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	HbA1c (%)	Fasting Plasma Glu (mg/dL)	OGTT (mg/dL)
Normal	≤ 5.6	< 99	< 148
Prediabetes	5.7 – 6.4	100 - 125	149 - 199
Diabetes	≥ 6.5	≥ 126	≥ 200

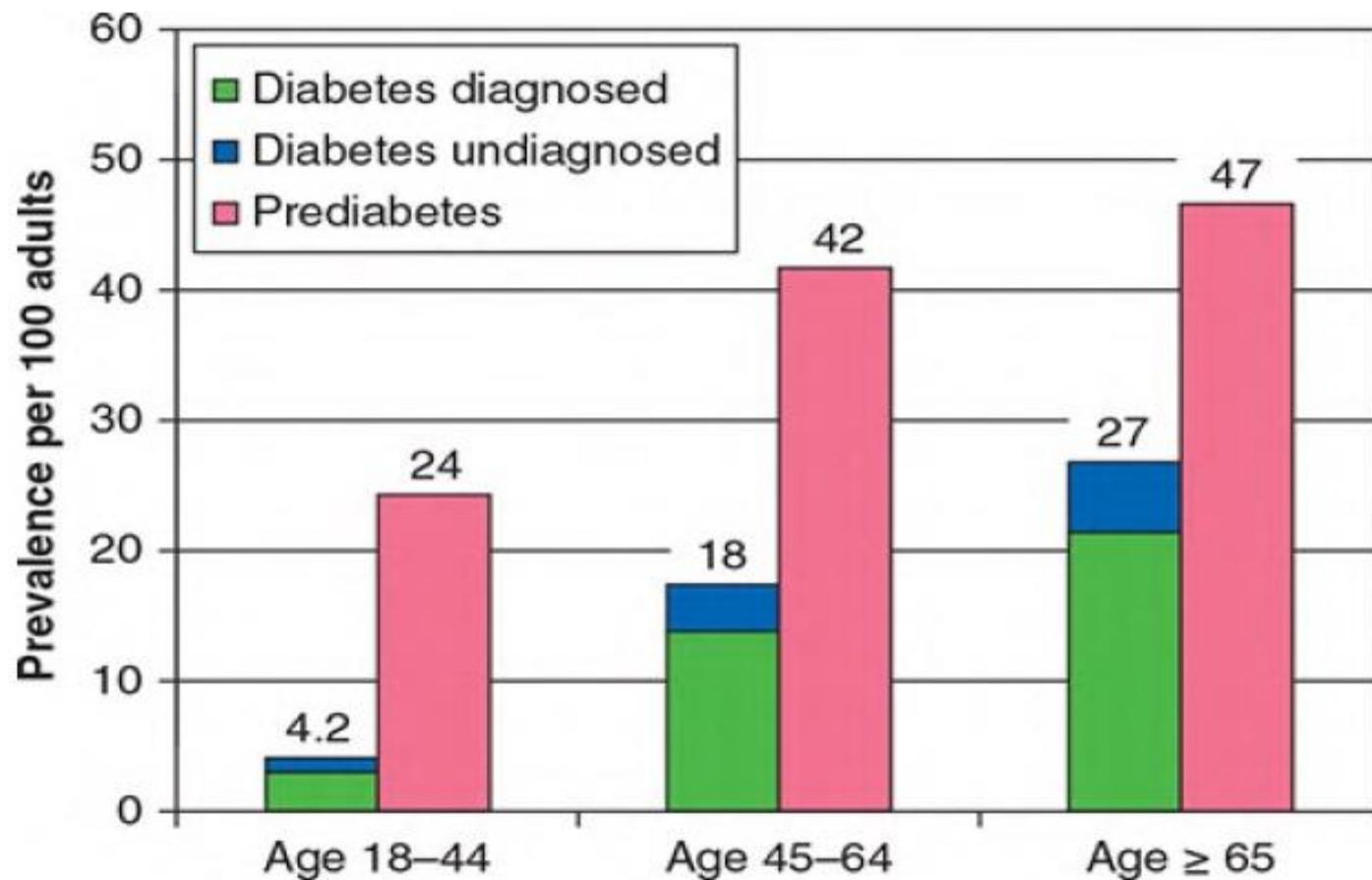
## اپیدمیولوژی دیابت

۱۴۰ درصد افراد ۲۰ ساله و بالاتر

یک سوم این افراد تشخیص داده نمی شوند.

