Brigham and Women's Hospital
Founding Member, Mass General Brigham

Diabetes Update: New guidelines, approaches and drugs

Marie E. McDonnell, MD

Director, Brigham and Women's Diabetes Program

Division of Endocrinology, Diabetes and Hypertension

Brigham and Women's Hospital

Associate Professor of Medicine

Harvard Medical School

CONTINUING MEDICAL EDUCATION
DEPARTMENT OF MEDICINE

HARVARD MEDICAL SCHOOL
TEACHING HOSPITAL

Marie E. McDonnell, MD

Boston University School of Medicine

Medicine Residency: Columbia Presbyterian, New York

Endocrinology Fellowship: Boston Medical Center

Chief, Diabetes section, Division of Endocrinology Diabetes and Hypertension at Brigham and Women's Hospital

Associate Professor of Medicine at HMS

- *Clinical focus:* Diabetes care in complex patient populations
- *Research focus:* Health outcomes research and care model design for people with diabetes

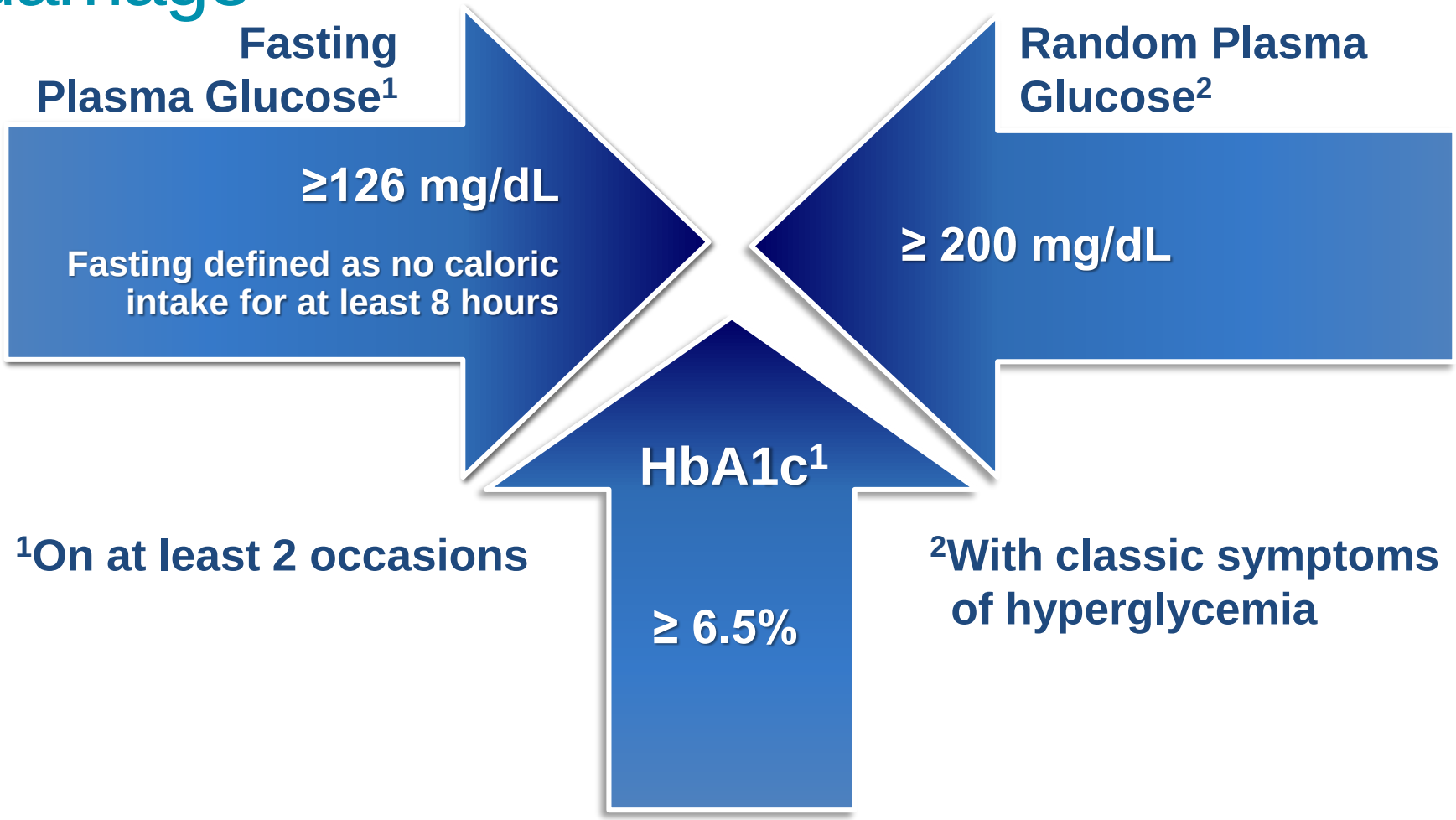
Disclosures

Research funding paid directly to institution: Dexcom, Inc

Learning Objectives

- Review basics of diagnosis and when to think beyond type 2
- Understand how to prescribe the available noninsulin pharmacologic therapies for type 2 diabetes
- Learn what is new in individualizing therapeutic strategies for type 2 diabetes based on comorbidities, goals as well as concerns and side effects

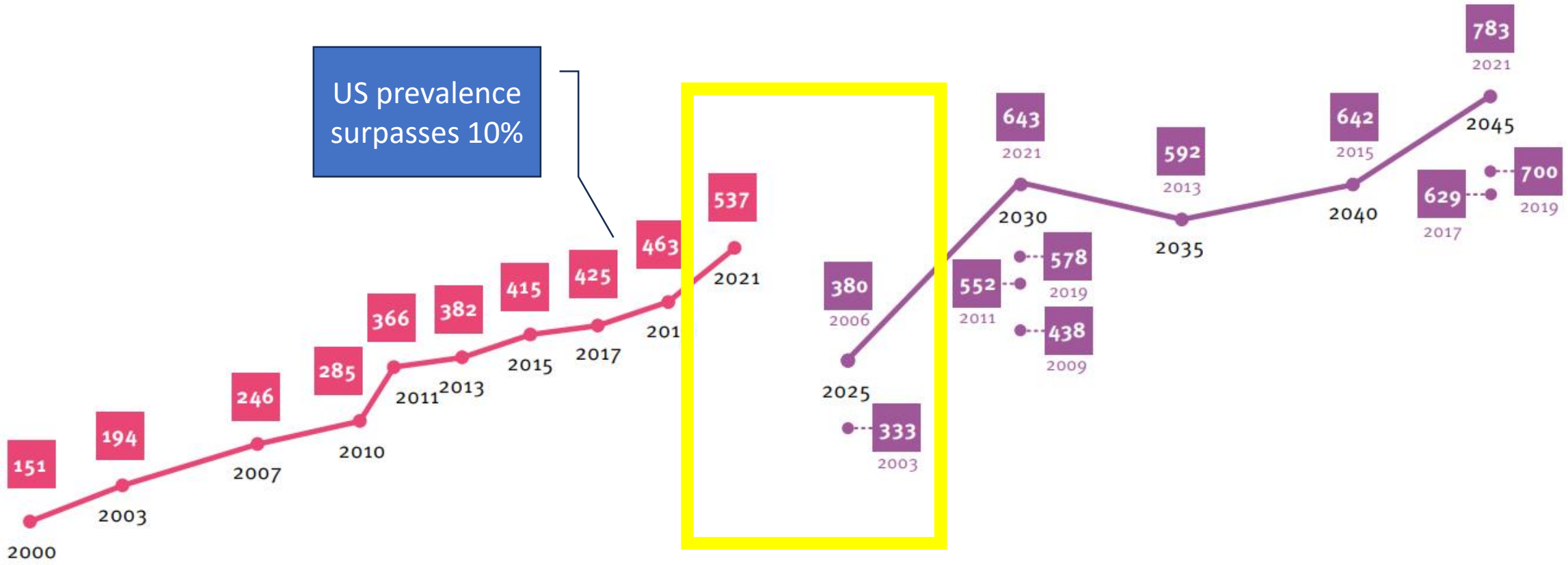
What is Diabetes?:
Persistent Hyperglycemia that over time leads to organ damage



[1]On at least 2 occasions

[2]With classic symptoms of hyperglycemia

GLOBALLY: OUTPACING PROJECTIONS



Key

151 Number of people with diabetes in millions

Key

333 Projection in millions

2003 Year projection made

YOUTH-ONSET DIABETES

Projections of type 1 and type 2 diabetes burden in the U.S. population aged <20 years through 2060: The SEARCH for Diabetes in Youth Study

Objective

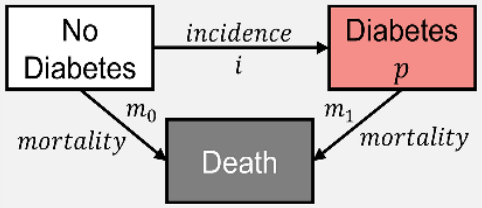
To project the prevalence and number of youth aged <20 years with diabetes through 2060

Input data

Prevalence in 2017 and incidence between 2002 and 2017 by

- Diabetes type
- Age
- Sex
- Race and ethnicity

Illness-Death Model



Two projection scenarios:

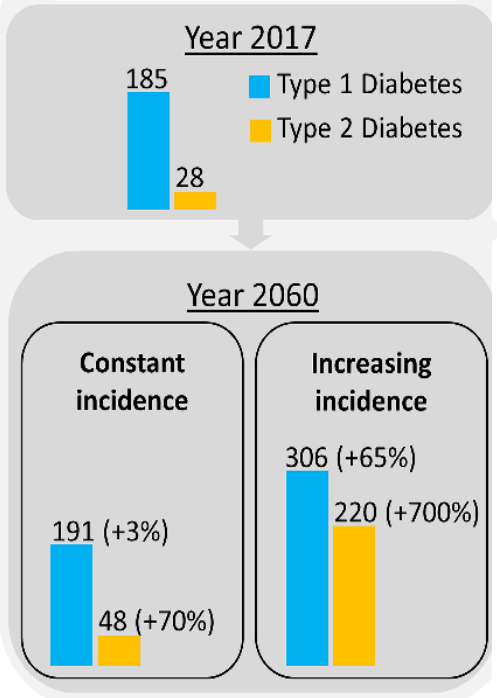
1. Constant incidence:

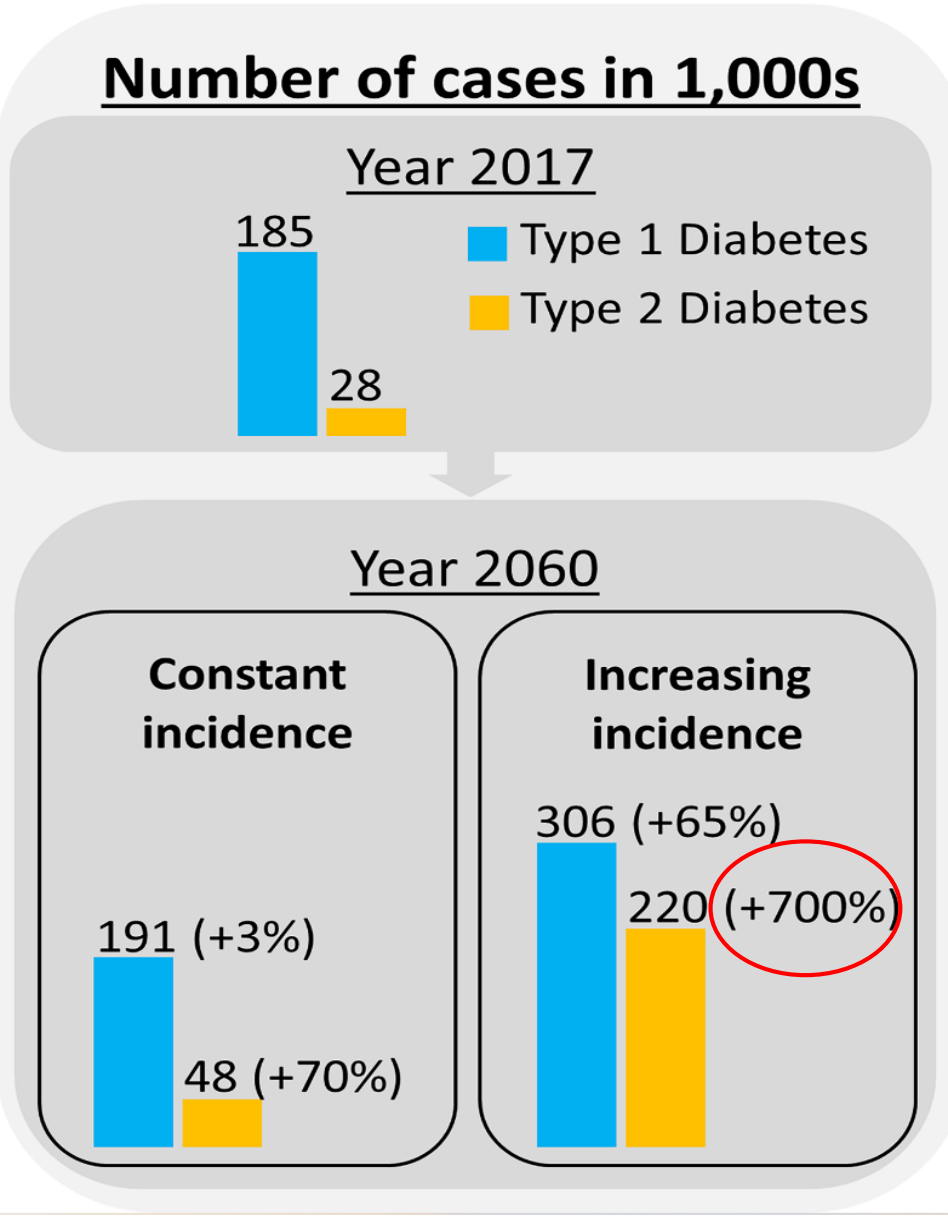
   Incidence remains constant between 2017 and 2060

2. Increasing incidence:

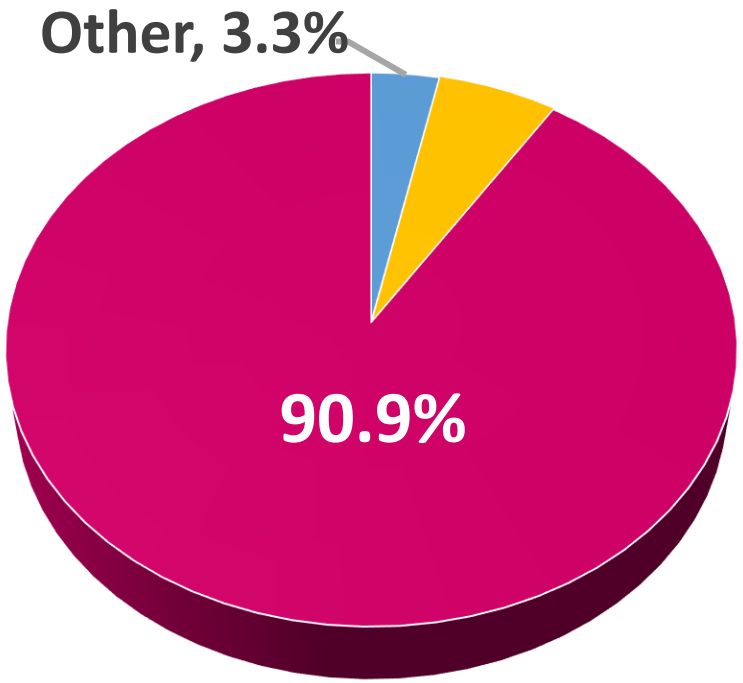
   Incidence continues to increase as observed between 2002 and 2017

