DiabetesEd Training Conference Syllabus

October 9th-11th, 2024

Presented By:

Coach Beverly Thomassian, RN, MPH, CDCES, BC-ADM

Diana Isaacs, PharmD, BCPS, BC-ADM, BCACP, CDCES, FADCES

Jessica Jones, MS, RDN, CDCES

DiabetesEd Training Conference – San Diego
October 9th-11th, 2024

Welcome

We are proud to welcome you to our 25th Annual DiabetesEd Training Conference. Your attendance demonstrates a commitment to advocating for best diabetes care for the 38.4 million Americans with diabetes. We encourage you to share the new ideas and information garnered from this conference with your community and colleagues. As advocates, specialists, and coaches, we believe we can make a dramatic difference in improving the quality of life for people with prediabetes and diabetes using a person-centered, evidenced-based, compassionate approach coupled with curiosity. Thank you for your participation, and we invite you to enjoy the program.

Faculty Biographies

Beverly Dyck Thomassian, RN, MPH, BC-ADM, CDCES

As president of Diabetes Education Services, Beverly Thomassian, RN, MPH, CDCES, BC-ADM, believes that we can improve diabetes care through education, advocacy and curiosity. As a diabetes coach, she promotes excellence in care through her live courses and webinar presentations. As a Diabetes Nurse Specialist who is Board Certified in Advanced Diabetes Management, Beverly has a twenty-year history of being an innovator, leader and mentor.

In addition to running her company, she is an Associate Clinical Professor at the University of California, San Francisco, (UCSF) and a visiting professor at California State University, Chico (CSU Chico). As a Diabetes Nurse Specialist at a local Indian Health Services Health Center, she keeps her clinical skills fresh through one-on-one consultation, provider collaboration and quality improvement initiatives.

Diana Isaacs, PharmD, BCPS, BCACP, CDCES, BC-ADM, FADCES, FCCP

Diana Isaacs was 2020 ADCES Diabetes Educator of the Year for her educational platform promoting the use of CGM for people with diabetes and other innovations. Dr. Isaacs was awarded the Ohio Pharmacists Association Under 40 Award in 2019. She serves in leadership roles for several pharmacies and diabetes organizations. She has numerous diabetes publications and research projects with a focus on medications, CGM and diabetes technology. Dr. Isaacs is a contributing author for the 2023 ADA Standards of Care.

For the past three years, Dr. Isaacs has served as a contributing author for the ADA Standards of Care. As the Program Coordinator and clinical pharmacist specialist in the Cleveland Clinic Diabetes Center, Dr. Isaacs brings a wealth of clinical knowledge combined with extensive research and speaking experience to this program.

Jessica Jones, MS, RDN, CDCES

Jessica is a nationally recognized Registered Dietitian Nutritionist and Certified Diabetes Care & Education Specialist committed to making nutrition education accessible to everyone. As the CEO and co-founder of Diabetes Digital, Jessica has been pivotal in developing an innovative telehealth platform that provides tailored nutrition counseling for individuals with diabetes and prediabetes. Additionally, she co-hosts the Diabetes Digital Podcast, engaging listeners with thoughtful conversations on managing diabetes. With over a decade of clinical experience, Jessica has contributed significantly to the field through her co-authorship of the "28-Day Plant-Powered Health Reboot" cookbook and "A Diabetes Guide to Enjoying the Foods of the World." She also wrote the Diabetes Chapter for the Food and Nutrition Care Manual Textbook and regularly shares her insights as a columnist for SELF magazine.

As a co-founder of Food Heaven, an online platform and podcast with more than 5 million downloads, she offers essential resources on cooking, intuitive eating, and embracing body respect. Jessica's contributions have been celebrated in prominent publications, including Oprah Magazine, Women's Health, The Food Network Magazine, SELF Magazine, the Huffington Post, and Bon Appetit.

Staff Biographies and Accreditation

Lonnie Vaughn, RNC, BSN, CDCES – Onsite Program Manager
As a leader in the field of diabetes management, Lonnie has been championing best care practices at Doctor's Hospital in Modesto for over 30 years. As a certified diabetes educator, trainer, mentor and advocate, her passion and commitment to improving diabetes care is valued by patients and professionals alike. Lonnie's expertise and experience uniquely qualify her to address a multitude of diabetes related topics that not only inform but inspire.

Tiffany Bergeron – Onsite Customer Advocate
Tiffany brings a wealth of experience and a strong commitment to supporting the customer experience at Diabetes Education Services. Her background includes managing CRM and website content, event coordination, and administrative duties. She excels in ensuring seamless communication with customers. Her ability to respond effectively to customer service calls and guide customer inquiries demonstrates her dedication to providing exceptional support.

Accreditation Info
Diabetes Education Services is an approved provider by the California Board of Registered Nursing, Provider 12640, and our CPEU courses have received Prior Approval* from the Commission of Dietetic Registration (CDR), Provider DI002. Need hours for your CDCES? We have great news. This program is accredited by the CDR so all hours of instruction can be used to renew your CDCES regardless of your profession.

We are overjoyed that you are joining us! Please let us know how we can be of more service!

Sincerely,

Coach Beverly Thomassian

Beverly Thomassian, RN, MPH, CDCES, BC-ADM
President and Founder, Diabetes Education Services
DiabetesEd.Net

DiabetesEd Training Conference |San Diego *

Day One | October 9, 2024 (Pacific Time)

Standards of Care, Meds for Type 2 & Addressing Cardiovascular Disease

Time	Topic	Speakers
7:30 – 8:00am	**Breakfast & Welcome**	
8:00 – 10:00	**Current State of Diabetes ADA Standards of Care** **Person Centered Care for Type 1, Type 2, LADA, GDM**	Beverly Dyck Thomassian, RN, BC-ADM, MPH, CDCES and
10:00 – 10:15	**Break**	Diana Isaacs, PharmD, BCPS, BCACP, CDCES, BC-ADM, FADCES, FCCP
10:15 – 12:00	**Medical Evaluation, Risk Identification** **Diabetes Prevention** **Glycemic targets across the Lifespan**	
12:00 – 1:00	**Lunch Break**	
1:00 – 2:30	**Hypoglycemia prevention & treatment** **Landmark Studies** **Medications for Type 2**	
2:30 – 2:45	**Break**	
2:45– 3:15	**Pharmacology Algorithms - AACE and ADA**	
3:30 – 4:30	**Cardiovascular Monitoring and Management**	
4:30 – 4:45	**Delivering Extraordinary Diabetes Care**	

**Topics, Timing and Speakers Subject to Change*

Diabetes Education Services Presents:

DiabetesEd Specialist Training Conference – Day 1

October 9th – 11th, 2024

Diabetes Education Services and Team

www.DiabetesEd.net

Thank you to our Speakers

Coach Beverly Thomassian

Dr. Diana Isaacs

Jessica Jones

www.DiabetesEd.net

Diabetes Education SERVICES 25 years

Coach Bev has no Conflict of Interest

- She’s not on any speaker's bureau
- Does not invest or have any financial relationships with diabetes related companies.
- Gathers information from reading package inserts, research and articles
- The ADA Standards of Medical Care is main resource for course content

Disclosures for Dr. Isaacs

- Diana Isaacs, PharmD, BCPS, BCACP, CDCES, BC-ADM, FADCES, FCCP declares the following disclosures:
- Speaker: Abbott, Dexcom, Novo Nordisk, Insulet, Medtronic, Lilly, Cequr
- Consultant: Sanofi, Undermyfork
- ADCES Board Member

Diabetes Overview and Glycemic Goals

Objectives:

1. Discuss current Diabetes ADA Standards
2. Describe person-centered care for Type 1, Type 2, LADA, GDM
3. List steps for Medical Evaluation, Risk Identification and Prevention
4. State glycemic targets across the lifespan
5. Discuss hypoglycemia prevention & treatment
6. Describe significance of Landmark Diabetes Studies
7. List medications considerations for Type 2
8. Describe the pharmacology Algorithms
9. Discuss most recent cardiovascular risk mitigation strategies and goals.

17. Diabetes Advocacy

- People living with diabetes deserve to be free from the burden of discrimination.
- We need to all be a part of advocating to ensure a healthy and productive life for people living with diabetes.
- Decrease barriers to diabetes self-management.

Diabetes Care needs to meet outlined standards in all settings.

- In school setting
- Young children in childcare
- For occupational drivers
- In work settings
- In Correctional Institutions

FREE

Global Epidemic

537 million adults are living with diabetes

3 in 4 adults with diabetes live in low- and middle-income countries

Diabetes around the world in 2021

www. DiabetesAtlas.org

- World Diabetes Day is November 14

CDC Announces

35% of Americans will have Diabetes by 2050

Boyle, Thompson, Barker, Williamson

2010, Oct 22:8(1)29

www.pophealthmetrics.com

Poll Question 1

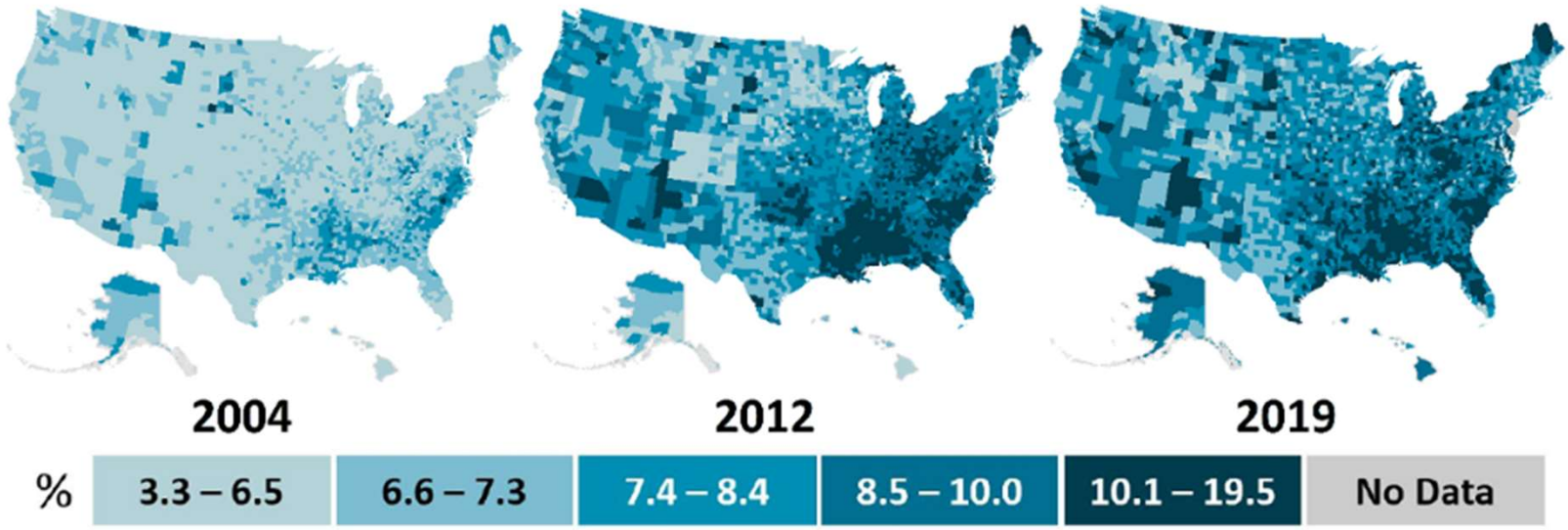
- According to the CDC, what best describes the current prevalence of prediabetes and diabetes in the U.S.?

a. 30% of people above the age of 20 have type 2 diabetes.
b. The rate of type 1 and type 2 diabetes have tripled since 2010.
c. A total of 50% of people have prediabetes or diabetes.
d. 1 out of 2 persons above age 20 have prediabetes.

Type 2 Diabetes in America 2024

- 11.3% with Diabetes - 37 million adults
  - 23% don't know they have it
- 38% with Prediabetes – 96 million adults

Figure 3. Age-adjusted, county-level prevalence of diagnosed diabetes among adults aged 20 years or older, United States, 2004, 2012, and 2019



Data sources: US Diabetes Surveillance System; Behavioral Risk Factor Surveillance System.

Centers for Disease Control and Prevention. National Diabetes Stats Report https://www.cdc.gov/diabetes/data/statistics-report/index.html. Accessed 1/23

1. Improving Care and Promoting Health in Populations

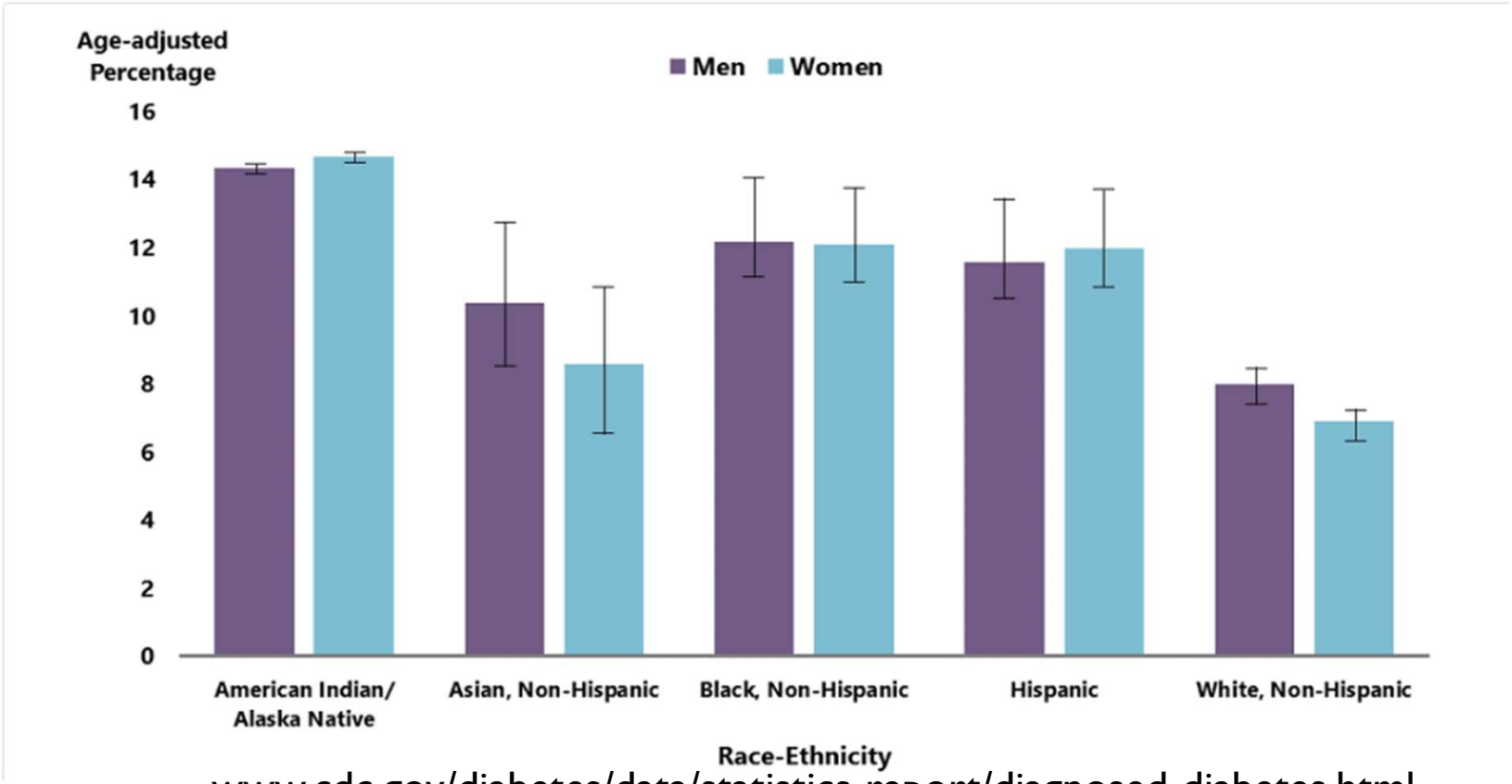
- "Health outcomes of a group of individuals -
  - including the distribution of health outcomes within the group"
- These outcomes can be measured in terms of health:
  - mortality, morbidity, health, and functional status
  - disease burden
    - (incidence and prevalence)
  - behavioral and metabolic factors
    - (exercise, diet, A1C, etc.)

ADA Standards 2024

Diabetes Prevalence by Ethnic Group

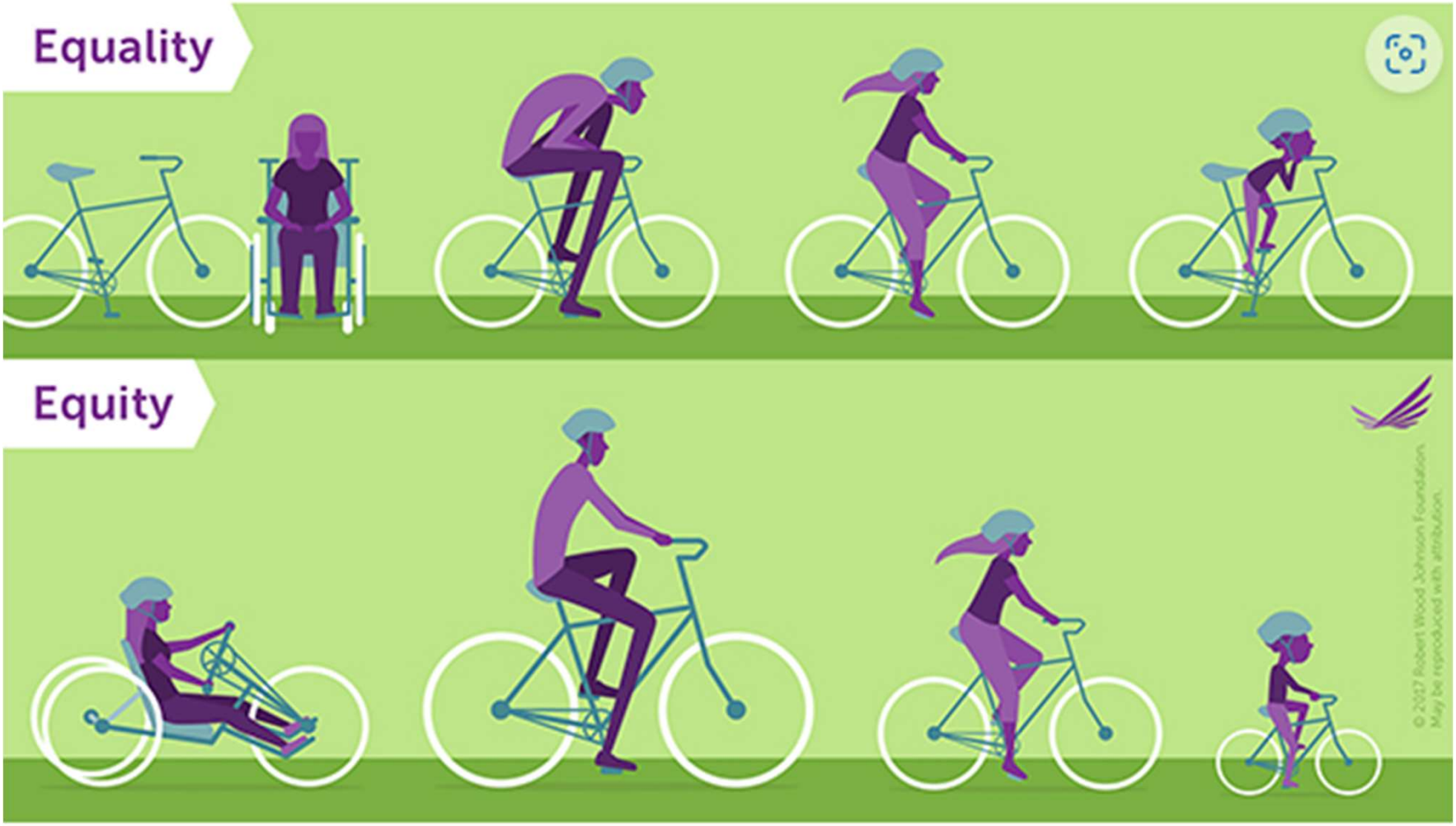
- For adults, diabetes prevalence highest among:
  - American Indians and Alaska Natives (14.5%),
  - Non-Hispanic Blacks (12.1%),
  - People of Hispanic origin (11.8%),
  - Non-Hispanic Asians (9.5%)

Figure 2. Age-adjusted estimated prevalence of diagnosed diabetes by race/ethnicity group and sex for adults aged 18 years or older, United States, 2018–2019



www.cdc.gov/diabetes/data/statistics-report/diagnosed-diabetes.html

Equality vs Equity

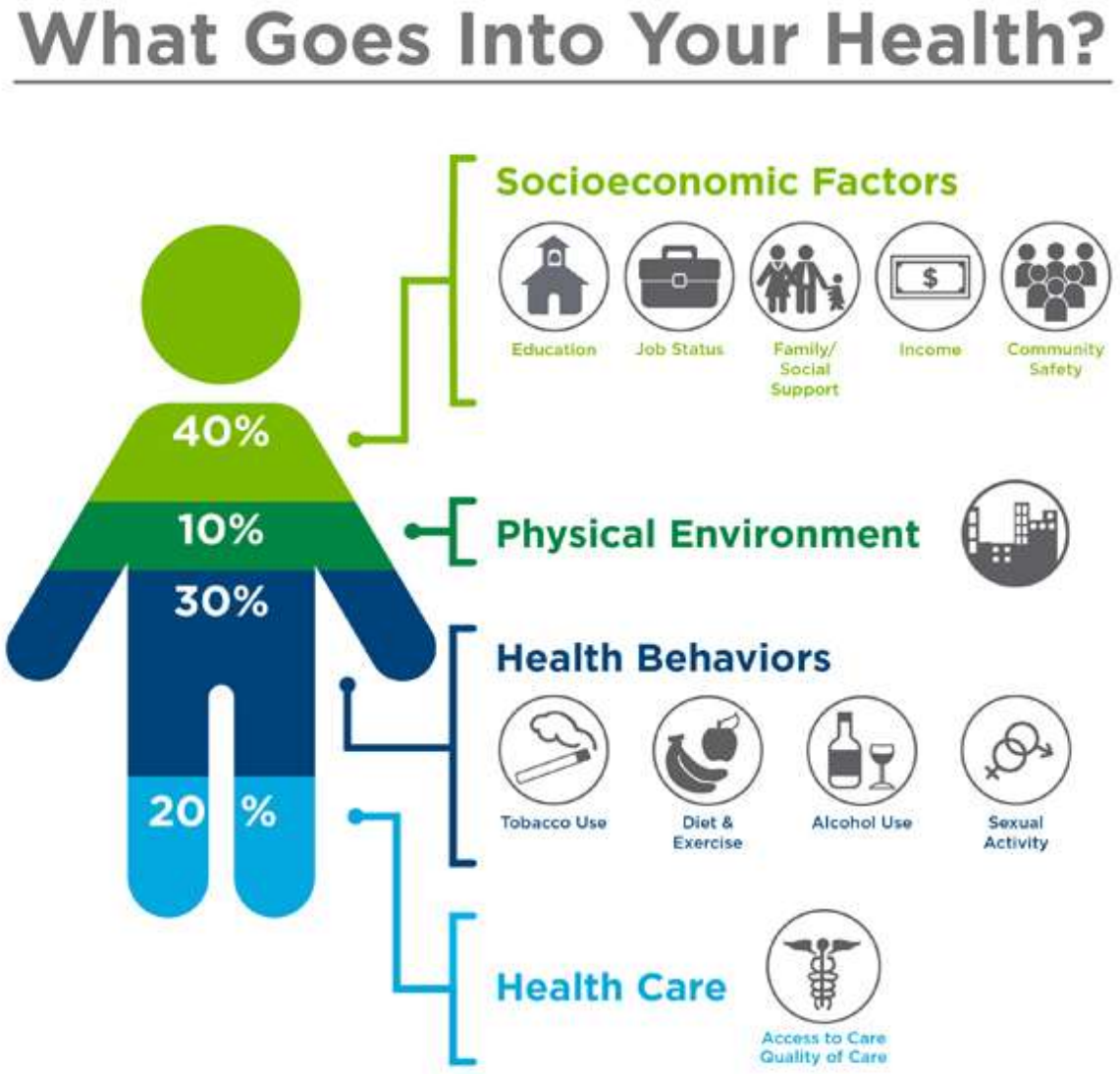


Design and deliver diabetes care with goal of **health equity** across all populations.

https://coveragetoolkit.org/health-equity/defining-health-equity/

Address Barriers to Self Management

- **Barriers exist** within health system, payer, health care professional & individual.
- **Address barriers** through innovation, including community health workers, telehealth, other digital health solutions.
- **Consider social determinants of health** in the target population when designing care.



Source: Institute for Clinical Systems Improvement, Going Beyond Clinical Walls: Solving Complex Problems (October 2014)

https://coveragetoolkit.org/health-equity/defining-health-equity/

5. Facilitating Positive Health Behaviors and Well-being to Improve Health Outcomes: *Standards of Care in Diabetes—2024* FREE

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Social Determinants of Health

- The conditions in which people:
  - Play
  - Live
  - Work
  - Learn
  - Pray

Directly affects their health risks and outcome

AADE Population Health & Diabetes Educators Evolving Role 2019

Status of Diabetes Care

- In 2015–2018, U.S. community-dwelling adults with diabetes achieved:
  - A1C <7% by 50.5%
    - 75.4% achieved A1C <8%.
  - BP target of <130/80 achieved by 47.7%
    - 70.4% achieved blood pressure <140/90 mmHg.
  - Lipid control (non-HDL cholesterol) <130 mg/dL, achieved by 55.7%
- 22.2% met targets for all three risk factors
- Many not receiving adequate lifestyle or pharmacotherapy.

1. Improving Care and Promoting Health in Populations: *Standards of Care in Diabetes—2024* FREE

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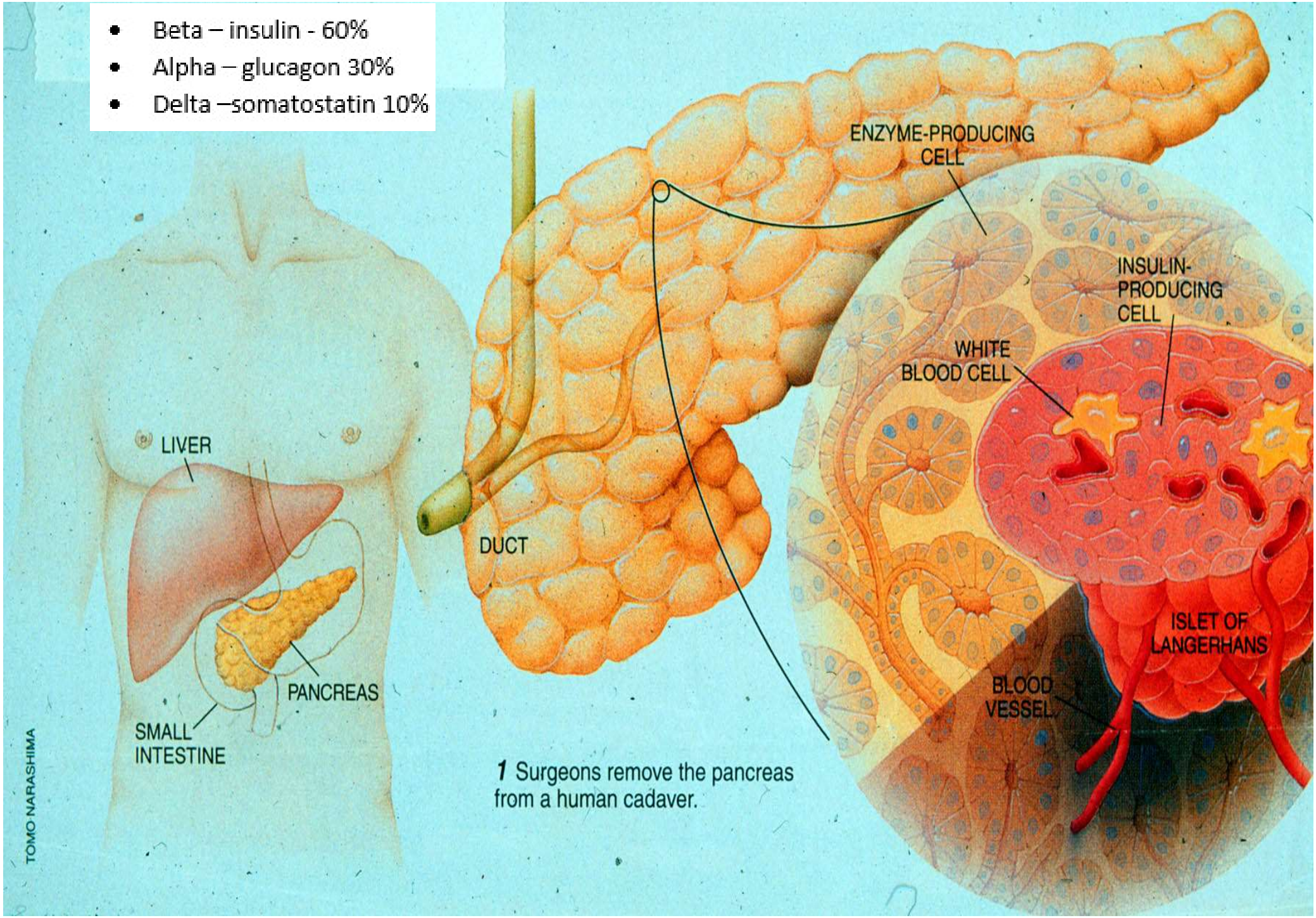
Abstracts | View article | PDF

Topics: chronic care, chronic disease, food insecurity, guidelines, health personnel

Diabetes Care December 2023, Vol.47, S11-S19. doi:https://doi.org/10.2337/dc24-S001

- Beta – insulin - 60%
- Alpha – glucagon 30%
- Delta –somatostatin 10%



Hormones Effect on Glucose

Hormone	Effect
Glucagon (pancreas)	↑
Stress hormones (kidney)	↑
Epinephrine (kidney)	↑
Insulin (pancreas)	↓
Amylin (pancreas)	↓
Gut hormones - incretins (GLP-1) released by L cells of intestinal mucosa, beta cell has receptors)	↓

Pre Diabetes & Type 2- Screening Guidelines (ADA 2024 Clinical Practice Guidelines)

1. Start screening all people at age 35.
2. Screen at any age if BMI ≥ 25 (Asians BMI ≥ 23) plus one or > additional **risk factor**:

- First-degree relative w/ diabetes
- Member of a high-risk ethnic population
- Habitual physical inactivity
- *PreDiabetes
- History of heart disease
- *Taking high risk meds; antiretrovirals, 2nd generation antipsychotics or steroids
- History of pancreatitis

2. Diagnosis and Classification of Diabetes: *Standards of Care in Diabetes—2024* FREE

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Second-Generation Antipsychotic Meds and Diabetes Risk

- People taking these meds require frequent monitoring due to increased risk of hyperglycemia and other metabolic effects.
- There is a range of effects across second-generation antipsychotic medications;
  - Olanzapine, haloperidol, clozapine, quetiapine, and risperidone tend to have *more* metabolic effects.
  - Aripiprazole and ziprasidone tend to have *fewer* metabolic effects.
  - It taking these agents, screen for prediabetes or diabetes at baseline, rescreen at 12–16 weeks after medication initiation, and screen annually thereafter ADA 2024

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Diabetes 2 - Who is at Risk?

(ADA 2024 Clinical Practice Guidelines)

Screen using A1C, Fasting Blood Glucose or OGTT.

Repeat screening at least every 3 years if negative.

*If prediabetes or on high risk meds, recheck yearly

Risk factors cont'd

- HTN - BP > 130/80
- HDL < 35 or triglycerides > 250
- History of Gestational Diabetes Mellitus
- Polycystic ovary syndrome (PCOS)
- Other conditions associated w/ insulin resistance:
  - Elevated BMI, acanthosis nigricans (AN)

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RECOMMENDATIONS FOR DIAGNOSIS AND CLASSIFICATION OF DIABETES – 2024

CRITERIA FOR TESTING FOR DIABETES AND PREDIABETES IN ASYMPTOMATIC ADULTS – TABLE 1

DIABETES TYPE	RISK FACTORS and FREQUENCY OF SCREENING and TESTING FOR DIABETES
Type 1	Screen for presymptomatic type 1 diabetes, by testing autoantibodies to insulin, GAD, islet antigen 2, or ZnT8 is recommended. Also test antibodies for those with type 1 phenotypic risk (younger age, ketoacidosis , etc.)
Type 2	1. Test all adults starting at age **35** for prediabetes and diabetes using Fasting Plasma Glucose, A1C or OGTT. 2. Perform risk-based screening if BMI ≥ 25 or BMI ≥ 23 in Asian Americans with 1 or more risk factors: • History of cardiovascular disease • First or second degree relative with diabetes • HDL ≤ 35 mg/dl or triglyceride ≥ 250 mg/dl • If taking antipsychotic, antiretroviral meds* • Other conditions associated with insulin resistance (PCOS, Acanthosis Nigricans) • High risk ethnicity (African American, Latino, Native American, Asian American, Pacific Islanders) • Physical inactivity • History of GDM (repeat test at least every 3 years) • Hypertension ≥ 130/80 or on therapy for HTN • A1c ≥ 5.7% or Impaired Fasting Glucose (test yearly) 3. If results normal, repeat test at a minimum of 3-year intervals or more frequently based on risk status. 4. *Screen people with HIV, exposure to high-risk medicines, history of pancreatitis and re-check annually.

DiabetesEd.net Cheat Sheets – See appendix in back of syllabus

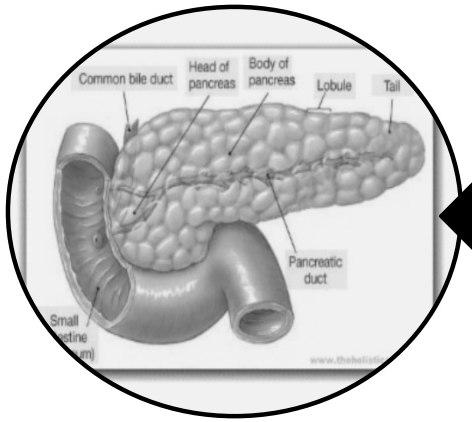
TESTS TO DIAGNOSE DIABETES - TABLE 2

STAGE	For all the below tests, in the absence of unequivocal hyperglycemia, Confirm results by repeat testing.			
	A1C *NGSP certified & standardized assay*	**Fasting* Plasma Glucose (FPG)** **No intake 8 hrs.*	**Random Plasma Glucose**	**Oral Glucose Tolerance Test (OGTT) 75-g** (Carb intake of ≥ 150 g/day for 3 days prior to test.)
Diabetes	A1C ≥ 6.5%	FPG ≥ 126 mg/dl	Random plasma glucose ≥ 200 mg/dl plus symptoms[1] [1]Random = any time-of-day w/out regard to time since last meal; symptoms include usual polyuria, polydipsia, and unexplained wt. loss.	Two-hour plasma glucose (2hPG) ≥ 200 mg/dl
Prediabetes	A1C 5.7 – 6.4%	Impaired Fasting BG (IFG) = FPG 100-125 mg/dl		Impaired Glucose Tolerance (IGT) = 2hPG 140 -199 mg/dl
Normal	A1C < 5.7%	FPG < 100 mg/dl		2hPG < 140 mg/dl

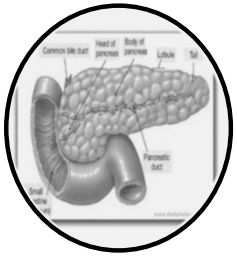
Poll Question 2

- Which of the following level is considered pre-diabetes range?
  a. Fasting BG of 62
  b. A1c of 5.9 %
  c. After meal BG of 137
  d. A1c of 7.1 %

Natural History of Diabetes



Yes!



NO

Healthy

FBG <100

Random <140

A1c <5.7%

Prediabetes

FBG 100-125

Random 140 - 199

A1c ~ 5.7- 6.4%

~ 50% working pancreas

Diabetes

FBG 126 +

Random 200 +

A1c 6.5% or +

~ 20% working pancreas

Development of type 2 diabetes happens over years or decades

PreDiabetes is FREAKING ME OUT

- 96 million people in US
- 80% don't know they have it
- In 3-5 years, about 30% of predm will get diabetes
- Associated with higher rates of heart attack, stroke, neuropathy and vessel disease

Do I look like I am freaking out?

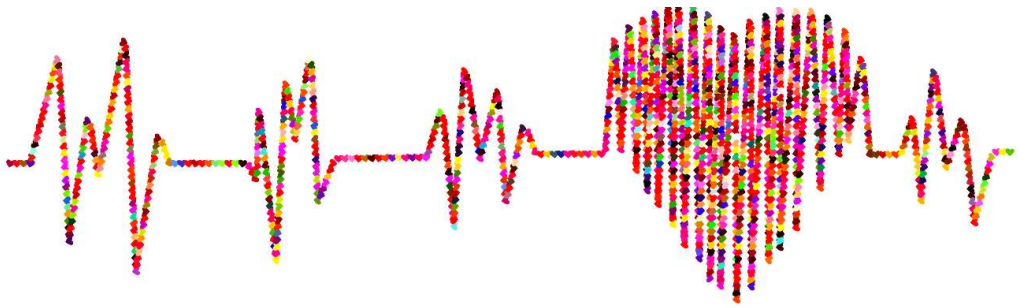
3. Prevention or Delay of Diabetes and Associated Comorbidities: *Standards of Care in Diabetes—2024*

Poll Question 3

- What best describes prediabetes?
  a. Prediabetes affects 18-20% of people above the age of 20.
  b. The prevalence of prediabetes and diabetes are almost equal.
  c. Most people with BMI of 30 or greater have prediabetes.
  d. Prediabetes is associated with increased risk of CV disease

3. Detecting PreDiabetes Matters

- Given the cost-effectiveness of lifestyle behavior modification programs for diabetes prevention:
  - Offer diabetes prevention programs to adults at high risk of type 2 diabetes
  - Should be covered by third-party payers,
  - Address inconsistencies in access
- Screening guidelines for people with Type 1



3. Prevention or Delay of Diabetes and Associated Comorbidities: *Standards of Care in Diabetes—2024*

3. Prevent or Delay Diabetes for those with Prediabetes

- Prediabetes defined as:
  - A1c 5.7 – 6.4% or fasting BG 100 -125mg/dl
- Action:
  - Screen yearly for diabetes
  - For adults with BMI 23/25
    - Refer to DPP approved programs
    - Includes intensive behavioral lifestyle interventions with 7% wt reduction goal + 150 min exercise week
    - Provide in person or certified assisted programs

3. Prevention or Delay of Diabetes and Associated Comorbidities: *Standards of Care in Diabetes—2024*

3. Prediabetes Pharmacologic Intervention

- No FDA approved med for prevention (off label)
- Consider Metformin Therapy for Prediabetes
- Especially for ages 25-59
  - BMI of 35+
  - If A1c is ~6.0 or FPG is 110mg/dL
  - Women with history of GDM
- Monitor B12 level (esp with neuropathy or anemia)

- CV Risk Mitigation important.
- Statin can increase BG, stop if notice elevation
- Consider low dose pioglitazone (Actos) if history of stroke.

