American Diabetes Association 2021 Standards of Medical Care in Diabetes

CLINICAL PRACTICE GUIDELINES ARE KEY TO IMPROVING POPULATION HEALTH

Glycemic recommendations for many nonpregnant adults with diabetes[a]

A1C <7.0%	eAG 154 mg/dL (123-185)[b] corresponds to A1C=7%	**Assess glycemic status (A1C or other glycemic measure) at least every 3 months if change in therapy and/or not at goal, or at least every 6 months if meeting treatment goals**
FPG 80-130 mg/dL	TIR >70% (70-180 mg/dL) with TBR <4% (<70 mg/dL)[c]	
PPG[d] <180 mg/dL		

ASCVD risk management

Assess CV risk factors at least annually in all patients with diabetes (dyslipidemia, hypertension, overweight/obesity, chronic kidney disease, smoking, albuminuria, and a family history of premature coronary disease)

Dyslipidemia:	Statins should be initiated for lipid management with varying intensity depending on ASCVD risk factors, 10-year ASCVD risk percent, and age in addition to lifestyle therapy			
Hypertension:	Goal of <140/90 mm Hg for patients with low CVD risk[e]			
Overweight and Obesity in T2D:	Treatment may be indicated for select motivated patients	BMI category (kg/m^2) ≥25[f]	≥27[g]	≥30[h]
	Diet, physical activity, and behavioral therapy	✓	✓	✓
	Pharmacotherapy		✓	✓
	Metabolic surgery			✓
Chronic Kidney Disease (CKD):	Annually assess[i] eGFR and urinary albumin when <30 mg/g Cr, or twice annually when >300 mg/g Cr and/or eGFR 30-60 mL/min/1.73 m^2			
Smoking:	Advise all patients not to use cigarettes and other tobacco products or e-cigarettes; provide smoking cessation counseling and other forms of treatment as needed			

Microvascular risk management

Diabetic Retinopathy:	Comprehensive dilated eye exam at diagnosis of T2D[j], at least annually if retinopathy is present, more frequently if progressing or sight-threatening, and every 1-2 years if there is no evidence of retinopathy and glycemia is well controlled
Peripheral Neuropathy:	All patients should be assessed for diabetic peripheral neuropathy starting at diagnosis of T2D[j] and at least annually thereafter

ASCVD=atherosclerotic cardiovascular disease; BMI=body mass index; Cr=creatinine; CVD=cardiovascular disease; eAG=estimated average glucose; eGFR=estimated glomerular filtration rate; FPG=preprandial capillary plasma glucose (fasting plasma glucose); LDL=low-density lipoprotein; PPG=Peak postprandial capillary plasma glucose; T2D=type 2 diabetes; TBR=time below range; TIR=time in range. [a]Goals should be individualized based on patient characteristics; [b]Based on ADAG trial data of ~2,700 readings over 3 months per A1C measurement in 507 adults with type 1, type 2, or no diabetes; [c]For use with CGM; [d]Peak postprandial capillary plasma glucose measured 1-2 hours after the start of a meal; [e]A goal of 130/80 mm Hg for patients at higher CVD risk; [f]25.0-26.9 (cut point is 23.0 to 24.9 for Asian American individuals); [g]Range 27.0-29.9 (cut point is 25.0 to 27.4 for Asian American individuals); [h]Cut point is ≥27.5 for Asian American individuals; [i]In all patients with type 2 diabetes, in patients with type 1 diabetes with duration of ≥5 years; [j]Within 5 years after the onset of type 1 diabetes.

Glucose-lowering medication in type 2 diabetes: Overall approach

First-line therapy is metformin and comprehensive lifestyle (including weight management and physical activity)

TO AVOID THERAPEUTIC INERTIA REASSESS AND MODIFY TREATMENT REGULARLY (3-6 MONTHS)

Indicators of high-risk or established ASCVD, CKD, or HF[†] — NO

Consider independently of baseline A1C, individualized A1C target, or metformin use*

+ASCVD/Indicators of high risk

- Established ASCVD
- Indicators of high ASCVD risk (age ≥55 years with coronary, carotid, or lower-extremity artery stenosis >50%, or LVH)

EITHER/OR

- GLP-1 RA with proven CVD benefit[1]
- SGLT2i with proven CVD benefit[1]

If A1C above target

If further intensification is required or patient is unable to tolerate GLP-1 RA and/or SGLT2i, choose agents demonstrating CV benefit and/or safety:

- For patients on a GLP-1 RA, consider adding SGLT2i with proven CVD benefit and vice versa[1]
- TZD[2]
- DPP-4i if not on GLP-1 RA
- Basal insulin[3]
- SU[4]

+HF

Particularly HFrEF (LVEF <45%)

SGLT2i with proven benefit in this population[5,6]

+CKD

DKD and Albuminuria[7] — NO

PREFERABLY

SGLT2i with primary evidence of reducing CKD progression

OR

SGLT2i with evidence of reducing CKD progression in CVOTs[5,7]

OR

GLP-1 RA with proven CVD benefit[1] if SGLT2i not tolerated or contraindicated

For patients with T2D and CKD[7] (eg, eGFR <60 mL/min/1.73 m²) and thus at increased risk of CV events

EITHER/OR

- GLP-1 RA with proven CVD benefit[1]
- SGLT2i with proven CVD benefit[1,6]

If A1C above individualized target, proceed as below

Compelling need to minimize hypoglycemia

- DPP-4i
- GLP-1 RA
- SGLT2i
- TZD

If A1C above target

- SGLT2i **OR** TZD
- SGLT2i **OR** TZD
- GLP-1 RA **OR** DPP-4i **OR** TZD
- SGLT2i **OR** DPP-4i **OR** GLP-1 RA

If A1C above target

Continue with addition of other agents as outlined above

If A1C above target

Consider the addition of SU[4] **OR** basal insulin:

- Choose later generation of SU with lower risk of hypo
- Consider basal insulin with lower risk of hypo

Compelling need to minimize weight gain or promote weight reduction

EITHER/OR

- GLP-1 RA with good efficacy for weight reduction
- SGLT2i

If A1C above target

- SGLT2i
- GLP-1 RA with good efficacy for weight reduction

If A1C above target

If quadruple therapy required, or SGLT2i and/or GLP-1 RA not tolerated or contraindicated, use regimen with lowest risk of weight gain

PREFERABLY

DPP-4i (if not on GLP-1 RA) based on weight neutrality

If DPP-4i not tolerated or contraindicated or patient already on GLP-1 RA, cautious addition of:

·SU[4] ·TZD[2] ·Basal insulin

Cost is a major issue[8,9]

- SU[4]
- TZD[9]

If A1C above target

- TZD[9]
- SU[4]

If A1C above target

Insulin therapy basal insulin with lowest cost

OR

Consider other therapies based on cost

[†]Actioned whenever these become new clinical considerations regardless of background glucose-lowering medications.

*Most patients enrolled in the relevant trials were on metformin at baseline as glucose-lowering therapy.

[1]Proven CVD benefit means it has label indication of reducing CVD events.

[2]Low dose may be better tolerated though less well studied for CVD effects.

[3]Some basal insulins have demonstrated CVD safety.

[4]Choose later generation SU to lower risk of hypoglycemia.

[5]Be aware that SGLT2i labelling varies by country and individual agent with regard to indicated level of eGFR for initiation and continued use.

[6]Proven benefit means it has a label indication of reducing HF in this population.

[7]Refer to full ADA Standards of Care Section 11: Microvascular Complications and Foot Care for more information.

[8]If no specific comorbidities (ie, no established CVD, low risk of hypo, and lower priority to avoid weight gain or no weight-related comorbidities).

[9]Consider country- and region-specific cost of drugs. In some countries, TZDs are relatively more expensive and DPP-4i are relatively cheaper.

Adapted with permission from the American Diabetes Association. Please see full algorithm for more information.

ASCVD=atherosclerotic cardiovascular disease; CKD=chronic kidney disease; CV=cardiovascular; CVD=cardiovascular disease; CVOT=cardiovascular outcomes trial; DKD=diabetic kidney disease; DPP-4i=dipeptidyl peptidase 4 inhibitor; eGFR=estimated glomerular filtration rate; GLP-1 RA=glucagon-like peptide-1 receptor agonist; HF=heart failure; HFrEF=heart failure reduced ejection fraction; hypo=hypoglycemia; LVEF=left ventricular ejection fraction; SGLT2i=sodium-glucose cotransporter 2 inhibitor; SU=sulfonylurea; T2D=type 2 diabetes; TZD=thiazolidinedione.

Intensifying to injectable therapies

Use principles for glucose-lowering medication in type 2 diabetes including reinforcement of behavioral interventions (weight management and physical activity) and provision of DSMES to meet individualized treatment goals

TO AVOID THERAPEUTIC INERTIA REASSESS AND MODIFY TREATMENT REGULARLY (3-6 MONTHS)

If injectable therapy is needed to reduce A1C[a]

Consider GLP-1 RA in most patients prior to insulin[a,b]

If already on GLP-1 RA or if GLP-1 RA not appropriate OR insulin preferred

If above A1C target

Add basal insulin[a]
Choice of basal insulin should be based on patient-specific considerations, including cost

Add basal analog or bedtime NPH insulin
INITIATION: Start 10 IU a day **OR** 0.1-0.2 IU/kg a day
TITRATION:
- Set FPG target
- Choose evidence-based titration algorithm (eg, increase 2 units every 3 days to reach FPG target without hypo)
- For hypoglycemia determine cause, if no clear reason lower dose by 10-20%

Assess adequacy of basal insulin dose
Consider clinical signals to evaluate for overbasalization and need to consider adjunctive therapies[a]

Consider GLP-1 RA if not already in regimen
For addition of GLP-1 RA, consider lowering insulin dose dependent on current glycemic assessment and patient factors

If above A1C target

If on bedtime NPH, consider converting to twice-daily NPH regimen[a]
Conversion based on individual needs and current glycemic control

Add prandial insulin[a]
Usually one dose with the largest meal or meal with greatest PPG excursion; prandial insulin can be dosed individually or mixed with NPH as appropriate

If above A1C target

If above A1C target

Stepwise additional injections of prandial insulin
(ie, 2, then 3 additional injections)

Consider self-mixed/split insulin regimen[a]
Can adjust NPH and short or rapid-acting insulins separately

Consider twice daily premix insulin regimen[a]

Proceed to full basal-bolus regimen
(ie, basal insulin and prandial insulin with each meal)

[a]**Refer to complete algorithm in the ADA Standards of Care for additional information;** [b]**When selecting GLP-1 RA, consider: patient preference, A1C-lowering, weight-reduction effect, or frequency of injection. If CVD, consider GLP-1 RA with proven CVD benefit.**

CVD=cardiovascular disease; DSMES=diabetes self-management education and support; FPG=fasting plasma glucose; GLP-1 RA=glucagon-like peptide-1 receptor agonist; hypo=hypoglycemia; NPH=Neutral Protamine Hagedorn; PPG=postprandial glucose.

Reference: American Diabetes Association. Standards of medical care in diabetes—2021. *Diabetes Care.* 2021;*44*(suppl 1):S1-S232.

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