
Metabolic Surgery (continued)

8.23 People who undergo metabolic surgery should routinely be evaluated to assess the need for ongoing mental health services to help with the adjustment to medical and psychosocial changes after surgery. **C**

Pharmacologic Therapy for Type 1 Diabetes

- 9.1 Most individuals with type 1 diabetes should be treated with multiple daily injections of prandial and basal insulin, or continuous subcutaneous insulin infusion. **A**
- 9.2 Most individuals with type 1 diabetes should use rapid-acting insulin analogs to reduce hypoglycemia risk. **A**
- 9.3 Individuals with type 1 diabetes should receive education on how to match mealtime insulin doses to carbohydrate intake, fat and protein content, and anticipated physical activity. **C**

Pharmacologic Therapy for Type 2 Diabetes

- 9.4a** First-line therapy depends on comorbidities, patient-centered treatment factors, and management needs and generally includes metformin and comprehensive lifestyle modification. **A**
- 9.4b** Other medications (glucagonlike peptide 1 receptor agonists, sodium–glucose cotransporter 2 inhibitors), with or without metformin based on glycemic needs, are appropriate initial therapy for individuals with type 2 diabetes with or at high risk for atherosclerotic cardiovascular disease, heart failure, and/or chronic kidney disease **(Fig. 9.3)**. **A**
- 9.5** Metformin should be continued upon initiation of insulin therapy (unless contraindicated or not tolerated) for ongoing glycemic and metabolic benefits. **A**

Pharmacologic Therapy for Type 2 Diabetes (continued)

9.6 Early combination therapy can be considered in some patients at treatment initiation to extend the time to treatment failure. **E**

9.7 The early introduction of insulin should be considered if there is evidence of ongoing catabolism (weight loss), if symptoms of hyperglycemia are present, or when A1C levels ($>10\%$ [86 mmol/mol]) or blood glucose levels (>300 mg/dL [16.7 mmol/L]) are very high. **A**

Pharmacologic Therapy for Type 2 Diabetes (continued)

- 9.8 A patient-centered approach should guide the choice of pharmacologic agents. Consider the effects on cardiovascular and renal comorbidities, efficacy, hypoglycemia risk, impact on weight, cost and access, risk for side effects, and patient preferences (Table 9.2 and Fig. 9.3). **E**
- 9.9 Among individuals with type 2 diabetes who have established atherosclerotic cardiovascular disease or indicators of high cardiovascular risk, established kidney disease, or heart failure, a sodium–glucose cotransporter 2 inhibitor and/or glucagon-like peptide 1 receptor agonist with demonstrated cardiovascular benefit (Fig. 9.3, Table 9.2, Table 10.3B, and Table 10.3C) is recommended as part of the glucose-lowering regimen and comprehensive cardiovascular risk reduction, independent of A1C and in consideration of patient-specific factors (Fig. 9.3) (see Section 10, “Cardiovascular Disease and Risk Management,” <https://doi.org/10.2337/dc22-S010>, for details on cardiovascular risk reduction recommendations). **A**

Pharmacologic Therapy for Type 2 Diabetes (continued)

- 9.10 In patients with type 2 diabetes, a glucagon-like peptide 1 receptor agonist is preferred to insulin when possible. **A**
- 9.11 If insulin is used, combination therapy with a glucagon-like peptide 1 receptor agonist is recommended for greater efficacy and durability of treatment effect. **A**
- 9.12 Recommendation for treatment intensification for patients not meeting treatment goals should not be delayed. **A**

Pharmacologic Therapy for Type 2 Diabetes (continued)

9.13 Medication regimen and medication-taking behavior should be reevaluated at regular intervals (every 3–6 months) and adjusted as needed to incorporate specific factors that impact choice of treatment (Fig. 4.1 and Table 9.2). **E**

9.14 Clinicians should be aware of the potential for overbasalization with insulin therapy. Clinical signals that may prompt evaluation of overbasalization include basal dose more than 0.5 IU/kg/day, high bedtime-morning or postprandial glucose differential, hypoglycemia (aware or unaware), and high glycemic variability. Indication of overbasalization should prompt reevaluation to further individualize therapy. **E**

PHARMACOLOGIC APPROACHES TO GLYCEMIC TREATMENT

Representative relative attributes of insulin delivery approaches in people with type 1 diabetes¹

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	+++	+++	++++

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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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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.

