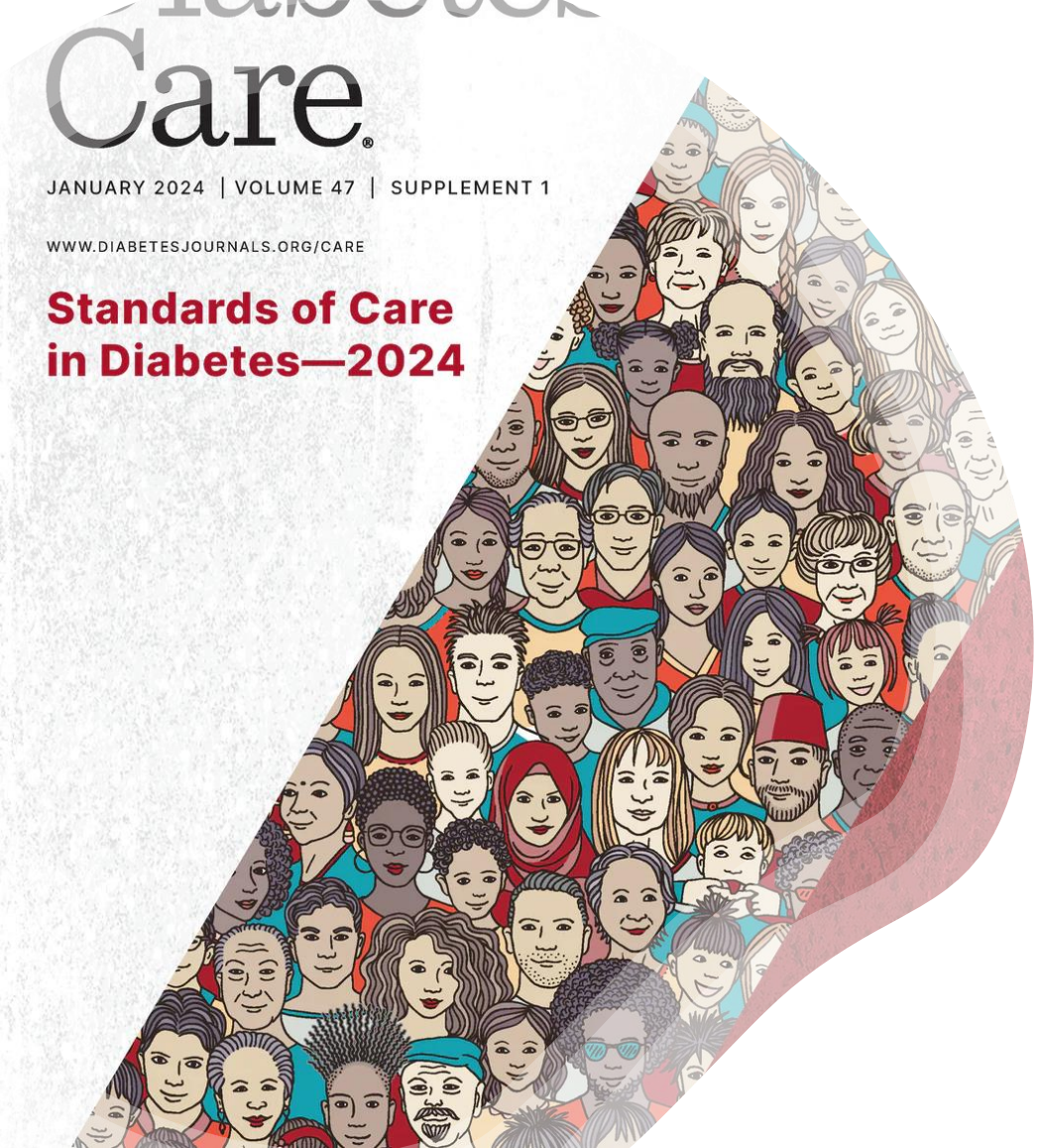


Diabetes Update Standards of Care 2024

Kelly Lang-Sheppard, APRN-CNS, CDCES

Relevant Financial Disclosure(s)
Kelly Lang-Sheppard

I have nothing to disclose

Objectives

Apply diabetes treatment goals and guidelines to guide practice in caring for people with diabetes.

Review pharmacologic approaches to glycemic treatment

Update on diabetes technology

National Diabetes Statistics Report

Fast Facts on Diabetes

Diabetes

- **Total:** 37.3 million people have diabetes (11.3% of the US population)
- **Diagnosed:** 28.7 million people, including 28.5 million adults
- **Undiagnosed:** 8.5 million people (23.0% of adults are undiagnosed)

Prediabetes

- **Total:** 96 million people aged 18 years or older have prediabetes (38.0% of the adult US population)
- **65 years or older:** 26.4 million people aged 65 years or older (48.8%) have prediabetes

Centers for Disease Control and Prevention. National Diabetes Statistics Report website. https://www.cdc.gov/diabetes/data/statistics-report/index.html. Accessed [2023].

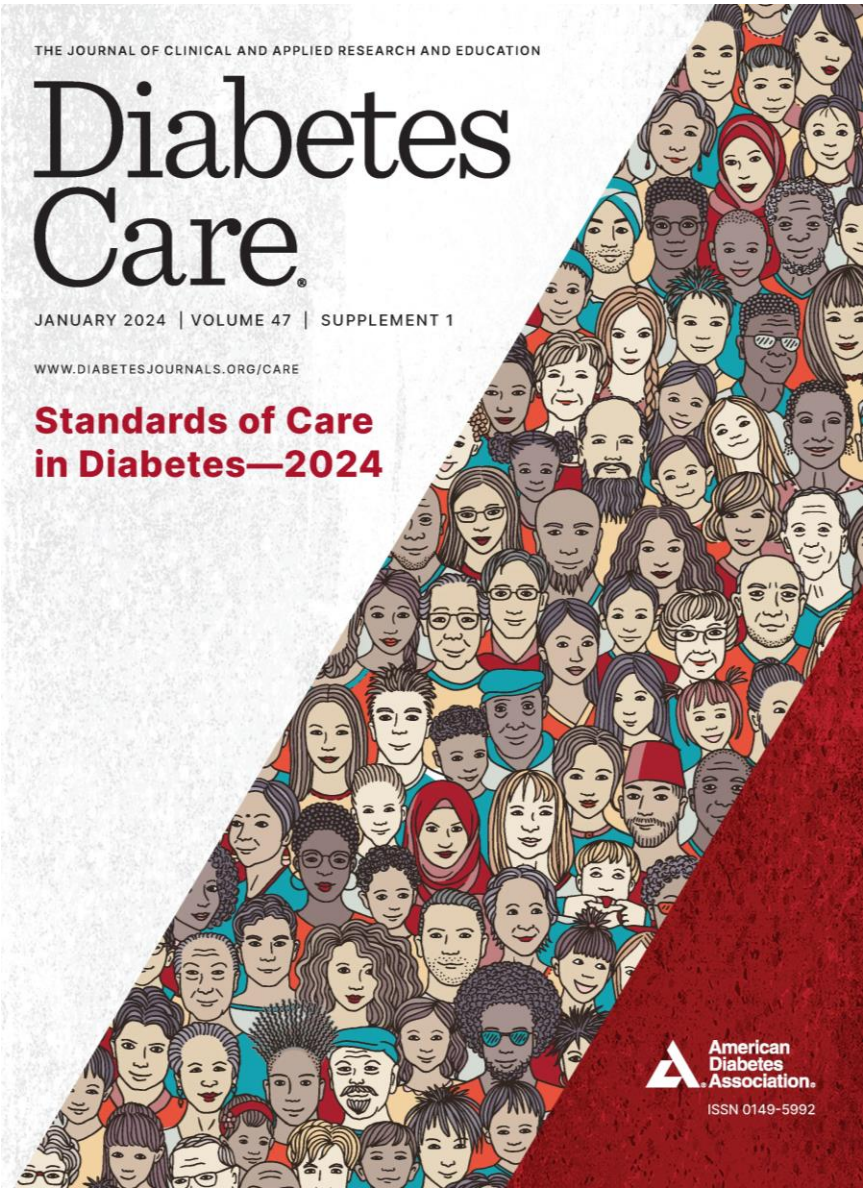
Diabetes Classifications

- Type 1 diabetes (due to autoimmune B-cell destruction, usually leading to absolute insulin deficiency, including latent autoimmune diabetes in Adult (LADA).

- Type 2 diabetes (due to non-autoimmune progressive loss of adequate B-cell secretion, frequently on the background of insulin resistance & metabolic syndrome).

- Specific type of diabetes due to other causes: monogenic diabetes (such as neonatal diabetes and maturity-onset diabetes of the young, diseases of the exocrine pancreas (such as cystic fibrosis and pancreatitis), and drug or chemical-induced diabetes (such as glucocorticoid use, in the treatment of people with HIV, or after organ transplantation.

- Gestational diabetes (diabetes diagnosed in the second or 3rd trimester of pregnancy that was not clearly overt diabetes prior to gestation or other types of diabetes occurring throughout pregnancy, such as Type 1 diabetes.



Review of Diabetes Diagnosis with A1c

Result*	A1C Test	Fasting Blood Sugar Test	Glucose Tolerance Test	Random Blood Sugar Test
Diabetes	6.5% or above	126 mg/dL or above	200 mg/dL or above	200 mg/dL or above
Prediabetes	5.7 – 6.4%	100 – 125 mg/dL	140 – 199 mg/dL	N/A
Normal	Below 5.7%	99 mg/dL or below	140 mg/dL or below	N/A

Risk Reduction Interventions

- PWD & HTN qualify for anti-hypertensive drug therapy when the BP is persistently elevated greater than or equal to 130/80.
- ACE-I/ARBs are recommended first-line treatment.
- For PWD & atherosclerotic CV disease, treatment with high-intensity statin therapy is recommended to target an LDL cholesterol reduction of greater than or equal of 50% from baseline and an LDL cholesterol goal of < 70 mg/dL.

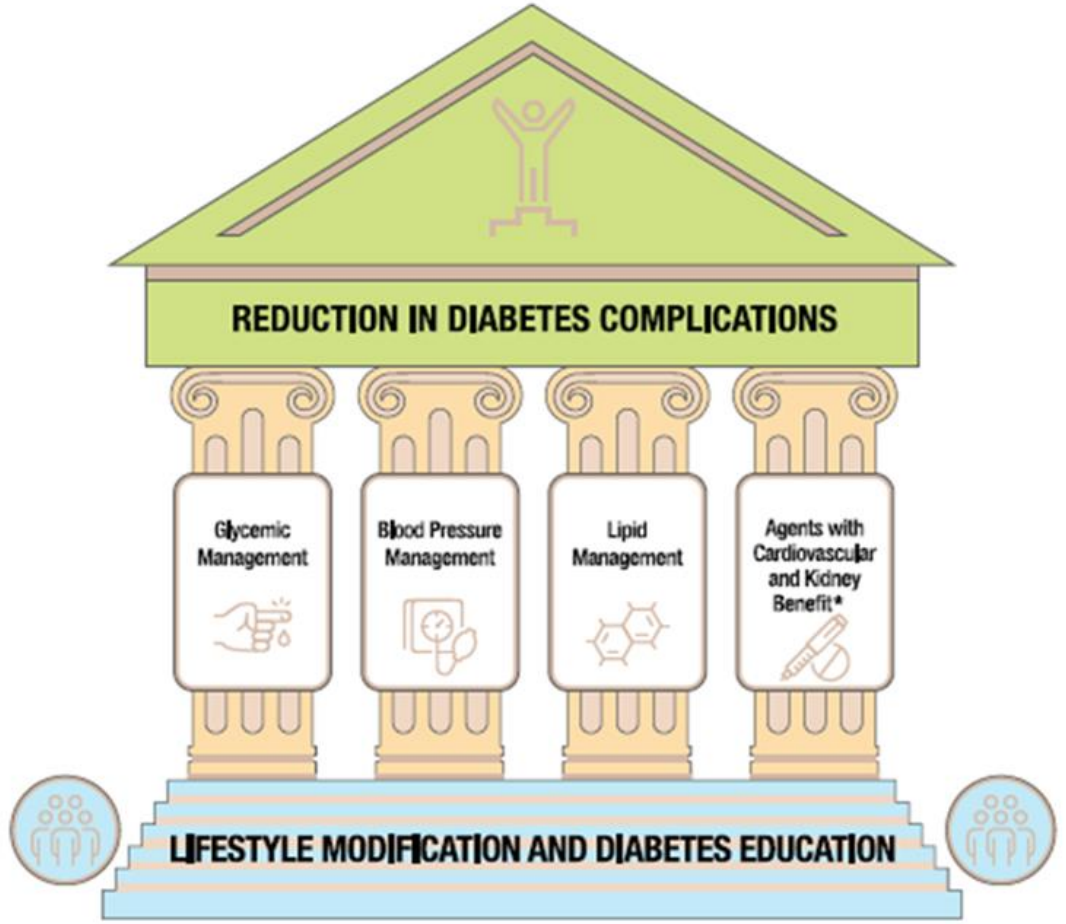


Figure 10.1—Multifactorial approach to reduction in risk of diabetes complications. *Risk reduction interventions to be applied as individually appropriate.

