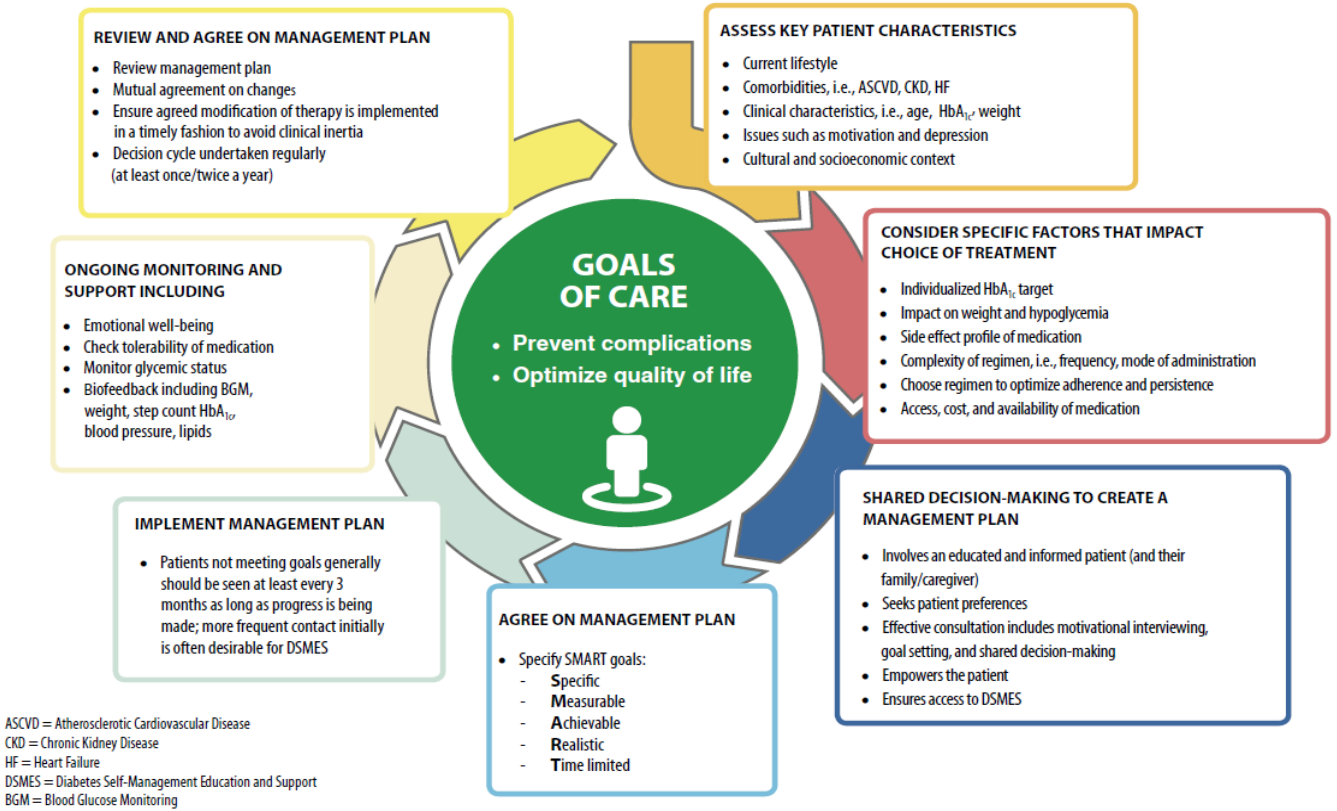
ADA Guidelines

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



ASCVD = Atherosclerotic Cardiovascular Disease
CKD = Chronic Kidney Disease
HF = Heart Failure
DSMES = Diabetes Self-Management Education and Support
BGM = Blood Glucose Monitoring

Comprehensive Medical Evaluation and Assessment of Comorbidities:
Standards of Medical Care in Diabetes - 2022. *Diabetes Care* 2022;45(Suppl. 1):S46-S59

Table 4.1 - Components of the comprehensive diabetes medical evaluation at initial, follow-up, and annual visits

		INITIAL VISIT	EVERY FOLLOW-UP VISIT	ANNUAL VISIT
PAST MEDICAL AND FAMILY HISTORY	**Diabetes history**			
	▪ Characteristics at onset (e.g., age, symptoms)	✓		
	▪ Review of previous treatment regimens and response	✓		
	▪ Assess frequency/cause/severity of past hospitalizations	✓		
	Family history			
	▪ Family history of diabetes in a first-degree relative	✓		
	▪ Family history of autoimmune disorder	✓		
	Personal history of complications and common comorbidities			
	▪ Common comorbidities (e.g., obesity, OSA, NAFLD)	✓		✓
	▪ High blood pressure or abnormal lipids	✓		✓
	▪ Macrovascular and microvascular complications	✓		✓
	▪ Hypoglycemia: awareness/frequency/causes/timing of episodes	✓	✓	✓
	▪ Presence of hemoglobinopathies or anemias	✓		✓
	▪ Last dental visit	✓		✓
	▪ Last dilated eye exam	✓		✓
	▪ Visits to specialists	✓	✓	✓
	Interval history			
	▪ Changes in medical/family history since last visit		✓	✓

Comprehensive Medical Evaluation and Assessment of Comorbidities:
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BEHAVIORAL FACTORS	▪ Eating patterns and weight history	✓	✓	✓
	▪ Assess familiarity with carbohydrate counting (e.g., type 1 diabetes, type 2 diabetes treated with MDI)	✓		✓
	▪ Physical activity and sleep behaviors	✓	✓	✓
	▪ Tobacco, alcohol, and substance use	✓		✓
MEDICATIONS AND VACCINATIONS	▪ Current medication regimen	✓	✓	✓
	▪ Medication-taking behavior	✓	✓	✓
	▪ Medication intolerance 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 and use, connected pen and glucose data	✓	✓	✓
SOCIAL LIFE ASSESSMENT	**Social network**			
	▪ Identify existing social supports	✓		✓
	▪ Identify surrogate decision maker, advanced care plan	✓		✓
	▪ Identify social determinants of health (e.g.., food security, housing stability & homelessness, transportation access, financial security, community safety)	✓		✓

Comprehensive Medical Evaluation and Assessment of Comorbidities:
Standards of Medical Care in Diabetes - 2022. *Diabetes Care* 2022;45(Suppl. 1):S46-S59

PHYSICAL EXAMINATION	▪ Height, weight, and BMI; growth/pubertal development in children and adolescents	✓	✓	✓
	▪ Blood pressure determination	✓	✓	✓
	▪ Orthostatic blood pressure measures (when indicated)	✓		
	▪ Fundoscopic 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	✓		✓
	▪ Screen for depression, anxiety, and disordered eating	✓		✓
	▪ Consider assessment for functional performance*	✓		✓
	▪ Consider assessment for functional performance*	✓		✓

Comprehensive Medical Evaluation and Assessment of Comorbidities:
Standards of Medical Care in Diabetes - 2022. *Diabetes Care* 2022;44(Suppl. 1):S46-S59

LABORATORY EVALUATION	■ A1C, if the results 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 tests#	✓		✓
	• Spot urinary albumin-to-creatinine ratio	✓		✓
	• Serum creatinine and estimated glomerular filtration rate+	✓		✓
	• Thyroid-stimulating hormone in patients with type 1 diabetes#	✓		✓
	• Vitamin B12 if on metformin	✓		✓
	• Serum potassium levels in patients on ACE inhibitors, ARBs, or diuretics+	✓		✓

ABI, ankle-brachial pressure index; ARBs, angiotensin receptor blockers; CGM, continuous glucose monitors; MDI, multiple daily injections; NAFLD, nonalcoholic fatty liver disease; OSA obstructive sleep apnea;PAD, peripheral arterial disease

*At 65 years of age or older

+May be needed more frequently in patients with known chronic kidney disease or with changes in medications that affect kidney function and serum potassium (see Table 11.1)

#May also need to be checked after initiation or dose changes of medications that affect these laboratory values (i.e., diabetes medications, blood pressure medications, cholesterol medications, or thyroid medications)

^In people without dyslipidemia and not on cholesterol-lowering therapy, testing may be less frequent

**Should be performed at every visit in patients with sensory loss, previous foot ulcers, or amputations

Comprehensive Medical Evaluation and Assessment of Comorbidities:
Standards of Medical Care in Diabetes - 2022. *Diabetes Care* 2022;45(Suppl. 1):S46-S59

Table 4.2—Assessment and treatment plan*

Assessing risk of diabetes complications

- ASCVD and heart failure history
- ASCVD risk factors and 10-year ASCVD risk assessment
- Staging of chronic kidney disease (see **Table 11.1**)
- Hypoglycemia risk (see **Table 4.3**)
- Assessment for retinopathy
- Assessment for neuropathy

Goal setting

- Set A1C/blood glucose/time in range target
- If hypertension is present, establish blood pressure target
- Diabetes self-management goals

Therapeutic treatment plans

- Lifestyle management
- Pharmacologic therapy: glucose lowering
- Pharmacologic therapy: cardiovascular and renal disease risk factors
- Use of glucose monitoring and insulin delivery devices
- Referral to diabetes education and medical specialists (as needed)

ASCVD, atherosclerotic cardiovascular disease. *Assessment and treatment planning are essential components of initial and all follow-up visits.