۳۳ درصد افراد ۶۵ ساله و بالاتر

در سه دهه اخیر، شیوع و بروز دیابت، افزایش یافته است



## علل ایجاد دیابت:

- تخریب سلول های بتا در پانکراس دیابت نوع یک
- برهم کنش ژنتیک، افزایش سن و سبک زندگی دیابت نوع دو
- بیماری های بخش اگزوکرین پانکراس
- افزایش هورمون های مقابله کننده با اثر انسولین
- داروهای ایجاد کننده اختلال در ترشح یا عملکرد انسولین

## اثرات افزایش سن بر قند خون

- کاهش حساسیت به اثرات متابولیک انسولین
- اختلال در ترشح انسولین
- عدم تحمل گلوکز

-افزایش خفیف FBS

-تاخیر در بازگشت قند خون به میزان طبیعی، پس از مصرف گلوکز

## علام معمول ہایپرگلیسمی

- پلی اوری
- پلی دیپسی پلی فاژی
- کاہش وزن

## علائم بالینی دیابت در سالمندان

- بالابودن میزان قند خون در ارزیابی های معمول آزمایشگاهی
- کاهش وزن تدریجی و غیر قابل توجیه
- زمین خوردن
- خستگی
- گیجی
- بی اختیاری ادراری

## تشخیص دیابت

- معیارهای تشخیص دیابت با افزایش سن، تغییر نمی کنند.
- برای تشخیص دیابت، به دو نتیجه مختل در آزمایش ها، نیاز است.
- استفاده از معیار HbA1c امکان شناسایی افراد بدون علامت را افزایش می دهد.

## غربالگری

- همه افراد بالای ۴۵ سال، در فواصل زمانی ۳ ساله

در بیماران پر خطر، پایش سالانه توصیه می شود:

$$BMI \geq 25$$

- سابقه خانوادگی قوی برای ابتلا به دیابت
- سابقه قبلی دیابت بارداری
- ابتلا به فشارخون بالا یا اختلال لیپید ( TG بالا یا HDL پایین)
- اختلال در OGTT، FBS، HbA1c یا در تست های قبلی

## CRITERIA FOR ANNUAL SCREENING FOR DIABETES OR PREDIABETES IN HIGH-RISK OLDER ADULTS

- Presence of overweight or obesity ( $\text{BMI} \geq 25 \text{ kg/m}^2$ )
- First-degree relative with diabetes
- High-risk race/ethnicity (eg, African American, Latino, American Indian, Asian, Pacific Islander)
- History of CVD
- Hypertension ( $\geq 140/90 \text{ mm Hg}$  or on therapy for hypertension)
- HDL cholesterol level  $< 35 \text{ mg/dL}$  ( $0.90 \text{ mmol/L}$ ) and/or a triglyceride level  $> 250 \text{ mg/dL}$  ( $2.82 \text{ mmol/L}$ )
- Women with polycystic ovary syndrome or history of GDM
- Physical inactivity
- Other clinical conditions associated with insulin resistance (eg, glucocorticoid therapy, acanthosis nigricans)
- Prior diagnosis of prediabetes
- HIV on antiretroviral therapies

## ارزیابی سالمند مبتلا به دیابت

- بررسی عوارض دیابت
- بررسی سایر عوامل خطر و بیماری های همراه
- ارزیابی سابقه دارویی
- اختلال شناختی
- وضعیت عملکردی
- میزان امید به زندگی
- بررسی شنوایی
- کانسرها
- ریسک Fall
- انوریسم شکمی
- بررسی پروفایل لیپید
- بررسی عوارض میکروواسکوک
- دانسیتومتری استخوان