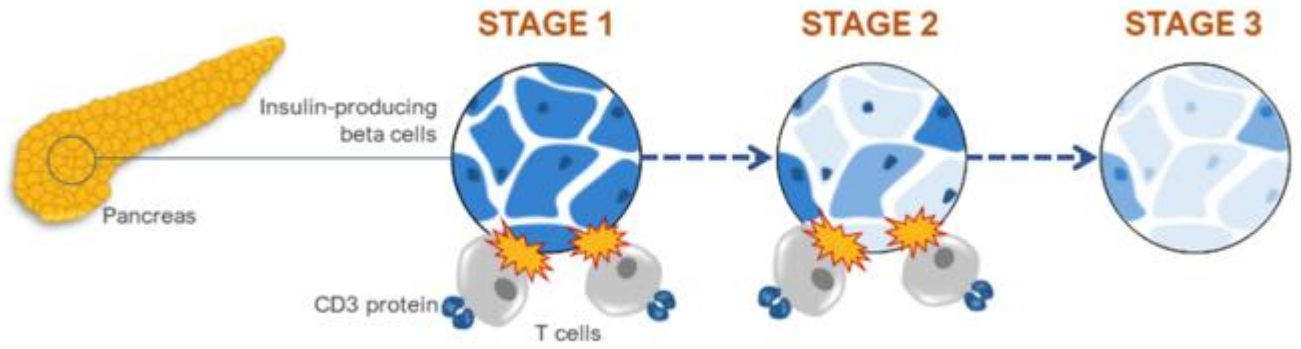
Prevention
Lifestyle Behavior Change for Type 2 Diabetes

- Refer adults with overweight or obesity at high risk of T2DM as seen in the **Diabetes Prevention Program (DPP)**, to an intensive lifestyle behavior change program.
- Recommended weight reduction at least 7%.
- A variety of eating patterns can be considered. The DPP study included a reduction of total dietary fat & calories.
- Moderate-intensity physical activity, such as brisk walking for 150 min./wk, has shown beneficial effects in people with prediabetes.
- **Can consider metformin**

Prevention
Pharmacologic Interventions to Delay Symptomatic Type 1 Diabetes

Table 2.1—Staging of type 1 diabetes (8,9)

	Stage 1	Stage 2	Stage 3
Characteristics	• Autoimmunity • Normoglycemia • Presymptomatic	• Autoimmunity • Dysglycemia • Presymptomatic	• New-onset hyperglycemia • Symptomatic
Diagnostic criteria	• Multiple autoantibodies • No IGT or IFG	• Multiple autoantibodies • Dysglycemia: IFG and/or IGT • FPG 100–125 mg/dL (5.6–6.9 mmol/L) • 2-h PG 140–199 mg/dL (7.8–11.0 mmol/L) • A1C 5.7–6.4% (39–47 mmol/mol) or ≥10% increase in A1C	• Clinical symptoms • Diabetes by standard criteria



Teplizumab-mzwv Infusion

- Teplizumab has been approved to delay the onset of stage 3 type 1 DM in people 8 years or older with stage 2 type 1 DM based in part on the results of a single trial in relatives of people with type 1 DM.

- The median time to stage 3 type 1 DM diagnoses was 48.4 months in the teplizumab group and 24.4 months in the placebo group.

Facilitating Positive Health Behaviors & Well-being to Improve Health Outcomes
Diabetes Self-Management Education & Support

- Strongly recommend all PWD to participate in **Diabetes Self-Management Education and Support (DSMES)**

- **There are 5 critical time points when the need for DSMES should be evaluated by the healthcare professional and referrals made, as needed:**

1. *At diagnosis*
2. *Annually*
3. *When not meeting treatment goals*
4. *When complicating factors occur*
5. *When transition in life and care occur*

Facilitating Positive Health Behaviors & Well-being to Improve Health Outcomes

Medical Nutrition Therapy

- To promote & support healthful eating patterns, emphasizing a variety of nutrient-dense foods in appropriate portion sizes, to improve over all health.
- Referral to be made for MNT to a RDN at diagnosis & as needed throughout the lifespan, similar to DSMES.

Can have a 2% reduction in A1c for people with T2DM and a 1% reduction in A1c for people with Type1 DM

Look at eating patterns versus carb amount recommendations

https://fda.gov/food/food-additives-petitions/aspartame-and-other-sweeteners-food

Nonnutritive sweeteners are still considered safe over sugary drinks

https://lifestylemedicine.org/

The most important DRUG is behavior change. The wins are behaviors not necessarily outcomes (TIR & A1c)

Facilitating Positive Health Behaviors & Well-being to Improve Health Outcomes

Physical Activity

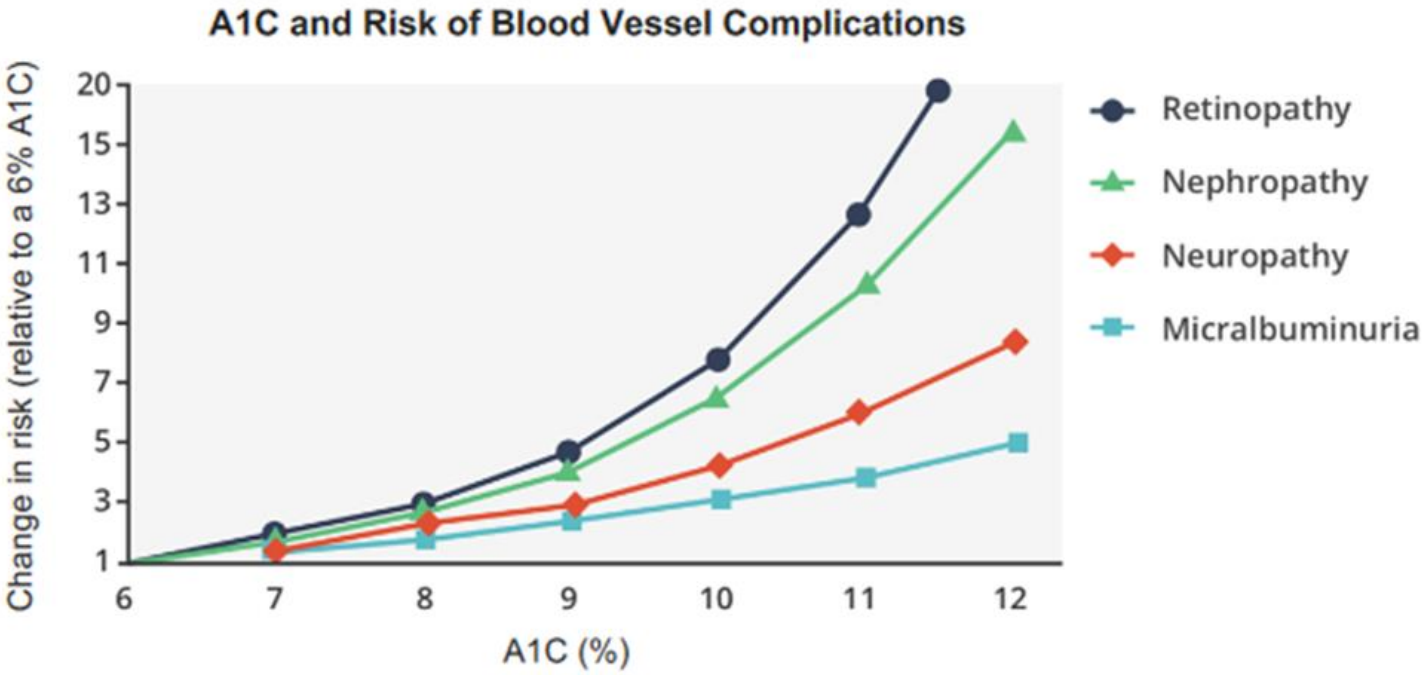
Physical activity is a general term that includes all movement that increases energy use and is an important part of the diabetes management plan.

Exercise is a more specific form of physical activity that is structured and designed to improve physical fitness.

Both are important…physical activity has been shown to improve blood glucose levels, reduce CV risk factors, contribute to weight loss, & improve well-being.

- **ADA recommendations include PWD to engage in 150 minutes or more of moderate-to-vigorous-intensity aerobic activity a week.**
- **For people who do not meet activity guidelines, encourage increased physical activity above baseline.**

Glycemic Control & Diabetes Complications



DCCT, Diabetes Control and Complications Trial

1. Adapted from Skyler JS. *Endocrinol Metab Clin North Am.* 1996;25:243-254.
2. DCCT. *N Engl J Med.* 1993;329:977-986
3. DCCT. *Diabetes.* 1995;44:968-983

Cardiorenal Complications in PWD

- People with diabetes (PWD) are twice as likely to have CVD & CVA
- CVD is the leading cause of morbidity & mortality
- HF hospitalization rates double for PWD
- 37% of adults with DM have CKD – ½ stages 3-4

