PACE Pharmaceutical Assistance Contract for the Elderly

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Balanced information for better care

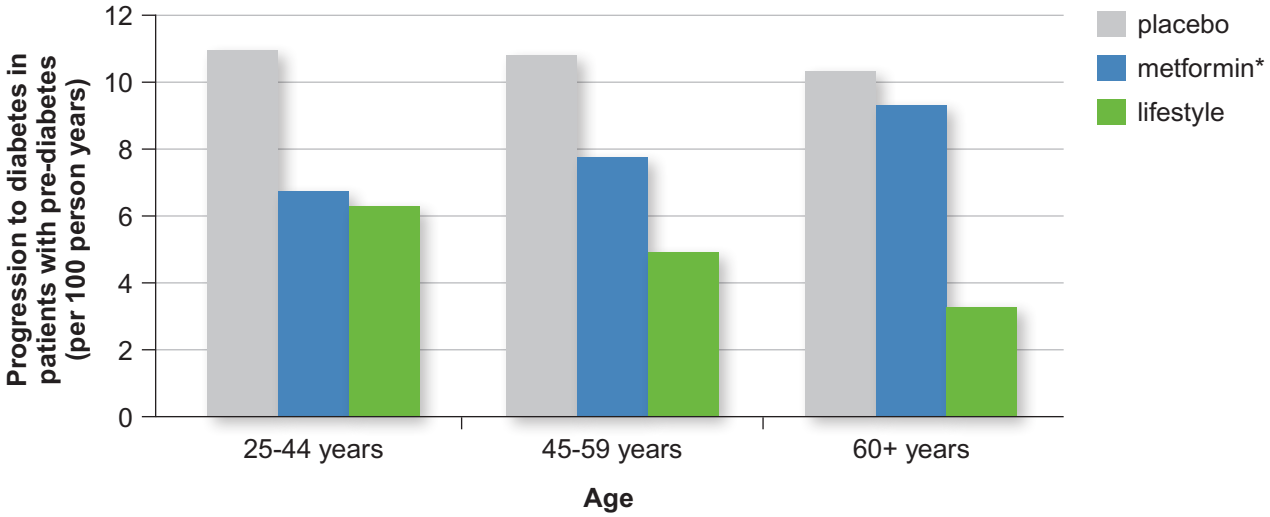
Managing type 2 diabetes

New guidelines are transforming medication use

Type 2 diabetes is common, but its risk can be reduced with lifestyle changes

Prediabetes (HbA1c 5.7-6.4%) affects more than 96 million Americans.[1]

FIGURE 1. A randomized trial found that diet and exercise can reduce or delay the progression from prediabetes to diabetes, especially in older adults.[2]



*Metformin can delay the onset of diabetes in patients with pre-diabetes, but it is less effective than lifestyle modification and may not reduce long-term complications. It is not recommended for routine use in these patients.

Diabetes Prevention Programs

These initiatives support lifestyle changes in patients with prediabetes through exercise and wellness programs certified by the CDC. To learn more about referring patients and to find programs in your area, visit **AlosaHealth.org/Prediabetes**.

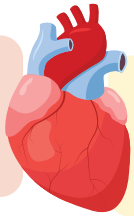
Over **37 million** Americans have diabetes (HbA1c ≥6.5%), including nearly **10%** of adult Pennsylvanians.[1,3]

Two major goals now guide the medical management of type 2 diabetes

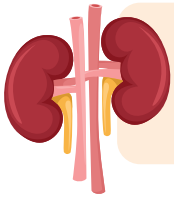
It's not just about HbA1c levels anymore.

1 **Use medications that can reduce the risk of complications and death** from cardiovascular and kidney disease.[4]

Prevent atherosclerotic cardiovascular disease (ASCVD), including myocardial infarction and stroke.



Reduce symptoms and progression of heart failure.