Comprehensive Medical Evaluation and Assessment of Comorbidities:
Standards of Medical Care in Diabetes - 2022. *Diabetes Care* 2022;45(Suppl. 1):S46-S59

Table 4.3—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 behavioral response to hypoglycemia
- Alcohol use
- Polypharmacy (especially ACE inhibitors, angiotensin receptor blockers, nonselective β-blockers)
- History of severe hypoglycemic event

In addition to individual risk factors, consider use of comprehensive risk prediction models (105).

See references 106–110.

Comprehensive Medical Evaluation and Assessment of Comorbidities:
Standards of Medical Care in Diabetes - 2022. *Diabetes Care* 2022;45(Suppl. 1):S46-S59

Table 4.4—Referrals for initial care management

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

Comprehensive Medical Evaluation and Assessment of Comorbidities:
Standards of Medical Care in Diabetes - 2022. *Diabetes Care* 2022;44(Suppl. 1):S46-S59

Medical Nutrition Therapy

Table 5.1—Medical nutrition therapy recommendations

Topic	Recommendation
Effectiveness of nutrition therapy	**5.9** An individualized medical nutrition therapy program as needed to achieve treatment goals, provided by a registered dietitian nutritionist (RD/RDN), preferably one who has comprehensive knowledge and experience in diabetes care, is recommended for all people with type 1 or type 2 diabetes, prediabetes, and gestational diabetes mellitus. **A** **5.10** Because diabetes medical nutrition therapy can result in cost savings **B** and improved outcomes (e.g., A1C reduction, reduced weight, decrease in cholesterol) **A**, medical nutrition therapy should be adequately reimbursed by insurance and other payers. **E**
Energy balance	**5.11** For all patients with overweight or obesity, behavioral modification to achieve and maintain a minimum weight loss of 5% is recommended. **A**
Eating patterns and macronutrient distribution	**5.12** There is no ideal macronutrient pattern for people with diabetes; meal plans should be individualized while keeping total calorie and metabolic goals in mind. **E** **5.13** A variety of eating patterns can be considered for the management of type 2 diabetes and to prevent diabetes in individuals with prediabetes. **B** **5.14** Reducing overall carbohydrate intake for individuals with diabetes has demonstrated the most evidence for improving glycemia and may be applied in a variety of eating patterns that meet individual needs and preferences. **B**

Facilitating Behavior Change and Well-being to Improve Health Outcomes:
Standards of Medical Care in Diabetes - 2021. *Diabetes Care* 2021;44(Suppl. 1):S53-S72

Medical Nutrition Therapy (continued)

Carbohydrates	**5.15** Carbohydrate intake should emphasize nutrient-dense carbohydrate sources that are high in fiber (at least 14 g fiber per 1,000 kcal) and minimally processed. Eating plans should emphasize nonstarchy vegetables, fruits, and whole grains, as well as dairy products, with minimal added sugars. **B** **5.16** People with diabetes and those at risk are advised to replace sugar-sweetened beverages (including fruit juices) with water as much as possible 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** **5.17** When using a flexible insulin therapy program, education on the glycemic impact of carbohydrate **A**, fat, and protein **B** should be tailored to an individual's needs and preferences and used to optimize mealtime insulin dosing. **5.18** When using fixed insulin doses, individuals should be provided education about consistent pattern of carbohydrate intake with respect to time and amount, while considering the insulin action time, as it can result in improved glycemia and reduce the risk for hypoglycemia. **B**
Protein	**5.19** 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**

Facilitating Behavior Change and Well-being to Improve Health Outcomes:
Standards of Medical Care in Diabetes - 2021. *Diabetes Care* 2021;44(Suppl. 1):S53-S72

Medical Nutrition Therapy (continued)

Dietary fat	**5.20** An eating plan emphasizing elements of a Mediterranean-style eating pattern rich in monounsaturated and polyunsaturated fats may be considered to improve glucose metabolism and lower cardiovascular disease risk. **B** **5.21** 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**
Micronutrients and herbal supplements	**5.22** 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	**5.23** 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** **5.24** Educating people with diabetes about the signs, symptoms, and self-management of delayed hypoglycemia after drinking alcohol, especially when using insulin or insulin secretagogues, is recommended. The importance of glucose monitoring after drinking alcoholic beverages to reduce hypoglycemia risk should be emphasized. **B**
Sodium	**5.25** Sodium consumption should be limited to <2,300 mg/day. **B**
Nonnutritive sweeteners	**5.26** The use of nonnutritive sweeteners as a replacement for sugar-sweetened products may reduce overall calorie and carbohydrate intake as long as there is not a compensatory increase of energy intake from other sources. Overall, people are encouraged to decrease both sweetened and nonnutritive-sweetened beverages, with an emphasis on water intake. **B**

Facilitating Behavior Change and Well-being to Improve Health Outcomes:
Standards of Medical Care in Diabetes - 2021. *Diabetes Care* 2021;44(Suppl. 1):S53-S72

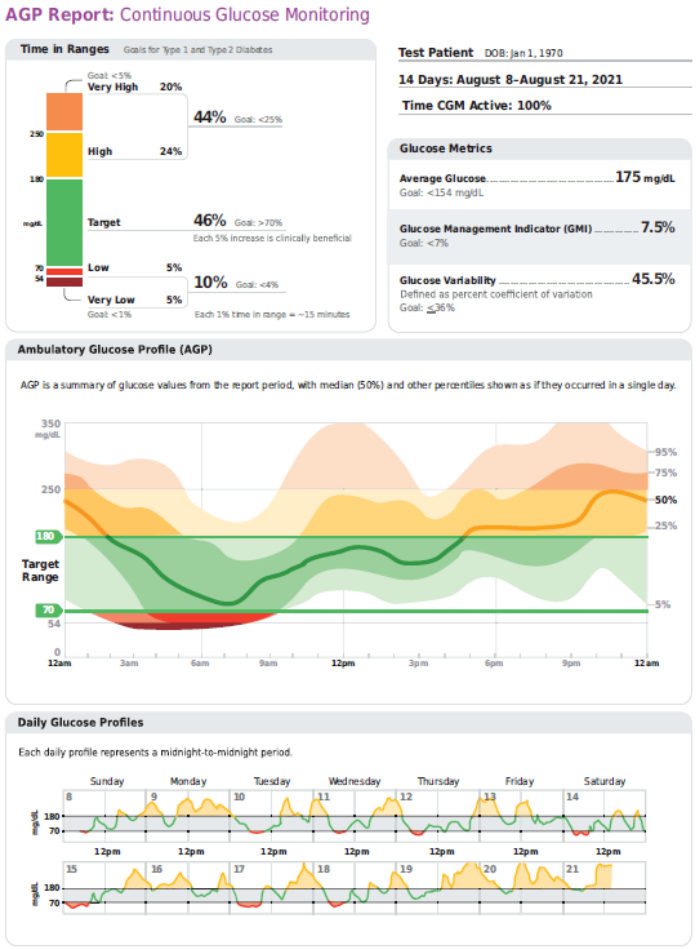
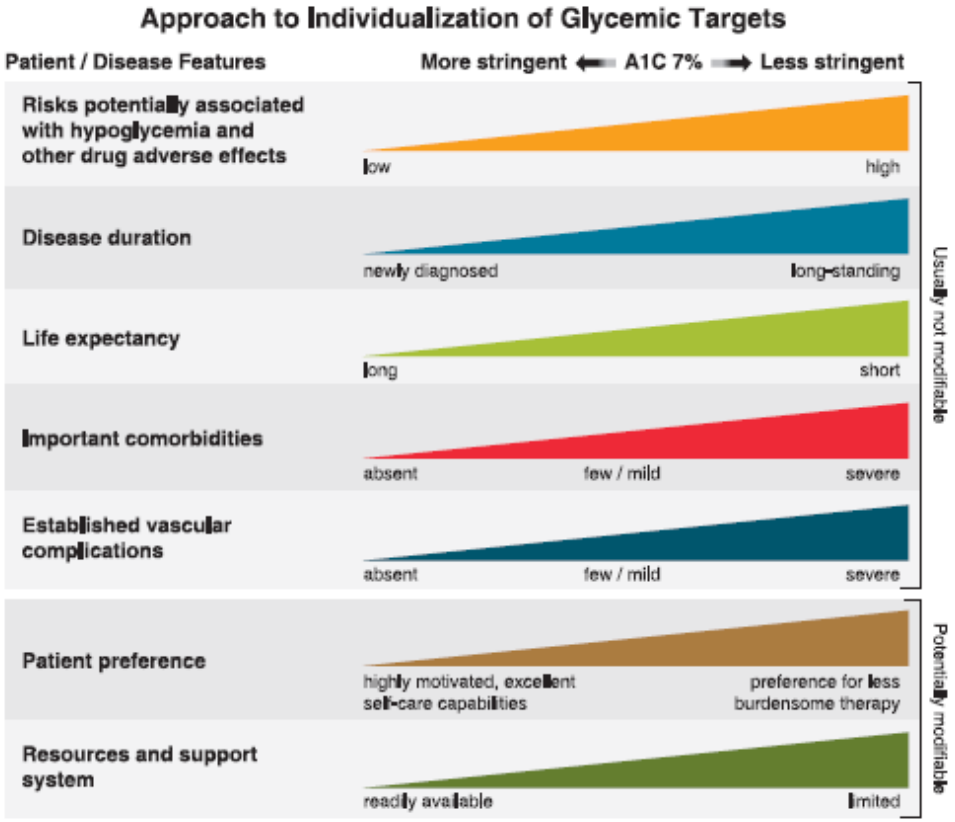