Glycemic Targets

For the general population

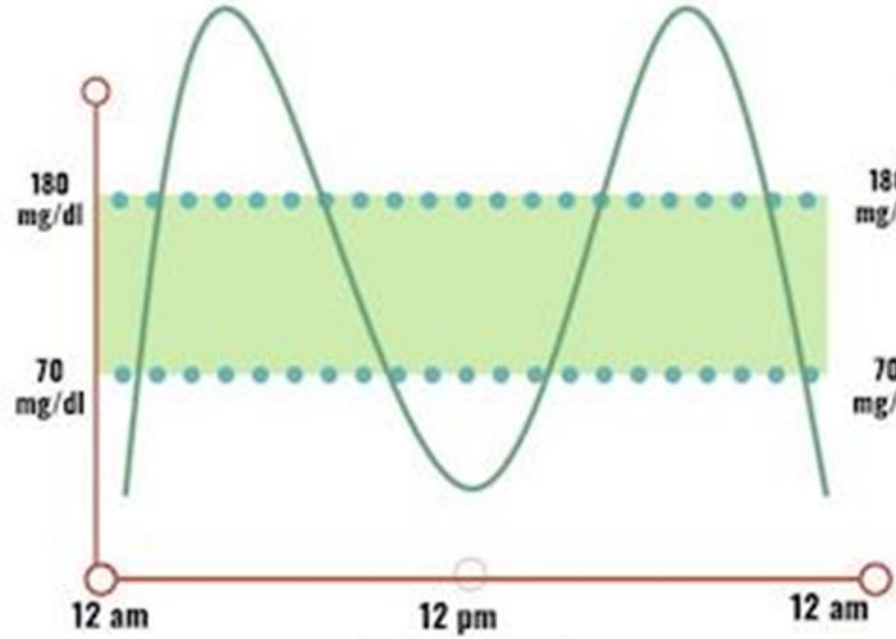
<7%

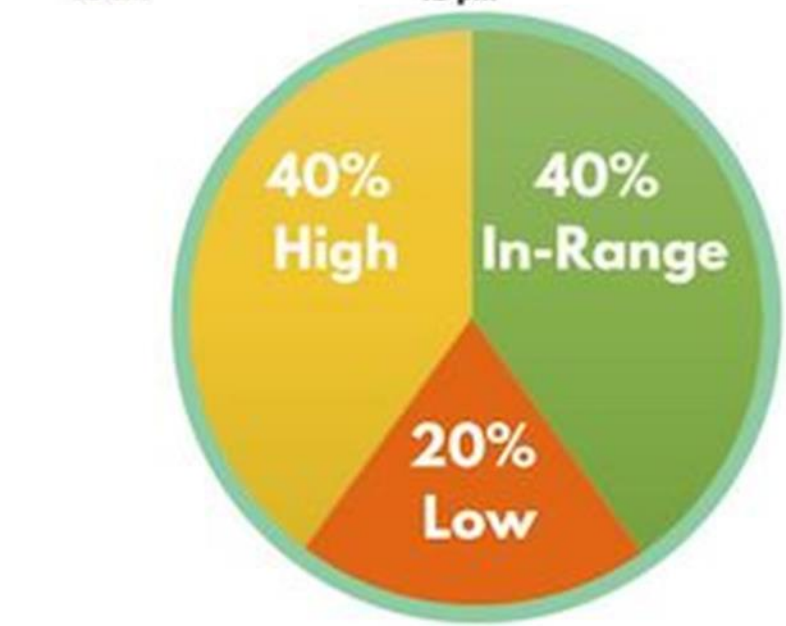
80-130 mg/dL

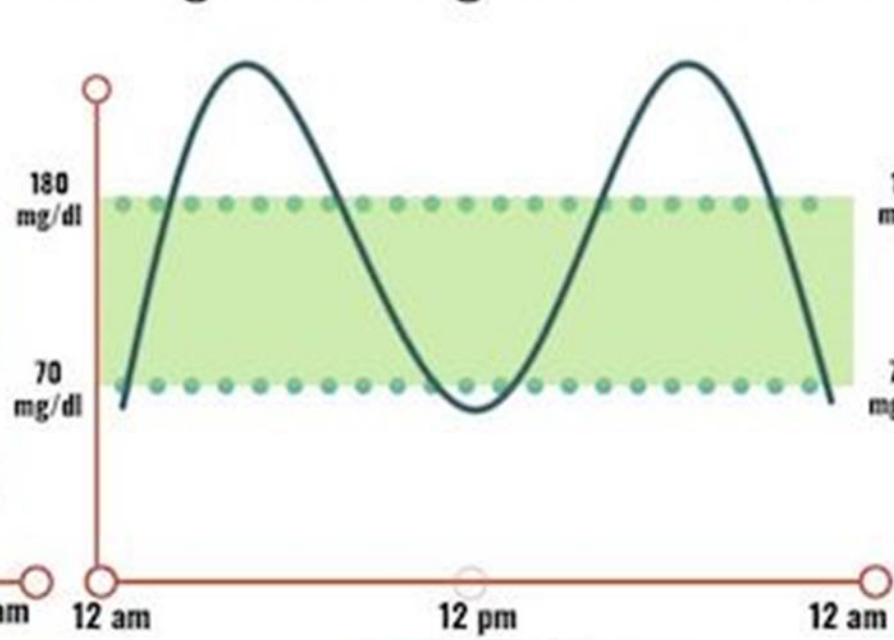
<180 mg/dL

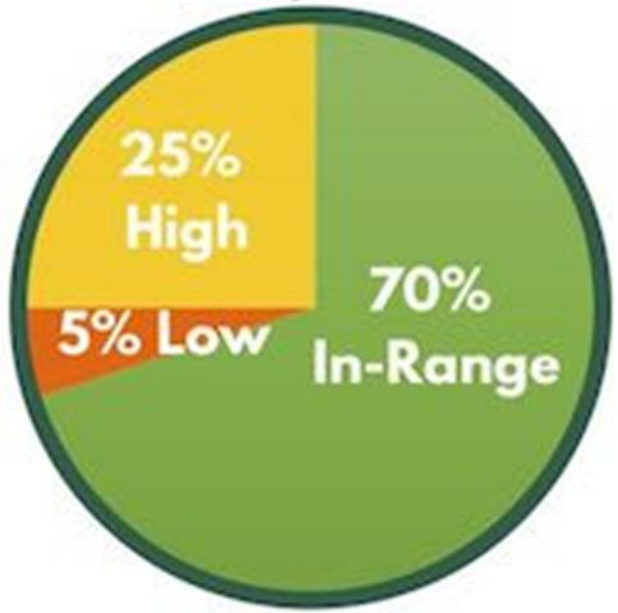
THE MANY FACES OF A 7% A1C

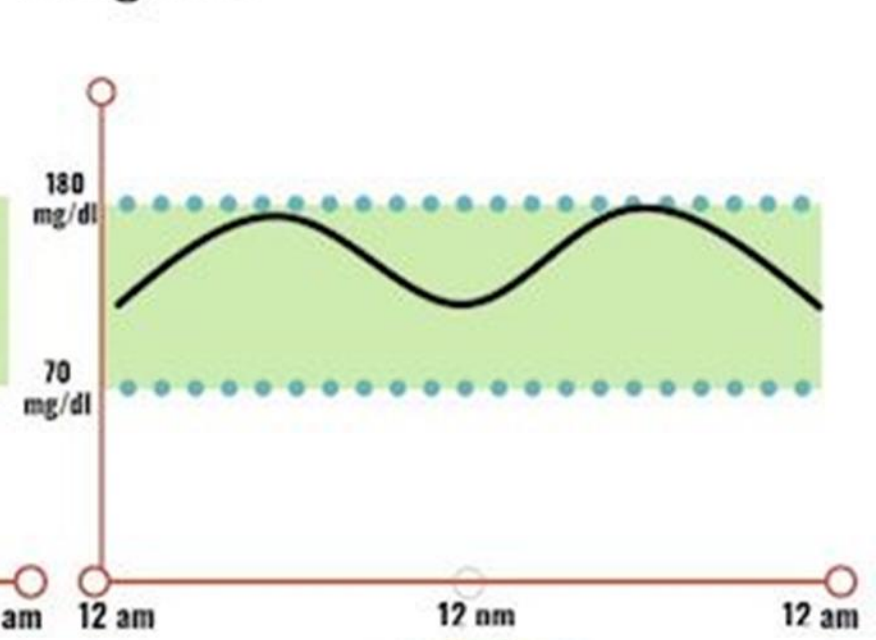
(and an average blood glucose of 154 mg/dl)





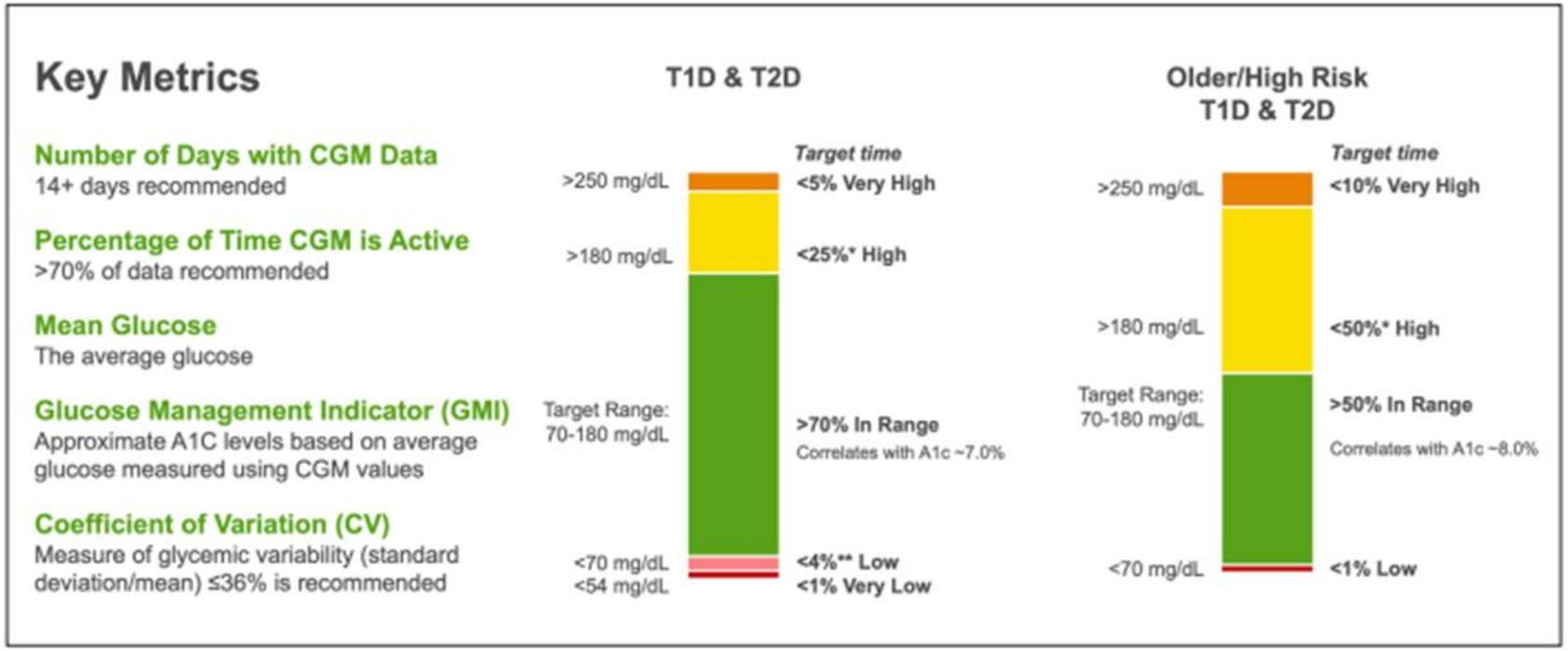




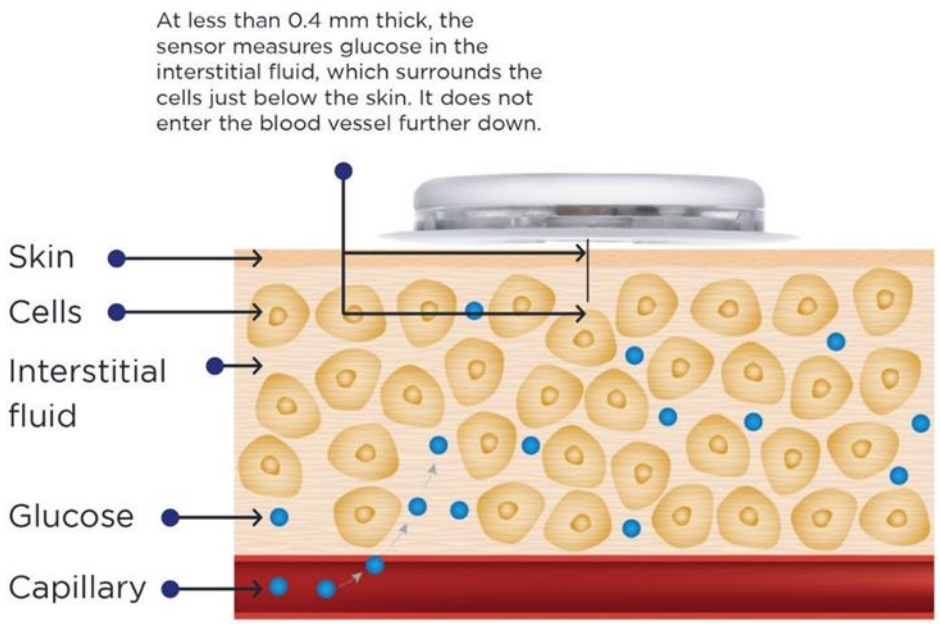


Glycemic Targets
Time in Range (TIR)

Figure 1: Core CGM Metrics and Goals for Time in Range (TIR)



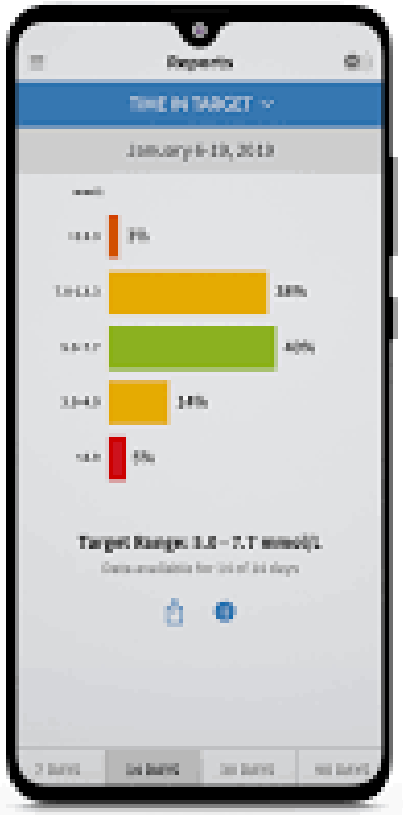
Glycemic Goals and Hypoglycemia
CGM



- Most personal CGMs eliminate the need for fingerstick blood sugars or decrease the amount of fingerstick blood sugars that need to be checked. CGMs give you continuous readings by checking the sugar every 1 to 5 minutes depending on what CGM you are using, like a movie or video. Fingerstick blood sugars give you only a snapshot in time, like a photograph. All CGMs tell you where your sugar has been, your current sugar, and what direction your sugar is headed 😊

- Your sensor glucose and fingerstick blood glucose results may not always match. One reason is that the sensor glucose is measuring your glucose/sugar in the interstitial fluid and your fingerstick is measuring the glucose/sugar in the blood/capillary. The glucose goes into the blood/capillary first, then into the interstitial fluid.

Glycemic Goals and Hypoglycemia *AGP Report*



AGP Report

Name

MRN

GLUCOSE STATISTICS AND TARGETS

26 Feb 2019 - 10 Mar 2019	13 days
% Time CGM is Active	99.9%

Glucose Ranges	Targets [% of Readings (Time/Day)]
Target Range 70-180 mg/dL	Greater than 70% (16h 48min)
Below 70 mg/dL	Less than 4% (58min)
Below 54 mg/dL	Less than 1% (14min)
Above 250 mg/dL	Less than 5% (1h 12min)

Each 5% increase in time in range (70-180 mg/dL) is clinically beneficial.

Average Glucose	173 mg/dL
Glucose Management Indicator (GMI)	7.6%
Glucose Variability	49.5%

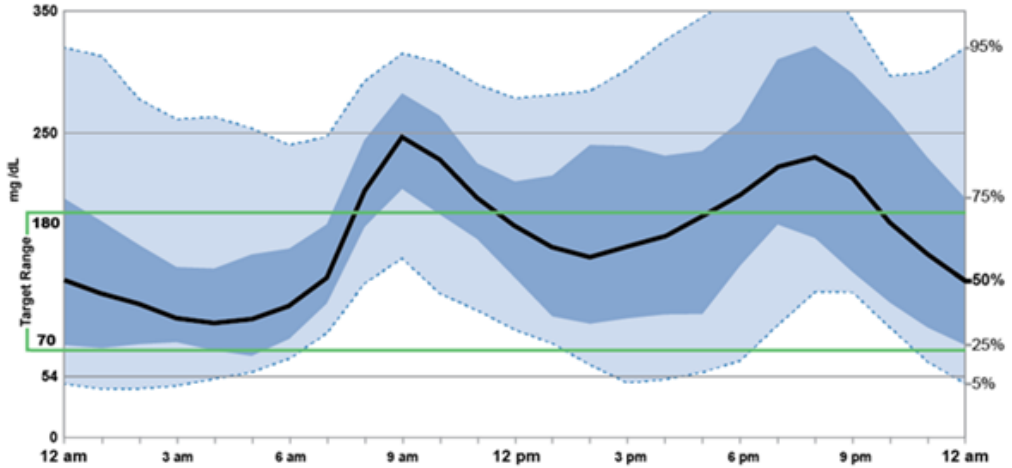
Defined as percent coefficient of variation (%CV); target ≤36%

TIME IN RANGES

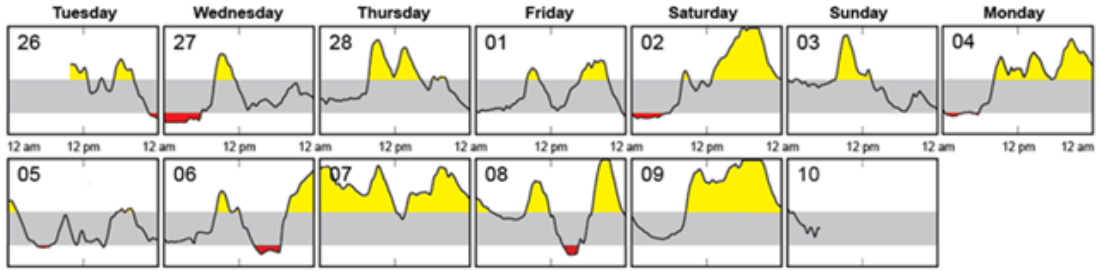
- Very High (>250 mg/dL) 20% (4h 48min)
- High (181–250 mg/dL) 23% (5h 31min)
- Target Range (70–180 mg/dL) 47% (11h 17min)
- Low (54–69 mg/dL) 4% (58min)
- Very Low (<54 mg/dL) 6% (1h 26min)

AMBULATORY GLUCOSE PROFILE (AGP)

AGP is a summary of glucose values from the report period, with median (50%) and other percentiles shown as if occurring in a single day.