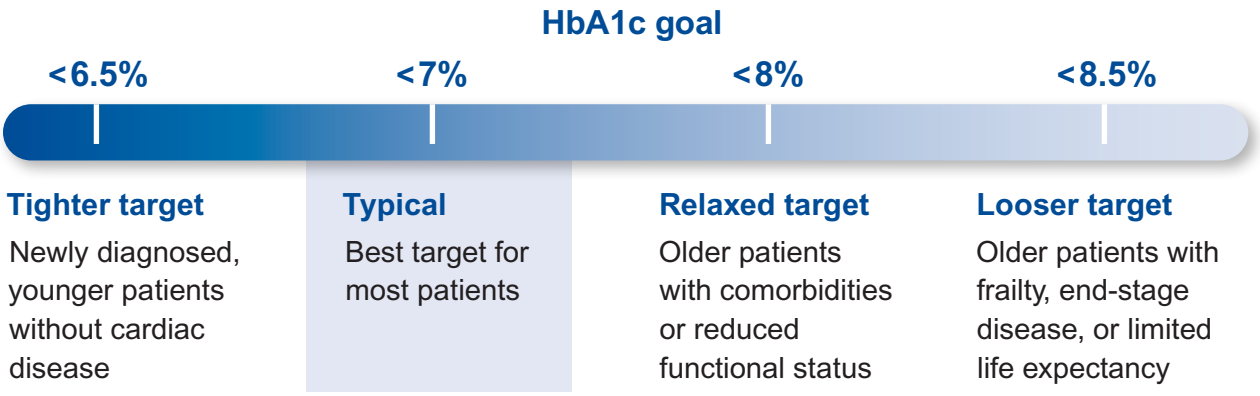


Slow progression of kidney disease and reduce the risk of requiring dialysis.

2 **Control blood glucose** to reduce the microvascular complications of diabetes, including retinopathy and neuropathy.

Select an HbA1c goal based on the patient's clinical characteristics.

FIGURE 2. For most adults, the HbA1c target is <7%. But this goal can change as patients age, especially in older adults with comorbidities, cognitive decline, or frailty.[4]



Select an initial medication based on comorbidities

For the first time, the American Diabetes Association now recommends drugs other than metformin as first-line treatment for type 2 diabetes. These two classes reduce the risk of cardiovascular and renal events for many patients with comorbidities.[4]

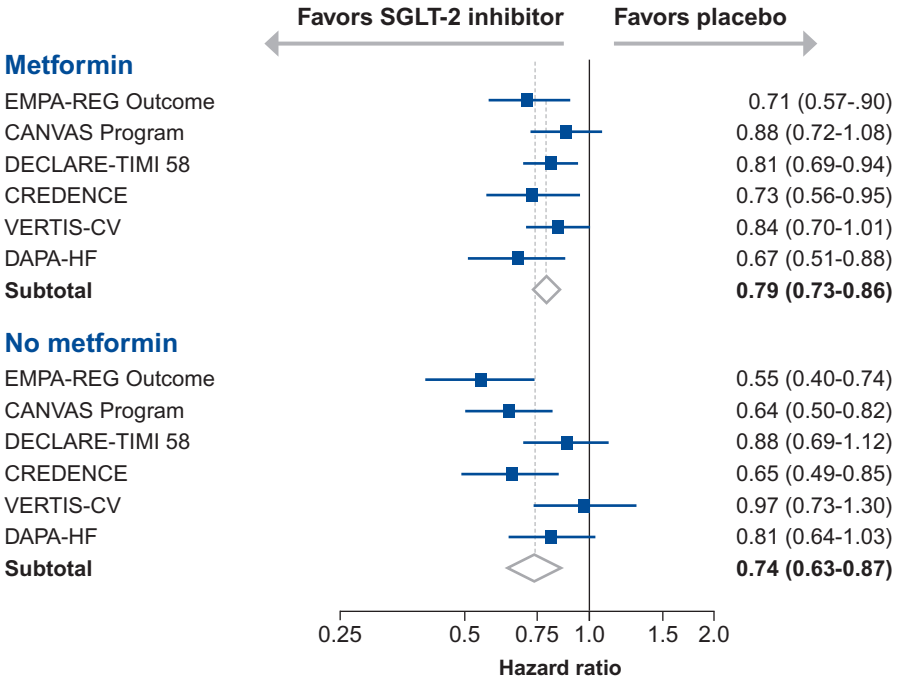
FIGURE 3. In patients with HbA1c < 10%, use one of these three medication classes* for initial treatment of diabetes, with the goal of preventing end-organ damage.

