Diabetes Mellitus

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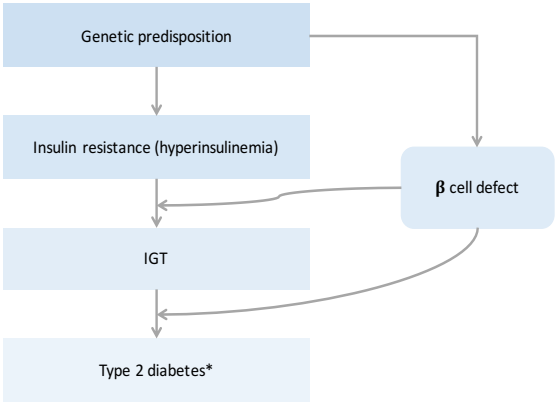
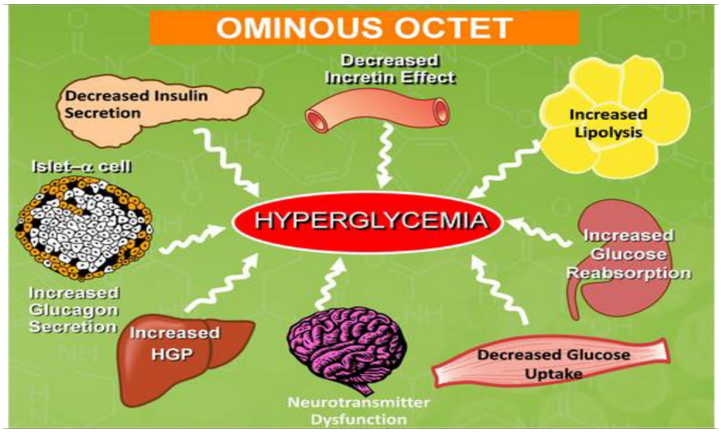
Pathophysiology



* Usually 50% of β cells are functioning at time of diagnosis, with time those β cells will continue to be destroyed and maybe will be completely distorted so the patient will need insulin



DM is not only problem in β cells, and insulin resistance there are so many problems on so many organs. Because of that there are so many drugs classifications which work on specific organ

Prevalence of DM in Saudi Arabia

- A community-based study of 17232 subjects conducted between 1995 and 2000 in KSA.
- The examining age group, 30-70 years of selected households during 5-year period
- The overall prevalence of DM obtained from this study is 23.7% in KSA.
- The prevalence in males and females were 26.2% and 21.5% respectively (p<0.00001).
- A large number of diabetics 1116 (27.9%) were unaware of having DM.

[1] هذي المحاضرة فيها حكي واااجد خصوصًا في recommendations، ركزوا بس على الأحمر والباقي مب مهم ومعظمه أصلًا الدكتور سحب عليه وما قراه. أهم شي ركزوا على الأدوية هي المهمة مع الأحمر

Classification diagnosis of diabetes

- Type I diabetes (due to autoimmune **β**-cell destruction, usually leading to absolute insulin deficiency)
- Type 2 diabetes (due to a progressive loss of **β**-cell insulin secretion frequently on the background of insulin resistance)
- Gestational diabetes mellitus (GDM) (diabetes diagnosed in the second or third trimester of pregnancy that was not clearly overt diabetes prior to gestation)
- Specific types of diabetes due to other causes, e.g., monogenic diabetes syndromes (such as neonatal diabetes and maturity-onset diabetes of the young), diseases of the exocrine pancreas (such as cystic fibrosis and pancreatitis), and drug-or chemical-induced diabetes (such as with glucocorticoid use, in the treatment of HIV/AIDS, or after organ transplantation)

Diagnostic Tests for Diabetes (very important)

- FPG ≥ 126 mg/dL (7.0 mmol/L). Fasting is defined as caloric intake for at least 8 h.*

Or

- 2-h PG ≥ 200 mg/dL (11.1 mmol/L) during OGTT. The test should be performed as described by the WHO, using glucose load containing the equivalent of 75-g anhydrous glucose dissolved in water.*

Or

- A1C ≥ 6.5% (48 mmol/mol). The test should be performed in a laboratory using a method that is NGSP certified and standardized to the DCCT assay*

Or

- In a patient with classic symptoms of hyperglycemia or hyperglycemic crisis, a random plasma glucose ≥ 200 mg/dL (11.1 mmol/L)

*in the absence of unequivocal hyperglycemia, diagnosis requires two abnormal test results from the same sample or in 2 separate test sample, **so if the patient came asymptomatic with abnormal reading repeat the test before labeling the patient as diabetic**

Pre-diabetic

- FPG ≥ 100 mg/dL (5.6 mmol/L) to 125 g/dL (6.9 mmol/L) (Impaired Fasting Glucose 'IFG')

Or

- 2-h PG in the 75-g OGTT 140 mg/dL (7.8 mmol/L) to 199 mg/dL (11.0 mmol/L) (Impaired Glucose Test 'IGT')

Or

- A1C 5.7-6.4% (39-46 mmol/mol)

*for all three tests, risk is continuous, extending below the lower limit of the range and becoming disproportionately greater at the higher end of the range

**There is no preferable test, you can choose any test but we usually do all the tests

Diagnostic Tests for Diabetes (very important)

Screening for diabetes

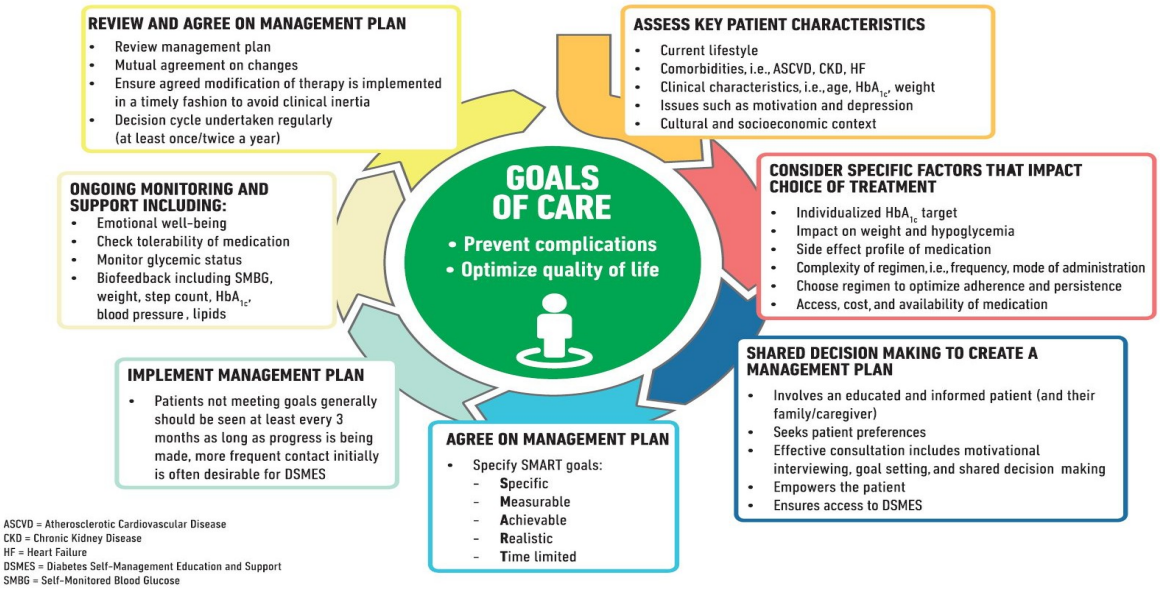
1. Testing should be consider in overweight or obese (BMI ≥ 25 kg/m^2 in Asian Americans) adults who have one or more of the following risk factors:
    - First-degree relative with diabetes
    - High-risk race/ethnicity (e.g., African American, Native American, Pacific Islander)
    - History of CVD
    - Hypertension (≥ 140/90 mmHg or in therapy for hypertension)
    - HDL cholesterol level < 35 mg/dL (0.90 mmol/L) and/or a triglyceride level > 250 mg/dL (2.82 mmol/L)
    - Women with PCOS
    - Physical inactivity
    - Other clinical conditions associated with insulin resistance (e.g., sever obesity, acanthosis nigricans)
2. Patients with prediabetes (A1C ≥ 5.7 [39mmol/mol], IGT or IFG) should be tested yearly.
3. Women who were diagnosed with GDM should have lifelong testing at least every 3 years.
4. For all other patients, testing should begin at the age 45 years.
5. If results are normal, testing should be repeated at a minimum of 3-year intervals, with consideration of more frequent testing depending on initial results and risk status