Continued on p. S130

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PHARMACOLOGIC APPROACHES TO GLYCEMIC TREATMENT

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).

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

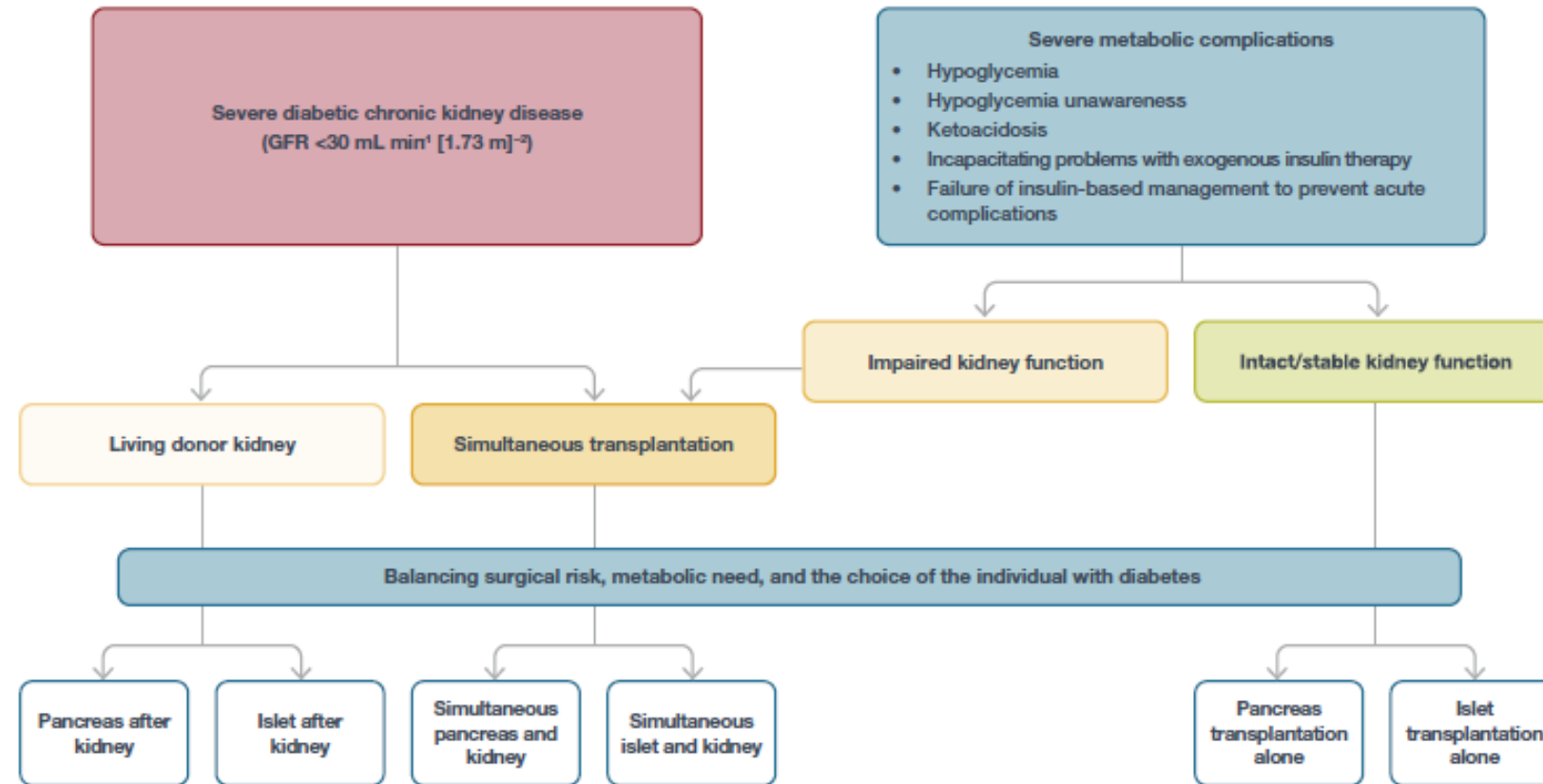


Figure 9.2—Simplified overview of indications for β -cell replacement therapy in people with type 1 diabetes. The two main forms of β -cell replacement therapy are whole-pancreas transplantation or islet cell transplantation. β -Cell replacement therapy can be combined with kidney transplantation if 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:

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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	<ul style="list-style-type: none">Contraindicated with eGFR <30 mL/min/1.73 m²	<ul style="list-style-type: none">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 [§]	<ul style="list-style-type: none">See labels for renal dose considerations of individual agentsGlucose-lowering effect is lower for SGLT2 inhibitors at lower eGFR	<ul style="list-style-type: none">Should be discontinued before any scheduled surgery to avoid potential risk for DKADKA risk (all agents, rare in T2D)Risk of bone fractures (canagliflozin)Genitourinary infectionsRisk of volume depletion, hypotension↑LDL cholesterolRisk of Fournier's gangrene
GLP-1 RAs		High	No	Loss	Benefit: dulaglutide [‡] , liraglutide [‡] , semaglutide (SQ) [‡]	Neutral	High	SQ; oral (semaglutide)	Benefit on renal end points in CVOTs, driven by albuminuria outcomes: liraglutide, semaglutide (SQ), dulaglutide	<ul style="list-style-type: none">See labels for renal dose considerations of individual agentsNo dose adjustment for dulaglutide, liraglutide, semaglutideCaution 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.	<ul style="list-style-type: none">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 reactionsPancreatitis has been reported in clinical trials but causality has not been established. Discontinue if pancreatitis is suspected.
					Neutral: exenatide once weekly, lixisenatide						
DPP-4 inhibitors		Intermediate	No	Neutral	Neutral	Potential risk: saxagliptin	High	Oral	Neutral	<ul style="list-style-type: none">Renal dose adjustment required (sitagliptin, saxagliptin, alogliptin); can be used in renal impairmentNo dose adjustment required for linagliptin	<ul style="list-style-type: none">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	<ul style="list-style-type: none">No dose adjustment requiredGenerally not recommended in renal impairment due to potential for fluid retention	<ul style="list-style-type: none">FDA Black Box: Congestive heart failure (pioglitazone, rosiglitazone)Fluid retention (edema; heart failure)Benefit in NASHRisk of bone fracturesBladder cancer (pioglitazone)↑LDL cholesterol (rosiglitazone)
Sulfonylureas (2nd generation)		High	Yes	Gain	Neutral	Neutral	Low	Oral	Neutral	<ul style="list-style-type: none">Glyburide: generally not recommended in chronic kidney diseaseGlipizide and glimepiride: initiate conservatively to avoid hypoglycemia	<ul style="list-style-type: none">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	<ul style="list-style-type: none">Lower insulin doses required with a decrease in eGFR; titrate per clinical response	<ul style="list-style-type: none">Injection site reactionsHigher risk of hypoglycemia with human insulin (NPH or premixed formulations) vs. analogs
	Analog						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.

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PHARMACOLOGIC TREATMENT OF HYPERGLYCEMIA IN ADULTS WITH TYPE 2 DIABETES

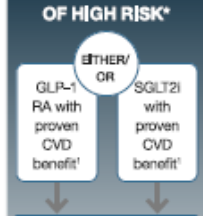
FIRST-LINE THERAPY depends on comorbidities, patient-centered treatment factors, including cost and access considerations, and management needs and generally includes metformin and comprehensive lifestyle modification^A



ASCVD/INDICATORS OF HIGH RISK, HF, CKD†

RECOMMEND INDEPENDENTLY OF BASELINE A1C, INDIVIDUALIZED A1C TARGET, OR METFORMIN USE‡

+ASCVD/INDICATORS OF HIGH RISK*

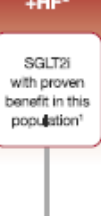


IF A1C ABOVE TARGET

- For patients on a GLP-1 RA, consider incorporating SGLT2i with proven CVD benefit and vice versa†
- TZD§

IF A1C remains above target, consider treatment intensification based on comorbidities, patient-centered treatment factors, and management needs