	ASCVD	Heart failure	Chronic kidney disease**	Overweight or obesity	All other patients
Sodium-glucose co-transporter 2 inhibitor (SGLT-2i)	✓	✓	✓		
Glucagon-like peptide-1 receptor agonist (GLP-1 RA)	✓		✓	✓	
Biguanide (metformin)					✓

*Select a medication within the class that targets a patient's comorbidities; see table on page 7.
**In patients with chronic kidney disease, SGLT-2is are preferred if urine albumin-to-creatinine ratio > 200.

SGLT-2 inhibitors or GLP-1 receptor agonists used as initial treatment do not require concurrent use of metformin.[5,6]

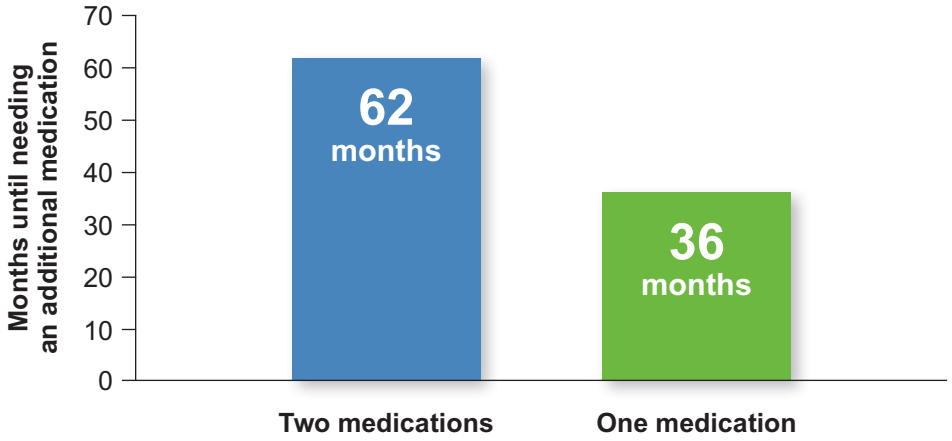
FIGURE 4. Even in patients not taking metformin, starting an SGLT-2 inhibitor reduced heart failure hospitalization and CV death in randomized controlled trials.[6]



Starting two medications can benefit some patients

In patients with HbA1c 1.5% or more above their goal, starting two medications can improve control.[4]

FIGURE 5. Patients who started and titrated metformin over three weeks then added a DPP-4 inhibitor went for a longer time before an additional drug was needed.[7]



Starting one medication a short time ahead of another may be advisable in order to address common drug-specific adverse effects.

Continue to counsel all patients with diabetes on the key role of maintaining a healthy lifestyle along with medication treatment.

DIET

- Reduce calories to achieve weight loss.
- Favor whole grains, nuts, fruits, and vegetables (such as the Mediterranean or DASH diets) over processed foods.