Prevention or delay of type 2 diabetes

Recommendation

A	• Refer patients with prediabetes to an intensive behavioral lifestyle intervention program modeled on the Diabetes Prevention Program to achieve and maintain 7% loss of initial body weight and increase moderate-intensity physical activity (such as brisk walking) to at least I50 min/week. • Metformin therapy for prevention of type 2 diabetes should be considered in those with prediabetes, especially for those with BMI 35 kg/m2, those aged <60 years, and women with prior GDM.
B	• Prediabetes is associated with heightened cardiovascular risk; therefore, screening for and treatment of modifiable risk factors for cardiovascular disease is suggested.
E	• At least annual monitoring for the development of type 2 diabetes in those with prediabetes is suggested.

Comprehensive medical evaluation and assessment of comorbidities



Recommendation

B	• A complete medical evaluation should be performed at the initial visit to: Confirm the diagnosis and classify diabetes. • Evaluate for diabetes complications and potential comorbid conditions. • Review previous treatment and risk factor control in patients with established diabetes. • Begin patient engagement in the formulation of a care management plan. • Develop a plan for continuing care.

Components of the comprehensive diabetes medical evaluation at initial and follow up visits (this helps you in OSCE)

		Initial visit	Every follow up visit	Annual visit
Past medical and family history	**Diabetic history**			
	• Characteristics at onset (e.g. age, symptoms)	✓		
	• Review of previous treatment regimens and response	✓		
	• Assess frequency/causes/severity of past hospitalizations	✓		
	Family history			
	• Family history of diabetes in a first degree relative	✓		
	• Family history of autoimmune disorder	✓		

		Initial visit	Every follow up visit	Annual visit
Past medical and family history	**Personal history of complications and common comorbidities**			
	• Macrovascular and microvascular	✓		
	• Common comorbidities	✓		
	• Presence of Hemoglobinopathies or anemias	✓		
	• High blood pressure or abnormal lipids	✓		
	• Last dental visit	✓		✓
	• Last dilated eye exam	✓		✓
	• Visits to specialists	✓	✓	✓
	Interval history			
	• Change in medical/family history since last visit		✓	✓
Social history	**Assess lifestyle and behavior patterns**			
	• Eating patterns and weight history	✓	✓	✓
	• Sleep behaviors and physical activity	✓	✓	✓
	• Familiarity with carbohydrate counting in type 1 diabetes	✓		
	• Tobacco, alcohol , and substance use	✓		
	• Identify existing social support	✓		
	Interval history			
	• Change in social history since last visit		✓	✓
Medication and vaccination	• Medication-taking behavior	✓	✓	✓
	• Medication tolerance or side effects	✓	✓	✓
	• Complementary and alternative medicine use	✓	✓	✓
	• Vaccination history and needs	✓		✓
Technology use	• Assess use of health apps, online education, patient portals, etc.	✓		✓
	• Glucose monitoring (meter/CGM): results and data use	✓	✓	✓
	• Review insulin pump settings	✓	✓	✓

		Initial visit	Every follow up visit	Annual visit
Screening	**Psychosocial conditions**			
	• Screen for depression, anxiety, and disordered eating; refer for further assessment or intervention if warranted	✓		✓
	• Consider assessment for cognitive impairment	✓		✓
	Diabetic self-management education and support			
	• History of dietitian/diabetic educator visits	✓	✓	✓
	• Screen for barriers to diabetes self-management	✓		✓
	• Refer or offer local resources and support as needed	✓	✓	✓
	Hypoglycemia			
	• Timing of episodes, awareness, frequency and causes	✓	✓	✓
	Pregnancy planning			
	• For women with childbearing capacity, review contraceptive needs and preconception planning	✓	✓	✓
Physical examination	• Height, weight, and BMI; growth/pubertal development in children and adolescents	✓	✓	✓
	• Blood pressure determination	✓	✓	✓
	• Orthostatic blood pressure measures (when indicated)	✓		
	• Funduscopic examination (refer to eye specialist)	✓		✓
	• Thyroid palpation	✓		✓
	• Skin examination (e.g., acanthosis nigricans, insulin injection or insertion sites, lipodystrophy)	✓		✓
	Comprehensive foot examination			
	• Visual inspection (e.g., skin integrity, callous formation, foot deformity or ulcer, toenails)	✓	✓	✓
	• Screen for PAD (pedal pulses; refer for ABI if diminished)	✓		✓
	• Determination of temperature, vibration, or pinprick sensation, and 10-g monofilament exam	✓		✓

		Initial visit	Every follow up visit	Annual visit
Laboratory evaluation	• A1C if the result are not available within the past 3 months	✓	✓	✓
	If not performed/available within the past year			
	• Lipid profile, including total, LDL, and HDL cholesterol and triglycerides	✓		✓
	• Liver function test	✓		✓
	• Spot urinary albumin-to-creatinine ratio	✓		✓
	• Serum creatinine and estimated GFR	✓		✓
	• TSH in patients with with DM1	✓		✓
	• Vitamin B12 if on metformin (if indicated)	✓		✓
	• Serum K^+ levels in patients on ACE inhibitors, ARBs, or diuretics	✓		✓
Assessment and plan	**Goal setting**			
	• Set A1C/blood glucose target and monitoring frequency	✓	✓	✓
	• If HTN diagnosed, establish blood pressure goal	✓		✓
	• Incorporate new members to the care team as needed	✓	✓	✓
	• Diabetes education and self-management support needs	✓	✓	✓
	Cardiovascular risk assessment and staging of CKD			
	• History of ASCVD	✓	✓	✓
	• Presence of ASCVD risk factor	✓	✓	✓
	• Staging of CKD	✓	✓	✓
	Therapeutic treatment plan			
	• Lifestyle management	✓	✓	✓
	• Pharmacologic therapy	✓	✓	✓
	• Referrals to specialists (including dietitian and diabetic educator) as needed	✓	✓	✓
	• Use of glucose monitoring and insulin devices	✓	✓	✓

