



# Clinical Updates: Pre-Diabetes and Diabetes Management 2024

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# Objectives

1. Identify criteria defining prediabetes in nonpregnant individuals.
2. Identify first line agents for type 2 diabetes management based on comorbidities of CAD/ASCVD, heart failure, and chronic kidney disease versus glucose lowering and weight loss.

# Criteria defining Prediabetes in non pregnant individuals

- ▶ A1 C 5.7 to 6.4% or
- ▶ Fasting glucose 100 to 125 mg/dl (IFG ) or
- ▶ 2-h glucose during 75g OGTT 140mg/dl to 199 mg/dl (IGT)
- ▶ People should consume a mixed diet with at least 150 grams of carbohydrate on the three days prior to the glucose tolerance test. Fasting or restriction in carbohydrate can falsely elevate glucose levels on oral glucose tolerance challenge.

# Screening criteria for diabetes or prediabetes in asymptomatic adults

- ▶ Testing should be considered in adults who are overweight or obese who have one or more of the following risk factors.
  - First degree relative with diabetes
  - High risk race or ethnicity (ie., African American, Latino, Native American, Asian American, Pacific Islander)
  - History of cardiovascular disease
  - Hypertension ( $\geq 130/80$  or on therapy for hypertension)
  - Dyslipidemia with HDL cholesterol level  $< 35\text{mg/dl}$  and/or triglyceride level  $> 250\text{ mg/dl}$
  - Individuals with polycystic ovarian syndrome
  - Physical inactivity
  - Other clinical conditions associated with insulin resistance like severe obesity, acanthosis nigricans, skin tags

# Screening criteria for diabetes or prediabetes in asymptomatic adults

- ▶ People with prediabetes or impaired glucose tolerance or impaired fasting glucose should be tested yearly.
- ▶ People who were diagnosed with GDM should have lifelong testing at least every three years.
- ▶ For all other people testing should begin at age 35
- ▶ If results are normal testing, should be repeated in a minimum of 3-year intervals, with consideration for more frequent testing depending on initial results and risk status.
- ▶ People with HIV, exposure to high-risk medication, history of pancreatitis. Examples of high-risk medication would include glucocorticoids, statins, PCSK 9 inhibitors, thiazide diuretics, HIV medications, second generation antipsychotic medications

# PreDiabetes: Which test do you use?

- ▶ Pre-diabetes with elevated A1C, elevated fasting blood glucose and abnormal OGTT are predictors of cardiovascular risk.
- ▶ A fasting sugar and A1C it's probably the easiest way to test for prediabetes but may miss impaired glucose tolerance as often post meal excursions are the earliest abnormalities of glucose homeostasis. You need to look at the patient's other risk factors and classifications.

# Prevention or Delay of diabetes and associated comorbidities

- ▶ In people with Prediabetes, monitor for development of type 2 diabetes at least annually.
- ▶ Refer to an intensive lifestyle behavior change program, such as the Diabetes Prevention Program to achieve and maintain a weight reduction of at least 7% of the initial body weight through a healthy reduced calorie diet and  $\geq 150$  minutes week of moderate intensity physical activity. Program is sponsored by the CDC and is available in multiple locations in central Minnesota including the Whitney center as well as the Diabetes Center.
- ▶ The DPP with weight loss and exercise, showed greater reduction in the incidence of diabetes compared to metformin when used in people with pre-diabetes. The reduction was 58% versus 31%
- ▶ In patients with a history of GDM, metformin and intensive lifestyle modification have led to 50% percent reduction in diabetes risk

# Medication

- No medications has FDA approval to treat Pre-DM



# Medication

- Metformin--Metformin for the prevention of type 2 diabetes should be considered in adults with high risk for type 2 diabetes especially age 25 to 59 with a BMI  $\geq 35$ , fasting glucose  $\geq 110$  and a higher A1C,  $\geq 6\%$  and individuals with prior gestational diabetes. Metformin may result in B12 deficiency with prolonged use. Consider periodic assessment of vitamin B12 level in metformin treated patients especially those with anemia or peripheral neuropathy
- Alpha Glucosidase inhibitors Pre-cose (Acarbose)
- Orlistat
- Nateglinide or Starlix
- GLP-1 Agonist-unlikely to be covered by insurance unless using one of the GLP-1's for obesity
- TZDs
- Dapagliflozin
- Weight loss surgery

# Pre-diabetes

- ▶ One author concluded that pre-diabetes is a major but silent incubator for future morbidity.