+HF*

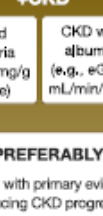


IF A1C ABOVE TARGET

- For patients on a GLP-1 RA, consider incorporating SGLT2i with proven CVD benefit and vice versa†
- TZD§

IF A1C remains above target, consider treatment intensification based on comorbidities, patient-centered treatment factors, and management needs

+CKD**



PREFERABLY

- SGLT2i with primary evidence of reducing CKD progression
- OR
- SGLT2i with evidence of reducing CKD progression in CVOTs
- OR
- GLP-1 RA with proven CVD benefit† if SGLT2i not tolerated or contraindicated

IF A1C remains above target, consider treatment intensification based on comorbidities, patient-centered treatment factors, and management needs

For patients with CKD (e.g., eGFR <60 mL/min/1.73 m²) without albuminuria, recommend the following to decrease cardiovascular risk



IF A1C ABOVE TARGET

- For patients on a GLP-1 RA, consider incorporating SGLT2i and vice versa
- For patients on a SGLT2i, consider incorporating a GLP-1 RA and vice versa

IF A1C remains above target, consider treatment intensification based on comorbidities, patient-centered treatment factors, and management needs

NONE

Incorporate agents that provide adequate EFFICACY to achieve and maintain glycemic goals

Higher glycemic efficacy therapy: GLP-1 RA; insulin; combination approaches (Table 9.2)

- Consider additional comorbidities, patient-centered treatment factors, and management needs in choice of therapy, as below:

MINIMIZE HYPOGLYCEMIA

- No/low inherent risk of hypoglycemia: DPP-4i, GLP-1 RA, SGLT2i, TZD
- For SU or basal insulin, consider agents with lower risk of hypoglycemia^{1,4}

IF A1C ABOVE TARGET

- Incorporate additional agents based on comorbidities, patient-centered treatment factors, and management needs

MINIMIZE WEIGHT GAIN/PROMOTE WEIGHT LOSS

- PREFERABLY**
- GLP-1 RA with good efficacy for weight loss
- OR
- SGLT2i

IF A1C ABOVE TARGET

- For patients on a GLP-1 RA, consider incorporating SGLT2i and vice versa
- If GLP-1 RA not tolerated or indicated, consider DPP-4i (weight neutral)

- Incorporate additional agents based on comorbidities, patient-centered treatment factors, and management needs

CONSIDER COST AND ACCESS

- Available in generic form at lower cost:
- Certain insulins: consider insulin available at the lowest acquisition cost
- SU
- TZD

IF A1C ABOVE TARGET

- Incorporate additional agents based on comorbidities, patient-centered treatment factors, and management needs

- Proven benefit refers to label indication (see Table 9.2)
- Low dose may be better tolerated though less well studied for CVD effects
- Choose later generation SU to lower risk of hypoglycemia
- Risk of hypoglycemia: degludec / glargine U-300 < glargine U-100 / detemir < NPH insulin
- Consider country- and region-specific cost of drugs

