

## **Type 2 Diabetes Update**

We are seeking an author or author group to write a manuscript for this edition of *FP Essentials* that will update family physicians about type 2 diabetes. This edition will cover four topics:

1. Screening, Prevention, and Team-Based Care
2. Nonpharmacologic Treatment and Continuous Glucose Monitoring
3. Pharmacologic Treatment
4. Preventing and Managing Retinopathy, Nephropathy, and Neuropathy

The main text of the manuscript should be approximately 10,000 words in length, divided into four sections of approximately 2,500 words each, plus an abstract of approximately 200 words for each section. In addition, there should be key practice recommendations, a maximum of 15 tables/figures total, and up to 200 references to provide support for all recommendations and factual statements in the manuscript. References must be numbered sequentially by section, with each new section starting over at “1.”

This edition should focus on what is new in each topic and should answer the key questions listed for each section. Each section should begin with an illustrative case, similar to the examples provided, with modifications to emphasize key points; each case should have a conclusion that demonstrates resolution of the clinical situation. The references provided here include information that should be considered in preparation of this edition of *FP Essentials*. However, these should be used only as a starting point in identifying the most current guidelines and references to include in the edition.

### **Needs Assessment**

In the United States, nearly 15% of adults, 1 in 5 adolescents, and 1 in 11 pregnant individuals have diabetes. Its prevalence is expected to double in the coming decades. Care for patients with type 2 diabetes incur direct and indirect medical costs of up to \$300 billion, and it remains one of the most common diagnoses made and managed by family physicians. Use of newer medications with evidence of cardiovascular, renal, weight loss, and mortality benefits have gained traction in recent years, but management decisions have become more nuanced and complicated, with various medical guidelines providing different recommendations for first-line treatment and subsequent management of type 2 diabetes. Therapeutic decisions are further complicated by evidence that social determinants of health and unequal access to care and resources lead to different health outcomes among patients. This edition of *FP Essentials* will review type 2 diabetes screening and prevention recommendations, explore the evidence behind nonpharmacologic and pharmacologic therapies, and evaluate effective preventive and therapeutic interventions for diabetic retinopathy, nephropathy, and neuropathy.

## Section 1: Screening, Prevention, and Team-Based Care

### Example Case

CS is a 59-year-old with type 2 diabetes (T2D), hypertension, and obesity who visits your clinic with a superficial diabetic foot ulcer that appears to be responding well to offloading. You notice, however, that his dressing is saturated, and his socks and boots are dirty. With curiosity and openness, you discover he has been living in his car since he lost his job and apartment and has no access to running water. You quickly take action by notifying your clinic social worker and care management team to begin engaging the patient and assessing his needs.

### Key Questions to Consider

Prevalence, Disease Burden, Health Disparities

- How prevalent are prediabetes and type 2 diabetes among adults in the United States and worldwide (based upon current diagnostic definitions and criteria)? How is the prevalence projected to change in coming years?
- What are the economic, personal, and societal impacts of T2D?
- What social determinants affect the prevalence of T2D, and what health disparities exist in the provision of care and outcomes for patients with T2D?

Screening

- What are the United States Preventive Services Task Force (USPSTF) recommendations regarding screening for prediabetes and T2D in adults? How do they compare to the American Diabetes Association (ADA) and American Association of Clinical Endocrinology (AACE) recommendations? When should screening begin in person from groups at high risk of diabetes?
- Does screening asymptomatic patients improve health outcomes (eg, all-cause mortality, disease-specific mortality or morbidity, quality of life)?
- What screening tests (and laboratory criteria/cutoffs) are used to diagnose prediabetes and T2D (eg, fasting plasma glucose, hemoglobin A1c, oral glucose tolerance test)? How often should screening be done? What are the current limitations of using hemoglobin A1c for screening patients for T2D, and what medical conditions will limit its use?

Prevention

- How effective are the following interventions for preventing or delaying the progression from prediabetes to T2D? How well do they improve health outcomes (mortality, morbidity, quality of life) in patients with prediabetes?
- Lifestyle interventions: diet, physical activity, weight loss or maintenance of healthy body weight, smoking cessation/abstinence
- Medications: metformin, dipeptidyl peptidase-4 inhibitors (pioglitazone, rosiglitazone), glucagon-like peptide-1 receptor agonists, or dual glucose-dependent insulinotropic polypeptide agonists/glucagon-like peptide-1 receptor agonists. *Note: Please add statement in the discussion that none of these medications are currently FDA-approved for prevention.*
- Complementary treatments: vitamin D, omega-3, omega-6, polyunsaturated fat
- For older adults, what is the prognosis/natural history of prediabetes? What percentage of patients with prediabetes will eventually develop T2D? What are the benefits and harms of preventive interventions?