DAILY GLUCOSE PROFILES



Each daily profile represents a midnight to midnight period.

captürAGP

Glycemic Goals and Hypoglycemia

Hypoglycemia treatment

People at the highest risk are those treated with insulin, sulfonylureas, or meglitinides

Prior hypoglycemia events, especially **level 2** (< 54 mg/dL) or **level 3** (altered mental/physical status requiring assistance) events.

Impaired hypoglycemia awareness ~ a person not experiencing the typical counterregulatory hormone release at low glucose levels or the associated symptoms.

Glycemic Goals and Hypoglycemia

Glucagon

Name/Delivery	Supplied	Dose Range		Age / Route / Storage
		Adult	Peds / Age WT Dosing	
Glucagon Emergency Kit Injection requires mixing glucagon powder	1mg / 1mL vial + syringe	1mg	0.03mg/kg or < 6yrs or < 25 kgs|0.5mg ≥ 6yrs or > 25kgs | 1mg	All ages approved SubQ or IM admin Expires in 2 years at room temp.
Baqsimi Nasal glucagon powder	3 mg intranasal device	3 mg	< 4 yrs: not recommended 4 yrs or older | 3mg dose	Approved Age 4+ Nasal admin Expires ~ 2 years at room temp (keep in shrink-wrapped tube).
Gvoke Injectable liquid stable glucagon solution	0.5mg/1.0mg prefilled syringe or 0.5mg/1.0mg HypoPen auto-injector	1 mg	< 2yrs: not recommended 2- 12 yrs < 45kg | 0.5mg ≥ 45kg | 1mg 12 yrs or older | 1mg	Approved Age 2+ SubQ admin in arm, thigh, abdomen Expires in 2 years at room temp (keep in foil pouch).
Dasiglucagon (Zegalogue) Stable liquid glucagon analog	0.6mg/0.6mL Prefilled syringe Autoinjector	0.6mg	< 6yrs: not recommended 6 yrs or older | 0.6mg	Approved Age 6+ SubQ in abdomen, buttocks, thigh outer upper arm Expires in 1 year at room temp. (store in red protective case).

**All raise BG 20+ points. Can cause nausea, vomiting. After admin, roll person on side. Seek medical help. If no response after 1st dose, give 2nd dose in 15 mins. When awake, give oral carbs ASAP when safe to swallow. Please consult package insert for detailed info.*

All PocketCard content is for educational purposes only. Please consult prescribing information for detailed guidelines.

Pharmacologic Approaches to Glycemic Treatment

CVOT were initiated after following the much-publicized CV safety concerns with rosiglitazone, (found to have a risk of MI & CV death) the FDA mandated in 2008 the all-new diabetes drugs conduct studies demonstrating CV safety.

Clinic trails must have a parallel arm for Major Adverse Cardiovascular Events (MACE) versus the control group. The main Cardiovascular events being non-fatal MI, CV death, & non-fatal stroke.

Then, if CV safety was demonstrated with the prespecified margins compared to placebo, these trial could test for SUPERIORITY for reduction of CV events.

Class	Examples	When to hold?	If NPO, ↑ risk of hypoglycemia?
Biguanide	Metformin	Lactic acidosis ↑ risk of developing AKI GFR <30	No
Sulfonylurea	Glipizide	↓ or variable oral intake GFR <30	Yes
TZD	Pioglitazone Rosiglitazone	Risk of heart failure or MI ALT >2.5x ULN	No
DPP-4 inhibitor	Alogliptin Saxagliptin	Prior or current pancreatitis Avoid saxagliptin in heart failure	No
GLP-1 receptor agonist	Dulaglutide Liraglutide Semaglutide	Prior or current pancreatitis Nausea and/or vomiting Ileus or gastric dysmotility	No
SGLT2i	Empagliflozin Dapagliflozin	Hold for 72 hours pre-operatively ↓ or variable oral intake Hypovolemia	No*
Meglitinide	Repaglinide	NPO	Yes
α-glucosidase inhibitor	Acarbose Miglitol	Cirrhosis Partial bowel obstruction Cr >2	No

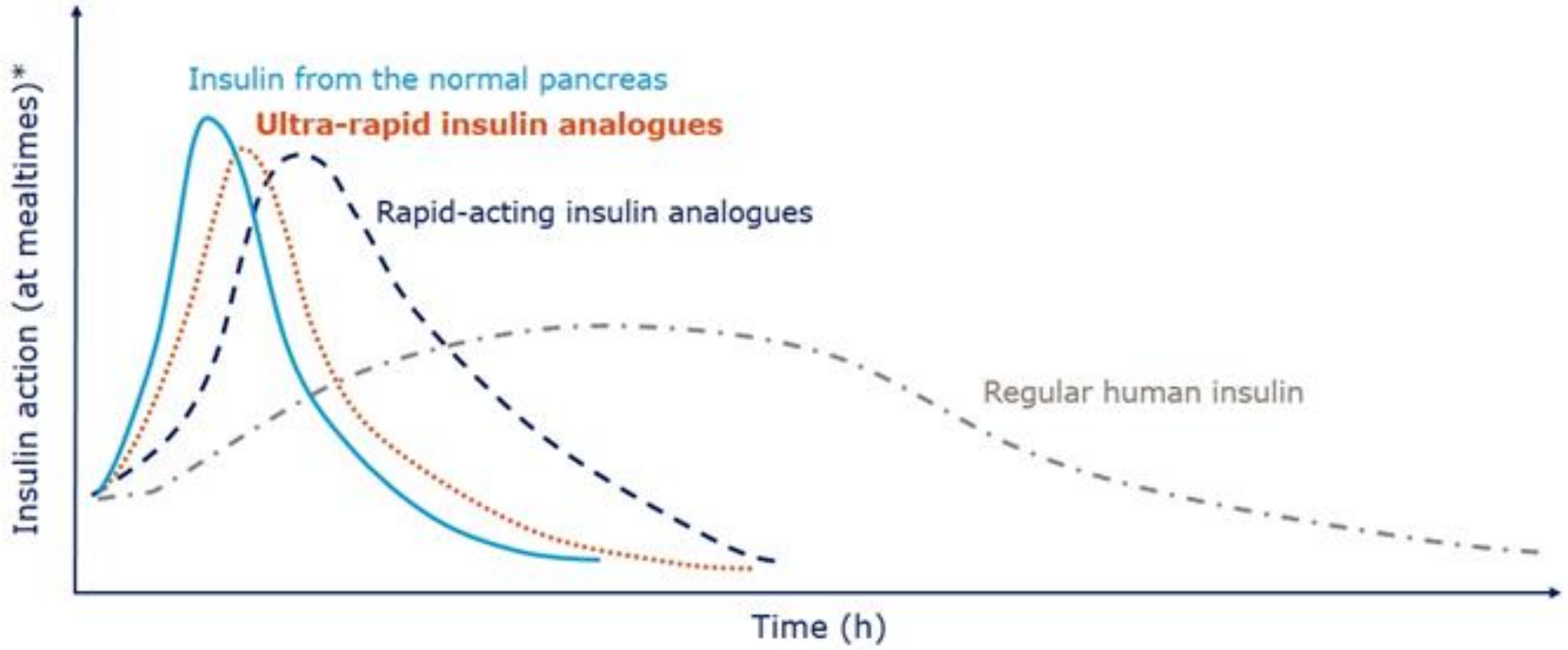
Types of insulin	Common Insulin Names	When it's usually taken	How soon it starts working*	When it's working the most*	How long it lasts*
Fast-acting insulin	NovoLog Humalog Apidra	Right before a meal	15 minutes	30 to 90 minutes	3 to 5 hours
Long-acting insulin	Lantus Levemir	30 minutes before the evening meal or at bedtime	1 hour	Steady over time	Up to 24 hours
Short-acting insulin (also called regular insulin)	Novolin R Humulin R	30 minutes before a meal	30 to 60 minutes	2 to 4 hours	5 to 8 hours
Medium-acting (intermediate-acting) (NPH) insulin	Humulin N Novolin N	30 minutes before breakfast or at bedtime	1 to 3 hours	8 hours	10 to 16 hours
Premixed mixture of fast-acting and medium-acting (NPH) insulin	Humalog Mix 75/25 Humalog Mix 50/50 NovoLog 70/30	Before breakfast and/or before the evening meal	5 to 15 minutes	Varies	10 to 16 hours
Premixed mixture of short-acting (regular) and medium-acting (NPH) insulin	Humulin 70/30 Novolin 70/30 Humulin 50/50	30 minutes before breakfast and/or before the evening meal	30 to 60 minutes	Varies	10 to 16 hours
Ultra-long-acting insulin*	Toujeo Tresiba	Once-a-day at about the same time.	Over a number of hours.	Constant	32 to 42 hours

*These insulins must only be taken using a pen device. Never a syringe.

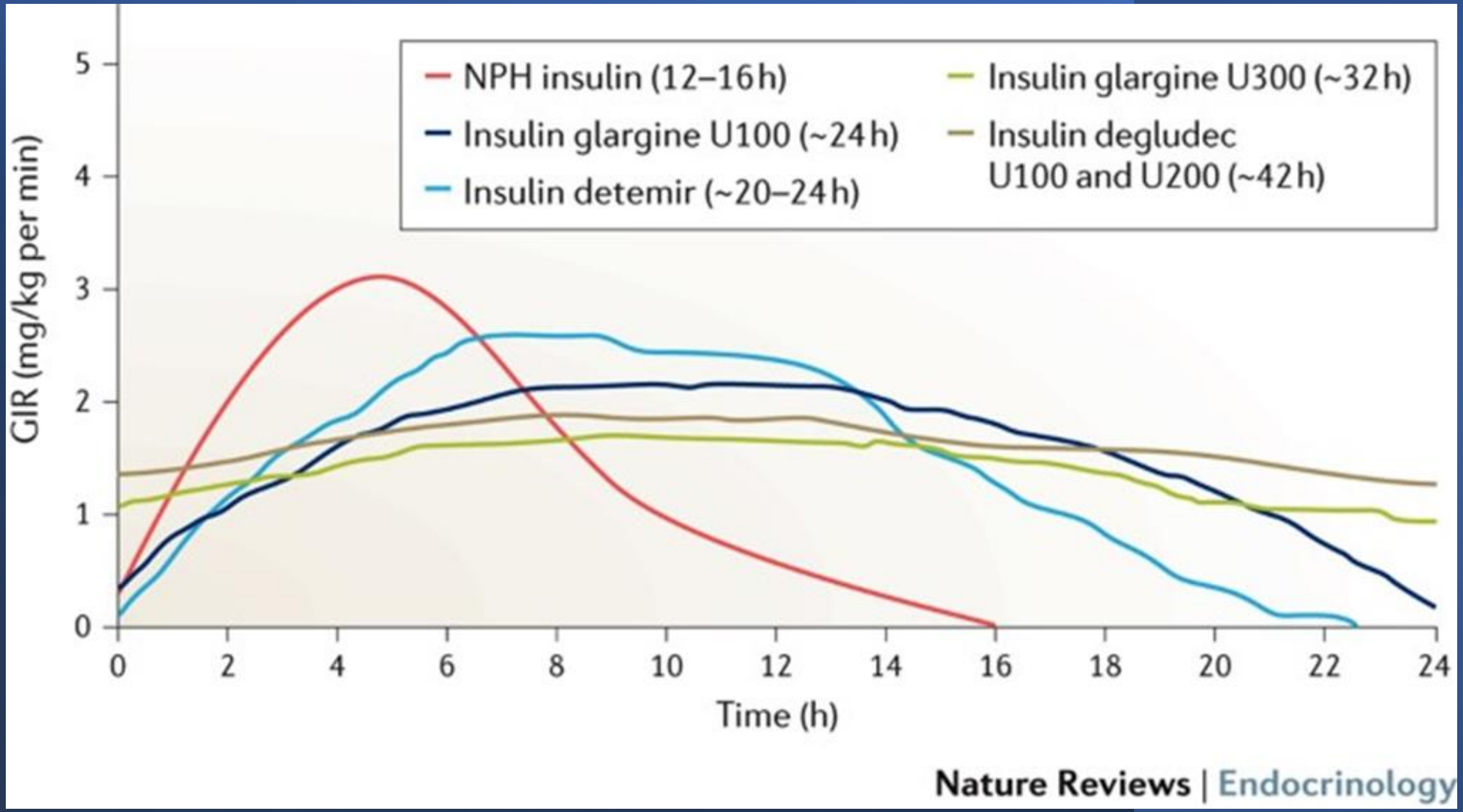
Ultra Rapid-acting Insulins:

- Fiasp (insulin aspart)
- Lyumjev (insulin lispro)

Bolus insulins with time action profiles that more closely mimic physiological insulin



*Schematic representation
Adapted from Home PD. *Diabetes Obes Metabo* 2015;17:1011–20


NPH insulin (12–16 h)
Insulin glargine U100 (~24 h)
Insulin detemir (~20–24 h)
Insulin glargine U300 (~32 h)
Insulin degludec U100 and U200 (~42 h)
GIR (mg/kg per min)
0
1
2
3
4
5
0
2
4
6
8
10
12
14
16
18
20
22
24
Time (h)
Nature Reviews | Endocrinology

Pharmacologic Approaches to Glycemic Treatment
Medications for Lowering Glucose Summary of Characteristics