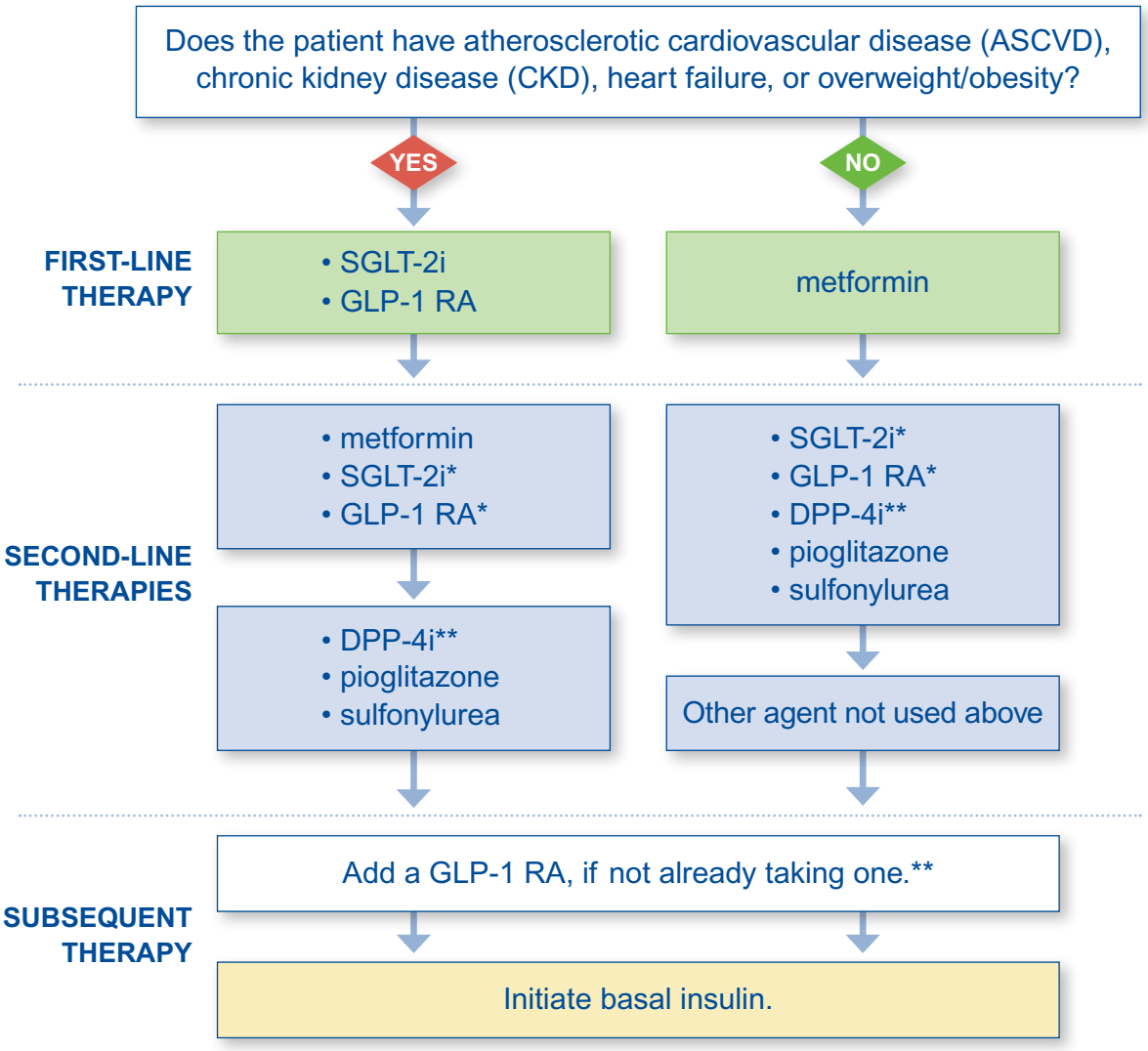
EXERCISE

- Set a goal of 150 minutes of physical activity per week.
- A combination of aerobic and resistance training is best at lowering HbA1c.

A framework for adding and adjusting drugs

- Each time a medication is added or adjusted, reinforce diet and exercise, assess adherence to current medications, and optimize doses.
- Add additional medications if needed to achieve the patient's HbA1c goal and/or reduce the risk of end-organ damage.
- Optimize treatment with multiple non-insulin options before adding insulin.

FIGURE 6. Treatment paths for patients who are not at HbA1c goal. Use the patient's characteristics, preferences, and insurance coverage to select the best regimen.[4]



*SGLT-2is and GLP-1 RAs can be used in combination to address specific comorbidities, but this approach has not yet been formally evaluated in a randomized clinical trial.[8]

**Avoid co-prescribing a DPP-4i and GLP-1 RA, because they act through overlapping mechanisms.

Select medications based on patient factors

TABLE 1. Medication effects and considerations for choosing among them

Class / medication	CV outcome: ASCVD	CV outcome: HF	Worsening renal function	Weight change	Hypoglycemia	Other safety considerations
biguanide metformin (Glucophage)	potential benefit	*	*	loss	no	GI intolerance (start with low dose to minimize, or use extended release)
SGLT-2 inhibitors (flozins) canagliflozin (Invokana) empagliflozin (Jardiance)	benefit	benefit	benefit	loss	no	UTI, ketoacidosis, genital infections, hypotension, fractures (cana), amputation (cana)
dapagliflozin (Farxiga)	neutral					
ertugliflozin (Steglatro)			neutral			
GLP-1 receptor agonists liraglutide (Victoza) semaglutide† (Ozempic) dulaglutide† (Trulicity)	benefit	neutral	potential benefit	loss	no	GI side effects common pancreatitis
exenatide† (Bydureon) lixisenatide (Adlyxin) semaglutide (Rybelsus)§	neutral	neutral	*			
exenatide (Byetta)	*	*	*			
DPP-4 inhibitors (gliptins) linagliptin (Tradjenta) sitagliptin (Januvia)	neutral	neutral	*	*	no	joint pain, pancreatitis
alogliptin (Nesina) saxagliptin (Onglyza)	*	potential risk	*	*		
thiazolidinediones (TZD) pioglitazone (Actos)	potential benefit	increased risk	*	gain	no	fractures, bladder cancer
sulfonylureas glyburide (DiaBeta, Glynase) glimepiride (Amaryl)	neutral	*	*	gain	yes	
glipizide (Glucotrol)	*	*	*			
insulin lispro, aspart, glulisine, regular, NPH	*	*	*	gain	yes	
glargine, degludec, detemir	neutral	*	*			