Figure 6.1—Key points included in standard ambulatory glucose profile (AGP) report. Reprinted from Holt et al. (33).

Glycemic Targets:
Standards of Medical Care in Diabetes - 2022. *Diabetes Care* 2022;45(Suppl. 1)



Glycemic Targets:
Standards of Medical Care in Diabetes - 2022. *Diabetes Care* 2022;45(Suppl. 1)

Glycemic targets

Table 6.3—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. #CGM may be used to assess glycemic target as noted in Recommendation 6.5b and **Fig. 6.1**. 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 (as per **Fig.6.2**). †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.

Glycemic Targets:
Standards of Medical Care in Diabetes - 2022. *Diabetes Care* 2022;45(Suppl. 1)

Representative relative attributes of insulin delivery approaches in people with type 1 diabetes[1]

Injected insulin regimens	Flexibility	Lower risk of hypoglycemia	Higher costs
MDI with LAA + RAA or URAA	+++	+++	+++
Less-preferred, alternative injected insulin regimens			
MDI with NPH + RAA or URAA	++	++	++
MDI with NPH + short-acting (regular) insulin	++	+	+
Two daily injections with NPH + short-acting (regular) insulin or premixed	+	+	+

Continuous insulin infusion regimens	Flexibility	Lower risk of hypoglycemia	Higher costs
Hybrid closed-loop technology	+++++	+++++	++++++
Insulin pump with threshold/ predictive low-glucose suspend	++++	++++	+++++
Insulin pump therapy without automation	+++	+++	++++

Pharmacologic Approaches to Glycemic Management: *Standards of Medical Care in Diabetes - 2022*. *Diabetes Care* 2022;45(Suppl. 1):S125-S143

Table 9.1—Examples of subcutaneous insulin regimens

Regimen	Timing and distribution	Advantages	Disadvantages	Adjusting doses
Regimens that more closely mimic normal insulin secretion				
Insulin pump therapy (hybrid closed-loop, low-glucose suspend, CGM-augmented open-loop, BGM-augmented open-loop)	Basal delivery of URAA or RAA; generally 40–60% of TDD. Mealtime and correction: URAA or RAA by bolus based on ICR and/or ISF and target glucose, with pre-meal insulin ~15 min before eating.	Can adjust basal rates for varying insulin sensitivity by time of day, for exercise and for sick days. Flexibility in meal timing and content. Pump can deliver insulin in increments of fractions of units. Potential for integration with CGM for low-glucose suspend or hybrid closed-loop. TIR % highest and TBR % lowest with: hybrid closed-loop > low-glucose suspend > CGM-augmented open-loop > BGM-augmented open-loop.	Most expensive regimen. Must continuously wear one or more devices. Risk of rapid development of ketosis or DKA with interruption of insulin delivery. Potential reactions to adhesives and site infections. Most technically complex approach (harder for people with lower numeracy or literacy skills).	Mealtime insulin: if carbohydrate counting is accurate, change ICR if glucose after meal consistently out of target. Correction insulin: adjust ISF and/or target glucose if correction does not consistently bring glucose into range. Basal rates: adjust based on overnight, fasting, or daytime glucose outside of activity of URAA/RAA bolus.
MDI: LAA + flexible doses of URAA or RAA at meals	LAA once daily (insulin detemir or insulin glargine may require twice-daily dosing); generally 50% of TDD. Mealtime and correction: URAA or RAA based on ICR and/or ISF and target glucose.	Can use pens for all components. Flexibility in meal timing and content. Insulin analogs cause less hypoglycemia than human insulins.	At least four daily injections. Most costly insulins. Smallest increment of insulin is 1 unit (0.5 unit with some pens). LAAs may not cover strong dawn phenomenon (rise in glucose in early morning hours) as well as pump therapy.	Mealtime insulin: if carbohydrate counting is accurate, change ICR if glucose after meal consistently out of target. Correction insulin: adjust ISF and/or target glucose if correction does not consistently bring glucose into range. LAA: based on overnight or fasting glucose or daytime glucose outside of activity time course, or URAA or RAA injections.

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Pharmacologic Approaches to Glycemic Management: *Standards of Medical Care in Diabetes - 2022*. *Diabetes Care* 2022;45(Suppl. 1):S125-S143

Table 9.1—Continued

Regimen	Timing and distribution	Advantages	Disadvantages	Adjusting doses
MDI regimens with less flexibility				
Four injections daily with fixed doses of N and RAA	Pre-breakfast: RAA ~20% of TDD. Pre-lunch: RAA ~10% of TDD. Pre-dinner: RAA ~10% of TDD. Bedtime: N ~50% of TDD.	May be feasible if unable to carbohydrate count. All meals have RAA coverage. N less expensive than LAAs.	Shorter duration RAA may lead to basal deficit during day; may need twice-daily N. Greater risk of nocturnal hypoglycemia with N. Requires relatively consistent mealtimes and carbohydrate intake.	Pre-breakfast RAA: based on BGM after breakfast or before lunch. Pre-lunch RAA: based on BGM after lunch or before dinner. Pre-dinner RAA: based on BGM after dinner or at bedtime. Evening N: based on fasting or overnight BGM.
Four injections daily with fixed doses of N and R	Pre-breakfast: R ~20% of TDD. Pre-lunch: R ~10% of TDD. Pre-dinner: R ~10% of TDD. Bedtime: N ~50% of TDD.	May be feasible if unable to carbohydrate count. R can be dosed based on ICR and correction. All meals have R coverage. Least expensive insulins.	Greater risk of nocturnal hypoglycemia with N. Greater risk of delayed post-meal hypoglycemia with R. Requires relatively consistent mealtimes and carbohydrate intake. R must be injected at least 30 min before meal for better effect.	Pre-breakfast R: based on BGM after breakfast or before lunch. Pre-lunch R: based on BGM after lunch or before dinner. Pre-dinner R: based on BGM after dinner or at bedtime. Evening N: based on fasting or overnight BGM.
Regimens with fewer daily injections				
Three injections daily: N+R or N+RAA	Pre-breakfast: ~40% N + ~15% R or RAA. Pre-dinner: ~15% R or RAA. Bedtime: 30% N.	Morning insulins can be mixed in one syringe. May be appropriate for those who cannot take injections in middle of day. Morning N covers lunch to some extent. Same advantages of RAAs over R. Least (N + R) or less expensive insulins than MDI with analogs.	Greater risk of nocturnal hypoglycemia with N than LAAs. Greater risk of delayed post-meal hypoglycemia with R than RAAs. Requires relatively consistent mealtimes and carbohydrate intake. Coverage of post-lunch glucose often suboptimal. R must be injected at least 30 min before meal for better effect.	Morning N: based on pre-dinner BGM. Morning R: based on pre-lunch BGM. Morning RAA: based on post-breakfast or pre-lunch BGM. Pre-dinner R: based on bedtime BGM. Pre-dinner RAA: based on post-dinner or bedtime BGM. Evening N: based on fasting BGM.

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Pharmacologic Approaches to Glycemic Management: *Standards of Medical Care in Diabetes - 2022*. *Diabetes Care* 2022;45(Suppl. 1):S125-S143

Table 9.1—Continued

Regimen	Timing and distribution	Advantages	Disadvantages	Adjusting doses
Twice-daily "split-mixed": N+R or N+RAA	Pre-breakfast: ~40% N + ~15% R or RAA. Pre-dinner: ~30% N + ~15% R or RAA.	Least number of injections for people with strong preference for this. Insulins can be mixed in one syringe. Least (N+R) or less (N+RAA) expensive insulins vs analogs. Eliminates need for doses during the day.	Risk of hypoglycemia in afternoon or middle of night from N. Fixed mealtimes and meal content. Coverage of post-lunch glucose often suboptimal. Difficult to reach targets for blood glucose without hypoglycemia.	Morning N: based on pre-dinner BGM. Morning R: based on pre-lunch BGM. Morning RAA: based on post-breakfast or pre-lunch BGM. Evening R: based on bedtime BGM. Evening RAA: based on post-dinner or bedtime BGM. Evening N: based on fasting BGM.