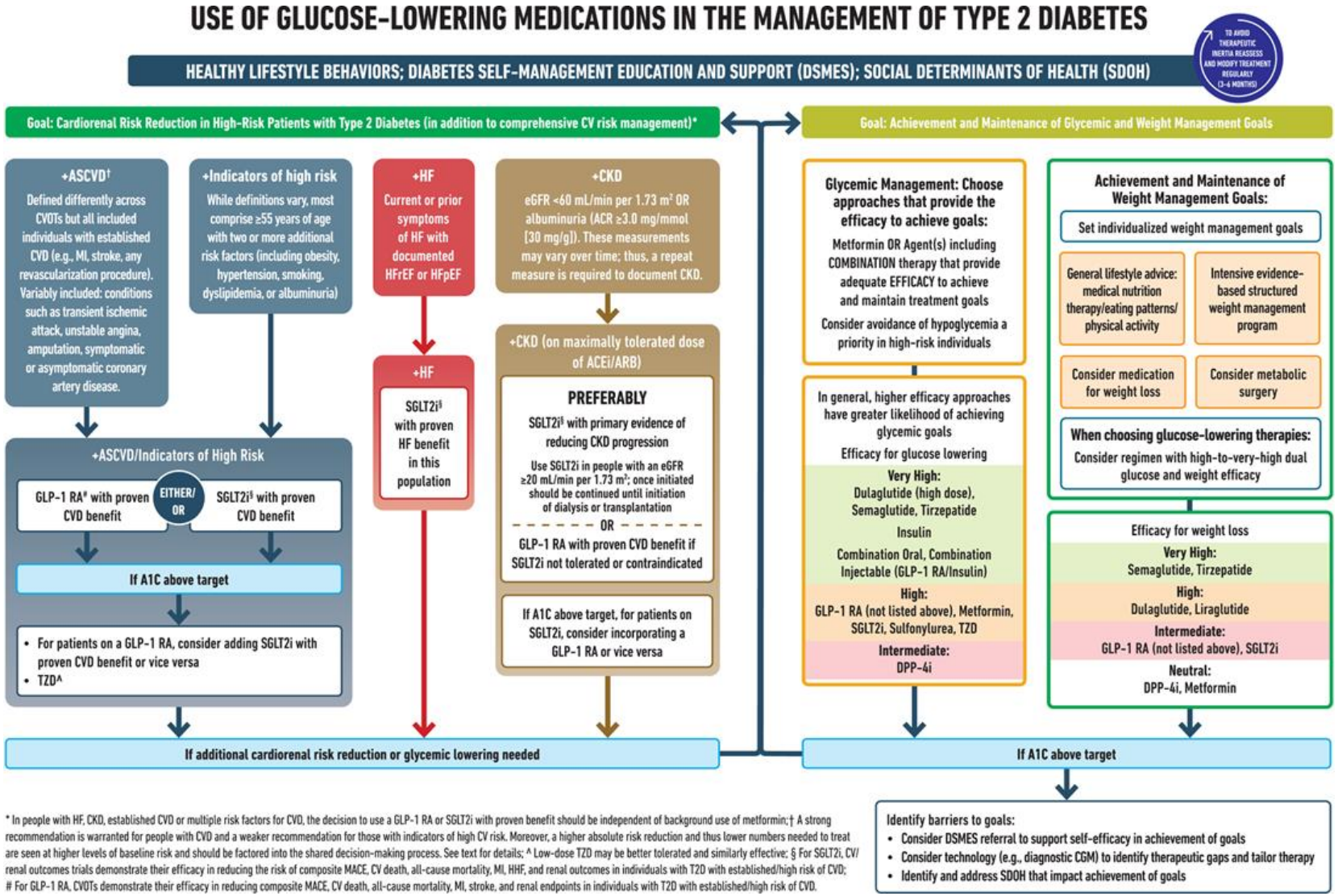
Diabetes Education SERVICES™

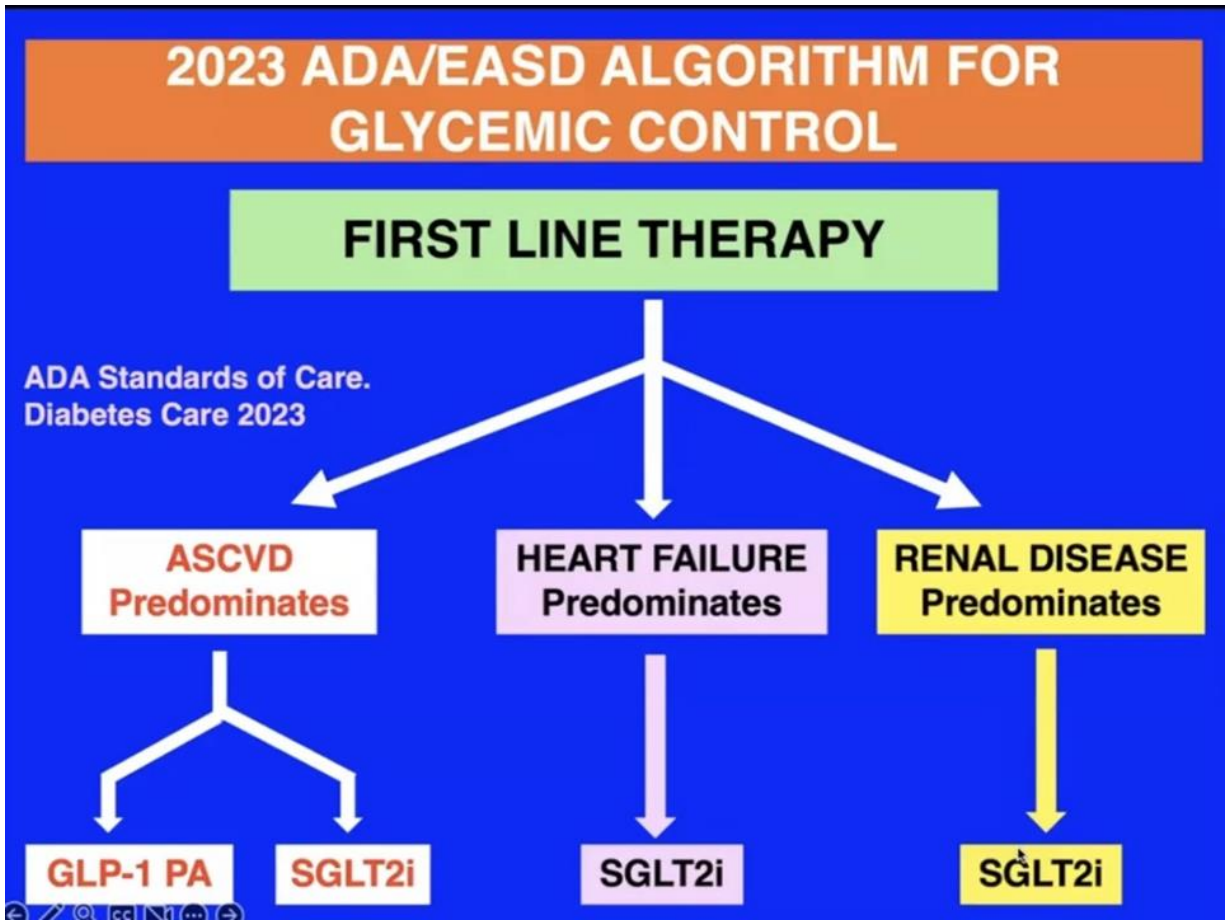
Diabetes Med & Insulin Pocket Cards

https://diabetesed.net/pocket-cards-insulin-and-diabetes-medication/

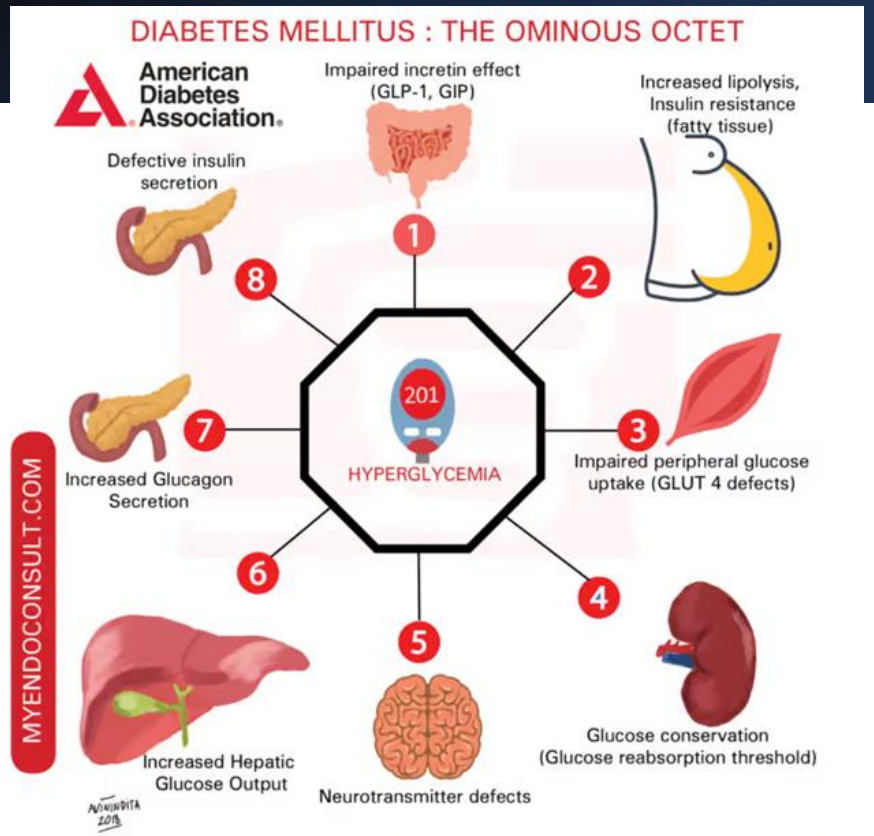
Type 2 Diabetes Medication/Treatment Decision Tree

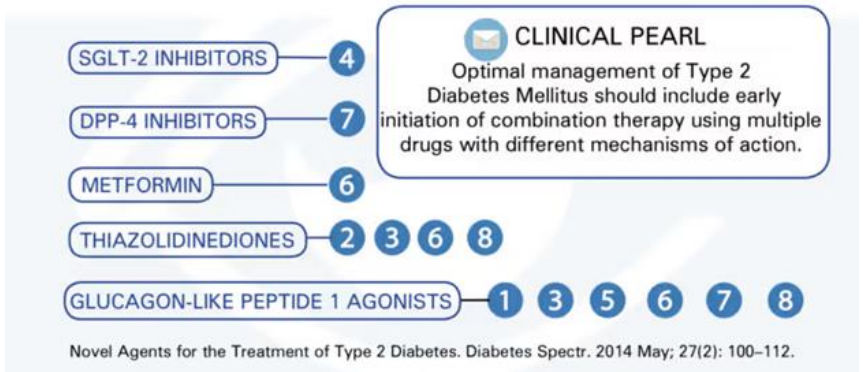
ADA Guidelines 2024




2023 ADA/EASD ALGORITHM FOR GLYCEMIC CONTROL
FIRST LINE THERAPY
ADA Standards of Care.
Diabetes Care 2023
ASCVD Predominates
HEART FAILURE Predominates
RENAL DISEASE Predominates
GLP-1 PA
SGLT2i
SGLT2i
SGLT2i

Ominous Octet of Type 2 Diabetes Mellitus





- Optimal management of Type 2 Diabetes should include early initiation of combination therapy using multiple drugs with different mechanisms of action versus a treat to fail approach.

- The goal in treating PWD is to preserve pancreatic function ~ combination therapy helps meet this goal.

DeFronzo, Ralph (2009) From the triumvirate to the ominous octet: A new paradigm for the treatment of type 2 diabetes mellitus. Diabetes, vol. 58.

Dr. Ralph DeFronzo

"The Godfather of Diabetes" 😆

https://youtu.be/aiojX2mJVqA

Obesity & Weight Management for the Prevention & Treatment of Type 2 Diabetes

In people with T2DM and overweight or obesity, modest weight loss improves glycemia and reduces the need for glucose lowering medications, and larger weight loss, strongly improves glycemia and often leads to remission of diabetes, improved quality of life, CV outcomes, & mortality.

Obesity & Weight Management for the Prevention & Treatment of Type 2 Diabetes

Recommendations for Obesity Management

Behavioral

Pharmacological

Surgical

Obesity & Weight Management for the Prevention & Treatment of Type 2 Diabetes

Pharmacotherapy

Preferred therapy is a glucagon-like peptide 1 receptor agonist or dual glucose dependent insulinotropic polypeptide and glucagon-like peptide 1 receptor agonist with greater weight loss efficacy.

semaglutide (Ozempic)

tirzepatide (Mounjaro)

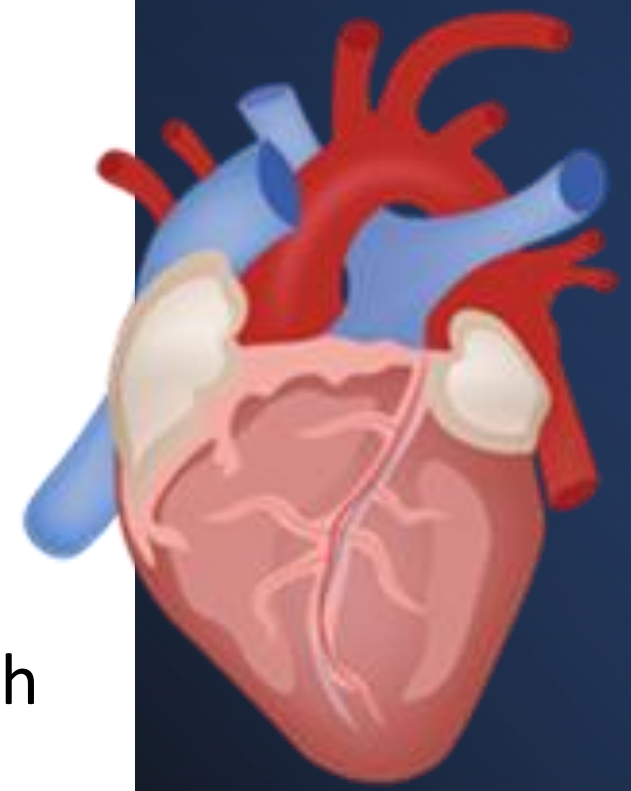
Obesity & Weight Management for the Prevention & Treatment of Type 2 Diabetes

GLP-1 or GLP-1/GIP Agonist

"Background nausea" is common	Reduce risk of nausea with smaller portions and avoiding fried, fatty, greasy foods	Go to the hospital if severe abdominal pain	Report mass in neck, dysphagia, dyspnea, persistent hoarseness
It is not medication OR lifestyle modification. It should be both!	Strength training and resistance training to prevent loss of muscle mass	Double weight loss with lifestyle changes	Recommend high protein foods, fruits, vegetables and weight/resistance training to help prevent muscle loss.