# DETERMINING CLINICAL TARGETS IN ADULTS AGED 65 AND OLDER

OVERALL HEALTH CATEGORY	GROUP 1: GOOD HEALTH	GROUP 2: INTERMEDIATE HEALTH	GROUP 3: POOR HEALTH	
Patient characteristics	No comorbidities <b>or</b> 1–2 non-diabetes chronic illnesses <sup>a</sup> <b>and</b> No ADL <sup>c</sup> impairments and $\leq 1$ IADL impairment	3 or more non-diabetes chronic illnesses <sup>a</sup> <b>and/or</b> Any one of the following: Mild cognitive impairment or early dementia $\geq 2$ IADL impairments	Any <b>one</b> of the following: End-stage medical condition(s) <sup>b</sup> Moderate to severe dementia $\geq 2$ ADL impairments Residence in a long-term nursing facility	
Reasonable glucose target ranges and HbA1C by group				
Shared decision-making: individualized goal may be lower or higher				
Use of drugs that may cause hypoglycemia (eg, insulin, sulfonylurea, glinides)	No	Fasting: 90–130 mg/dL Bedtime: 90–150 mg/dL $<7.5\%$	Fasting: 90–150 mg/dL Bedtime: 100–180 mg/dL $<8\%$	Fasting: 100–180 mg/dL Bedtime: 110–200 mg/dL $<8.5\%^d$
	Yes <sup>c</sup>	Fasting: 90–150 mg/dL Bedtime: 100–180 mg/dL $\geq 7.0$ and $<7.5\%$	Fasting: 100–150 mg/dL Bedtime: 150–180 mg/dL $\geq 7.5$ and $<8.0\%$	Fasting: 100–180 mg/dL Bedtime: 150–250 mg/dL $\geq 8.0$ and $<8.5\%^d$

1. Dyslipidemia
  - Statin therapy and an annual lipid profile are recommended to achieve levels for reducing absolute CVD events and mortality.
  - If statin therapy is inadequate for reaching the LDL-C reduction goal, then alternative or additional drugs (such as ezetimibe or proprotein convertase subtilisin/kexin type 9 inhibitors) should be initiated.
  - In patients with fasting triglycerides  $> 500$  mg/dL, the use of fish oil and/or fenofibrate is recommended to reduce the risk of pancreatitis.
2. Hypertension
  - A target BP of  $< 140/90$  mm Hg is recommended to decrease the risk of CVD outcomes, stroke, and progressive CKD.
  - An angiotensin-converting enzyme inhibitor or an angiotensin receptor blocker is recommended as first-line therapy for hypertension in patients with nephropathy.
3. Use of aspirin
  - Low-dosage aspirin (75–162 mg/d) is recommended for secondary prevention of cardiovascular disease after careful assessment of bleeding risk and collaborative decision-making with the patient, family, and other caregivers.

BP, blood pressure; CKD, chronic kidney disease; CVD, cardiovascular disease; LDL-C, low-density lipoprotein cholesterol.

*Data from LeRoith D, Biessels GJ, Braithwaite SS, et al. Treatment of diabetes in older adults: an Endocrine Society® clinical practice guideline. J Clin Endocrinol Metab. 2019;104(5):1520–1574.*