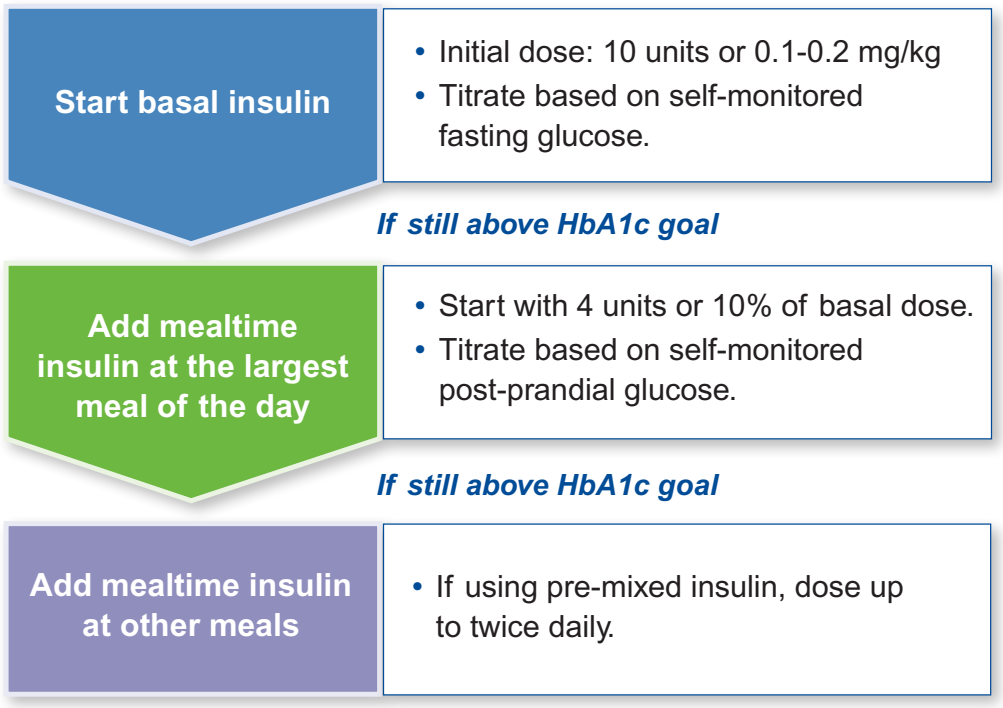
*no data available; †given weekly; §oral formulation

Renal dose adjustment is required for metformin, GLP-1 receptor agonists, and SGLT-2 inhibitors.

Some patients will still require insulin

If insulin is needed, start with a long-acting basal formulation that can be taken once a day, such as glargine, detemir, or degludec.

FIGURE 7. Titrate insulin dose, optimizing basal insulin before advancing to prandial doses.



Titrate insulin using a documented plan, such as Treat to Target,[9] with more gradual titration in older adults to avoid hypoglycemia.