BGM, blood glucose monitoring; CGM, continuous glucose monitoring; ICR, insulin:carbohydrate ratio; ISF, insulin sensitivity factor; LAA, long-acting analog; MDI, multiple daily injections; N, NPH insulin; R, short-acting (regular) insulin; RAA, rapid-acting analog; TDD, total daily insulin dose; URAA, ultra-rapid-acting analog. Reprinted from Holt et al. (5).

Pharmacologic Approaches to Glycemic Management:
Standards of Medical Care in Diabetes - 2022. *Diabetes Care* 2022;45(Suppl. 1):S125-S143

Simplified overview of indications for β-cell replacement therapy in people with type 1 diabetes

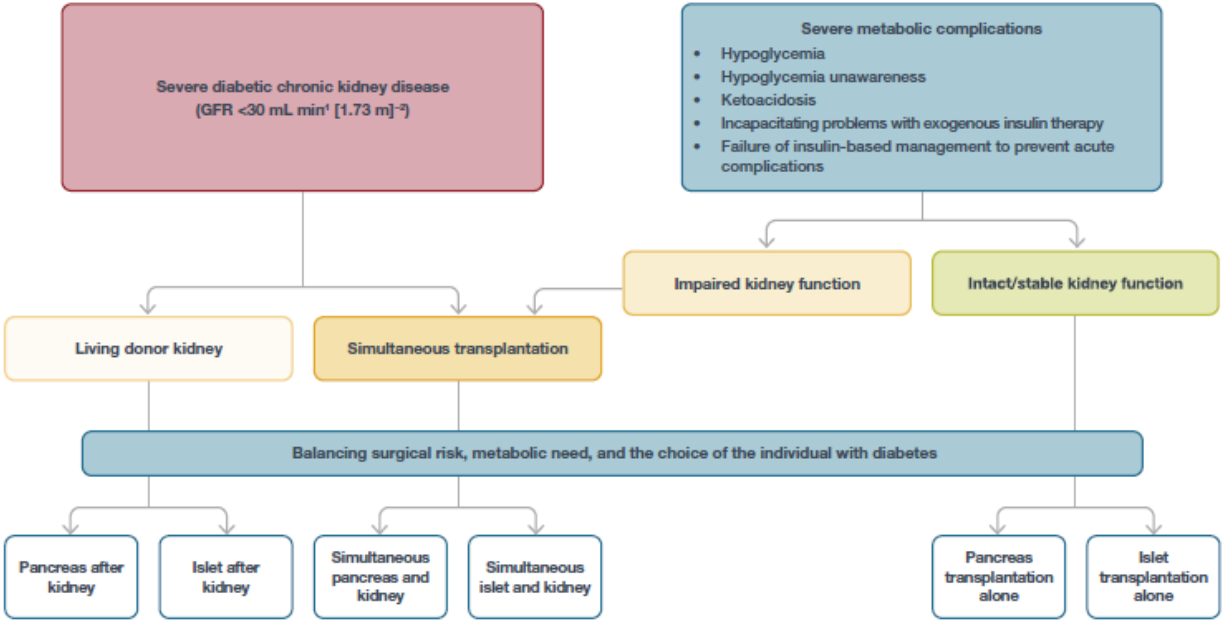

Figure 9.2—Simplified overview of indications for β-cell replacement therapy in people with type 1 diabetes. The two main forms of β-cell replacement therapy are whole-pancreas transplantation or islet cell transplantation. β-Cell replacement therapy can be combined with kidney transplantation if the individual has end-stage renal disease, which may be performed simultaneously or after kidney transplantation. All decisions about transplantation must balance the surgical risk, metabolic need, and the choice of the individual with diabetes. GFR, glomerular filtration rate. Reprinted from Holt et al. (5).

Pharmacologic Approaches to Glycemic Management:
Standards of Medical Care in Diabetes - 2022. *Diabetes Care* 2022;45(Suppl. 1):S125-S143

Table 9.2—Drug-specific and patient factors to consider when selecting antihyperglycemic treatment in adults with type 2 diabetes

	Efficacy (60)	Hypoglycemia	Weight change (109)	CV effects		Cost	Oral/SQ	Renal effects		Additional considerations
				ASCVD	HF			Progression of DKD	Dosing/use considerations*	
Metformin	High	No	Neutral (potential for modest loss)	Potential benefit	Neutral	Low	Oral	Neutral	▪ Contraindicated with eGFR <30 mL/min/1.73 m^2	▪ Gastrointestinal side effects common (diarrhea, nausea) ▪ Potential for B12 deficiency
SGLT2 inhibitors	Intermediate	No	Loss	Benefit: empagliflozin†, canagliflozin†	Benefit: empagliflozin†, canagliflozin, dapagliflozin‡, ertugliflozin	High	Oral	Benefit: canagliflozin§, empagliflozin, dapagliflozin§	▪ See labels for renal dose considerations of individual agents ▪ Glucose-lowering effect is lower for SGLT2 inhibitors at lower eGFR	▪ Should be discontinued before any scheduled surgery to avoid potential risk for DKA ▪ DKA risk (all agents, rare in T2D) ▪ Risk of bone fractures (canagliflozin) ▪ Genitourinary infections ▪ Risk of volume depletion, hypotension ▪ ↑LDL cholesterol ▪ Risk of Fournier's gangrene
GLP-1 RAs	High	No	Loss	Benefit: dulaglutide†, liraglutide†, semaglutide (SQ)† Neutral: exenatide once weekly, lixisenatide	Neutral	High	SQ; oral (semaglutide)	Benefit on renal end points in CVOTs, driven by albuminuria outcomes: liraglutide, semaglutide (SQ), dulaglutide	▪ See labels for renal dose considerations of individual agents ▪ No dose adjustment for dulaglutide, liraglutide, semaglutide ▪ Caution when initiating or increasing dose due to potential risk of nausea, vomiting, diarrhea, or dehydration. Monitor renal function in patients reporting severe adverse GI reactions when initiating or increasing dose of therapy.	▪ **FDA Black Box:** Risk of thyroid C-cell tumors in rodents; human relevance not determined **(liraglutide, dulaglutide, exenatide extended release, semaglutide)** ▪ GI side effects common (nausea, vomiting, diarrhea) ▪ Injection site reactions ▪ Pancreatitis has been reported in clinical trials but causality has not been established. Discontinue if pancreatitis is suspected.
DPP-4 inhibitors	Intermediate	No	Neutral	Neutral	Potential risk: saxagliptin	High	Oral	Neutral	▪ Renal dose adjustment required (sitagliptin, saxagliptin, alogliptin); can be used in renal impairment ▪ No dose adjustment required for linagliptin	▪ Pancreatitis has been reported in clinical trials but causality has not been established. Discontinue if pancreatitis is suspected. ▪ 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: generally not recommended in chronic kidney disease ▪ 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	High	Yes	Gain	Neutral	Neutral	Low (SQ)	SQ; inhaled	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
Insulin — Analogs						High	SQ			

ASCVD, atherosclerotic cardiovascular disease; CV, cardiovascular; CVOT, cardiovascular outcomes trial; DPP-4, dipeptidyl peptidase 4; DKA, diabetic ketoacidosis; DKD, diabetic kidney disease; eGFR, estimated glomerular filtration rate; GI, gastrointestinal; GLP-1 RAs, glucagon-like peptide 1 receptor agonists; HF, heart failure; NASH, nonalcoholic steatohepatitis; SGLT2, sodium–glucose cotransporter 2; SQ, subcutaneous; T2D, type 2 diabetes. *For agent-specific dosing recommendations, please refer to the manufacturers' prescribing information. †FDA-approved for cardiovascular disease benefit. ‡FDA-approved for heart failure indication. §FDA-approved for chronic kidney disease indication.