# Type 2 Diabetes Management

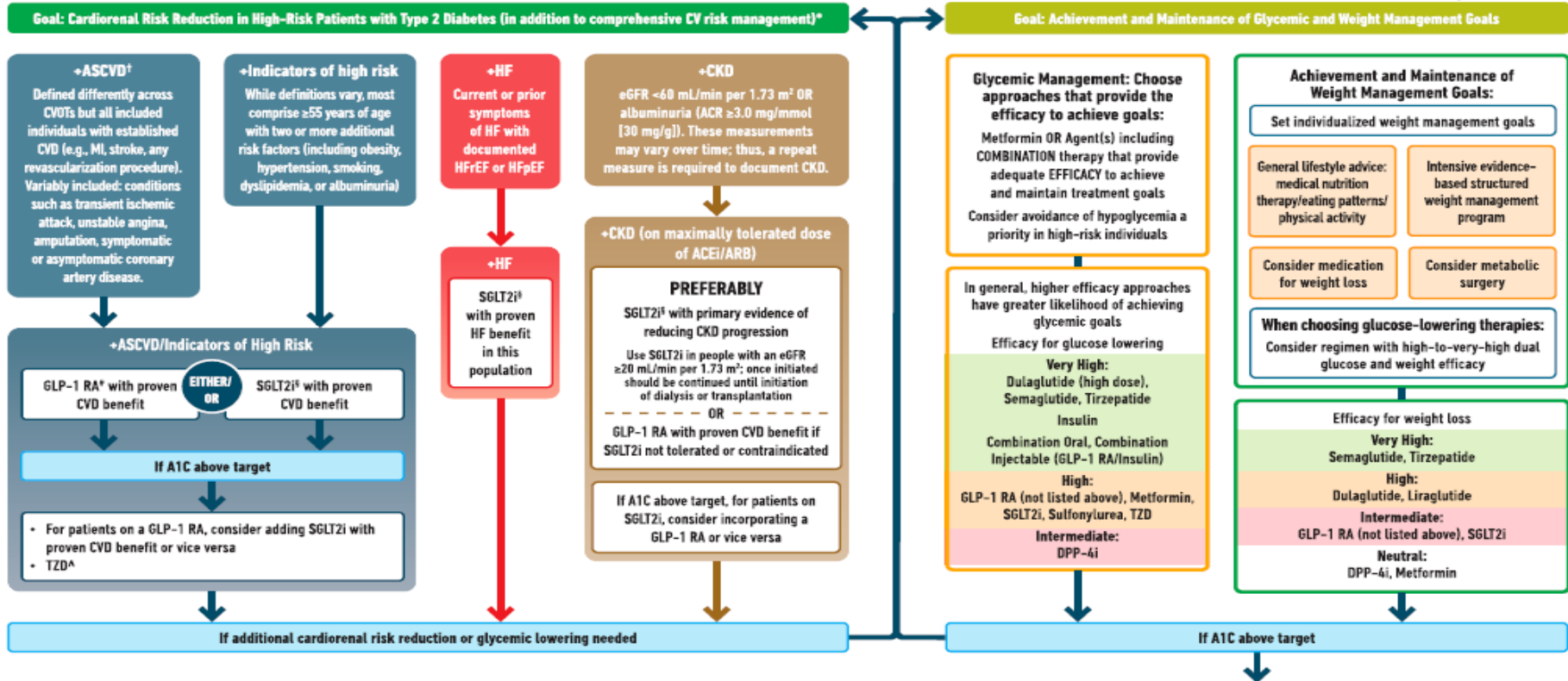
# First line therapy

1. Healthy Lifestyle Behaviors, Monitor BG (Blood Glucose)
2. DSMES-DM self management education and support , Refer to Diabetes Education/ Nurse and Registered Dietitian, Walk 30 minutes, 5 days per week plus resistance training
3. Social Determinants of Health-Psychological support/motivation, Assess for anxiety &/or depression, DM distress, Food insecurity
4. Avoid Therapeutic Inertia—reassess and modify treatment every 3-6 months
5. Other things to consider: Patient-Centered treatment factors, Cost, Access considerations
6. The first line drugs depends on the GOAL OF THERAPY!!! Metformin is no longer listed as first line but is still effective in glucose lowering.