Number of cases in 1,000s





Breakdown of diabetes in United States



Autoimmune diabetes 5.8%:

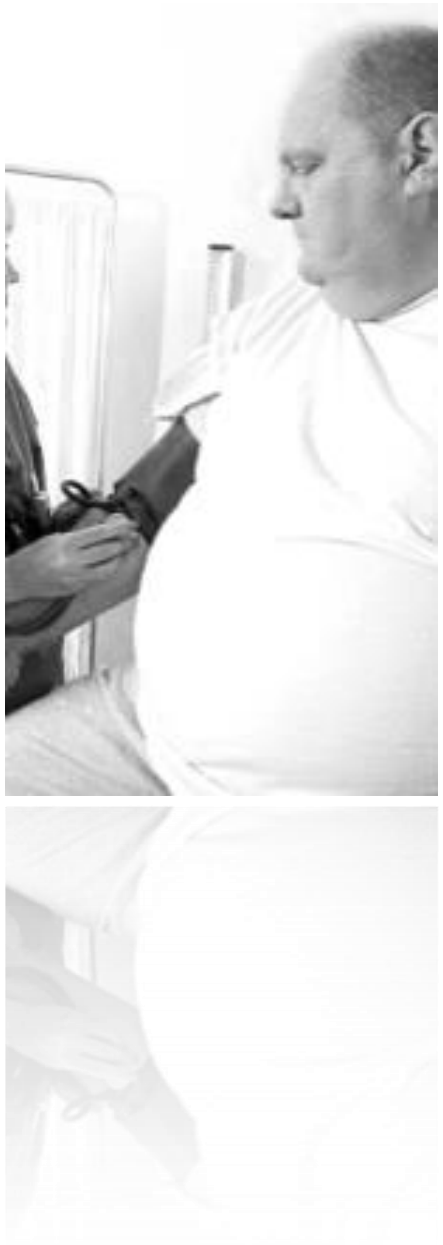
Positive GAD, IA2, insulin, or zinc ZnT8 Antibodies; Often lack features of metabolic syndrome

Type 2 diabetes: ***Older age, higher BMI, features of metabolic syndrome***

MMWR Morb Mortal Wkly Rep. 2018 Mar 30; 67(12): 359–361.

Standards of Medical Care in Diabetes, Diabetes Care, 2022

Slide : Miriam Udler



When to suspect autoimmune/type 1 diabetes?

Normal or mildly overweight

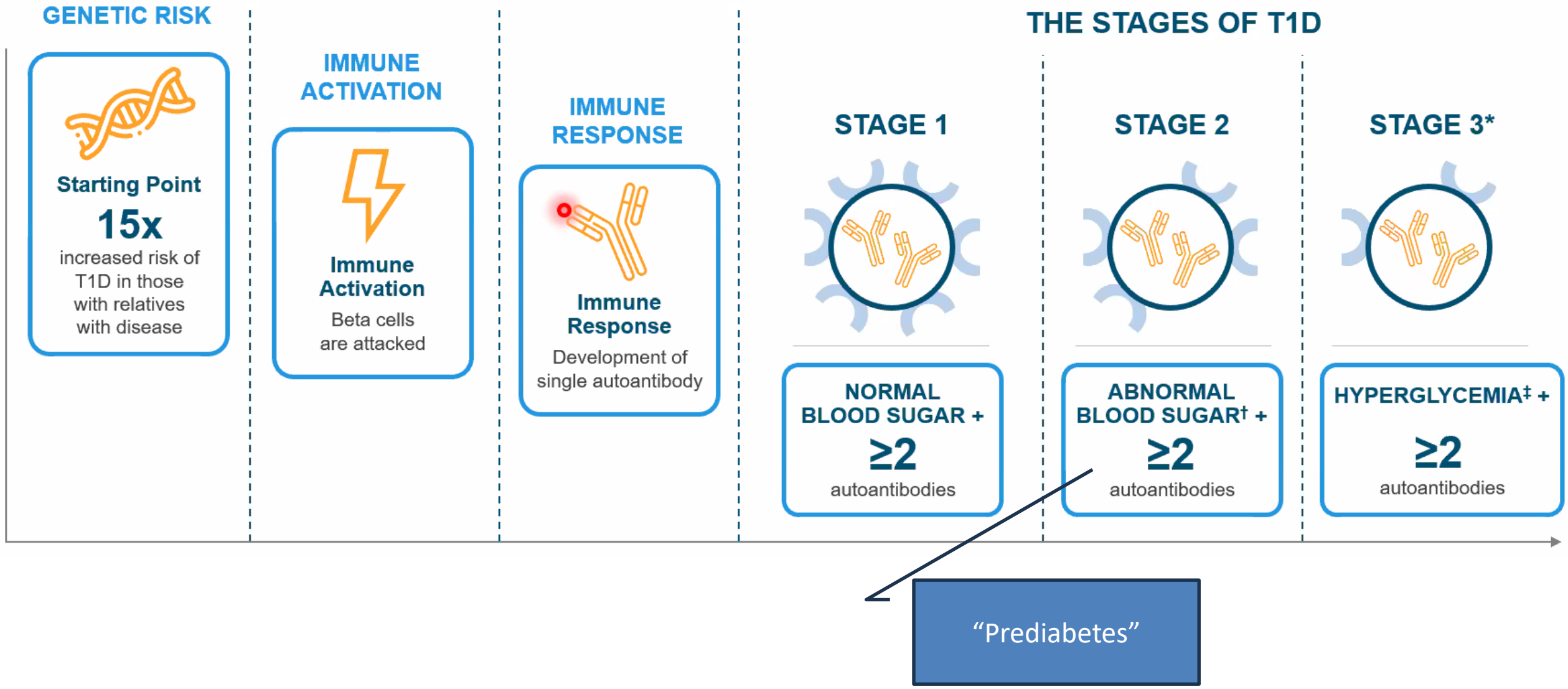
Lack of family history

Absence of other features of the metabolic syndrome (e.g. HTN, HL)

Suspect Type 1 ?

- ✓ Islet Cell Antibodies: Glutamic acid decarboxylase- 65
- ✓ Glucose and c-peptide (c-peptide *may* be lower than expected for glucose level)

New concept: Type 1 diabetes in stages



Can we prevent Type 1 DM or delay the onset?

- **Most trials of immunomodulator therapy have not shown ability to prevent new Type 1 DM in high risk groups**
- **Recently approved for delaying onset T1D: Teplizumab**
  - Anti-CD3 Antibody Teplizumab in children and adults with Stage 2 type 1 diabetes showed that it can delay the onset of type 1, with about half as many patients receiving the drug having the diagnosis after 4 years, compared with those who did not receive the drug
- **Ongoing trials: Youth new onset in honeymoon OR adult with prediabetes and 2 + antibodies**

Herold KC,et cal. An Anti-CD3 Antibody, Teplizumab, in Relatives at Risk for Type 1 Diabetes. N Engl J Med. 2019 Aug 15;381(7):603-613. doi: 10.1056/NEJMoa1902226. Epub 2019 Jun 9. Erratum in: N Engl J Med. 2020 Feb 6;382(6):586.

What is monogenic diabetes?

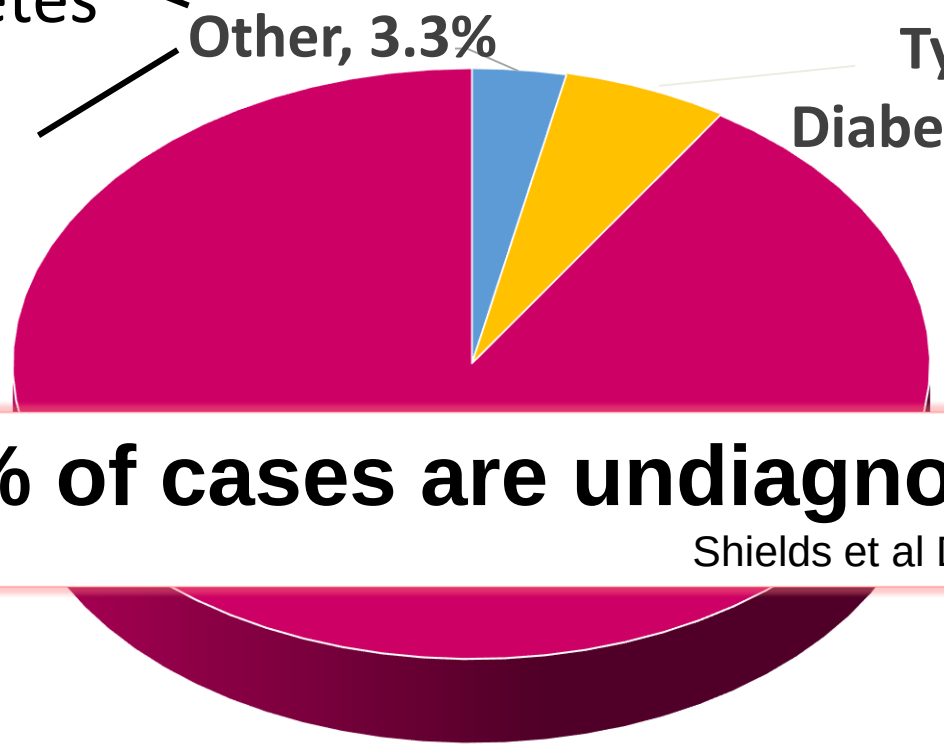
Diabetes caused by variation in <u>1 gene.</u>

Maturity Onset Diabetes of the Young (MODY) is the most common form.

~0.4% = Monogenic diabetes

- 1-3% of diabetes in young adults

~ 1/ 250 all diabetes cases



~80% of cases are undiagnosed!

Shields et al Diabetologia, 2010

Standards of Medical Care in Diabetes 2022; MMWR Morb Mortal Wkly Rep. 2018 Mar 30; 67(12): 359–361; Shields BM, et al. Diabetes Care 2017; 40: 1017-25.

When to suspect MODY?

Young Age at Onset (<35)

Parental diabetes/Runs in family

Non-obese, lack of metabolic syndrome

<u>Negative</u> Islet Cell Antibodies

Compared to Type 2

Lower BMI

Younger Age at Dx

Compared to Type 1

Older Age at Dx

Negative Antibodies

Detectable C-Peptide >3 Yrs post Dx

No history of DKA

Types of MODY and treatment implications

Most common forms of MODY:

- ~30-50% *GCK*
- ~40-60% *HNF1A* or *HNF4A*
- ~10% other genes

Patients typically **do not need diabetes medications.**

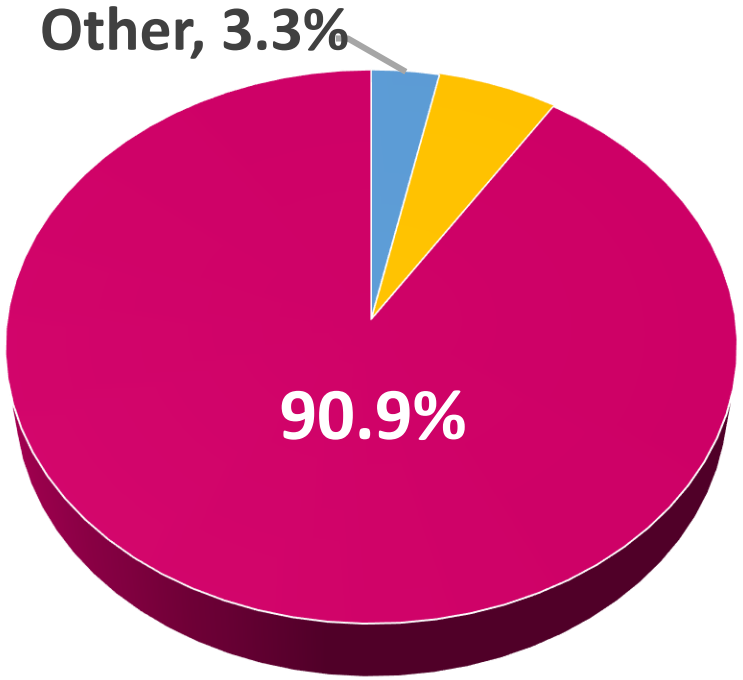
Patients can often be **transitioned from insulin injections to non-insulin agents.**

Most patients treated with insulin. **Gene can inform other related phenotypes** (e.g. *HNF1B* with renal cysts, elevated LFTs).

Slide : Miriam Udler

Pearson *et al*., Lancet 2003; Shields *et al*. Diabetologia 2010; Murphy *et a*l. Nat Clin Practice, End & Metabolism, 2008; Fajans *et al*, NEJM 2001.