## Team-Based Care

*Please include medical (eg, pharmacists, dietician, nurses, subspecialists) and nonmedical team members (eg, social worker, peer support, community health workers)*

- What is team-based care and how can it enhance the management of patients with prediabetes and T2D? How effective is it compared to usual care? Is it cost-effective?
- What are the barriers and facilitators to effective team-based care?

## Initial References to Consider

- US Preventive Services Task Force; Davidson KW, Barry MJ, Mangione CM, et al. Screening for Prediabetes and Type 2 Diabetes: US Preventive Services Task Force Recommendation Statement. *JAMA*. 2021;326(8):736-743.
- Peer N, Balakrishna Y, Durao S. Screening for type 2 diabetes mellitus. *Cochrane Database Syst Rev*. 2020;5(5):CD005266.
- Centers for Disease Control and Prevention. National diabetes statistics report. Estimates of diabetes and its burden in the United States. 2024. <https://www.cdc.gov/diabetes/php/data-research/index.html>
- Lin J, Thompson TJ, Cheng YJ, et al. Projection of the future diabetes burden in the United States through 2060. *Popul Health Metr*. 2018;16(1):9.
- Hassan S, Gujral UP, Quarells RC, et al. Disparities in diabetes prevalence and management by race and ethnicity in the USA: defining a path forward. *Lancet Diabetes Endocrinol*. 2023;11(7):509-524.
- Kalyani RR, Neumiller JJ, Maruthur NM, Wexler DJ. Diagnosis and Treatment of Type 2 Diabetes in Adults: A Review. *JAMA*. 2025;334(11):984-1002.
- Knowler WC, Barrett-Connor E, Fowler SE, et al. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. *N Engl J Med*. 2002;346(6):393-403.
- Goldberg RB, Orchard TJ, Crandall JP, et al. Effects of Long-term Metformin and Lifestyle Interventions on Cardiovascular Events in the Diabetes Prevention Program and Its Outcome Study. *Circulation*. 2022;145(22):1632-1641.
- Hemmingsen B, Gimenez-Perez G, Mauricio D, et al. Diet, physical activity or both for prevention or delay of type 2 diabetes mellitus and its associated complications in people at increased risk of developing type 2 diabetes mellitus. *Cochrane Database Syst Rev*. 2017;12(12):CD003054.
- Khan TA, Field D, Chen V, et al. Combination of Multiple Low-Risk Lifestyle Behaviors and Incident Type 2 Diabetes: A Systematic Review and Dose-Response Meta-analysis of Prospective Cohort Studies. *Diabetes Care*. 2023;46(3):643-656.
- Madsen KS, Chi Y, Metzendorf MI, et al. Metformin for prevention or delay of type 2 diabetes mellitus and its associated complications in persons at increased risk for the development of type 2 diabetes mellitus. *Cochrane Database Syst Rev*. 2019;12(12):CD008558.
- Moelands SV, Lucassen PL, Akkermans RP, et al. Alpha-glucosidase inhibitors for prevention or delay of type 2 diabetes mellitus and its associated complications in people at increased risk of developing type 2 diabetes mellitus. *Cochrane Database Syst Rev*. 2018;12(12):CD005061.
- Diabetes Prevention Program Research Group. Long-term effects of lifestyle intervention or metformin on diabetes development and microvascular complications over 15-year

follow-up: The Diabetes Prevention Program Outcomes Study. *Lancet Diabetes Endocrinol.* 2015;3(11):866-875.