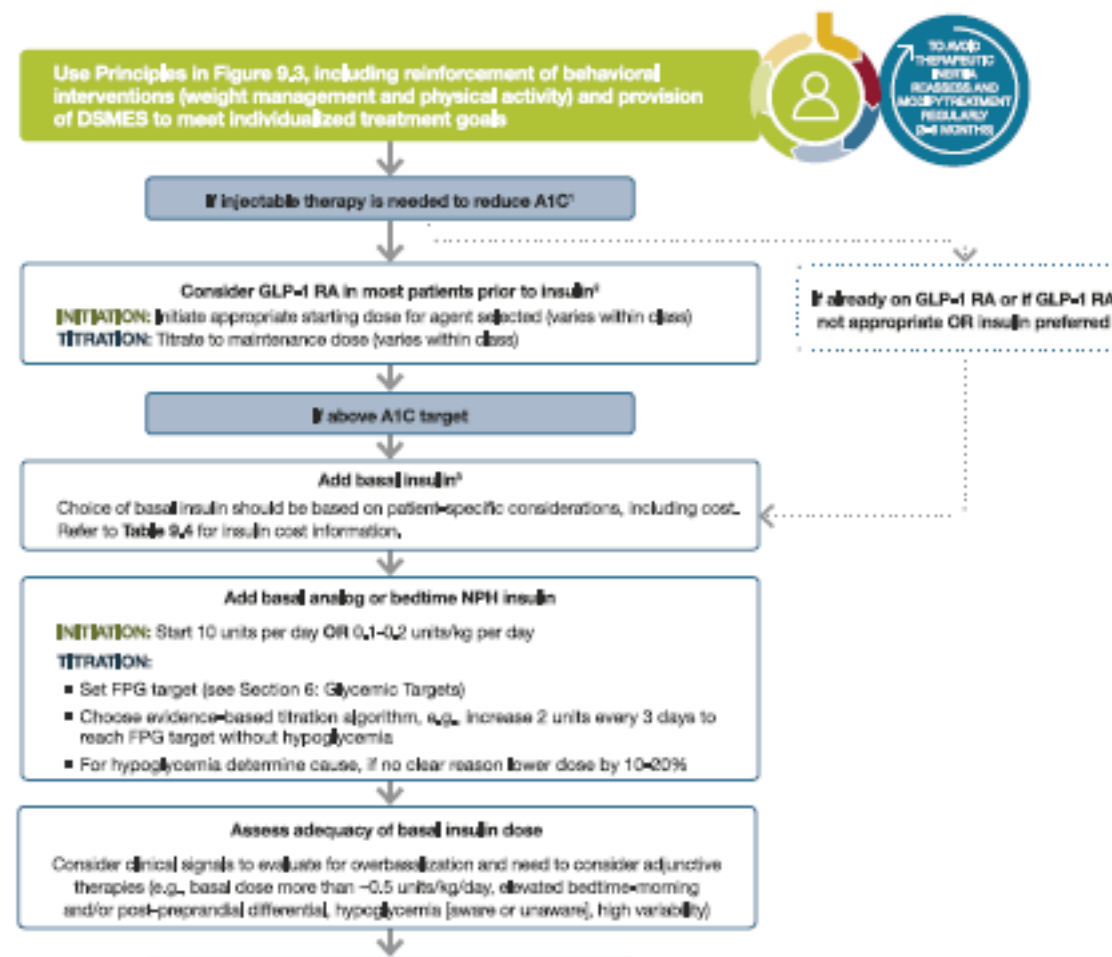
- ^AFor adults with overweight or obesity, lifestyle modification to achieve and maintain ≥5% weight loss and ≥150 min/week of moderate- to vigorous-intensity physical activity is recommended (See Section 5: Facilitating Behavior Change and Well-being to Improve Health Outcomes).
- [†]Actioned whenever 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.
- [§]Refer to Section 11: Cardiovascular Disease and Risk Management.
- ^{||}Refer to Section 11: Chronic Kidney Disease and Risk Management and specific medication label for eGFR criteria.