Breakdown of diabetes in United States



Autoimmune diabetes 5.8%:

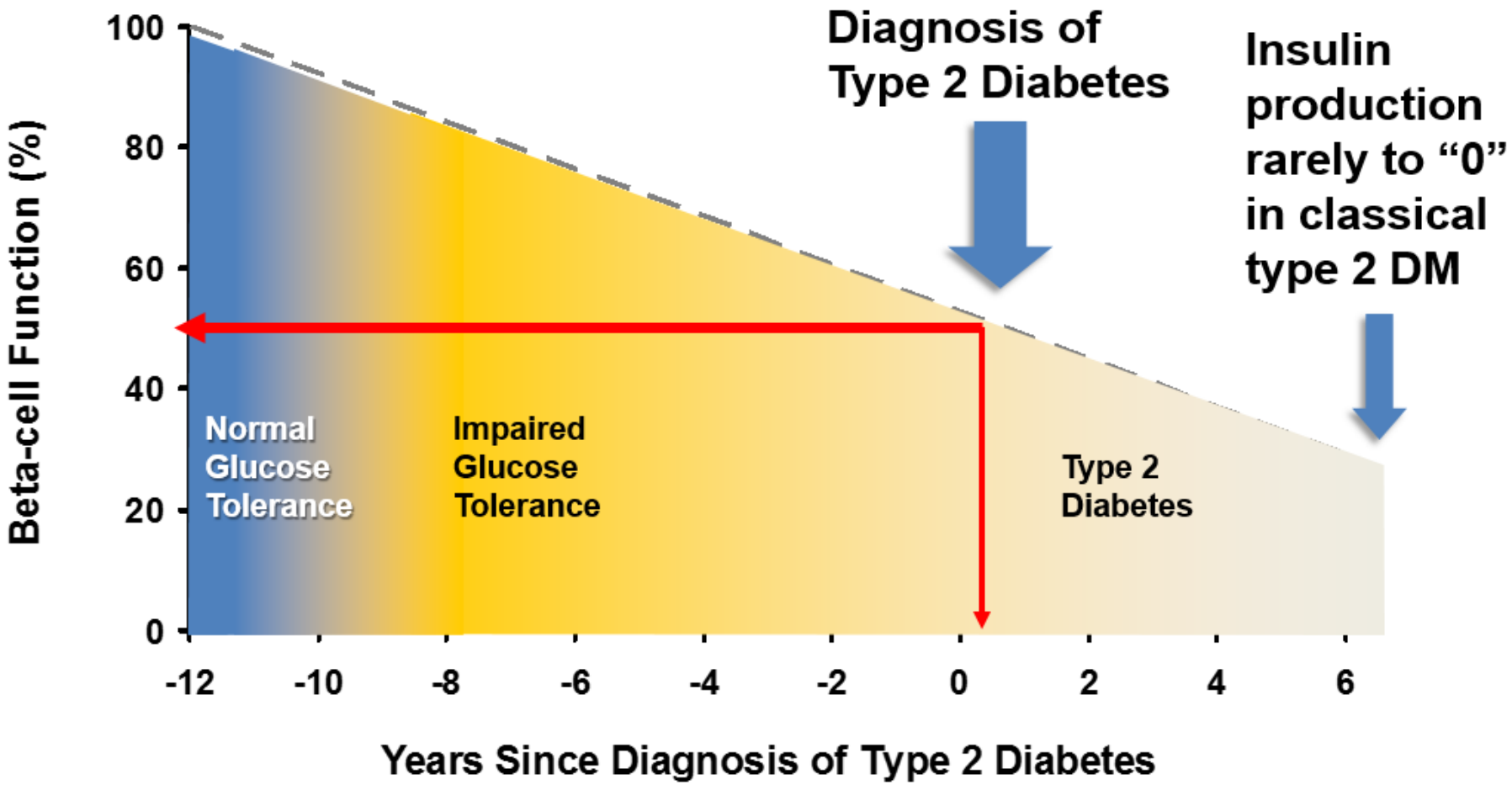
Positive GAD, IA2, insulin, or zinc ZnT8 Antibodies; Often lack features of metabolic syndrome

Type 2 diabetes: ***Older age, higher BMI, features of metabolic syndrome***

MMWR Morb Mortal Wkly Rep. 2018 Mar 30; 67(12): 359–361.

Standards of Medical Care in Diabetes, Diabetes Care, 2022

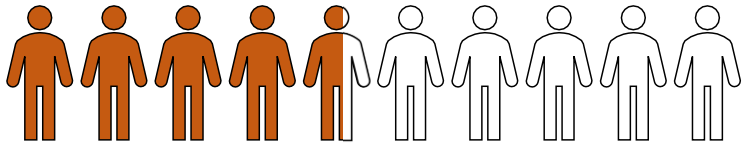
T2D is a **challenging disease** because it is progressive and requires changes to therapeutic strategy over time



Adapted from UKPDS16. Diabetes. 1995:44:1249-1258.

Doc, do I need to take medications? Diabetes remissions in the DiRECT study

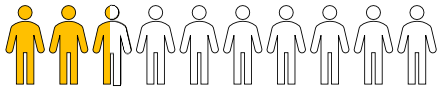
At 1 year[1]



46% achieved diabetes remission within 6 years of diagnosis

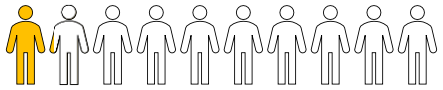
Weight loss of **10–15 kg**: 57% achieved diabetes remissions
Weight loss of **≥15 kg**: 86% achieved diabetes remissions

At 2 years[2]



24%

Maintained **≥10 kg** weight loss



11%

Maintained **≥15 kg** weight loss

At 2 years[2]

64%

Achieved diabetes remission

70%

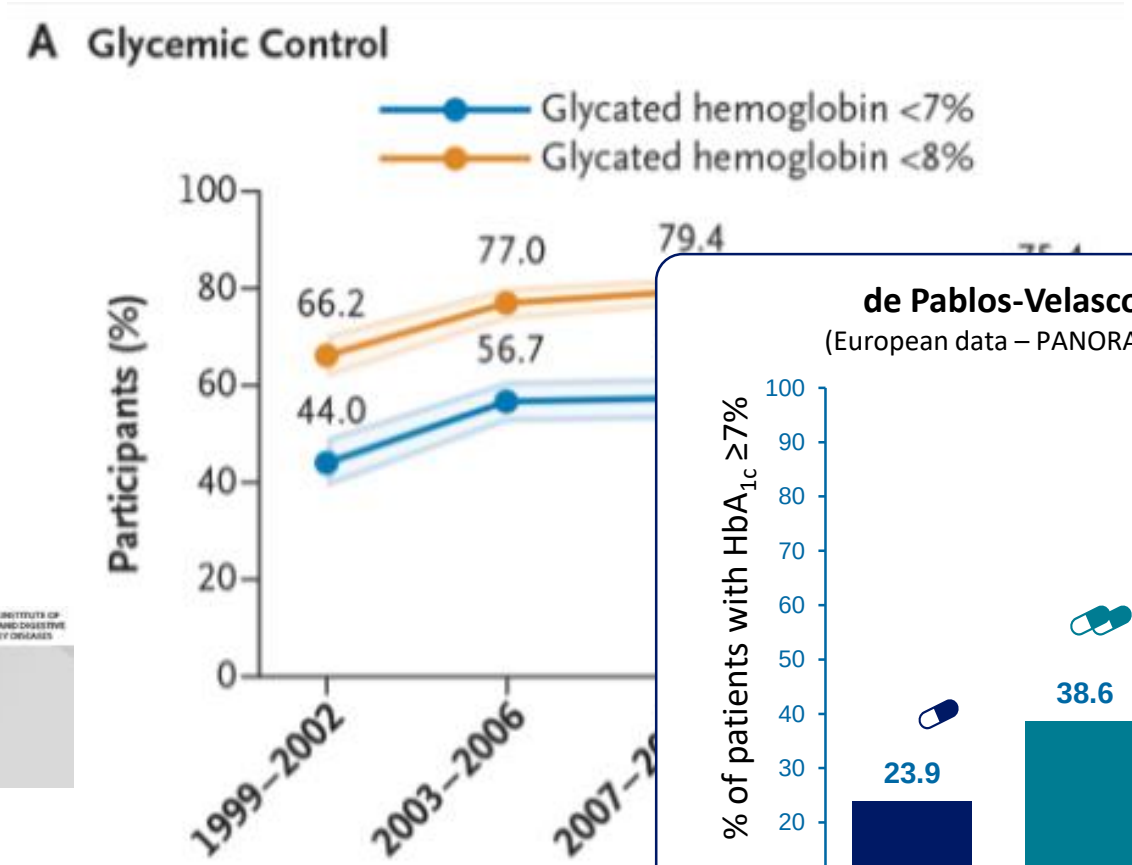
Achieved diabetes remission

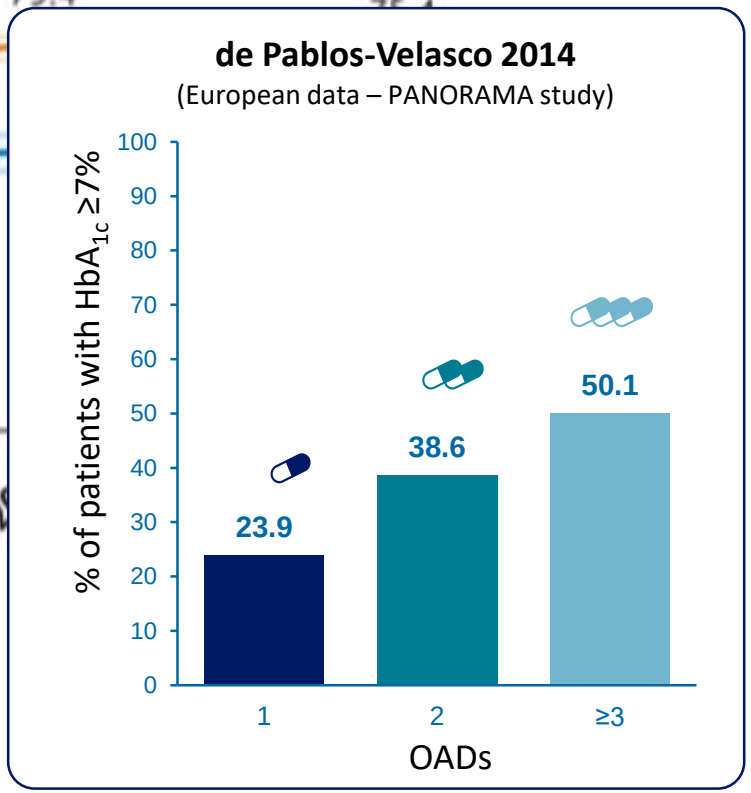
1. Lean ME *et al. Lancet.* 2018;391:541–51; 2. Lean ME *et al. Lancet Diabetes Endocrinol.* 2019;7:344–355; 3. Al-Mrabeh A, et al; Lancet Diabetes Endocrinol 2020; 8:939-48

Glycemic control remains elusive for many

- "After more than a decade of progress from 1999 to the early 2010s, glycemic and blood-pressure control declined in adult NHANES participants with diabetes"

70% of subjects had an A1c >7% by study end





Fang M, et al. *N Engl J Med*. 2021 Jun 10;384(23):2219-2228.

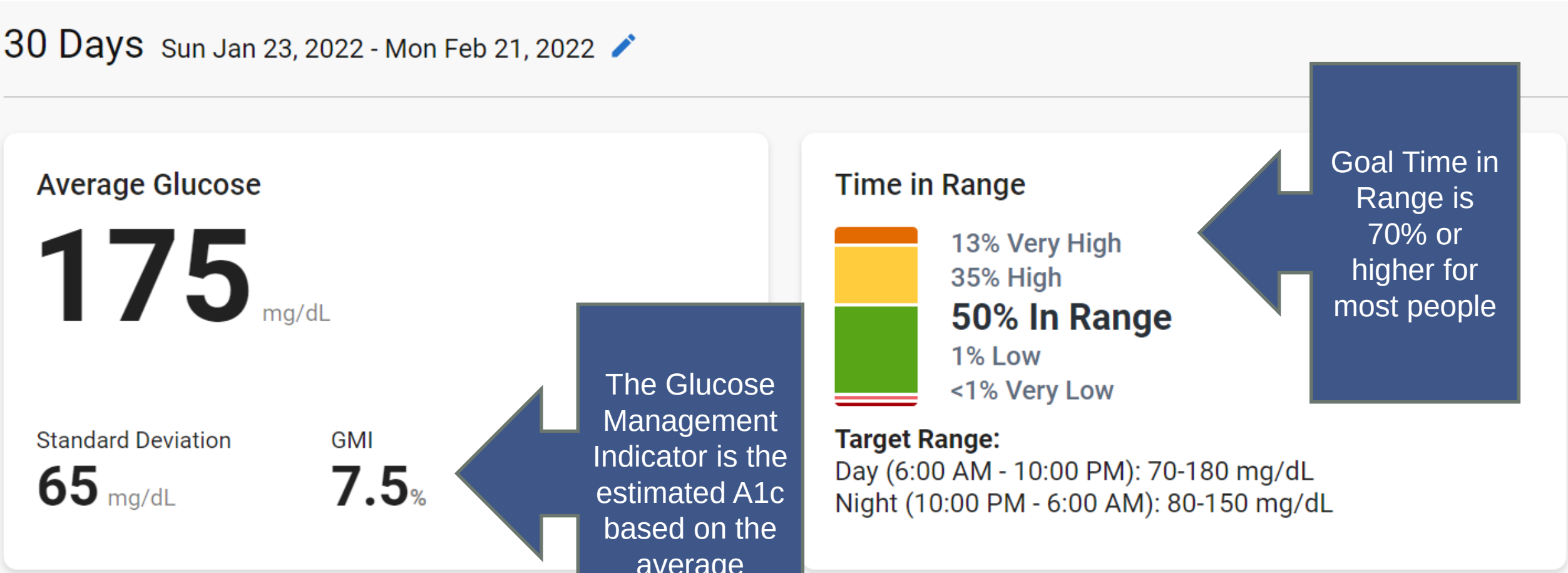
Let’s start with Targets: *How do we define “glycemic control”?*

Expert recommendations: ?Consensus

Organization	HbA1c goal
American Association of Clinical Endocrinologists (AACE) – American College of Endocrinology (ACE)	**≤6.5%**
American Diabetes Association (ADA) – European Association for the Study of Diabetes (EASD)	**≤7%**
ADA Standards of Care	**≤7%**
American College of Physicians (ACP) -- endorsed by American Academy of Family Physicians (AAFP)*	**7-8%**
American Geriatric Society (AGS)*	**7.5-8%**