Assessment and treatment plan

- Assess risk of diabetes complications
  - ASCVD and heart failure history
  - ASCVD risk factors and 10-year ASCVD risk assessment
  - Staging of chronic kidney disease
  - Hypoglycemia risk
- Goal setting
  - Set A1C/blood glucose target
  - If HTN present, establish blood pressure target
  - Diabetes self-management goals (e.g., monitoring frequency)
- Therapeutic treatment plan
  - Lifestyle management
  - Pharmacologic therapy (glucose lowering)
  - Pharmacologic therapy (cardiovascular disease risk factors and renal)
  - Use of glucose monitoring and insulin delivery devices
  - Referral to diabetes education and medical specialist

Assessment of hypoglycemia risk

Factors that increase risk of treatment-associated hypoglycemia

- Use of insulin or insulin secretagogues (i.e., sulfonylureas, meglitinides)
- Impaired kidney or hepatic function
- Longer duration of diabetes
- Frailty and older age
- Cognitive impairment
- Impaired counterregulatory response, hypoglycemia unawareness
- Physical or intellectual disability that may impair behavior response to hypoglycemia
- Alcohol use
- Polypharmacy (especially ACE inhibitors, angiotensin receptor blockers, nonselective **β**-blockers)

Referral for initial care management

- Eye care professional for annual dilated eye exam
- Family planning for women of reproductive age
- Registered dietitian for medical nutrition therapy
- Diabetes self-management education and support
- Dentist for comprehensive dental and periodontal examination
- Mental health professional, if indicated

Glycemic targets

A1C Testing recommendation

E	• Perform the A1C test at least two times a year in patients who are meeting treatment goals (and who have stable glycemic control). • Perform the A1C test quarterly in patients whose therapy has changed or who are not meeting glycemic goals. • Point-of-care testing for A1C provides the opportunity for more timely treatment changes.

A1C goals recommendation

A	• A reasonable A1C goal for many nonpregnant adults is <7% (53 mmol/mol).
B	• Less stringent A1C goals (such as <8% [64 mmol/mol]) may be appropriate for patients with a history of level 3 hypoglycemia (altered mental and/or physical state requiring assistance), limited life expectancy, advanced microvascular or macrovascular complications, extensive comorbid conditions, or long-standing diabetes in whom the goal is difficult to achieve despite diabetes self-management education, appropriate glucose monitoring, and effective doses of multiple glucose-lowering agents including insulin.
C	• Providers might reasonably suggest more stringent AIC goals (such as <6.5% [48 mmol/mol]) for selected individual patients if this can be achieved without significant hypoglycemia or other adverse effects of treatment (i.e., polypharmacy). Appropriate patients might include those with short duration of diabetes, type 2 diabetes treated with lifestyle or metformin only, long life expectancy, or no significant cardiovascular disease.
E	• Reassess glycemic targets over time based on the criteria.

TABLE 4. Summary of Glycemic Recommendations for Many Nonpregnant Adults With Diabetes

A1C	<7.0% (53 mmol/mol)*
Preprandial capillary plasma glucose	80–130 mg/dL* (4.4–7.2 mmol/L)
Peak postprandial capillary plasma glucose†	<180 mg/dL* (10.0 mmol/L)

**More or less stringent glycemic goals may be appropriate for individual patients. Goals should be individualized based on duration of diabetes, age/life expectancy, comorbid conditions, known CVD or advanced microvascular complications, hypoglycemia unawareness, and individual patient considerations. †Postprandial glucose may be targeted if A1C goals are not met despite reaching preprandial glucose goals. Postprandial glucose measurements should be made 1–2 h after the beginning of the meal, generally peak levels in patients with diabetes.*

Hypoglycemia

- Level 1 hypoglycemia is defined as a measurable glucose concentration <70 mg/dL (3.9 mmol/L).
- Level 2 hypoglycemia (defined as a blood glucose concentration <54 mg/dL [3.0 mmol/L]) is the threshold at which neuroglycopenic symptoms begin to occur and requires immediate action to resolve the hypoglycemic event.
- Level 3 hypoglycemia is defined as a severe event characterized by altered mental and/or physical functioning that requires assistance from another person for recovery.

Recommendation

A	• Insulin-treated patients with hypoglycemia unawareness or an episode of level 2 hypoglycemia should be advised to raise their glycemic targets to strictly avoid hypoglycemia for at least several weeks in order to partially reverse hypoglycemia unawareness and reduce risk of future episodes.
B	• Ongoing assessment of cognitive function is suggested with increased vigilance for hypoglycemia by the clinician, patient, and caregivers if low cognition or declining cognition is found.
C	• Individuals at risk for hypoglycemia should be asked about symptomatic and asymptomatic hypoglycemia at each encounter.
E	• Glucose (15–20 g) is the preferred treatment for the conscious individual with blood glucose <70 mg/dL (3.9 mmol/L), although any form of carbohydrate that contains glucose may be used. Fifteen minutes after treatment, if SMBG shows continued hypoglycemia, the treatment should be repeated. Once SMBG returns to normal, the individual should consume a meal or snack to prevent recurrence of hypoglycemia. • Glucagon should be prescribed for all individuals at increased risk of level 2 hypoglycemia, defined as blood glucose <54 mg/dL (3.0 mmol/L), so it is available should it be needed. Caregivers, school personnel, or family members of these individuals should know where it is and when and how to administer it. Glucagon administration is not limited to health care professionals. • Hypoglycemia unawareness or one or more episodes of level 3 hypoglycemia should trigger reevaluation of the treatment regimen.

Hypertension/Blood Pressure Control: Recommendations for Screening and Diagnosis

B	• Blood pressure should be measured at every routine clinical visit. Patients found to have elevated blood pressure (140/90 mmHg) should have blood pressure confirmed using multiple readings, including measurements on a separate day, to diagnose hypertension. • All hypertensive patients with diabetes should monitor their blood pressure at home.

Cardiovascular Disease: Recommendations for Screening

A	• In asymptomatic patients, routine screening for coronary artery disease is not recommended as it does not improve outcomes as long as ASCVD risk factors are treated.
E	• Consider investigations for coronary artery disease in the presence of any of the following: atypical cardiac symptoms (e.g., unexplained dyspnea, chest discomfort); signs or symptoms of associated vascular disease including carotid bruits, transient ischemic attack, stroke, claudication, or peripheral arterial disease; or electrocardiogram abnormalities (e.g., Q waves).

