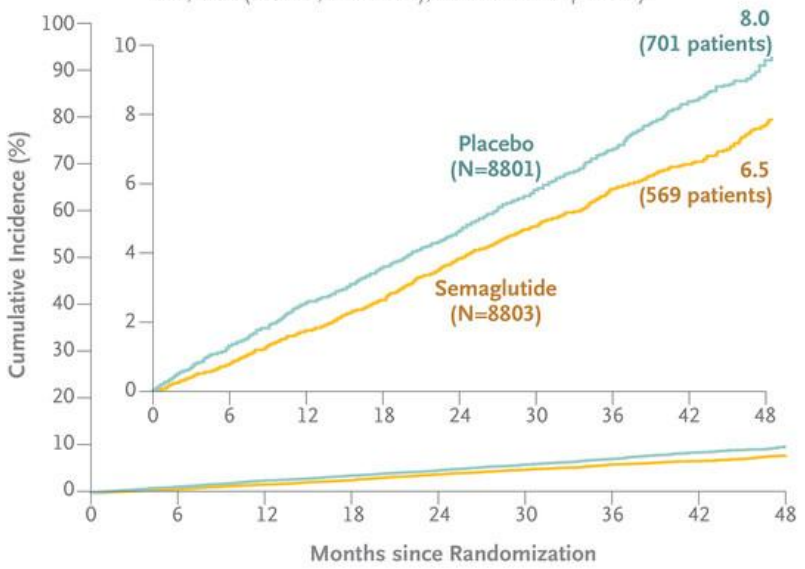
Design: An international, double-blind, event-driven, randomized, placebo-controlled, superiority trial assessed the safety and efficacy of semaglutide in patients with preexisting cardiovascular disease, overweight or obesity (body-mass index, ≥27), and no history of diabetes.

Intervention: 17,604 adults ≥45 years of age were assigned to receive once-weekly subcutaneous semaglutide (2.4 mg) or placebo. The primary cardiovascular end point was a composite of the first occurrence of death from cardiovascular causes, nonfatal myocardial infarction, or nonfatal stroke in a time-to-event analysis.

RESULTS

Death from Cardiovascular Causes, Nonfatal MI, or Nonfatal Stroke

HR, 0.80 (95% CI, 0.72–0.90); P<0.001 for superiority



Adverse Events Leading to Permanent Discontinuation of Regimen

CONCLUSIONS

In patients with preexisting cardiovascular disease and overweight or obesity but without diabetes, once-weekly subcutaneous semaglutide at a dose of 2.4 mg was superior to placebo in reducing the incidence of death from cardiovascular causes, nonfatal myocardial infarction, or nonfatal stroke during a mean follow-up of approximately 40 months.