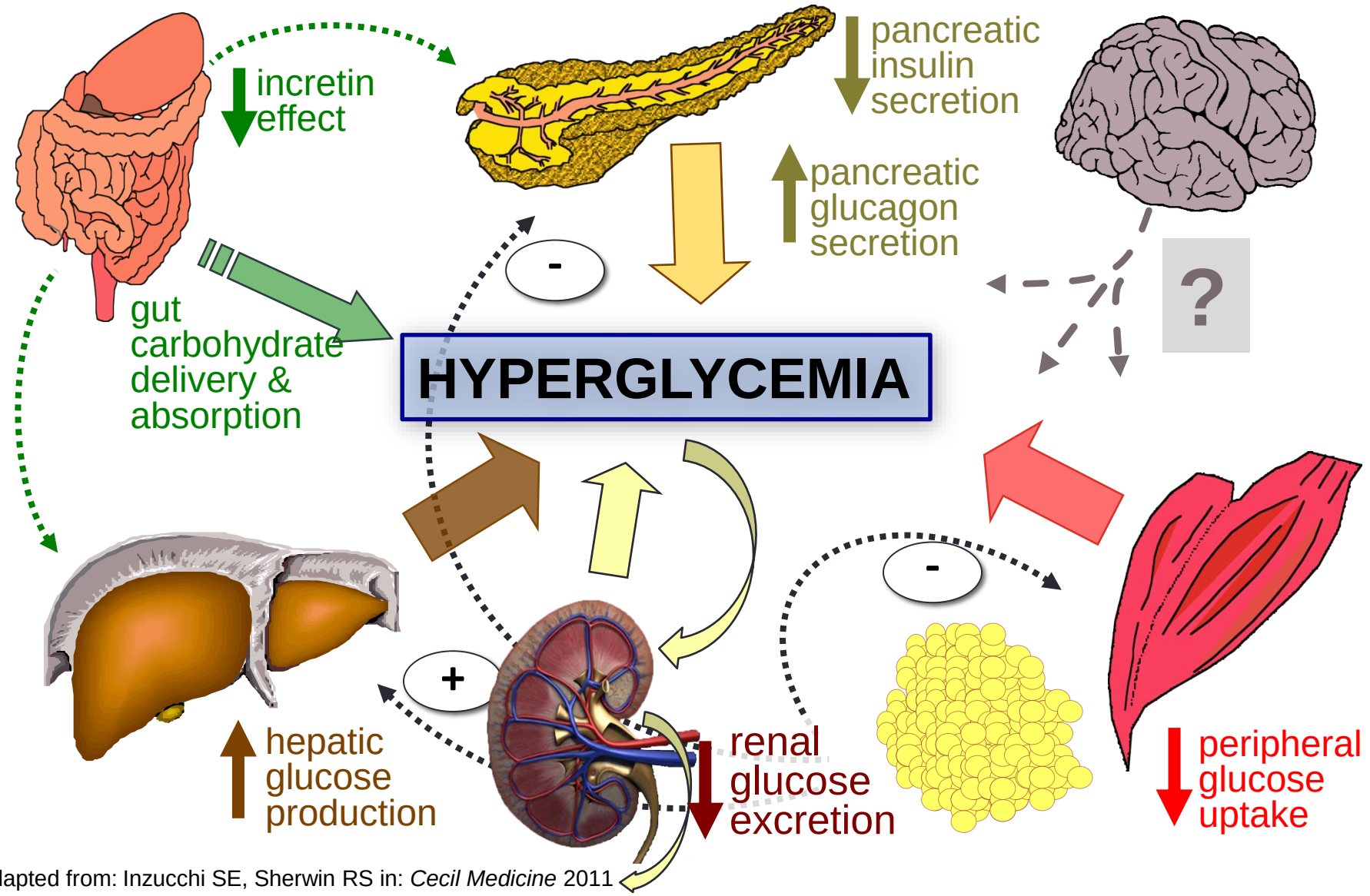
* Both statements have caveats allowing for more aggressive HbA1c goals based on patient preference and overall health.

“Glycemic status” = HA1c or the GMI on CGM…*huh?*



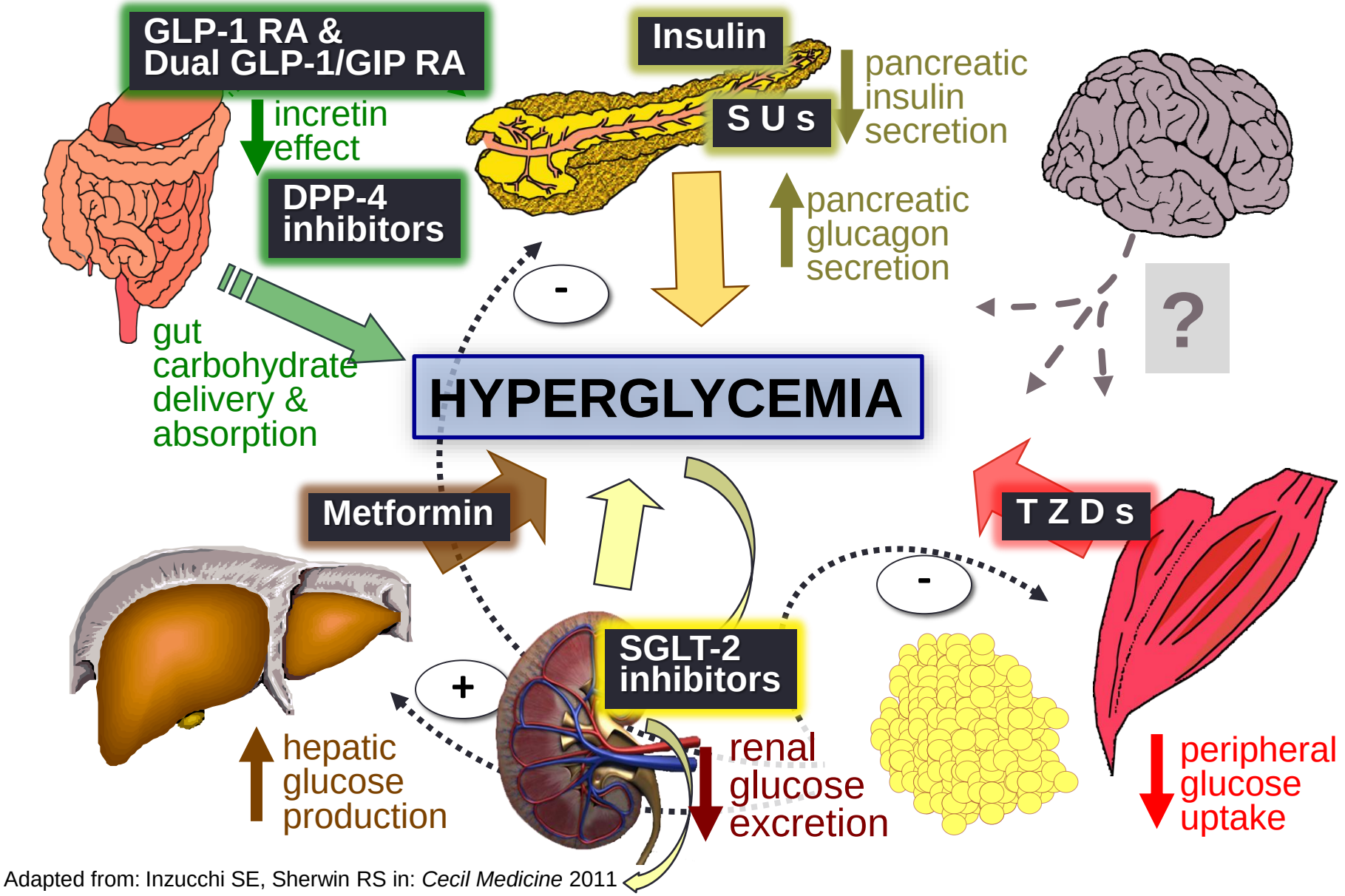
What are the options for medication management in Type 2 Diabetes: *An Overview*

Multiple Complex Pathophysiological Abnormalities in T2DM

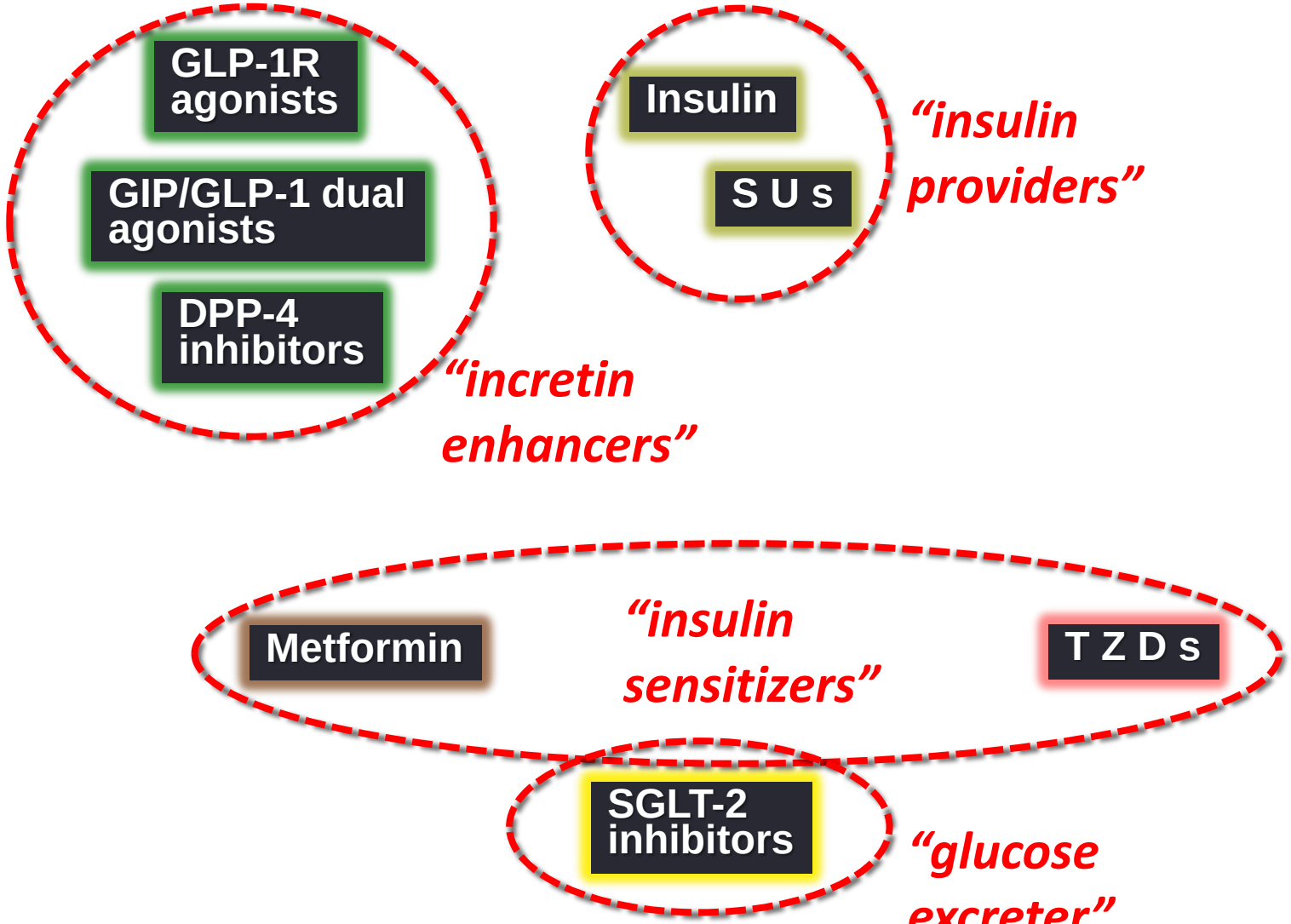


Adapted from: Inzucchi SE, Sherwin RS in: *Cecil Medicine* 2011

Major Pathophysiologically-Based Therapies for T2DM



Adapted from: Inzucchi SE, Sherwin RS in: *Cecil Medicine* 2011


GLP-1R agonists
GIP/GLP-1 dual agonists
DPP-4 inhibitors
"incretin enhancers"
Insulin
S U s
"insulin providers"
Metformin
"insulin sensitizers"
T Z D s
SGLT-2 inhibitors
"glucose excreter"

GLP-1R and dual GLP1/GIP agonists

Insulin

S U s

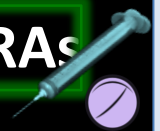
DPP-4 inhibitors

Metformin

T Z D s

SGLT-2 inhibitors

Glucose Lowering Drugs Classes

Classes	Generic Names	↓ A1c	Side effects
Insulin 	Degludec, Glargine, Detemir, NPH, Regular, Lispro, Aspart, Glulisine	1+ %	Hypoglycemia, weight gain, Injections
SU's 	Glyburide, Glipizide, Glimepiride	1-1.5%	Hypoglycemia, weight gain
Metformin 	Metformin	1-1.5%	GI, B-12 deficiency, lactic acidosis,
TZD's 	Rosiglitazone, Pioglitazone	1-1.5%	CHF, Weight gain, edema, bone fx's, ?bladder ca
DPP-4 i's 	Sitagliptin, Saxagliptin, Alogliptin, Linagliptin (GLIPTINS)	**0.5-1%**	Urticaria, arthralgias (rare) pancreatitis
Incretin RAs 	GLP-1: Exenatide, Lira-, Dula-,Sema- GLP-1/GIP dRA: Tirzepatide	1-1.5%	GI, gallbladder, ?pancreatitis, injections
SGLT2-i's 	Canagliflozin, Dapagliflozin, Empagliflozin, Bexaflozin (FLOZINS)	**0.5-1%**	GU infections, Polyuria, GU infections, DKA, ?fractures

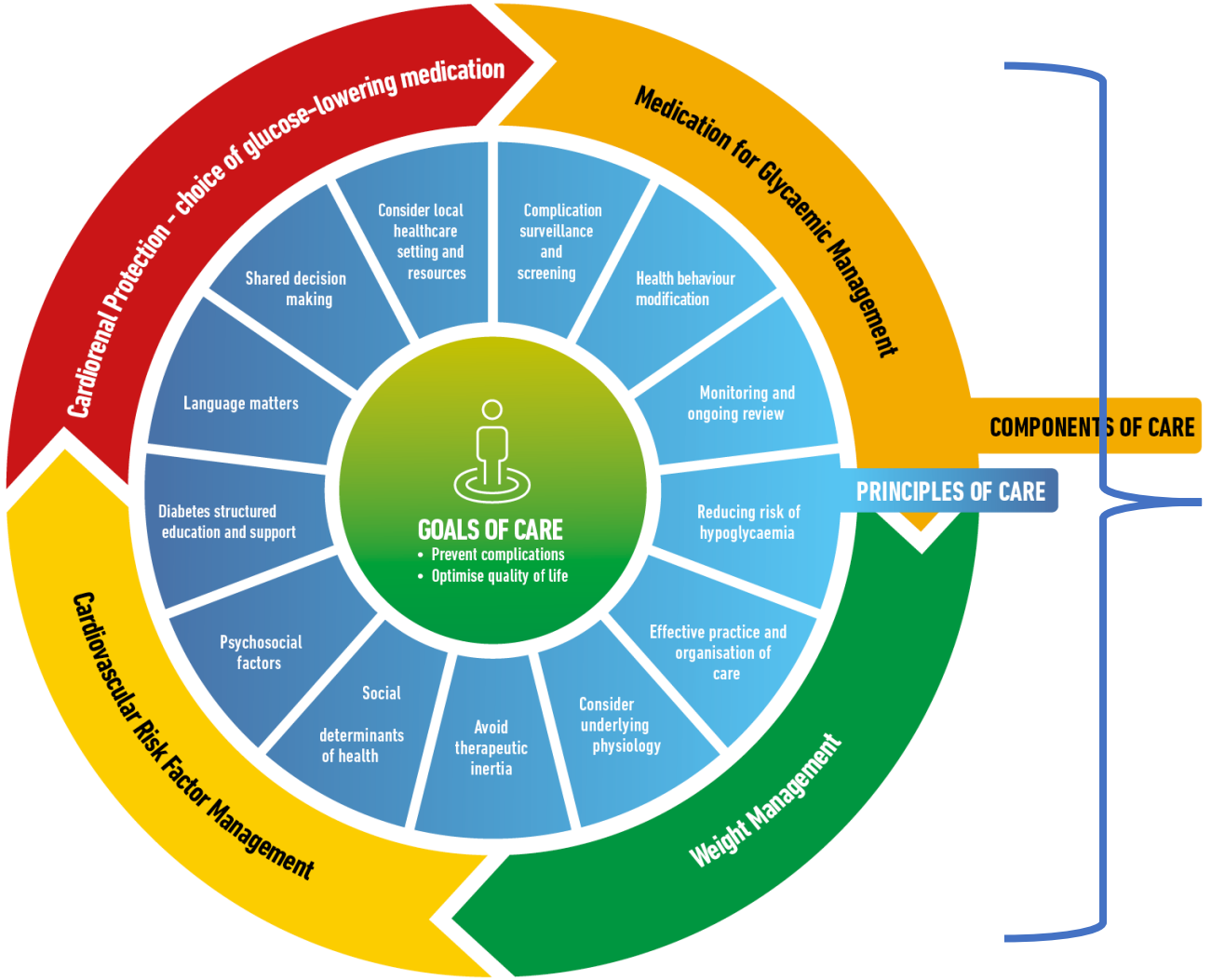
What is the new approach to medication selection and management in diabetes?