GLP- 1 RA Benefits

- **CV benefit**, weight loss, NAFLD benefits, some renal benefit
- Contraindication in medullary thyroid CA, pancreatitis, gastroparesis
- Warning for worsening retinopathy (can occur with large shifts in blood sugars, just like with insulin)
- Semaglutide (Ozempic) has a new warning for intestinal blockage.



GLP-1 & GLP-1/GIP Agonist

TAKING RYBELSUS
FIRST THING IN THE MORNING
ON AN EMPTY STOMACH
WITH ONLY 4oz PLAIN WATER
WAIT 30 MIN BEFORE FOOD AND OTHER MEDICATIONS

RESEARCH SUMMARY

Tirzepatide vs. Semaglutide Once Weekly in Patients with Type 2 Diabetes

Frías JP et al. DOI: 10.1056/NEJMoa2107519

CLINICAL PROBLEM

Not all patients with type 2 diabetes have adequate glucose control with metformin monotherapy. Tirzepatide is a dual glucose-dependent insulinotropic polypeptide and glucagon-like peptide-1 (GLP-1) receptor agonist under development for treatment of diabetes; how it compares with the selective GLP-1 receptor agonist semaglutide is unknown.

CLINICAL TRIAL

Design: An international, randomized, open-label, phase 3, noninferiority trial was conducted to compare tirzepatide with semaglutide in adults with type 2 diabetes.

Intervention: 1879 adults with inadequately controlled diabetes despite metformin treatment were assigned to a once-weekly subcutaneous injection of tirzepatide (5, 10, or 15 mg) or semaglutide (1 mg) for 40 weeks. The primary efficacy end point was the change in glycated hemoglobin level from baseline to 40 weeks.

RESULTS

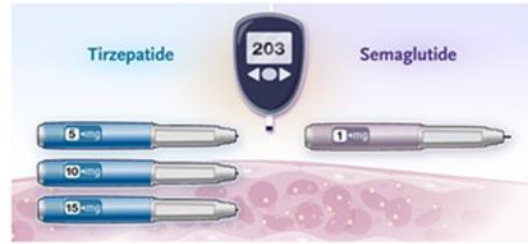
Efficacy: All three tirzepatide doses were noninferior to and also superior to semaglutide with respect to the mean reduction in glycated hemoglobin level. Patients in the tirzepatide groups also lost more weight than those in the semaglutide group.

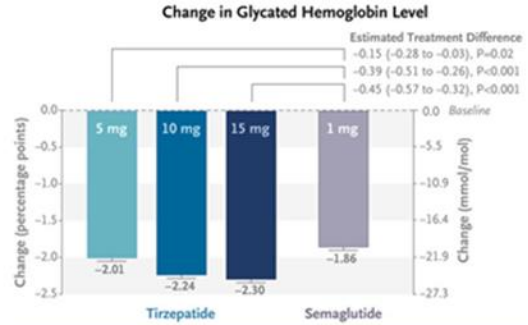
Safety: The percentage of patients reporting any adverse event was similar across the groups, with gastrointestinal events most common. However, serious adverse events were reported by 5.3 to 7.0% of patients in the tirzepatide groups and 2.8% of those in the semaglutide group.

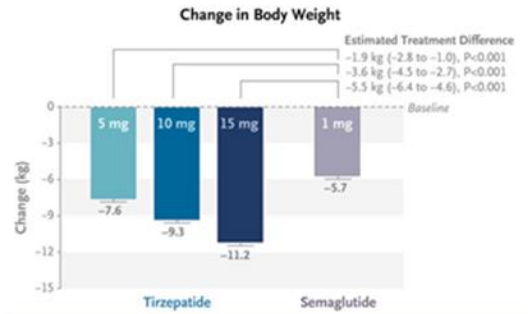
LIMITATIONS AND REMAINING QUESTIONS

- Treatments were not blinded because of differences in devices and dose-escalation schemes (although individual tirzepatide doses were blinded).
- Higher doses of semaglutide were not compared with tirzepatide.
- Black patients accounted for only 4% of the trial population, so generalizability of the findings is limited.
- How tirzepatide performs in patients with increased cardiovascular risk requires further study.

Links: Full Article | NEJM Quick Take | Editorial







CONCLUSIONS

Tirzepatide was noninferior and also superior to semaglutide in reducing glycated hemoglobin levels in adults with type 2 diabetes.

Retatrutide ~ Triple Hormone Receptor Agonist for Obesity

Contributes to a reduction in blood sugar

By boosting the release of insulin and lowering the release of glucagon, Retatrutide is able to combat obesity and type 2 diabetes. Glucagon is a hormone that contributes to an increase in blood sugar levels

Aids in the reduction of body fat

Retatrutide is effective in reducing appetite as well as preventing the formation of fat.

Reduces the severity of fatty liver disease

The synthesis of glucagon is boosted by Retatrutide, which in turn helps decrease fat in the liver. Glucagon not only causes an increase in glucose levels, but it also assists in the elimination of fat from the liver. Retatrutide, in conjunction with two additional methods, lowers both the amount of sugar in the blood and the amount of excess fatty acids in the liver.

Jasterboff et al. (2023) Triple-Horomone-Receptor Agonist Retatrutide for Obesity-A Phase 2 Trail. N. Engl J Med.

Diabetes Core Update Podcasts

Diabetes Core Update is a monthly audio podcast devoted to presenting and discussing the latest clinically relevant articles from ADA's four scholarly journals— ***Diabetes***, ***Diabetes Care***, ***Clinical Diabetes***, and ***Diabetes Spectrum***—as well as notable articles from other journals related to diabetes research and care. Each episode is approximately 30 minutes long and includes discussion of 4–6 recently published articles and interviews with authors. Intended for the busy health care professional Diabetes Core Update examines how the latest research and information published in ADA journals and beyond are relevant to clinical practice and can be applied in a treatment setting.

For more information about each of ADA's science and medical journals, please visit diabetesjournals.org.

Presented by:
Neil Skolnik, M.D. , Professor of Family and Community Medicine, Sidney Kimmel Medical College, Thomas Jefferson University; Associate Director, Family Medicine Residency Program, Abington Jefferson Health

https://diabetesjournals.org/journals/pages/podcasts_obesity

Nonalcoholic Fatty Liver Disease & Nonalcoholic Steatohepatitis
Medical Evaluation & Assessment of Comorbidities

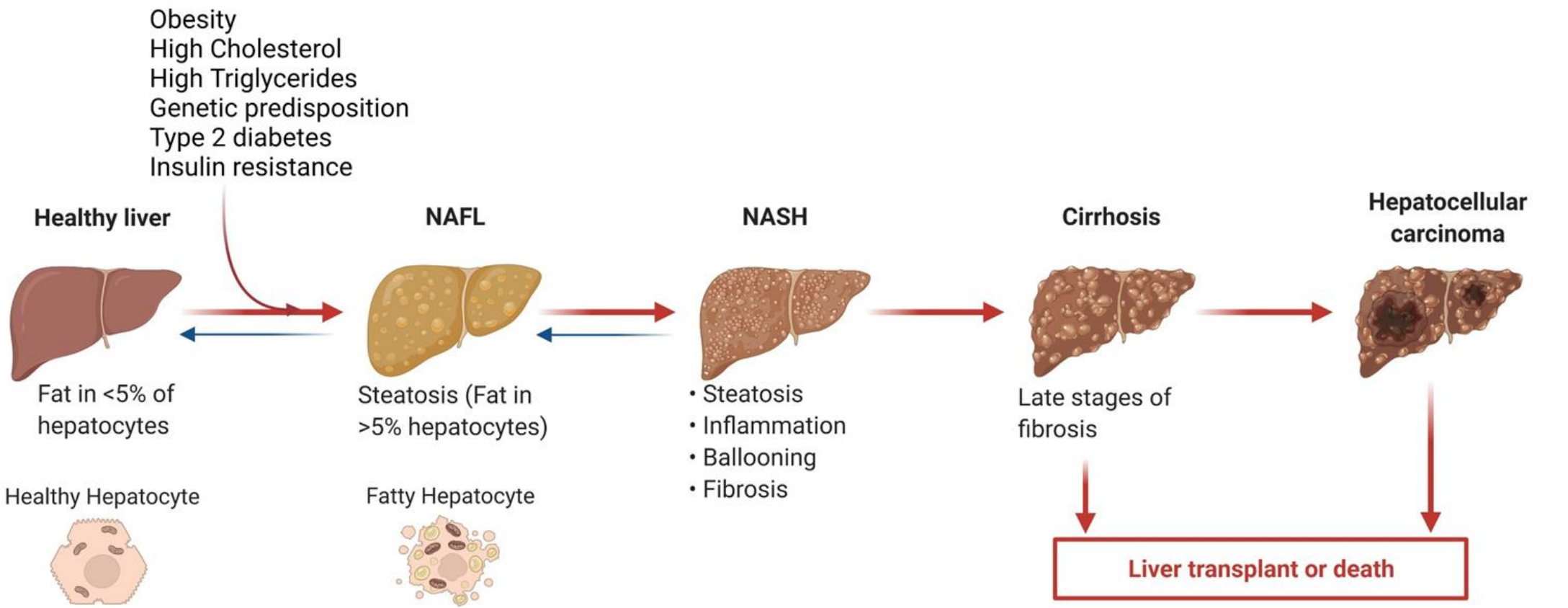
Nonalcoholic fatty liver disease (NAFLD) includes a broad spectrum of disease, ranging from hepatic steatosis (with & without inflammation) to nonalcoholic steatohepatitis (NASH).

Diabetes is a major risk factor for developing NASH, disease progression, and worse liver outcomes.

Recent studies in adults in the U.S. estimated that NAFLD is prevalent in > 70% of people with Type 2 diabetes.

The risk is higher in people who have central obesity and cardiometabolic risk factor or insulin resistance, are > 50 years of age, and/or have persistently elevated plasma aminotransferases (AST and/or ALT > 30 units/L or > 6 months).

While steatohepatitis and cirrhosis occur in lean PWD & are believed to be linked to genetic predisposition, IR, & environmental factors, there is ample evidence to implicate excess visceral & overall adiposity in people with overweight & obesity in the pathogenesis of the disease.



Created with BioRender.com

Nonalcoholic Fatty Liver Disease & Nonalcoholic Steatohepatitis

Management in people with T2DM

- *At present there are no FDA-approved drugs for the treatment of NASH ~* The treatment is centered on treating hyperglycemia & obesity.
- A minimum weight loss goal of 5%, but preferably greater or equal to 10% is needed to improve liver histology, with fibrosis requiring the larger weight reduction to promote change.
- Pioglitazone and some GLP-1 RA have been shown to be effective to treat steatohepatitis & may slow the progression & decrease CV disease, which is the number one cause of death in people with T2DM & NAFLD.

Pioglitazone

- Improves glucose & lipid metabolism and reverses steatohepatitis
- Causes dose-dependent weight gain (15 mg/day, mean of 1-2%; 45 mg/day , 3-5%) ~ need to ensure dietary changes and physical activity.
- Can also increase fracture risk, may promote heart failure, & may be a link to bladder cancer.

A meta-analysis concluded that pioglitazone treatment results in resolution of NASH and may improve fibrosis.

Musso G. Cassader m, Paschetta E, Gamino R. Thiazolidinediones and advanced liver fibrosis in nonalcoholic steatohepatitis: a meta-analysis. JAMA Intern Med 2017; 177: 633-640

Nonalcoholic Fatty Liver Disease & Nonalcoholic Steatohepatitis

GLP-1 RAs

Are effective at inducing weight loss and improve elevated plasma aminotransferases and steatosis. There are 2 RCTs of GLP-1 RA. A small study with liraglutide (Victoza) and more recently, with semaglutide (Ozempic).

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

A Placebo-Controlled Trial of Subcutaneous Semaglutide in Nonalcoholic Steatohepatitis

P.N. Newsome, K. Buchholtz, K. Cusi, M. Linder, T. Okanoue, V. Ratziu, A.J. Sanyal, A.-S. Sejling, and S.A. Harrison, for the NN9931-4296 Investigators*

ABSTRACT

BACKGROUND

Nonalcoholic steatohepatitis (NASH) is a common disease that is associated with increased morbidity and mortality, but treatment options are limited. The efficacy and safety of the glucagon-like peptide-1 receptor agonist semaglutide in patients with NASH is not known.