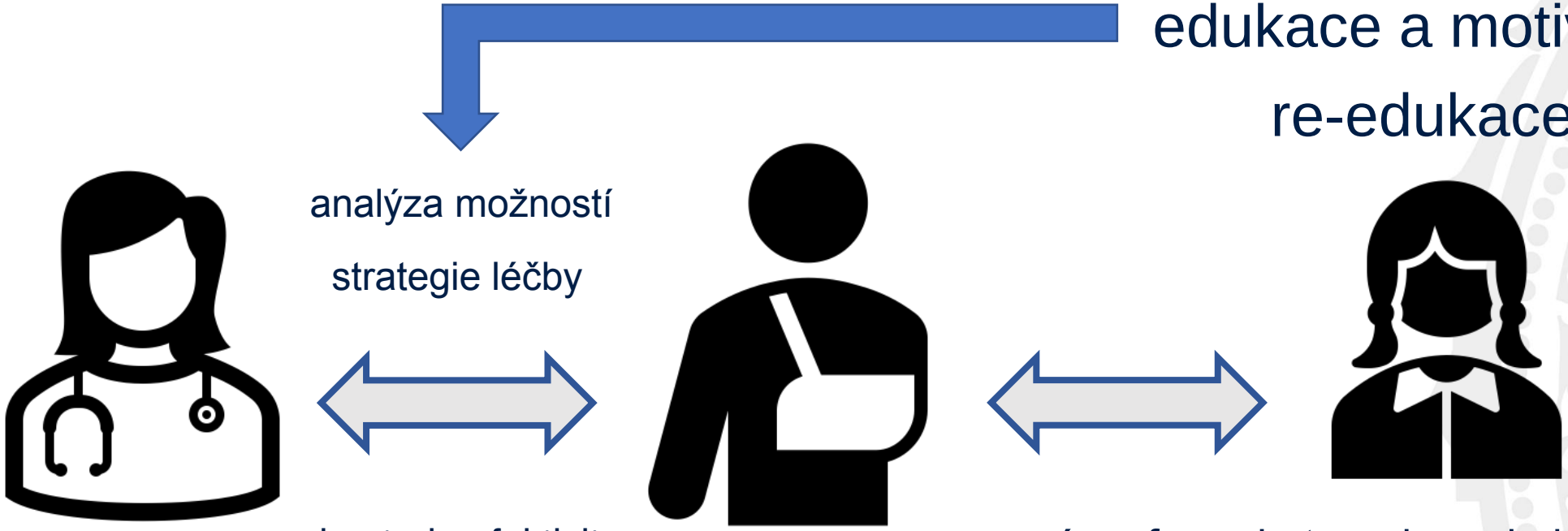
NUTRIČNÍ TERAPEUT

terapeutická intervence

NLZP

edukace a motivace

re-edukace



analýza možností

strategie léčby

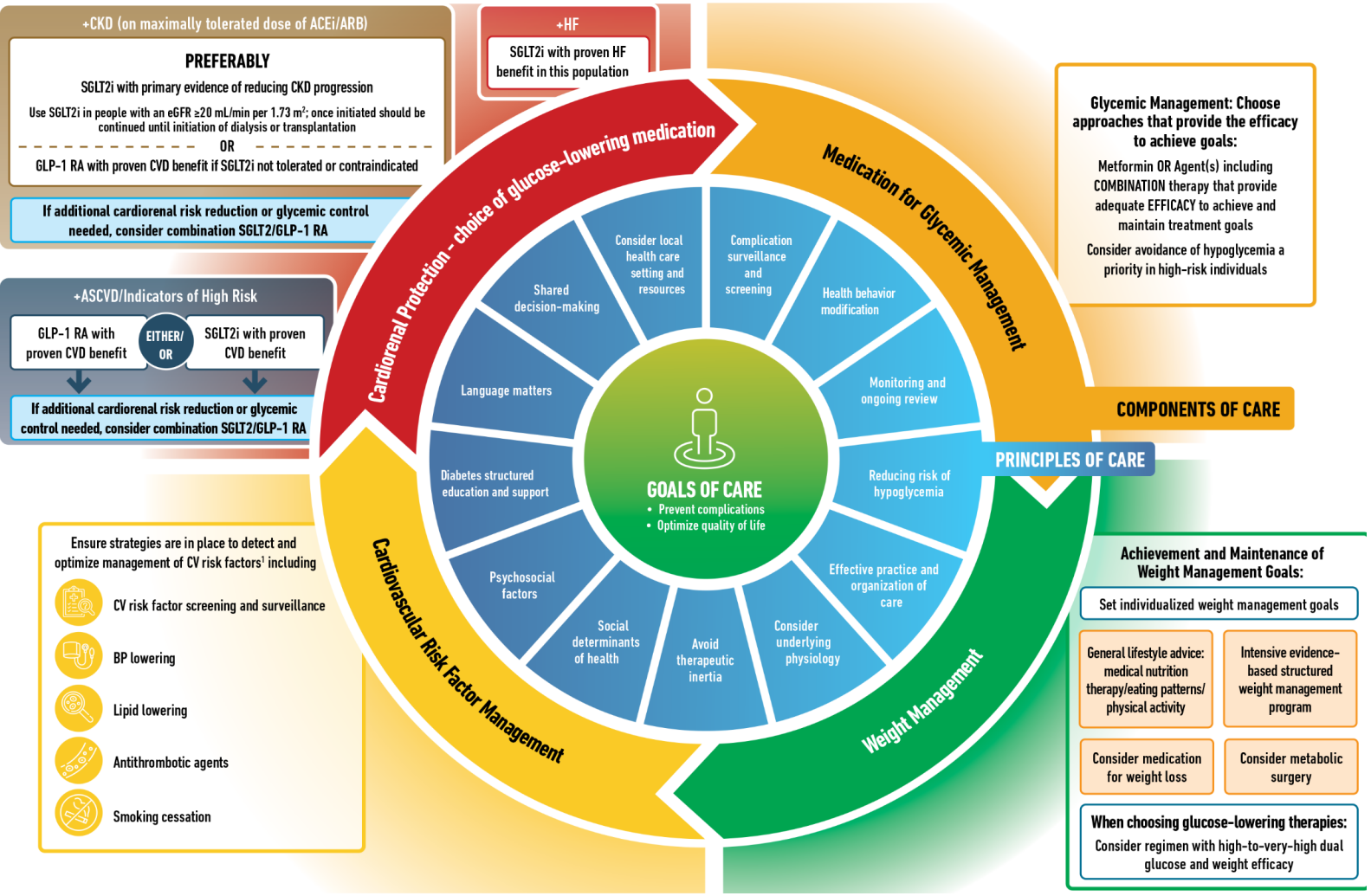
kontrola efektivity
a bezpečnosti léčby

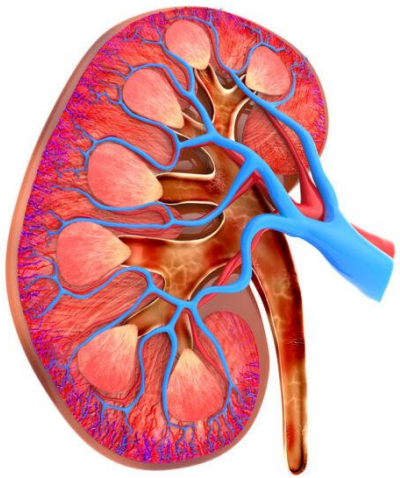
silné motivační prvky

anamnéza, farmakoterapie, pohyb, dieta, jídelníček a jeho analýza, hypoglykémie, antropometrie a analýza složení těla, technologie (CGM, pumpy, bolusový kalkulátor), flexibilní dávkování, fyzická aktivita, senzory CGM, kalkulace bolusu, automatické pumpy, trendové signály, kalibrace, specifické potřeby pacienta, individuální dietní plán

Glykemická a neglykemická prevence

- DIA: SGLT-2i, GLP-1 RA, multicretiny?
- CKD: SGLT-2i, finerenon, GLP-1 RA
- Atero: alirocumab, evolocumab, inclisiran, GLP1-RA
- MAFLD: GLP-1 RA
- OBE: liraglutid, semaglutid, tirzepatid, retatrutid





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