As a result of >10 RCTs and >50,000 patients studied… Step-wise therapy is out the window

ADA: Pharmacologic therapy should be guided by person-centered treatment factors, including comorbidities and treatment goals. Pharmacologic approaches that provide the efficacy to achieve treatment goals should be considered, such as metformin or other agents, including combination therapy, that provide adequate efficacy to achieve and maintain treatment goals.

Guidelines: It's Not just about the sugar

"I want to help to protect your organs from diabetes related problems"



"I want to help you to control your blood sugar and your weight"

1 = 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.

ACEi, Angiotensin-Converting Enzyme Inhibitor; ARB, Angiotensin Receptor Blockers; ASCVD, Atherosclerotic Cardiovascular Disease; BP, Blood Pressure; CKD, Chronic Kidney Disease; CV, Cardiovascular; eGFR, Estimated Glomerular Filtration Rate; GLP-1 RA, Glucagon-Like Peptide-1 Receptor Agonist; HF, Heart Failure; SGLT2i, Sodium-Glucose Cotransporter-2 Inhibitor; T2D, Type 2 Diabetes.

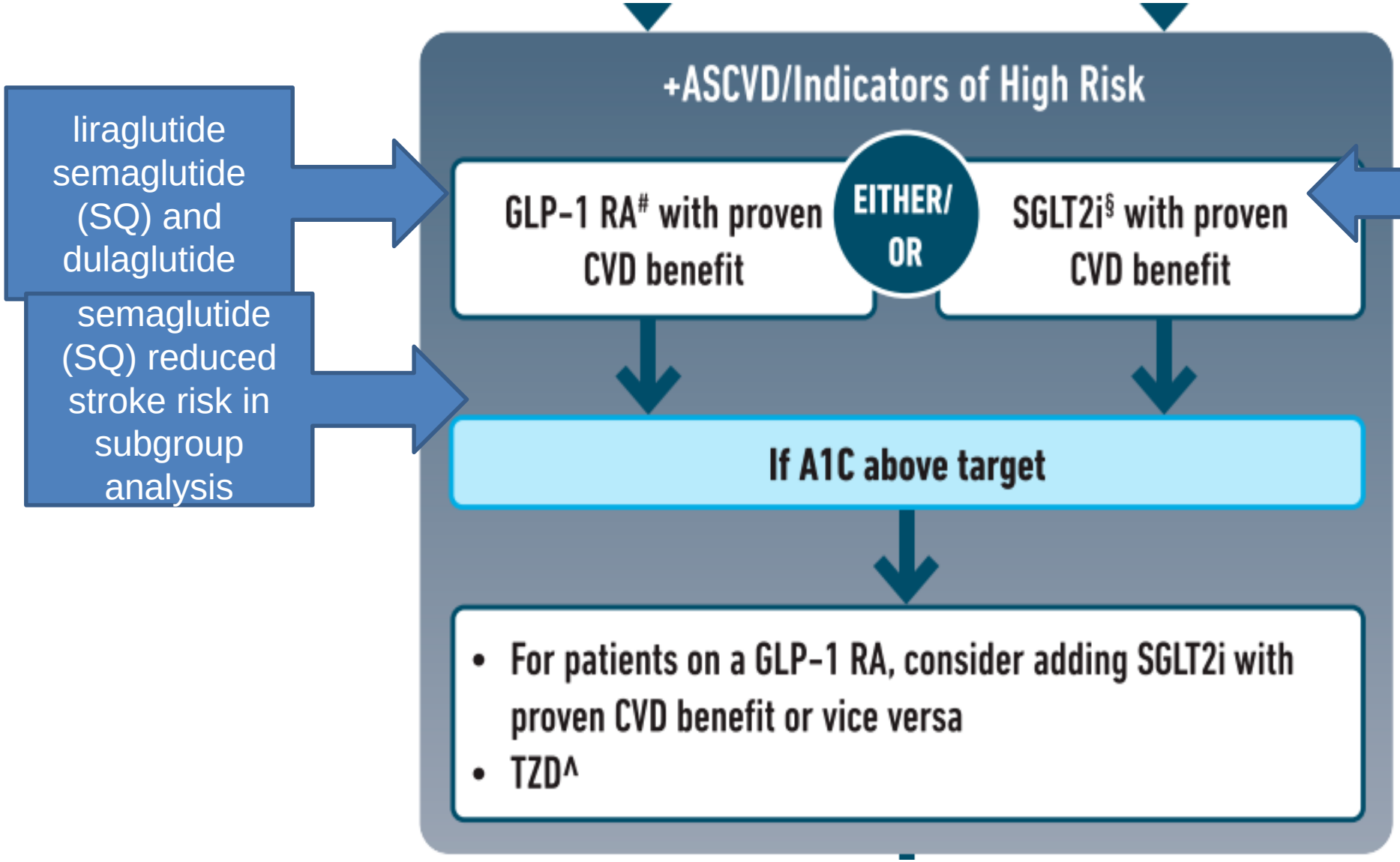
Davies MJ, Aroda VR, Collins BS, Gabbay RA, Green J, Maruthur NM, Rosas SE, Del Prato S, Mathieu C, Mingrone G, Rossing P, Tankova T, Tsapas A, Buse JB

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

American Diabetes Association.

EASD European Association for the Study of Diabetes

Atherosclerotic Cardiovascular Disease (ASCVD) *



ASCVD or High Risk*

- ***STROKE***

**end-organ damage* *including retinopathy or LVH*

Or

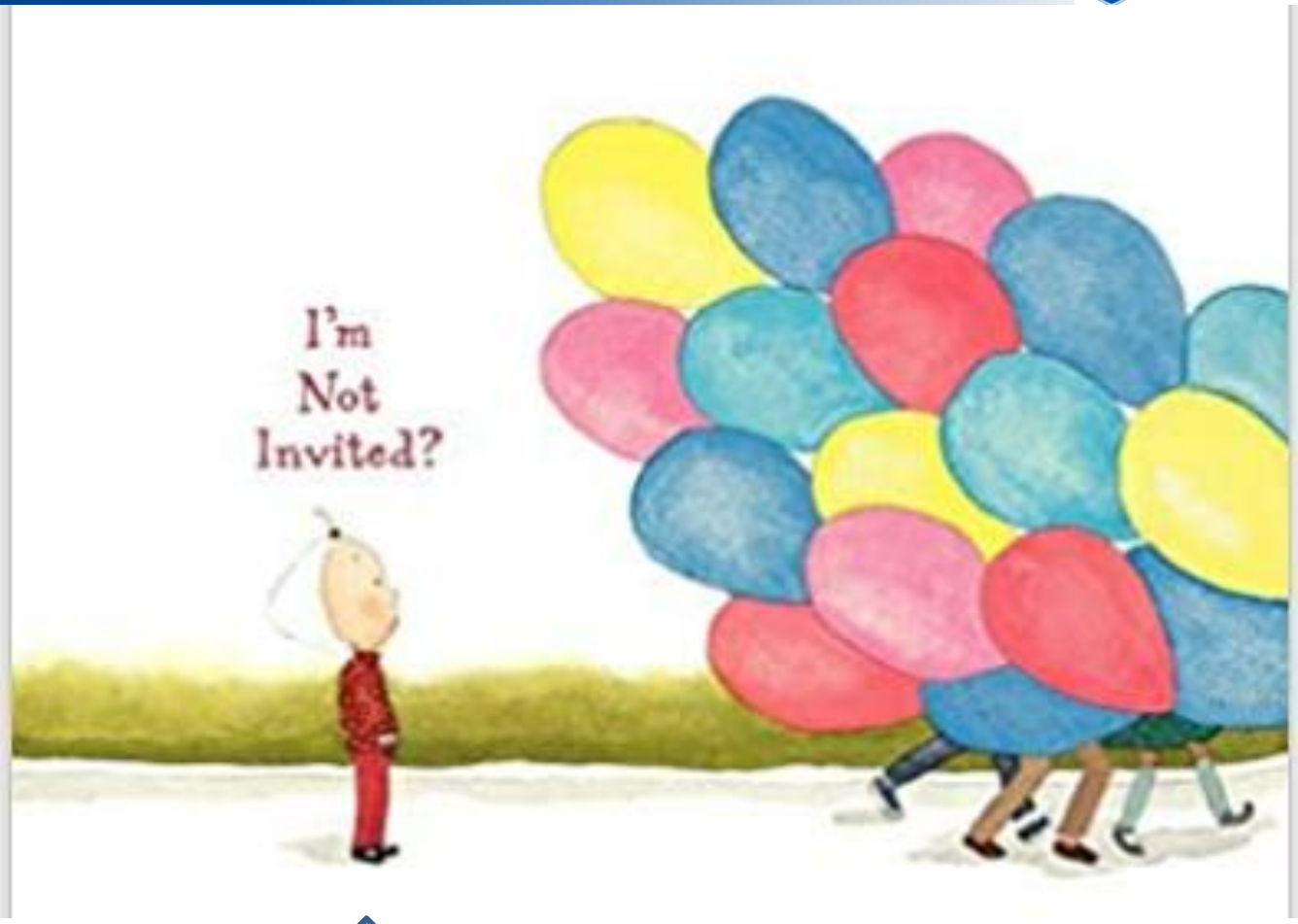
<u>Multiple</u> CV risk factors (age, HTN, smoking, dyslipidemia, obesity

GLP-1 receptor agonists and Analogs

	Initial dose	Final dose	Δ HbA1c	Δ Weight
Exenatide	5 mcg bid	10 mcg bid	-0.5 to -1.5	~ -2.8 kg
Liraglutide	0.6 mg qd	1.2-1.8 mg qd	-1.5	~ -3.24 kg
Exenatide LAR		2 mg qweek	-1.6	~ -2.3 kg
Dulaglutide	0.75mg/w	4.5 mg/w	-1.5	~ -2.5 kg
Semaglutide Inj	0.25mg/w	2.0 mg/w or 2.4mg/w in weight loss packaging	-1.8	~ -5 kg
Semaglutide oral	3mg daily tab	14mg daily tab	-1.2 to -1.4	~ -1.8-4kg

- Complements oral and insulin therapy in T2D
- Injectable via pen (daily, BID or weekly) or now oral Rybelsus (semaglutide)
- Does not cause hypoglycemia

Two GLP-1s have not been shown to reduce major adverse cardiac events nor slow the progression of CKD and are less commonly prescribed



Exenatide & Lixisenatide

What about oral semaglutide?

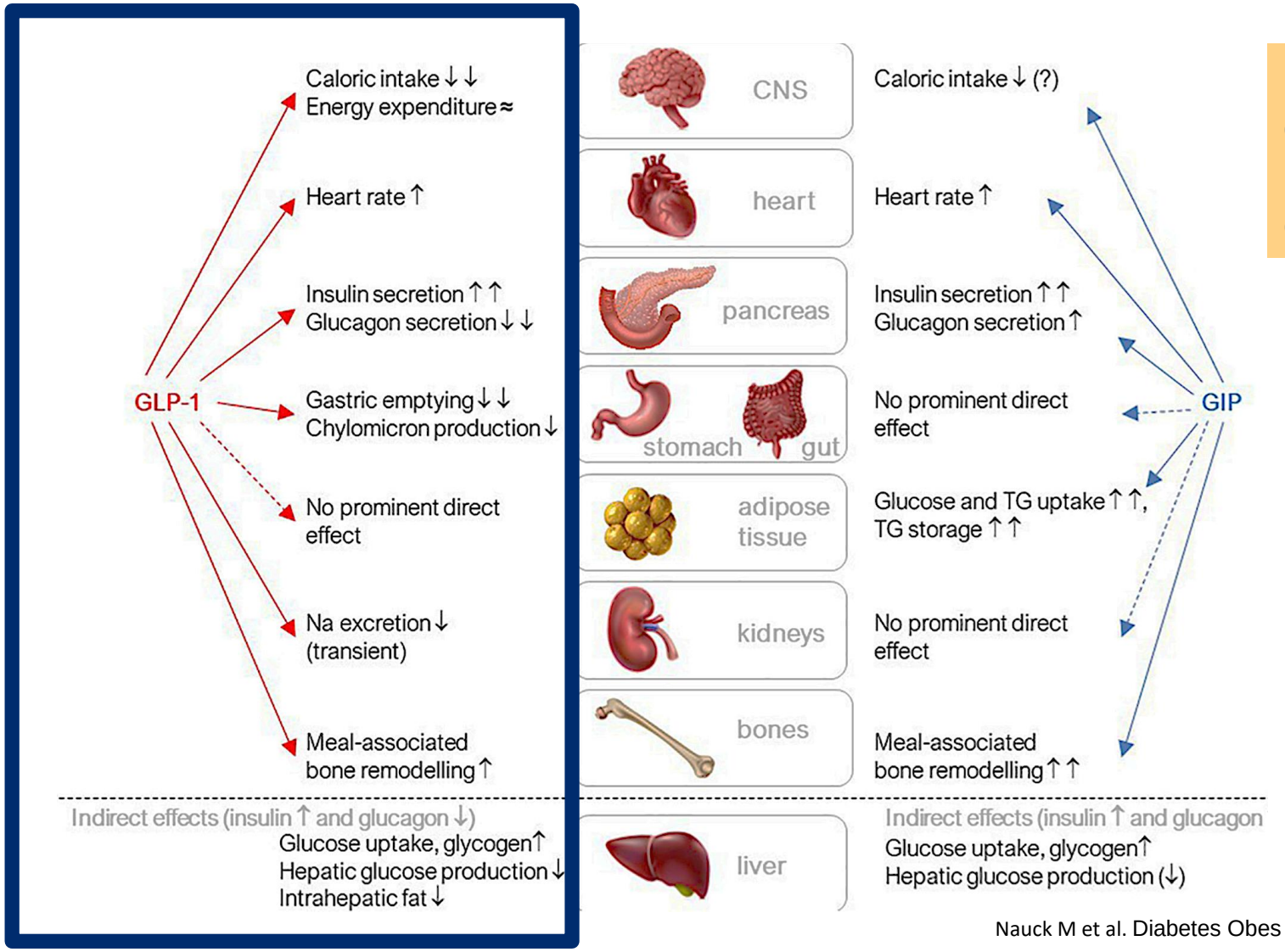
Oral Semaglutide: *on the B list for weight loss and CV risk mod*

The PIONEER Cardiovascular outcome trial showed CV safety but not benefit

No established renal benefit

Metanalysis/Comparative effectiveness study **did show** oral semaglutide to lower risk of mortality and CV death in those who were at high risk of ASCVD

Tirzepatide (Dual GLP-1 RA/GIP RA) Regulates Glucose Primarily through the GLP-1R;



Brain impact on caloric intake is likely more potent with the dual agonist

Nauck M et al. Diabetes Obes Metab. 2021;23(Suppl. 3):5–29.