# PHARMACOLOGIC THERAPY

## Summary of glucose-lowering interventions

Intervention	Expected decrease in A1C with monotherapy (%)	Advantages	Disadvantages
<b>Initial therapy</b>			
Lifestyle change to decrease weight and increase activity	1.0 to 2.0	Broad benefits	Insufficient for most within first year owing to inadequate weight loss and weight regain
Metformin	1.0 to 2.0	Weight neutral	GI side effects, contraindicated with renal insufficiency (eGFR <30 mL/min/1.73 m <sup>2</sup> )*
<b>Additional therapy<sup>1</sup></b>			
Insulin (usually with a single daily injection of intermediate- or long-acting insulin initially)	1.5 to 3.5	No dose limit, rapidly effective, improved lipid profile	1 to 4 injections daily, monitoring, weight gain, hypoglycemia, analogs are expensive
Sulfonylurea (shorter-acting agents preferred)	1.0 to 2.0	Rapidly effective	Weight gain, hypoglycemia (especially with glibenclamide or chlorpropamide)
GLP-1 receptor agonist (daily to weekly injections)	0.5 to 1.5	Weight loss, reduction in major adverse cardiovascular events (liraglutide, semaglutide, dulaglutide) in patients with established CVD and potentially for those at high risk for CVD	Requires injection, frequent GI side effects, expensive
Thiazolidinedione	0.5 to 1.4	Improved lipid profile (pioglitazone), potential decrease in MI (pioglitazone)	Fluid retention, HF, weight gain, bone fractures, potential increase in MI (rosiglitazone) and bladder cancer (pioglitazone)
Glinide	0.5 to 1.5 <sup>Δ</sup>	Rapidly effective	Weight gain, 3 times/day dosing, hypoglycemia
SGLT2 inhibitor	0.5 to 0.7	Weight loss, reduction in systolic blood pressure, reduced cardiovascular mortality in patients with established CVD, improved renal outcomes in patients with nephropathy	Vulvovaginal candidiasis, urinary tract infections, bone fractures, lower limb amputations, DKA
DPP-4 inhibitor	0.5 to 0.8	Weight neutral	Possible increased risk of HF with saxagliptin, expensive
Alpha-glucosidase inhibitor	0.5 to 0.8	Weight neutral	Frequent GI side effects, 3 times/day dosing
Pramlintide	0.5 to 1.0	Weight loss	3 injections daily, frequent GI side effects, long-term safety not established, expensive

A1C: glycated hemoglobin; GI: gastrointestinal; eGFR: estimated glomerular filtration rate; GLP-1: glucagon-like peptide-1; CVD: cardiovascular disease; MI: myocardial infarction; HF: heart failure; SGLT: sodium-glucose co-transporter 2; DKA: diabetic ketoacidosis; DPP-4: dipeptidyl peptidase 4.

## درمان دارویی دیابت مت فورمین:

داروی خوراکی خط اول در دیابت نیپ دو  
سرکوب تولید گلوکز در کبد و افزایش حساسیت به انسولین در بافت ها  
حداکثر دوز در سالمندان: ۲۵۰۰ میلی گرم در روز  
در نارسایی کلیوی، کبدی و قلبی پیشرونده منع مصرف دارد

## درمان دارویی دیابت

- سولفونیل اوره ها Glyburide, Glipizide, Gliclazide, Glimepiride
- افزایش ترشح انسولین از سلول های بتای پانکراس
- خطر بالای هایپوگلیسمی در نارسایی کلیه و بیماری شدید کبدی، نباید استفاده شوند.

- مهارکننده های آلفا گلیکوزیداز Acarbose, Miglitol
- کند کردن هضم و جذب کربوهیدرات ها در روده
- به عنوان درمان کمکی در کنار سایر داروها

## درمان دارویی دیابت

- تیازولیدیون ها افزایش حساسیت به انسولین در بافت های محیطی و کبد

### Pioglitazone, Rosiglitazone •

- دارایی عوارض جانبی قابل توجه: احتباس مایع، ادم محیطی، افزایش وزن، افزایش خطر نارسایی احتقانی قلب

- در مبتلایان به نارسایی قلبی منع مصرف دارد.

## درمان دارویی دیابت

Repaglinide, Nateglinide، Meglitinide

تحریک سریع ترشح انسولین با اثر مستقیم بر سلول های بتا

• در سالمندان، نیاز به تعديل دوز ندارند.

• در مبتلایان به نارسایی کلیه، ( با تعديل دوز ) قابل مصرف هستند.

انسولین:

با تعیین دوز مناسب و پایش سطح گلوکز

، در نارسایی کبدی یا کلیوی،

در بیماران با عدم توانایی خوردن و در مبتلایان به بیماری های جدی، قابل

استفاده است.

پایش مکرر در شروع درمان و پیشرفت تدریجی برنامه درمانی توصیه می

شود.