Monitoring glycemic control

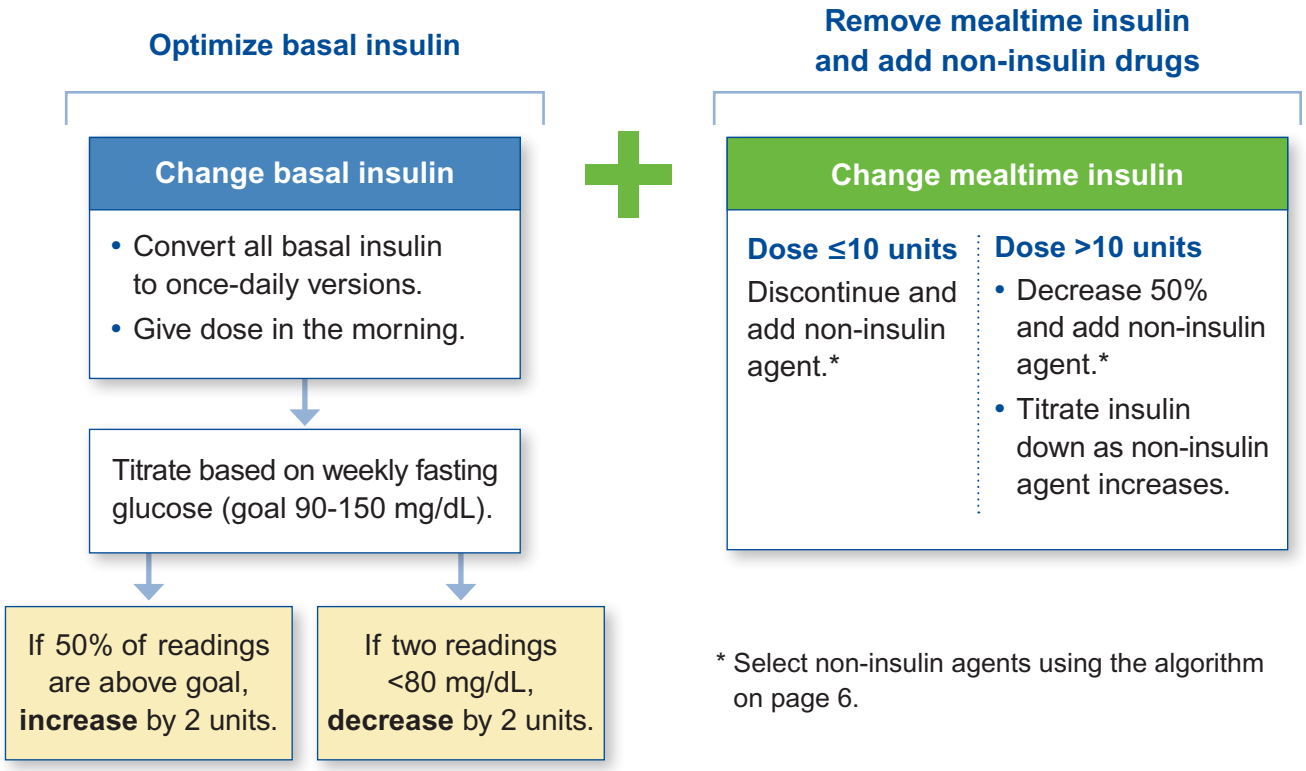
- All patients with type 2 diabetes require **HbA1c monitoring at least every 6 months**, or every 3 months if the HbA1c is inadequately controlled or medications are being adjusted.
- Patients taking insulin should monitor their glucose levels at home to prevent hypoglycemia. Patients not taking insulin typically do not need to check sugars at home.
- For patients taking basal and mealtime insulin, **continuous glucose monitoring** (CGM) can lead to better glycemic control and lower risk of hypoglycemia, compared to fingerstick glucose monitoring.[10,11]

Keep the burden of treatment manageable for older patients

In the elderly, constantly re-evaluate risks and benefits of the regimen.

- Avoid hypoglycemia, which is associated with cognitive decline and falls in older adults.
- Reassess the need for injectable therapies or reduce the number of injections.

FIGURE 8. A pragmatic implementation study in older people with diabetes used an algorithm to simplify the insulin regimen.[4,12]