Tirzepatide: Other benefits reported from SURPASS -2 study

Effects on Cardiovascular Risk Factors[1]

	Tirzepatide 5 mg	Tirzepatide 10 mg	Tirzepatide 15 mg	Semaglutide 1 mg
A1c (% change)	-2.01	-2.24	-2.3	-1.86
Weight (kg)	-7.6	-9.3	-11.2	-5.7
LDL (% change)	-7.7	-5.8	-5.2	-6.1
HDL (% change)	+6.8	+7.9	+7.1	+4.4
TG (% change)	-19.0	-24.1	-24.8	-11.5
BP (mm Hg)	-4.8/-1.9	-5.3/-2.5	-6.5/-2.9	-3.6/-1.0
Pulse (bpm)	+ 2.3	+2.2	+2.5	+2.6

- Decrease liver fat content by MRI[2]
- Decrease albuminuria[3]
- Slower decline in eGFR over time[3]

1. Frias JP et al, N Eng J Med,,2021, 2. Ludvik B, et al. *Lancet*. 2021;398:583-598, 3. Tuttle, K, presented at the 83rd Sci Sessions ADA

NAFLD is now *MAFLD* : Metabolic-dysfunction Associated Steatohepatitis

Rx:
-Weight loss
-GLP-1 – Semaglutide
-Pioglitazone (more advanced stages)
-Metabolic Surgery

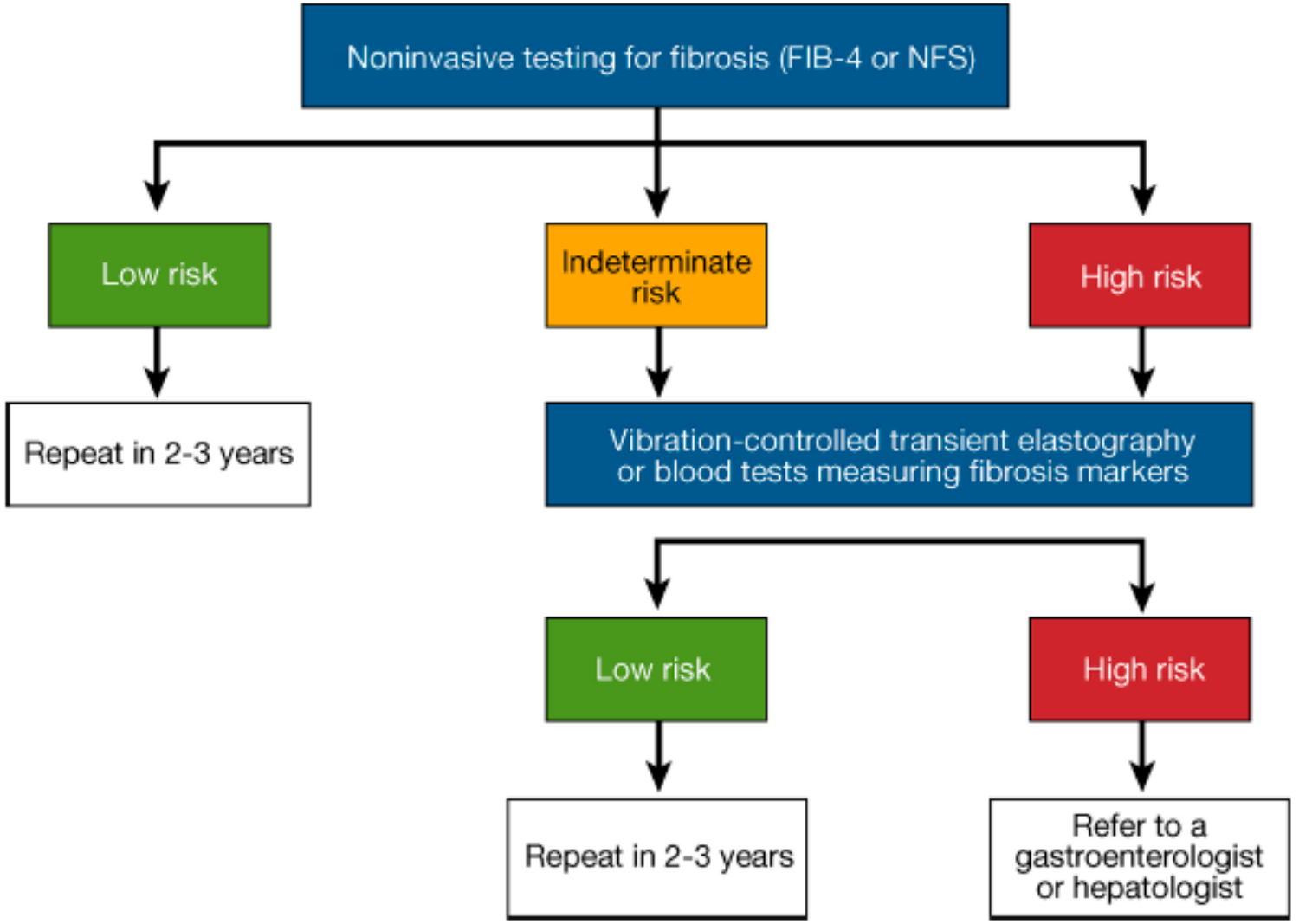
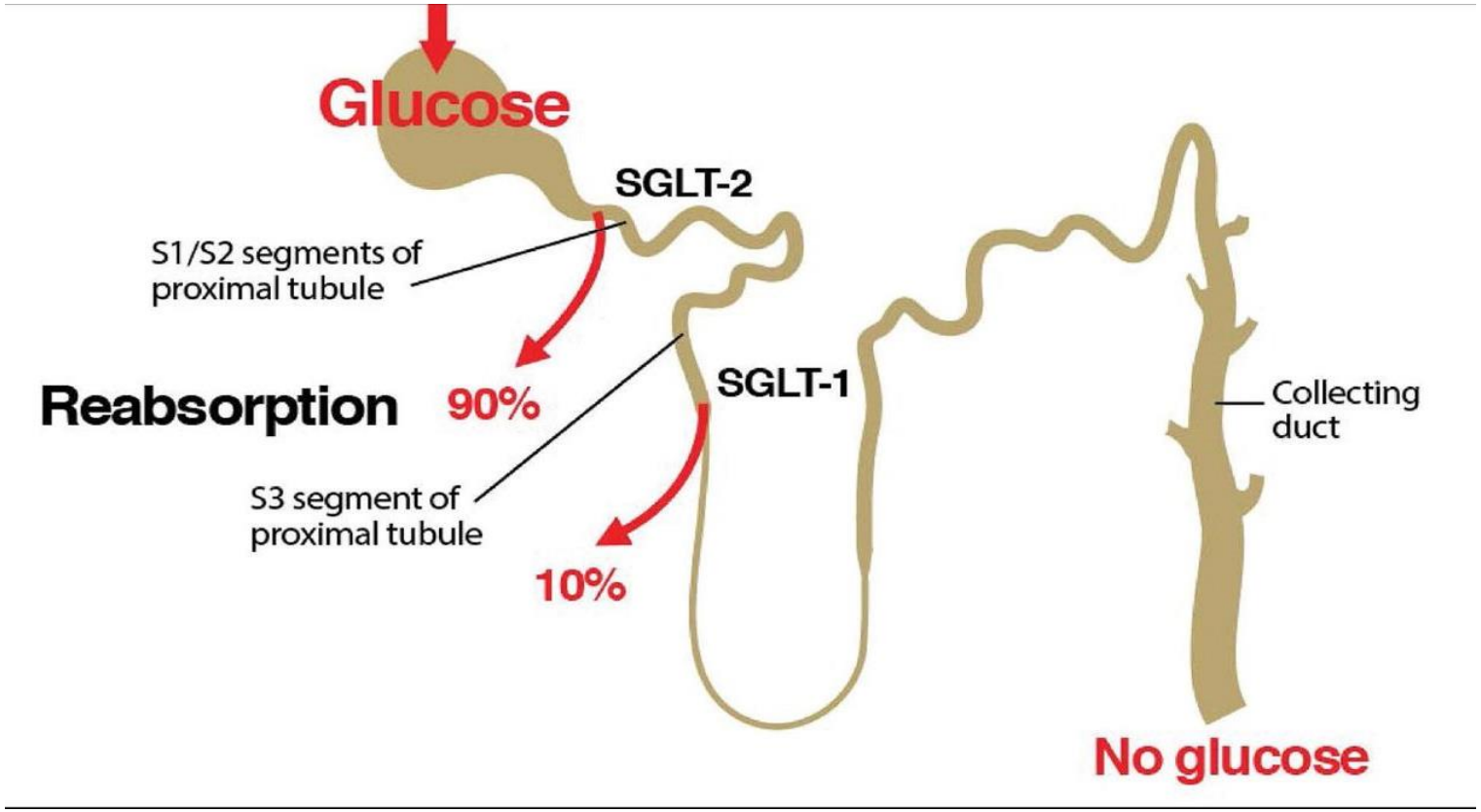


Figure 4.2—A proposed algorithm for risk stratification in individuals with nonalcoholic fatty liver disease (NAFLD) or nonalcoholic steatohepatitis (NASH). NFS, NAFLD fibrosis score created by a group of experts that included American Diabetes Association representatives. Reprinted from Kanwal et al. (64).

The Sodium Glucose Co-Transporters



SGLT-2 inhibitors

	Initial dose	Max dose	Δ HbA1c	Δ Weight
canagliflozin	100mg qd	300mg qd	-0.5 to -1.0	-1.5-2.5kg
empagliflozin	10mg	25mg		
dapagliflozin	5mg	10mg		
ertugliflozin	5mg	15mg		
bexagliflozin	20mg	20mg		

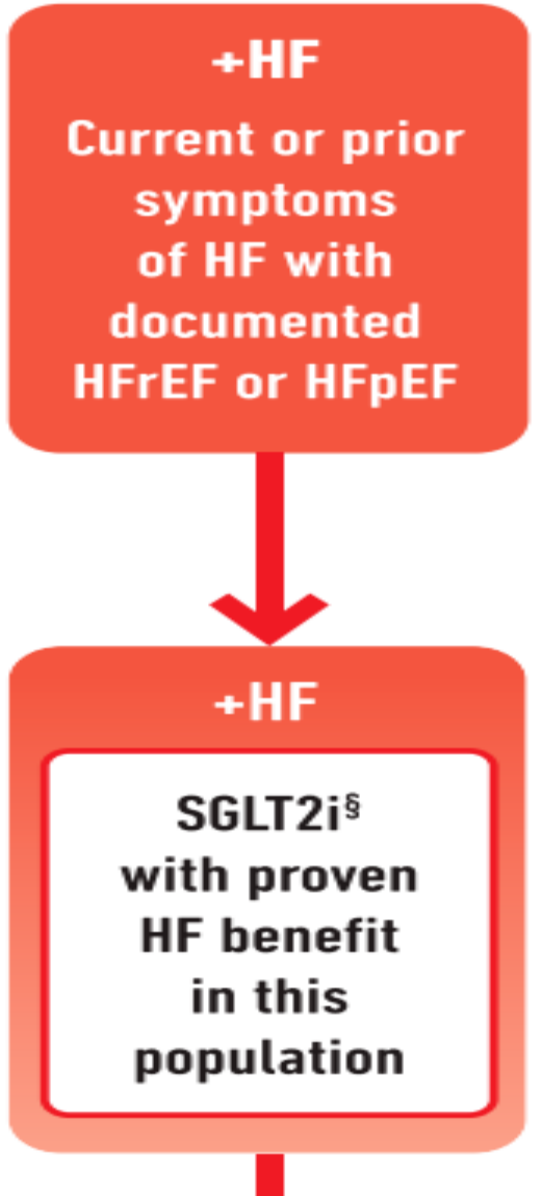
- Daily tablets
- Complements oral and insulin therapy in T2D
- Does not *independently* cause hypoglycemia

Heart Failure

- **SGLT2i now clearly indicated for <u>both</u> HFpEF and HFrEF**

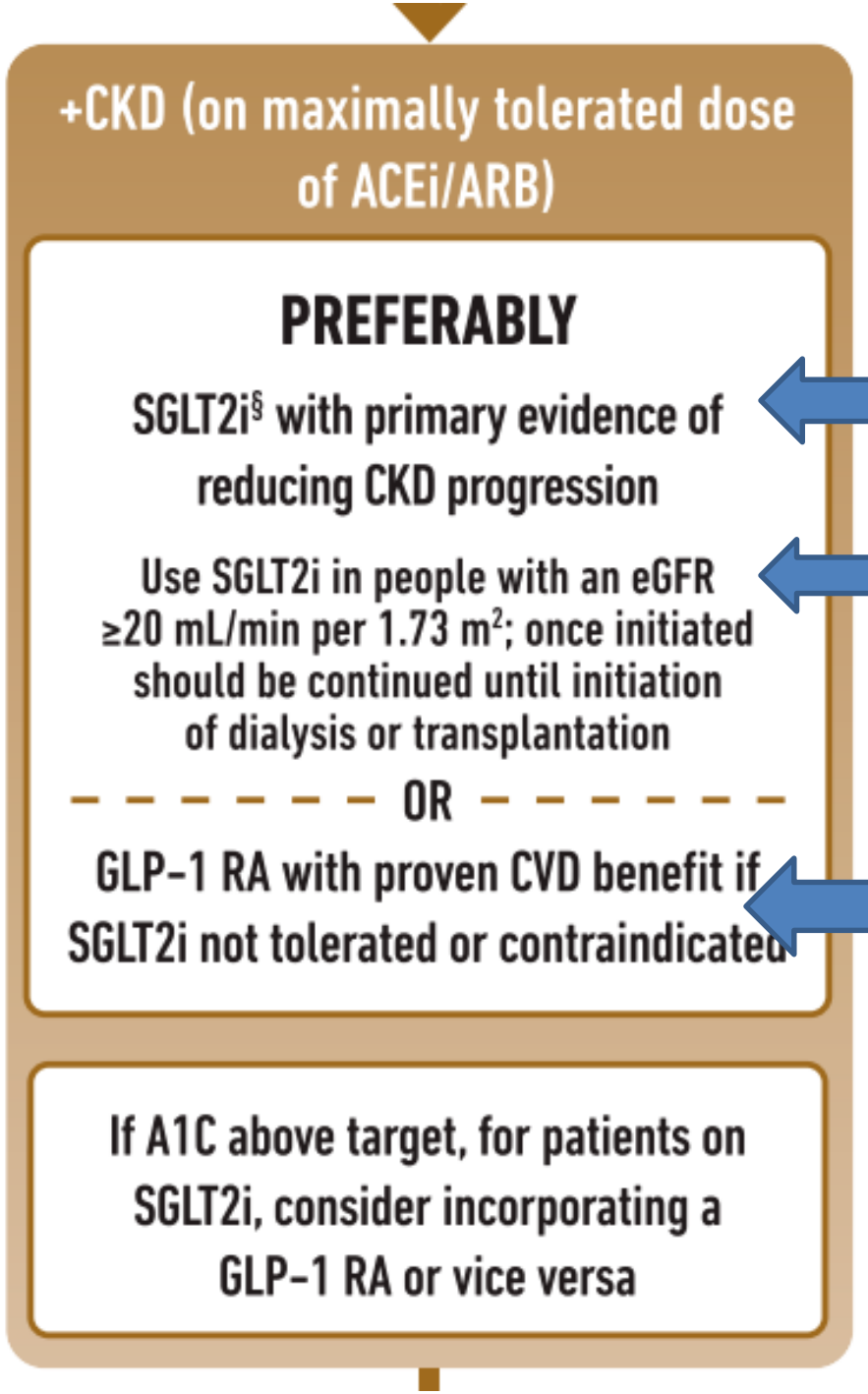
Dapagliflozin and empagliflozin have **primary** <u>heart failure</u> outcome data.