Pharmacologic Approaches to Glycemic Management: *Standards of Medical Care in Diabetes - 2022*. *Diabetes Care* 2022;45(Suppl. 1):S125-S143

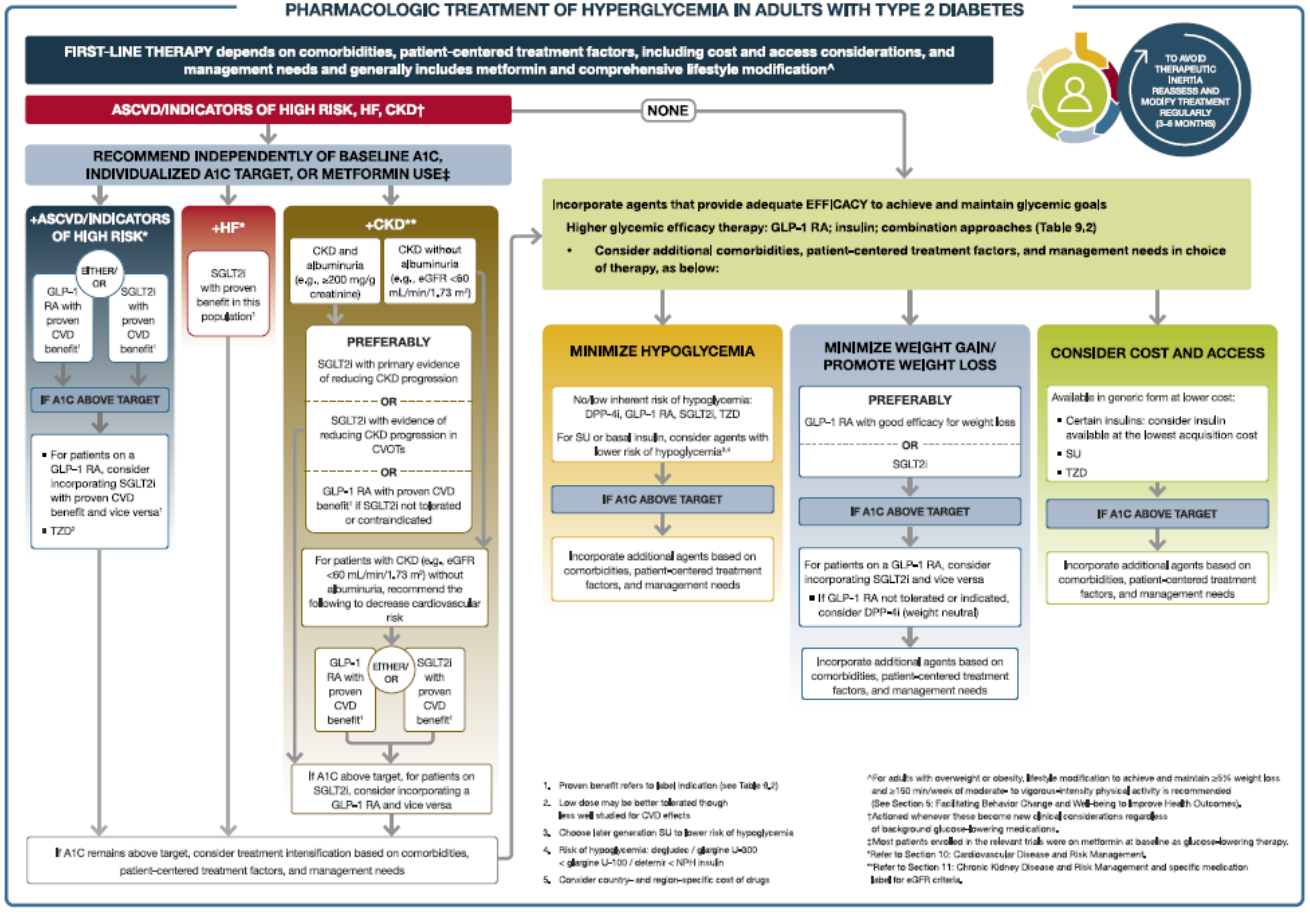

Figure 9.3—Pharmacologic treatment of hyperglycemia in adults with type 2 diabetes. 2022 ADA Professional Practice Committee (PPC) adaptation of Davies et al. (43) and Buse et al. (44). For appropriate context, see **Fig. 4.1**. The 2022 ADA PPC adaptation emphasizes incorporation of therapy rather than sequential add-on, which may require adjustment of current therapies. Therapeutic regimen should be tailored to comorbidities, patient-centered treatment factors, and management needs. ASCVD, atherosclerotic cardiovascular disease; CKD, chronic kidney disease; 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; T2D, type 2 diabetes; TZD, thiazolidinedione.

Glucose-lowering Medication in Type 2 Diabetes: 2021 ADA Professional Practice Committee (PPC) adaptation of Davies et al. and Buse et al.

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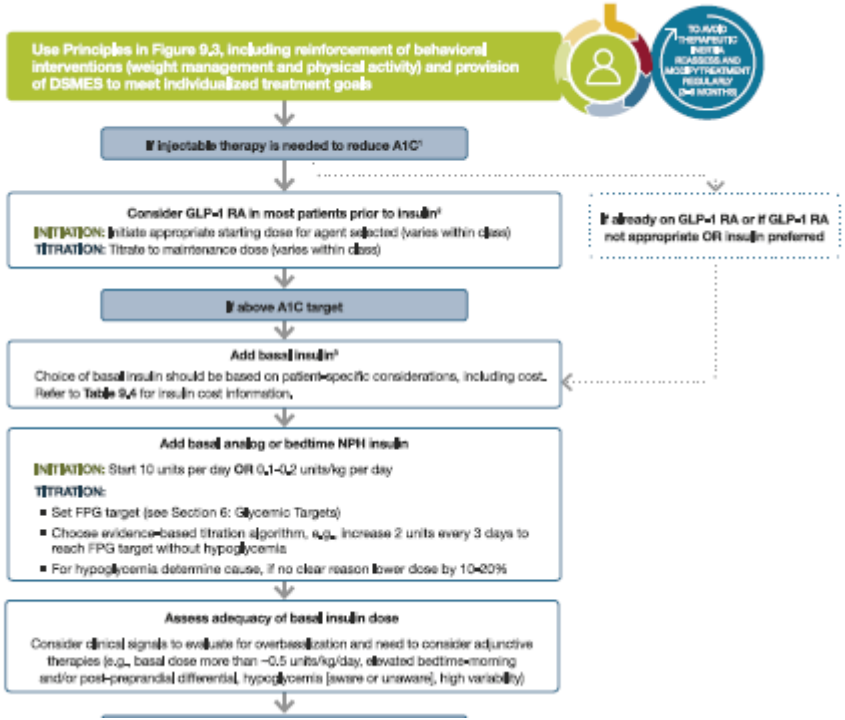
Intensifying to injectable therapies (1 of 2)



Pharmacologic Approaches to Glycemic Management:
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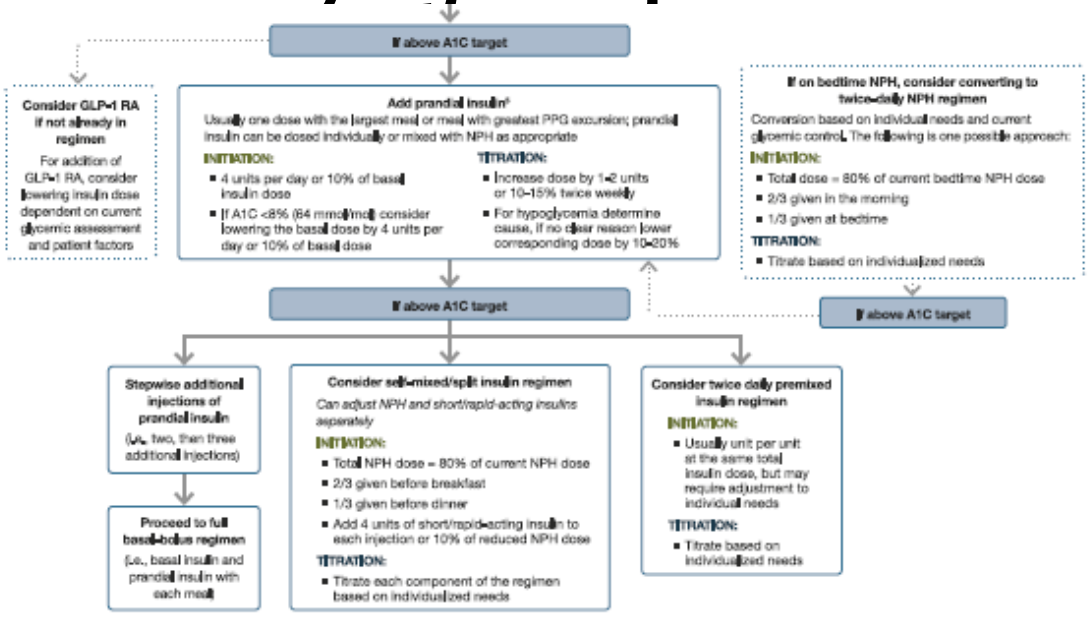
Intensifying to injectable therapies (2 of 2)



1. Consider insulin as the first injectable if evidence of ongoing catabolism, symptoms of hyperglycemia are present, when A1C levels (>10% [86 mmol/mol]) or blood glucose levels (≥300 mg/dL [16.7 mmol/L]) are very high, or a diagnosis of type 1 diabetes is a possibility.
2. When selecting GLP-1 RA, consider: patient preference, A1C lowering, weight-lowering effect, or frequency of injection. If CVD, consider GLP-1 RA with proven CVD benefit. Oral or injectable GLP-1 RA are appropriate.
3. For patients on GLP-1 RA and basal insulin combination, consider use of a fixed-ratio combination product (IDegLira or iGlarLixi).
4. Consider switching from evening NPH to a basal analog if the patient develops hypoglycemia and/or frequently forgets to administer NPH in the evening and would be better managed with an AM dose of a long-acting basal insulin.
5. If adding prandial insulin to NPH, consider initiation of a self-mixed or premixed insulin regimen to decrease the number of injections required.