3. Prevention or Delay of Diabetes and Associated Comorbidities: *Standards of Care in Diabetes—2024*

Diabetes is Complex

- Goal – achieve well being and negotiated outcomes
- Psychological factors:
  - Environmental
  - Social
  - Behavioral
  - Emotional
- Keep it person centered while integrating care into daily life
  - Consider the individual

Tailoring Treatment for Social Context

- "Social determinants of health (SDOH)—*often out of direct control of the individual* and potentially representing lifelong risk—contribute to health care and psychosocial outcomes and must be addressed to improve all health outcomes"

The ADA recognizes this relationship and is taking action.

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Remember by Joy Harjo – Poet Laureate

- Remember the earth whose skin you are:
  red earth, black earth, yellow earth, white earth, brown earth, we are earth.

- Remember the plants, trees, animal life who all have their tribes, their families, their histories, too. Talk to them, listen to them. They are alive poems.

- Remember the wind. Remember her voice. She knows the origin of this universe.

- Remember you are all people and all people are you.
  Remember you are this universe and this universe is you.
  Remember all is in motion, is growing, is you.
  Remember language comes from this.
  Remember the dance language is, that life is.
  Remember.

We are all connected

Person Centered Care

- Emphasize that a collaboratively developed plan improves well-being and outcomes.
- Provides care that is respectful and responsive to the individuals preferences, needs and values.
- Ensuring that the person's values guide all clinical decisions

Recognizes the expert within. Goal is to improve outcomes and encourage self-management for the long run.

Type 1 ~ Immune Mediated
5-10% of Diabetes

ADCES In Practice - March 2024

Recent Advances in Type 1 Diabetes: Teplizumab (Tzeild®)

Karen S. Fiano, PHARMD, BCACP, Devada Singh-Franco, PHARMD, CDCES, Young M. Kwon, BS, PHD

1.5 Million people have type 1 in U.S.

Prevalence increasing:

2001 – 1.48 per 1000 youths diagnosed with diabetes

2017 - 2.15 per 1000 youths diagnosed with diabetes

Incidence & Prevalence increasing

Highest incidence in Finland or Northern Europe.

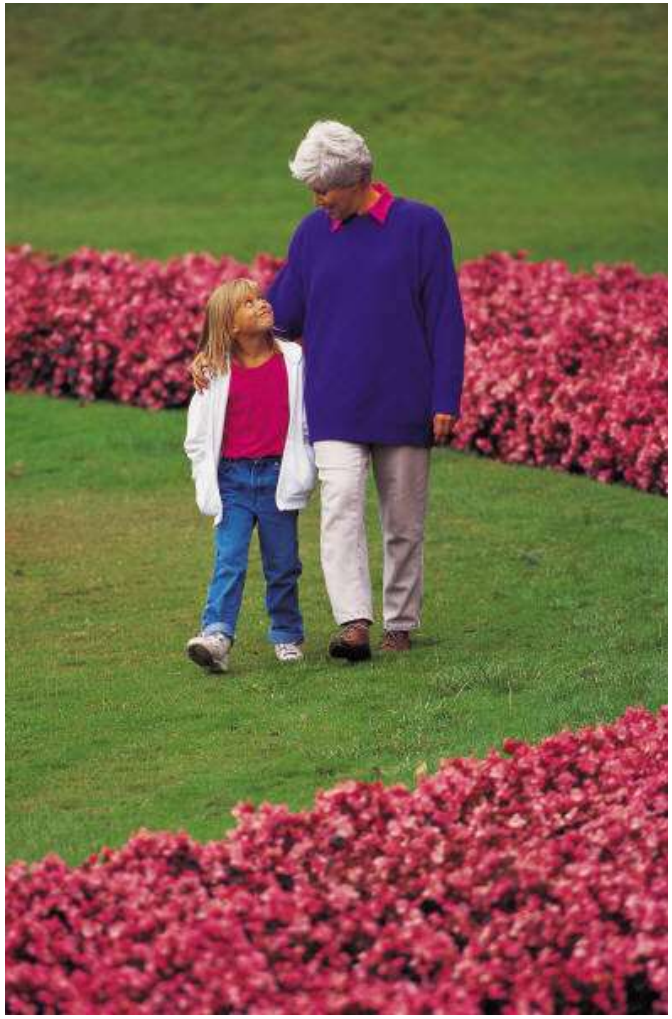
Poll Question 4

JR's mom has type 1 diabetes and JR's dad has type 2 diabetes. JR is 28 years old and in the emergency room with a glucose of 482 mg/dl. Besides checking glucose, ketones and A1C levels, which of the following lab test can be used to determine if someone has autoimmune diabetes?

1. Endogenous insulin titer
2. Glutamic Acid Decarboxylase
3. Beta cells auto antibodies
4. Langerhan's antibody

How do we know someone has Type 1 vs Type 2?

- Type 1 - Positive antibodies
  - GAD - glutamic acid decarboxylase (primary)
  - IA2 - islet antigen 2, or
  - ZnT8 - zinc transporter 8
- Can also check C-peptide levels to determine endogenous insulin production
- Younger people develop quickly
- Older people take longer to develop
- "misdiagnosis is common and can occur in ~40% of adults with new type 1 diabetes"



2. Diagnosis and Classification of Diabetes: *Standards of Care in Diabetes—2024* FREE

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Determine if Type 1 - Use AABBCC Approach

- **A**ge
  - e.g., for individuals <35 years old, consider type 1 diabetes
- **A**utoimmunity
  - e.g., personal or family history of autoimmune disease or polyglandular autoimmune syndromes
- **B**ody habitus
  - e.g., BMI <25 kg/m2
- **B**ackground
  - e.g., family history of type 1 diabetes
- **C**ontrol
  - e.g., level of glucose control on noninsulin therapies
- **C**omorbidities
  - e.g., treatment with immune checkpoint inhibitors for cancer can cause acute autoimmune type 1 diabetes or presence of other autoimmune conditions

2. Diagnosis and Classification of Diabetes: *Standards of Care in Diabetes—2024* FREE

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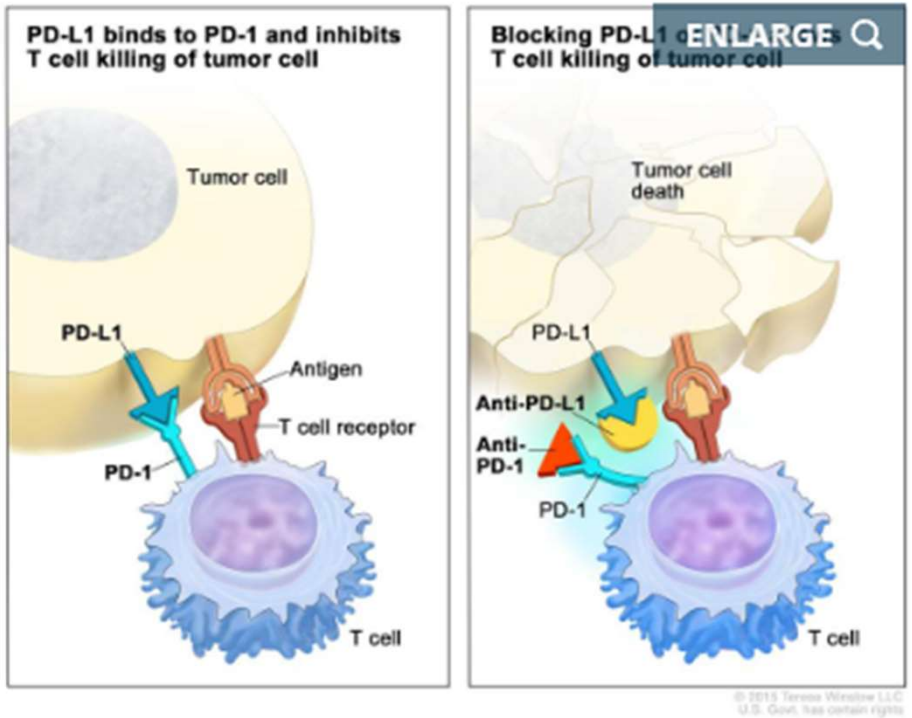
Diabetes Care, June 2023

Immune Checkpoint Inhibitors



Checkpoint proteins, such as PD-L1 on tumor cells and PD-1 on T cells, help keep immune responses in check. The binding of PD-L1 to PD-1 keeps T cells from killing tumor cells in the body (left panel). Blocking the binding of PD-L1 to PD-1 with an immune checkpoint inhibitor (anti-PD-L1 or anti-PD-1) allows the T cells to kill tumor cells (right panel).

Credit: © Terese Winslow

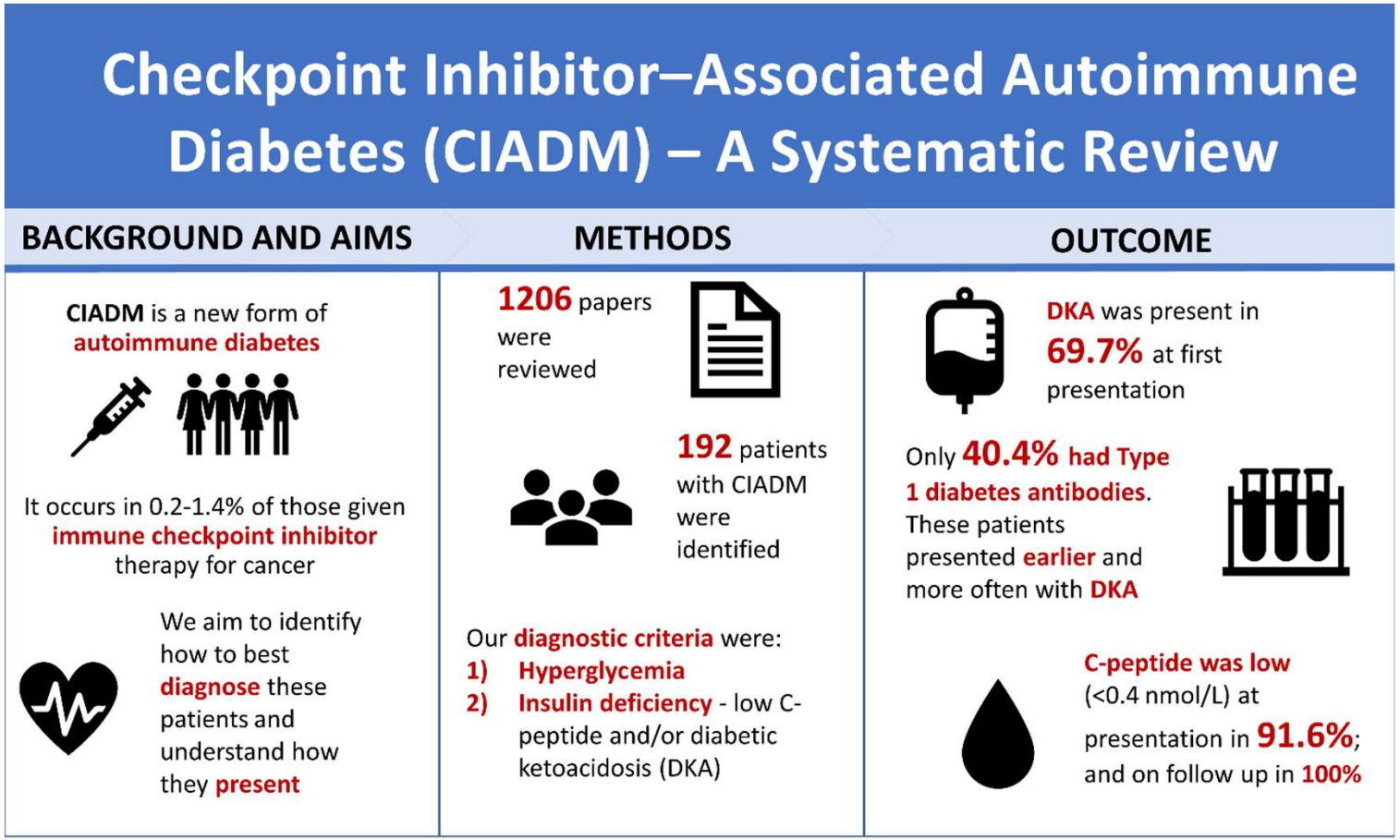
Approved to treat cancer types, including:

- breast cancer
- bladder cancer
- cervical cancer
- colon cancer
- head and neck cancer
- Hodgkin lymphoma
- liver cancer
- lung cancer
- renal cell cancer (a type of kidney cancer)
- skin cancer, including melanoma
- stomach cancer
- rectal cancer
- any solid tumor that is not able to repair errors in its DNA that occur when the DNA is copied

https://www.cancer.gov/about-cancer/treatment/types/immunotherapy/checkpoint-inhibitors

Checkpoint Inhibitors cause immune meditated diabetes

"treatment with immune checkpoint inhibitors for cancer can cause acute autoimmune type 1 diabetes or presence of other autoimmune conditions."



2. Diagnosis and Classification of Diabetes: *Standards of Care in Diabetes—2024* FREE
American Diabetes Association Professional Practice Committee

Linda Wu, Venessa Tsang, Alexander M. Menzies, Sarah C. Sasson, Matteo S. Carlino, David A. Brown, Roderick Clifton-Bligh, Jenny E. Gunton; Risk Factors and Characteristics of Checkpoint Inhibitor–Associated Autoimmune Diabetes Mellitus (CIADM): A Systematic Review and Delineation From Type 1 Diabetes. Diabetes Care 1 June 2023; 46 (6): 1292–1299. https://doi.org/10.2337/dc22-2202

Type 1 Diabetes Features?

- For JR, a 28 admitted to the ICU with a blood glucose of 476 mg/dl, pH of 7.1, anion gap of 15. Recently lost 13 pounds.

Type 1 Most Discriminative Features

- Younger than 35 years at diagnosis
- Lower BMI (<25 kg/m^2)
- Unintentional weight loss
- Ketoacidosis
- Glucose 360 mg/dl or greater.

CONSENSUS REPORT | OCTOBER 18 2021

The Management of Type 1 Diabetes in Adults. A Consensus Report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD) FREE

3. Prevention or Delay of Diabetes and Associated Comorbidities: *Standards of Care in Diabetes—2024*

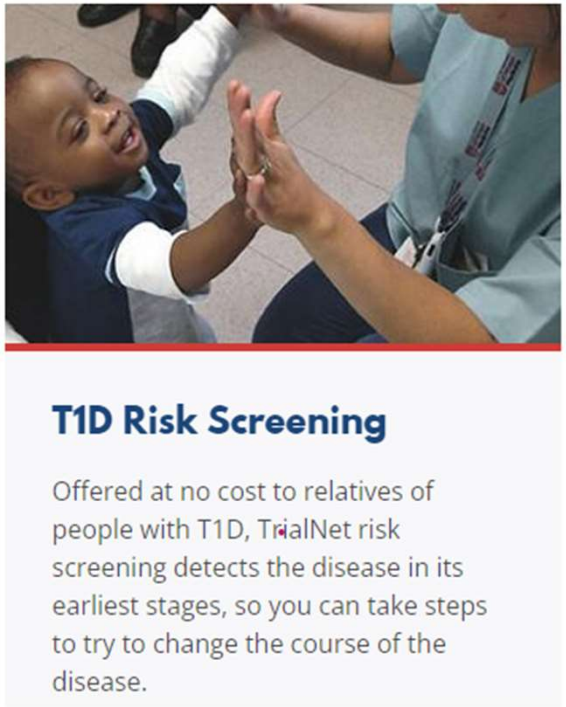
Type 1 Diabetes Progression

	Stage 1	Stage 2	Stage 3
Characteristics	• Autoimmunity	• Autoimmunity	• Autoimmunity
	• Normoglycemia	• Dysglycemia	• Overt hyperglycemia
	• Presymptomatic	• Presymptomatic	• Symptomatic
Diagnostic criteria	• Multiple islet autoantibodies - GAD, glutamic acid decarboxylase - islet antigen 2 - Zinc transporter 8 (ZnT8) - Islet cell autoantibody (ICA)	• Islet autoantibodies Dysglycemia: Elevated IFG and/or IGT • FPG 100–125 mg/dL • 2-h PG 140–199 mg/dL • A1C 5.7–6.4% or ≥10% increase in A1C	• Autoantibodies may disappear over time (5-10% may not express antibodies) • Diabetes diagnosed by standard criteria

2. Diagnosis and Classification of Diabetes: *Standards of Care in Diabetes—2024* FREE
American Diabetes Association Professional Practice Committee

3. Prevention or Delay of Diabetes and Associated Comorbidities (for Preclinical Type 1 Diabetes)

- Positive Antibodies with Prediabetes:
  - A1c 5.7 – 6.4% or fasting BG 100 -125mg/dl
- Action:
  - Screen A1C every 6 months
  - 75- OGTT every year
  - Modify screening based on antibodies and glycemic metrics.
  - May benefit from CGM to monitor progression



Trialnet.org

3. Prevention or Delay of Diabetes and Associated Comorbidities: *Standards of Care in Diabetes—2024*

Type 1 & Lifestyle Prevention

- Observational studies in those with antibodies, shed light on factors that ***increase*** β-cell demand:
  - Less physical activity
  - Consuming higher glycemic index foods
  - Sugar intake
- Factors that **reduced risk** of progression from TEDDY study:
- Daily minutes spent doing vigorous physical exercise.
- More info needed

3. Prevention or Delay of Diabetes and Associated Comorbidities: *Standards of Care in Diabetes—2024*

Pharmacologic Intervention to Delay Symptomatic Type 1 (in Stage 2)

- Teplizumab-Tzield (CD3-monoclonal antibody)
- 14-day infusion can delay the onset of symptomatic type 1 diabetes (stage 3)
- An option in selected individuals aged ≥8 years with stage 2 type 1 diabetes.
- In a single trial, 44 individuals received 14-day course of teplizumab vs 32 placebo.
- The median time to stage 3 diagnosis of type 1
  - 48.4 months in tep group
  - 24.4 months placebo
- Cost: $193,000
- Sanofi has financial assist programs.

126. Herold KC, Bundy BN, Long SA, et al.; Type 1 Diabetes TrialNet Study Group. An anti-CD3 antibody, teplizumab, in relatives at risk for type 1 diabetes. *N Engl J Med* 2019;381:603–613

Type 1 (stage 2) Delayed with Teplizumab by 2 years TrialNet

- **How to get families linked to screening?**

Quick Question

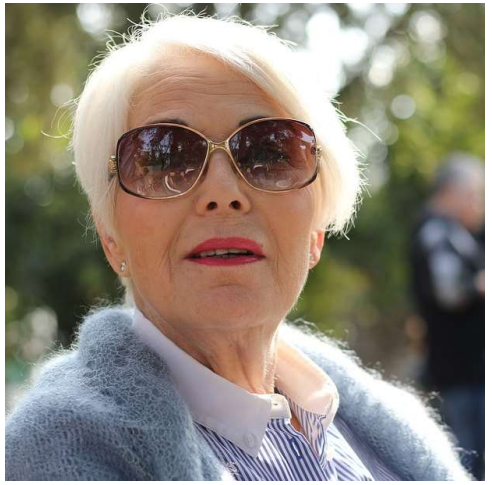
- **Question:** LT has just been diagnosed with stage 2, type 1 diabetes. They have 2 positive antibodies and their blood sugars are slightly elevated. They ask you if they are a candidate for "that therapy" that can protect their beta cells and slow progression of type 1 diabetes. **What is the most accurate response?**
  - Unfortunately, you are not a candidate, since you already have 2 positive antibodies.
  - Let's talk to your provider about the possibility of starting Teplizumab therapy.
  - With your blood sugar elevation, the best early intervention is insulin therapy.
  - Since you are already in stage 2, the monoclonal antibody therapy won't be effective.

Medalist Study – Harvard Joslin Diabetes Center

- After 50 years with diabetes
  - Many still produced some insulin
  - Many had no eye disease

What kind of Diabetes?

- 58 yr old, states she has had type 1 diabetes for 18 years. Quit smoking a year ago and gained about 20 lbs. BMI 25.
- Meds
  - Humalog 18-23 units before each meal
  - Glargine 28 units at bedtime
  - Metformin 500mg TID
- What tests would you recommend?



25% of ind's with Type 1 also have type 2 diabetes.

ADA Post Grad, 2010

What type of Diabetes?

- 72 Years old
- A1c 3 months prior 6.2%
- A1c now 13.9%
- BMI 24.5
- Lost about 10 pounds over last month

Latent AutoImmunity Diabetes in Adults (LADA)

- Antibody positive to 1-2 of below
  - GAD-65 autoantibodies
  - Insulin Autoantibodies
  - Islet Cell antigen-2
  - ZnT8
- Adult Age at onset
- Usually benefit from insulin w/in first 6 months of diagnosis
- Early insulin therapy may preserve beta cell function

Latent Autoimmune Diabetes

Venkatraman Rajkumar; Steven N. Levine.

Author Information and Affiliations

Last Update: June 21, 2022.

Diabetes Care 26:536-538, 2003
Jerry P. Palmer, MD and Irl B. Hirsch, MD

LADA Clinical Features Compared to Type 2

Feature	LADA	Type 2
Age <50	63%	19%
Acute hyperglycemia	66	24
BMI < 25	33	13
Hx of autoimmune dx	27	12
Family hx autoimmune	46	35

Latent Autoimmune Diabetes

Venkatraman Rajkumar; Steven N. Levine.

Author Information and Affiliations

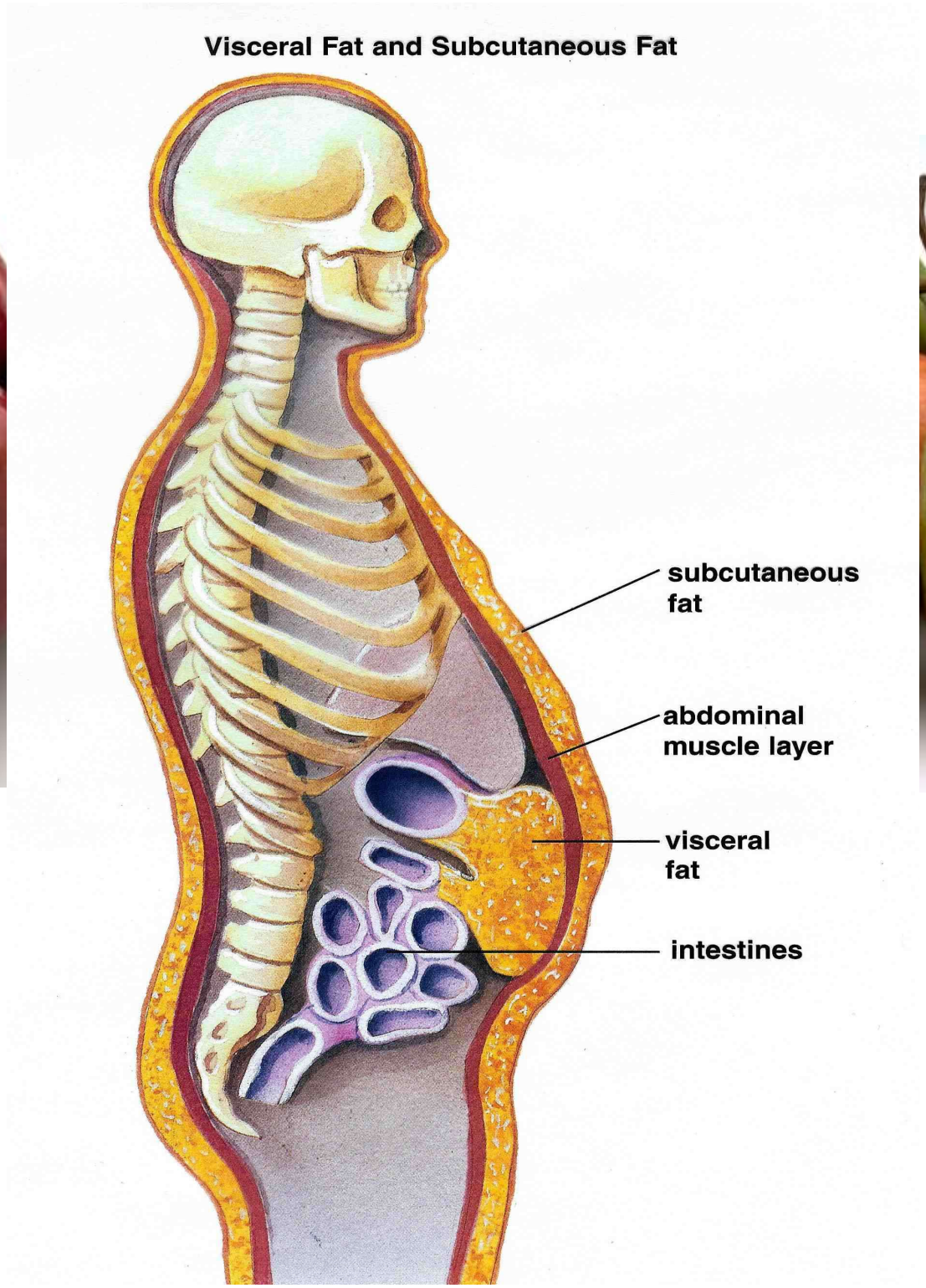
Last Update: June 21, 2022.

Practical Diabetology March 08, Unger MD

Signs of Diabetes

- Polyuria
- Polydipsia
- Polyphasia
- Weight loss
- Fatigue
- Skin and other infections
- Blurry vision

- Glycosuria, H_2O losses
- Dehydration
- Fuel Depletion
- Loss of body tissue, H_2O
- Poor energy utilization
- Hyperglycemia increases incidence of infection
- Osmotic changes


Visceral Fat and Subcutaneous Fat
subcutaneous fat
abdominal muscle layer
visceral fat
intestines

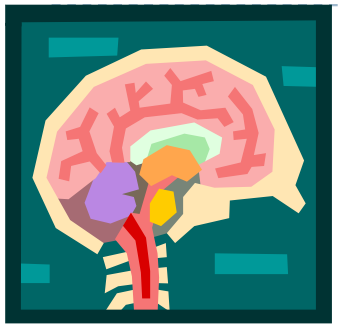
What is Type 2 Diabetes?

- Complex metabolic disorder ….
  (Insulin resistance and deficiency)

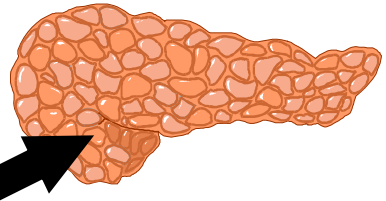
with social, behavioral and environmental risk factors unmasking the effects of genetic susceptibility.

New Diagnosis?
Call 800 – DIABETES to request "Getting Started Kit"
www.Diabetes.org

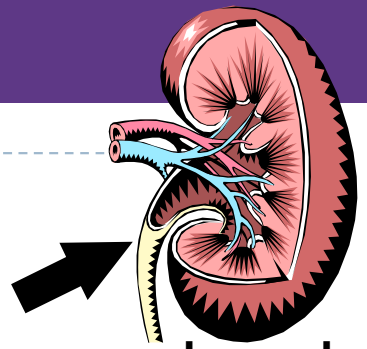
Ominous Octet



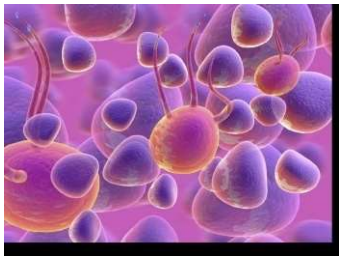
Decreased satiation neuro-transmission



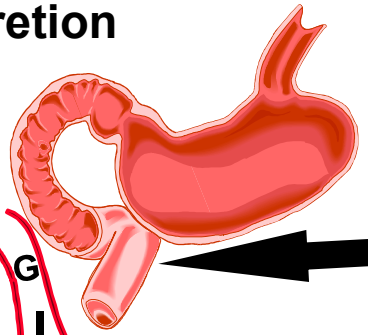
Decreased amylin, β-cell secretion
80% loss at dx



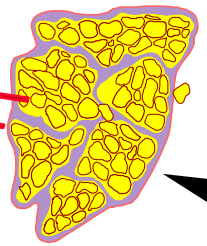
Increased renal glucose reabsorption



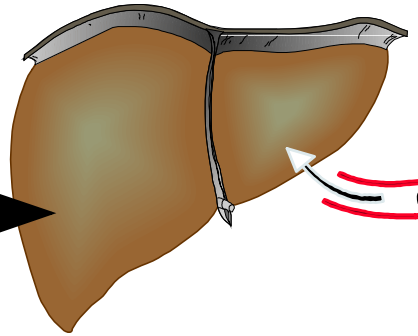
Increased glucagon secretion



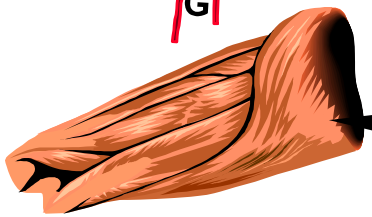
Decreased Gut hormones



Increased lipolysis

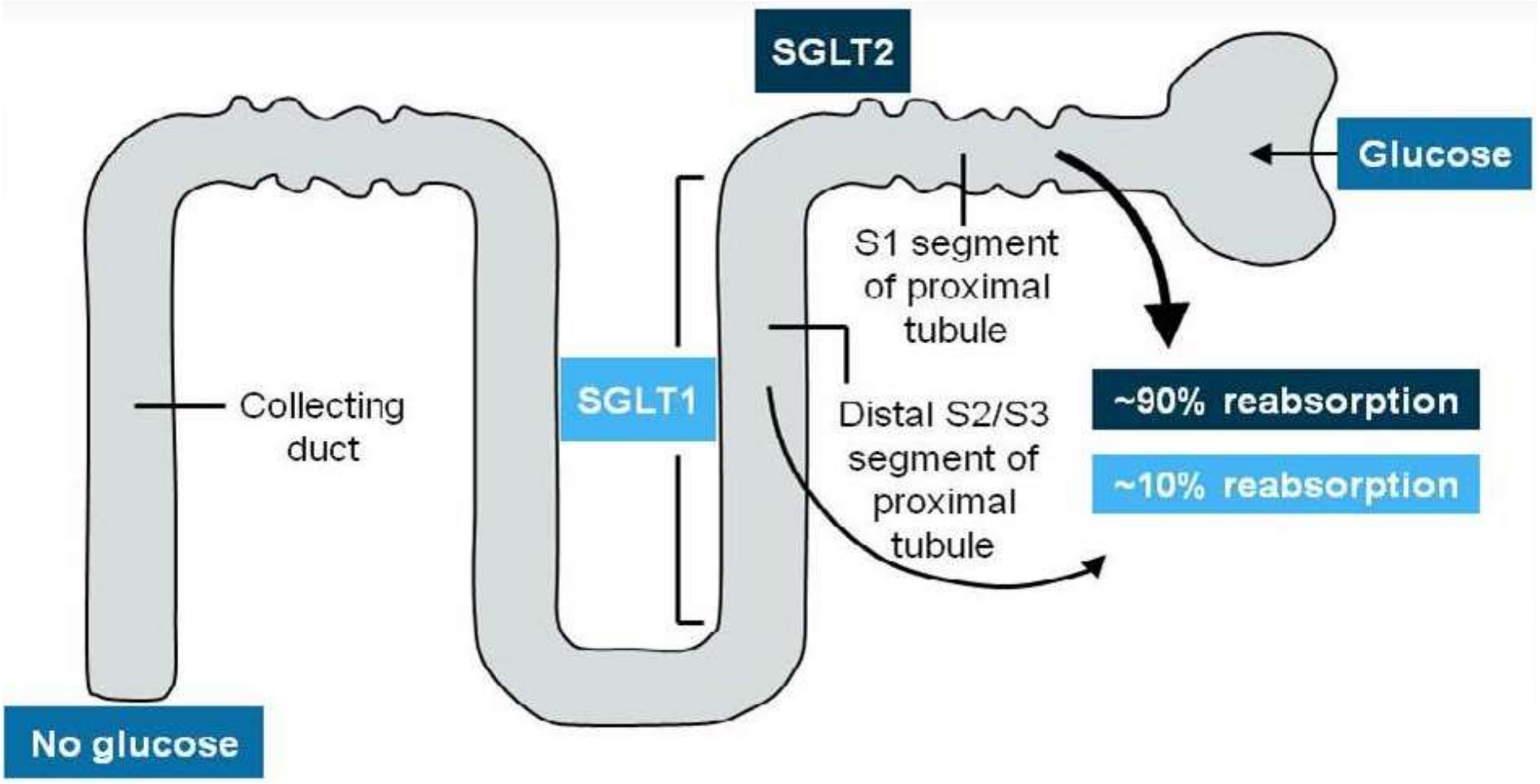


Increase glucose production



Decreased glucose uptake

SGLT and the Kidney



Poll Question 7

- A potential side effect of SGLT-2 Inhibitors is:

a. Urinary tract infections
b. Hypertension
c. Kidney tenderness
d. Increased uric acid

SGLT2 Inhibitors- "Glucoretics"

- **Action**: decreases renal reabsorption of glucose proximal tubule of kidneys (reset renal threshold)
- **Preferred** diabetes treatment for people with heart and kidney failure. Decreases BG & CV Risk.

Class/Main Action	Name(s)	Daily Dose Range	Considerations
SGLT2 Inhibitors "Glucoretic" • Decreases glucose reabsorption in kidneys	Canagliflozin* (Invokana) Dapagliflozin*† (Farxiga) Empagliflozin*† (Jardiance) Ertugliflozin (Steglatro) Bexagliflozin (Brenzavvy)	100 - 300 mg 1x daily 5 - 10 mg 1x daily 10 - 25 mg 1x daily 5 – 15 mg 1x daily 20 mg 1x daily	**Side effects:** hypotension, UTIs, genital infections, increased urination, weight loss, ketoacidosis. **Heart Failure, CV & Kidney Protection:** 1st line therapy for Heart Failure (HF), Kidney Disease (CKD), Cardiovascular Disease, before or with metformin. **Considerations:** See Package Insert (PI) for GFR cut-offs, dosing. Limited BG lowering effect if GFR < 45, still benefits kidneys & heart at lower GFR. If CKD & GFR ≥20, use SGLT-2 to reduce CVD, HF, preserve renal function. (ADA/EASD) **Benefits:** SGLT-2s* reduce BG, CV death & HF, slow CKD. †Approved for peds, 10 yrs +. Lowers A1C 0.6% to 1.5%.

SGLT-2 Inhibitor Dosing and Renal Adjustments

Drug	Dose	Renal Adjustment
Ertugliflozin (Steglatro)	5-15 mg daily	Not recommended for eGFR <45
Dapagliflozin (Farxiga)	5-10 mg daily	Not recommended to initiate with eGFR <45 (glycemic control) or <25 (other conditions): may continue for CV, CKD benefits
Empagliflozin (Jardiance)	10-25 mg daily	Not recommended to initiate for eGFR <30 (glycemic control) , may continue for CV, CKD benefits
Canagliflozin (Invokana)	100-300 mg daily	eGFR 30 to <60: 100 mg once daily eGFR <30: avoid initiation, may continue 100mg daily until ESRD
Bexagliflozin (Brenzavvy)	20 mg daily	Not recommended for eGFR <30

Package inserts, dailymed.nlm.nih.gov

SGLT-2i Indications Summary

Drug	Lowers BG	Reduces CV Risk?	Used to treat Heart Failure?	Slows renal disease?
Dapagliflozin (Farxiga)	Yes, for 10 yrs and older	Yes	Yes +/- Diabetes	Yes +/- Diabetes
Empagliflozin (Jardiance)	Yes for 10 yrs and older	Yes	Yes +/- Diabetes	Yes +/- Diabetes
Canagliflozin (Invokana)	Yes	Yes	Yes w/ Diabetes	Yes w/ Diabetes
Ertugliflozin (Steglatro)	Yes	No	Yes w/ Diabetes	No
Bexagliflozin (Brenzavvy)	Yes	NA	NA	NA

Benefits of SGLT-2 Inhibitors

A1C lowering

Weight loss

Cardiovascular

Renal

Heart failure

Blood pressure lowering

Side Effects of SGLT-2 Inhibitors

Genitourinary infections	Volume depletion	Increased urination
Hypotension	UTI	Diabetes ketoacidosis (DKA)

Amputation risk? Fournier's gangrene?

SGLT2i: Managing Adverse Effects

- Maintain good hygiene to reduce risk of genital mycotic infections
  - Higher risk with higher glucose
- DKA risk
  - Use caution with reducing insulin dose
- Monitor BP
  - May need to reduce antihypertensive meds
- UTI risk greater with hyperglycemia
- Amputations observed with canagliflozin
  - Good foot care, check feet daily
- Monitor renal function/potassium
- Discontinue 3 days prior to surgery or procedures that require prolonged fasting

Case Study: Rick

- Rick is a 51yoM diagnosed with type 2 diabetes 5 years ago.
- He takes metformin 1000mg twice daily and semaglutide 2mg weekly. His A1C=7.3%.
- In the last 3 months, he was diagnosed with kidney disease. He has albuminuria and eGFR=50.
- Weight: 205lbs, 5”7, BMI=32kg/m^2
- He lost 20lbs in the last year

Case Study: Rick (No Poll)

- What is the best drug to add to Rick's regimen?

A. Glipizide
B. Dapagliflozin (Farxiga)
C. Pioglitazone (Actos)
D. Linagliptin (Tradjenta)
E. More than 1 correct answer

SGLT2 Inhibitors- How do they rate?