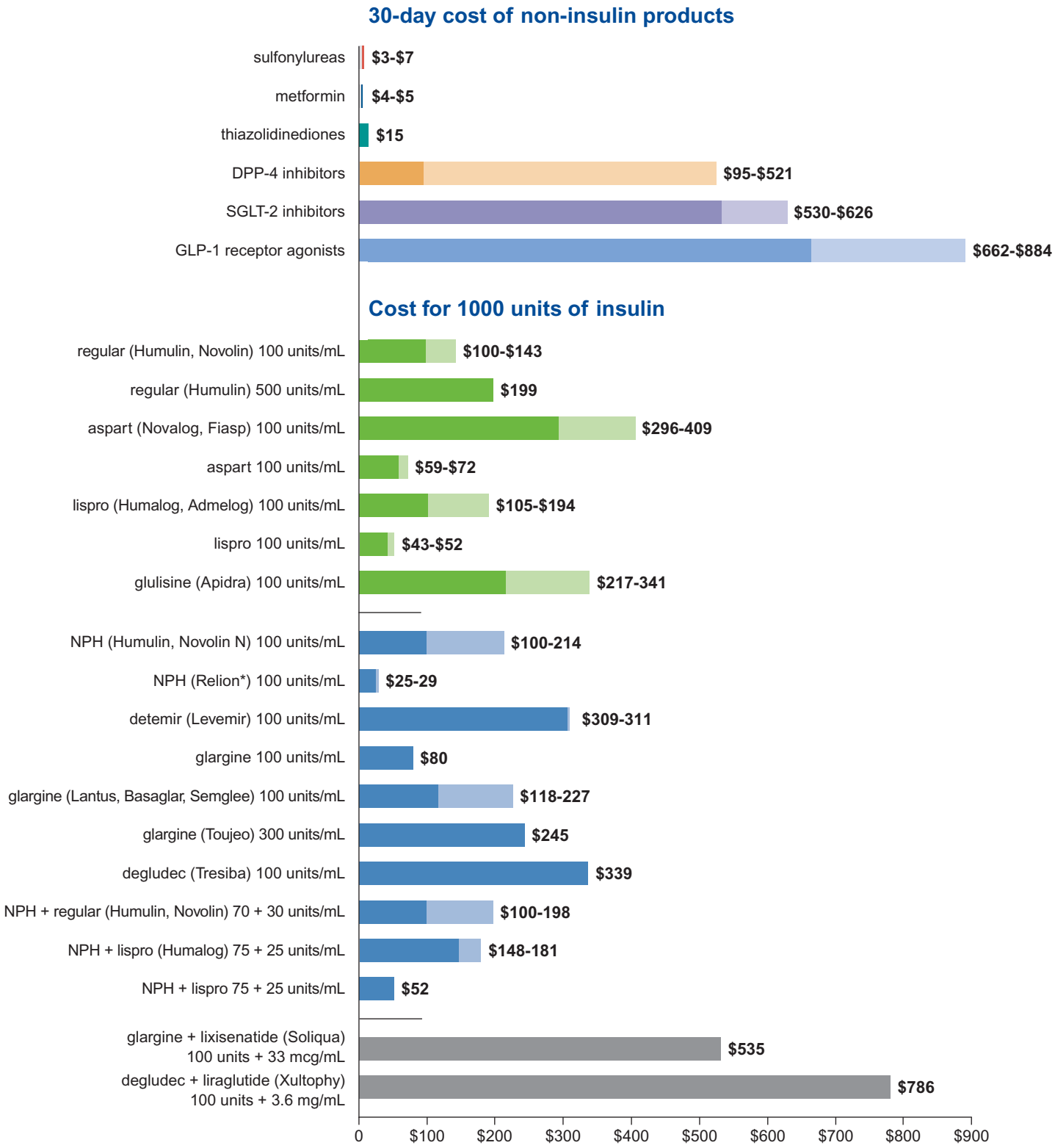
* Select non-insulin agents using the algorithm on page 6.

Reducing treatment burden or simplifying the insulin regimen can lead to:[12]

- ✓ reduced time spent in hypoglycemia (by nearly three-fold),
- ✓ reduced number of insulin injections (from four injections to one a day), and
- ✓ similar HbA1c control.

Costs

FIGURE 9. Costs of medications for diabetes



Prices from goodrx.com, March 2022. Listed doses are based on Defined Daily Doses by the World Health Organization and should not be used for dosing in all patients. All doses shown are generics when available, unless otherwise noted. These prices are a guide; patient costs will be subject to copays, rebates, and other incentives. *Relion is available only at Walmart.