Figure 9.4—Intensifying to injectable therapies in type 2 diabetes. DSMES, diabetes self-management education and support; FPG, fasting plasma glucose; GLP-1 RA, glucagon-like peptide 1 receptor agonist; max, maximum; PPG, postprandial glucose. Adapted from Davies et al. (43).

Pharmacologic Approaches to Glycemic Management: *Standards of Medical Care in Diabetes - 2022*. *Diabetes Care* 2022;45(Suppl. 1):S125-S143

Table 9.3—Median monthly (30-day) AWP and NADAC of maximum approved daily dose of noninsulin glucose-lowering agents in the U.S.

Class	Compound(s)	Dosage strength/ product (if applicable)	Median AWP (min, max)†	Median NADAC (min, max)†	Maximum approved daily dose*
Biguanides	• Metformin	850 mg (IR)	$108 ($5, $109)	$3	2,550 mg
		1,000 mg (IR)	$87 ($5, $88)	$2	2,000 mg
		1,000 mg (ER)	$242 ($242, $7,214)	$102 ($102, $430)	2,000 mg
Sulfonylureas (2nd generation)	• Glimepiride	4 mg	$74 ($71, $198)	$3	8 mg
	• Glipizide	10 mg (IR)	$68 ($67, $70)	$3	40 mg
		10 mg (XL/ER)	$48	$12	20 mg
	• Glyburide	6 mg (micronized)	$52 ($48, $71)	$11	12 mg
		5 mg	$82 ($63, $93)	$12	20 mg
Thiazolidinediones	• Pioglitazone	45 mg	$348 ($7, $349)	$5	45 mg
	• Rosiglitazone	4 mg	N/A	$324	8 mg
α-Glucosidase inhibitors	• Acarbose	100 mg	$106 ($104, $106)	$26	300 mg
	• Miglitol	100 mg	$284 ($241, $346)	N/A	300 mg
Meglitinides (glinides)	• Nateglinide	120 mg	$155	$28	360 mg
	• Repaglinide	2 mg	$878 ($58, $897)	$34	16 mg
DPP-4 inhibitors	• Alogliptin	25 mg	$234	$166	25 mg
	• Saxagliptin	5 mg	$549	$438	5 mg
	• Linagliptin	5 mg	$583	$466	5 mg
	• Sitagliptin	100 mg	$596	$477	100 mg
SGLT2 inhibitors	• Ertugliflozin	15 mg	$372	$297	15 mg
	• Dapagliflozin	10 mg	$639	$511	10 mg
	• Canagliflozin	300 mg	$652	$521	300 mg
	• Empagliflozin	25 mg	$658	$526	25 mg
GLP-1 RAs	• Exenatide (extended release)	2 mg powder for suspension or pen	$909	$727	2 mg**
	• Exenatide	10 μg pen	$933	$746	20 μg
	• Dulaglutide	4.5 mg mL pen	$1,013	$811	4.5 mg**
	• Semaglutide	1 mg pen	$1,022	$822	1 mg**
		14 mg (tablet)	$1,022	$819	14 mg
	• Liraglutide	1.8 mg pen	$1,220	$975	1.8 mg
	• Lixisenatide	20 μg pen	$814	N/A	20 μg
Bile acid sequestrant	• Colesevelam	625 mg tabs	$710 ($674, $712)	$75	3.75 g
		3.75 g suspension	$674	$222	3.75 g
Dopamine-2 agonist	• Bromocriptine	0.8 mg	$1,036	$833	4.8 mg
Amylin mimetic	• Pramlintide	120 μg pen	$2,702	N/A	120 μg/injection††

AWP, average wholesale price; DPP-4, dipeptidyl peptidase 4; ER and XL, extended release; GLP-1 RA, glucagon-like peptide 1 receptor agonist; IR, immediate release; max, maximum; min, minimum; N/A, data not available; NADAC, National Average Drug Acquisition Cost; SGLT2, sodium–glucose cotransporter 2. †Calculated for 30-day supply (AWP [70] or NADAC [71] unit price × number of doses required to provide maximum approved daily dose × 30 days); median AWP or NADAC listed alone when only one product and/or price. *Utilized to calculate median AWP and NADAC (min, max); generic prices used, if available commercially. **Administered once weekly. ††AWP and NADAC calculated based on 120 μg three times daily.

Median monthly cost of maximum approved daily dose of noninsulin glucose-lowering agents in the U.S.

Pharmacologic Approaches to Glycemic Management: *Standards of Medical Care in Diabetes - 2022*. *Diabetes Care* 2022;45(Suppl. 1):S125-S143

Table 9.4—Median cost of insulin products in the U.S. calculated as AWP (70) and NADAC (71) per 1,000 units of specified dosage form/product

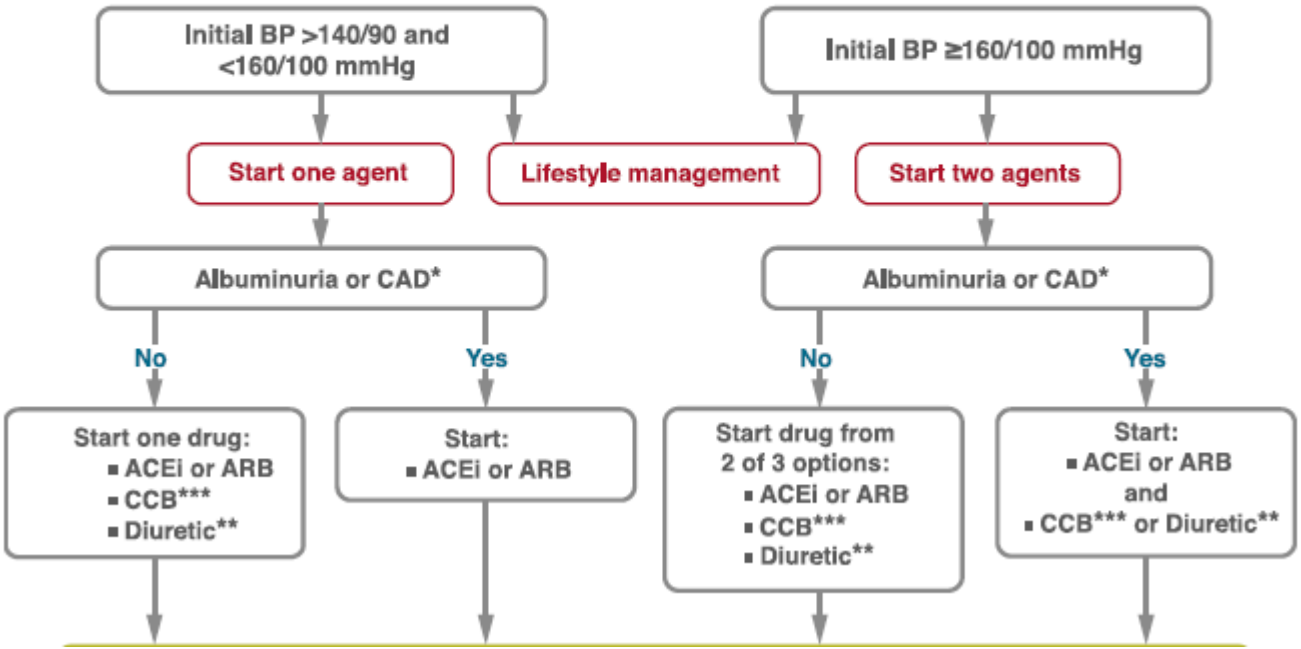
Insulins	Compounds	Dosage form/product	Median AWP (min, max)*	Median NADAC*
Rapid-acting	• Lispro follow-on product	U-100 vial	$157	$125
		U-100 prefilled pen	$202	$161
	• Lispro	U-100 vial	$165†	$132†
		U-100 cartridge	$408	$325
		U-100 prefilled pen	$212†	$170†
		U-200 prefilled pen	$424	$339
	• Lispro-aabc	U-100 vial	$330	N/A
		U-100 prefilled pen	$424	N/A
		U-200 prefilled pen	$424	N/A
	• Glulisine	U-100 vial	$341	$272
		U-100 prefilled pen	$439	$352
	• Aspart	U-100 vial	$174†	$139†
		U-100 cartridge	$215	$172
		U-100 prefilled pen	$223†	$179†
	• Aspart ("faster acting product")	U-100 vial	$347	$278
		U-100 cartridge	$430	N/A
		U-100 prefilled pen	$447	$356
	• Inhaled insulin	Inhalation cartridges	$1,325	$606
Short-acting	• human regular	U-100 vial	$165††	$132††
		U-100 prefilled pen	$208	$167
Intermediate-acting	• human NPH	U-100 vial	$165††	$132††
		U-100 prefilled pen	$208	$167
Concentrated human regular insulin	• U-500 human regular insulin	U-500 vial	$178	$143
		U-500 prefilled pen	$230	$184
Long-acting	• Glargine follow-on products	U-100 prefilled pen	$118	$96
		U-100 vial	$190 (118, 261)	$95
	• Glargine	U-100 vial; U-100 prefilled pen	$340	$277
		U-300 prefilled pen	$340	$272
	• Detemir	U-100 vial; U-100 prefilled pen	$370	$296
	• Degludec	U-100 vial; U-100 prefilled pen; U-200 prefilled pen	$407	$325
Premixed insulin products	• NPH/regular 70/30	U-100 vial	$165††	$133††
		U-100 prefilled pen	$208	$167
	• Lispro 50/50	U-100 vial	$342	$274
		U-100 prefilled pen	$424	$338
	• Lispro 75/25	U-100 vial	$152	$273
		U-100 prefilled pen	$212	$170
	• Aspart 70/30	U-100 vial	$180	$144
		U-100 prefilled pen	$224	$179
Premixed insulin/GLP-1 RA products	• Glargine/Lixisenatide	100/33 μg prefilled pen	$619	$495
	• Degludec/Liraglutide	100/3.6 μg prefilled pen	$917	$732