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

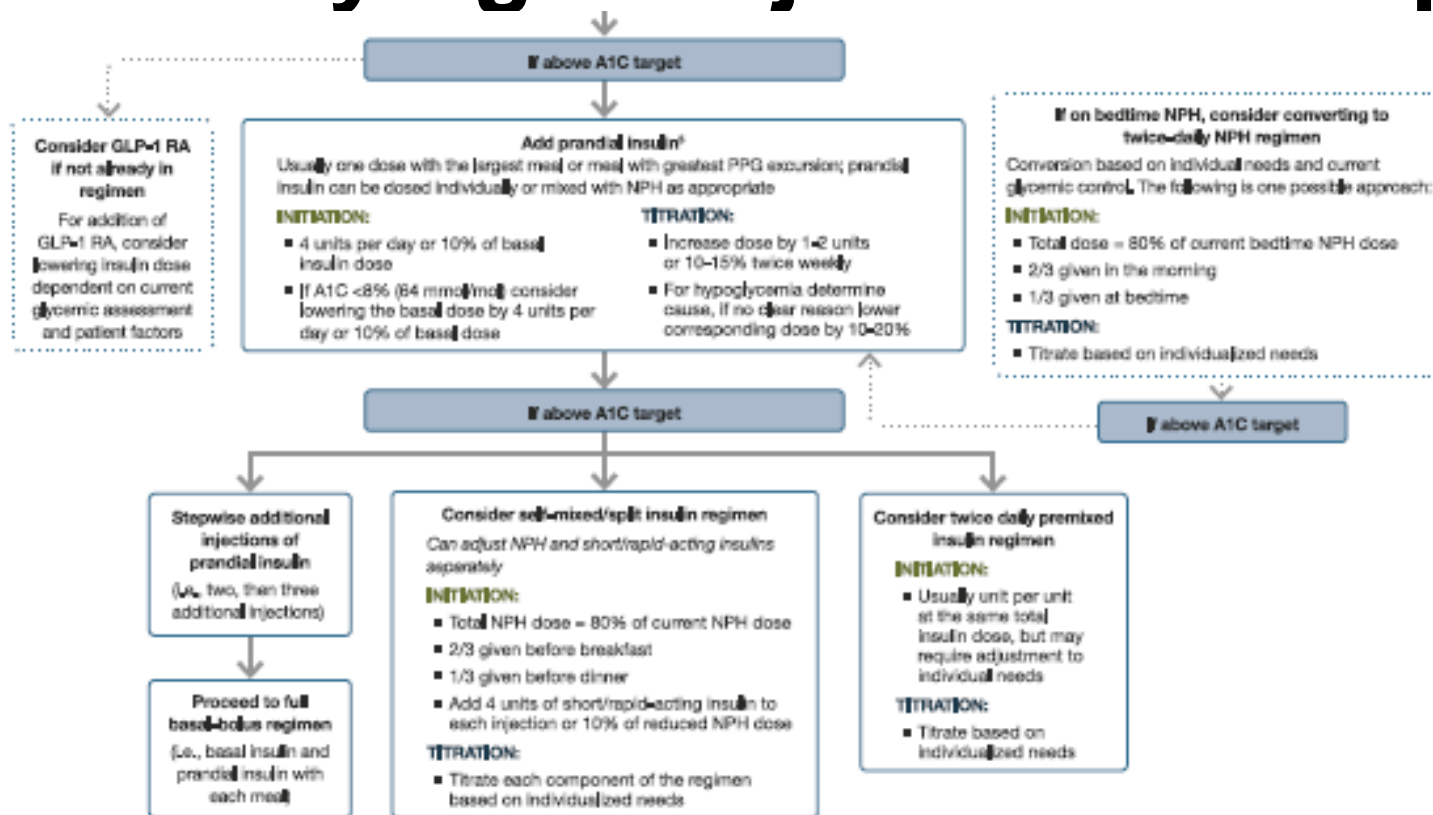
Pharmacologic Approaches to Glycemic Management: *Standards of Medical Care in Diabetes - 2022. Diabetes Care* 2022;45(Suppl. 1):S125-S143

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; TZD, type 2 diabetes; TZD, thiazolidinedione.

Intensifying to injectable therapies (1 of 2)



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-loss 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 (DegLin or IDegLid).
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).

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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
		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.

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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
	• Aspart	U-100 prefilled pen	\$439	\$352
		U-100 vial	\$174†	\$139†
	• Aspart ("faster acting product")	U-100 cartridge	\$215	\$172
		U-100 prefilled pen	\$223†	\$179†
		U-100 vial	\$347	\$278
		U-100 cartridge	\$430	N/A
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

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Screening and Diagnosis

- 10.1** Blood pressure should be measured at every routine clinical visit. When possible, patients found to have elevated blood pressure ($\geq 140/90$ mmHg) should have blood pressure confirmed using multiple readings, including measurements on a separate day, to diagnose hypertension. **A**
- Patients with blood pressure $\geq 180/110$ mmHg and cardiovascular disease could be diagnosed with hypertension at a single visit. **E**
- 10.2** All hypertensive patients with diabetes should monitor their blood pressure at home. **A**