Antiplatelet Agents: Recommendations

A	• Use aspirin therapy (75–162 mg/day) as secondary prevention in those with diabetes and history of ASCVD.
B	• For patients with ASCVD & aspirin allergy, clopidogrel (75 mg/day) should be used. • Dual antiplatelet therapy is reasonable for up to a year after an acute coronary syndrome.

C	• Consider aspirin therapy (75–162 mg/day) as a primary prevention strategy in those with type 1 or type 2 diabetes at increased cardiovascular risk
	  ○ includes most men or women with diabetes age 50 years who have at least one additional major risk factor, including:
	  1. Family history of premature ASCVD
	  2. Hypertension
	  3. smoking
	  4. Dyslipidemia
	  5. Albuminuria
	• Aspirin is not recommended for ASCVD prevention for adults with DM at low ASCVD risk, since potential adverse effect from bleeding likely onset potential benefits.
	  ○ Low risks such as in men or women with diabetes aged <50 years with no major additional ASCVD risk factors)

E	• In patients with diabetes <50 years of age with multiple other risk factors (e.g., 10-year risk 5–10%), clinical judgment is required.

Lipid management in diabetic patients

Table 10.2—Recommendations for statin and combination treatment in adults with diabetes

Age	ASCVD or 10-year ASCVD risk >20%	Recommended statin intensity^ and combination treatment*
<40 years	No	None†
	Yes	High • In patients with ASCVD, if LDL cholesterol ≥70 mg/dL despite maximally tolerated statin dose, consider adding additional LDL-lowering therapy (such as ezetimibe or PCSK9 inhibitor)#
≥40 years	No	Moderate‡
	Yes	High • In patients with ASCVD, if LDL cholesterol ≥70 mg/dL despite maximally tolerated statin dose, consider adding additional LDL-lowering therapy (such as ezetimibe or PCSK9 inhibitor)

ASCVD, atherosclerotic cardiovascular disease; PCSK9, proprotein convertase subtilisin/kexin type 9. *In addition to lifestyle therapy. ^For patients who do not tolerate the intended intensity of statin, the maximally tolerated statin dose should be used. †Moderate-intensity statin may be considered based on risk-benefit profile and presence of ASCVD risk factors. ASCVD risk factors include LDL cholesterol ≥100 mg/dL (2.6 mmol/L), high blood pressure, smoking, chronic kidney disease, albuminuria, and family history of premature ASCVD. ‡High-intensity statin may be considered based on risk-benefit profile and presence of ASCVD risk factors. #Adults aged <40 years with prevalent ASCVD were not well represented in clinical trials of non-statin–based LDL reduction. Before initiating combination lipid-lowering therapy, consider the potential for further ASCVD risk reduction, drug-specific adverse effects, and patient preferences.

Table 10.3—High-intensity and moderate-intensity statin therapy*

High-intensity statin therapy (lowers LDL cholesterol by ≥50%)	Moderate-intensity statin therapy (lowers LDL cholesterol by 30–50%)
Atorvastatin 40–80 mg	Atorvastatin 10–20 mg
Rosuvastatin 20–40 mg	Rosuvastatin 5–10 mg
	Simvastatin 20–40 mg
	Pravastatin 40–80 mg
	Lovastatin 40 mg
	Fluvastatin XL 80 mg
	Pitavastatin 2–4 mg

*Once-daily dosing. XL, extended release.

Other combination therapy: recommendations

A	• Combination therapy (statin/fibrate) has not been shown to improve atherosclerotic cardiovascular disease outcomes and is generally not recommended • Combination therapy (statin/niacin) has not been shown to provide additional cardiovascular benefit above statin therapy alone, may increase the risk of stroke with additional side effects, and is generally not recommended

Chronic Kidney Disease: Recommendations for Screening

B	• At least once a year, assess urinary albumin (e.g., spot urinary albumin-to-creatinine ratio) and eGFR in patients with type I diabetes with duration of 50 years, in all patients with type 2 diabetes, and in all patients with comorbid hypertension.

Diabetic Retinopathy: Recommendations

A	• Optimize glycemic control to reduce the risk or slow the progression of diabetic retinopathy. • Optimize blood pressure and serum lipid control to reduce the risk or slow the progression of diabetic retinopathy.
B	• Adults with type 1 diabetes should have an initial dilated and comprehensive eye examination by an ophthalmologist or optometrist within 5 years after the onset of diabetes. • Patients with type 2 diabetes should have an initial dilated and comprehensive eye examination by an ophthalmologist or optometrist at the time of the diabetes diagnosis. • If there is no evidence of retinopathy for one or more annual eye exam and glycaemia is well controlled, then exams every 1–2 years may be considered. If any level of diabetic retinopathy is present, subsequent dilated retinal examinations should be repeated at least annually by an ophthalmologist or optometrist. If retinopathy is progressing or sight-threatening, then examinations will be required more frequently. • Telemedicine programs that use validated retinal photography with remote reading by an ophthalmologist or optometrist and timely referral for a comprehensive eye examination when indicated can be an appropriate screening strategy for diabetic retinopathy. • Women with preexisting type I or type 2 diabetes who are planning pregnancy or who are pregnant should be counseled on the risk of development and/or progression of diabetic retinopathy. • Eye examinations should occur before pregnancy or in the first trimester in patients with preexisting type1 or type 2 diabetes, and then patients should be monitored every trimester and for 1-year postpartum as indicated by the degree of retinopathy.

Neuropathy: Recommendations for Screening

B	• All patients should be assessed for diabetic peripheral neuropathy starting at diagnosis of type 2 diabetes and 5 years after the diagnosis of type 1 diabetes and at least annually thereafter. • Assessment for distal symmetric polyneuropathy should include a careful history and assessment of either temperature or pinprick sensation (small-fiber function) and vibration sensation using a I28-Hz tuning fork (for large-fiber function). All patients should have annual I0-g monofilament testing to identify feet at risk for ulceration and amputation.
E	• Symptoms and signs of autonomic neuropathy should be assessed in patients with microvascular complications.

Foot Care: Recommendations

B	• Perform a comprehensive foot evaluation at least annually to identify risk factors for ulcers and amputations. • Obtain a prior history of ulceration, amputation, Charcot foot, angioplasty or vascular surgery, cigarette smoking, retinopathy, and renal disease and assess current symptoms of neuropathy (pain, burning, numbness) and vascular disease (leg fatigue, claudication). • The examination should include inspection of the skin, assessment of foot deformities, neurological assessment (10-g monofilament testing with at least one other assessment: pinprick, temperature, vibration), and vascular assessment including pulses in the legs and feet. • A multidisciplinary approach is recommended for individuals with foot ulcers and high-risk feet (e.g., dialysis patients and those with Charcot foot or prior ulcers or amputation). • Provide general preventive foot self-care education to all patients with diabetes. • The use of specialized therapeutic footwear is recommended for high-risk patients with diabetes including those with severe neuropathy, foot deformities, or history of amputation.
C	• Patients with evidence of sensory loss or prior ulceration or amputation should have their feet inspected at every visit. • Patients with symptoms of claudication or decreased or absent pedal pulses should be referred for ankle-brachial index and for further vascular assessment as appropriate. • Refer patients who smoke or who have histories of prior lower-extremity complications, loss of protective sensation, structural abnormalities, or peripheral arterial disease to foot care specialists for ongoing preventive care and lifelong surveillance.