Question	Answer
Cause hypoglycemia?	No
Cause weight gain?	No
Affordable?	No
Lowers Cardiorenal risk?	Yes
Can most tolerate /use?	Yes

Comparison of Type 1,Type 2, LADA

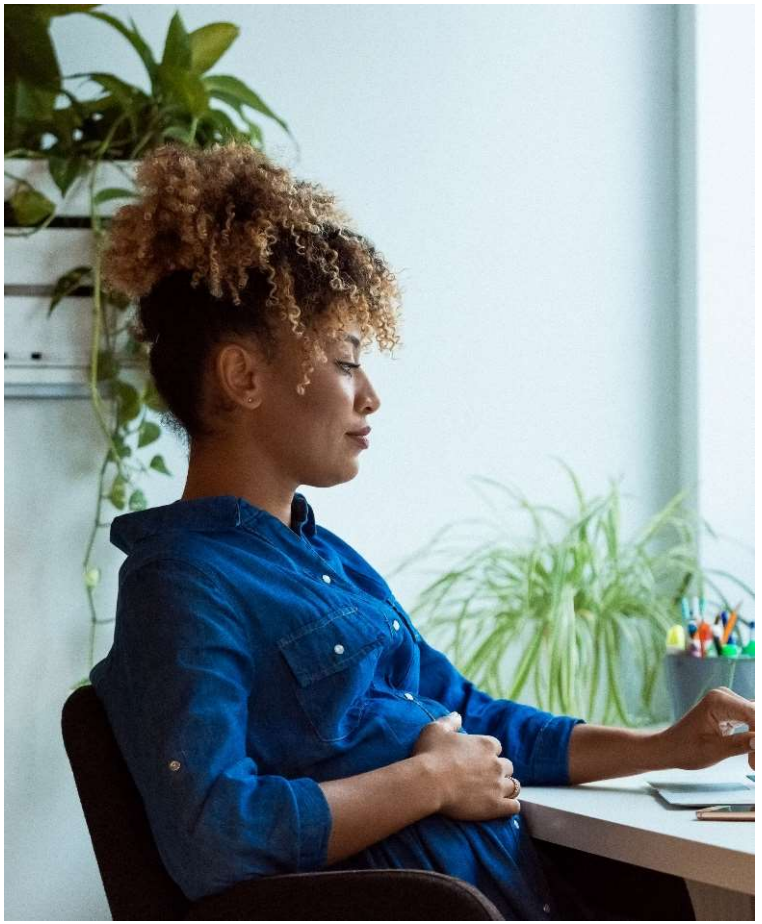
	Type I	Type 2	LADA
Excess weight	x	xxx	x
Insulin dependence	xxx	30%	6mos
Respond to oral agents	0	xxx	x
Ketosis	xxx	x	x
Antibodies present	xxx	0	xx
Typical Age of onset	teens	adult	adult
Insulin Resistance	0	xxx	x

Other Types of Diabetes

- Gestational
- Other specific types of diabetes

Screening in early Pregnancy

- Checking glucose levels before 15 weeks of gestation:
  - Can find undetected diabetes or hyperglycemia
  - Prevent fetal exposure to hyperglycemia
  - Allows providers and pregnant people to take action to prevent complications
- Use standard diabetes diagnostic criteria.
  - If positive, diagnosis “Diabetes complicating pregnancy”
- If fasting BG 110+ or A1C 5.9%+
  - At higher risk of adverse outcomes and more likely to experience GDM and need insulin.



15. Management of Diabetes in Pregnancy: *Standards of Care in Diabetes—2024* FREE

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Poll question 6

- What best describes gestational diabetes?

a. Diabetes discovered within the first 12 weeks of pregnancy.
b. Diabetes discovered in the 24-28 weeks of pregnancy.
c. Risk of getting diabetes before pregnancy.
d. Diabetes discovered at any point during pregnancy.

Gestational DM ~ 9% of all Pregnancies

- Detected at 24-28 weeks of pregnancy (most insulin resistant phase)
- 50% chance of getting diabetes post delivery
- Offspring at greater risk of insulin resistance and diabetes

Rates of Gestational Diabetes (GDM) and Diabetes in Pregnancy increasing

- 1% to 2% have type 1 or type 2 during pregnancy
- 6% to 9% develop GDM.
- From 2000 to 2010
  - GDM rates increased 56%
  - Type 1 or type 2 before pregnancy increased 37%.
- Asian and Hispanic women have higher rates of GDM
- Black and Hispanic women have higher rates of type 1 or type 2 diabetes during pregnancy.

CDC
https://www.cdc.gov/reproductivehealth/maternalinfanthealth/diabetes-during-pregnancy.htm

See Diabetes and Pregnancy Level 2

Screening and Diagnosis of Diabetes Cheat Sheet

GESTATIONAL DIABETES (GDM)*

PREGNANCY SCREENING	TEST	DIAGNOSTIC CRITERIA
Screen to identify abnormal glucose metabolism before 15 weeks gestation Test those w/ risk factors (table 1) to identify undiagnosed prediabetes or diabetes at first prenatal visit.	Standard Diagnostic Testing and Criteria as listed in Diagnosing Diabetes –Table 2	Standard Diagnostic Testing and Criteria as listed in Diagnosing Diabetes –Table 2 Those with fasting of 110-125 or A1C of 5.9% to 6.4% are at higher risk of adverse outcomes (GDM, need insulin, preeclampisa and other)
Screen for GDM at 24–28 wks gestation for those without known diabetes. Screen those with GDM for diabetes 4 - 12 wks postpartum with 75-g OGTT. Lifelong screening at least every 3 yrs. **Please see reference below for complete guidelines.*	Can use either IADPSG consensus: **"One Step" 75-g OGTT** fasting and at 1 and 2 h (perform after overnight fast of at least 8 h) **"Two step" NIH Consensus – Step 1:** 50gm glucose load (non fasting) w/ plasma BG test at 1 hr. If BG ≥ 130-140*, go to **Step 2 >**	**One Step:** GDM diagnosis when ANY of following BG values are exceeded: • Fasting ≥92 mg/dl, • 1 h ≥180 mg/dl • 2 h ≥153 mg/dl **Two Step -Step 2** - 100g OGTT (fasting) GDM diagnosis if at least 2 of 4 BG measured at fasting, 1h, 2h, 3h after OGTT meet or exceed 95, 180, 155, 140 mg/dL respectively.

***Reference** – Diagnosis & Classification of Diabetes. American Diabetes Association Standards of Medical Care in Diabetes. Diabetes Care 2024 Jan; 47 (Supplement 1): S20-S42. **Compliments of Diabetes Education Services www.DiabetesEd.net**

See appendix in back of syllabus

15. Management of Diabetes in Pregnancy: *Standards of Care in Diabetes—2024* FREE

American Diabetes Association Professional Practice Committee

Gestational Diabetes and Pregnancy

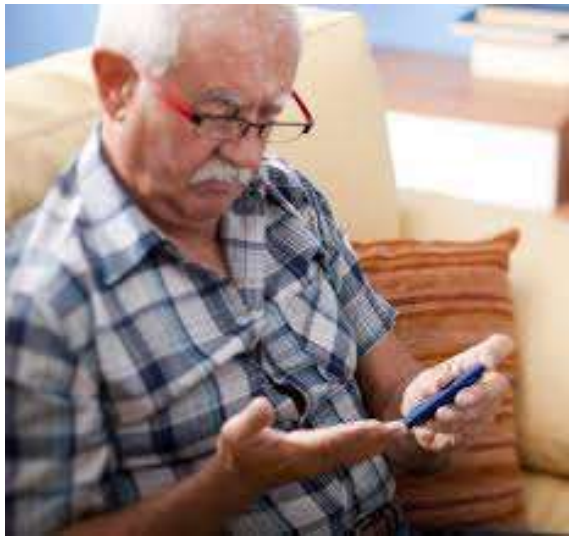
- Test for GDM at 24-28 weeks
- Test GDM women for post partum diabetes at 4-12 weeks, using OGTT
- Women with GDM need lifelong screening for prediabetes/diabetes at least every 3 yrs
- Women with hx of GDM, found to have prediabetes need intensive lifestyle interventions or metformin to prevent diabetes.

15. Management of Diabetes in Pregnancy: *Standards of Care in Diabetes—2024* FREE

American Diabetes Association Professional Practice Committee

Other Specific Types of DM

- Medications such as: steroids, protease inhibitors and Prograf®
- Secondary to Agent Orange
- Liver failure
- TPN or tube feedings
- Pancreatic cancers or removal
- Cystic fibrosis, pancreatitis
- Other



DiaBingo

B Frequent skin and yeast infections

B A BMI of ____ or greater indicates increased pre/diabetes risk?

B To reduce complications, control **A**1c, **B**lood pressure, **C**holesterol

B PreDiabetes – fasting glucose level of ___ to ____

B Erectile dysfunction indicates greater risk for ____

B Diabetes – fasting glucose level____ or greater

B Type 1 diabetes is best described as an _____ disease

B People with diabetes are _____ times more likely to die of heart dx

B Elevated triglycerides, < HDL, smaller dense LDL

B Each percentage point of A1C = _____ mg/dl glucose

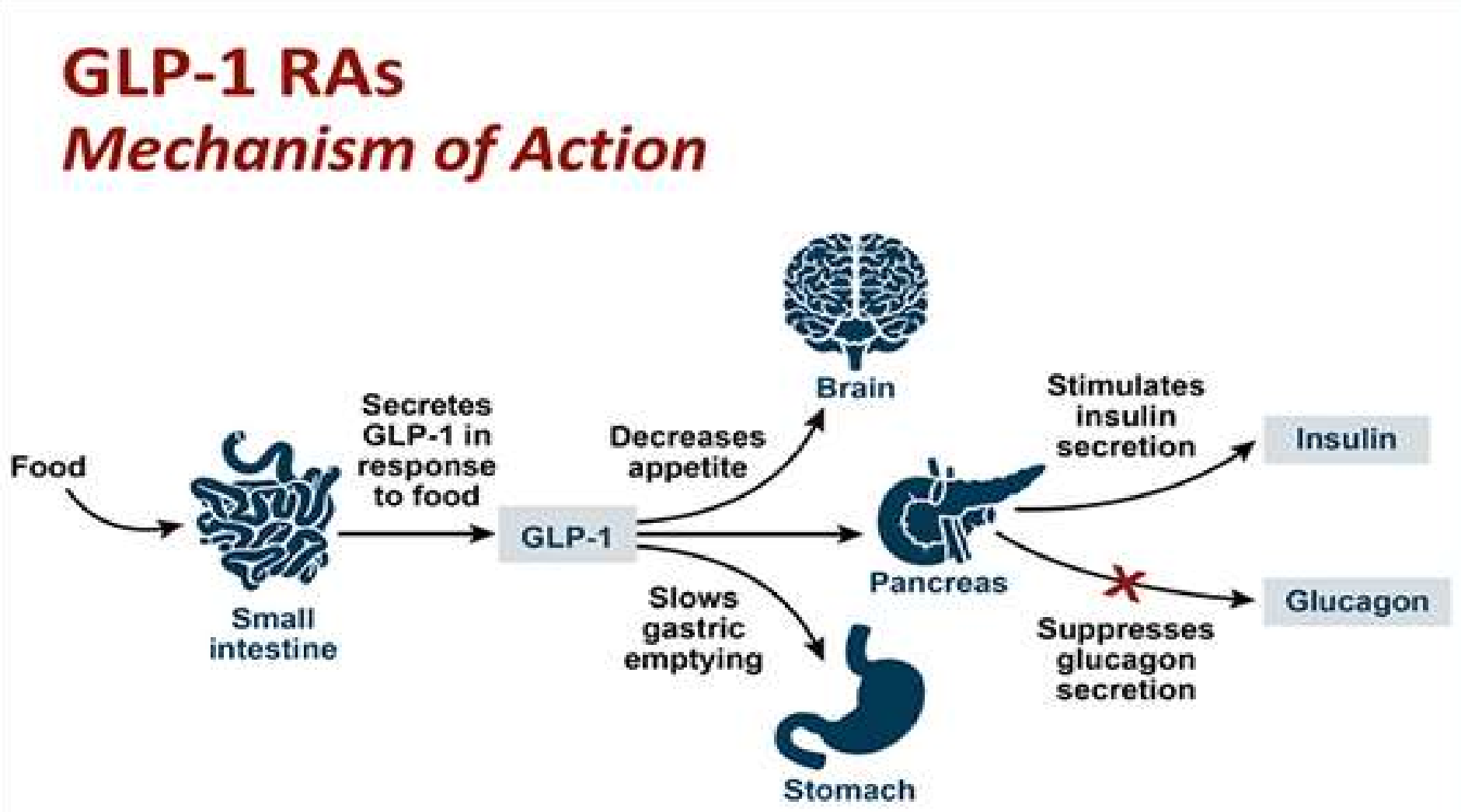
B At dx of type 2, about __% of the beta cell function is lost

B Diabetes – random glucose ____ or greater

Incretins:
GLP-1 & GLP-1/GIP Receptor Agonists

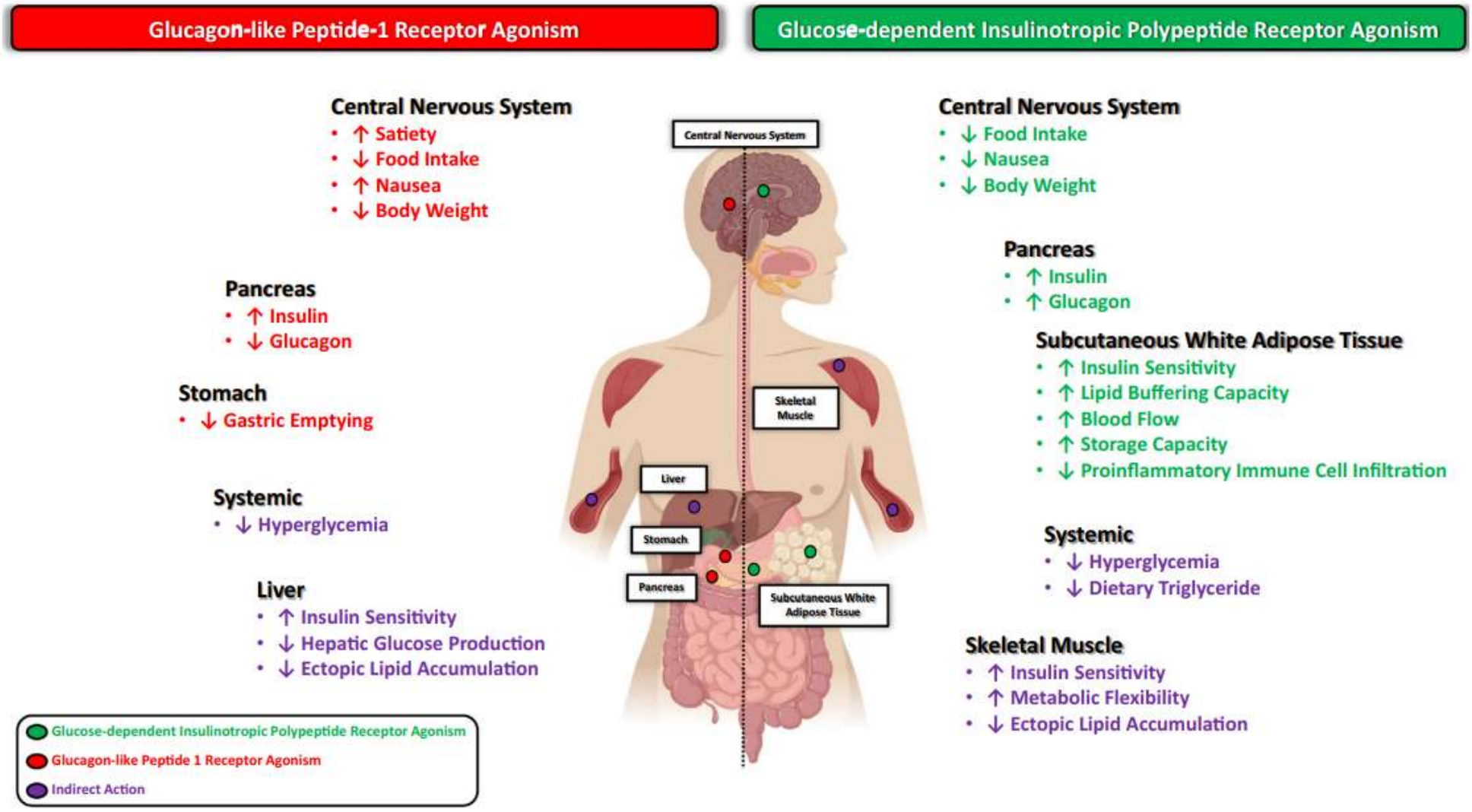
GLP-1: glucagon like peptide 1
GIP: glucose-dependent insulinotropic polypeptide

GLP-1 Receptor Agonist Mechanism



Meier JJ. *Nat Rev Endocrinol*. 2012;8:728-742.

Action of GLP-1 and GIP



Samms RJ, Coghlan MP, Sloop KW. How May GIP Enhance the Therapeutic Efficacy of GLP-1? Trends Endocrinol Metab. 2020 Jun;31(6):410-421.

Pocket Card: GLP-1 & GIP RA

GLP-1 & GIP Receptor Agonists

Class/Main Action	Name	Dose Range	Considerations
GLP-1 RA - Glucagon Like Peptide Receptor Agonist **"Incretin Mimetic"** • Increases insulin release with food • Slows gastric emptying • Promotes satiety • Suppresses glucagon	exenatide (Byetta)	5 and 10 mcg BID	**Side effects:** nausea, vomiting, weight loss, injection site reaction. Report signs of acute pancreatitis or intestinal blockage (ileus) and stop med. Increase dose monthly to achieve targets. **Black box warning:** Thyroid C-cell tumor warning (avoid if family history of medullary thyroid tumor). *Significantly reduces risk of CV death, heart attack, and stroke. †Approved for pediatrics 10-17 yrs Lowers A1C 0.5 – 1.6% Weight loss: 4-6% body weight loss.
	exenatide XR† (Bydureon)	2 mg 1x a week Pen injector - Bydureon BCise	
	liraglutide (Victoza)*†	0.6, 1.2 and 1.8 mg daily	
	dulaglutide* (Trulicity)†	0.75, 1.5, 3.0 and 4.5 mg 1x a week pen injector	
	semaglutide* (Ozempic)	0.25, 0.5, 1.0 and 2.0 mg 1x a week pen injector	
	(Rybelsus) Oral tablet	3, 7, and 14 mg daily in a.m. Take on empty stomach with sip of water	
GLP-1 & GIP Receptor Agonist Activates receptors for GLP-1 (see above) & Glucose-dependent Insulinotropic Polypeptide (GIP).	Tirzepatide (Mounjaro)	2.5, 5.0, 7.5, 10, 12.5 and 15 mg 1x a week prefilled single dose pen Increase dose by 2.5 mg once monthly to reach targets.	**Side effects:** nausea, diarrhea, injection site reaction. Report pancreatitis, signs of intestinal blockage. **Black box warning:** Avoid if family history of medullary thyroid tumor. Lowers A1C ~ 1.8 - 2.4% Weight loss: 7-13% body weight loss at max dose.

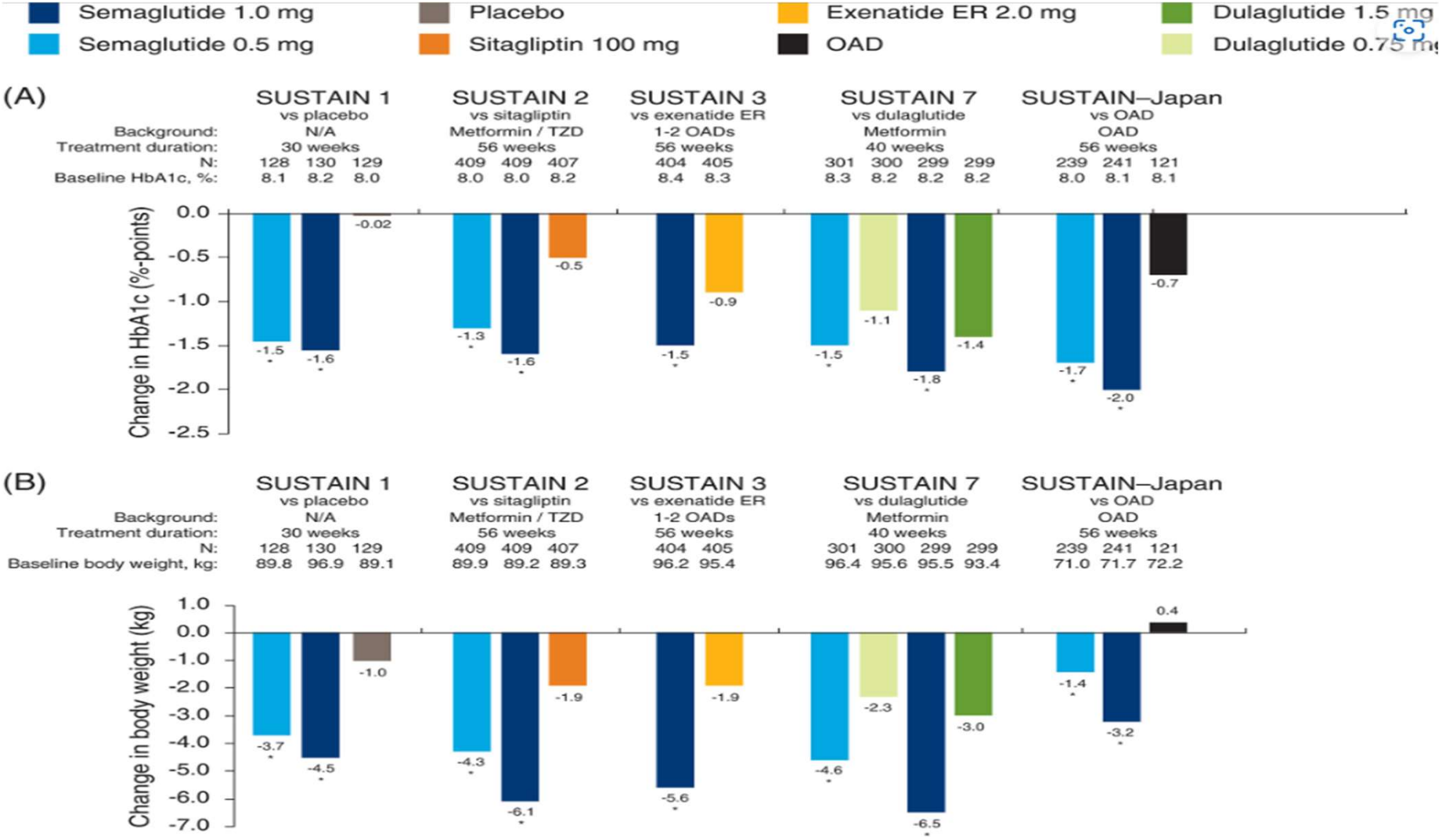
Oral Semaglutide (Rybelsus)

- Barriers to GLP-1 oral absorption:
  - Degradation by gastrointestinal enzymes
  - pH induced conformational changes
  - Limited protein permeability of the intestinal membrane
- Semaglutide co-formulated with sodium N-(8-[2-hydroxybenzoyl] amino) caprylate (**SNAC**), an absorption enhancer
- Absorbed in stomach where SNAC causes a localized increase in pH, leading to higher solubility and protection against proteolytic degradation
- Take daily at least 30 mins before first food, beverage, or other oral meds
- Take with no more than 4 ounces of plain water
- Swallow tablets whole (don't cut or crush)

Incretin Summary

	Drug	Approval date (US, EMA)	Phase III clinical trial program	Base	Homology to native GLP-1 (%)	Dose and frequency	Route	T_{max}	Half-life
Short-acting	Exenatide (Byetta®)	28 April 2005, 20 November 2006	AMIGO	Exendin-4	53	5–10 mcg twice daily	SC	2.1 h	2.4 h
	Lixisenatide (Adlyxin®, Lyxumia®)	28 July 2016, 1 February 2013	GetGoal	Exendin-4	50	10–20 mcg once daily	SC	1–3.5 h	3 h
Long-acting	Liraglutide (Victoza®)	25 January 2010, 30 June 2009	LEAD	Human GLP-1	97	0.6–1.8 mg once daily	SC	8–12 h	13 h
	Exenatide (Bydureon®)	26 January 2012, 17 June 2011	DURATION	Exendin-4	53	2 mg once weekly	SC	2.1–5.1 h	NR
	Dulaglutide (Trulicity®)	18 September 2014, 21 November 2014	AWARD	Human GLP-1	90	0.75–1.5 mg once weekly	SC	24–72 h	5 days
	Semaglutide (Ozempic®)	5 December 2017, 8 February 2018	SUSTAIN	Human GLP-1	94	0.25–1 mg once weekly	SC	1–3 days	1 week
	Oral Semaglutide (Rybelsus®)	20 September 2019, 3 April 2020	PIONEER	Human GLP-1	94	3–14 mg once daily	PO	1 h	1 week

SUSTAIN (semaglutide)clinical program



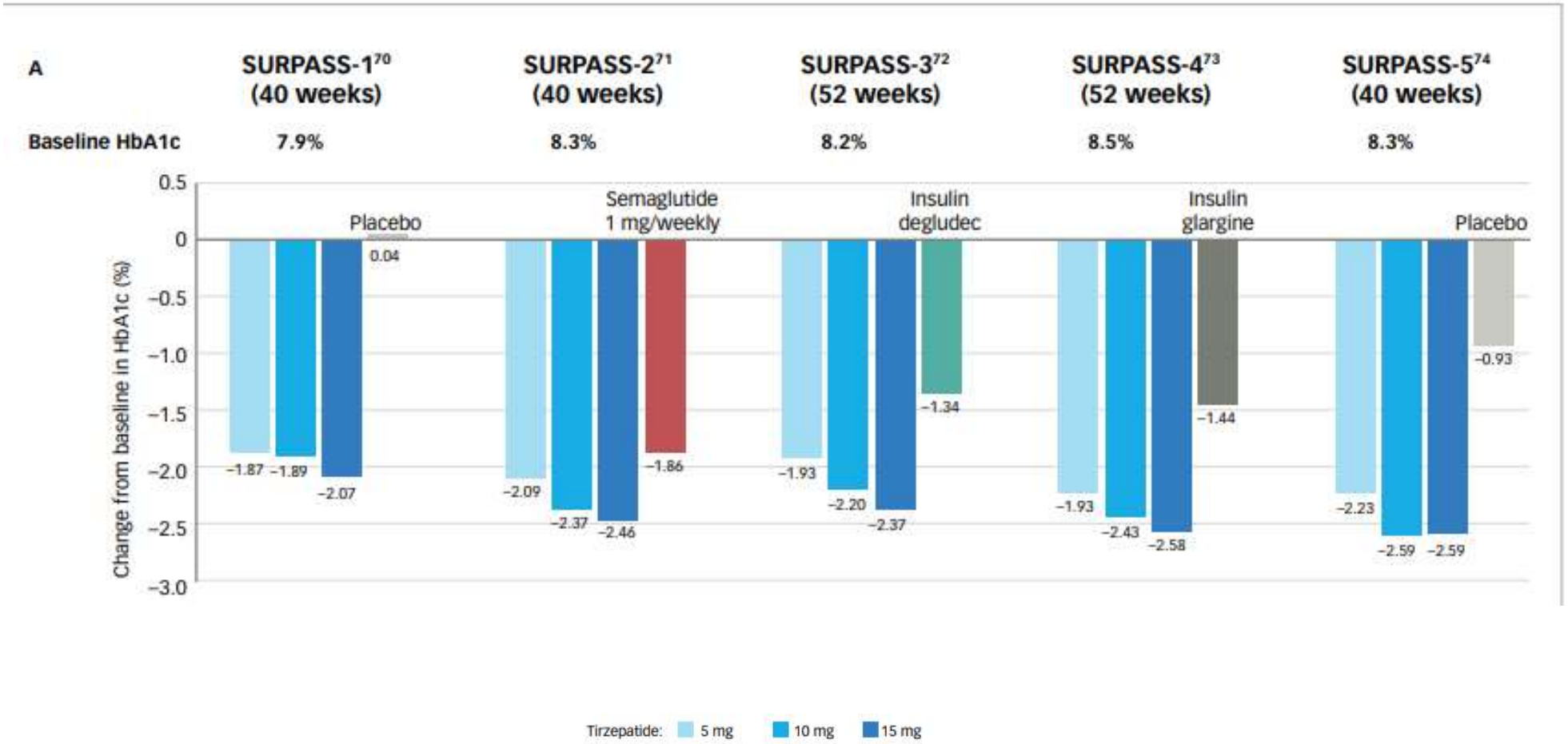
Chudleigh RA, Platts J, Bain SC. Comparative Effectiveness of Long-Acting GLP-1 Receptor Agonists in Type 2 Diabetes: A Short Review on the Emerging Data. Diabetes Metab Syndr Obes. 2020 Feb 18;13:433-438.

Poll Question 9

Alice injects tirzepatide once a week. Which of the following is true?

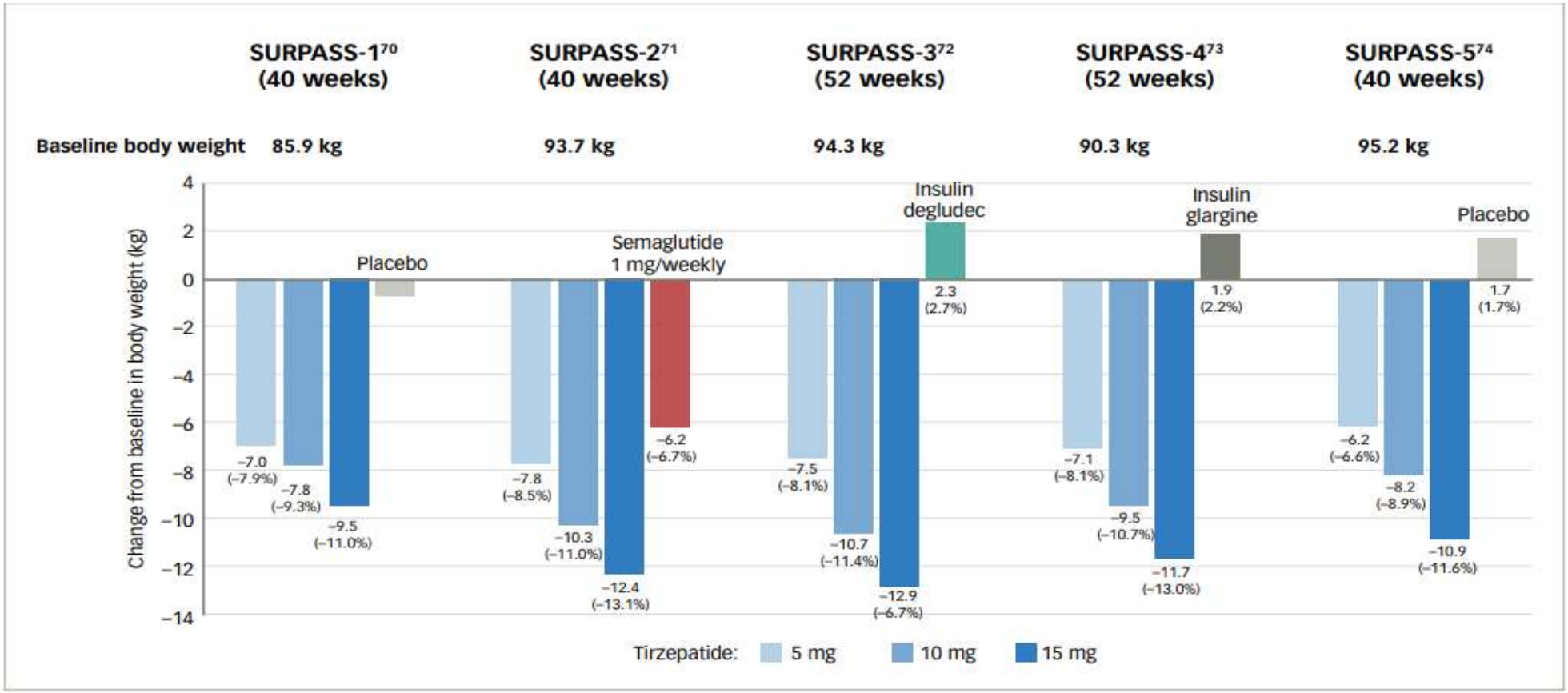
a. May experience nausea
b. May cause hypoglycemia
c. Muscle aches are common
d. Doubles risk of pancreatic cancer

SURPASS (Tirzepatide): A1C Change



Rosenstock J, et al. Lancet. 2021;398:143–55. Frias JP, et al. N Engl J Med. 2021;358:503–15. 82. Ludvik B, et al. Lancet. 2021;398:583–98. 83. Del Prato S et al. Lancet. 2021;398:1811–24. 84. Dahl Det al. Diabetologia. 2021:64(Suppl. 1):S13. Abstr 20. Kaneko S.. touchREV Endocrinol. 2022 Jun;18(1):10-19.

SURPASS (Tirzepatide): Change in Body Weight



Rosenstock J, et al. Lancet. 2021;398:143–55. Frias JP, et al. N Engl J Med. 2021;358:503–15. 82. Ludvik B, et al. Lancet. 2021;398:583–98. 83. Del Prato S et al. Lancet. 2021;398:1811–24. 84. Dahl Det al. Diabetologia. 2021:64(Suppl. 1):S13. Abstr 20. Kaneko S.. touchREV Endocrinol. 2022 Jun;18(1):10-19.

Tirzepatide & GLP-1 RA Safety Profile

- GI side effects
  - Nausea, appetite loss, diarrhea, constipation, dyspepsia, abdominal pain
- Pancreatitis
- Hypoglycemia with concomitant use of insulin or secretagogues
- Hypersensitivity reactions
- Acute kidney injury
- Thyroid C-Cell tumors –black box warning
- Acute gallbladder disease
- Worsening retinopathy

Package inserts.

Counseling Points: GLP-1 RA & GLP-1/GIP

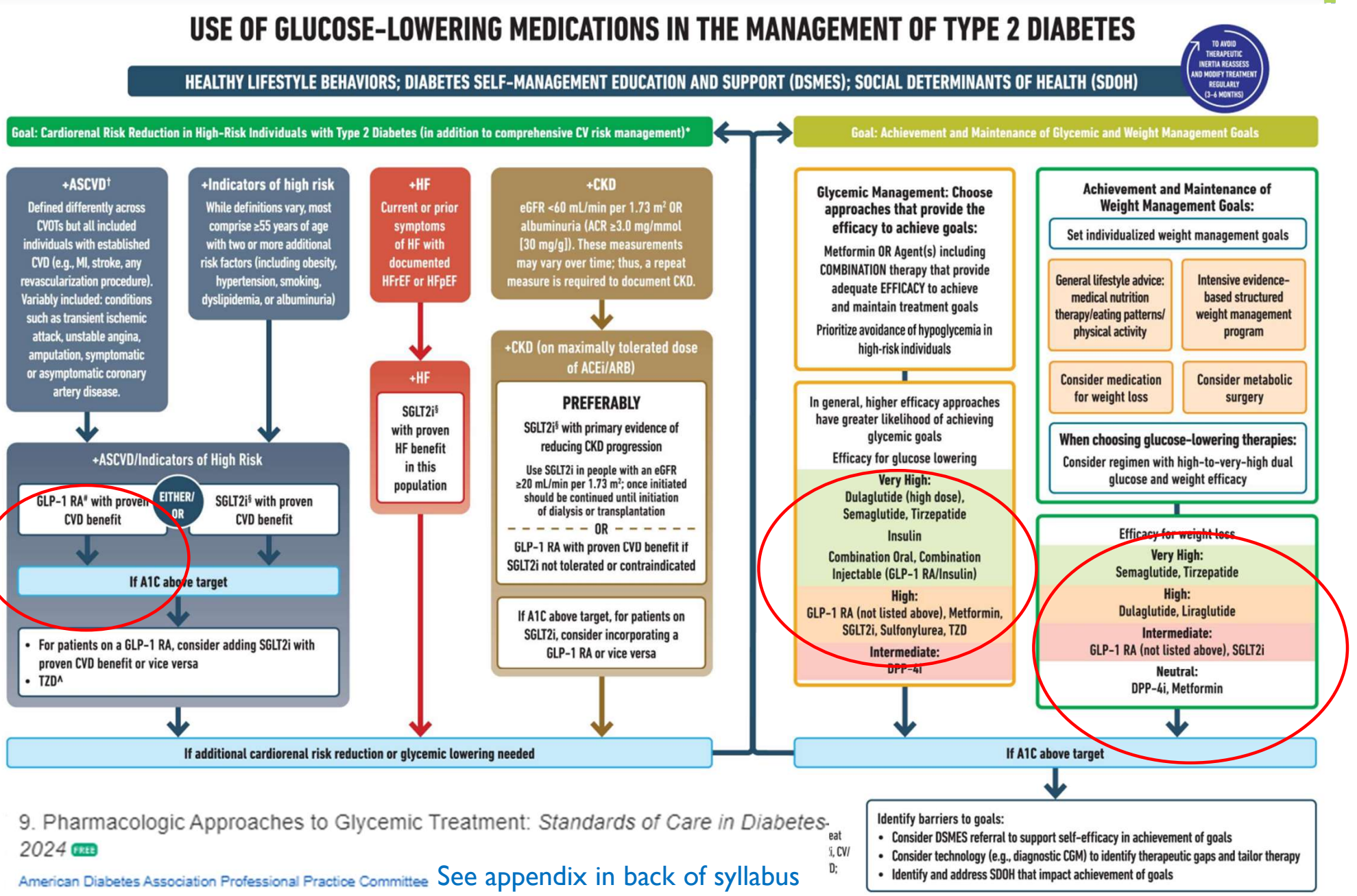
- Avoid if personal or family history of medullary thyroid cancer
- Start at lower dose and titrate
- Eat smaller *nourishing* meals to reduce nausea
- Avoid high fat meals -
- Reconsider nausea as feeling full
- Store extra pens in fridge
- Avoid in combo with DPP-4 inhibitors
- Report any sudden abdominal pain or pancreatitis symptoms
- Ask about recent eye exam
  - Potential increase in diabetes retinopathy

Poll Question 10

AR is 36 years old with type 2 diabetes and a BMI of 41kg/m^2. Current diabetes medications include: metformin, sitagliptin (Januvia) and empagliflozin (Jardiance) at maximum doses. AR is prescribed tirzepatide (Mounjaro). Based on this information, what action do you recommend to the provider?

A. Verify kidney function first.
B. Stop the sitagliptin when initiating tirzepatide.
C. Decrease the dose of metformin to prevent hypoglycemia.
D. Evaluate thyroid function before starting tirzepatide.

ADA Algorithm: Where do GLP-1 Fit?