- Haw JS, Galaviz KI, Straus AN, et al. Long-term sustainability of diabetes prevention approaches: A systematic review and meta-analysis of randomized clinical trials. *JAMA Intern Med.* 2017;177(12):1808-1817.
- Ipsen EØ, Madsen KS, Chi Y, et al. Pioglitazone for prevention or delay of type 2 diabetes mellitus and its associated complications in people at risk for the development of type 2 diabetes mellitus. *Cochrane Database Syst Rev.* 2020;11(11):CD013516.
- Hemmingsen B, Sonne DP, Metzendorf MI, Richter B. Insulin secretagogues for prevention or delay of type 2 diabetes mellitus and its associated complications in persons at increased risk for the development of type 2 diabetes mellitus. *Cochrane Database Syst Rev.* 2016;10(10):CD012151.
- Hemmingsen B, Sonne DP, Metzendorf MI, Richter B. Dipeptidyl-peptidase (DPP)-4 inhibitors and glucagon-like peptide (GLP)-1 analogues for prevention or delay of type 2 diabetes mellitus and its associated complications in people at increased risk for the development of type 2 diabetes mellitus. *Cochrane Database Syst Rev.* 2017;5(5):CD012204.
- Lincoff AM, Brown-Frandsen K, Colhoun HM, et al. Semaglutide and Cardiovascular Outcomes in Obesity without Diabetes. *N Engl J Med.* 2023;389(24):2221-2232.
- Jastreboff AM, le Roux CW, Stefanski A, et al. Tirzepatide for Obesity Treatment and Diabetes Prevention. *N Engl J Med.* 2025;392(10):958-971.
- Hemmingsen B, Krogh J, Metzendorf MI, Richter B. Sodium-glucose cotransporter (SGLT) 2 inhibitors for prevention or delay of type 2 diabetes mellitus and its associated complications in people at risk for the development of type 2 diabetes mellitus. *Cochrane Database Syst Rev.* 2016;4(4):CD012106.
- Pittas AG, Dawson-Hughes B, Sheehan P, et al. Vitamin D Supplementation and Prevention of Type 2 Diabetes. *N Engl J Med.* 2019;381(6):520-530.
- Brown TJ, Brainard J, Song F, et al. PUFAH Group. Omega-3, omega-6, and total dietary polyunsaturated fat for prevention and treatment of type 2 diabetes mellitus: Systematic review and meta-analysis of randomised controlled trials. *BMJ.* 2019;366:l4697.
- Lazris A, Roth AR, Haskell H, James J. Prediabetes Diagnosis: Helpful or Harmful? *Am Fam Physician.* 2021;104(6):649-651.
- Community Preventive Services Task Force. Team-Based Care to Improve Type 2 Diabetes Management: Recommendation of the Community Preventive Services Task Force. *Am J Prev Med.* 2019;57(1):e27-e29.
- Konnyu KJ, Yogasingam S, Lépine J, et al. Quality improvement strategies for diabetes care: Effects on outcomes for adults living with diabetes. *Cochrane Database Syst Rev.* 2023;5(5):CD014513.
- Sims Gould J, Tong C, Ly J, et al. Process evaluation of team-based care in people aged >65 years with type 2 diabetes mellitus. *BMJ Open.* 2019;9(8):e029965.
- Torti JMI, Szafran O, Kennett SL, Bell NR. Interprofessional care of patients with type 2 diabetes mellitus in primary care: family physicians' perspectives. *BMC Prim Care.* 2022;23(1):74.
- Werner JJ, Ufholz K, Yamajala P. Recent Findings on the Effectiveness of Peer Support for Patients with Type 2 Diabetes. *Curr Cardiovasc Risk Rep.* 2024;18:65-79.

- Chen C, Zhou Y, Xu JY, et al. Effect of peer support interventions in patients with type 2 diabetes: A systematic review. *Patient Educ Couns*. 2024;122:108172.

## Section 2: Nonpharmacologic Treatment and Continuous Glucose Monitoring

### Example Case

NJ is a 70-year-old with type 2 diabetes (T2D), stage 3 chronic kidney disease, hypertension, and obesity, who has struggled to keep her hemoglobin A1c below 9% despite being on empagliflozin, semaglutide, and basal plus prandial insulin. She is fairly sedentary and struggles to make adequate nutritional changes. Her brother suggested she talk to you about obtaining a continuous glucose monitoring (CGM) device, as this has been a game-changer for him in tracking his glucose as it relates to his diet and insulin doses.

### Key Questions to Consider

#### Lifestyle Interventions

- What is the role of diet, physical activity, weight loss, and behavioral interventions in the management of T2D? How well do they improve health outcomes (mortality, morbidity, quality of life)?
- How has the emphasis from professional guidelines on medical nutrition therapy shifted away from macronutrients and micronutrients toward a focus on eating patterns (dietary or food patterns), the totality of consumption of food and beverages, and nutrient-dense food choices? How should patients with diabetes be counseled on nutrition with this in mind? What are the best diets to recommend to diabetic patients? Consider individualized nutrition education that may include carbohydrate counting for patients on insulin regimens, while emphasizing broader dietary patterns. *Note: An upcoming monograph on obesity management will be published in April 2026, so please keep your discussions focused on diabetes.*

#### Behavioral Interventions, Including Self-Management

- How well do group-based and individual diabetes self-management educational interventions improve T2D health outcomes?
- How effective are educational interventions provided by formally trained diabetes educators (eg, nurses, dieticians, pharmacists) vs brief in-office physician advice? At what level of diabetes control (ie, hemoglobin A1c) should patients be referred for these services? Is there benefit for individuals with good control or prediabetes to see a diabetic educator?
- How effective are mobile, virtual, artificial intelligence, or other technology-based behavioral interventions and self-management tools in improving health outcomes in patients with diabetes? Consider a table or algorithm for readers as a “how to” implement in practice and provide specific examples/links/resources of these interventions.