Non- Pharmacological: Diet and Exercise

Table 5.1—Medical nutrition therapy recommendations

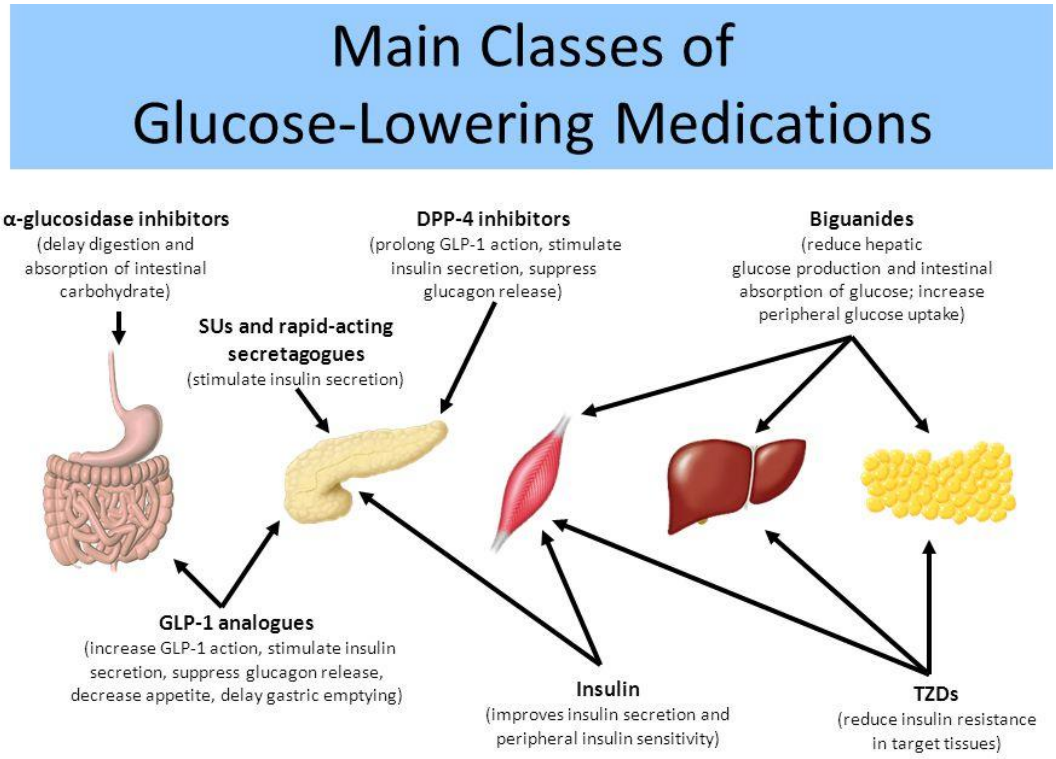
Topic	Recommendations	Evidence rating
Effectiveness of nutrition therapy	**5.6** An individualized medical nutrition therapy program as needed to achieve treatment goals, preferably provided by a registered dietitian, is recommended for all people with type 1 or type 2 diabetes, prediabetes, and gestational diabetes mellitus.	A
	5.7 A simple and effective approach to glycemia and weight management emphasizing portion control and healthy food choices may be considered for those with type 2 diabetes who are not taking insulin, who have limited health literacy or numeracy, or who are older and prone to hypoglycemia.	B
	5.8 Because diabetes nutrition therapy can result in cost savings **B** and improved outcomes (e.g., A1C reduction) **A**, medical nutrition therapy should be adequately reimbursed by insurance and other payers. **E**	B, A, E
Energy balance	**5.9** Weight loss (>5%) achievable by the combination of reduction of calorie intake and lifestyle modification benefits overweight or obese adults with type 2 diabetes and also those with prediabetes. Intervention programs to facilitate weight loss are recommended.	A
Eating patterns and macronutrient distribution	**5.10** There is no single ideal dietary distribution of calories among carbohydrates, fats, and proteins for people with diabetes; therefore, meal plans should be individualized while keeping total calorie and metabolic goals in mind.	E
	5.11 A variety of eating patterns are acceptable for the management of type 2 diabetes and prediabetes.	B
Carbohydrates	**5.12** Carbohydrate intake should emphasize nutrient-dense carbohydrate sources that are high in fiber, including vegetables, fruits, legumes, whole grains, as well as dairy products.	B
	5.13 For people with type 1 diabetes and those with type 2 diabetes who are prescribed a flexible insulin therapy program, education on how to use carbohydrate counting **A** and in some cases how to consider fat and protein content **B** to determine mealtime insulin dosing is recommended to improve glycemic control.	A, B
	5.14 For individuals whose daily insulin dosing is fixed, a consistent pattern of carbohydrate intake with respect to time and amount may be recommended to improve glycemic control and reduce the risk of hypoglycemia.	B
	5.15 People with diabetes and those at risk are advised to avoid sugar-sweetened beverages (including fruit juices) in order to control glycemia and weight and reduce their risk for cardiovascular disease and fatty liver **B** and should minimize the consumption of foods with added sugar that have the capacity to displace healthier, more nutrient-dense food choices. **A**	B, A
Protein	**5.16** In individuals with type 2 diabetes, ingested protein appears to increase insulin response without increasing plasma glucose concentrations. Therefore, carbohydrate sources high in protein should be avoided when trying to treat or prevent hypoglycemia.	B
Dietary fat	**5.17** Data on the ideal total dietary fat content for people with diabetes are inconclusive, so an eating plan emphasizing elements of a Mediterranean-style diet rich in monounsaturated and polyunsaturated fats may be considered to improve glucose metabolism and lower cardiovascular disease risk and can be an effective alternative to a diet low in total fat but relatively high in carbohydrates.	B
	5.18 Eating foods rich in long-chain n-3 fatty acids, such as fatty fish (EPA and DHA) and nuts and seeds (ALA), is recommended to prevent or treat cardiovascular disease **B**; however, evidence does not support a beneficial role for the routine use of n-3 dietary supplements. **A**	B, A
Micronutrients and herbal supplements	**5.19** There is no clear evidence that dietary supplementation with vitamins, minerals (such as chromium and vitamin D), herbs, or spices (such as cinnamon or aloe vera) can improve outcomes in people with diabetes who do not have underlying deficiencies and they are not generally recommended for glycemic control.	C
Alcohol	**5.20** Adults with diabetes who drink alcohol should do so in moderation (no more than one drink per day for adult women and no more than two drinks per day for adult men).	C
	5.21 Alcohol consumption may place people with diabetes at increased risk for hypoglycemia, especially if taking insulin or insulin secretagogues. Education and awareness regarding the recognition and management of delayed hypoglycemia are warranted.	B
Sodium	**5.22** As for the general population, people with diabetes should limit sodium consumption to <2,300 mg/day.	B
Nonnutritive sweeteners	**5.23** The use of nonnutritive sweeteners may have the potential to reduce overall calorie and carbohydrate intake if substituted for caloric (sugar) sweeteners and without compensation by intake of additional calories from other food sources. For those who consume sugar-sweetened beverages regularly, a low-calorie or nonnutritive-sweetened beverage may serve as a short-term replacement strategy, but overall, people are encouraged to decrease both sweetened and nonnutritive-sweetened beverages and use other alternatives, with an emphasis on water intake.	B