Empagliflozin, canagliflozin, and dapagliflozin and ertugliflozin have shown reduction in HF in CVOTs.



Kidney disease (CKD)

- **Key points:**
- **SGLT2i's reduce CKD progression mainly in those with significant albuminuria = UACR >/= 200 mg/g creatinine**
- **In those with UACR >/= 300 goal is to reduce UACR by 30%+**
- **Combination therapy with both drugs *as needed* to achieve A1c target is recommended**



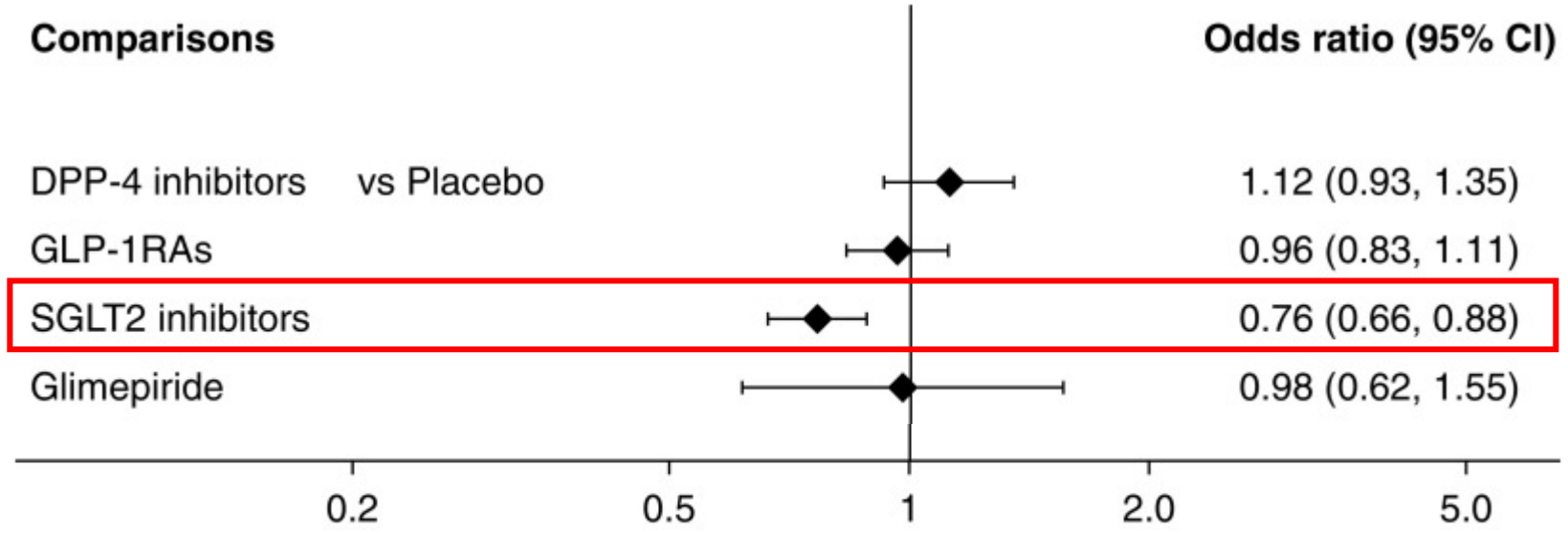
canagliflozin, dapagliflozin

empagliflozin

liraglutide semaglutide (SQ) and dulaglutide

SGLT2 inhibitors: No increased AKI risk with initiation

Meta-analysis of AKI in CANVAS, CREDENCE, EMPA-REG OUTCOME, DECLARE-TIMI 58, VERTIS-CV



Additional outcome data:

- Multiple retrospective cohort studies show no difference or significant decrease in incident AKI with SGLT2 inhibitor initiation
- Measured by increase in serum Cr, hospital discharge codes for AKI
- SGLT2is Probably protective down to GFR 20

Zhao et al, Clin J Am Soc Nephrol 2021; 16(1):70–78
Rampersad et al, Am J Kidney Dis 2020; 76(4):471-479
Cahn et al, Diabetes Obes Metab 2019; 21:340-348
Zhuo et al, Am J Kidney Dis 2021; 79(6):858-867

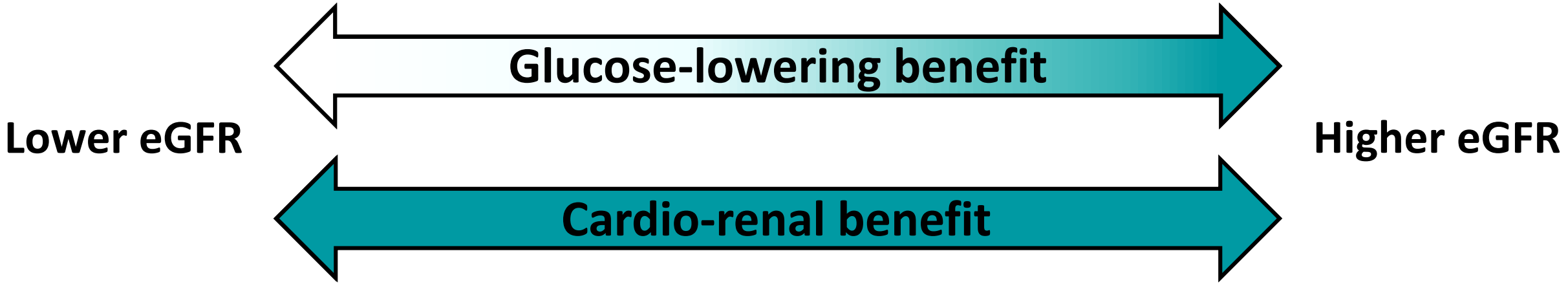
SGLT2 inhibitors: Benefits based on eGFR

eGFR <30

* **Cana + empa**: Not recommended for glycemic control

eGFR <45

* **Dapa + ertu**: Not recommended for glycemic control



* Per prescribing information

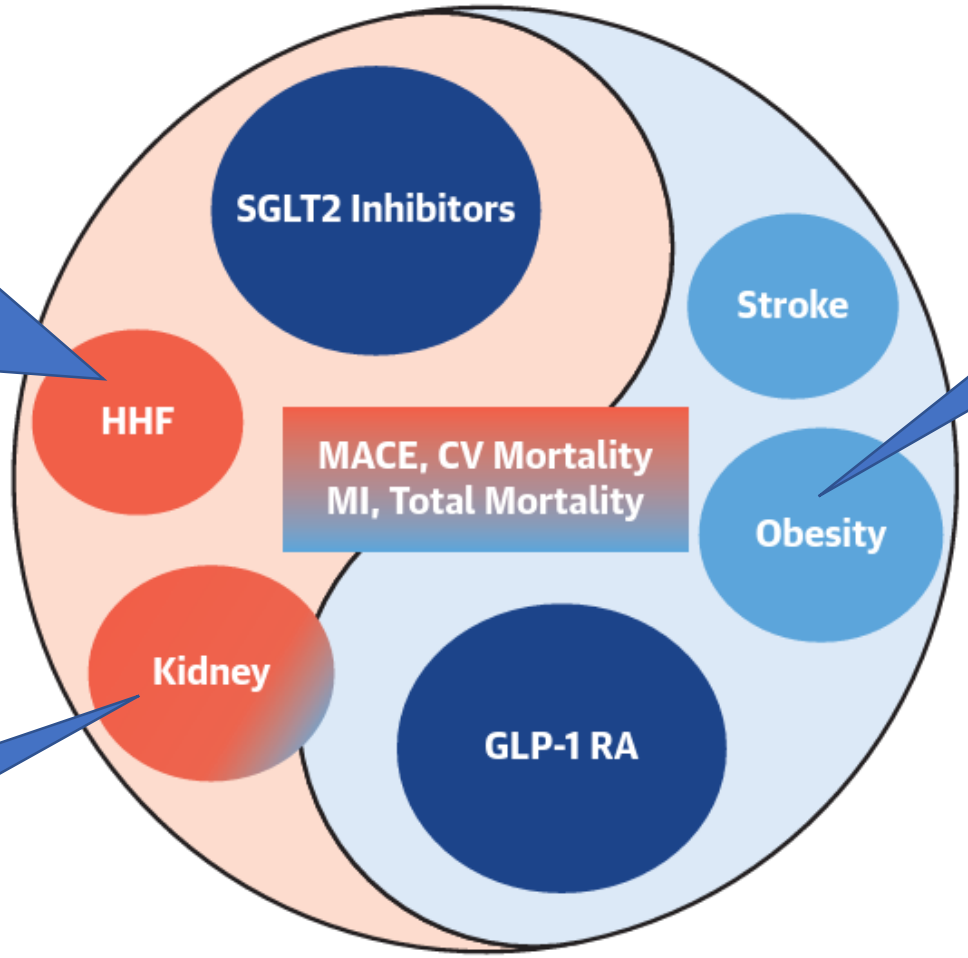
- Slide courtesy of Lee-Shing Chang

https://www.janssenlabels.com/package-insert/product-monograph/prescribing-information/INVOKANA-pi.pdf
https://den8dhaj6zs0e.cloudfront.net/50fd68b9-106b-4550-b5d0-12b045f8b184/0be9cb1b-3b33-41c7-bfc2-04c9f718e442/0be9cb1b-3b33-41c7-bfc2-04c9f718e442_viewable_rendition__v.pdf
https://content.boehringer-ingelheim.com/DAM/7d9c411c-ec33-4f82-886f-af1e011f35bb/jardiance-us-pi.pdf
https://www.merck.com/product/usa/pi_circulars/s/steglatro/steglatro_pi.pdf

Big picture for organ protection in type 2 diabetes

Semaglutide reduces symptoms and improves functional status in HFpEF in people with obesity (no overt diabetes)
Kosiborod MN, et al. N Engl J Med. 2023 Sep 21

SURPASS CVOT: Semaglutide CVOT results shows 20% reduction in MACE in people with obesity =/- prediabetes (no overt diabetes)

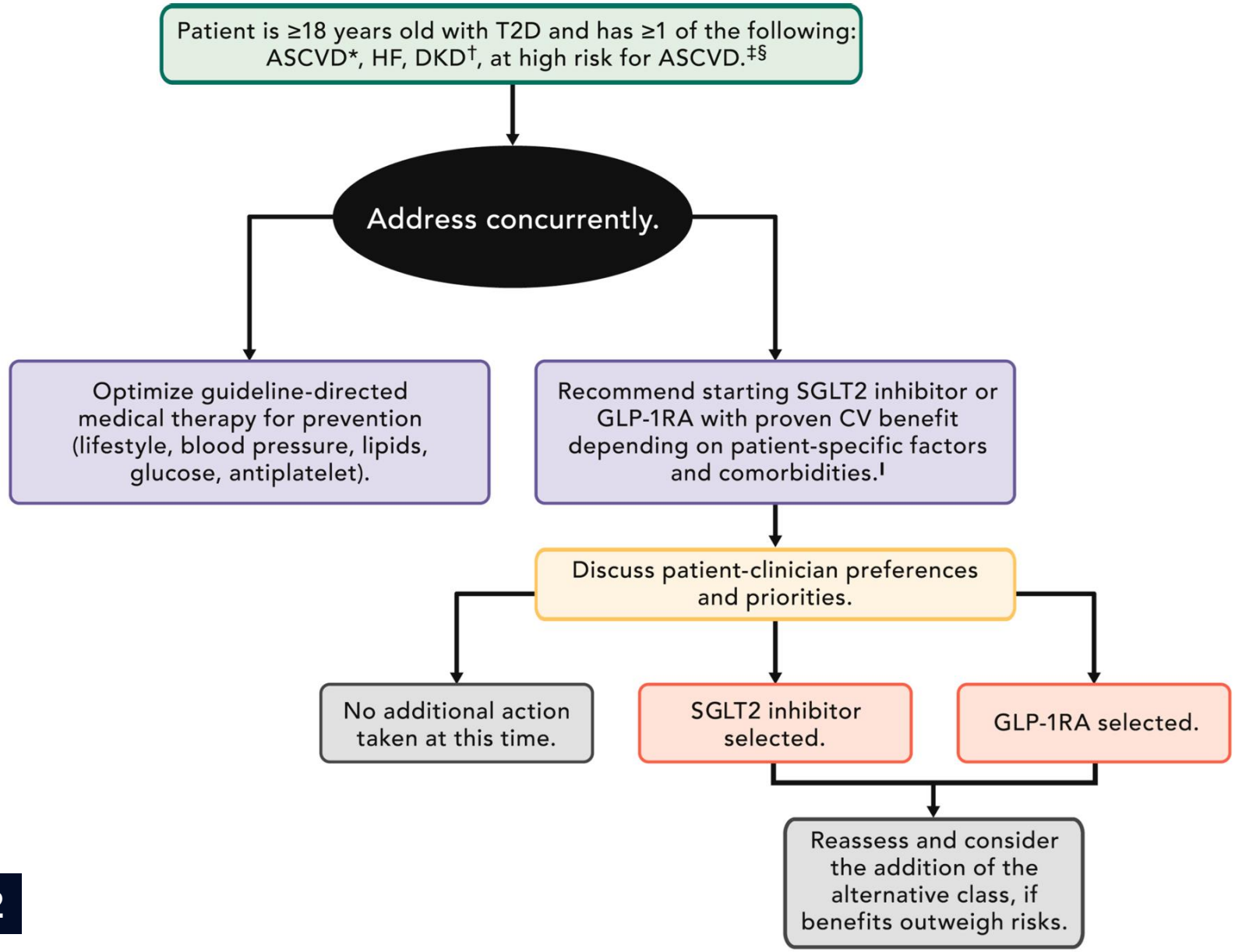


Semaglutide's FLOW study was stopped early for renal benefit

EDITORIAL COMMENT

GLP-1 RA and SGLT2 Inhibitors
In Harmony for Organ Protection*

Vanita R. Aroda, MD,[a,b] Liana K. Billings, MD, MMSc[c,d]


Patient is ≥18 years old with T2D and has ≥1 of the following: ASCVD*, HF, DKD†, at high risk for ASCVD.‡§
Address concurrently.
Optimize guideline-directed medical therapy for prevention (lifestyle, blood pressure, lipids, glucose, antiplatelet).
Recommend starting SGLT2 inhibitor or GLP-1RA with proven CV benefit depending on patient-specific factors and comorbidities.‖
Discuss patient-clinician preferences and priorities.
No additional action taken at this time.
SGLT2 inhibitor selected.
GLP-1RA selected.
Reassess and consider the addition of the alternative class, if benefits outweigh risks.