METHODS

We conducted a 72-week, double-blind phase 2 trial involving patients with biopsy-confirmed NASH and liver fibrosis of stage F1, F2, or F3. Patients were randomly assigned, in a 3:3:3:1:1:1 ratio, to receive once-daily subcutaneous semaglutide at a dose of 0.1, 0.2, or 0.4 mg or corresponding placebo. The primary end point was resolution of NASH with no worsening of fibrosis. The confirmatory secondary end point was an improvement of at least one fibrosis stage with no worsening of NASH. The analyses of these end points were performed only in patients with stage F2 or F3 fibrosis; other analyses were performed in all the patients.

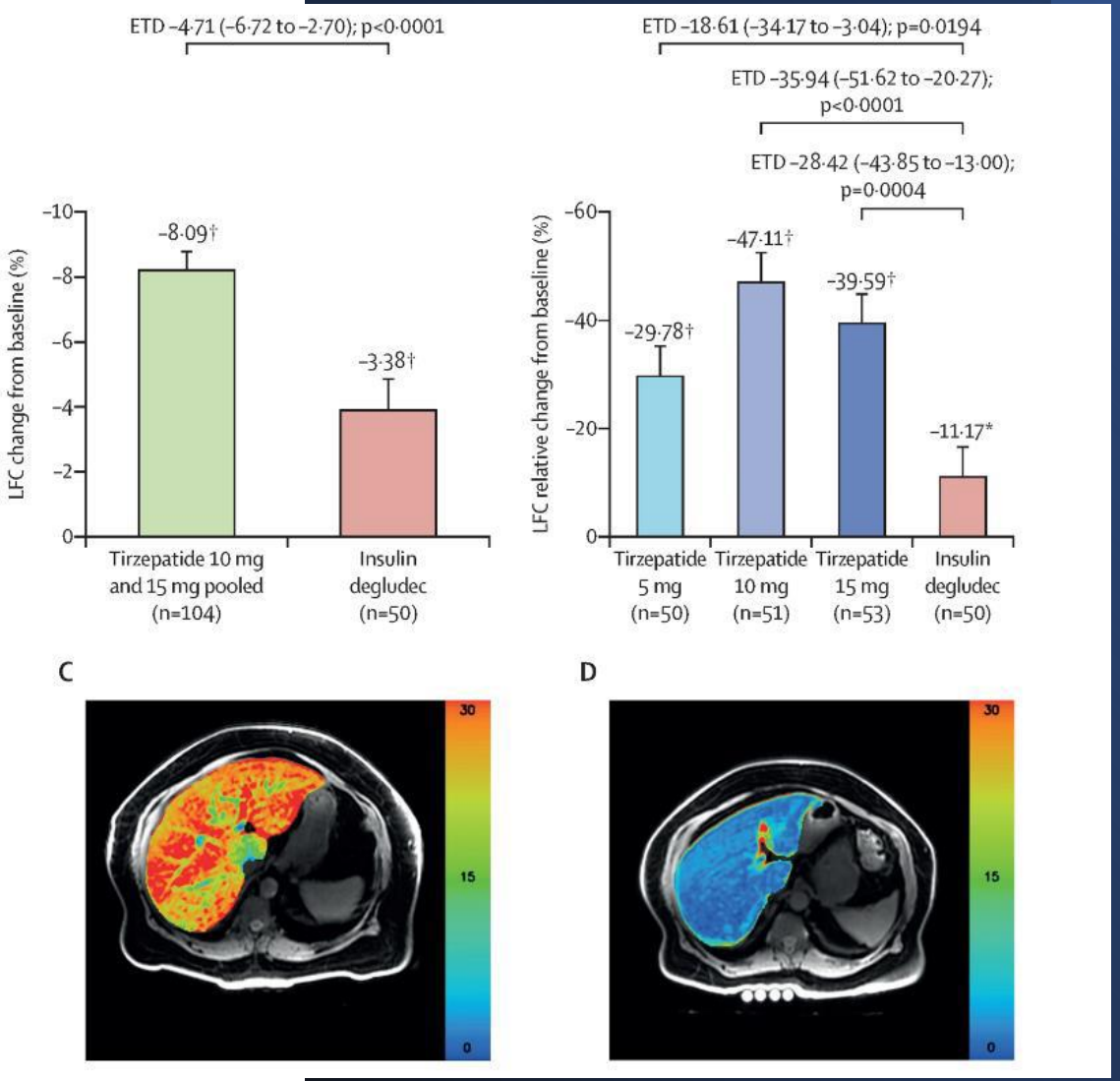
RESULTS

In total, 320 patients (of whom 230 had stage F2 or F3 fibrosis) were randomly assigned to receive semaglutide at a dose of 0.1 mg (80 patients), 0.2 mg (78 patients), or 0.4 mg (82 patients) or to receive placebo (80 patients). The percentage of patients in whom NASH resolution was achieved with no worsening of fibrosis was 40% in the 0.1-mg group, 36% in the 0.2-mg group, 59% in the 0.4-mg group, and 17% in the placebo group ($P<0.001$ for semaglutide 0.4 mg vs. placebo). An improvement in fibrosis stage occurred in 43% of the patients in the 0.4-mg group and in 33% of the patients in the placebo group ($P=0.48$). The mean percent weight loss was 13% in the 0.4-mg group and 1% in the placebo group. The incidence of nausea, constipation, and vomiting was higher in the 0.4-mg group than in the placebo group (nausea, 42% vs. 11%; constipation, 22% vs. 12%; and vomiting, 15% vs. 2%). Malignant neoplasms were reported in 3 patients who received semaglutide (1%) and in no patients who received placebo. Overall, neoplasms (benign, malignant, or unspecified) were reported in 15% of the patients in the semaglutide groups and in 8% in the placebo group; no pattern of occurrence in specific organs was observed.

Nonalcoholic Fatty Liver Disease & Nonalcoholic Steatohepatitis

GLP-1 RA/GIP

Another study is almost completed on the effect of tirzepatide (Mounjaro) versus degludec (Tresiba) on liver fat content and abdominal adipose tissue in people with T2DM (SURPASS-3 MRI): a substudy of the randomized, open label, parallel-group, phase 3 SURPASS-3 trial.



Gastaldelli A et al. (2022). Lancet Diabetes Endocrinol. 10:393-406

Nonalcoholic Fatty Liver Disease & Nonalcoholic Steatohepatitis

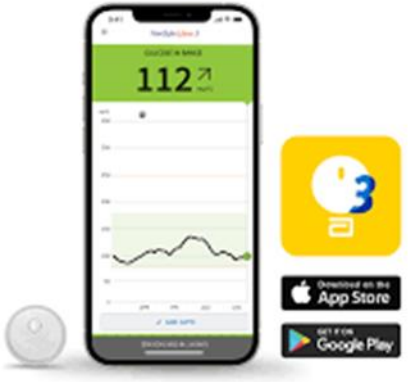
Metabolic Surgery

Metabolic surgery improves NASH & cardiometabolic health.

Meta-analyses report that 70-80% of people have improvement of hepatic steatosis, 50-75% in inflammation & hepatocyte ballooning (necrosis), and 30-40% in fibrosis.

Diabetes Technology
CGMs

Dexcom G7 & G6



FreeStyle Libre 3

Medtronic Guardian 4

Eversense

Diabetes Technology

Tandem Insulin Pumps

Diabetes Technology
Omnipod 5 Insulin Pump

Diabetes Technology
Medtronic 780G Insulin Pump

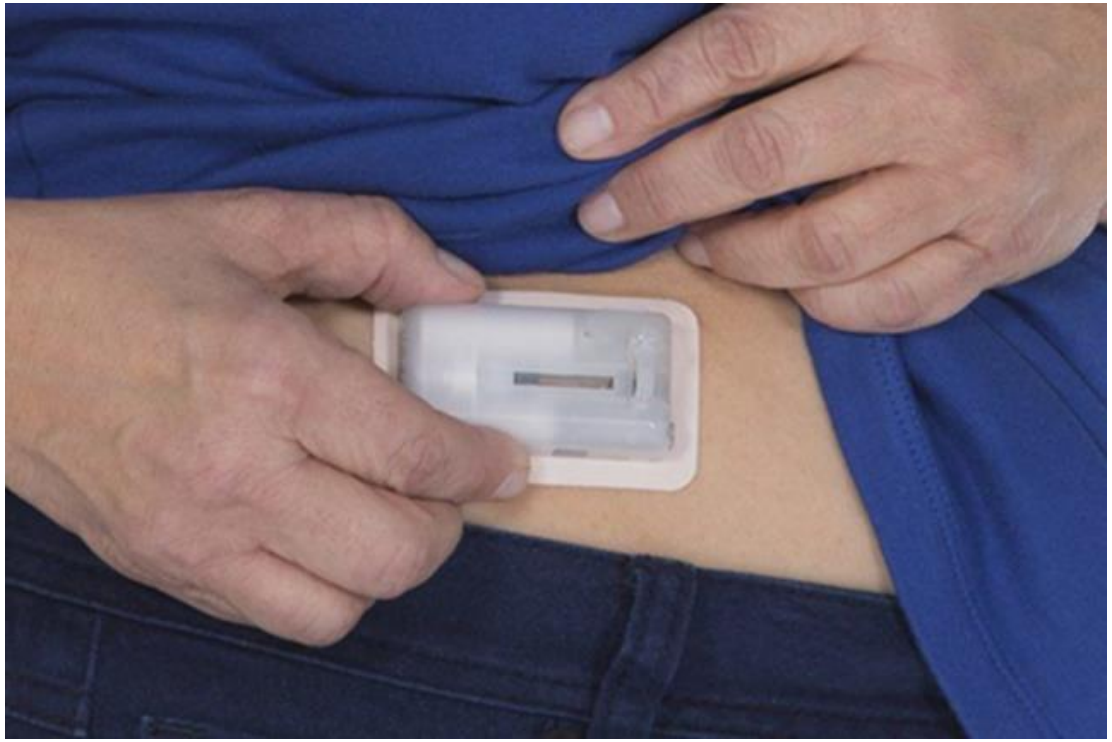
Diabetes Technology

Beta Bionic Insulin Pump

NO Carb Counting!

Diabetes Technology
Patch Pumps

Simplicity Patch Pump



V-Go Patch Pump

Diabetes Technology
Smart Pens

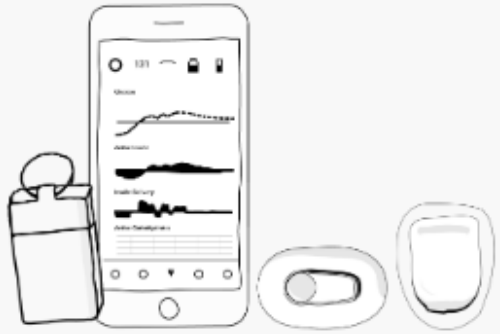
InPen

Tempo

Compare ☐

SENSOR WITH SMART PUMP

Loop with Dexcom G6 & OmniPod Smart System



Loop is a DIY (do-it-yourself) system. It takes some work to set up, but allows you to think about diabetes less by automating basal insulin delivery based on predicted glucose levels.

Compare ☐

SENSOR WITH SMART PUMP

Loop with Dexcom G6 & Medtronic Pump Smart System

Loop is a DIY (do-it-yourself) system. It takes some work to set up but allows you to think about diabetes less by automating basal insulin delivery based on predicted glucose levels.

Compare ☐

SENSOR & PUMP

Dexcom G6 & Omnipod

Omnipod is the only tubeless pump option. This paired with the G6 is a common choice for active people.

https://diabeteswise.org/

Diabetes Care in the Hospital
Glycemic Goals

Perform an A1c test on all PWD or hyperglycemia (random glucose > 140 mg/dL)

Institutions should develop structured order sets/ hyperglycemic protocols.

Insulin and or other therapies should be initiated or intensified for treatment of persistent hyperglycemia starting at a threshold of > 180 mg/dL.

Goal of 140-180 mg/dL is recommended for most critically ill (ICU) people with hyperglycemia.

Goal of 100-180 mg/dL recommended for the noncritical care setting.

Diabetes Care in the Hospital
Glucose Monitoring/Self Management

In PWD using a CGM, the use of it should be continued, if appropriate, with a confirmatory POC glucose measurements for insulin dosing.

For PWD using an AID system along with CGM should be continued, if clinically appropriate, with a confirmatory POC glucose measurements for insulin dosing. This is to be done with proper staff training and supervision.