9. Pharmacologic Approaches to Glycemic Treatment: *Standards of Care in Diabetes-2024* FREE

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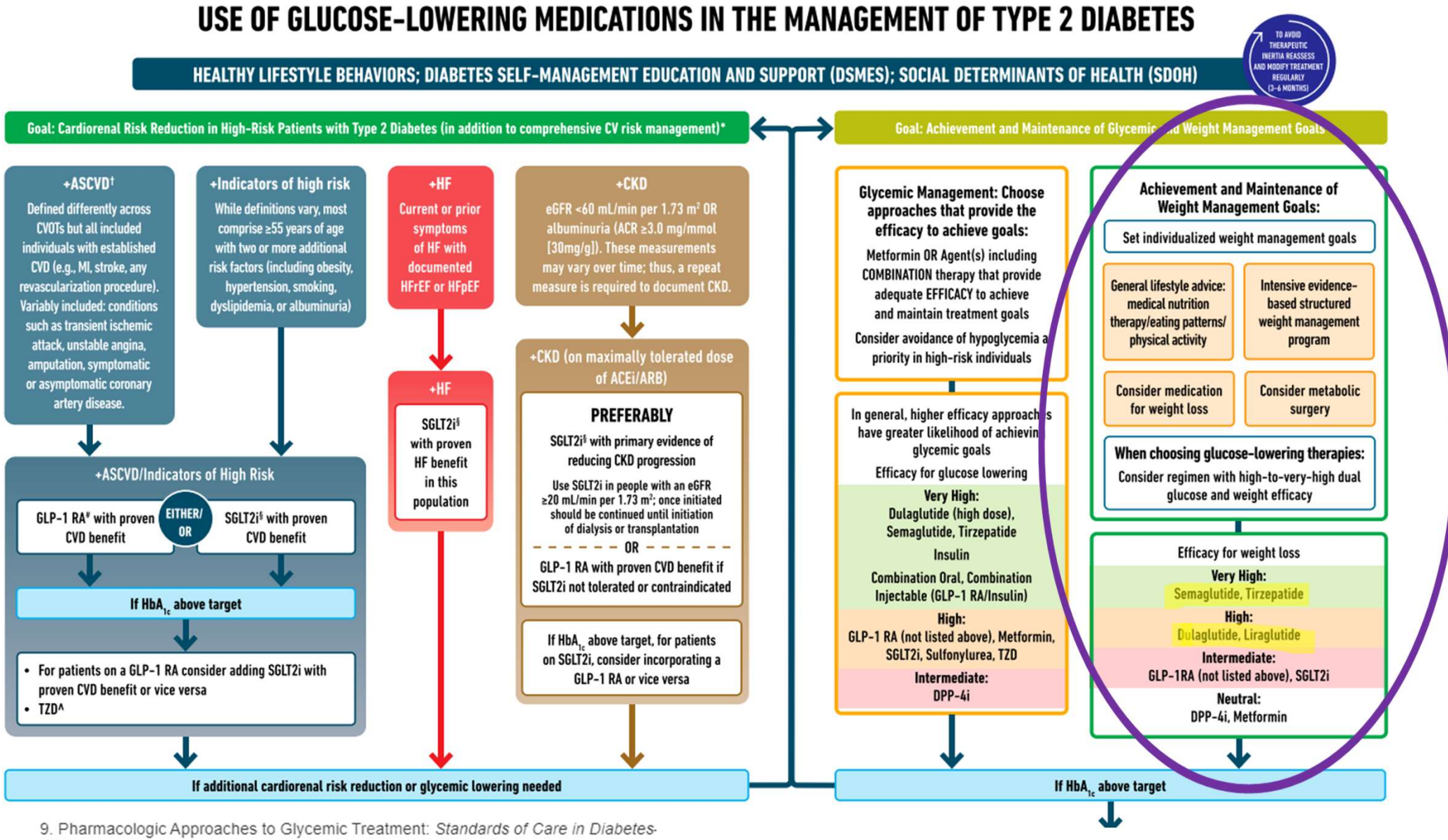
See appendix in back of syllabus

ADA Meds Algorithm



9. Pharmacologic Approaches to Glycemic Treatment: *Standards of Care in Diabetes-2024* FREE

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GLP-1 /GIPs Approved for Weight Loss

- Liraglutide:
  - Victoza 1.8 mg (diabetes)
  - Saxenda 3 mg (wt loss)
- Semaglutide:
  - Ozempic 2mg (diabetes)
    - Wegovy 2.4mg (wt loss)
- Tirzepatide
  - Mounjaro 15mg (diabetes)
  - Zepbound 15mg (wt loss)

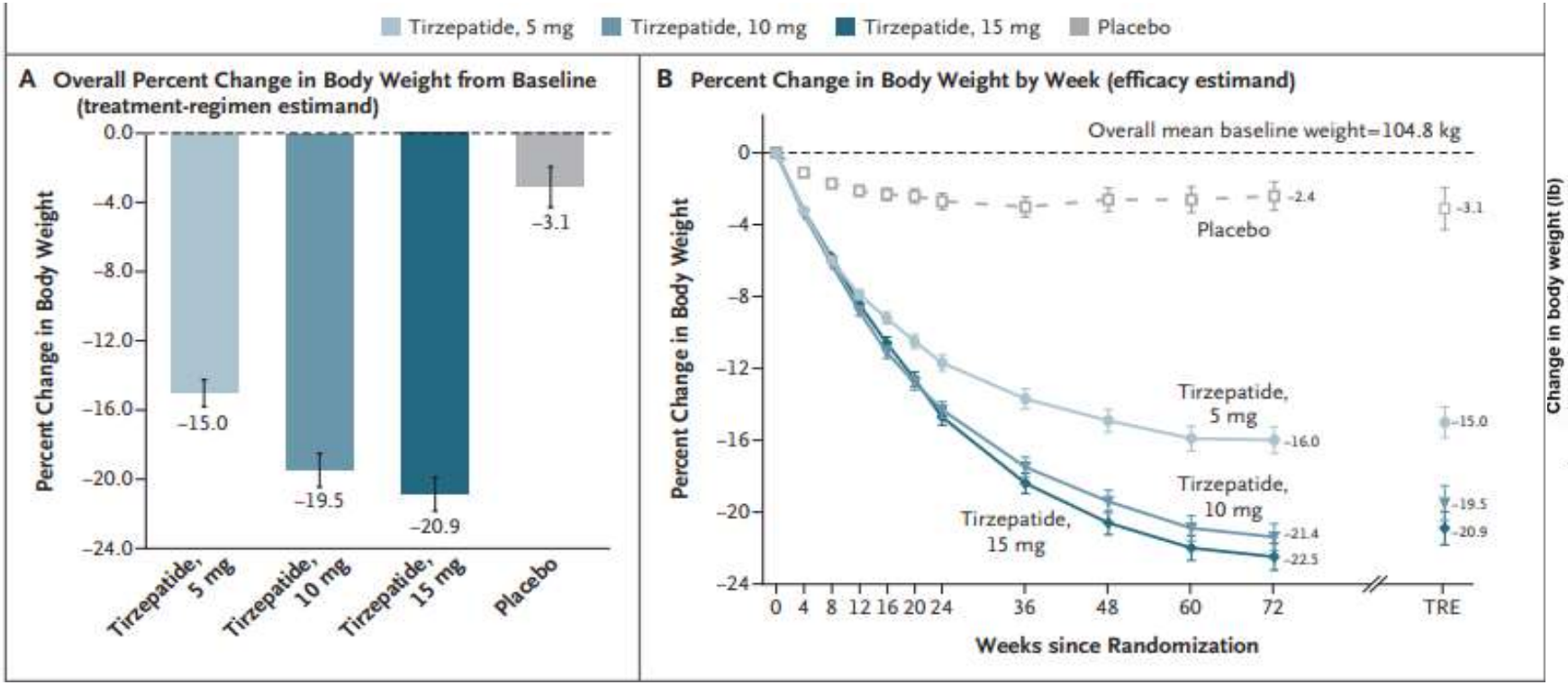
All 3 Approved for use in adults with a:

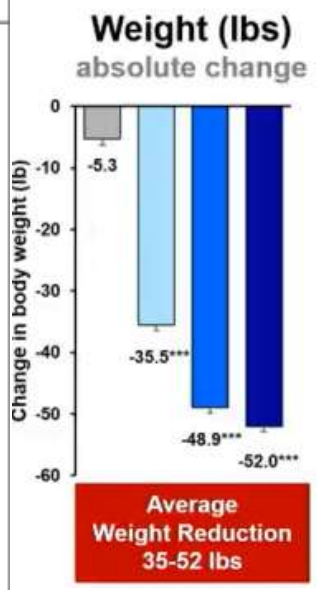
- BMI of ≥ 30 or
- BMI of ≥ 27 or greater who have hypertension, type 2 diabetes, or dyslipidemia.

Wegovy also indicated for those overweight/obesity ASCVD to reduce CVD events

Tirzepatide for Weight Loss: SURMOUNT-1

- 20.9% weight loss with 15mg dose and 35-52lbs lost!





Jastreboff AM, et al., on behalf of the SURMOUNT-1 Investigators. Tirzepatide Once Weekly for the Treatment of Obesity. *N Engl J Med* 2022;387:205-16.

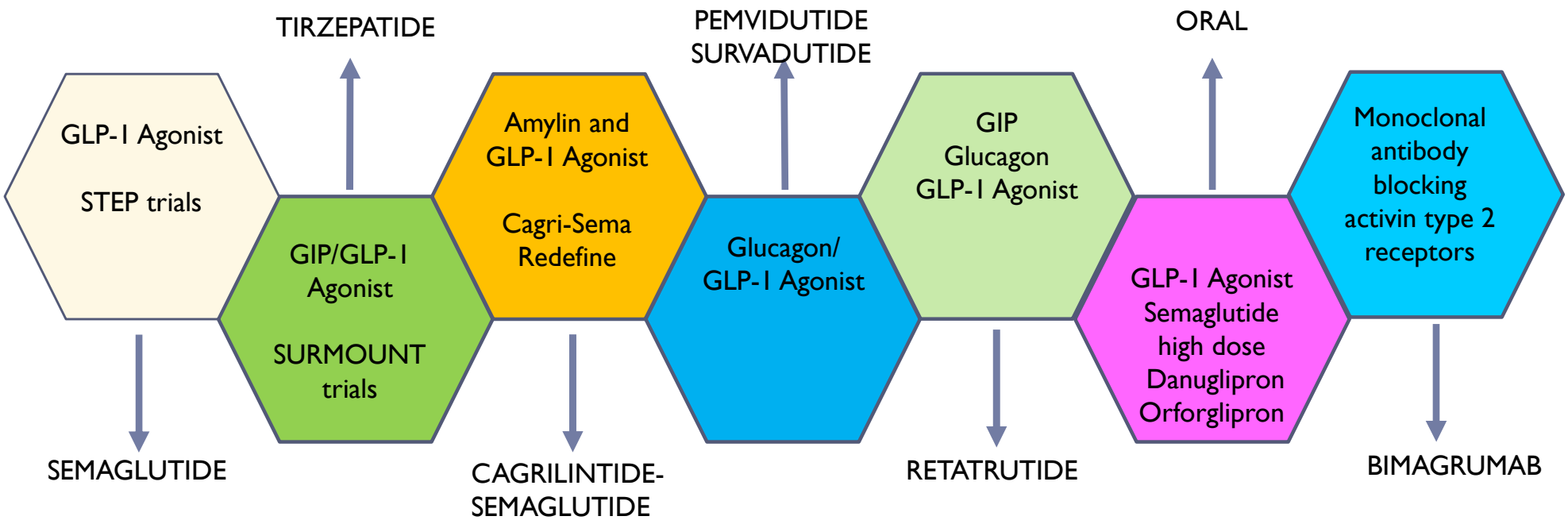
GLP-1/GIP Receptor Agonist Indications

Drug	Lower BG	Reduce CV Risk?	Wt loss approved?
Exenatide IR **(Byetta)** Lixisenatide **(Adlyxin)** Semaglutide **(Rybelsus)**	Yes	No	No
Exenatide ER **(Bydureon)**	Yes for 10 yrs and older	No	No
Dulaglutide **(Trulicity)**	Yes for 10 yrs and older	Yes	No
Semaglutide **(Ozempic)**	Yes	Yes	Yes Wegovy 2.4mg
Liraglutide **(Victoza)**	Yes for 10 yrs and older	Yes	Yes Saxenda 3mg
Tirzepatide **(Mounjaro)**	Yes	?	Yes, Zepbound 15 mg

Incretins– How Do They Rate?

Question	Answer
Cause hypoglycemia?	No
Cause weight gain?	No
Affordable?	No, $1000/+month
Lowers CV risk*?	*Liraglutide / Semaglutide/Dulaglutide
Can most tolerate /use?	Yes/No (GI)

The Future of Incretins is Bright



Medication Taking Behaviors

- Adequate medication taking is defined as 80%
- 23% of time, if A1c, B/P, lipids above target - due to med taking behavior
- Assess for barriers
- If taking meds 80% of time and goals not met, consider medication intensification

Barriers include:
Forgetting to fill Rx, forgetting to take, fear, depression, health beliefs, med complexity, cost, knowledge gap, system factors, etc.

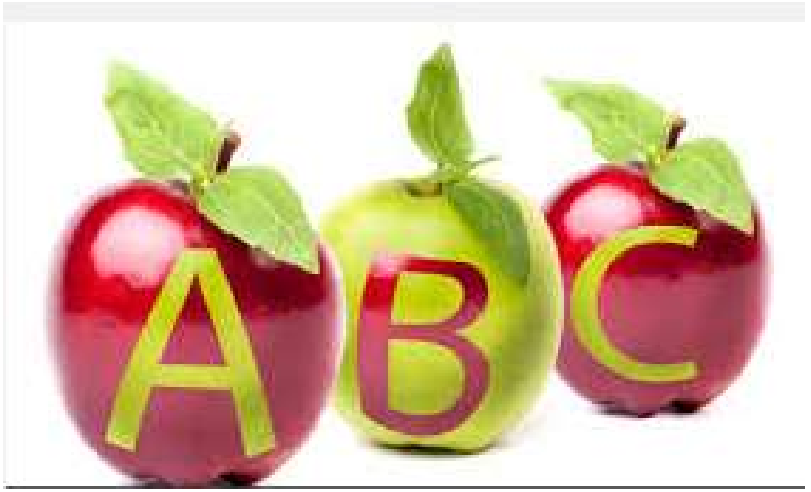
Work on targeted approach for specific barrier

6. Glycemic Goals & Hypo

A1C

Blood Pressure

Cardiovascular risk reduction



ABC's of Diabetes

- A1c less than 7% (individualize)
  - Pre-meal BG 80-130
  - Post meal BG <180
  - AGP - Time in Range (70-180) 70% of time
- Blood Pressure < 130/80
- Cholesterol
  - Statin therapy based on age & risk status
  - If 40+ with ASCVD Risk, decrease 50%, LDL <70
  - If 40+ with ASCVD, decrease 50%, LDL <55

6. Glycemic Targets for Non-Pregnant Adults

- **A1c < 7%** - a reasonable goal for adults.
- **A1c < 6.5%** - for those without significant risk of hypoglycemia
- **A1c < 8%** - for those with history of hypoglycemia, limited life expectancy, or those with longstanding diabetes and vascular complications.
- **A1c Check Frequency:**
  - If meeting goal - At least 2 times a year
  - If *not* meeting goal – Quarterly

- **Also review Ambulatory Glucose Profile**

6. Glycemic Targets
Individualize Targets – ADA

- Pre-Prandial BG 80- 130
- 1-2 hr post prandial < than 180

  *for nonpregnant adults
- Time in Range: 70%
  - BG of 70-180 mg/dL

A1c and Estimated Avg Glucose (eAG)

A1c (%)	eAG
5	**97** (76-120)
6	**126** (100-152)
7	**154** (123-185)
8	**183** (147-217)
9	**212** (170 -249)
10	**240** (193-282)
11	**269** (217-314)
12	**298** (240-347)

eAG = 28.7 x A1c-46.7 ~ 29 pts per 1%
Translating the A1c Assay Into eAG – ADAG Study

6. Glycemic Goals and Hypoglycemia: *Standards of Care in Diabetes—2024*

BGM vs CGM

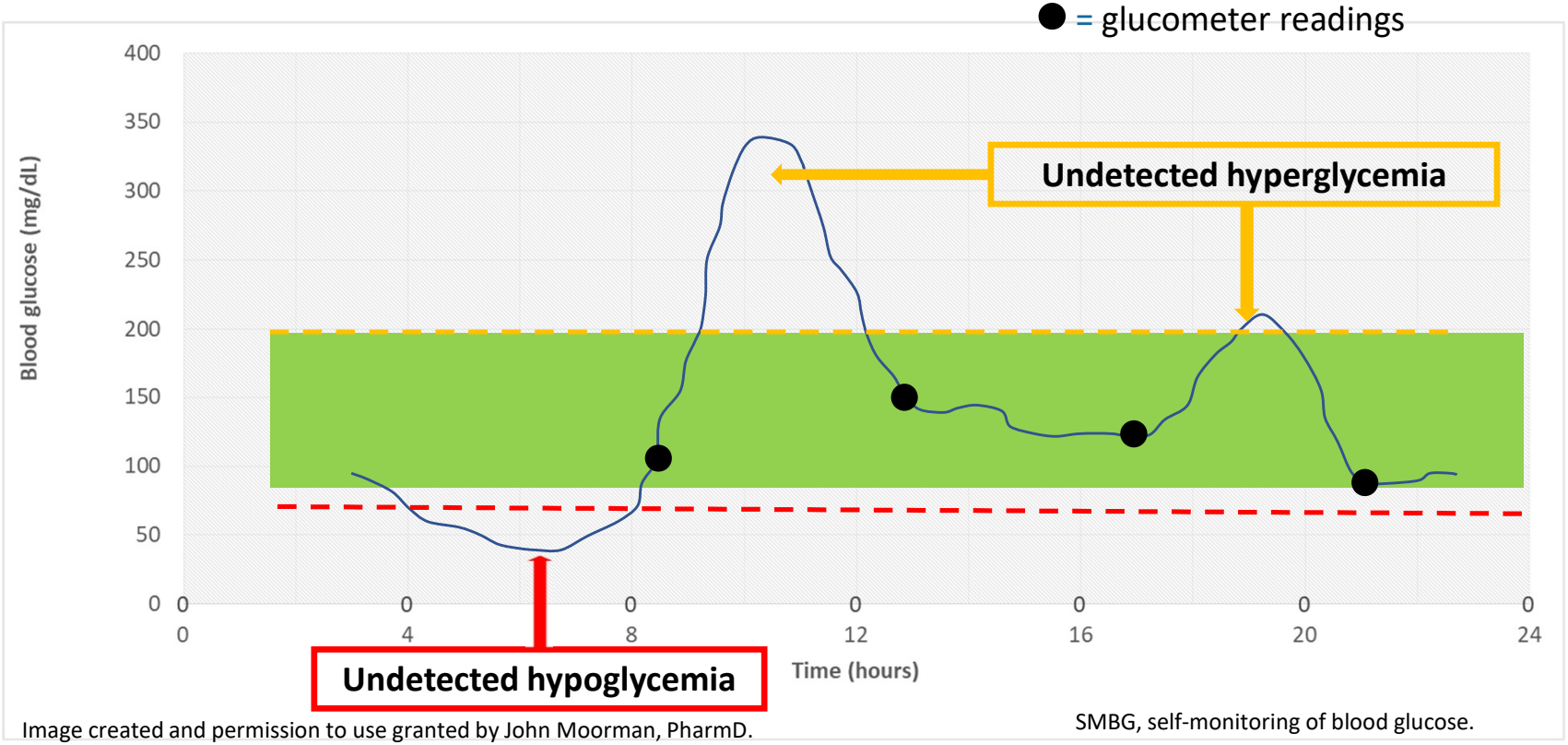
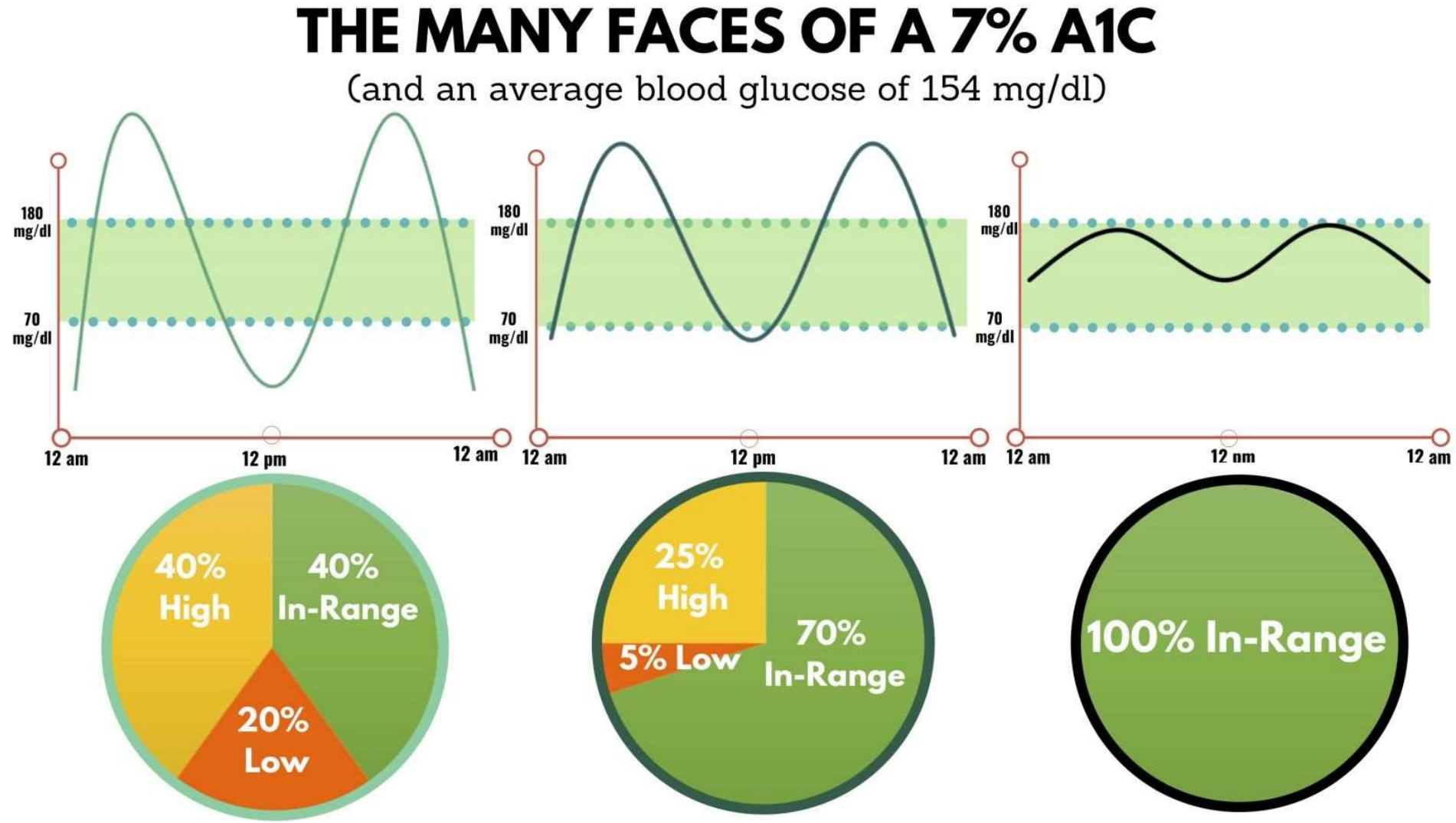


Image created and permission to use granted by John Moorman, PharmD.

SMBG, self-monitoring of blood glucose.

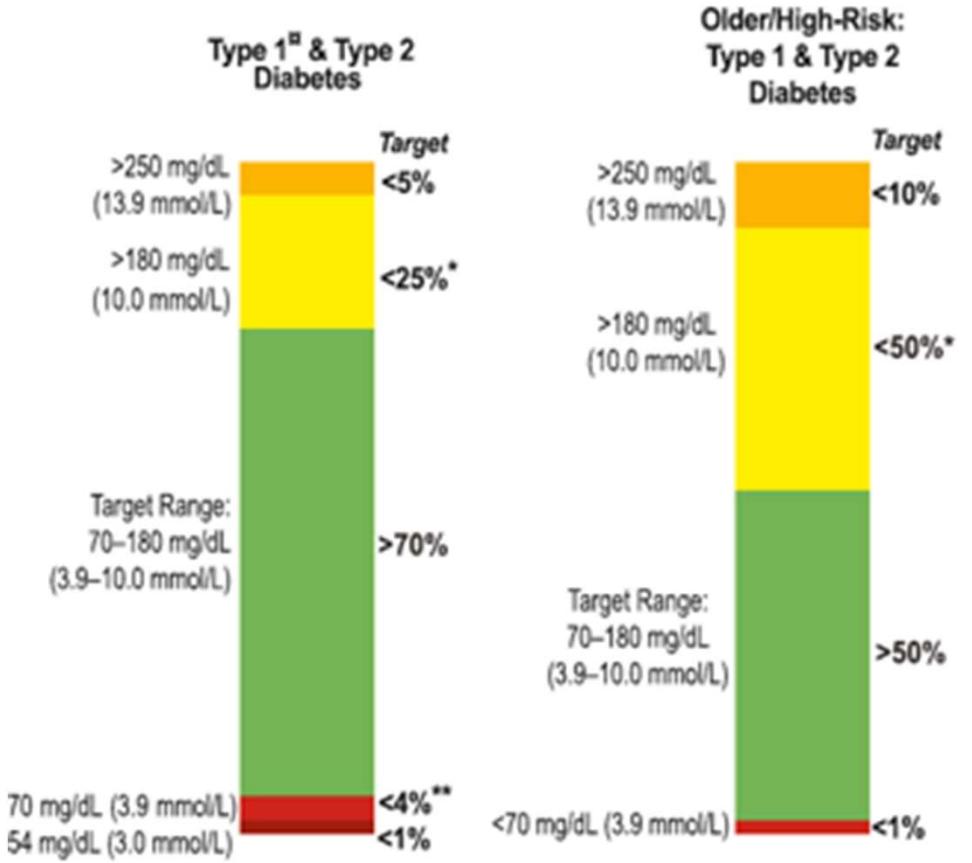
A1C Alone is Just Not Enough



https://diatribe.org/time-range.

Time in Range

- Evaluate Time in Range (TIR)
  - Target 70-180 mg/dl
  - Target time *below* goal
    - Less than 70
    - Less than 54
  - Target time *above* goal
    - Above 180
    - Above 250



Battelino T, et al. *Diabetes Care*. 2019;42(8):1593-1603.

6. Glycemic Goals and Hypoglycemia: *Standards of Care in Diabetes—2024*

Estimation of A1c for a Given TIR

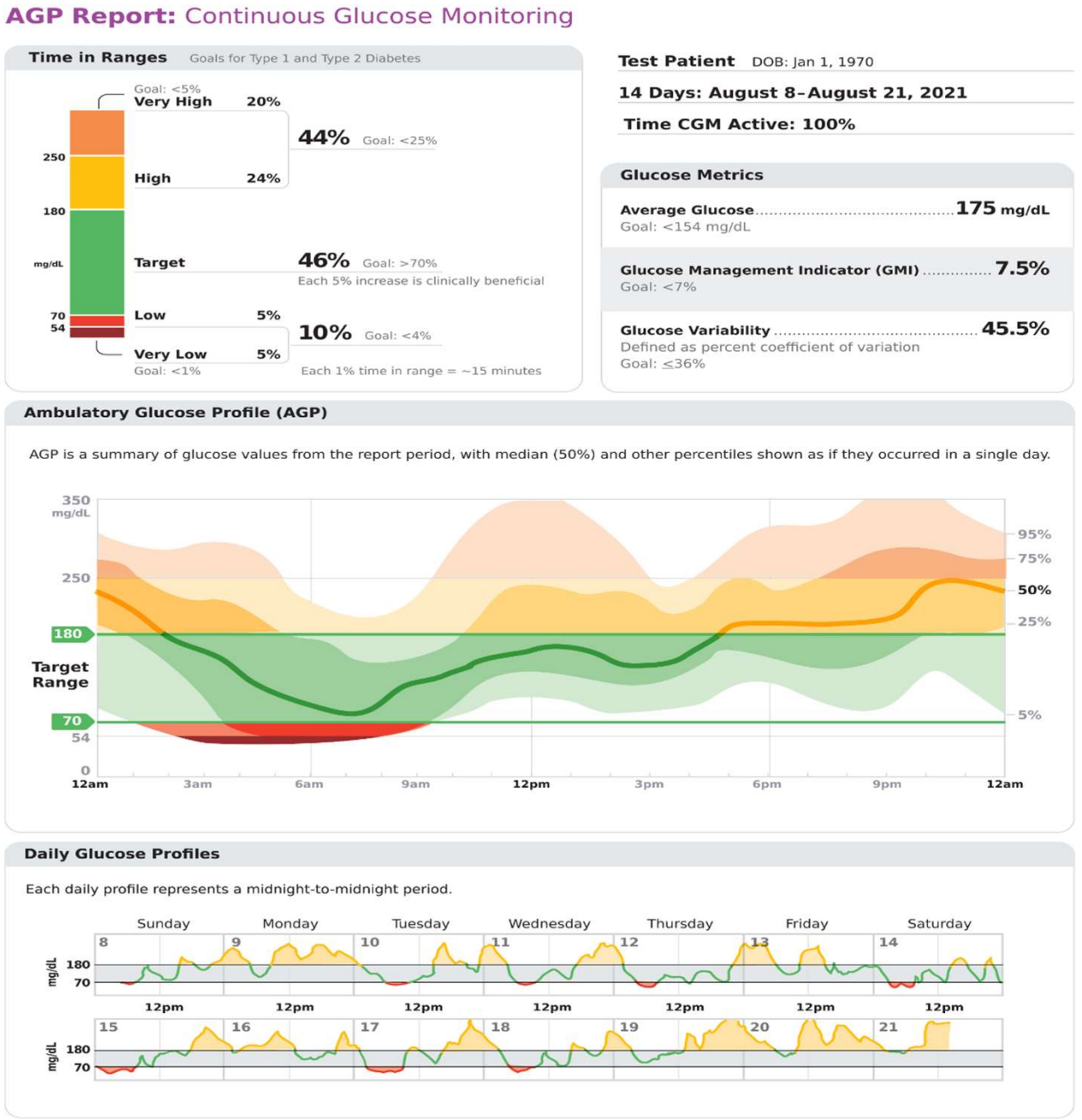
TIR$^{70\text{-}180}$ (%)	Estimated HbA1c (%)	95% CI for the predicted value
20	9.4	(8.0, 10.7)
30	8.9	(7.7, 10.2)
40	8.4	(7.1, 9.7)
50	**7.9**	**(6.6, 9.2)**
60	7.4	(6.1, 8.8)
70	**7.0**	**(5.6, 8.3)**
80	6.5	(5.2, 7.8)
90	6.0	(4.7, 7.3)

10% ΔTIR ≈ 0.5% ΔHbA1c

Beck RW, et al. J Diabetes Sci Technol. 2019;13:614-626.

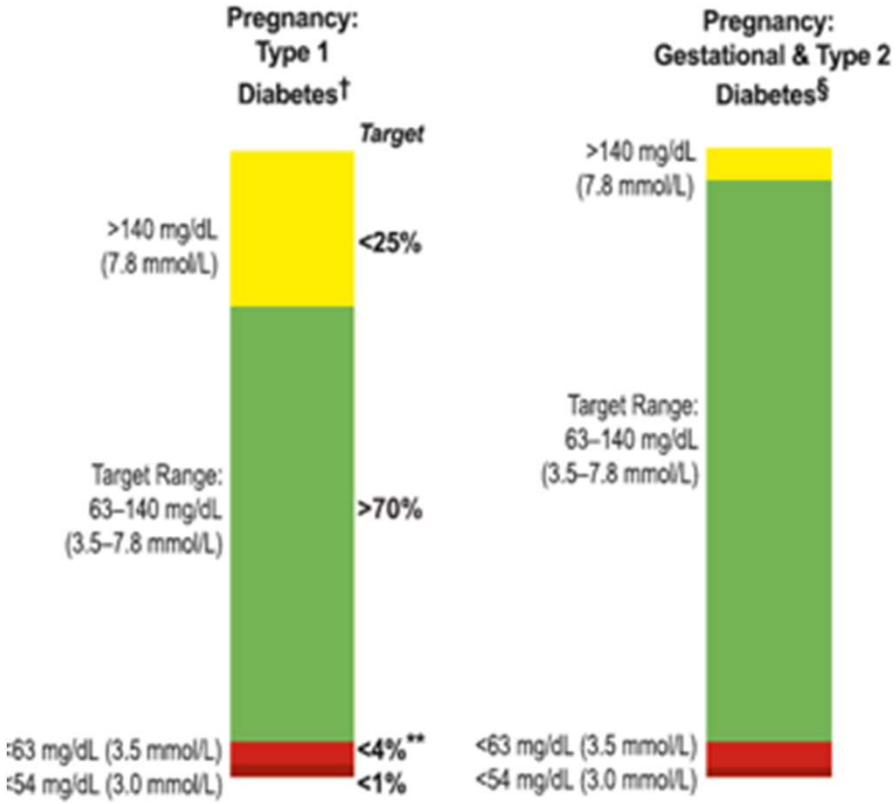
Ambulatory Glucose Profile Report

- CGM key metrics
- AGP
- Daily tracings



15. ADA Pregnancy Targets – For those with type 1, type 2 and GDM

- A1c < 6-6.5% (closer to 6 in 2nd/3rd tri)
- Fasting and Post Meal BG Goals
  - Fasting glucose 70–95 mg/dL and either
  - One-hour postprandial glucose 110–140 mg/dL or
  - Two-hour postprandial glucose 100–120 mg/dL
- Time in range: 63-140 mg/dL



Battelino T, et al. *Diabetes Care*. 2019;42(8):1593-1603.

6. Glycemic Goals and Hypoglycemia: *Standards of Care in Diabetes—2024*

Pharmacologic Treatment during Pregnancy

- Insulin is preferred therapy for GDM, type 1 and 2
  - Does not cross placenta
  - Can overcome insulin resistance assoc w/ type 2
- Sulfonylureas pass through placenta / associated with neonatal hypo (glyburide)
- Metformin – lower risk of hypo and maternal wt gain but may increase prematurity rate
  - Passes through placenta
  - If using for PCOS, stop by end of first trimester
- Refer to specialized center

15. Management of Diabetes in Pregnancy: *Standards of Care in Diabetes—2024* FREE

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Pregnancy and Hypertension

- If pregnant with diabetes and chronic hypertension
  - Blood pressure target of 110–135/85 mmHg
    - Reduces risk for accelerated maternal hypertension
    - Minimizes impaired fetal growth
  - Stop potentially harmful medications in prep for pregnancy
    - Avoid ACE inhibitors, angiotensin receptor blockers (ARBs), statins in sexually active women of childbearing age if not using reliable contraception
    - Stop these meds at conception
    - Preferred meds: labetolol, nifedipine

15. Management of Diabetes in Pregnancy: *Standards of Care in Diabetes—2024* FREE

American Diabetes Association Professional Practice Committee

Case Study - Ricki

Ricki is a 36yoF with a history of GDM and newly diagnosed with type 2 diabetes. A1C=7.4%. Normal kidney function. Past medical history includes hypertension for which she takes HCTZ 25mg daily.

Weight: 220lbs, BMI=34kg/m^2

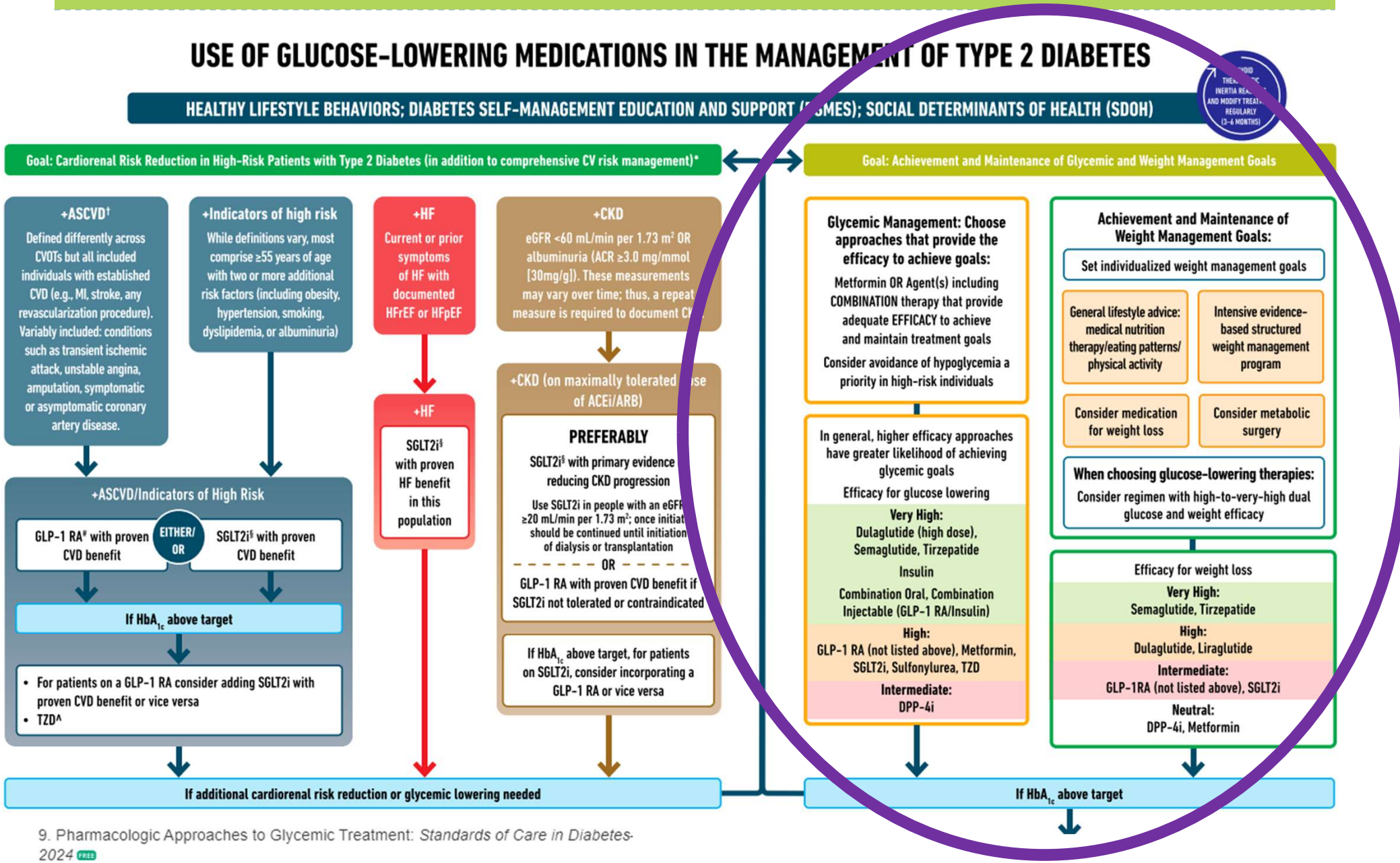
Social history

- Works full time as an accountant
- Skips breakfast, eats a small lunch, eats a large dinner, snacks in evening
- No Exercise
- Loves Starbucks Frappuccino's

Poll 11. What Treatment Should Ricki Be Started On?