Diabetes management

Non- Pharmacological: Exercise recommendations

B	• Most adults with type 1 C and type 2 B diabetes should engage in 150 min or more of moderate−to−vigorous intensity aerobic activity per week, spread over at least 3 days/week, with no more than 2 consecutive days without activity. Shorter durations (minimum 75 min/week) of vigorous−intensity or interval training may be sufficient for younger and more physically fit individuals. • Adults with type 1 C and type 2 B diabetes should engage in 2−3 sessions /week of resistance exercise on nonconsecutive days. • All adults, and particularly those with type 2 diabetes, should decrease the amount of time spent in daily sedentary behavior.
C	• Children and adolescents with type 1 or type 2 diabetes or prediabetes should engage in 60 min/day or more of moderate− or vigorous−intensity aerobic activity, with vigorous muscle−strengthening and bone−strengthening activities at least 3 days/week. • Flexibility training and balance training are recommended 2−3 times/week for older adults with diabetes. Yoga and tai chi may be included based on individual preferences to increase flexibility, muscular strength, and balance.

Pharmacological:



TZD = thiazolidinedione; DPP = dipeptidyl peptidase; GLP = glucagon-like peptide
Krentz AJ, Bailey CJ. Drugs 2005;65:385-411

	M.O.A	HbA1C lowering %	Advantage	Disadvantage	Adverse effect
Insulin–sensitizing agents: reduce blood sugar by making the body's tissues more sensitive to insulin.					
Biguanides (Metformin)	the main mechanism is decrease hepatic gluconeogenesis	Decrease HgA1C by 1.0 to 2.0 %	• The first line for oral treatment of type 2 diabetes • High efficacy with no hypoglycemia. • Weight neutral • lipid–lowering activity • Decreased all–cause mortality and a decreased rate of (MI) in overweight and obese patients	• GI side effects • Potential for vitamin B–12 def • Lactic acidosis (rare) • Discontinue during acute illness and before radiographic procedures requiring contrast • Contraindicated in Renal insufficiency (discontinues if eGFR ≤ 30) if GFR 30 - 45 decrease the dose into half	
Insulin Secretagogues: stimulate release of insulin from pancreatic beta cells					
Sulfonylureas • Glipizide • Gliclazide • Glibenclamide • Glimepiride		Lower A1c by 1–2 %	Safe in CVD and renal impairment (except glyburide)		• Hypoglycemia (most common) • Nausea, skin reactions (including photosensitivity) • Weight gain
	Use				
Meglitinides (Glinides) • Repeglinide • Nateglinide	before each meal, if you skip the meal skip the medication		Repeglinide safe in pt. with decrease GFR or renal failure .		• Hypoglycemia & weight gain (less than sulfa) • Dosing frequency .

	M.O.A	HbA1C lowering %	Advantage	Disadvantage	Adverse effect
Insulin–sensitizing agents					
Thiazolidinediones (TZD) • Pioglitazone • Rosiglitazone	Increase insulin sensitivity by acting on adipose, muscle, and liver to increase glucose utilization and decrease glucose production.	When used as monotherapy, they reduce hemoglobin (A1C) values by 1.5 %.	• High efficacy with no hypoglycemia. • Show benefit in NASH • No dose adjustment	• Increase risk for bladder cancer (Pioglitazone) • Increased risk for cardiovascular event (Progressive ischemia ,MI, HF) in Rosiglitazone • Increased LDL (Rosiglitazone)	• Fluid retention/heart failure (Peripheral edema occurs in 4 to 6 %) • Decrease bone density and increase fracture risk, particularly in women • All thiazolidinediones cause weight gain • FDA Black Box: CHF >> pioglitazone & rosiglitazone. • Not recommended in renal impairment due to fluid retention
Incretin Based Therapy: after eating carbs, they will go to the intestine which will stimulate incretin (GLP-1) which will 1- delay gastric empty. 2- stimulate pancreas to stimulate insulin and suppress glucagon. 3- decrease the appetite. GLP-1 never stimulate unless there is carbs, so it is responsible for insulin secretion postprandial					
DPP-4 inhibitors • Sitagliptin • Saxagliptin • Vildagliptin • Linagliptin • Alogliptin	Incretin stays 30 min and then get degregated by DDP-4 enzyme. Those drugs will inhibit DDP-4 drugs to prolong incretin effect	Reduce HbA1c between 0.6– 1.1%	• Intermediate efficacy with no hypoglycemia (bc it will only cause hypoglycemia after consuming carbs, and the patient is not consuming carbs while having the medication) • No effects on body weight	Require dose adjustment except Linagliptin	• Potential CV risk in saxagliptin and alogliptin. • Headache, nasopharyngitis, and upper respiratory tract infection • Joint pain, myalgias, muscle weakness, and muscle spasms. • Urticarial & angioedema • Acute pancreatitis

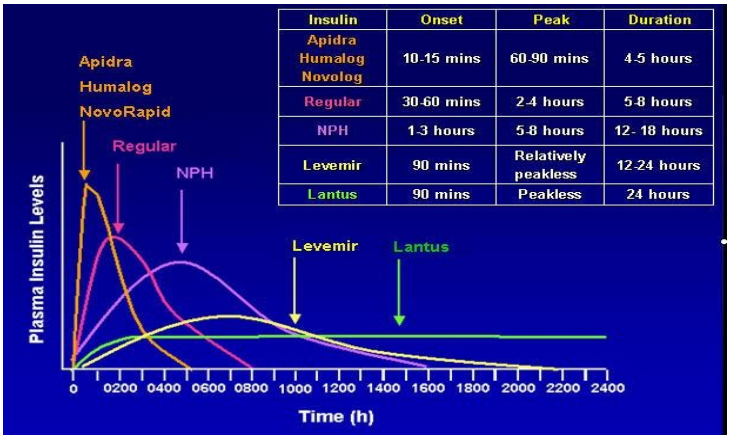
	M.O.A	HbA1C lowering %	Advantage	Disadvantage	Adverse effect
Incretin Based Therapy					
GLP-1 receptor agonists • Liraglutide • Semaglutide • Dulaglutide • Exenatide			• High efficacy with no hypoglycemia • **Weight reduction** • Decrease ASCVD in Liraglutide > Semaglutide > Exenatide ER • ↓ 2-3 mmHg of BP • ↑ 2-3 beats/min	Injectable	• GI side effect (nausea, vomiting, diarrhea) • Initiating/increasing dose >> Potential risk of AKI (Liraglutide is safe) • FDA Black Box >> – cell hyperplasia/medullary thyroid tumors (avoid it only for family or personal history of thyroid cancer) • Pancreatitis • injection site reaction.
Others					
Glucosidase Inhibitors • Acarbose • Miglitol • Voglibose	Slow absorption of glucose and reduce postprandial blood glucose concentration	lowering (A1C) by only 0.4 to 0.9%	if the A1c is not high and the post prandial is the main problem, those drugs are very effective		• Flatulence • Diarrhea
SGLT-2 Inhibitors • Canagliflozin • Dapagliflozin • Empagliflozin	Inhibit the reabsorption of glucose in the distal tubules of the kidney		• **Weight loss** • **Good CV effect and specifically heart failure patient** (Empagliflozin and Canagliflozin) • **Delay progression of CKD** (empagliflozin and canagliflozin) • Intermediate efficacy with no hypoglycemia • lipid–lowering activity	• FDA Black Box: risk of amputation (Canagliflozin) • It needs GFR > 45 to initiate the treatment	• Genitourinary infections • Risk of bone fracture (Canagliflozin) • DKA risk (all agents, rare in T2DM) • Increase LDL cholesterol • Risk of volume depletion and hypotension, so we advise the patient to drink lots of water • Acute kidney injury