Key messages

- **Diet and exercise** can slow the progression of prediabetes to type 2 diabetes and improve glucose control in patients with established diabetes.
- **Choose medications** that will reduce the risk of end-organ damage (e.g., heart and kidney disease) as well as lowering blood sugar.
- **Aim for a target HbA1c of 7% for most patients,** but modify the goal (to as high as <8.5%) for frail older patients in whom overtreatment can increase the risk of hypoglycemia and falls.
- **First-line treatment with an SGLT-2 inhibitor and/or GLP-1 receptor agonist** is preferred for patients with heart disease (or are at high risk for it), chronic kidney disease, or obesity. Metformin is a more affordable alternative for patients without these comorbidities.
- Other medications (DPP-4 inhibitors, sulfonylureas, thiazolidinediones) can be used as **second- or third-line options** for patients who cannot use first-line treatments or continue to have HbA1c levels above goal.
- **Intensify treatment early** (within weeks) for patients who are 1.5% or more above their HbA1c goal.
- **Add insulin when other agents are not sufficient** to achieve the HbA1c goal.
- Continuously **assess for adherence to medications.**

More information is available at AlosaHealth.org/Diabetes.

References:

(1) Centers for Disease Control and Prevention. Diagnosed diabetes. gis.cdc.gov/grasp/diabetes/DiabetesAtlas.html. Accessed March 9, 2022. **(2)** Crandall J, Schade D, Ma Y, et al. The influence of age on the effects of lifestyle modification and metformin in prevention of diabetes. *J Gerontol A Biol Sci Med Sci.* 2006;61(10):1075-1081. **(3)** Centers for Disease Control and Prevention. National diabetes statistics report: estimates of diabetes and its burden in the United States. www.cdc.gov/diabetes/data/statistics-report. Published January 18, 2022. Accessed March 9, 2022. **(4)** Draznin B, Aroda VR, Bakris G, et al. Standards of Medical Care in Diabetes-2022. *Diabetes Care.* 2022;45(Suppl 1):S1-S258. **(5)** Baker C, Retzik-Stahr C, Singh V, et al. Should metformin remain the first-line therapy for treatment of type 2 diabetes? *Ther Adv Endocrinol Metab.* 2021;12:2042018820980225. **(6)** Neuen BL, Arnott C, Perkovic V, et al. Sodium-glucose co-transporter-2 inhibitors with and without metformin: A meta-analysis of cardiovascular, kidney and mortality outcomes. *Diabetes Obes Metab.* 2021;23(2):382-390. **(7)** Matthews DR, Paldánius PM, Proot P, et al. Glycaemic durability of an early combination therapy with vildagliptin and metformin versus sequential metformin monotherapy in newly diagnosed type 2 diabetes (VERIFY): a 5-year, multicentre, randomised, double-blind trial. *Lancet.* 2019;394(10208): 1519-1529. **(8)** Lam CSP, Ramasundarahettige C, Branch KRH, et al. Efpeglenatide and Clinical Outcomes With and Without Concomitant Sodium-Glucose Cotransporter-2 Inhibition Use in Type 2 Diabetes: Exploratory Analysis of the AMPLITUDE-O Trial. *Circulation.* 2022;145(8): 565-574. **(9)** Riddle MC, Rosenstock J, Gerich J. The treat-to-target trial: randomized addition of glargine or human NPH insulin to oral therapy of type 2 diabetic patients. *Diabetes Care.* 2003;26(11):3080-3086. **(10)** Beck RW, Riddlesworth TD, Ruedy K, et al. Continuous Glucose Monitoring Versus Usual Care in Patients With Type 2 Diabetes Receiving Multiple Daily Insulin Injections: A Randomized Trial. *Ann Intern Med.* 2017;167(6):365-374. **(11)** Martens T, Beck RW, Bailey R, et al. Effect of Continuous Glucose Monitoring on Glycemic Control in Patients With Type 2 Diabetes Treated With Basal Insulin: A Randomized Clinical Trial. *JAMA.* 2021;325(22):2262-2272. **(12)** Munshi MN, Slyne C, Segal AR, et al. Simplification of Insulin Regimen in Older Adults and Risk of Hypoglycemia. *JAMA Intern Med.* 2016;176(7):1023-1025.

About this publication

These are general recommendations only; specific clinical decisions should be made by the treating clinician based on an individual patient's clinical condition. More detailed information on this topic is provided in a longer evidence document at AlosaHealth.org.

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