A. Glipizide (sulfonylurea)
B. Linagliptin (DPP-4 inhibitor)
C. Empagliflozin (SGLT-2 inhibitor)
D. Metformin (Biguanide)
E. Lifestyle modifications only

ADA Meds Management



9. Pharmacologic Approaches to Glycemic Treatment: *Standards of Care in Diabetes-2024* FREE

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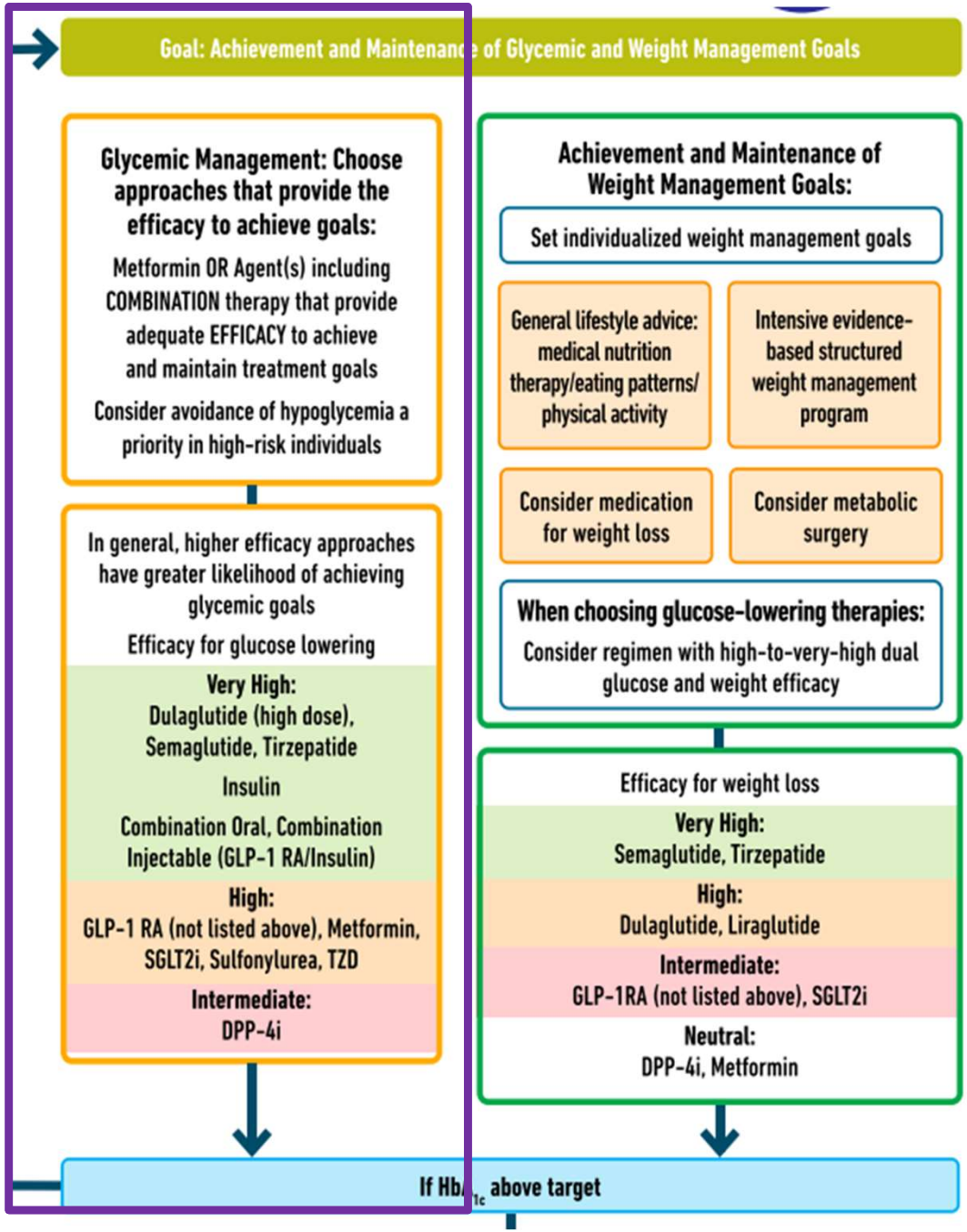
Metformin is "Usually" 1st Line



- Why metformin?
  - Longstanding evidence
  - High efficacy and safety
  - Inexpensive - 3 months for $12
  - Weight neutral

- If ASCVD, HF or CKD or high ASCVD risk, use SGLT2i or GLP-1 RA +/- metformin
- If A1C ≥ 8.5%, consider combo therapy.

9. Pharmacologic Approaches to Glycemic Treatment: *Standards of Care in Diabetes-2024* FREE

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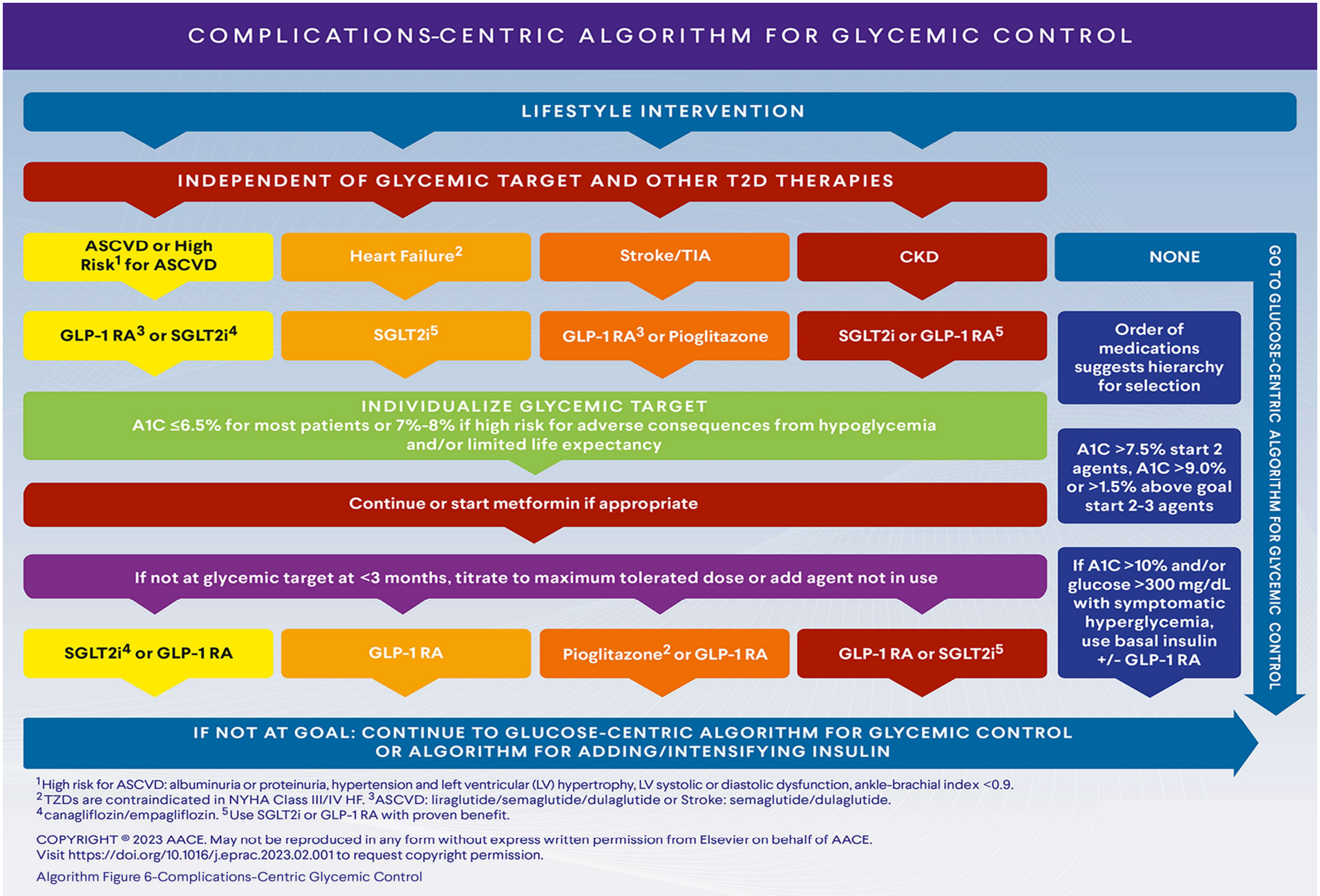
AACE 2023 Diabetes Guideline



[1]High risk for ASCVD: albuminuria or proteinuria, hypertension and left ventricular (LV) hypertrophy, LV systolic or diastolic dysfunction, ankle-brachial index <0.9.
[2]TZDs are contraindicated in NYHA Class III/IV HF. [3]ASCVD: liraglutide/semaglutide/dulaglutide or Stroke: semaglutide/dulaglutide.
[4]canagliflozin/empagliflozin. [5]Use SGLT2i or GLP-1 RA with proven benefit.

Algorithm Figure 6-Complications-Centric Glycemic Control

Common Oral Diabetes Meds

Class/Main Action	Name(s)	Daily Dose Range	Considerations
Biguanides • Decreases hepatic glucose output • First line med at diagnosis of type 2	metformin (Glucophage) Riomet (liquid metformin)	500 - 2550 mg (usually BID w/ meal) 500 - 2550 mg 500mg/5mL	**Side effects:** nausea, bloating, diarrhea, B12 deficiency. To minimize GI Side effects, use XR and take w/ meals. **Obtain GFR before starting.** • If GFR <30, do not use. • If GFR <45, don't start Meformin • If pt on Metformin and GFR falls to 30-45, eval risk vs. benefit; consider decreasing dose. **For dye study,** if GFR <60, liver disease, alcoholism or heart failure, restart metformin after 48 hours if renal function stable. **Benefits:** lowers cholesterol, no hypo or weight gain, cheap. Approved for pediatrics, 10 yrs + Lowers A1c 1.0%-2.0%.
	Extended Release-XR (Glucophage XR) (Glumetza) (Fortamet)	(1x daily w/dinner) 500 – 2000 mg 500 – 2000 mg 500 – 2500 mg	

Biguanide derived from:
Goat's Rue *Galega officinalis*,
French Lilac
Does NOT harm kidneys
$10 for 3-month supply from
Walmart & other pharmacies

Poll Question 12

- Ricki is started on Metformin 500mg BID. Which of the following is true?

a. Hold metformin if blood glucose is below 80 mg/dL
b. If you forget to take metformin before the meal, hold the dose
c. Metformin may cause loose stools
d. Avoid Metformin if eGFR is less than 60

Metformin Dosing and Mechanism

- Mechanism: decreases hepatic glucose production
  - Data suggest metformin may be safely continued with eGFR of 30-45 mL/min/1.73m^2 with dose reductions
  - Do not initiate when eGFR < 45
  - Max effective dose: 2000mg/day
- Monitor vitamin B12 levels and renal function
- GI issues: nausea, vomiting, diarrhea
  - Consider long-acting formulation, dose reduction

Metformin – How Does it Rate?

Question	Answer
Cause hypoglycemia?	No
Cause weight gain?	No
Affordable?	Yes
Lowers CV risk?	Yes
Can most tolerate /use?	Yes/No (GI, creat)

Risk-Based Screening for PreDiabetes or Type 2 in Children and Youth

- Test youth with excess weight (BMI >85% percentile)
- Plus any ONE of following risk factors:
  - Maternal diabetes or GDM during child's gestation
  - Family history type 2 in 1st or 2nd degree relative
  - Native American, African American, Latin, Asian, Pacific Islander
  - Signs of insulin resistance (acanthosis nigricans, HTN, dyslipidemia, Polycystic Ovary Syndrome – PCOS or small for gestational age birth weight

2. Diagnosis and Classification of Diabetes: *Standards of Care in Diabetes—2024* FREE

American Diabetes Association Professional Practice Committee

- Test at 10 yrs or puberty (whichever is first) and at least every 3 yrs or more frequently if indicated. Consider earlier screening if multiple risk factors.

14. Type 2 and Kids Goals

- A1c goal of 7% if on oral meds alone
- A1c goal of 7.5% if at risk for hypoglycemia
- Some children benefit from A1c of 6.5% or less

- Initiate pharmacologic therapy, in addition to lifestyle therapy, at diagnosis
- Confirm diagnosis with antibody testing
- Treat glucose, B/P and lipids
- Engage in lifestyle coaching
- **Please see Kids and Diabetes Level 2 Course**

14. Children and Adolescents: *Standards of Care in Diabetes—2024* FREE

14. Pediatric Glycemic Targets

- **A1c goal 6.5 – 8.0% for Type 1**
  - Generally, goal is <7.0%
  - Individualization is encouraged.
  - A goal <6.5% may be considered for those at low risk of excessive hypoglycemia
  - A goal of <8.0 may be needed
  - CGM / Insulin pump important tools.

14. Children and Adolescents: *Standards of Care in Diabetes—2024* FREE

Poll Question 13

- What percent of the population over the age of 65 has type 2 diabetes?

A. 9.3%
B. 18%
C. 26%
D. 34%

13. Older Adults Goals – Whole Picture

- Consider the assessment of medical, psychological and self-care domains to provide context to determine targets and therapeutic approaches for management.
- Screen for geriatric issues
  - polypharmacy,
  - cognitive impairment, depression
  - urinary incontinence, falls, and persistent pain

  that can affect diabetes self-management and diminish quality of life

See Level 2 Course, Older Adults and Diabetes

Treatment Goals Based On:

- Length of time living with diabetes (new onset, undiagnosed for many years or longer history)
- Presence or absence of complications
- Comorbidities
- Degree of frailty
- Cognitive function
- Life expectancy (often longer than expected)
- Functional status

Poll Question 14

- RT, is a healthy 74-year-old who is on metformin 1000mg BID. Has had diabetes for 11 years. Latest A1c was 7.3% What is best response?
  - A. Good job, let's get the A1c less than 7%
  - B. Have you been snacking more than usual?
  - C. What do you think about your A1c level?
  - D. Let's add on another medication to get your A1c to target.

Healthy & Good Functional Status

- Set more intensive goals if:
  - Good cognitive and physical function
  - Expected to live long enough to reap benefits of intensive management,
- Ongoing follow-up to eval safety and hypoglycemia frequency

- **Goals:**
  - Reasonable A1c goal <7.0 - 7.5%
  - Fasting BG 80 – 130
  - Bedtime Glucose 80-180
  - Blood Pressure < 130/80
  - Statin unless contraindicated or not tolerated

Poll 15 – Review Question

- HR is a 78-year-old with a stroke and limited cognition. She has had diabetes for 8 years and is on intensive insulin therapy: Bolus coverage at meals and basal at night. Her A1c is 6.2%. She has a part time care taker. What do you suggest?
- A. Evaluate food intake
- B. Discuss de-intensifying insulin regimen
- C. Move Lantus to morning
- D. Stop insulin and start on oral medications

Older Adults and Medications

- In older **adults** at increased risk of hypoglycemia, meds with low risk of hypoglycemia are preferred.
- Overtreatment of diabetes is common in older adults and should be avoided.
- Deintensification (or simplification) of complex regimens is recommended to reduce the risk of hypoglycemia, if it can be achieved within the individualized A1C target.

Older Adults with Complications and Reduced Functionality - Less Intense Goals

- Intermediate remaining life expectancy, high treatment burden, hypo and fall risk.
- Consider DE-Intensification
- Goals:
  - Reasonable A1c goal <8.0%
  - Fasting BG 90 – 150
  - Bedtime BG 100-180
  - Blood Pressure < 130/80
  - Statin unless contraindicated or not tolerated

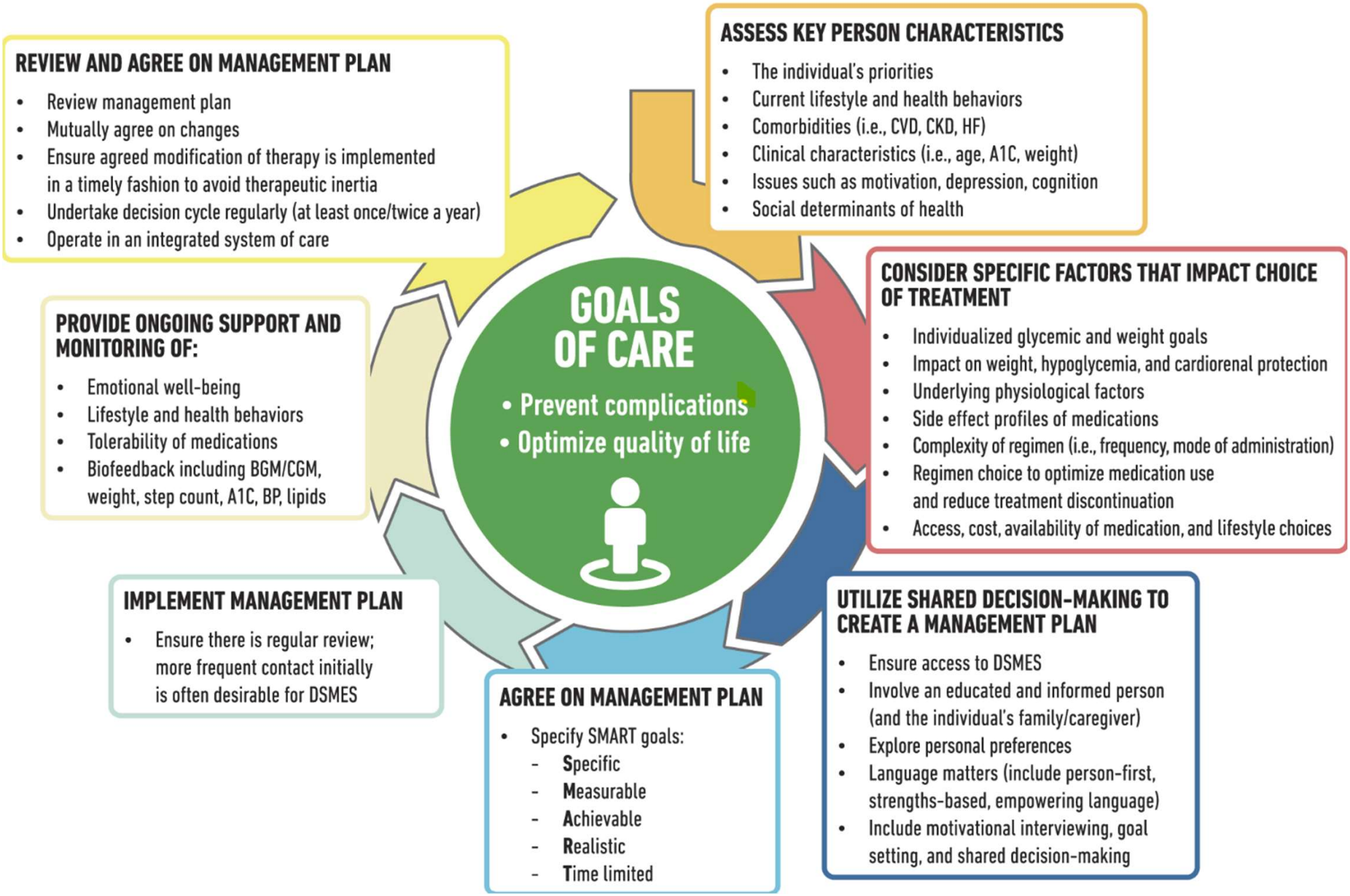
Older Adults (≥65 years) with diabetes

- Annual screening for early detection of mild cognitive impairment or dementia
- High priority population for depression screening and treatment
- Avoid hypoglycemia in this high risk group
  - Prevent hypo by adjusting glycemic targets and adjusting pharmacologic interventions

4. ADA – Complete Medical Evaluation

- At initial visit :
  - Whole person care and psychosocial evaluation
  - Explore diabetes self-management and health status
  - Evaluate if changes in diabetes treatment would improve well being.
- Engagement in formulation of a care management plan
- Develop a plan for continuing care

DECISION CYCLE FOR PERSON-CENTERED GLYCEMIC MANAGEMENT IN TYPE 2 DIABETES



4. Comprehensive Medical Evaluation and Assessment of Comorbidities: *Standards of Care in Diabetes—2024*

American Diabetes Association Professional Practice Committee

ADA Assess and Treatment Plan

- **Assess risk of diabetes complications**
  - ASCVD risk factors and heart failure history
  - Stage chronic kidney disease
  - Hypoglycemia risk
  - Assess for neuropathy, retinopathy
- **Goal setting**
  - Set A1C/blood glucose targets & Time in Range
  - Address hypertension and lipids
  - Diabetes self-management goals
- **Therapeutic treatment plans**
  - Lifestyle management – referral to RD, DSME and specialists
  - Pharmacologic therapy: glucose lowering
  - Pharmacologic therapy: cardiorenal risk factors
  - Use of glucose monitoring and insulin delivery devices
  - Referral for DSME and RDN

Lab Eval at Initial & Annual Visit

- A1c (each 3-6 mo's)
- Each year
  - Lipids, CBC with platelets
  - Liver function
  - Spot urinary albumin-to-creat ratio (UACR))
  - Serum creat and GFR
  - TSH (type 1)
  - B12 if on metformin
  - Calcium, Vita D, and phosphorus if appropriate
- Serum K
  - If on ACE, ARBs or diuretics

4. Comprehensive Medical Evaluation and Assessment of Comorbidities: *Standards of Care in Diabetes—2024*

American Diabetes Association Professional Practice Committee

Referrals for Initial Care Mgmt

- Eye professional – annual check
- Family planning
- RD for nutrition therapy
- DSMES - Diabetes Self-Management Education Support
- Dentist for comprehensive dental examination
- Behavioral health professional & audiology, if indicated
- Social worker/community resources
- Rehab medicine for cog/disability eval

4. Comprehensive Medical Evaluation and Assessment of Comorbidities: *Standards of Care in Diabetes—2024* FREE

ADA – Follow-up Visit to include:

- **Interval medical history**
  - Psychosocial Status
  - Assess med taking behavior
- **Physical exam**
  - Skin appearance
  - Ambulation and gate
  - Lower extremities, feet
  - Activity levels strengthening and cardiovascular workout
- **Health**
  - Dental health, Bone health
  - Eye check
  - Mammogram
  - Vaccinations
  - RDN, CDCES, Diabetes Ed Program
- **Nutritional status and relationship with food**
  - GI health (constipation, diarrhea, gastroparesis, fatty liver)
  - GU health – continence, creat, GFR, creat /alb ratio
  - Menstruation and contraception
  - Thyroid – Symptoms + TSH
  - Heart – blood pressure, chest pain, heart rate, cholesterol

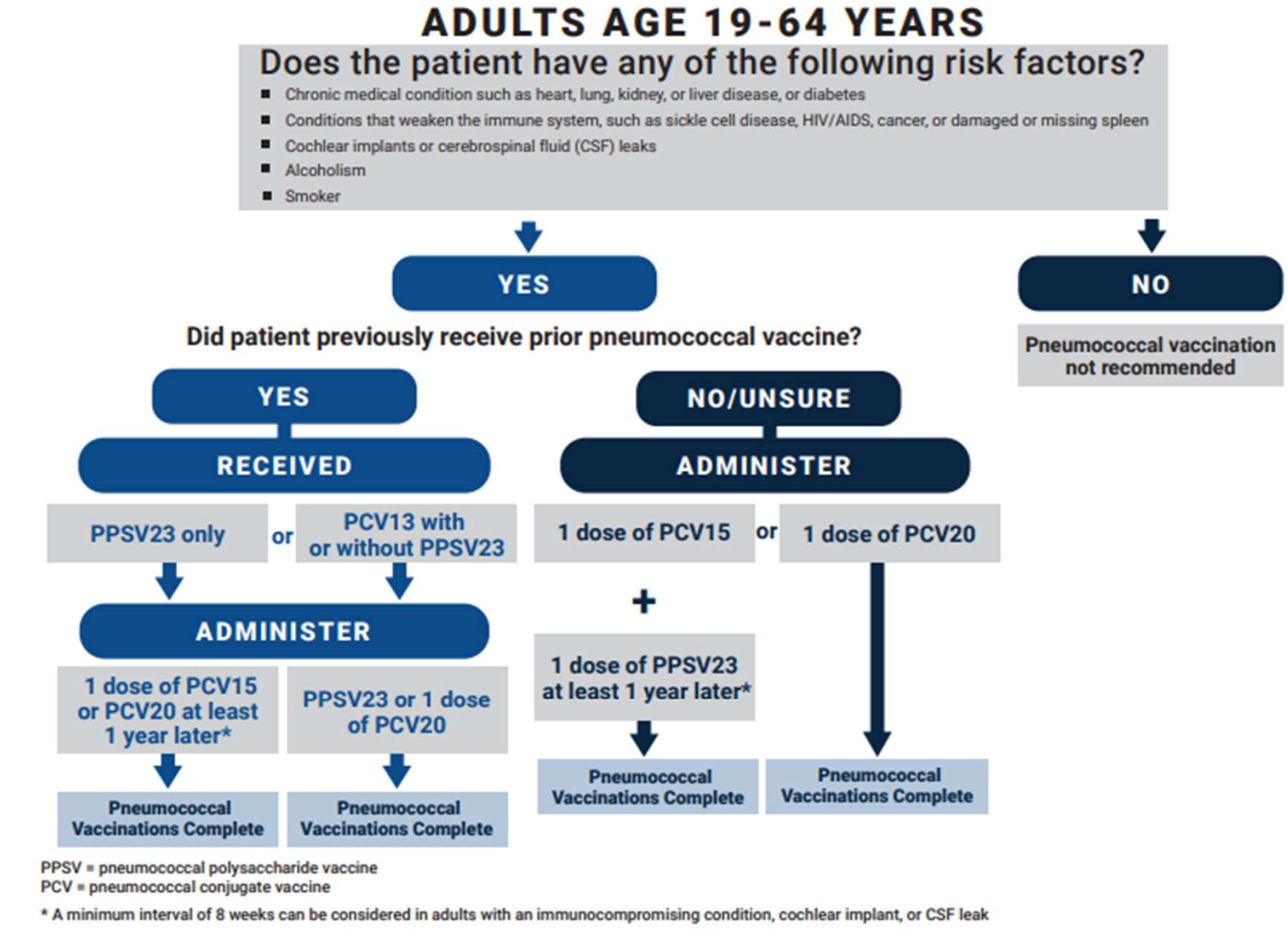
Immunization Schedule for Diabetes 2024

Vaccine	Who by Age	Series and Frequency
Hepatitis B Vaccine	Less than 60 years*	2-3 dose series
RSV	Adults ≥ 60 years	Single dose
Influenza (avoid live attenuated vaccine)	All	Annually
Tetanus, diphtheria, pertussis (TDAP)	All adults; extra dose during pregnancy	Booster every 10 years.
Zoster	50+	2 dose Shingrix
COVID-19	Starting at age 6 mo's	Initial vaccination and boosters
Pneumonia (PPSV23) Pneumovax	Adults19-64*	See Standards for schedule and details and for those 65 or older.
*Pneumococcal Conjugate Vaccine (PCV15, PCV20)	19-64 with underlying risk factors or no previous vaccination*.	May need PPSV23 follow-up vaccine ≥1 year.* If 65+, discuss with provider.

2024 ADA Standards, Vol.47, S52-S76.

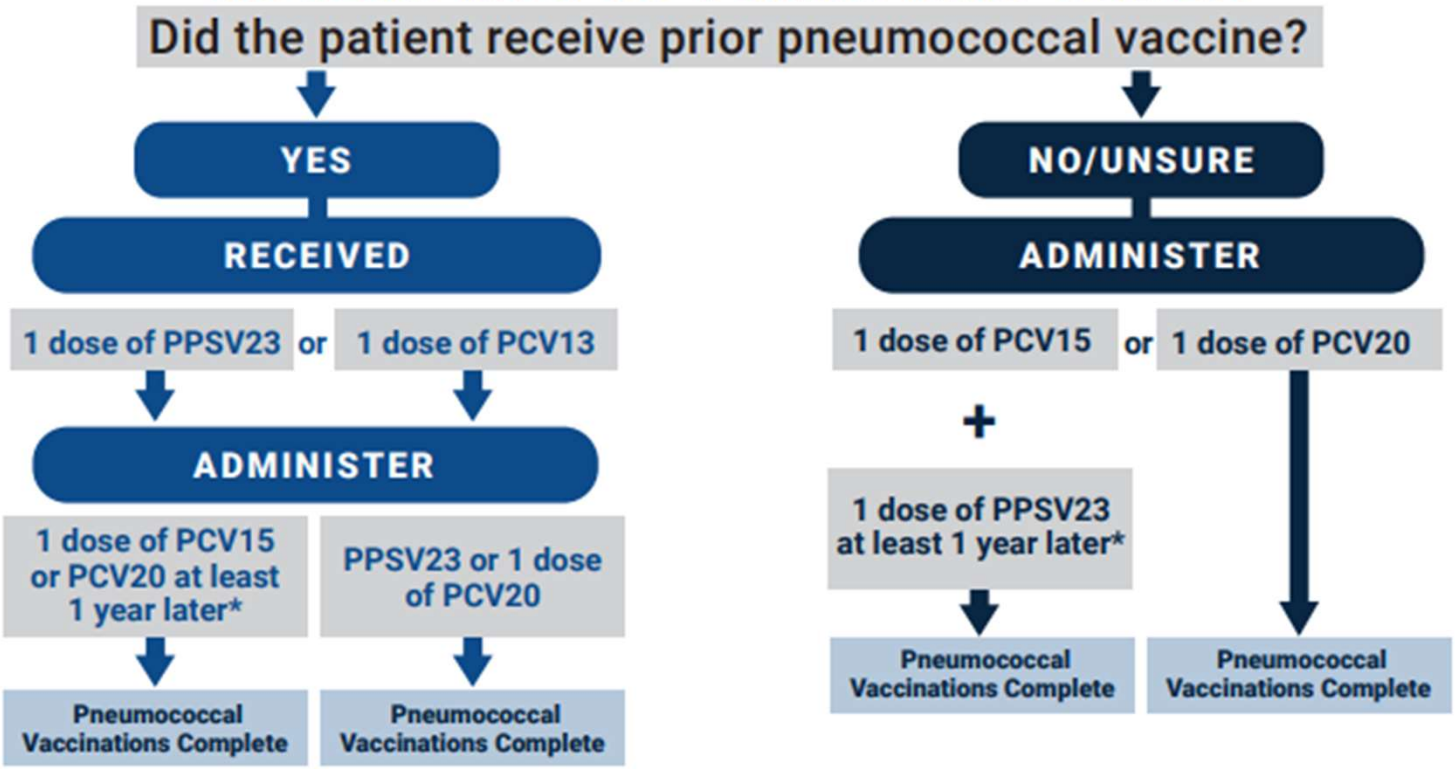
*See ADA Standards, Table 4.4 for detailed info/considerations.

Pneumococcal Vaccine for US Adults



PNEUMOCOCCAL VACCINE FOR US ADULTS

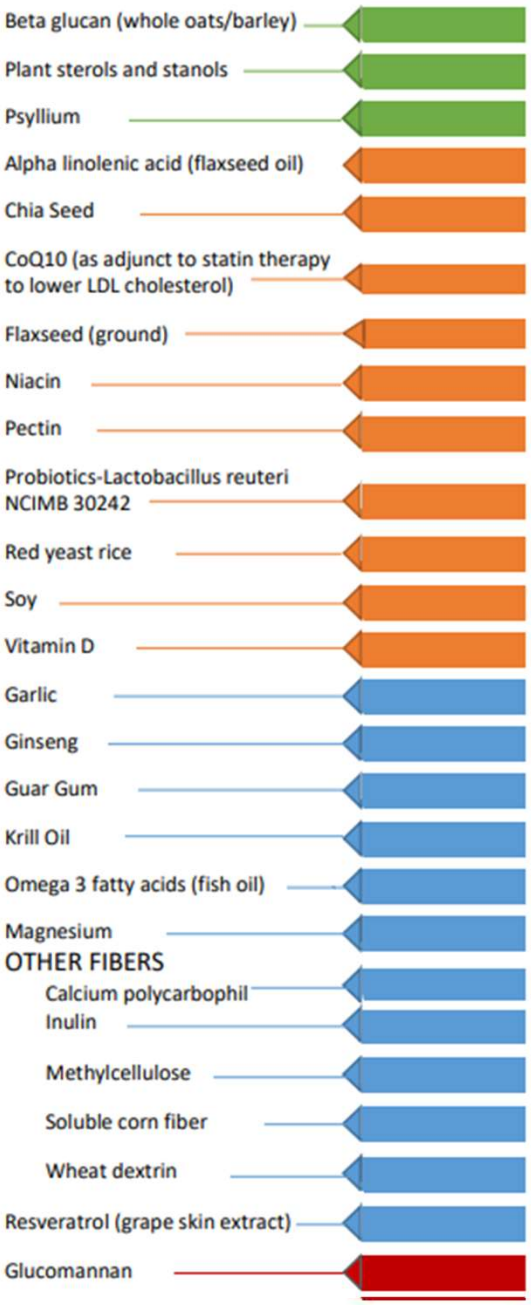
ADULTS AGE 65 YEARS AND OLDER



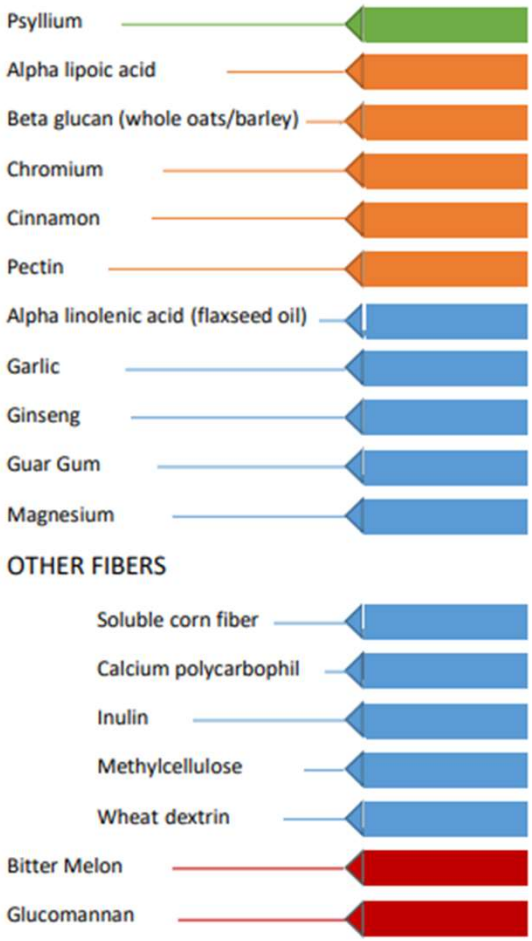
PPSV = pneumococcal polysaccharide vaccine
PCV = pneumococcal conjugate vaccine

* A minimum interval of 8 weeks can be considered in adults with an immunocompromising condition, cochlear implant, or CSF leak

Supplements to Help Manage Total Cholesterol, LDL, and HDL



Supplements to Help Lower Blood Sugar



This downloadable version is compliments of

www.DiabetesEd.net

Supplement Safety Ratings from Cleveland Clinic

Safety Rating Color Key

Recommended: Several well-designed studies in humans have shown positive benefit. Our team is confident about its therapeutic potential.

Recommended with Caution: Preliminary studies suggest some benefit. Future trials are needed before we can make a stronger recommendation.

Not Recommended-Evidence: Our team does not recommend this product because clinical trials to date suggest little to no benefit.

Not Recommended-High Risk: Our team recommends against using this product because clinical trials suggest substantial risk is greater than the benefit

This content was adapted from The Cleveland Clinic Wellness flyer. For more detailed information, access full supplement review at www.clevelandclinicwellness.com/supp review

2024

QuickHitCard.pdf (clevelandclinicwellness.com)

See appendix in back of syllabus

Diabetes Toolkit - Individualize

Meter

- Strips that aren't expired?

List of Meds

Plan for Lows

Emergency Plan

Power back-up

- BG Checks and logging results
- Diabetes ID
  - Phone, medic alert, on person
- Carbohydrate source
  - Granola bar, glucose tabs, GU, gummy bears
- Rescue Meds

Hypoglycemia (Glucose) Alert Values

- **BG <70mg/dl – Level 1**
- Follow 15/15 rule and contact provider to make needed changes. At increased hypo risk.