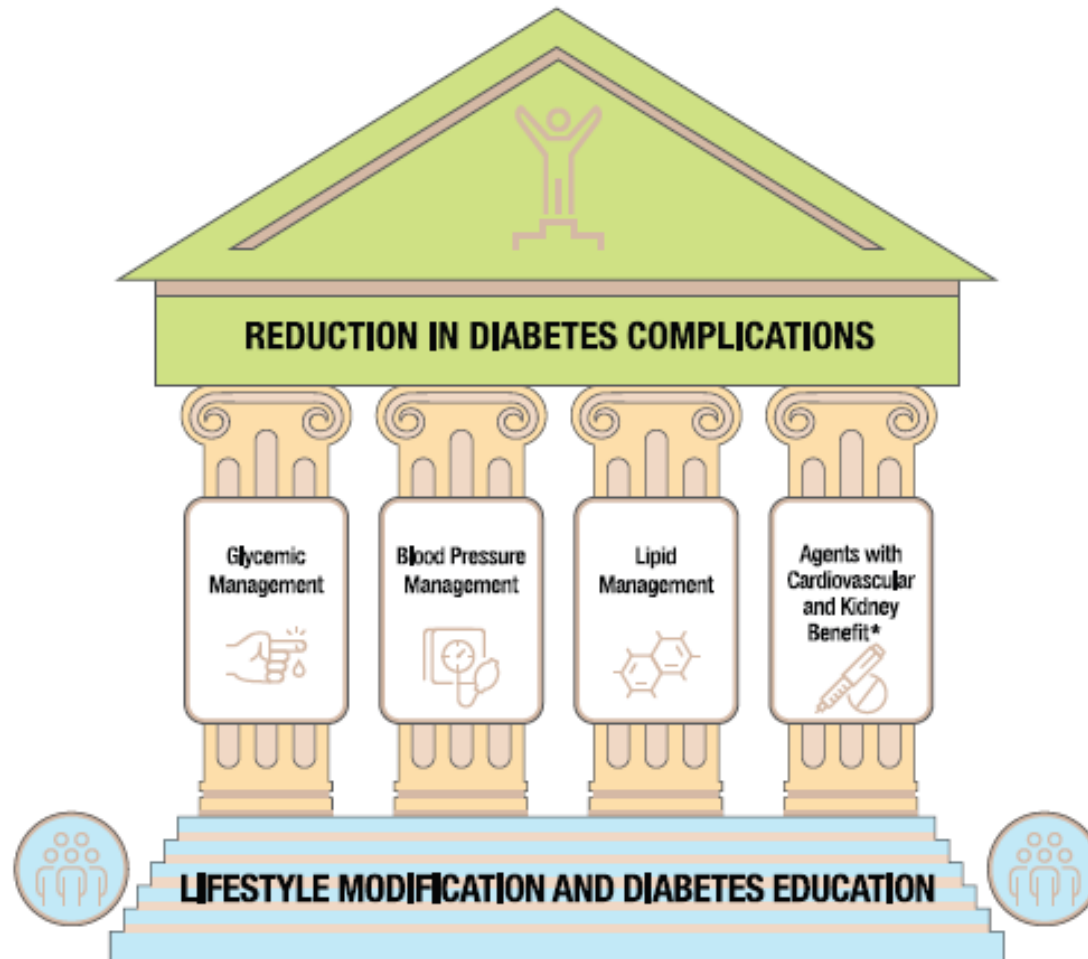


Figure 10.1—Multifactorial approach to reduction in risk of diabetes complications. *Risk reduction interventions to be applied as individually appropriate.

Treatment Goals

- 10.3** For patients with diabetes and hypertension, blood pressure targets should be individualized through a shared decision-making process that addresses cardiovascular risk, potential adverse effects of antihypertensive medications, and patient preferences. **B**
- 10.4** For individuals with diabetes and hypertension at higher cardiovascular risk (existing atherosclerotic cardiovascular disease [ASCVD] or 10-year ASCVD risk $\geq 15\%$), a blood pressure target of $<130/80$ mmHg may be appropriate, if it can be safely attained. **B**
- 10.5** For individuals with diabetes and hypertension at lower risk for cardiovascular disease (10-year atherosclerotic cardiovascular disease risk $<15\%$), treat to a blood pressure target of $<140/90$ mmHg. **A**

Treatment Goals (continued)

10.6 In pregnant patients with diabetes and preexisting hypertension, a blood pressure target of 110–135/85 mmHg is suggested in the interest of reducing the risk for accelerated maternal hypertension A and minimizing impaired fetal growth. **E**