#### Surgical Interventions

- With increasing availability of safe, effective pharmacologic treatment of obesity and T2D, when should metabolic bariatric surgery be considered? For which patients should both therapies be considered? What are the eligibility criteria for Medicare? *Note: A brief discussion should be sufficient since this topic will be thoroughly covered in the monograph on obesity management.*

#### Complementary Treatments

- Which complementary and alternative therapies are effective for T2D treatment or as adjunctive therapy?

#### Continuous Glucose Monitoring

- What is continuous glucose monitoring (CGM)? Which patients are good candidates for CGM / what are the common insurance requirements for patients to qualify? How does it affect health outcomes for patients with T2D (ie, benefits, harms)?
- Which CGM devices are available (both prescription and over-the-counter)? Using a table, please provide a summary of the following CGM device features:
  - Approved ages
  - Frequency of readings
  - Bluetooth range
  - Compatibility with mobile phone vs use of a separate reader (for patients without mobile phone)
  - Body location for sensor placement
  - Sensor life
  - Warm-up time
- What are the common restrictions on coverage (eg, insulin use, hypoglycemia unawareness)? For patients paying out of pocket, what are the retail prices for the sensors (and readers if applicable)? Please use tables to summarize key information.
- How should ambulatory glucose profile in CGM reports be interpreted (eg, average glucose, time in range, time above range, time below range, glycemic variability)? If appropriate, consider tables to summarize key information.
- Given the time constraints in clinical practice, how can family physicians effectively and efficiently incorporate CGM in caring for patients with T2D (eg, CGM integration with electronic health records, pharmacists within team-based care)?

### Initial References to Consider

- American Diabetes Association Professional Practice Committee. 5. Facilitating Positive Health Behaviors and Well-being to Improve Health Outcomes: Standards of Care in Diabetes-2025. *Diabetes Care*. 2024;47(Suppl 1):S77-S110.
- Norris SL, Zhang X, Avenell A, et al. Long-term non-pharmacological weight loss interventions for adults with type 2 diabetes mellitus. *Sao Paulo Med J*. 2016;134(2):184.
- Sigal RJ, Kenny GP, Boulé NG, et al. Effects of aerobic training, resistance training, or both on glycemic control in type 2 diabetes: a randomized trial. *Ann Intern Med*. 2007;147(6):357-369.
- Gregg EW, Chen H, Wagenknecht LE, et al.; Look AHEAD Research Group. Association of an intensive lifestyle intervention with remission of type 2 diabetes. *JAMA*. 2012;308(23):2489-2496.
- Thomas DE, Elliott EJ, Naughton GA. Exercise for type 2 diabetes mellitus. *Cochrane Database Syst Rev*. 2006;2006(3):CD002968.
- Rejeski WJ, Ip EH, Bertoni AG, et al. Lifestyle change and mobility in obese adults with type 2 diabetes. *N Engl J Med*. 2012;366(13):1209-1217.
- Kanaley JA, Colberg SR, Corcoran MH, et al. Exercise/Physical Activity in Individuals with Type 2 Diabetes: A Consensus Statement from the American College of Sports Medicine. *Med Sci Sports Exerc*. 2022;54(2):353-368.
- Look AHEAD Research Group; Wing RR, Bolin P, Brancati FL, et al. Cardiovascular effects of intensive lifestyle intervention in type 2 diabetes. *N Engl J Med*. 2013;369(2):145-154.