- **BG < 54mg/dl – Level 2**
- Indicates serious hypo. Reassess BG Goals. Consider med decrease. Predictive of Level 3 Hypo. Needs Glucagon Emergency Kit

- **Severe Hypoglycemia – Level 3**
- Altered mental, physical functioning.
- Requires external assistance – no threshold

6. Glycemic Goals and Hypoglycemia: *Standards of Care in Diabetes—2024* FREE

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Hypoglycemia: Clinical Risk Factors

Table 6.5

Assessment of hypoglycemia risk among individuals treated with insulin, sulfonylureas, or meglitinides

Clinical/biological risk factors	Social, cultural, and economic risk factors
Major risk factors • Recent (within the past 3–6 months) level 2 or 3 hypoglycemia • Intensive insulin therapy* • Impaired hypoglycemia awareness • End-stage kidney disease • Cognitive impairment or dementia	Major risk factors • Food insecurity • Low-income status§ • Homelessness • Fasting for religious or cultural reasons
Other risk factors • Multiple recent episodes of level 1 hypoglycemia • Basal insulin therapy* • Age ≥75 years‡ • Female sex • High glycemic variability‡ • Polypharmacy • Cardiovascular disease • Chronic kidney disease (eGFR <60 mL/min/1.73 m^2 or albuminuria) • Neuropathy • Retinopathy • Major depressive disorder	Other risk factors • Low health literacy • Alcohol or substance use disorder

6. Glycemic Goals and Hypoglycemia: *Standards of Care in Diabetes—2024* FREE

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Components of hypoglycemia prevention for high-risk individuals at initial, follow-up, and annual visits

Hypoglycemia prevention action 6. Glycemic Goals and Hypoglycemia: *Standards of Care in Diabetes—2024* FREE American Diabetes Association Professional Practice Committee	**Initial visit**	**Follow-up visit**	**Annual visit**
Hypoglycemia history assessment	✓	✓	✓
Hypoglycemia awareness assessment	✓		✓
Cognitive function and other hypoglycemia risk factor assessment	✓		✓
Structured education for hypoglycemia prevention and treatment	✓	✓*	✓*
Consideration of continuous glucose monitoring needs	✓	✓	✓
Reevaluation of diabetes treatment plan with deintensification, simplification, or agent modification as appropriate	✓	✓†	✓†
Glucagon prescription and training for close contacts for insulin-treated individuals or those at high hypoglycemic risk	✓		✓
Training to reestablish awareness of hypoglycemia	✓		✓

Tx of Level 2 & 3 Hypoglycemia

- If can swallow w/out risk of aspiration, try gel, honey, etc. inside cheek
- If unable to swallow, D50 IV or Glucagon
- Glucagon injection (need Rx)
  - Inform and instruct caregivers, school personnel, family, coworkers of hypo signs and appropriate action
  - Dosing: Adults 1mg, Children <20kg 0.5mg
  - Glycemic effect 20 - 30mg, short lived
  - Must intake carb as soon as able
- If on Insulin or level 2 or 3 hypo, (<54), get Glucagon ER Kit. Re-evaluate diabetes med treatment plan.

Hypoglycemia: Identify, Treat, & Prevent

Step 1

Identify your signs of hypoglycemia or low blood sugar:

- Sweaty
- Shaky
- Hungry
- Can't think straight
- Headache
- Irritated, grouchy
- Other

Step 2

If have signs of hypo, treat with carbs until glucose reaches 70+, then eat usual meal.

- Sugary drink, 4–8oz
- Piece of fruit
- Raisins, handful
- Glucose tabs, 4+
- Honey/glucose gel
- Skittles candy, 15+

Step 3

Have glucagon rescue meds available.

In case of severe hypo, identify someone (ahead of time) who can get medical help & give a glucagon rescue medication.

Notify your provider of low blood sugar events.

Hypoglycemia Levels:

Level 1 – Glucose less than 70
Level 2 – Glucose less than 54
Level 3 - Severe, needs assistance

Identify Causes of Hypo & Problem Solve to Prevent Future Episodes

» Low carb meal
» Extra activity
» Drinking alcohol
» Delayed, missed meal
» Too much insulin/meds
» Insulin timing

Poll Question 1

- JL is 78 and drinks a “few cocktails” every night. Lives with partner and takes basal insulin at night and bolus insulin as needed. Checks BG a few times a week. Most recent A1c was 5.9%. What is the BG target for JL?

- A. A1c less than 6.5%
- B. Fasting BG 100 +
- C. Ask JL to determine their A1c target.
- D. A1c less than 7% based on the Legacy Trial results.

If on insulin or sulfonylurea – special precautions required

- Carb source on person, car, by bed at all times
- Identification
  - Phone (ICE)
  - Wallet Card
  - Bracelet
- If pattern of lows, med adjustment required
- Pre-meal target
  - 100-130?
- Post meal
  - Less than 180
- Bedtime
  - 110 - 180

Sulfonylureas - Secretagogues or "Squirters"

- Mechanism: Stimulate beta cells to release insulin
- Dosed 1-2x daily before meals
- Adverse effects
  - Hypoglycemia, Weight gain, watch renal function
- Low cost, $12 for 3 months supply
- Can help with glucose toxicity, lowers A1C 1-2%

Sulfonylureas • Stimulates sustained insulin release	glyburide: (Diabeta) (Glynase PresTabs)	 1.25 – 20 mg 0.75 – 12 mg	Can take once or twice daily before meals. Low cost generic. **Side effects**: hypoglycemia and weight gain. Eliminated via kidney. **Caution**: Glyburide most likely to cause hypoglycemia. Lowers A1c 1.0% – 2.0%.
	glipizide: (Glucotrol) (Glucotrol XL)	2.5 – 40 mg 2.5 – 20 mg	
	glimepiride (Amaryl)	1.0 – 8 mg	

Meglitinides - Squirts

- **Action**: stimulate insulin secretion (rapid and short duration) when glucose present
- **Names**:
  - repaglinide (Prandin)
    - **Dosing**: 0.5 to 4 mg a.c. Max dose 16mg
    - Metabolized by liver and mostly excreted in feces (some renally).
  - nateglinide (Starlix)
    - **Dosing**: 120 mg tid with meals
    - Metabolized by liver, excreted by kidney
- Efficacy:
  - Decreases peak postprandial glucose
  - Decreases plasma glucose 60-70 mg/dl
  - Reduce A1C 1.0-2.0

Case Study Ken – Poll 2

Ken is a 67yoM with type 2 diabetes x 5 years. He complains of dizziness/shakiness 3x/week. Last A1C=6.7%. Which of his medications is most likely causing hypoglycemia?

A. Metformin

B. Sitagliptin (Januvia)

C. Glimepiride (Amaryl)

D. Pioglitazone (Actos)

Reducing Hypoglycemia

- Which are the only diabetes meds that directly cause hypoglycemia?

- ❑ Insulin
- ❑ Secretagogues (sulfonylureas, glitinides)

6. Glycemic Goals and Hypoglycemia: *Standards of Care in Diabetes—2024* FREE

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Glucagon Rescue Medications for Diabetes-Related Hypoglycemia

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 or 1.0mg in -Prefilled syringe -HypoPen auto-injector -Kit with vial and syringe	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.

Quick Question 3

- JZ is excited about his A1c of 5.4%. He takes rapid acting insulin 4-6 times a day using a pen to keep his BG to target. Plus, adjusts glargine as needed if his pm BG is elevated. What is your biggest concern?

A. Does he change his needle each time?

B. Why is he adjusting glargine?

C. Is he adjusting insulin for exercise?

D. How many hypoglycemic events per week?

Preventing Hypoglycemia

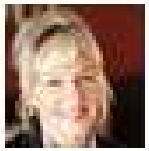
Nocturnal Lows

- If bedtime glucose <110, reduce meds
- If increased daytime activity, may need extra snack
- Eval pre-dinner insulin/meds

Other

- Monitor kidney function / wt loss
- Monitor BG trends
- Too much meds?
- Skipped /delayed meals?
- Plan ahead
- Alcohol precautions
- Exercise planning
- CGM

"The highest form of wisdom is kindness."
The Talmud



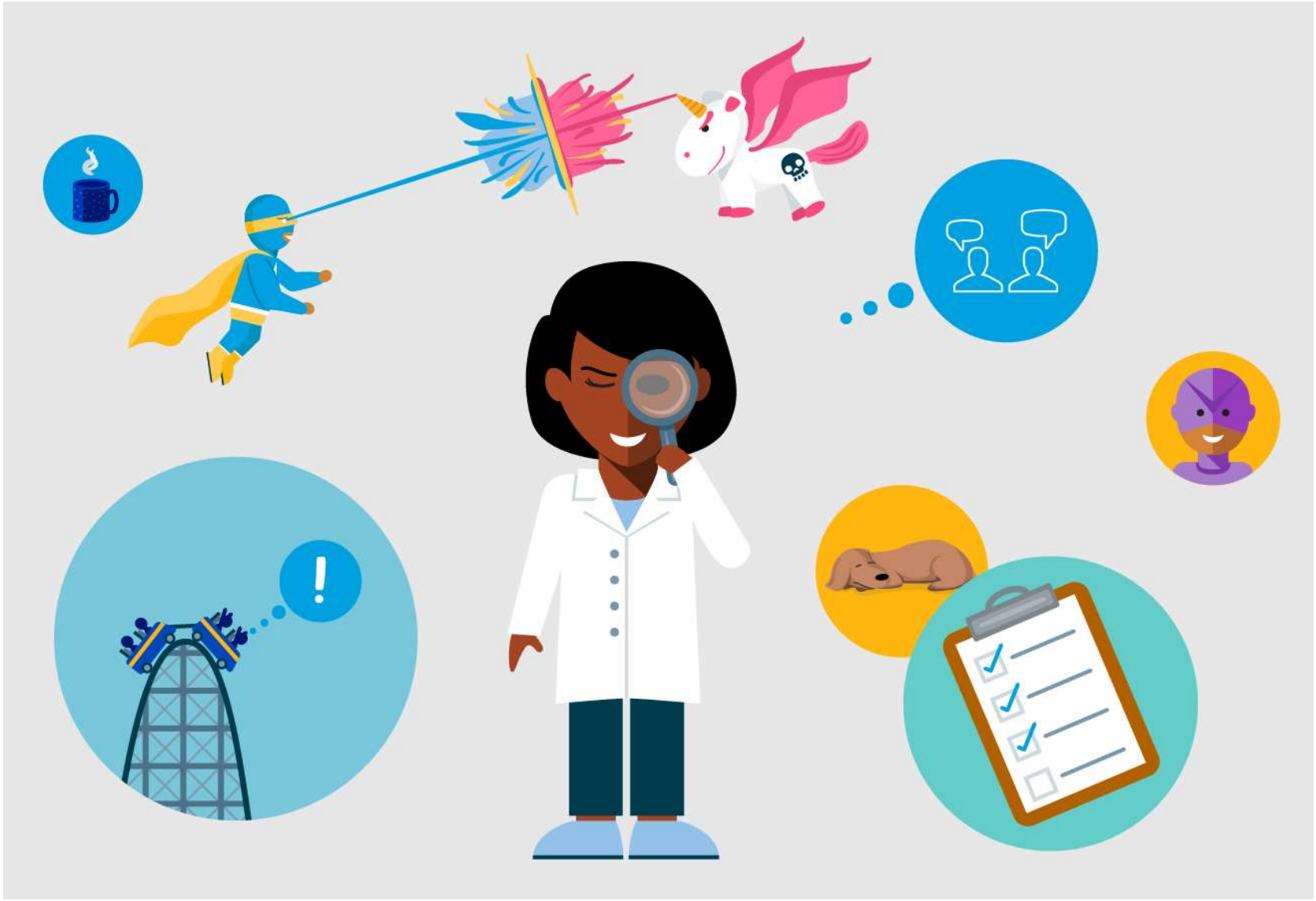
Kindness matters!
Learning to be less harsh or judgmental and more compassionate to oneself may help people with diabetes manage their disease and stave off depression, a recent study suggests.

Self-compassion may help people with diabetes achieve better glucose control and less depression

By Reyna Gobel(Reuters Health) – Learning to be less harsh or judgmental and more...

REUTERS.COM | BY REYNA GOBEL

Landmark Trials



Quick Question 3A

Which study demonstrated that keeping A1c less than 7% reduces complications for Type 1?

a. Diabetes Prevention Trial
b. Diabetes Control and Complications Trial
c. United Kingdom Prospective Diabetes Study
d. YOUTH Trial

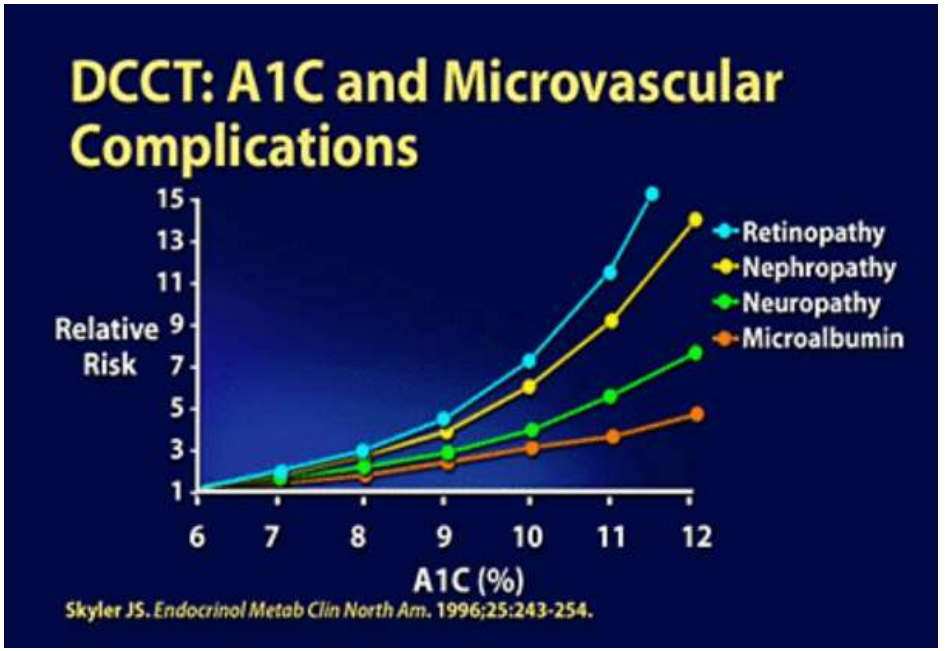
Diabetes Control and Complications Trial (DCCT) Type 1 – Does getting A1c <7% matter?

The largest, most comprehensive diabetes study ever conducted.

10 year study involved more than 1400 subjects with Type 1 DM.

Compared the effects of two treatment regimens:

- standard therapy and
- intensive control-on the complications of diabetes.



DCCT Conclusions

By maintaining A1C < 7%:

- Eye disease - 76% reduced risk
- Kidney disease - 50% reduced risk
- Nerve disease - 60% reduced risk

Management elements included:

- SMBG 4 or more times a day
- 4 daily insulin injections or insulin pump
- Greater risk of hypoglycemia
- More associated weight gain

UKPDS Results

United kingdom Prospective Diabetes Study

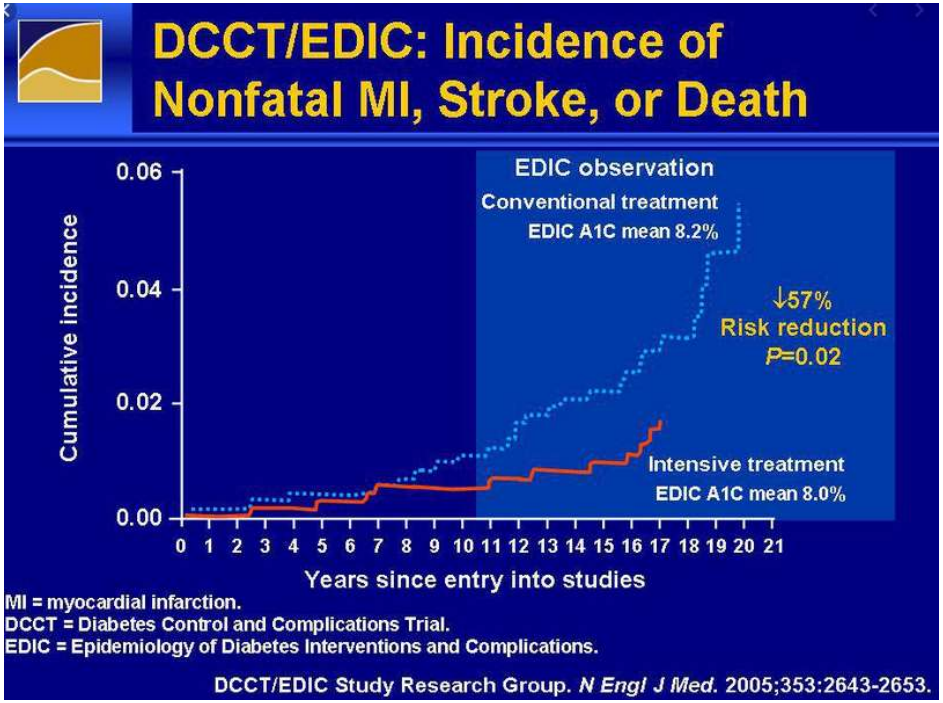
- Conducted over 20 years involving over 5,100 patients with Type 2 diabetes

- 1% decrease in A_1c reduces microvascular complications by 35%
- 1% decrease in A_1c reduces diabetes related deaths by 25%
- B/P control (144/82) reduced risk of:
  - Heart failure (56%)
  - Stroke (44%)
  - Death from diabetes (32%)

Lancet 352: 837-865, 1998

“Legacy Effect”

- For participants of DCCT and UKPDS
  - long lasting benefit of early intensive BG control prevents
    - Microvascular complications
    - Macrovascular complications (15-55% decrease)
  - Even though their BG levels increased over time
  - Message – Catch early and Treat aggressively



DiaBingo- G

G ADA goal for A1c is less than ____%

G People with DM need to see their provider at least every month

G Blood pressure goal is less than

G People with DM should see eye doctor (ophthalmologist) at least

G The goal for triglyceride level is less than

G Goal for my HDL cholesterol is more than

G The goal for blood sugars 1-2 hours after a meal is less than:

G People with DM should get this shot every year

G People with DM need to get urine tested yearly for _____

G Periodontal disease indicates increased risk for heart disease

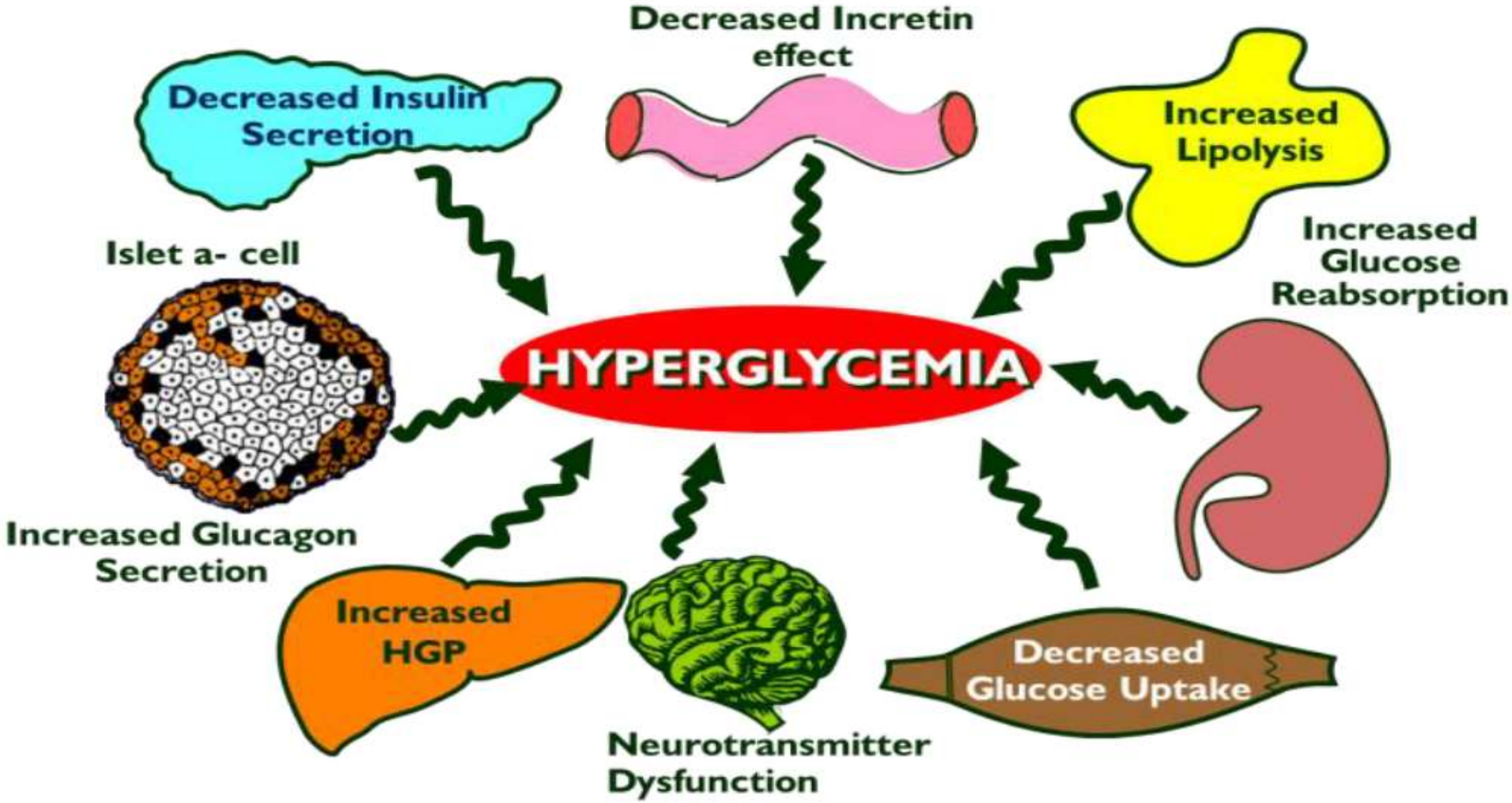
G The goal for blood sugar levels before meals is:

G The activity goal is to do ___ minutes on most days

How Many Drug Options for Diabetes?

- Biguanide
- Sulfonylureas
- Meglitinides
- Glucagon-like-peptide-1 (GLP-1) receptor agonists
- GLP/GIP receptor agonist
- Sodium glucose cotransporter-2 (SGLT-2) inhibitors
- Thiazolidinediones (TZD's)
- Dipeptidylpeptidase-4 (DPP-4) inhibitors
- Alpha-glucosidase inhibitors
- Bile acid sequestrant
- Dopamine-2-agonist
- Amylin mimetic
- Insulin

Drug Targets in Diabetes



DeFronzo et al. Diabetes Spectrum Volume 27, Number 2, 2014

Section 9- Pharmacologic Approaches to Glycemic Treatment for Type 2 Diabetes

- Person centered with focus on addressing:
  - Atherosclerotic CV Disease (ASCVD)
  - Heart failure (HF) and
  - Chronic Kidney Disease (CKD),
  - Weight loss
- Updated chart on cost and attributes of different meds.

9. Pharmacologic Approaches to Glycemic Treatment: *Standards of Care in Diabetes-2024* FREE

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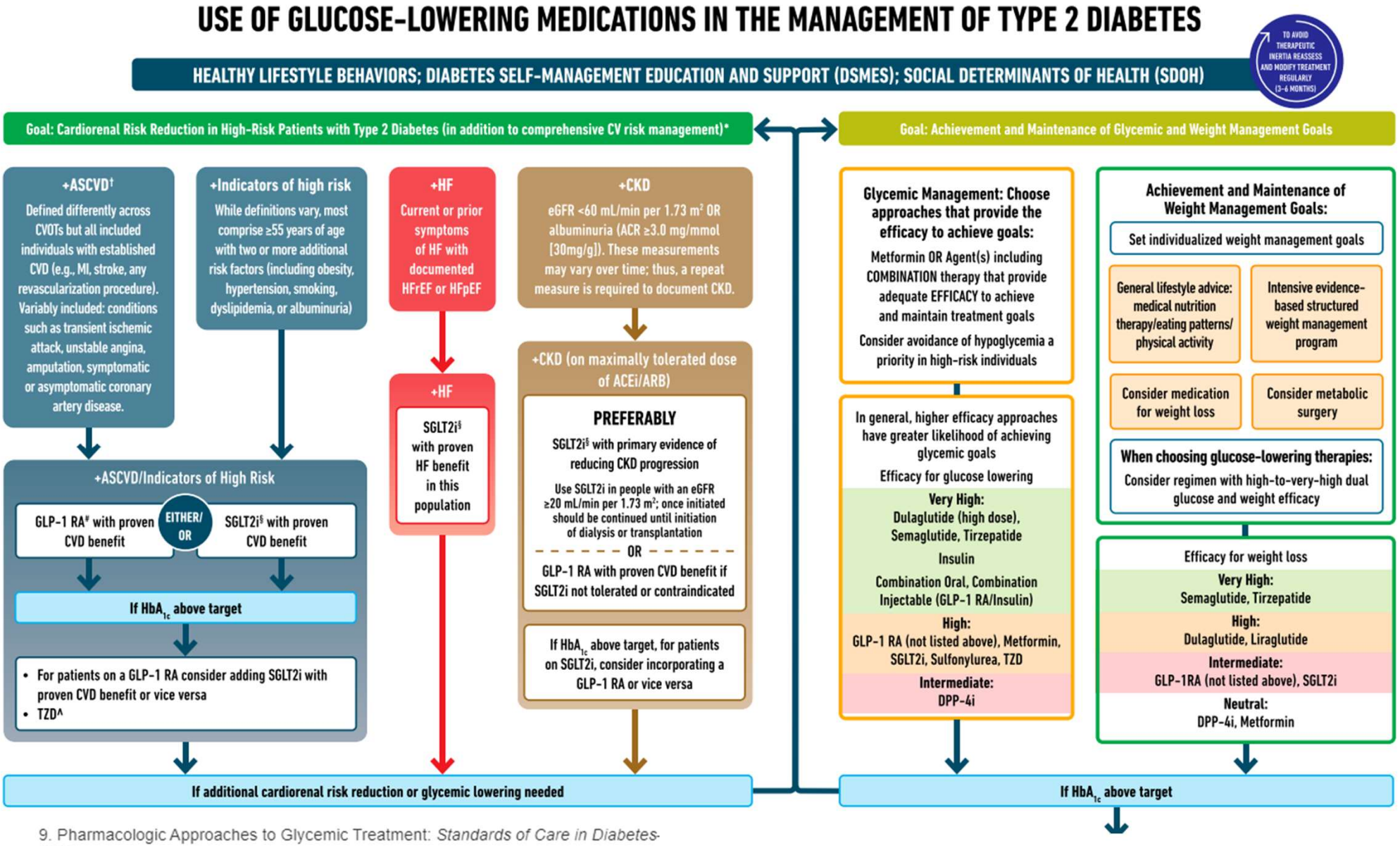
ADA Meds Management for Type 2



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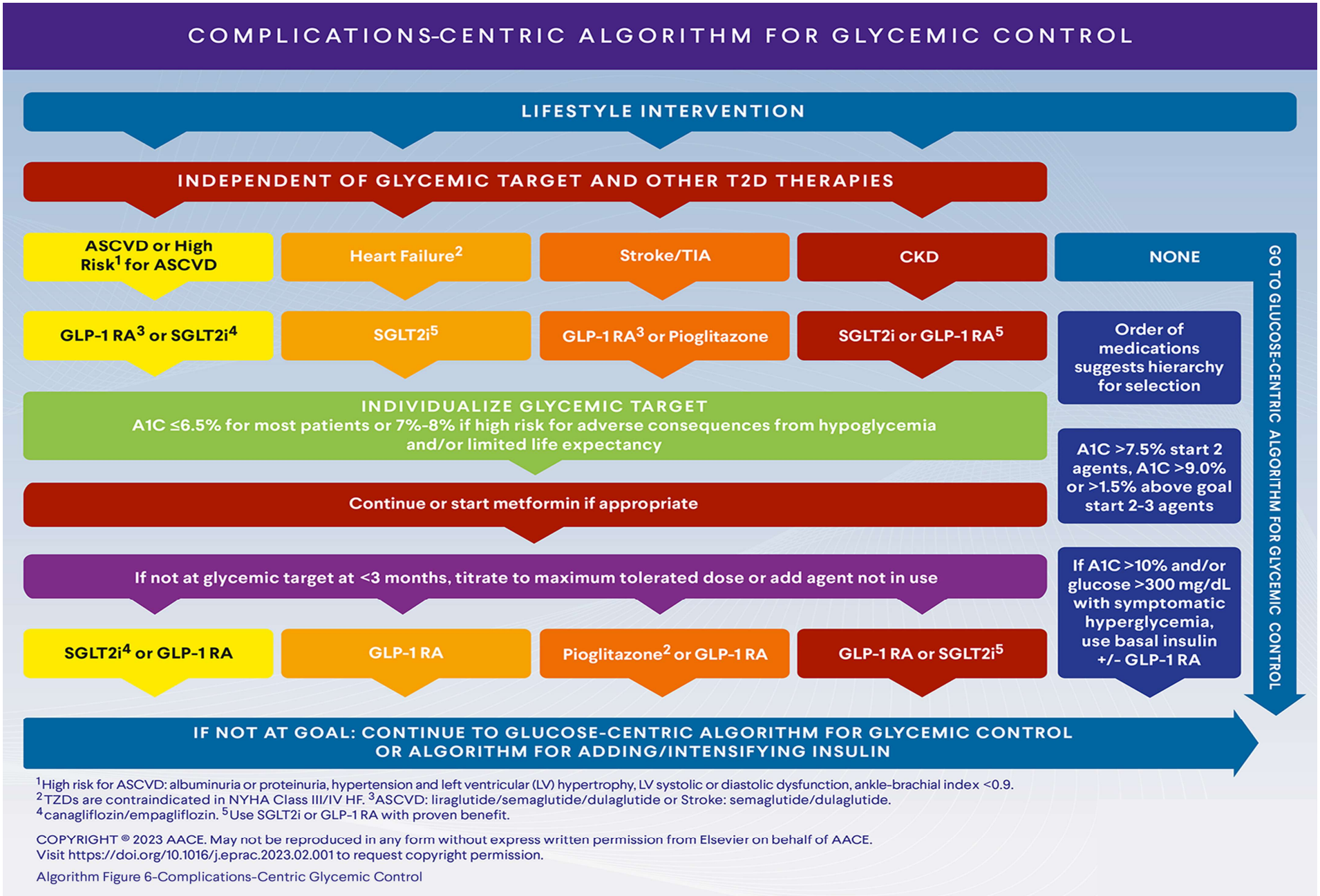
AACE 2023 Diabetes Guideline



[1]High risk for ASCVD: albuminuria or proteinuria, hypertension and left ventricular (LV) hypertrophy, LV systolic or diastolic dysfunction, ankle-brachial index <0.9.
[2]TZDs are contraindicated in NYHA Class III/IV HF. [3]ASCVD: liraglutide/semaglutide/dulaglutide or Stroke: semaglutide/dulaglutide.
[4]canagliflozin/empagliflozin. [5]Use SGLT2i or GLP-1 RA with proven benefit.

Algorithm Figure 6-Complications-Centric Glycemic Control

Indications for Insulin Sensitizers

Rosiglitazone (Avandia), Pioglitazone (Actos)

- **Action**: decrease insulin resistance by making muscle and adipose cells more sensitive to insulin. Decrease free fatty acids

- **Names**:
  - pioglitazone (Actos) – bladder cancer warning
    - Dosing: 15-45 mg daily
    - Consider adding low dose if history of stroke or have steatosis
  - rosiglitazone (Avandia)
    - Dosing: 4-8 mg daily

- **Efficacy/ Considerations**
  - Reduce A1C ~0.5-1.0%
  - 6 weeks for maximum effect
  - Actos $5 a month, Avandia $300 a month
  - Can cause fluid retention, not indicated w/ CHF

Thiazolidinediones "TZDs" • Increases insulin sensitivity	pioglitazone (Actos) rosiglitazone (Avandia)	15 – 45 mg daily 4 – 8 mg daily	Black Box Warning: TZDs may cause or worsen CHF. Monitor for edema and weight gain. Increased peripheral fracture risk. Actos may increase risk of bladder cancer. Lowers A1c 0.5% – 1.0%

TZDs – How Do They Rate?

Question	Answer
Cause hypoglycemia?	No
Cause weight gain?	Yes
Affordable?	Generic
Lowers CV risk?	??
Can most tolerate /use?	Watch HF

Dipeptidyl Peptidase-4 (DPP-4) Inhibitors

Mechanism of action

- Prevents the breakdown of GLP-1 and GIP, resulting in 2-3X increased endogenous incretin levels

Efficacy

- Hemoglobin A1C reduction by **0.6%–0.8%**
- Primarily lowers postprandial glucose levels
- Not as efficacious as GLP-1 agonists
- CV neutral, increased HF hospitalization with alogliptin/saxagliptin

Adverse effects

- Generally well tolerated, dosed once daily
- Avoid in combo with GLP-1 agonist
- Caution with h/o pancreatitis
- Potential joint pain

DPP4 Inhibitor Dosing

Drug	Dose	Renal Adjustment
Sitagliptin	100 mg daily	50 mg/day eGFR 30–45 mL/min/1.73m^2 25 mg/day eGFR <30 mL/min/1.73m^2
Linagliptin	5 mg daily	None necessary
Saxagliptin	5 mg daily	2.5 mg/day eGFR < 45 mL/min/1.73m^2
Alogliptin	25 mg daily	12.5 mg/day eGFR 30–59 mL/min/1.73m^2 6.25 mg/day for eGFR <30 mL/min/1.73m^2

DPP – 4 Inhibitors "Incretin Enhancers" • Prolongs action of gut hormones • Increases insulin secretion • Delays gastric emptying	sitagliptin (Januvia)	25 - 100 mg daily – eliminated via kidney*	*If creat elevated, see med insert for dosing. **Side effects:** headache and flu-like symptoms. **Can cause severe, disabling joint pain.** Contact MD, stop med. Report signs of pancreatitis. †Alogliptin can increase risk of heart failure. Notify MD for shortness of breath, edema, weakness, etc. No wt gain or hypoglycemia. Lowers A1c 0.6%-0.8%.
	linagliptin (Tradjenta)	5 mg daily – eliminated via feces	
	alogliptin (Nesina)†	6.25 - 25 mg daily – eliminated via kidney*	

- DPP-IV Dosing and Diabetes Med PocketCards

Alpha-glucosidase Inhibitors

- **Action**: blocks enzymes that digest starches in the small intestine
- **Name**: acarbose (Precose) or miglitol (Glyset)
  - Dosing: 25-100mg TID, max 300mg/day
- Efficacy
  - Decrease postprandial glucose 40-50 mg/dl
  - Decrease A1C 0.5-1.0%
- Other Effects
  - Flatulence or abdominal discomfort
  - Contraindicated in patients with inflammatory bowel disease or cirrhosis
- Special Consideration
  - In case of hypoglycemia, treat with glucose tabs or milk
  - (other starches are blocked by medication)

Other Med Classes

Other Oral Diabetes Medications

Class/Main Action	Name(s)	Daily Dose Range	Considerations
Thiazolidinediones "TZDs" • Increases insulin sensitivity	pioglitazone (Actos) rosiglitazone (Avandia)	15 – 45 mg daily 4 – 8 mg daily	Black Box Warning: TZDs may cause or worsen CHF. Monitor for edema and weight gain. Increased peripheral fracture risk. Actos may increase risk of bladder cancer. Lowers A1c 0.5% – 1.0%
Glucosidase Inhibitors • Delays carb absorption	acarbose (Precose) miglitol (Glyset)	25 – 100 mg w/meals; 300 mg max daily dose	Start low dose, increase at 4-8 wk intervals to decrease GI effects. Caution with liver or kidney problems. In case of hypo, treat w/ glucose tabs. Lowers A1c 0.5– 1.0%.
Meglitinides • Stimulates rapid insulin burst	repaglinide (Prandin) nateglinide (Starlix)	0.5 – 4 mg w/meals (metabolized in liver) 60 – 120 mg w/meals (eliminated via kidney)	Take before meals. Side effects may include hypoglycemia and weight gain. Lowers A1c 1.0% – 2.0%.
Dopamine Receptor Agonists • Resets circadian rhythm	bromocriptine mesylate—Quick Release "QR" (Cycloset)	1.6 to 4.8 mg a day (each tab 0.8 mg)	Take within 2 hrs of waking. Side effects: nausea, headache, fatigue, hypotension, syncope, somnolence. Lowers A1c 0.6% – 0.9%.
Bile Acid Sequestrants • Decreases cholesterol / BG levels.	Colesevelam HCL (Welchol)	Up to six (6) 625 mg pills (3 tabs am, 3 tabs pm) 3.75gm packet in 4-8 ounces of fluid	Do not use if history of bowel obstruction, triglycerides >500, or pancreatitis. Can decrease absorption of certain meds, soluble vitamins. Lowers LDL by 15-30%. Side effects GI in nature. Lowers A1c 0.5%

Drug Comparison

Class	Efficacy	Hypoglycemia	Weight Change	Effect on MACE	Heart Failure	Renal	Cost
Metformin	High	No	Neutral/ Loss	Potential benefit	Neutral	Neutral	Low
SGLT2 Inhibitors	Intermediate to High	No	Loss, intermediate	Benefit	Benefit	Benefit	High
GLP-1 RA	High to Very High	No	Loss, intermediate to high	Benefit	Neutral	Benefit	High
GIP and GLP-1 RA	High to Very High	No	Loss, very high	Under investigation	Under investigation	Under investigation	High
DPP-4 Inhibitors	Intermediate	No	Neutral	Neutral	Risk: saxa/alogliptin	Neutral	High
TZD	High	No	Gain	Potential benefit: Pio	Risk	Neutral	Low
Sulfonylurea	High	Yes	Gain	Neutral	Neutral	Neutral	Low

Check Your Knowledge – No Poll

Which of the following medications is **least** affordable?

A. Pioglitazone (Actos)
B. Metformin (Glucophage)
C. Glimepiride (Amaryl)
D. Ozempic (semaglutide)

Medication Cost Considerations

- Lowest cost medications - AWP for a month
  - Metformin - $3
  - Sulfonylureas $3
  - TZD – Pioglitazone $3
  - Lower cost insulin
  - Brenzavvy-$48, costplus
  - Insulin-$35
- Highest cost medications – AWP for a month
  - GLP-1 RA - $1000+
  - GLP-1/GIP RA - 1000+
  - SGLT2i - $650
  - DPP-IV's - $550-600

Cost Related Barriers

- Among people with chronic illnesses, 2/3 of those who reported not taking medications as prescribed due to CRB never shared this with their physician.
- Especially associated with diabetes medications and insulin.