CLASS	ROUTE OF ADMINISTRATION AND USUAL DAILY DOSAGE	PRIMARY PHYSIOLOGIC ACTION	ADVANTAGES	DISADVANTAGES
Biguanide • Metformin • Metformin ER	Oral • 500–1000 mg BID • Max 2500 mg/d • 500–2000 mg qd	• ↓ Hepatic glucose production, possible ↑ insulin-mediated uptake of glucose in muscles	• No weight gain • Minimal hypoglycemia • Likely ↓ in both microvascular and macrovascular events • Extensive clinical experience • Lower cost	• Gastrointestinal side effects (diarrhea and abdominal discomfort; less GI side effects with metformin ER) • Lactic acidosis (rare) • Contraindicated in presence of progressive liver, kidney, or cardiac failure • Contraindicated if eGFR < 30 mL/min/1.73 m <sup>2</sup>
Sulfonylureas • Glipizide • Glyburide • Glimepiride • Gliclazide <sup>a</sup>	Oral • 2.5–10 mg qd BID • 2.5–20 mg qd • 1–4 mg qd • 40 mg qd–160 mg BID	• ↑ Insulin secretion from pancreatic β-cells	• ↓ Microvascular events • Extensive clinical experience • Lower cost	• Hypoglycemia (esp. with longer half-life: glyburide) • Weight gain • Skin rash (including photosensitivity)
DPP-4 inhibitors • Sitagliptin • Saxagliptin • Vildagliptin • Linagliptin • Alogliptin	Oral • 100 mg qd • 2.5–5 mg qd • 50 mg qd BID • 5 mg qd • 25 mg qd	• ↑ Insulin secretion (glucose-dependent) • ↑ Glucagon secretion (glucose-dependent)	• Minimal hypoglycemia • Well tolerated • Once a day dosing • OK to use in renal impairment • No renal dose adjustment (Linagliptin)	• Urticaria/angioedema • Renal dose adjustment (sitagliptin, saxagliptin, alogliptin) • ? ↑ risk of pancreatitis • ? ↑ Heart failure hospitalization • Higher cost
GLP-1 receptor agonists • Exenatide • Exenatide extended release • Liraglutide • Dulaglutide • Lixisenatide • Semaglutide • Insulin glargine/lixisenatide • Insulin degludec/liraglutide 100/3.6	Injection • 5–10 µg SC bid • 2 mg SC qwk • 0.6–1.8 mg SC qd • 0.75 mg/0.5 mL SC qwk • 10–20 µg SC qd • Oral 3–14 mg qd • 0.25–1 mg SC qwk • 15–60 units SC qd • 16–50 units SC qd	• ↑ Insulin secretion (glucose-dependent) • ↓ Glucagon secretion (glucose-dependent) • Slows gastric emptying • ↑ Satiety	• Minimal hypoglycemia risk (lower risk for the fixed combination with insulin than insulin alone) • Weight reduction (weight neutrality for the fixed combination with insulin) • ↓ Blood pressure • ↓ Postprandial glucose excursions • No renal dose adjustment (liraglutide, semaglutide, and dulaglutide) • ↓ CVD events (liraglutide, semaglutide, and dulaglutide) • May ↓ CKD progression (liraglutide, semaglutide, dulaglutide)	• Gastrointestinal side effects (nausea, vomiting) • ↑ Heart rate • ? Acute pancreatitis • Thyroid C-cell hyperplasia/tumors in rodents (human relevance uncertain) • Avoid if eGFR < 30 mL/min/1.73 m <sup>2</sup> (exenatide, lixisenatide) • Higher cost