AWP, average wholesale price; GLP-1 RA, glucagon-like peptide 1 receptor agonist; N/A, not available; NADAC, National Average Drug Acquisition Cost *AWP or NADAC calculated as in **Table 9.3**. †Generic prices used when available. ††AWP and NADAC data presented do not include vials of regular human insulin and NPH available at Walmart for approximately $25/vial; median listed alone when only one product and/or price.

Median cost of insulin products in the U.S. calculated as AWP and NADAC per 1,000 units of specified dosage

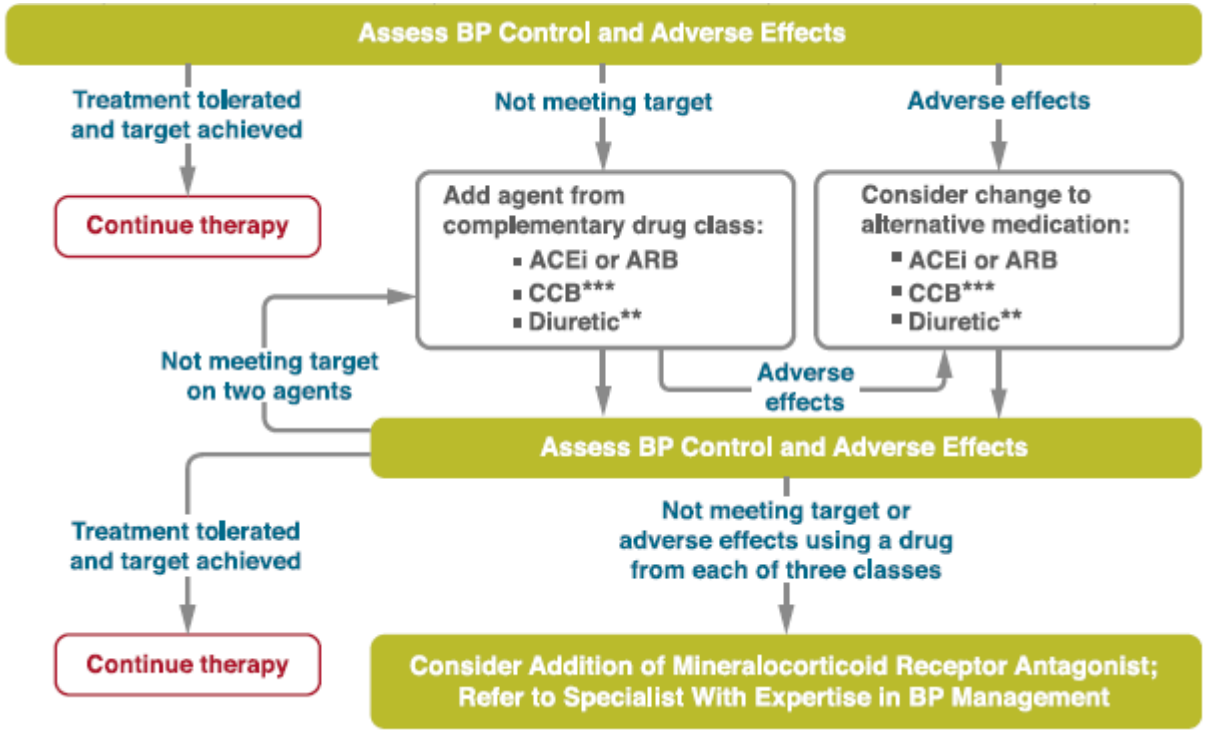
Pharmacologic Approaches to Glycemic Management: *Standards of Medical Care in Diabetes - 2022*. *Diabetes Care* 2022;45(Suppl. 1):S125-S143

Recommendations for the Treatment of Confirmed Hypertension in People With Diabetes



Recommendations for the Treatment of Confirmed Hypertension in People with Diabetes (1 of 2)

Cardiovascular Disease and Risk Management:
Standards of Medical Care in Diabetes - 2022. *Diabetes Care* 2022;45(Suppl. 1):S144-S174



Recommendations for the Treatment of Confirmed Hypertension in People with Diabetes (2 of 2)

Cardiovascular Disease and Risk Management:
Standards of Medical Care in Diabetes - 2022. *Diabetes Care* 2022;45(Suppl. 1):S144-S174

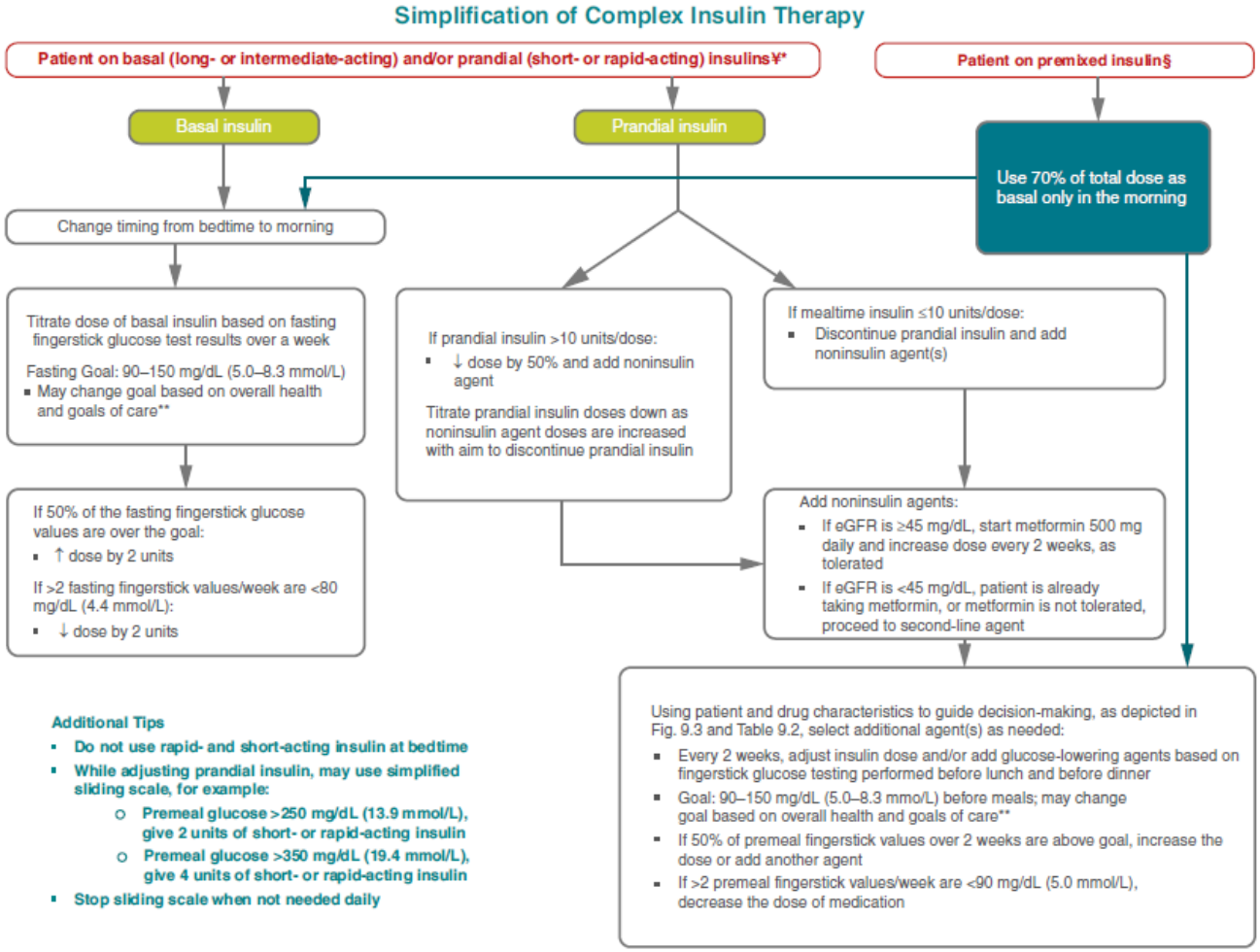


Figure 13.1—Algorithm to simplify insulin regimen for older patients with type 2 diabetes.