KDIGO 2022

GLP1 RA vs. SGLT2i: *when you need to make a choice*

Prefer SGLT2i when	**Prefer GLP1 RA when…**
Heart failure	TIA/Stroke/MI/PAD
HA1c <9%	Weight loss is a priority
Renal protection: GFR <60, significant albuminuria	**Renal protection:** when glycemic control *and* ASCVD risk are priority
Preference for oral medication *(oral Semaglutide unclear CV benefits)*	eGFR <20
Contraindications to GLP1 RA are present, such as: - History of pancreatitis ***with ongoing risk*** - History of **severe** gastroparesis - History of medullary thyroid cancer or MEN2 (rare!!)	Relative Contraindications to SGLT2i are present, such as: - History of severe recurrent genital mycotic infections - History of recurrent UTI while on SGLT2i - History of diabetic ketoacidosis

Oldies but goodies: *special considerations*

Sulfonylureas

- **Choose glimepiride as first line**
  - Only SU tested in a CVOT
  - Was compared with linagliptin
  - No difference in CV risk and hypoglycemia risk was lower than expected
- **Remember that SUs will fail**
  - Can appear to happen suddenly
  - Typically not useful to increase beyond 10mg daily if A1c has risen >0.5%
  - Best approach is to add another agent and taper the SU off (stopping suddenly can cause hyperglycemia even when effectiveness is reduced)

Thiazolidinediones (TZD)

- **Pros:** ok in euvolemic advanced kidney disease, potent
- **Cons:** weight gain, edema/CHF, CV controversy, increased fractures in women, (urologic cancers? unclear, FDA avoid if family history)
- **Select the right *patient & dose*:**
  - Fatty liver
  - TIA, stroke history
  - MI history, normal EF, unable to take SGLT2i or GLP-1
  - Side effects are dose-dependent – use 15mg, avoid max dose

Nissen SE, et al. *N Engl J Med.* 2007; 356: 2457-71.
Singh S, et al. *JAMA*. 2007; 298: 1189-1195.
Lincoff AM, et al. *JAMA*. 2007; 298: 1180-1188.

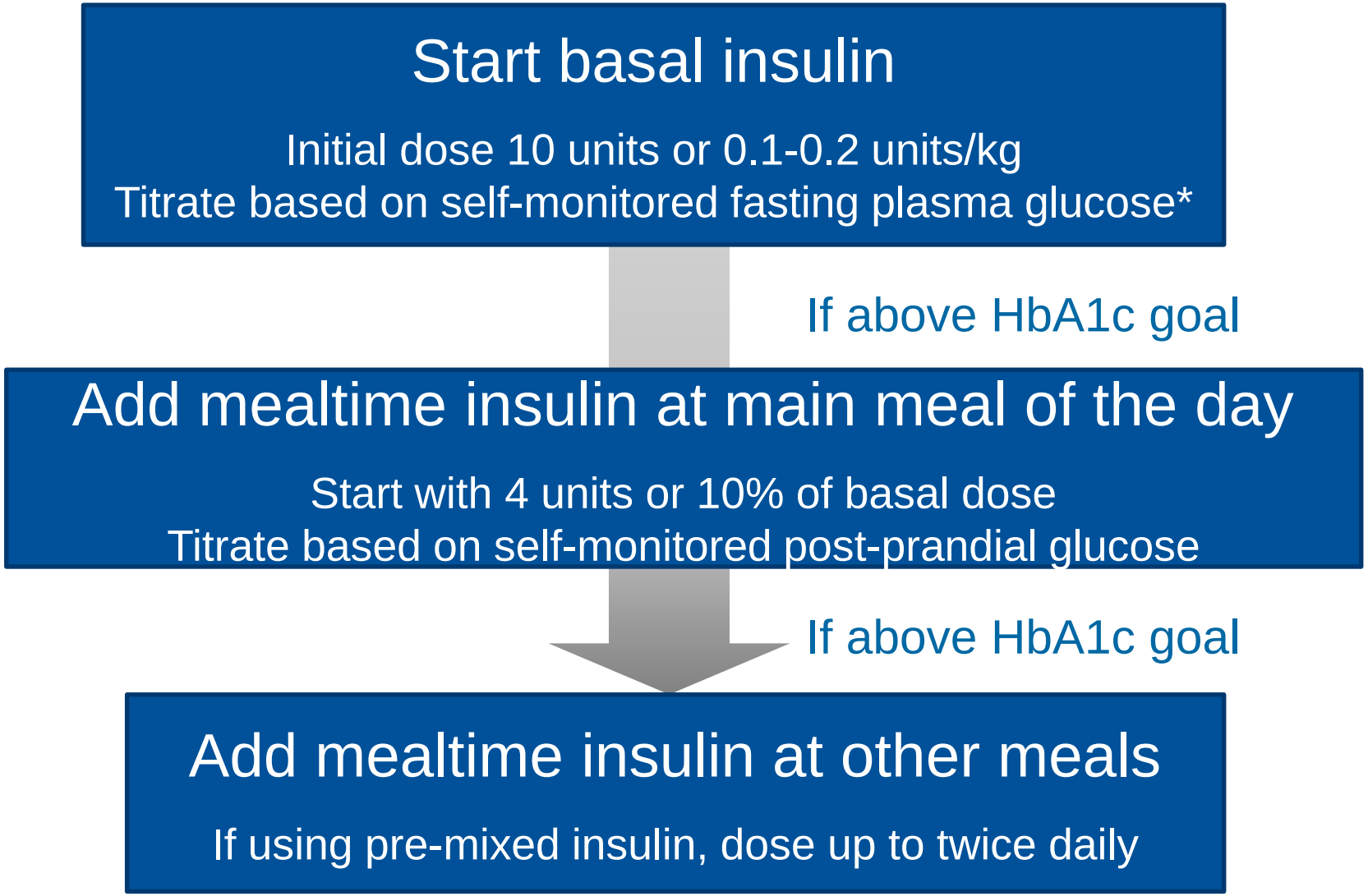
Thiazolidinediones (TZD)

Data to Know!

- Lowers progression to cirrhosis in Nonalcoholic Steatohepatitis (Cusi, 2016)
- Pioglitazone *reduces* MACE (Lincoff, 2007)
- Lowers risk of stroke after TIA (Kernan, 2016)
- Prevents progression from prediabetes to diabetes (Kernan, 2016)

Nissen SE, et al. *N Engl J Med.* 2007; 356: 2457-71.
Singh S, et al. *JAMA*. 2007; 298: 1189-1195.
Lincoff AM, et al. *JAMA*. 2007; 298: 1180-1188.

Initiating insulin: *nothing new*



Based on ADA Standards of Care. 2023.

What is on the horizon in Diabetes Care?

Once weekly basal insulin coming (very) soon

November 26, 2020
N Engl J Med 2020; 383:2107-2116
DOI: 10.1056/NEJMoa2022474
Chinese Translation 中文翻译

- ***Icodec (Novonordisk)***

  Approved in Canada in March, 2024!

  Type 2 diabetes: Compared with Glargine, no difference in efficacy, modest increase in non-severe hypoglycemia risk

  Type 1 diabetes: The ONWARDS phase 3 studies of icodec vs. glargine show similar results (higher rates of non-severe hypoglycemia than degludec in type 1 diabetes)

  Takes 3-4 weekly injections to achieve steady state

  Will require a dosing ramp-up

- ***Basal insulin Fc (BIF) (Eli Lilly)***

More and simpler CGM-augmented insulin therapy with automatic insulin delivery

The ILET: "Bionic pancreas"
Patients only enter their weight and "press go"
First version with insulin only, later bi-hormonal with glucagon
Phase 3 Clinical Trial with insulin completed 2021
Approved 2023

OMNIPOD 5 integration with Dexcom
Requires programming but mostly uses learned algorithm after 2 days of regular use
Can chose from 5 different target glucoses
FDA approved

New drugs, some new targets

- **Small molecule oral GLP-1**
- **CagriSemma (Semaglutide + cagrilintide)**
  - **GLP-1 RA + Amylin agonist**
  - **15% weight loss in people with diabetes !**
- **Retatrutide (single peptide, 3 targets: GLP-1, GIP and Glucagon)**
  - **Will be mainly an obesity agent (may increase A1c over time)**
- **Others –**

Myostatin inhibitors for weight loss related sarcopenia

GIP antagonists

Key points for the PCP

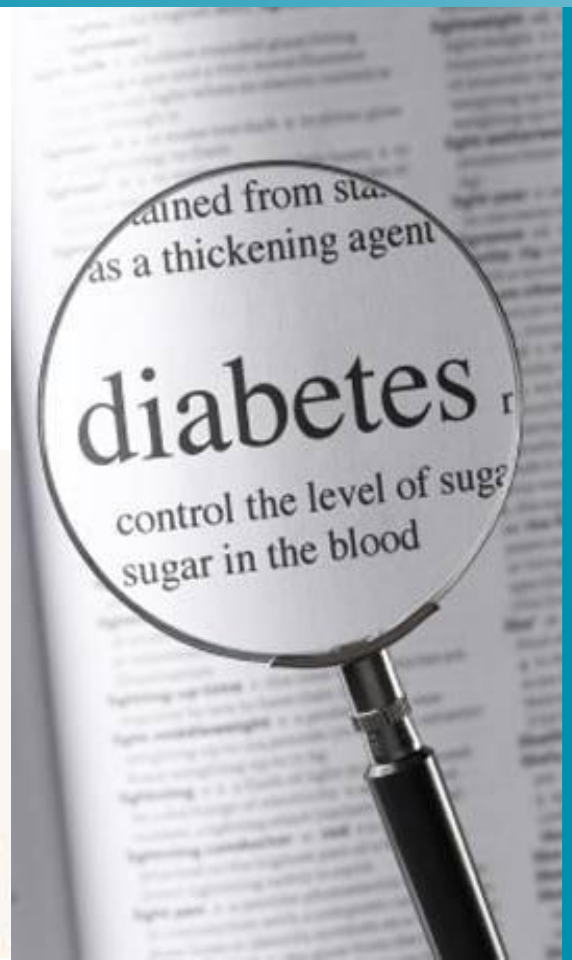
- Remember that not all Diabetes is Type 2
- Type 2 diabetes management is *no longer glucocentric*
- A comorbidity-first approach *supports* durable glucose control over time
  - In other words, the right approach should achieve good glycemic control and control comorbities
- *Preventing and treating obesity* as the underlying disease in most prediabetes and type 2 diabetes (along with other key features of the obesity syndrome) is a priority for overall health and survival of the individual

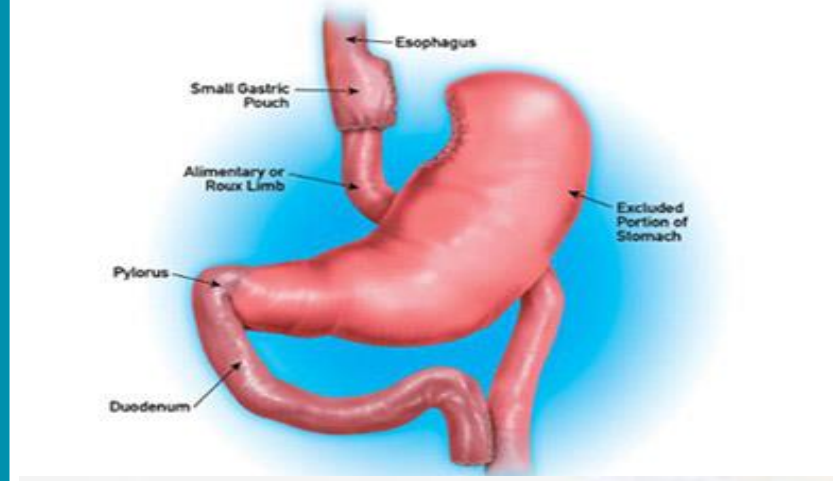
Next Best Steps for the PCP

- Individualize therapeutic strategies for type 2 diabetes based mainly on cardiovascular risk and kidney health. Consider the patient's priorities, concerns and side effects to make the final choice.


BRIGHAM AND
WOMEN'S HOSPITAL

Thank you!


as a thickening agent
diabetes
control the level of sug
sugar in the blood


Esophagus
Small Gastric Pouch
Alimentary or Roux Limb
Excluded Portion of Stomach
Pylorus
Duodenum

Selected references

- American Diabetes Association Professional Practice Committee. 9. Pharmacologic Approaches to Glycemic Treatment: Standards of Care in Diabetes-2024. Diabetes Care. 2024 Jan 1;47(Suppl 1):S158-S178. doi: 10.2337/dc24-S009. PMID: 38078590; PMCID: PMC10725810.

- Tsapas A, Avgerinos I, Karagiannis T, Malandris K, Manolopoulos A, Andreadis P, Liakos A, Matthews DR, Bekiari E. Comparative Effectiveness of Glucose-Lowering Drugs for Type 2 Diabetes: A Systematic Review and Network Meta-analysis. Ann Intern Med. 2020 Aug 18;173(4):278-286. PMID: 32598218.

- Wang L, Li X, Wang Z, Bancks MP, Carnethon MR, Greenland P, Feng YQ, Wang H, Zhong VW. Trends in Prevalence of Diabetes and Control of Risk Factors in Diabetes Among US Adults, 1999-2018. JAMA. 2021 Jun 25;326(8):1–13. doi: 10.1001/jama.2021.9883. Epub ahead of print. PMID: 34170288; PMCID: PMC8233946.