SGLT-2 inhibitors • Canagliflozin • Empagliflozin • Dapagliflozin • Ertugliflozin	Oral • 100–300 mg qd • 10–25 mg qd • 5–10 mg qd • 5–15 mg qd	• ↓ Glucose reabsorption by the kidney • ↑ Urinary glucose excretion	• Minimal hypoglycemia • Weight reduction • ↓ Blood pressure • Once-a-day dosing • ↓ CVD events (empagliflozin, canagliflozin, and dapagliflozin) • ↓ CKD progression	• Renal dose adjustment and avoid if eGFR < 25–30 mL/min/1.73 m <sup>2</sup> • Genitourinary infections • Genital yeast infections • Polyuria • Hyperkalemia • Orthostatic hypotension • DKA (rare in T2DM) • ↑ fractures (canagliflozin) • Higher cost
α-Glucosidase inhibitors • Acarbose • Miglitol	Oral • 25–100 mg TID with meals • 25–100 mg TID with meals	• Slows intestinal carbohydrate digestion or absorption	• Minimal hypoglycemia • ↓ Postprandial glucose excursions • ? ↓ CVD events • Lower cost (acarbose)	• Generally modest A1C reduction • Flatulence • Abdominal discomfort • Contraindicated in cirrhosis • Frequent dosing schedule (with meals)
Thiazolidinediones • Pioglitazone • Rosiglitazone <sup>b</sup>	Oral • 15–45 mg qd • 2–8 mg qd or divided BID	• ↑ Insulin sensitivity	• Minimal hypoglycemia • ↑ HDL-C • ↓ Triglycerides (pioglitazone) • Lower cost (pioglitazone)	• Weight gain • Edema/heart failure (avoid in renal impairment) • Bone fractures • ↑ LDL-C (rosiglitazone) • ? ↑ MI
Meglitinides • Repaglinide • Nateglinide	Oral • 0.5–4 mg QAC • 60–120 mg QAC	• ↑ Insulin secretion from pancreatic β-cells	• ↓ Postprandial glucose excursions • Dosing flexibility (before meals)	• Hypoglycemia • Weight gain • Frequent dosing schedule • Intermediate cost
Amylin-like • Pramlintide <sup>c</sup>	Injection • 60–120 µg SC QAC	• ↓ Glucagon secretion • Slows gastric emptying • ↑ Satiety	• ↓ Postprandial glucose excursions • Weight reduction	• GI side effects (nausea; vomiting) • ↑ Hypoglycemic risk of insulin • Frequent dosing schedule • Higher cost
Bile acid sequestrant • Colesevelam <sup>d</sup>	Oral • 3750 mg qd (or 1875 mg BID) with meals	• Unclear • ? ↓ Hepatic glucose production • ? ↑ Incretin levels	• Minimal hypoglycemia • ↓ LDL-C	• Generally modest A1C efficacy • Constipation • ↑ Triglycerides • Reduce absorption of fat soluble vitamins • Higher cost
Dopamine-2 agonist • Bromocriptine, immediate-release form <sup>c</sup>	Oral • 1.6–4.8 mg QAM	• Modulates hypothalamic regulation of metabolism • ↑ Insulin sensitivity	• Minimal hypoglycemia	• Nausea; headache; orthostatic hypotension; potential exacerbation of psychosis • Higher cost

BID, twice a day; CKD, chronic kidney disease; CVD, cardiovascular disease; DKA, diabetic ketoacidosis; DPP-4, dipeptidyl peptidase-4; eGFR, estimated glomerular filtration; GLP-1, glucagon-like peptide 1; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; MI, myocardial infarction; QAC, before meals; QAM, every morning; qd, once daily; SC, subcutaneous injection; SGLT2 inhibitors, inhibitors of sodium glucose cotransporter 2; T2DM, type 2 diabetes mellitus; TID, three times a day.

<sup>a</sup>Not licensed in United States.

<sup>b</sup>Prescribing highly restricted in the United States; withdrawn in Europe.

Long-acting			
• Glargine 100	• About 2 h	• No peak	• 20–24 h
• Detemir	• About 2 h	• 3–9 h	• 6–24 h (duration of action is dose-dependent; at $\geq 0.8$ units/kg, mean duration of action is longer and less variable—22–23 h)
Ultra-long acting			
• Degludec	• About 2 h	• No peak	• > 40 h
• Glargine 300	• About 6 h	• No peak	• 28–36 h
Intermediate acting			
• Human NPH	• About 2 h	• 4–12 h	• 18–28 h
• Neutral protamine lispro <sup>a</sup>	• About 2 h	• 6 h	• 15 h
Short acting			
• Human regular	• About 30 min	• 2–4 h	• 5–8 h
Rapid acting			
• Lispro	• 5–15 min	• 45–75 min	• 2–4 h
• Aspart			
• Glulisine			
Inhalation powder			
• Human insulin <sup>b</sup>	• 5–15 min	• 50 min (wide variation)	• 2–3 h
Premixed insulins			
• NPH/Regular 70/30	• About 30 min	• 4–12 h	• 18–24 h
• Lispro 50/50 (lispro protamine and lispro)	• 5–15 min	• 1–5 h	• 11–22 h
• Lispro 75/25 (Lispro protamine and lispro)	• 5–15 min	• 1–6 h	• 13–22 h
• NovoLog Mix 70/30 (aspart protamine and aspart)	• 5–15 min	• 1–4 h	• Up to 24 h