Combo Oral Medications PocketCard™

Medications	Doses in mg	Medications	Doses in mg	Medications	Doses in mg
Trijardy XR (3 meds) empagliflozin linagliptin metformin XR	 5 - 25 2.5 -5 1000	Janumet (sitagliptin/ metformin)	50/500 50/1000	Prandimet (repaglinide/ metformin)	1/500 2/500
ACTOplus Met* (pioglitazone/ metformin)	15/500 15/850	Janumet XR (sitagliptin/ metformin)	50/500 50/1000 or 100/1000	Qtern (saxagliptin / dapagliflozin)	5/10
ACTOplus Met XR (pioglitazone/ metformin	15/1000 30/1000	Jentadueto (linagliptin/ metformin)	2.5/500 2.5/850 or 2.5/1000	Segluromet (ertugliflozin/ metformin)	2.5/500 or 2.5/1000 or 7.5/500 or 7.5/1000
Duetact* (pioglitazone/ glimepiride)	30/2 30/4	Kazano (alogliptin/ metformin)	12.5/500 12.5/1000	Steglujan (ertugliflozin/ sitagliptin)	5/100 or 15/100
Glucovance* (glyburide/ metformin)	1.25/250 2.5/500 5/500	Metaglip* (glipizide/ metformin)	2.5/250 2.5/500 or 5/500	Synjardy (empagliflozin/ metformin)	5/500 or 12.5/500 5/1000 or 12.5/1000
Glyxambi (empagliflozin and linagliptin)	10/5 25/5	Oseni (alogliptin/ pioglitazone)	12.5/15 or 25/15 12.5/30 or 25/30 12.5/45 or 25/45	Synjardy XR† (empagliflozin/ metformin XR)	5/1000 or 10/1000 12.5/1000, 25/1000 †Approved for peds
Invokamet (canagliflozin/ metformin)	50/500 or 50/1000 150/500 or 150/1000			Xigduo XR (dapagliflozin/ metformin)	5/500 or 10/500 5/1000 or 10/1000

Available in generic. Observe precautions of each component drug.

ADA 2024 Standard 11 - Chronic Kidney Disease and Risk Management

- Optimize glucose and BP to protect kidneys
- Screen Urine Albumin Creatinine ratio (UACR) & GFR
  - Type 2 at dx then yearly
  - Type 1 with diabetes for 5 years, then yearly
  - If urinary albumin ≥300 and GFR 30–60 monitor 1-4 times a year to guide therapy.
- Treat hypertension with ACEI or ARB and for elevated albumin-to-creatinine ratio of 30 -299.
- Monitor serum creat and K+
  - if on ACE, ARB or diuretics

Albuminuria Categories	Urinary Albumin Creatine Ratio (UACR)
Normal to mildly increased – A1	< 30 mg/g
Moderately increased – A2	30 – 299 mg/g
Severely increased – A3	300 mg/g +

Kidney Disease Stage	GFR
Stage 1 – Normal	90+
Stage 2 – Mild loss	89 - 60
Stage 3a – Mild to Mod	59 - 45
Stage 3b – Mod to Severe	44 - 30
Stage 4 – Severe loss	29 -15
Stage 5 – Kidney failure	14 - 0

11. Chronic Kidney Disease and Risk Management: *Standards of Care in Diabetes—2024*
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Poll Question 5

- Evaluating kidney function is important to determine most beneficial treatment interventions. Which of the following measurements would indicate that JR has healthy kidney function?

A. Urinary albumin creatinine ratio of 30-299 mg/g with GFR of 45.
B. GFR of 60 or greater and urinary albumin creatinine ratio of 12 mg/g.
C. Urinary albumin creatinine ratio less than 30 mg/g and GFR of 30-45.

- Creatinine of 1.5 and urinary albumin creatinine ratio of 300 mg/g or greater.

11. Chronic Kidney Disease and Risk Management: *Standards of Care in Diabetes—2024*

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				Albuminuria categories Description and range		
				A1	**A2**	**A3**
CKD is classified based on: **• Cause (C)** **• GFR (G)** **• Albuminuria (A)**				Normal to mildly increased	Moderately increased	Severely increased
				<30 mg/g <3 mg/mmol	30–299 mg/g 3–29 mg/mmol	≥300 mg/g ≥30 mg/mmol
GFR categories (mL/min/1.73 m²) Description and range	**G1**	Normal or high	≥90	Screen 1	Treat 1	Treat and refer 3
	G2	Mildly decreased	60–89	Screen 1	Treat 1	Treat and refer 3
	G3a	Mildly to moderately decreased	45–59	Treat 1	Treat 2	Treat and refer 3
	G3b	Moderately to severely decreased	30–44	Treat 2	Treat and refer 3	Treat and refer 3
	G4	Severely decreased	15–29	Treat and refer* 3	Treat and refer* 3	Treat and refer 4+
	G5	Kidney failure	<15	Treat and refer 4+	Treat and refer 4+	Treat and refer 4+

Low risk (if no other markers of kidney disease, no CKD)

Moderately increased risk

High risk

Very high risk

Diabetes + CKD – Increases CVD Risk

- Chronic kidney disease (CKD) is a frequent complication in diabetes
  - Type 1 diabetes ~30%
  - Type 2 diabetes ~40%
- In several studies, participants on SGLT2i with GFRs of 30-60 (stage 3) reduced ASCVD risk and improved renal function
  - Slowed kidney disease or death
  - Reduced albuminuria

National Kidney Foundation.
https://www.kidney.org/atoz/content/diabetes

Standard 11 – Protect Kidneys

- Diabetes with a
  - GFR ≥20 and
  - UACR ≥200 mg/g
- Start SGLT2 to reduce chronic kidney disease progression and cardiovascular events.

- If type 2 diabetes and established Chronic Kidney Disease (CKD)
  - Start nonsteroidal mineralocorticoid receptor antagonist (finerenone) and/or GLP-1 RA recommended for cardiovascular risk reduction.

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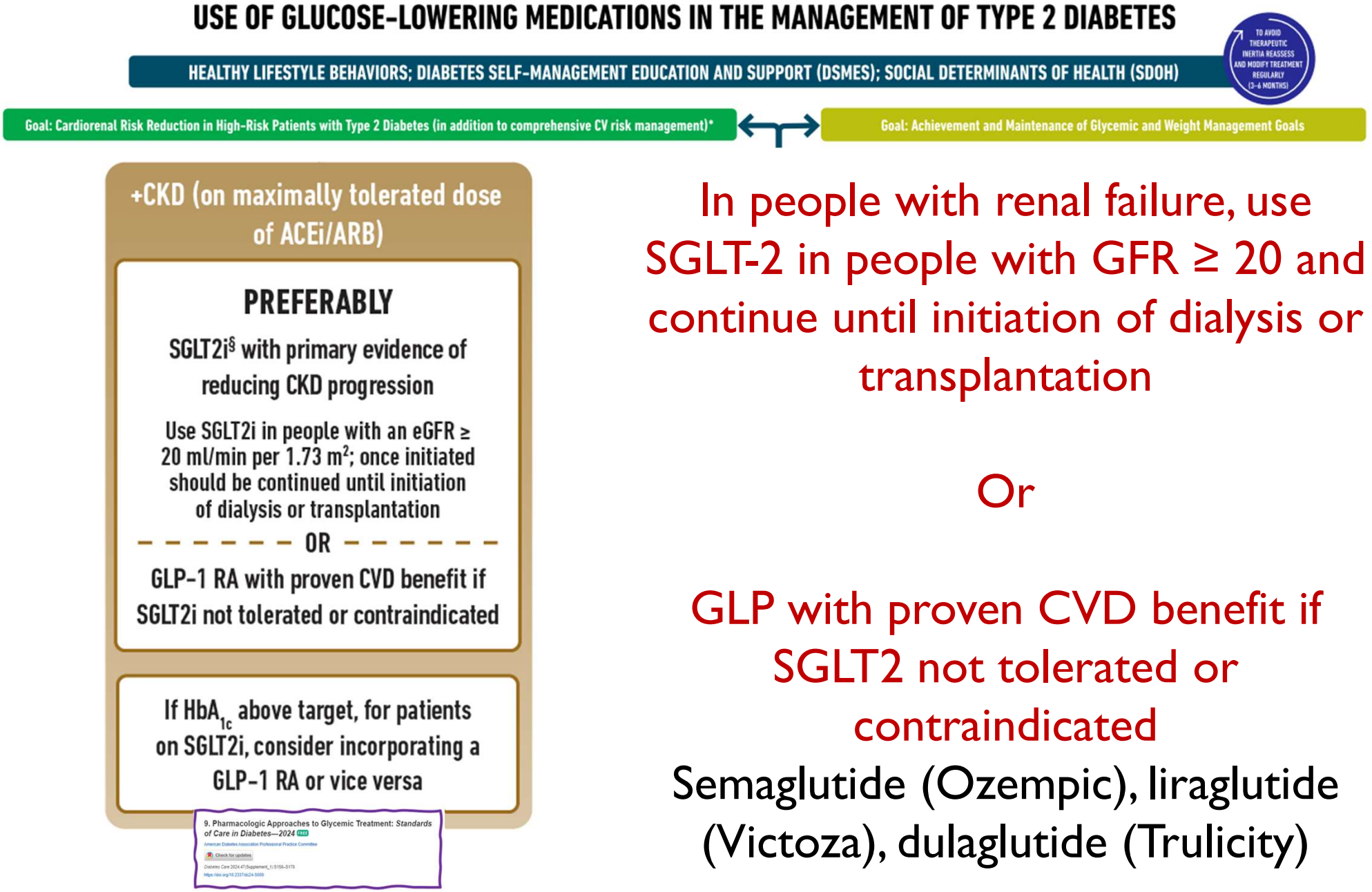
Choosing glucose-lowering medication in people with Chronic Kidney Disease



In people with renal failure, use SGLT-2 in people with GFR ≥ 20 and continue until initiation of dialysis or transplantation

Or

GLP with proven CVD benefit if SGLT2 not tolerated or contraindicated

Semaglutide (Ozempic), liraglutide (Victoza), dulaglutide (Trulicity)

SGLT2 Inhibitor CKD Evidence Summary

Trial Name	SGLT2 Inhibitor vs placebo	Outcomes (Primary Bolded)
CREDENCE	Canagliflozin	N=4401, Median follow-up 2.6 years, Prior CVD 50.4% **ESRD, doubling of create or death from renal or CV cause** (primary): 0.70 (0.59-0.82), 3 point MACE 0.80 (0.67-0.95)
DAPA-CKD	Dapagliflozin	N=4304, 2906 with diabetes, Median follow-up 2.4 years, Prior CVD 37.4% **>50% decline in eGFR, ESKD or renal/CV death (primary**): 0.61 (0.51-0.72)
EMPA-Kidney	Empagliflozin	N=6609, Median follow-up 2.0 years, Prior CVD 27%, 46% with DM **ESRD, >40% decline in eGFR, ESKD, or renal/CV death (primary**): 0.72 (0.64-0.82), stopped early due to positive benefit

Perkovic V, Jardine MJ, Neal B, et al. Canagliflozin and renal outcomes in type 2 diabetes and nephropathy. N Engl J Med. 2019;380:2295–2306.
Heerspink HJL, Stefansson BV, Correa-Rotter R, et al. Dapagliflozin in patients with chronic kidney disease. N Engl J Med. 2020;383:1436–1446.
EMPA-KIDNEY Collaborative Group, Herrington WG, Staplin N, Wanner C, et al. Empagliflozin in Patients with Chronic Kidney Disease. N Engl J Med. 2022 Nov 4. doi: 10.1056/NEJMoa2204233. Epub ahead of print. PMID: 36331190.

SGLT-2 Inhibitor Dosing & Indication

Once an SGLT2i is initiated, it is reasonable to continue an SGLT2i even if the eGFR falls below 20 ml/min/1.73 m2 , unless it is not tolerated or kidney replacement therapy is initiated.

Drug	Dose	FDA Approved Indications
Ertugliflozin (Steglatro)	5-15 mg daily	As an adjunct to diet and exercise to improve glycemic control in adults with T2DM (All)
Dapagliflozin (Farxiga)	5-10 mg daily	• To reduce the risk of hospitalization for HF in adults with T2DM and established CVD or multiple CV risk factors. • To reduce the risk of CV death and hospitalization for HF, and urgent HF visit in adults **with HF.** • To reduce the risk of sustained eGFR decline, ESKD, CV death, and hospitalization for HF in **adults with CKD** at risk of progression.
Empagliflozin (Jardiance)	10-25 mg daily	• To reduce the risk of CV death in adults with T2DM and established CVD. • To reduce the risk of CV death and hospitalization for HF in **adults with HF** • **To reduce the risk of sustained decline in eGFR, ESKD, CV death, and hospitalization in adults with CKD at risk of progression.**
Canagliflozin (Invokana)	100-300mg daily	• To reduce MACE in adults with T2DM and established CVD. • To reduce the risk of ESKD, doubling of serum creatinine, CV death, and hospitalization for HF in adults with T2DM and diabetic nephropathy with albuminuria >300 mg/day.
Bexagliflozin	20mg daily	As an adjunct to diet and exercise to improve glycemic control in adults with T2DM

Finereone's Place in Therapy

- In people with CKD and albuminuria who are at increased risk for CV events or CKD progression
  - a nonsteroidal mineralocorticoid receptor antagonist (finerenone) is recommended to reduce CKD progression and CV events.
- First optimize ACEI or ARB

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Finerenone Resource

New nonsteroidal MRAs for Type 2 and Chronic Kidney Disease

Nonsteroidal Selective Mineralocorticoid Antagonist

Indicated for people with chronic kidney disease (CKD) associated with Type 2 diabetes. Reduces the risk of kidney function decline, kidney failure, cardiovascular death, non-fatal heart attacks, and hospitalization for heart failure in adults with chronic kidney disease associated with type 2 diabetes. The mineralocorticoid receptor antagonist blocks the effects of aldosterone and reduces the risk of kidney function decline as well as heart failure.

Class / Action	Generic / Trade Name	Daily Dose	Frequency	Considerations
Nonsteroidal, selective mineralocorticoid antagonist. Blocks mineralocorticoid receptor mediated sodium reabsorption and mineralocorticoid overactivation in epithelial (for example kidneys) and nonepithelial (for example heart, blood vessels) tissues.	**Finerenone / Kerendia**	**10-20 mg**	**Once daily**	Monitor potassium 4 weeks after initiation or dose adjustment (although impact on potassium is much less than non-slective mineralocorticoid antagonists like spironolactone). Since medication is a CYP3A4 substrate, avoid taking with other strong cype3A4 inhibitors. Avoid grapefruit or grapefruit juice. May take with or without food.

Contributor: Diana Isaacs, PharmD, BCPS, BCACP, BC-ADM, CDCES, FADCES, FCCP 2022

Kidney Goals and MNT

- In people with chronic kidney disease with UACR ≥300 mg/g
- Goal is a reduction of 30% or greater in mg/g urinary albumin to slow chronic kidney disease progression

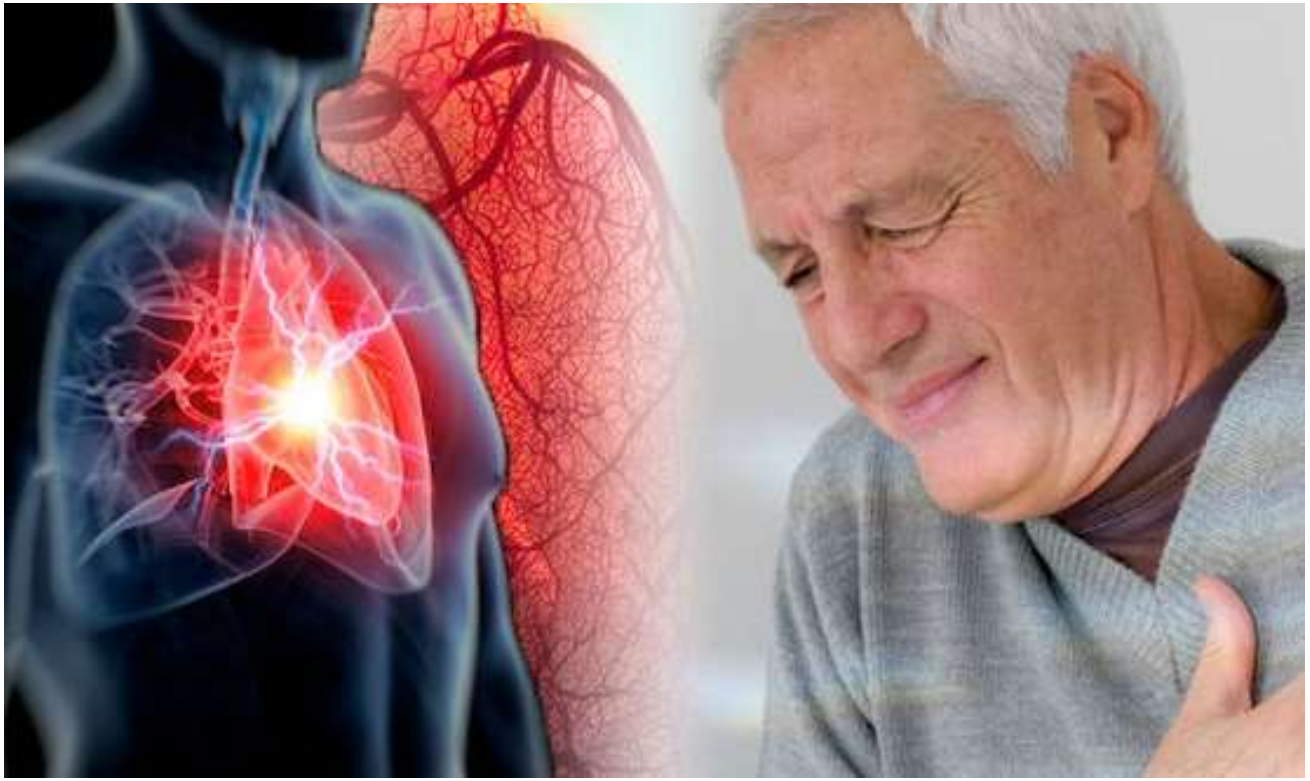
- **Nutrition Recommendations**
- For people with non–dialysis-dependent stage 3 or higher chronic kidney disease
  - dietary protein intake aimed to a target level of 0.8 g/kg body weight per day.
- For those on dialysis,
  - consider higher levels of dietary protein intake since protein energy wasting can be of concern

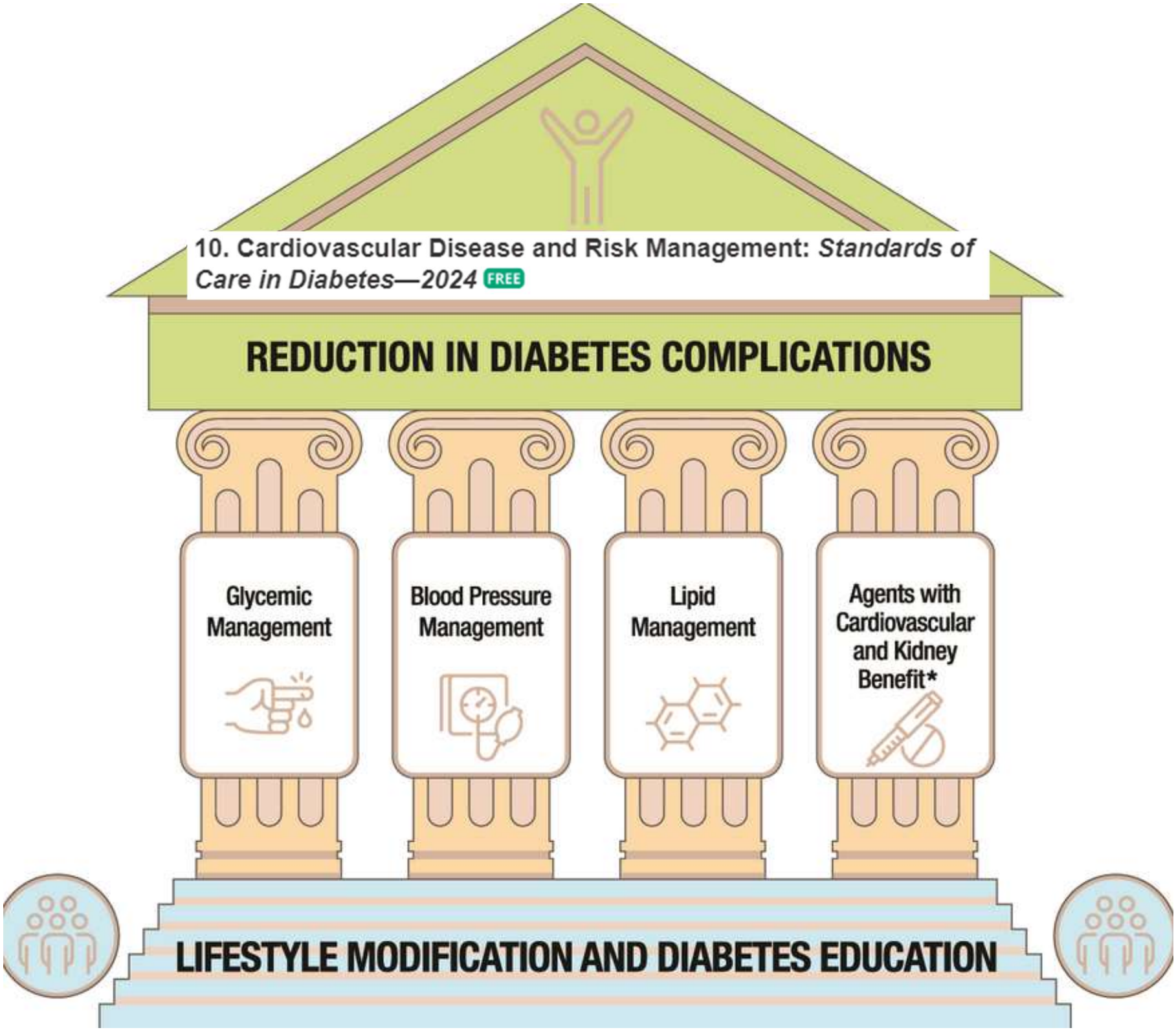
11. Chronic Kidney Disease and Risk Management: *Standards of Care in Diabetes—2023* FREE

DiaBingo - O

- SGLT-2 Inhibitors main action
- Januvia(sitagliptin) belongs to which class?
- These classes of diabetes pills increase insulin release
- Which treatments help lower elevated fasting BG
- On Acarbose (Precose) should treat hypo with ___
- On Metformin (Glucophage) Stop med if GFR ___
- On which med should ind's know about hypoglycemia SE's
- Possible side effects of TZD's include
- Metformin can damage kidney function
- What warning for DPP- IV and GLP-1 RA
- GLP-1 Receptor agonists cause increased satiety
- Side effects of Canagliflozin (Invokana) include
- If GI side effects on Metformin try ____

Cardiovascular Disease is the Leading Cause of Death in Diabetes




10. Cardiovascular Disease and Risk Management: *Standards of Care in Diabetes—2024* FREE
REDUCTION IN DIABETES COMPLICATIONS
Glycemic Management
Blood Pressure Management
Lipid Management
Agents with Cardiovascular and Kidney Benefit*
LIFESTYLE MODIFICATION AND DIABETES EDUCATION

Stroke and Heart Attack

- Pain or discomfort in your arms, back, jaw, neck, or stomach
- Shortness of breathing
- Sweating
- Nausea
- Light-headedness

Make sure people with diabetes know the signs and seek immediate help.

People with diabetes may not experience intense chest or jaw pain during heart attack due to neuropathy.

10. Cardiovascular Disease and Risk Management

- Atherosclerotic cardiovascular disease (ASCVD) and Heart Failure are leadings causes of morbidity and mortality in diabetes.
- ASCVD includes:
  - coronary heart disease (CHD),
  - cerebrovascular disease, or
  - peripheral arterial disease
- $39.4 billion in cardiovascular-related spending per year

Large benefits are seen when multiple CV risk factors are addressed simultaneously

With more aggressive goals, rates of CVD have decreased over past decade

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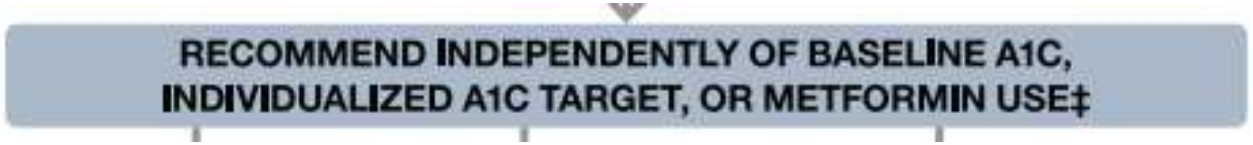
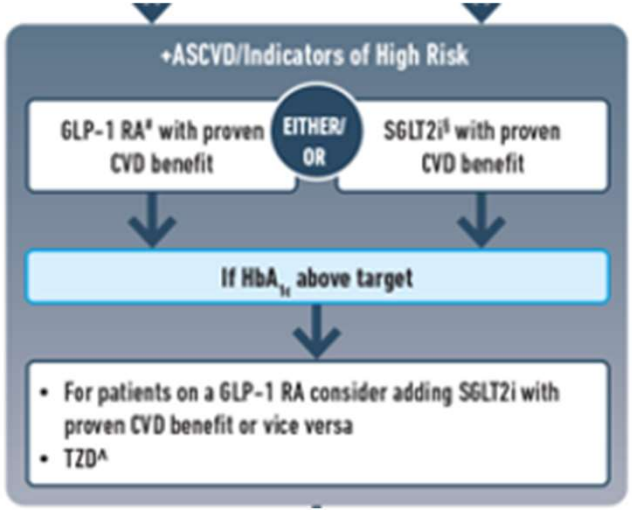
Atherosclerotic Cardiovascular Disease

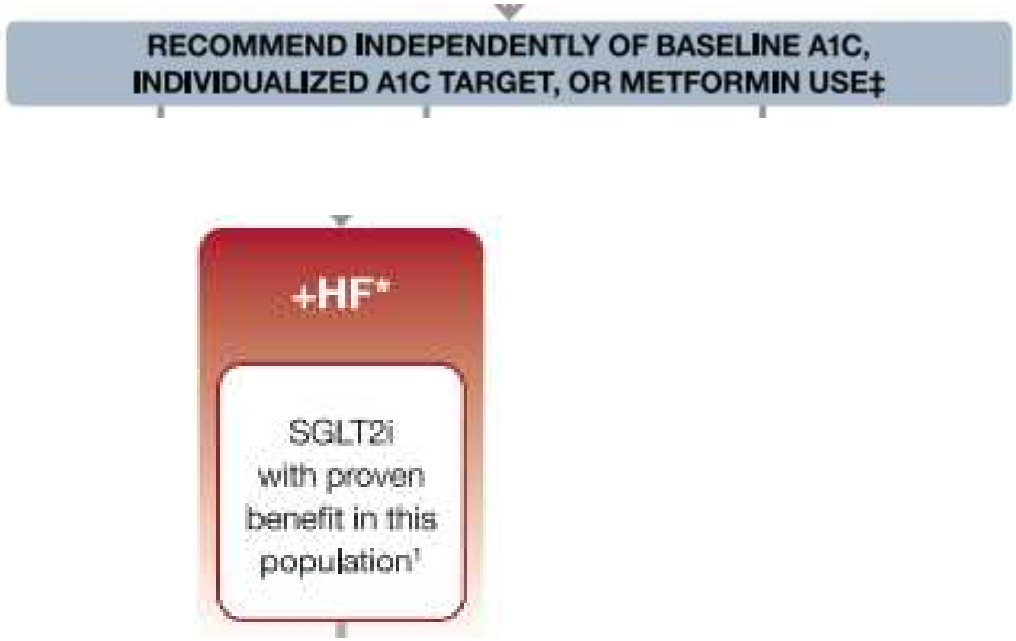
- ASCVD risk
  - Established CV disease
  - High CV Risk
    - 55+ with 2 or more risk factors
    - Risk factors include obesity, HTN, dyslipidemia, albuminuria, smoking
  - Most effective meds based on Cardiovascular Outcomes Trials (CVOT)
    - SGLT2i - Empagliflozin (Jardiance), canagliflozin (Invokana), Dapagliflozn (Farxiga)
    - GLP-1 RAs - Semaglutide (Ozempic), liraglutide (Victoza), dulaglutide (Trulicity), semaglutide (Wegovy)





Diabetes Care 2023;46(Suppl. 1):S125-S143.

Heart Failure



- If HF or reduced Ejection Fraction (rEF) and Left Ventricular Ejection Fraction (LVEF) <45% (all except bexagliflozin)
- Empagliflozin and dapagliflozin FDA approved for preserved EF
- SGLT-2 inhibitor if eGFR is adequate (>20 to start, may continue until ESRD)
- Avoid TZD
- If using a DPP4 inhibitor, avoid saxagliptin and alogliptin

Proven benefit: All

9. Pharmacologic Approaches to Glycemic Treatment: *Standards of Care in Diabetes—2024* FREE

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Sotagliflozin (Impefa)

- SGLT1/SGLT2 inhibitor
- Indicated to reduce risk of CV death, hospitalization for HF, and urgent HF visit in adults with:
  - HF or
  - T2D, CKD, and other CV risk factors
- Dose: 200mg once daily not more than 1 hour before first meal
- Titrate up to 400mg daily after at least 2 weeks
- Studied in the SCORED and SOLOIST trials.
- SCORED: A total of 10.584 people with T2D and additional CV risk factors
  - After 16 months, rate of primary endpoint (death from CV causes, hospitalization for HF and urgent visits for GF) was reduced (5.6 events/100 patient years with sotagliflozin compared to 7.5/100 patient years with placebo)

SGLT2 Inhibitor HF/ASCVD Evidence Summary

Trial Name	SGLT2 Inhibitor vs. placebo	Outcomes (Primary Bolded)
EMPA-REG Outcome	Empagliflozin	N=7020, Median follow-up 3.1 years, Prior CVD 99% **3 Point MACE (primary)**: 0.86 (0.74-0.99), CV death: 0.62 (0.49-0.77)
EMPEROR Reduced	Empagliflozin	N=3730, 1856 with diabetes, Median follow-up 1.3 years, 100% HF with reduced EF **CV death or HF hospitalization (primary)** 0.75 (0.65-0.86)
EMPEROR Preserved	Empagliflozin	N=5988, 2938 with diabetes, Median follow-up 2.2 years, 100% HF with EF > 40% **CV death or HF hospitalization (primary)** 0.79 (0.69-0.90)
CANVAS Program	Canagliflozin	N=10142, Median follow-up 3.6 years, Prior CVD 65.6% **3 point MACE (primary)**: 0.86 (0.75-0.97), Worsening nephropathy 0.60 (0.47-0.77)
DECLARE-TIMI 58	Dapagliflozin	N=17160, Median follow-up 4.2 years, Prior CVD 40% **3 point MACE (primary)**: 0.93 (0.84-1.03) CV death or HF hospitalization: 0.83 (0.73-0.95),
DAPA-HF	Dapagliflozin	N=4744 (1983 with diabetes), Median follow-up 1.5 years, 100% HF **Worsening Hf or CV death (primary)** 0.74 (0.65-0.85)
DELIVER	Dapagliflozin	N=6263, 2807 with diabetes, Median follow-up 2.3 years, 100% with HF with EF > 40% **Worsening HF or CV death (primary)** 0.82 (0.73-0.92)
VERTIS-CV	Ertugliflozin	N=8246, Median follow-up 3.5 years, Prior CVD 99.9% **3 point MACE (primary)** 0.97 (0.85-1.11), HF hospitalization 0.70 (0.51-0.90)

American Diabetes Association. 10. Cardiovascular disease and risk management: Standards of Care in Diabetes—2023. Diabetes Care 2023;46(Suppl. 1):S158–S190

GLP-1 Analog CVOT Data Summary

Trial Name	GLP-1 Agent/ Comparator	Outcomes (Primary Bolded)	FDA Indication
LEADER	**Liraglutide**/placebo	81% Prior CVD**, 3 point MACE** 0.87 (0.58-0.95) N=9340, Median follow-up 3.8 years Worsening nephropathy 0.78 (0.67-0.92)	As an adjunct to diet and exercise to improve glycemic control in patients **10 years and older** with type 2 DM To reduce the risk of **major adverse CV events** in adults with type 2 DM and **established CVD**
ELIXA	**Lixesenatide**/placebo	100% Prior CVD, **4 point MACE** 1.02 (0.89-1.17) N=6068, Median follow-up 2.1 years	As an adjunct to diet and exercise to improve glycemic control in adults with type 2 DM
SUSTAIN-6	**Semaglutide inj**/ placebo	60% Prior CVD, **3 point MACE** 0.74 (0.58-0.95) N=3297, Median follow-up 2.1 years Worsening nephropathy 0.64 (0.46-0.88)	As an adjunct to diet and exercise to improve glycemic control in adults with type 2 DM To reduce the risk of **major adverse CV events** in adults with type 2 DM and **established CVD**
PIONEER-6	**Semaglutide oral**/ placebo	84.7% Prior CVD, **3 point MACE** 0.79 (0.57-1.11) N=3183, Median follow-up 1.3 years	As an adjunct to diet and exercise to improve glycemic control in adults with type 2 DM
EXSCEL	**Exenatide** – (weekly)/ placebo	73.1% Prior CVD, **3 point MACE** 0.91 (0.83-1.00) N=14752, Median follow-up 3.2 years	As an adjunct to diet and exercise to improve glycemic control in patients **10 years and older** with type 2 DM
REWIND	**Dulaglutide**/placebo	32% Prior CVD, **3 point MACE** 0.88 (0.79-0.99) N=9901, Median follow up 5. 4 years Worsening nephropathy 0.85 (0.77-0.93)	As an adjunct to diet and exercise to improve glycemic control in adults with type 2 DM To reduce the risk of **major adverse CV events** in adults with type 2 DM and **established CVD** or **multiple CVD risk factors**

American Diabetes Association. 10. Cardiovascular disease and risk management: Standards of Care in Diabetes—2023. Diabetes Care 2023;46(Suppl. 1):S158–S190

Meet Alice

Alice is a 56yo AAF presenting for follow-up for type 2 diabetes. Alice reports that her blood pressure has been higher lately. Denies s/sx of hypoglycemia.

- **PMH**
  - Type 2 diabetes x5 years
  - HTN x 5 years
  - Depression
- **Meds**
  - Metformin1000mg PO bid
  - Glipizide 10mg PO qam
  - Chlorthalidone 25mg PO daily
  - Escitalopram 10mg PO daily
- **PE**
  - Ht: 5'3" Wt: 185lbs , BMI:32.8kg/m^2
  - BP: 140/88mmHg
  - A1c=6.9%, K: 4.5mEq/L, Scr:0.8mg/dL, ACR 202 mg/g
  - Tchol=204mg/dL, HDL=34mg/dL, LDL=120mg/dL, TG=250mg/dL

- Social history
  - (+)Alcohol: 1-2 drinks/week
  - (+) Tobacco use: 1/2ppd
  - Exercise: walks 15 min twice/week
  - Occ: receptionist
- Home monitoring
  - FBG and pre-meal: 110-130 mg/dL
  - BP: 140-150/80-90mmHg

Questions to Think About

- What are Alice's blood pressure, cholesterol and glucose targets?
- What lifestyle changes should be advised to reduce cardiovascular risk?
- What changes should be made to optimize Alice's medication regimen?

Hypertension Management in People with Diabetes

Classifying Hypertension

BP Category	SBP		DBP
Normal	<120 mmHg	And	<80mmHg
Elevated	120-129mmHg	And	<80mmHg
Hypertension			
Stage 1	130-139 mmHg	Or	80-89mmHg
Stage 2	≥140mmHg	Or	≥90mmHg

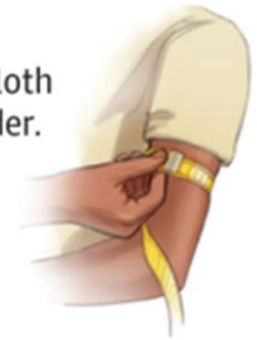
Individuals with SBP and DBP in 2 categories should be designated to the higher BP category

Whelton et al. 2017 High Blood Pressure Clinical Practice Guideline

Taking an accurate Blood Pressure

Choosing the correct blood pressure cuff size

Measure the circumference of your upper arm with a cloth measuring tape midway between the elbow and shoulder. Choose a cuff size that includes this measurement.



Position for taking your blood pressure at home

1. Rest for 5 minutes before measuring your blood pressure.
2. Sit in a chair with both feet flat on the ground and back straight.
3. Place your arm at the level of your heart or chest.
4. Stay still and do not talk as your blood pressure machine operates.

Measure your blood pressure in the morning right after you wake up or in the evening before you go to bed.

Try to measure your blood pressure at the same time every day.

BP and Diabetes Targets 2024

- **BP target <130/80**
  (if it can be safely attained)

- Confirm systolic BP ≥ 130 or diastolic BP ≥ 80 using multiple readings, including measurements on a separate day, to diagnose hypertension.
- If BP ≥ 180/110, can be diagnosed at single visit
- BP target based on ind assessment, shared decision making and potential adverse effects
- Monitor BP at home and at each visit
- During pregnancy, with previous history of HTN
  - B/P Target of 110 -135/85

10. Cardiovascular Disease and Risk Management: *Standards of Care in Diabetes—2024* FREE

BP Treatment in addition to Lifestyle

- **First Line B/P Drugs if 130/80 +**
  - With albuminuria* or ASCVD
    - Start either ACE or ARB
  - No albuminuria - Any of the 4 classes of BP meds can be used:
    - *ACE Inhibitors, *ARBs, *thiazide-like diuretics or calcium channel blockers.
    - *Monitor K+ 7-14 days after start/annually
  - Avoid ACE and ARB at same time
  - Multiple Drug Therapy often required
- **If B/P ≥ 150 /90 start 2 drug combo**

*Albuminuria = Urinary albumin creatinine ratio of 30+

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Recommendations for the Treatment of Confirmed Hypertension in Nonpregnant People With Diabetes

Initial BP ≥130/80 and <150/90 mmHg

Start one agent

Albuminuria or CAD*

No

Start one drug:
- ACEi or ARB
- CCB†
- Diuretic‡

Yes

Start:
- ACEi or ARB

Lifestyle management

Initial BP ≥150/90 mmHg

Start two agents

Albuminuria or CAD*

No

Start drug from 2 of 3 options:
- ACEi or ARB
- CCB†
- Diuretic‡

Yes

Start:
- ACEi or ARB

and

- CCB† or Diuretic‡

Assess BP Control and Adverse Effects

See Cheat Sheets & appendix in back of syllabus

10. Cardiovascular Disease and Risk Management: *Standards of Care in Diabetes—2024* FREE

Cost vs Benefit of Treating HTN

- Consider potential adverse effects of BP medications
  - Hypotension, syncope, falls, acute kidney injury, and electrolyte abnormalities
  - Older people, those with chronic kidney disease, and frailty have been shown to be at higher risk
  - People with orthostatic hypotension, substantial comorbidity, functional limitations, or polypharmacy higher risk and may prefer relaxed B/P targets to enhance quality of life.