Diabetes Care in the Hospital
Glucose-lowering Treatment ~ INSULIN

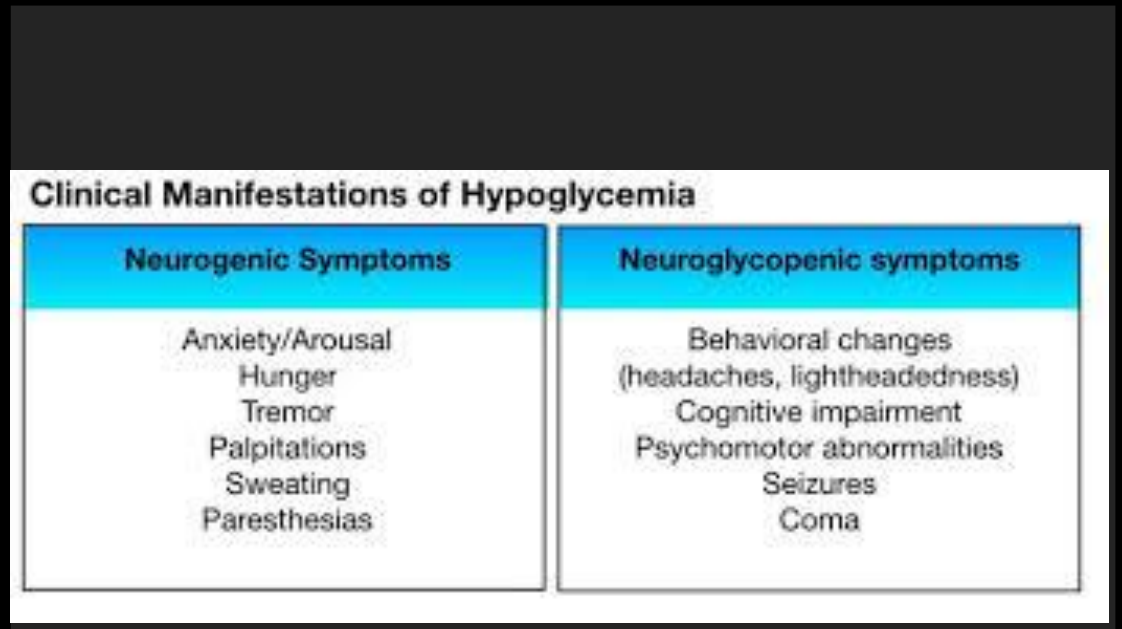
- Basal Insulin or a basal plus bolus correction plan is preferred treatment for non-critically ill individuals with poor intake or those who are NPO.
- An insulin plan with basal, prandial, and correction components is the preferred treatment for most non-critically ill individuals with adequate oral intake.
- For critically ill patients a continuous intravenous insulin infusion is the most effective method for achievement of glycemic goals.
- Recommendations to use one type of insulin and or oral agents to avoid confusion

Diabetes Care in the Hospital
Glucose-lowering Treatment ~ NONINSULIN THERAPIES

- DPP-4 inhibitors have demonstrated safety and efficacy.
  STOP alogliptin and saxagliptin in people who develop HF.

- GLP-1 RA are still mostly limited to research studies and select populations.

- SGLT-2 Inhibitors should be avoided in cases of severe illness, presence of ketonuria or ketonemia & during prolonged fasting and surgical procedure. The FDA has warned these drugs should be stopped 3 days before scheduled surgeries.



Diabetes Care in the Hospital
Hypoglycemia

A standardized hospital-wide, nurse-initiated hypoglycemia treatment protocol should be in place to immediately address BG levels < 70 mg/dL.

Diabetes Care in the Hospital
Perioperative Care

- Surgical stress and counterregulatory hormone release increase the risk of hyperglycemia, as well as mortality, infection, and LOS. An A1c goal of <8.0% when possible, for elective surgeries.

- BG goal 100-180 mg/dL.

Metformin should be held the day of surgery

SGLT-2 Inhibitors should be discontinued 3-4 days before surgery

Hold other oral glucose lowering agents the day of surgery

On morning of surgery or procedure give ½ of NPH dose

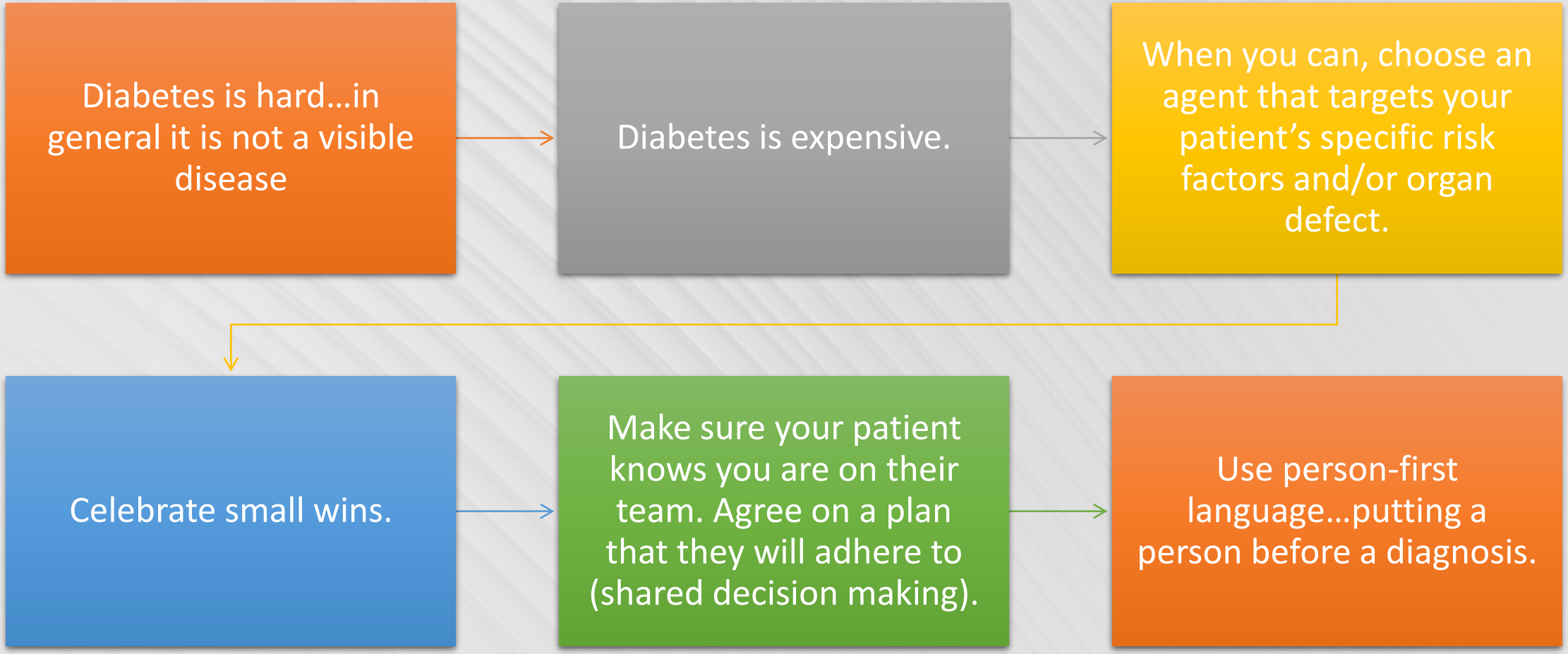
Lower the dose of long-acting insulin by 25% given the evening before surgery

Diabetes Care in the Hospital
Perioperative Care~ GLP-1 RA

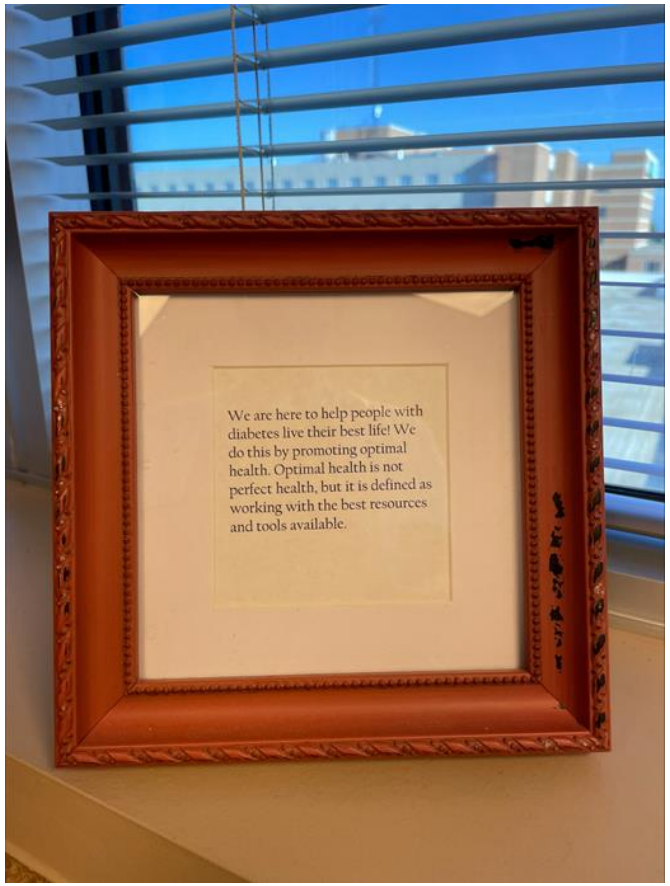
There is little data on the safe use of GLP-1 RA on glycemia and delayed gastric emptying. The **American Society of Anesthesiologists** has a consensus-based guidance on GLP-1RA for people with elective surgeries:

Hold on	For people on daily dosing can hold on the day of the procedure/surgery
Consider	For people on weekly dosing consider holding a week prior to procedure/surgery
Consider	If patient has any type of GI symptoms present, consider delaying elective procedure and discuss the concerns of potential risk of regurgitation and pulmonary aspiration of gastric contents.

Other Takeaways



Mission Statement



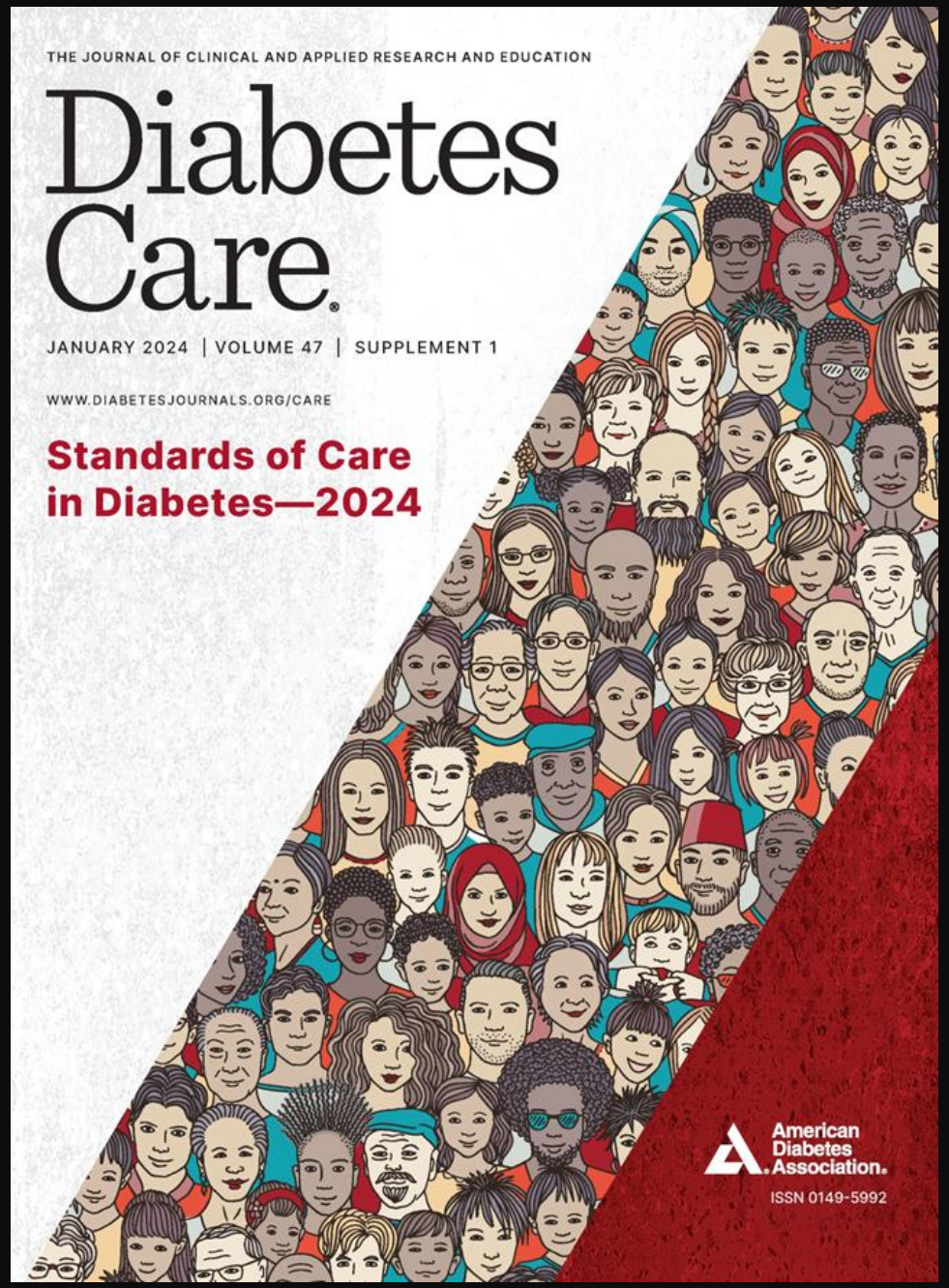
We are here to help people with diabetes live their best life!

We do this by promoting optimal health.

Optimal health is not perfect health, but it is defined as working with the best resources and tools available.

ADA Standards of Care 2024 Resources

https://diabetesjournals.org/care/issue/47/Supplement_1



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OKC, OK 73112

Kelly.lang@integrishealth.com

405-388-8216 cell

Resources

Centers for Disease Control and Prevention. National Diabetes Statistics Report website. https://www.cdc.gov/diabetes/data/statistics-report/index.html. Accessed [2023].

Diabetes Care. (January 2024, vol 47, supplement 1. www.diabetesjournal.org/care

DeFronzo, Ralph (2009) From the triumvirate to the ominous octet: A new paradigm for the treatment of type 2 diabetes mellitus. Diabetes, vol. 58.

Girish et. Al (2013) American Society of Anesthesiologists Consensus-Based Guidance on Preoperative Management of Patients on Glucagon-Like Peptide-1 Receptor Agonists

Jasterboff et al. (2023) Triple-Horomone-Receptor Agonist Retatrutide for Obesity-A Phase 2 Trail. N. Engl J Med.

Gastaldelli et al. (2022) Effect of tirzepatide versus insulin degludec on liver fat content and abdominal adipose tissue in people with Type 2 diabetes (SURPASS-# MRI): a substudy of the randomized, open-label, parallel-group, phase 3 SURPASS-3 trial. Lancet Diabetes Endocrinol. 10:393-406, 2022.