The insulin agents lead to increased glucose disposal and decreased hepatic glucose production. They are nearly universally responsive and likely lead to decreased microvascular risk (UK Prospective Diabetes Study [UKPDS]). Disadvantages are hypoglycemia risks, which vary based on the individual agent's dose and its course of the action.

<sup>a</sup>Only available in the United States in a premixed combination with insulin lispro.

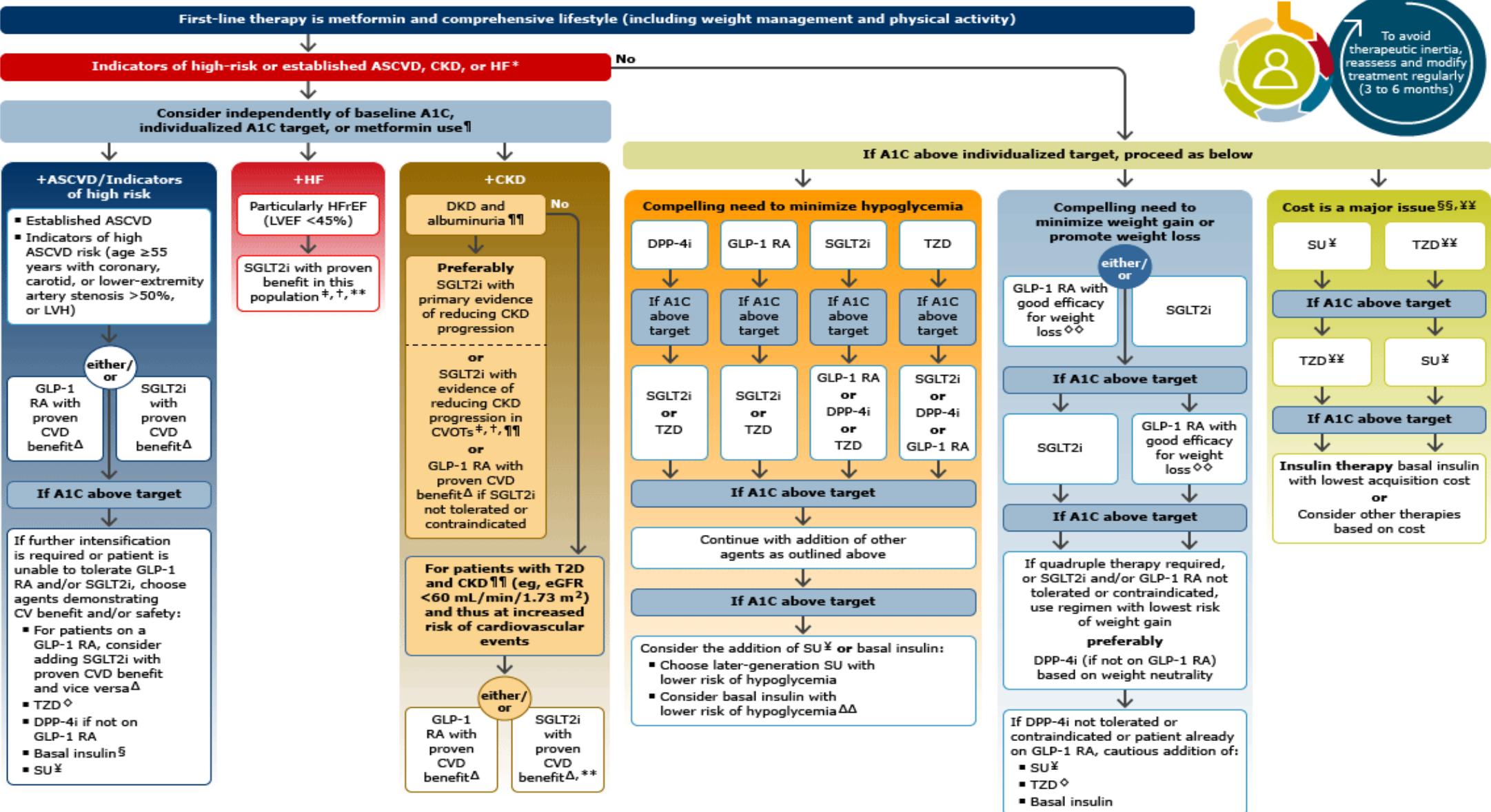
<sup>b</sup>Inhaled human insulin (Afrezza) is contraindicated in patients with chronic lung disease such as asthma or chronic obstructive pulmonary disease (COPD).