Administration of SGLT-2 inhibitors		
Canagliflozin: before the 1st meal of the day	Dapagliflozin: in the morning with or without food	Empagliflozin: in the morning with or without food

Diabetes management

Insulin

- Powerful agent
- Necessary in 2o-3o%
- Inexpensive
- Weight gain
- Hypoglycemia
- High level of patient fear



Insulin	Onset	Peak	Duration
Apidra Humalog Novolog	10-15 mins	60-90 mins	4-5 hours
Regular	30-60 mins	2-4 hours	5-8 hours
NPH	1-3 hours	5-8 hours	12- 18 hours
Levemir	90 mins	Relatively peakless	12-24 hours
Lantus	90 mins	Peakless	24 hours

TREATMENT REGIMENS OF TYPE 1 DM

- Conventional Insulin Therapy: Two injections of NPH and Regular Insulin
- Mixed Insulin: Two injections of 70/30 (70 basal 'long acting' insulin, 30 prandial insulin 'short acting') or 60/40 (60 basal insulin, 40 prandial insulin) or 50/50
- Multiple Insulin Injections
  - 1 or 2 injections of NPH plus 3 injections of Regular or Rapid Insulin.
  - One injection of Glargine or Detemir plus 3 injections of rapid insulin(Lispro /Aspart).

If you have DM pt on metformin with HbA1C above target, what to do?

- Estabilieshed ASCVD or CKD.
- Without established ASCVD or CKD:
  - To minimize hypoglycemia
  - To promote weight loss or minimize weight gain
  - Cost is a major issue

If HbA1c still above target despite dual/triple therapy, What to do?

- Consider GLP−1 RA in most prior to insulin.
- Consider insulin as first injectable if:
  - HbA1c very high > 11% (the doctor said 10)
  - Symptoms or evidence of catabolism: weight loss, polyuria, polydipsia which suggest insulin deficiency.
  - If type−1 diabetes is a possibility.
  - If already on GLP−1 RA or if GLP−1 RA not appropriate or Insulin preferred.

Table 9.1—Drug-specific and patient factors to consider when selecting antihyperglycemic treatment in adults with type 2 diabetes

		Efficacy	Hypoglycemia	Weight change	CV effects		Cost	Oral/SQ	Renal effects		Additional considerations
					ASCVD	CHF			Progression of DKD	Dosing/use considerations*	
Metformin		High	No	Neutral (potential for modest loss)	Potential benefit	Neutral	Low	Oral	Neutral	▪ Contraindicated with eGFR <30	▪ Gastrointestinal side effects common (diarrhea, nausea) ▪ Potential for B12 deficiency
SGLT-2 inhibitors		Intermediate	No	Loss	Benefit: empagliflozin†, canagliflozin	Benefit: empagliflozin†, canagliflozin	High	Oral	Benefit: canagliflozin, empagliflozin	▪ Renal dose adjustment required (canagliflozin, dapagliflozin, empagliflozin, ertugliflozin)	▪ **FDA Black Box:** Risk of amputation (**canagliflozin**) ▪ Risk of bone fractures (canagliflozin) ▪ DKA risk (all agents, rare in T2DM) ▪ Genitourinary infections ▪ Risk of volume depletion, hypotension ▪ ↑LDL cholesterol ▪ Risk of Fournier's gangrene
GLP-1 RAs		High	No	Loss	Neutral: lixisenatide Benefit: liraglutide† > semaglutide > exenatide extended release	Neutral	High	SQ	Benefit: liraglutide	▪ Renal dose adjustment required (exenatide, lixisenatide) ▪ Caution when initiating or increasing dose due to potential risk of acute kidney injury	▪ **FDA Black Box:** Risk of thyroid C-cell tumors (**liraglutide, albiglutide, dulaglutide, exenatide extended release**) ▪ Gastrointestinal side effects common (nausea, vomiting, diarrhea) ▪ Injection site reactions ▪ ?Acute pancreatitis risk
DPP-4 inhibitors		Intermediate	No	Neutral	Neutral	Potential risk: saxagliptin, alogliptin	High	Oral	Neutral	▪ Renal dose adjustment required (sitagliptin, saxagliptin, alogliptin); can be used in renal impairment ▪ No dose adjustment required for linagliptin	▪ Potential risk of acute pancreatitis ▪ Joint pain
Thiazolidinediones		High	No	Gain	Potential benefit: pioglitazone	Increased risk	Low	Oral	Neutral	▪ No dose adjustment required ▪ Generally not recommended in renal impairment due to potential for fluid retention	▪ **FDA Black Box:** Congestive heart failure [**pioglitazone, rosiglitazone**] ▪ Fluid retention (edema; heart failure) ▪ Benefit in NASH ▪ Risk of bone fractures ▪ Bladder cancer (pioglitazone) ▪ ↑LDL cholesterol (rosiglitazone)
Sulfonylureas (2nd generation)		High	Yes	Gain	Neutral	Neutral	Low	Oral	Neutral	▪ Glyburide: not recommended ▪ Glipizide and glimepiride: initiate conservatively to avoid hypoglycemia	▪ FDA Special Warning on increased risk of cardiovascular mortality based on studies of an older sulfonylurea (tolbutamide)
Insulin	**Human insulin**	Highest	Yes	Gain	Neutral	Neutral	Low	SQ	Neutral	▪ Lower insulin doses required with a decrease in eGFR; titrate per clinical response	▪ Injection site reactions ▪ Higher risk of hypoglycemia with human insulin (NPH or premixed formulations) vs. analogs
	Analogs						High	SQ			

*For agent-specific dosing recommendations, please refer to the manufacturers' prescribing information. †FDA approved for CVD benefit. CHF, congestive heart failure; CV, cardiovascular; DPP-4, dipeptidyl peptidase 4; DKA, diabetic ketoacidosis; DKD, diabetic kidney disease; GLP-1 RAs, glucagon-like peptide 1 receptor agonists; NASH, nonalcoholic steatohepatitis; SGLT2, sodium–glucose cotransporter 2; SQ, subcutaneous; T2DM, type 2 diabetes.