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



HEALTHY LIFESTYLE BEHAVIORS; DIABETES SELF-MANAGEMENT EDUCATION AND SUPPORT (DSMES); SOCIAL DETERMINANTS OF HEALTH (SDOH)



\* In people with HF, CKD, established CVD or multiple risk factors for CVD, the decision to use a GLP-1 RA or SGLT2i with proven benefit should be independent of background use of metformin; † A strong recommendation is warranted for people with CVD and a weaker recommendation for those with indicators of high CV risk. Moreover, a higher absolute risk reduction and thus lower numbers needed to treat are seen at higher levels of baseline risk and should be factored into the shared decision-making process. See text for details; <sup>Δ</sup> Low-dose TZD may be better tolerated and similarly effective; <sup>‡</sup> For SGLT2i, CV renal outcomes trials demonstrate their efficacy in reducing the risk of composite MACE, CV death, all-cause mortality, MI, HFrEF, and renal outcomes in individuals with T2D with established/high risk of CVD; <sup>††</sup> For GLP-1 RA, CVDs demonstrate their efficacy in reducing composite MACE, CV death, all-cause mortality, MI, stroke, and renal endpoints in individuals with T2D with established/high risk of CVD.

**Identify barriers to goals:**

- Consider DSMES referral to support self-efficacy in achievement of goals
- Consider technology (e.g., diagnostic CGM) to identify therapeutic gaps and tailor therapy
- Identify and address SDOH that impact achievement of goals

# Decision tree

Goal: Cardiorenal Risk reduction in High-risk Patients with T2DM (in addition to comprehensive CV risk management)



Goal: Achievement and Maintenance of Glycemic and Weight Management Goals

**Goal: Cardiorenal risk reduction in high-risk patients with type 2 diabetes ( in addition to comprehensive cardiorenal risk management)**

**Goal: Achievement and management of glycemic & weight management goals**

**+ASCVD**

**+  
Indicators  
of high  
risk**

**+ CHF**

**+CKD**

**Glycemic  
management:  
Focus on  
efficacy**

**Achievement  
and  
maintenance  
of weight  
management**

# If the patient has ASCVD, CHF, Renal Disease

- ▶ The options would be:
  - SGLT 2 inhibitor with proven cardiovascular benefit, heart failure benefit or renal benefit or
  - GLP 1 RA with proven cardiovascular benefit or
  - or both drugs if the A1C is elevated
  - The SGLT 2 inhibitors impact blood sugar, heart failure, kidney disease and proteinuria



# SGLT 2 use with a lower eGFR

- ▶ If the eGFR is decreased to under 45 , the glucose lowering effect of the drug is much less. It may not improve the glucose level but has positive impact on kidneys and heart
- ▶ A lower eGFR is not a reason not to use the drug. You will likely need an additional agent to bring the sugars down.
- ▶ A drop in the eGFR is also not a reason to stop the medication. We expect the creatinine to rise slightly and the eGFR to drop slightly but then it usually stabilizes.
- ▶ If the patient is acutely ill the medication should be held

# American College of Cardiology (ACC)

- ▶ Treatment approaches to improve CV outcomes in patients with T2D are a major priority
- ▶ Major medical societies such as the ACC recommend the use of T2D therapy with proven CVD benefit in patients with T2D and established CVD, or high risk for CVD. The decision to prescribe should not be contingent on a patient's A1C level.

Source: American College of Cardiology (ACC)

SGLT2-1	Brand Name	Clinical Benefit			
		ASCVD	CKD	HF	Wt Loss
Empagliflozin	Jardiance	+++	+++	+++	-
Canagliflozin	Invokana	+++	+++	+	-
Dapagliflozin	Farxiga	+++	+++	+++	-
GLP1-RA					
Semaglutide	Ozempic	+++	+	+	+
Semaglutide	Rybelsus	+	+	+	+
Semaglutide	Wegovy	+++	+	+	+++
Liraglutide	Victoza	+++	+	+	+
Liraglutide	Saxenda	+	+	+	+++
Dulaglutide	Trulicity	+++	+	+	+
Tirzepatide	Mounjaro	+	+	+	+
Tirzepatide	Zepbound	+	+	+	+++
+++	FDA-approved labeled indication				
++	Robust clinical data; considered off-label use				
+	Some evidence available				

# Decision tree

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# Goal: Achievement and Maintenance of Glycemic and Weight Management Goals

- ▶ Use the most efficient drugs with very high glucose lowering capability like Dulaglutide (high dose), Semaglutide, Tirzepatide, insulin, combination orals, combination injectables(GLP-1/insulin).
- ▶ Highly efficient drugs to lower sugars are the other GLP 1 agonists, metformin, SGLT 2 inhibitor, sulfonylurea, TZD
- ▶ Intermediate effective drugs include DPP 4 inhibitors

# Goal: Achievement and Maintenance of Glycemic and **Weight** Management Goals

- ▶ Very high efficacy: Semaglutide(9-14 pounds) and Tirzepatide(12-25 pounds)
- ▶ High efficacy: Dulaglutide and Liraglutide
- ▶ Intermediate: GLP-1 agonist not listed previously and SGLT 2 inhibitors
- ▶ Neutral: DPP 4 inhibitor and metformin

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