## Dual agent failure

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starting insulin therapy; sulfonylureas are discontinued

two oral agents and a GLP-1 receptor agonist



## MONITORING OF GLYCEMIA

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Glycated hemoglobin (A1C) :

**twice yearly** in whom are meeting treatment goals

**quarterly** in patients who are not meeting their glycemic goals

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**Self-monitoring of blood glucose (SMBG) :**

who take **medications** that can cause **hypoglycemia**

treated with **complex insulin regimens**

who would take action to **modify eating patterns or exercise**

# SCREENING FOR MICROVASCULAR COMPLICATIONS

## Monitoring in patients with diabetes mellitus

Intervention	Frequency	Notes
<b>History and physical examination</b>		
Height, weight, and BMI	Every visit	
Smoking cessation counseling	Every visit	For smokers only.
Blood pressure	Every visit	Goal systolic pressure 125 to 130 mmHg.*
Dilated eye examination	Annually <sup>¶</sup>	Begin at onset of type 2 diabetes, 3 to 5 years after onset of type 1 diabetes. Examine yearly (or more frequently) if retinopathy present, every 2 to 3 years if there is no evidence of retinopathy.
Comprehensive foot examination	Annually	Every visit if peripheral vascular disease or neuropathy.
Dental examination	Annually	Periodontal disease is more severe but not necessarily more prevalent in patients with diabetes.
<b>Laboratory studies</b>		
Lipid profile	Initially, as indicated	In people without dyslipidemia and not on cholesterol-lowering therapy, testing may be infrequent.
A1C	Every 3 to 6 months	Goal ≤7% (may be lower or higher in selected patients).
Urinary albumin-to-creatinine ratio	Annually	Begin 3 to 5 years after onset of type 1 diabetes and at diagnosis in patients with type 2 diabetes; protein excretion should also be monitored if persistent albuminuria is present.
Serum creatinine	Initially, as indicated	Typically annually; more often in the presence of chronic kidney disease.
<b>Vaccinations</b>		
Pneumococcus		
■ PPSV23	1 dose, ages 19 to 64 years	Once the patient is ≥65 years (and ≥1 year after PCV13 and >5 years after previous dose of PPSV23), give a second dose of PPSV23. Revaccinate every 10 years.
■ PCV13	1 dose at age ≥65 years	Once the patient is ≥65 years (and ≥1 year after PPSV23), give PCV13.
Influenza	Annually	
Hepatitis B	3-dose series	Administer to unvaccinated adults who are ages 19 to 59 years. For older patients, administer based upon risk of acquiring hepatitis B, including the need for assisted blood glucose monitoring and the likelihood of an adequate immune response to vaccination.
Provide other routine vaccinations for adults with diabetes according to age-related recommendations.		
<b>Education, self-management review</b>		
	Annually	More often at onset of diabetes and when there is a change in regimen.

BMI: body mass index; A1C: glycated hemoglobin.

\* When manual auscultatory method is used to measure blood pressure.

¶ Less frequent screening (every 2 to 3 years) may be appropriate for some patients (eg, patients with little or no retinopathy and near-normal A1C levels).