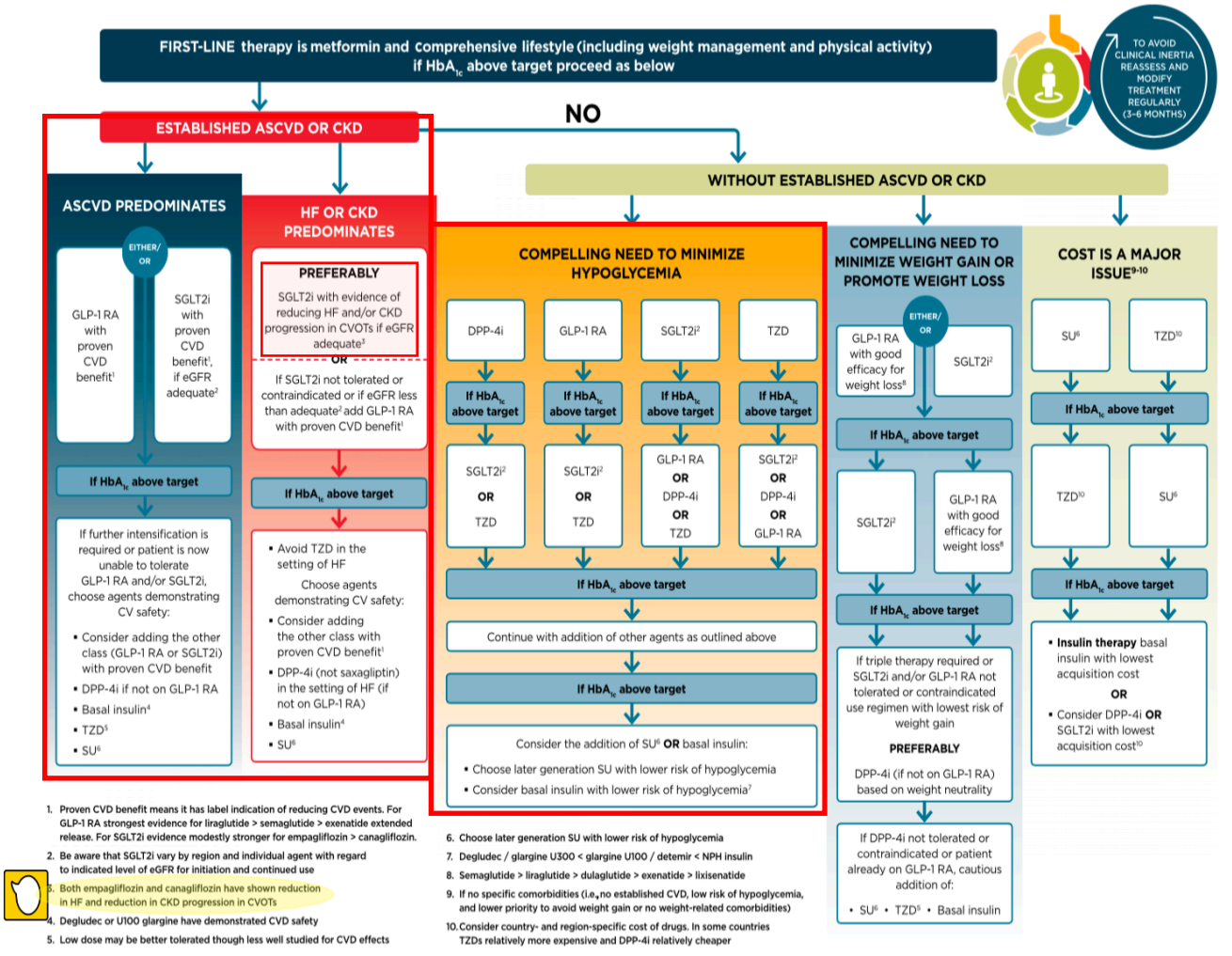


Figure 9.1—Glucose-lowering medication in type 2 diabetes: overall approach. For appropriate context, see **Fig. 4.1**. ASCVD, atherosclerotic cardiovascular disease; CKD, chronic kidney disease; CV, cardiovascular; CVD, cardiovascular disease; CVOTs, cardiovascular outcomes trials; DPP-4i, dipeptidyl peptidase 4 inhibitor; eGFR, estimated glomerular filtration rate; GLP-1 RA, glucagon-like peptide 1 receptor agonist; HF, heart failure; SGLT2i, sodium–glucose cotransporter 2 inhibitor; SU, sulfonylurea; TZD, thiazolidinedione. Adapted from Davies et al. (39).

Summary

	Advantages	Disadvantages/adverse effects
Metformin	• The first line for oral treatment of type 2 diabetes • no hypoglycemia. • Weight neutral	• GI side effects • vitamin B−12 def • Discontinues if GFR ≤ 30
Thiazolidinediones (TZD)	No hypoglycemia.	• Increase risk for bladder cancer (Pioglitazone) • Increased risk for cardiovascular event (Progressive ischemia ,MI, HF) in Rosiglitazone • Fluid retention • increase fracture risk
Sulfonylureas		• Hypoglycemia • Weight gain
Meglitinides (Glinides)	Safe in pt. with decrease GFR or renal failure .	• Hypoglycemia • weight gain
DPP-4 inhibitors	• No hypoglycemia • No effects on body weight	
GLP-1 receptor agonists	• High efficacy with no hypoglycemia • **Weight reduction** • Decrease ASCVD	• GI side effect (nausea, vomiting, diarrhea) • hyperplasia/medullary thyroid tumors
Glucosidase Inhibitors	Effective in lowering the postprandial glucose	
SGLT-2 Inhibitors	• **Weight loss** • **Good CV effect and specifically heart failure patient** • **Delay progression of CKD**	Genitourinary infections

We always start with lifestyle change and metformin then if the A1C still didn't reach the optimal (<7%) then we add. We add medication according to the patient situation, e.g. if the patient have high risk of CVD (previous Hx of strike, MI, angina, Hx of CHD or IHD) then we add GLP-1 agonist or SGLT-2 inhibitor (if the patient also have CKD we prefer SGLT-2i). If the patient doesn't have CVD risk then we see other factor: e.g. if the patient at risk of hypoglycemia like taxi driver we avoid hypoglycemic agent like Sulfonylureas or Glinides. If the patient has A1C 8.5 – 9% we should give TZD not Glucosidase Inhibitors

algorism from standard of medical care in diabetes 2019 for DM2 treatment
https://drive.google.com/file/d/1UfLuDy1kLcM9AANSsB8Z1q4ZKmIpToEv/view?usp=sharing