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HTN Lifestyle Treatment Strategies

- If BP > 120/80, start with lifestyle
- DASH Diet
- Weight loss if indicated
- Sodium intake <2,300mg/day
- Eat more fruits & veggies (8-10 a day)
- Low fat dairy products (2-3 servings/day)
- Limit alcohol 1-2 drinks a day
- Increase activity level

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Back to Alice

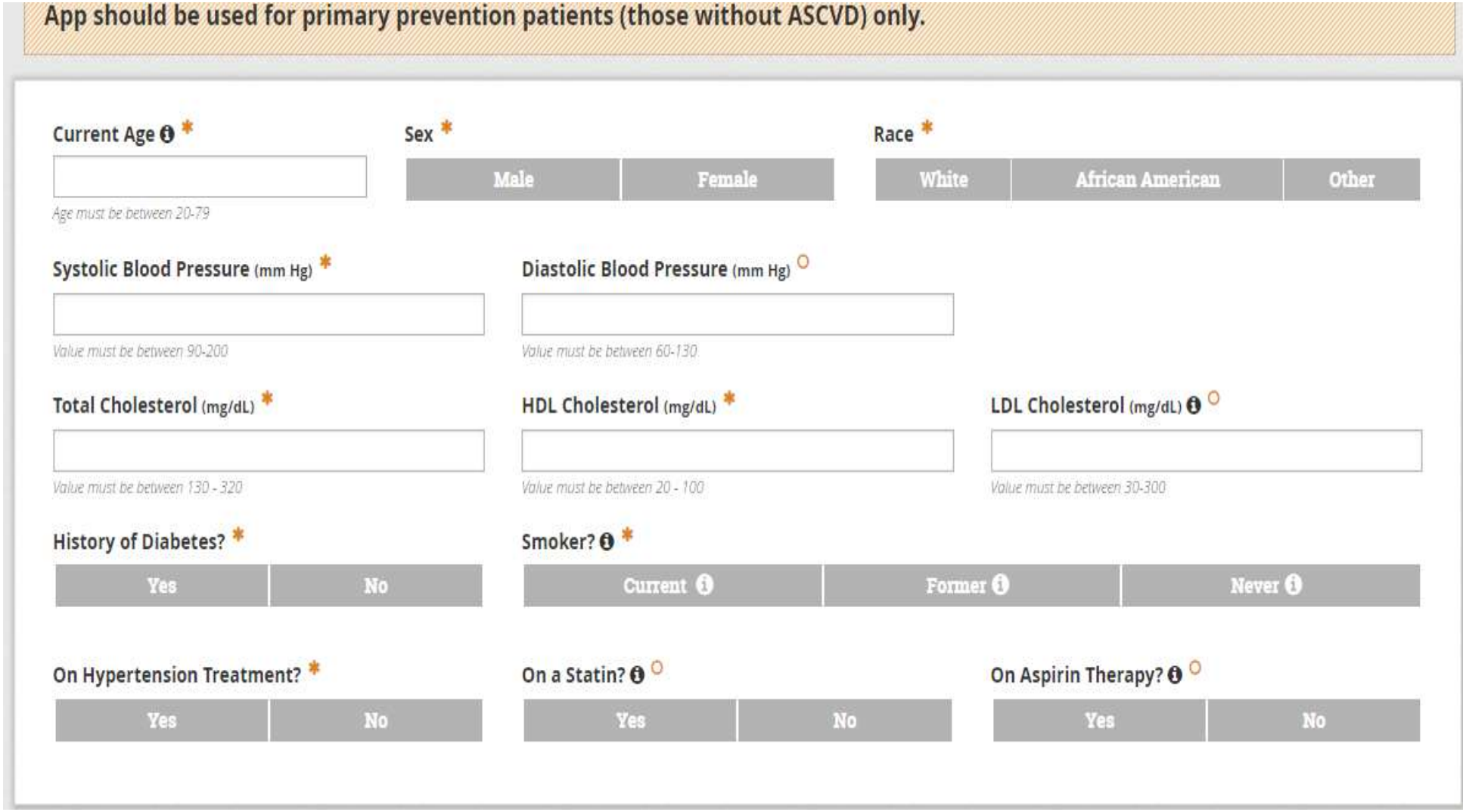
Alice is a 56yo AAF presenting for follow-up for type 2 diabetes. Alice reports that her blood pressure has been higher lately. Denies s/sx of hypoglycemia.

- **PMH**
  - Type 2 diabetes x5 years
  - HTN x 5 years
  - Depression
- **Meds**
  - Metformin1000mg PO bid
  - Glipizide 10mg PO qam
  - Chlorthalidone 25mg PO daily
  - Escitalopram 10mg PO daily
- **PE**
  - Ht: 5'3" Wt: 185lbs , BMI:32.8kg/m^2
  - BP: 140/88mmHg
  - A1c=6.9%, K: 4.5mEq/L, Scr:0.8mg/dL, ACR 202 mg/g
  - Tchol=204mg/dL, HDL=34mg/dL, LDL=120mg/dL, TG=250mg/dL

- Social history
  - (+)Alcohol: 1-2 drinks/week
  - (+) Tobacco use: 1/2ppd
  - Exercise: walks 15 min twice/week
  - Occ: receptionist
- Home monitoring
  - FBG and pre-meal: 110-130 mg/dL
  - BP: 140-150/80-90mmHg

Calculating ASCVD Risk

- http://tools.acc.org/ASCVD-Risk-Estimator-Plus/#!/calculate/estimate/



What Is Alice's ASCVD risk?

- 42% risk of a cardiovascular event in the next 10 years
- This puts Alice at HIGH risk

Poll 6 - What is the blood pressure goal for Alice?

A. BP<120/80 mmHg

B. BP<130/80 mmHg

C. BP<140/80 mmHg

D. BP<140/90 mmHg

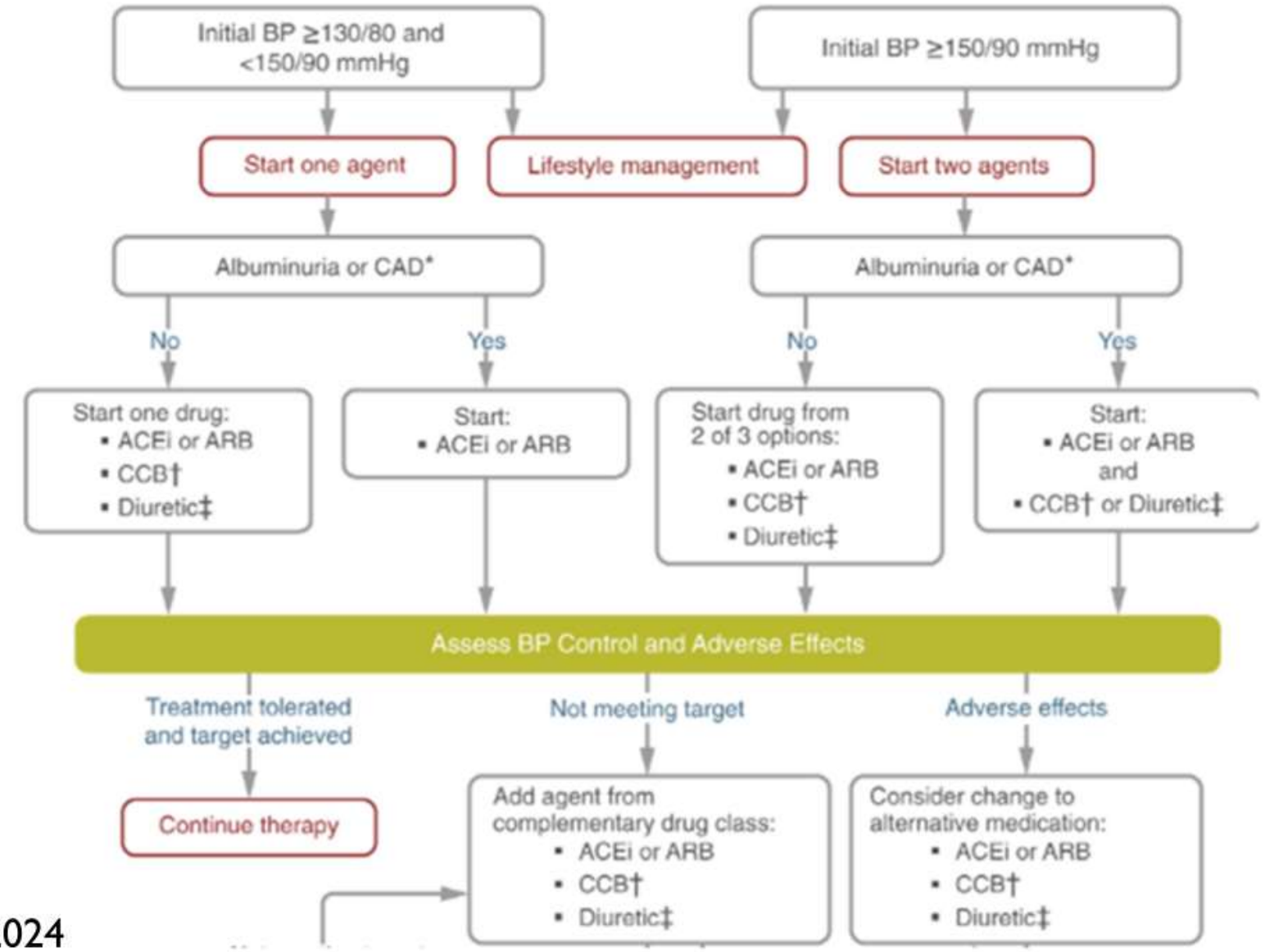
Does Alice have albuminuria?

Albumin to Creatinine ratio (ACR)= 202 mg/g

YES

Recommendations for the Treatment of Confirmed Hypertension in Nonpregnant People With Diabetes

ADA 2024 Standards of Diabetes Care
Figure 10.2 Vol.47, S179-218



ADASOC 2024

ACE Inhibitors

Class / Action	Generic / Trade Name	Usual Daily Dose Range	Frequency	Considerations
ACE Inhibitors Angiotensin Converting Enzyme **Action -** Block the conversion of AT-I to AT-II. Also stimulates release of nitric oxide causing vasodilation.	benazepril / Lotensin†	10 – 40 mg	1 x a day	Try to take same time each day. Effects seen w/in 1 hr of admin, max effects in 6 hrs. **Side effects**: Can cause cough (due to increased bradykinin) – can try different med in same class. Also can cause fatigue, dizziness, hypotension. †These meds are also available as a combo w/ low dose HCTZ (hydrochlorothiazide). ‡These meds are also available as a combo w/ CCB (calcium channel blocker) usually amlodipine
	captopril /Capoten*†	12.5 - 100 mg	2-3 x a day	
	Enalopril/ Vasotec*†	2.5 - 40 mg	1-2 x a day	
	Fosinopil / Monopril†	10- 40 mg	1 x a day	
	Lisinopril *† Prinivil Zestril	 10 – 40 mg 10 - 40 mg		
	Ramipril / Altace*†	2.5 – 10 mg		
	Moexipril / Univasc†	3.75 - 15 mg		
	Perindopril/Aceon‡ Perindopril/ Indapamide combo (Coversyl)	2-16 mg 2 - 8 mg 0.625 - 2.5 mg		
	Quinapril /Accupril†	5 – 40 mg		
	Trandolapril/ Mavik Trandolapril/ Verapamil combo (TARKA)	1.0 – 4 mg 1-4 mg 180 to 240 mg		

Initial dose adjustment may be needed for renal dysfunction or elderly

See Med Cheat Sheets

Angiotensin Receptor blockers (ARB's)

Class / Action	Generic / Trade Name	Usual Daily Dose Range	Frequency	Considerations
ARBs -Angiotensin Receptor Blockers **Action -**Block AT-I receptor which reduces aldosterone secretion and vasoconstriction	Azilsartan/Edarbi	40 - 80 mg	1 x daily	Try to take same time each day **Side effects**- Can cause dizziness, drowsiness, diarrhea, hyperkalemia, hypotension. †These meds are also available as a combo w/ low dose HCTZ (hydrochlorothiazide). ‡These meds are also available as a combo w/ CCB (calcium channel blocker) usually amlodipine
	Azilsartan/ Chlorthalidone combo (Edarbyclor)	40 mg 12.5 - 25 mg		
	Candesartan/Atacand†	8 – 32 mg		
	Eprosartan/Teveten†	400 - 600 mg		
	Irbesartan/ Avapro†	75 – 300 mg		
	Losartan / Cozaar*†	25 – 100 mg		
	Olmesartan / Benicar†‡ Tribenzor (triple combo)	20 – 40 mg		
	Telmisartan / Micardis	20 – 80 mg		
	Valsartan / Diovan†‡ Exforge HCT (triple combo)	80 – 320 mg		
	Valsartan/ Nebivolol combo (Byvalson)	80 mg 5 mg		

Initial dose adjustment may be needed for renal dysfunction or elderly

See Med Cheat Sheets

ACEI/ARB Adverse Effects

- Adverse effects
  - Dry cough with ACEI
    - Caused by inhibition of bradykinin breakdown
  - Hyperkalemia
  - Angioedema (< 1%)
    - Occurs 2-4x more frequently in African Americans
  - Bump in SCr
    - Up to 30% is acceptable
  - Orthostatic hypotension (initial dose)
  - Skin rash (captopril)

- Contraindications
  - Pregnancy
  - Bilateral renal artery stenosis

Thiazide diuretics

Class / Action	Generic / Trade Name	Usual Daily Dose Range	Considerations
Thiazide Diuretics **Action:** cause diuresis and decrease vascular resistance. (Many meds combined with this class)	Hydrochlorathiazide (HCTZ)* HydroDIURIL Microzide	12.5 – 25 mg Most frequently prescribed	1 x daily in am with or w/out food **Side effects**: lyte imbalances; hypokalemia, hypomagnesemia, hyperuricemia, hyperglycemia, hyperlipidemia and hyper/hypocalcemia. S/S include muscle cramps, fatigue, dizziness and cardiac arrhythmias .
	Chlorthalidone / Clorpres*	12.5 – 25 mg	
	Metolazone / Zaroxolyn*	2.5 – 20 mg	
	Indapamide / Lozol*	1.2 – 2.5 mg	

See Med Cheat Sheets

Calcium Channel Blockers

Calcium Channel Blockers are usually second or third line BP med for diabetes, since they have less impact on CVD. They may also be used for those who can't tolerate ACE or ARB Therapy.

Class / Action	Generic / Trade Name	Usual Daily Dose Range	Frequency	Considerations
Calcium Channel Blocker *Nondihydropyridine* Relaxes coronary blood vessels to decrease heart rate and cardiac output.	**Diltiazem immediate release***	30 – 360 mg	4 x day	**Monitor** BP, heart rate, liver enzymes and cardiac function a baseline and periodically. Take at the same time each day (with meals if possible). Take in evening if experience drowsiness. **Side Effects**: Watch for cardiac conduction abnormalities, bradycardia, CHF and edema. Can cause peripheral edema and constipation. Metabolized through CYP3A4, so review package insert for drug and food interactions (ie grapefruit).
	Diltiazem extended release*			
	Cardizem CD	120 – 480 mg	1 x day	
	Tiazac	120 – 540 mg	1 x day	
	Dilacor, Diltia	180 – 540 mg	1 x day	
	Verapamil immediate release* Calan	80 -320 mg	3 x day	
	Verapamil sustained release* Calan SR, Veralan	120 mg – 480 mg	1 -2 x day	
	Verapamil extended release*			
	Covera-HS	120 – 480 mg	1 x day	
	Verelan PM	100 – 400 mg		
Calcium Channel Blocker – *Dihydropyridine* Causes vasodilation and decreases peripheral vascular resistance.	Amlodipine/Norvasc	2.5 – 10 mg	1 x day	
	Felodipine / Plendil	2.5 – 10 mg	1 x day	
	Isradipine controlled release DynaCirc CR	2.5 – 10 mg	1 x day	
	Nicardipine sustained release / Cardene SR	30 – 60 mg	2 x day	
	Nifedipine long-acting* Adalat CC /Procardia XL	30 – 120 mg	1 x day	
	Nisoldipine / Sular	10 – 40 mg	1 x day	

Resistant hypertension

- Not meeting BP targets on 3 classes of antihypertensive meds (including a diuretic) at optimal doses
- Consider mineralocorticoid receptor antagonist
  - Spironolactone (Aldactone®) 25-100mg daily
  - Eplerenone (Inspira®) 50-100mg daily
- Monitor serum creatinine, potassium
- Avoid use with finerenone

Beta Blockers

- Use in recurrent MI, heart failure
- Side effects: depression, sexual dysfunction, exercise intolerance, sedation, dizziness
- Monitor BP, lipids, heart rate, glucose
- When stopping, taper dose gradually
- Can elevate glucose and mask adrenergic symptoms of hypoglycemia (ex. tachycardia)
  - Sweating will still occur (cholinergic mediated)

Beta Blockers are commonly prescribed as an add-on to other B/P meds for people with DM. Beta Blockers are beneficial for persons w/ concurrent cardiac problems and prevention of recurrent MI and heart failure. Caution in DM since Beta Blockers can cause hyperglycemia and mask hypoglycemia induced tachycardia (but do not block hypoglycemia related dizziness and sweating). Monitor B/P, heart rate, lipids and glucose.

Beta Blockers *β1- Selective* **Action:** Blockade β1 receptors & reduce cardiac output & kidney renin activation.g	Acebutolol / Sectral*	200 – 800 mg	2 x daily	Side Effects: Usually CNS related including sedation, dizziness, lightheaded . Watch for bradycardia, hypotension, depression and sexual dysfunction. Check heart rate each visit, adjust dose if HR <50. Can cause heart block – review package insert for drug-drug interactions. Watch for exercise intolerance. When stopping beta blockers, taper dose gradually. Use cautiously at lowest dose. †These meds are also available as a combo w/ low dose HCTZ (hydrochlorothiazide).
	Atenolol / Tenormin*	25 – 100 mg	1 x daily	
	Atenolol with Chlorthalidone/ Tenoretic	50 -100 mg 25 mg	1 x daily 1 x daily	
	Betaxolol / Kerlone	5 – 10 mg	2 x daily	
	Bisoprolol/ Zebeta†	2.5 – 10 mg		
	Metoprolol tartate/Lopressor*†	25 – 100 mg	1 x daily	
	Metoprolol succinate / Toprol XL	25 - 100 mg		
	Nebivolol/Bystolic	5 to 40 mg		
	Nebivolol with Valsartan/ Byvalson	5 mg 80 mg		
Beta Blockers *Non Selective* **Action**: Blockades β1 & β2	Nadolol / Corgard* Nadolol with Bendroflumethiazide	40 - 120 mg 40-80 mg 5 mg	1 x daily	
	Penbutolol / Levatol	10 - 40 mg	1 x daily	
	Pindolol / Visken	10 – 40 mg	2 x daily	
	Propanolol / Inderal* Inderal LA (extended)	40 – 160 mg 60 – 180 mg	2 x daily 1 x daily	
	Timolol / Blocadren*	10 – 60 mg	2 x daily	
Combined α- and β- Blockers	Corvedilol / Coreg Coreg CR	6.25 – 50 mg 20 – 80 mg	2 x daily 1 x daily	Same precautions as beta blockers.
	Labetalol / Normodyne*	100 – 2400 mg	2 x daily	

Other Hypertension Meds

- Direct renin inhibitors (Alsikiren-Tekturna®)
  - Similar side effects to ACEI/ARB, rarely used in clinical practice
- Combined alpha and beta blockers (ex. Carvedilol)
  - Similar precautions as beta blockers, additional MOA
- Loop diuretics (Furosemide, Torsemide, Bumetanide)
  - Use when eGFR<30 or if greater diuresis is needed, monitor electrolytes
- Potassium sparing diuretics (ex. Amiloride, Triamterene)
  - Use in combination with thiazide to retain potassium, minimal effect on BP

Other hypertension meds (cont)

- Alpha 1 blockers (Doxazosin, Prazosin, Terazosin)
  - Vasodilator, risk of orthostatic hypotension
  - Often used for people with DM + benign prostatic hypertrophy (BPH)
- Alpha 2 agonists (Clonidine, Methyldopa)
  - Centrally acting
  - Administer with a diuretic
  - Side effects: sedation, dry mouth, orthostatic hypotension, impotence
  - Avoid abrupt discontinuation

α1 – Receptor Blockers - Often used for pts with DM & benign prostatic hypertrophy (BPH).				
α1 – Receptor Blockers Vasodilation	Doxazoxin/Cardura*	1 – 8 mg	1 x day	Take at hs and low dose to reduce risk of postural hypotension/syncope.
	Prazosin / Minipress*	2 – 20 mg	2 - 3 day	
	Terazosin/ Hytrin*	1 – 10 mg	1 – 2 day	
α2 agonists- Not usually first line due to side effects. Effective in pts w/ renal disease, since does not compromise renal function.				
α2 agonists – Centrally act to block influence of norepinephrine on the heart and lower B/P	Clonidine / Catapres*	0.1 to 0.8 mg	2 x day	Administer w/ diuretic. Side effects: sedation, dry mouth, bradycardia orthostatic hypotension, impotence. Do not stop abruptly, can cause hypertensive crisis.
	Methyldopa / Aldomet*	250 – 1000 mg	2-3 x day	

Poll 7 - What Changes are Best to Make to Alice's Hypertension Regimen?

A. Add lisinopril
B. Replace chlorthalidone with lisinopril
C. Add amlodipine
D. Replace chlorthalidone with amlodipine

Assume all choices include lifestyle modifications

Cholesterol Management in People with Diabetes

- 1 minute stretch and Questions?

Poll Question 8

RZ is 47 years old with type 2 diabetes and hypertension. RZ takes metformin 1000 mg BID, plus lisinopril 20mg daily. RZs LDL is 130 mg/dL. Based on the most recent ADA Standards, what is the LDL Cholesterol target for RZ?

A. LDL less than 100 mg/dL.

B. Lower LDL by 30%.

C. LDL target of 65 mg/dL or less.

D. Determine LDL target based on ASCVD risk.

Lipid Goals – Primary Prevention

- For people with diabetes aged 40–75 at higher cardiovascular risk*
  - (*HTN, Smoke, CKD, BMI 30+ albuminuria, family hx ACSVD)
  - **High-intensity statin** therapy is recommended
  - **Reduce LDL cholesterol by at least 50% of baseline**

    AND
  - **Target LDL cholesterol <70 mg/dL.**

- **If LDL cholesterol 70 +**
  - it may be reasonable to add ezetimibe or a PCSK9 inhibitor to maximum tolerated statin therapy.

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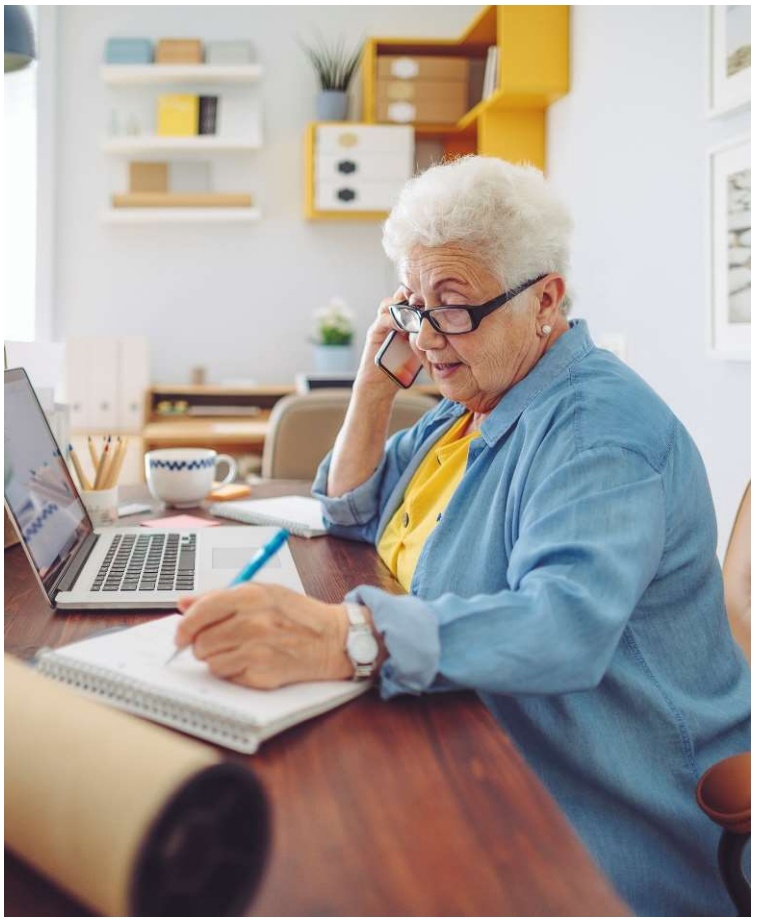
Lipid Goals for People *with* ASCVD

- For people of all ages with diabetes and atherosclerotic cardiovascular disease:
  - Add high-intensity statin to lifestyle therapy.
  - **Reduce LDL cholesterol by 50% or greater from baseline with LDL cholesterol goal of <55.**
  - Addition of ezetimibe or a PCSK9 inhibitor with proven benefit in recommended if goal is not achieved on maximum tolerated statin therapy.



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Lipid Therapy in Diabetes by Age

- All ages 20+ *with* ASCVD, add high-intensity statin
- 20–39 and additional ASCVD risk factors
  - may be reasonable to initiate statin therapy
  - 40-75 without ASCVD and low CV risk
    - Moderate intensity statin
  - 40-75 without ASCVD with 1 or more CV risk factor, reduce LDL by 50%, use high-intensity statin, LDL goal <70
- 75 years or older and already on statin
  - it is reasonable to continue statin treatment.
- 75 years or older
  - it may be reasonable to initiate moderate-intensity statin therapy after discussion of potential benefits and risks.

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Statin Dosing

High Intensity:
Lowers LDL ≥50%

- Lipitor (atorvastatin)
  - 40-80mg
- Crestor (rosuvastatin)
  - 20-40mg

Moderate Intensity:
Lower LDL 30-<50%

- Lipitor (atorvastatin)
  - 10-20mg
- Crestor (rosuvastatin)
  - 5-10mg
- Zocor (Simvastatin)
  - 20-40mg
- Pravachol (pravastatin)
  - 40 – 80mg
- Mevacor (lovastatin) 40 mg
- Lescol (fluvastatin) XL 80mg
- Livalo (pitavastatin) 2-4mg

*****If person can't tolerate intended statin dose, use maximally tolerated dose**

See Med Cheat Sheets

PCSK9 Inhibitors Lipid Medications

Proprotein convertase subtilisin/kexin type 9

	Alirocumab (Praluent)	Evolocumab (Repatha)
FDA-approved indications	• Primary hyperlipidemia (HLD) • Homozygous familial hypercholesterolemia (HoFH) • Secondary prevention of cardiac events	
Dosing	• **HoFH:** 150 mg SC q2 weeks • **HLD or secondary cardiac prevention:** 75 mg SC q2 weeks or 300 mg SC q4 weeks; if adequate LDL response not achieved, may increase to max of 150 mg q2 weeks	• **HoFH:** 420 mg SC q4 weeks; may increase to 420 mg q2 weeks if meaningful response not achieved in 12 weeks • **HLD or secondary cardiac prevention:** 140 mg q2 weeks or 420 mg q4 weeks
Dosage forms	• Auto-injector 75 mg/mL or 150 mg/mL	• Repatha Sure Click (auto-injector) 140 mg/mL • Repatha Pushtronex System (single use infusor with pre-filled cartridge) 420 mg/3.5 mL – administered over 9 minutes
Storage	• Store in refrigerator in outer carton until used • Once used, keep at room temperature, use within 30 days	
Injection clinical pearls	• Do not shake or warm with water • Administer by SC injection into thigh, abdomen, or upper arm • Rotate injection site with each injection	
Drug interactions	• No known significant interactions	
Monitoring parameters	• Lipid panel before initiating therapy, 4-12 weeks after initiating, and q3-12 months thereafter	
Side effects	• Injection site reaction (4-17%) • Hypersensitivity reaction (9%) • Influenza (6%) • Myalgia (4-6%) • Diarrhea (5%)	• Nasopharyngitis (6-11%) • Upper respiratory tract infection (9%) • Diabetes mellitus (9%) • Influenza (8-9%) • Injection site reaction (6%) • Myalgia (4%)

From Meds Cheat Sheet Page – Diabetesed.net

Lipid Monitoring and Lifestyle Treatment Strategies

- Lipid Goals
  - HDL >40
  - Triglycerides <150
  - LDL target based on risk

Monitoring:
If **not** taking statins and unde rage of 40.
- check at time of diagnosis and every 5 yrs.

On statin
Monitor lipids at diagnosis and yearly.
Monitor lipids 4-12 weeks after statin dose adjustment.

- Weight loss if indicated
- Mediterranean or DASH Diet
- Reduction of saturated fat intake
- Increase of omega-3 fatty acids, viscous fibers and plant stanols/sterols
- Increase activity level
- BG lowering helps lower triglycerides and increase HDL

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Statin Intolerant

- Primary Prevention
  - In people with diabetes intolerant to statin therapy, treatment with bempedoic acid is recommended to reduce cardiovascular event rates as an alternative cholesterol-lowering plan. (A)

- Secondary Prevention
  - For people with diabetes and ASCVD intolerant to statin ther apy, PCSK9 inhibitor therapy with monoclonal antibody treatment, (A), bempedoic acid (A) or PCSK9 inhibitor therapy with inclisiran siRNA (E) should be considered as an alternative cholesterol-lowering therapy.

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Additional Agents to Lower LDL

- Bempedoic acid (Nexltetol), lowers LDL by ~23% when added to statin
  - Reduced CVD events by 13% in people with CVD or high risk and intolerant to statin
  - Mechanism: adenosine triphosphate-citrate lyase (ACL) inhibitor that lowers LDL by inhibition of cholesterol synthesis in the liver.
  - ACL is an enzyme upstream of 3-hydroxy-3-methyl-glutaryl-coenzyme A (HMG-CoA) reductase in the cholesterol biosynthesis pathway.
  - Dose: 180mg orally once daily

Additional Agents to Lower LDL

- Iclisiran (Leqvio), lowers LDL by ~50% when added to statin
  - Studied in ORION-10 and ORION-11 trials
  - CV events reduced, being studied in a longer CVD outcome trial
  - Mechanism: double-stranded small interfering ribonucleic acid (siRNA), conjugated on the sense strand with triantennary N-Acetylgalactosamine (GalNAc) to facilitate uptake by hepatocytes.
  - In hepatocytes, inclisiran utilizes the RNA interference mechanism and directs catalytic breakdown of mRNA for PCSK9.
  - This increases LDL-C receptor recycling and expression on the hepatocyte cell surface, which increases LDL-C uptake and lowers LDL-C levels in the circulation.
  - SC injection, day 1, 90 days, then every 6 months

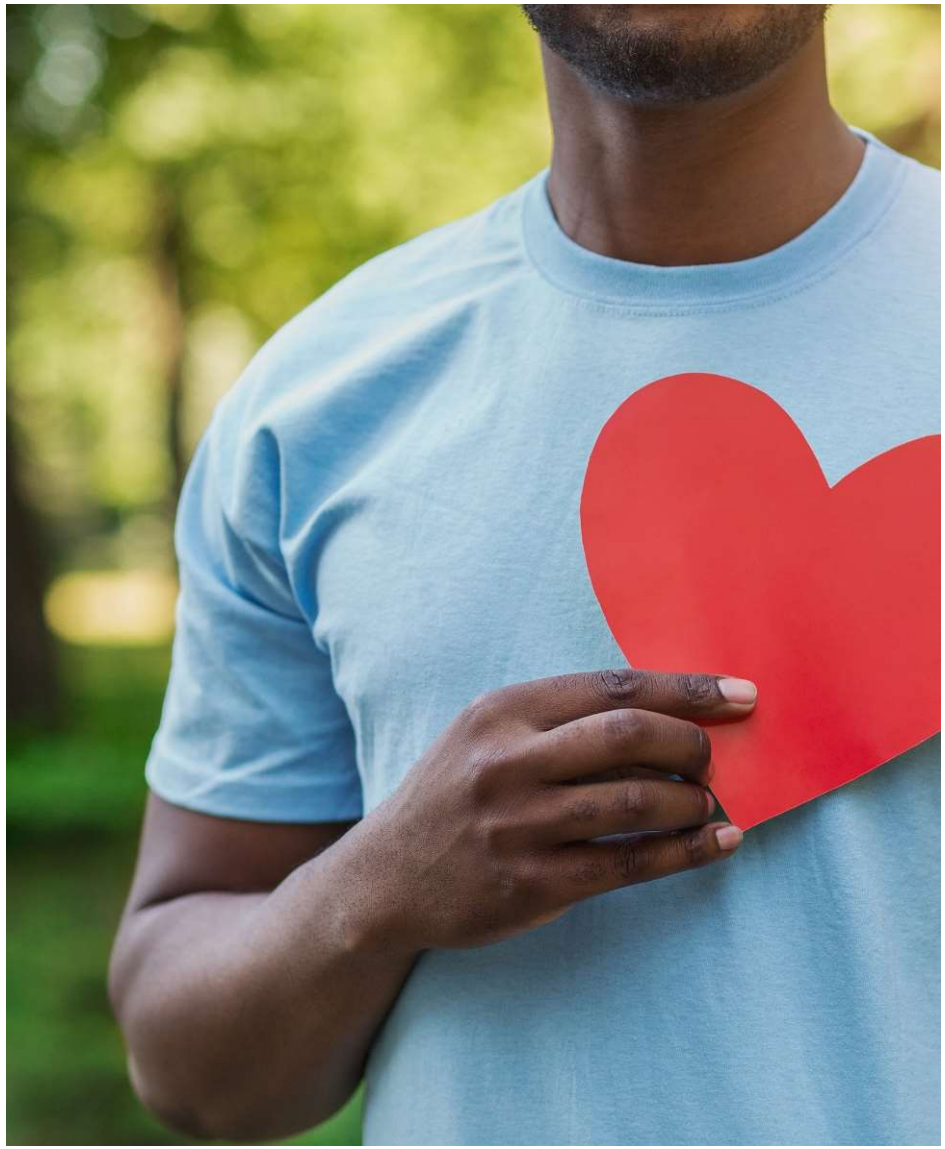
Treating High TG

- Consider fibrates or fish oil when TG>500mg/dL and definitely when TG>1000mg/dL
  - High TG puts people at increased pancreatitis risk
  - Rule out secondary causes

- In People with ASCVD on a statin with controlled LDL but elevated TG (135-499mg/dL), adding icosapent ethyl (Vascepa) can be considered to reduce CV risk (REDUCE-IT trial)
  - Individuals randomized to 2g BID who had either established CVD or diabetes + at least 1 risk factor, Vascepa demonstrated a 25% risk reduction in 3 point MACE

Diabetes Meds Lower CV Risk

- If diabetes plus ASCVD risk factors
  - SGLT-2s* and GLP-1s* reduce risk of major adverse CV events
  - Plus ACE or ARB
  - Post MI, continue beta blockers for 3 years.
- If type 2 diabetes and heart failure
  - SGLT-2s reduce risk of heart failure and hospitalization.
  - Also consider beta blocker



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Back to Alice

- Alice's lipid panel is as follows:
  - Total cholesterol: 204mg/dL
  - LDL: 120mg/dL
  - HDL: 34mg/dL
  - Triglycerides: 250mg/dL

- Which ASCVD risk factors does Alice have?

  Low HDL, smokes, obesity, HTN, albuminuria

- 10 year ASCVD risk=42%

Poll 8 - What is the best Lipid Recommendation for Alice?

A. Optimize lifestyle modifications only
B. Lifestyle + initiate a moderate intensity statin
C. Lifestyle + initiate a high intensity statin
D. Lifestyle + initiate high intensity statin + icosapent ethyl
E. Lifestyle + initiate high intensity statin + bempedoic acid

ADA 2024 Summary

A1c less than 7% (individualize)

- Pre-meal BG 80-130
- Post meal BG <180
- Time in Range (70-180) 70% of time

Blood Pressure <130/80

Cholesterol

- Statin therapy based on age & risk status
- If 40+ with ASCVD Risk, decrease LDL by 50%, LDL <70
- If 40+ with ASCVD, decrease LDL by 50%, LDL <55

10 - ADA Antiplatelet Agents

- Use aspirin therapy (75–162 mg/day) as a secondary prevention strategy in those with diabetes and a history of atherosclerotic cardiovascular disease.
  - Aspirin therapy dose (75–162 mg/day)
  - Increased bleeding risk
  - Dual antiplatelet therapy with a P2Y12 inhibitor for 1 year after acute coronary syndrome and may have benefits beyond
- Aspirin may be considered as a primary prevention strategy in diabetes (usually over age 50) with increased CV risk.
  - Requires **comprehensive discussion** w/ person on benefits versus increased risk of bleeding.
- Aspirin allergy, consider different agent

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Should Alice start aspirin?

A. Yes

B. No

Individualized discussed with shared decision making

Would you change Alice's Diabetes Regimen?

- Current meds
  - Metformin1000mg PO bid
  - Glipizide 10mg PO qam
  - Chlorthalidone 25mg PO daily
  - Escitalopram 10mg PO daily
- Home monitoring
  - FBG and pre-meal: 110-130mg/dL
  - Denies s/sx hypoglycemia.
- A1C=6.9%

Which of the Following Changes Would you Make to Alice's regimen? Poll 10

A. No changes since A1C is at target
B. Add empagliflozin (Jardiance)
C. Add dulaglutide (Trulicity)
D. Add linagliptin (Tradjenta)

If you add an agent, would you stop or decrease any of the others?

Lifestyle modifications

Category	Recommendations
Nutrition	• Maintain optimal weight • Calorie restriction • Plant based diet-high in polyunsaturated and monounsaturated fats • Avoid trans fats, limit saturated fats • Consider DASH/Mediterranean meal plans • Increase omega-3 fatty acids, viscous fiber, plant stanols/sterols (lipids)
Physical Activity	• 150 minutes/week moderate exertion • Strength training
Sleep	6-8 hours per night
Alcohol	• 2 drinks/day for men • 1 drink/day for women
Tobacco Cessation	Avoid tobacco products
Salt Intake	<2300mg/day

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Poll 11- What Lifestyle Modifications are Recommended for Alice?

A. Tobacco cessation
B. Weight loss
C. Increase physical activity
D. Reduce alcohol intake
E. Reduce salt intake

- Social history
  - (+)Alcohol: 1-2 drinks/week
  - (+) Tobacco use: 1/2ppd
  - Exercise: walks 15 min twice/week
  - Occ: receptionist
- BMI:32.8kg/m^2

Select all that apply

Thank You – Questions?

- Thanks for joining us!
- Questions?
- Info@diabetesed.net
- Call us at 530-893-8635
- www.DiabetesEd.net