Older Adults: *Standards of Medical Care in Diabetes - 2022*. *Diabetes Care* 2022;42(Suppl. 1)

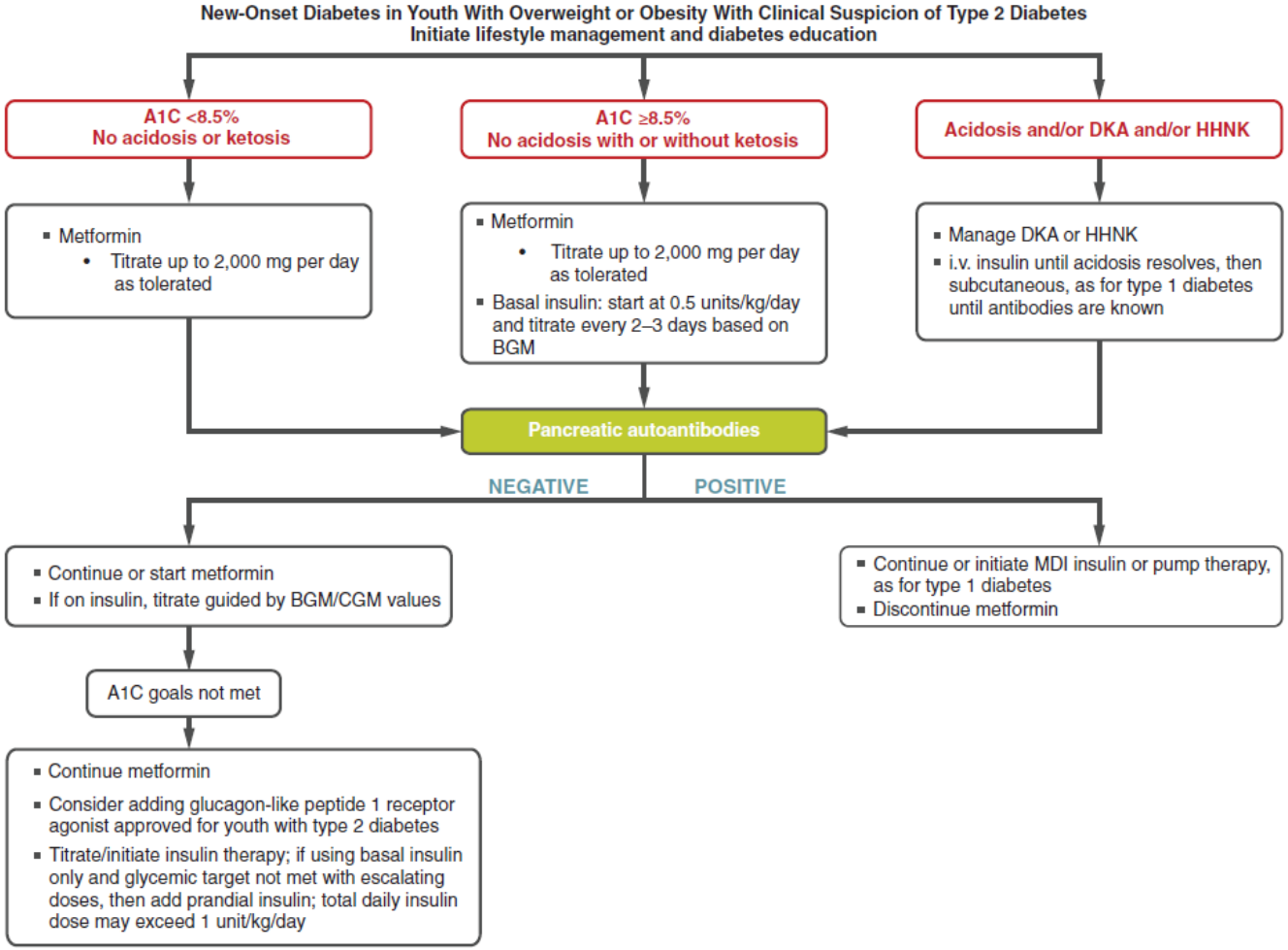


Figure 14.1—Management of new-onset diabetes in youth with overweight or obesity.

Children & Adolescents: *Standards of Medical Care in Diabetes - 2022*. *Diabetes Care* 2022;45(Suppl. 1)

MANAGEMENT OF DIABETES IN PREGNANCY

Table 15.1—Checklist for preconception care for women with diabetes (17,19)

Preconception education should include:

- ☐ Comprehensive nutrition assessment and recommendations for:
  - Overweight/obesity or underweight
  - Meal planning
  - Correction of dietary nutritional deficiencies
  - Caffeine intake
  - Safe food preparation technique
- ☐ Lifestyle recommendations for:
  - Regular moderate exercise
  - Avoidance of hyperthermia (hot tubs)
  - Adequate sleep
- ☐ Comprehensive diabetes self-management education
- ☐ Counseling on diabetes in pregnancy per current standards, including: natural history of insulin resistance in pregnancy and postpartum; preconception glycemic targets; avoidance of DKA/severe hyperglycemia; avoidance of severe hypoglycemia; progression of retinopathy; PCOS (if applicable); fertility in patients with diabetes; genetics of diabetes; risks to pregnancy including miscarriage, still birth, congenital malformations, macrosomia, preterm labor and delivery, hypertensive disorders in pregnancy, etc.
- ☐ Supplementation
  - Folic acid supplement (400 μg routine)
  - Appropriate use of over-the-counter medications and supplements

Medical assessment and plan should include:

- ☐ General evaluation of overall health
- ☐ Evaluation of diabetes and its comorbidities and complications, including: DKA/severe hyperglycemia; severe hypoglycemia/hypoglycemia unawareness; barriers to care; comorbidities such as hyperlipidemia, hypertension, NAFLD, PCOS, and thyroid dysfunction; complications such as macrovascular disease, nephropathy, neuropathy (including autonomic bowel and bladder dysfunction), and retinopathy
- ☐ Evaluation of obstetric/gynecologic history, including history of: cesarean section, congenital malformations or fetal loss, current methods of contraception, hypertensive disorders of pregnancy, postpartum hemorrhage, preterm delivery, previous macrosomia, Rh incompatibility, and thrombotic events (DVT/PE)
- ☐ Review of current medications and appropriateness during pregnancy

Management of Diabetes in Pregnancy:
Standards of Medical Care in Diabetes - 2022. *Diabetes Care* 2022;45(Suppl. 1)

MANAGEMENT OF DIABETES IN PREGNANCY

Screening should include:

- ☐ Diabetes complications and comorbidities, including: comprehensive foot exam; comprehensive ophthalmologic exam; ECG in women starting at age 35 years who have cardiac signs/symptoms or risk factors and, if abnormal, further evaluation; lipid panel; serum creatinine; TSH; and urine protein-to-creatinine ratio
- ☐ Anemia
- ☐ Genetic carrier status (based on history):
  - Cystic fibrosis
  - Sickle cell anemia
  - Tay-Sachs disease
  - Thalassemia
  - Others if indicated
- ☐ Infectious disease
  - *Neisseria gonorrhea/Chlamydia trachomatis*
  - Hepatitis C
  - HIV
  - Pap smear
  - Syphilis

Immunizations should include:

- ☐ Rubella
- ☐ Varicella
- ☐ Hepatitis B
- ☐ Influenza
- ☐ Others if indicated

Preconception plan should include:

- ☐ Nutrition and medication plan to achieve glycemic targets prior to conception, including appropriate implementation of monitoring, continuous glucose monitoring, and pump technology
- ☐ Contraceptive plan to prevent pregnancy until glycemic targets are achieved
- ☐ Management plan for general health, gynecologic concerns, comorbid conditions, or complications, if present, including: hypertension, nephropathy, retinopathy; Rh incompatibility; and thyroid dysfunction

Management of Diabetes in Pregnancy:
Standards of Medical Care in Diabetes - 2022. *Diabetes Care* 2022;45(Suppl. 1)