- Zhang Y, Yang Y, Huang Q, et al. The effectiveness of lifestyle interventions for diabetes remission on patients with type 2 diabetes mellitus: A systematic review and meta-analysis. *Worldviews Evid Based Nurs.* 2023;20(1):64-78.
- Zhang L, Zhang Y, Shen S, et al. Safety and effectiveness of metformin plus lifestyle intervention compared with lifestyle intervention alone in preventing progression to diabetes in a Chinese population with impaired glucose regulation: a multicentre, open-label, randomised controlled trial. *Lancet Diabetes Endocrinol.* 2023;11(8):567-577.
- Churuangsuk C, Hall J, Reynolds A, et al. Diets for weight management in adults with type 2 diabetes: an umbrella review of published meta-analyses and systematic review of trials of diets for diabetes remission. *Diabetologia.* 2022;65(1):14-36.
- Lohner S, Kuellenberg de Gaudry D, Toews I, et al. Non-nutritive sweeteners for diabetes mellitus. *Cochrane Database Syst Rev.* 2020;5(5):CD012885.
- American Diabetes Association Professional Practice Committee. 8. Obesity and Weight Management for the Prevention and Treatment of Type 2 Diabetes: Standards of Care in Diabetes-2025. *Diabetes Care.* 2025;48(1)(Suppl 1):S167-S180.
- Møller G, Andersen HK, Snorgaard O. A systematic review and meta-analysis of nutrition therapy compared with dietary advice in patients with type 2 diabetes. *Am J Clin Nutr.* 2017;106(6):1394-1400.
- Konnyu KJ, Yogasingam S, Lépine J, et al. Quality improvement strategies for diabetes care: Effects on outcomes for adults living with diabetes. *Cochrane Database Syst Rev.* 2023;5(5):CD014513.
- Powers MA, Bardsley JK, Cypress M, et al. Diabetes self-management education and support in adults with type 2 diabetes: a consensus report of the American Diabetes Association, the Association of Diabetes Care and Education Specialists, the Academy of Nutrition and Dietetics, the American Academy of Family Physicians, the American Academy of PAs, the American Association of Nurse Practitioners, and the American Pharmacists Association. *Diabetes Care.* 2020;43(7):1636-1649.
- Kerr D, Ahn D, Waki K, et al. Digital Interventions for Self-Management of Type 2 Diabetes Mellitus: Systematic Literature Review and Meta-Analysis. *J Med Internet Res.* 2024;26:e55757.
- da Rocha RB, Silva CS, Cardoso VS. Self-Care in Adults with Type 2 Diabetes Mellitus: A Systematic Review. *Curr Diabetes Rev.* 2020;16(6):598-607.
- He X, Li J, Wang B, et al. Diabetes self-management education reduces risk of all-cause mortality in type 2 diabetes patients: a systematic review and meta-analysis. *Endocrine.* 2017;55(3):712-731.
- Liu F, Li J, Li X, et al. Efficacy of telemedicine intervention in the self-management of patients with type 2 diabetes: a systematic review and meta-analysis. *Front Public Health.* 2024;12:1405770.
- Gokbulut P, Kuskonmaz SM, Onder CE, et al. Evaluation of ChatGPT-4 Performance in Answering Patients' Questions About the Management of Type 2 Diabetes. *Sisli Etfal Hastan Tip Bul.* 2024;58(4):483-490.
- Lum E, Jimenez G, Huang Z, et al. Decision Support and Alerts of Apps for Self-management of Blood Glucose for Type 2 Diabetes. *JAMA.* 2019;321(15):1530-1532.
- Pal K, Eastwood SV, Michie S, et al. Computer-based diabetes self-management interventions for adults with type 2 diabetes mellitus. *Cochrane Database Syst Rev.* 2013;2013(3):CD008776.

- Stenberg E, Ottosson J, Cao Y, et al. Cardiovascular and diabetes outcomes among patients with obesity and type 2 diabetes after metabolic bariatric surgery or glucagon-like peptide 1 receptor agonist treatment. *Br J Surg.* 2024;111(9):znae221.
- Kermansaravi M, Omar I, Finer N, et al. International expert consensus on surgery for type 2 diabetes mellitus. *BMC Endocr Disord.* 2025;25(1):151.
- Dicker D, Sagiv YW, Ramot N, et al. Bariatric Metabolic Surgery vs Glucagon-Like Peptide-1 Receptor Agonists and Mortality. *JAMA Netw Open.* 2024;7(6):e2415392.
- Liu JP, Zhang M, Wang WY, Grimsgaard S. Chinese herbal medicines for type 2 diabetes mellitus. *Cochrane Database Syst Rev.* 2004;2002(3):CD003642.
- American Diabetes Association Professional Practice Committee. 7. Diabetes Technology: Standards of Care in Diabetes-2025. *Diabetes Care.* 2025;48(1)(Suppl 1):S146-S166.
- Jancev M, Vissers TACM, Visseren FLJ, et al. Continuous glucose monitoring in adults with type 2 diabetes: a systematic review and meta-analysis. *Diabetologia.* 2024;67(5):798-810.
- Seidu S, Kunutsor SK, Ajjan RA, Choudhary P. Efficacy and Safety of Continuous Glucose Monitoring and Intermittently Scanned Continuous Glucose Monitoring in Patients With Type 2 Diabetes: A Systematic Review and Meta-analysis of Interventional Evidence. *Diabetes Care.* 2024;47(1):169-179.

## Section 3: Pharmacologic Treatment

### Example Case

JT is a 52-year-old male with type 2 diabetes (T2D), hypertension, obesity (BMI 40 kg/m<sup>2</sup>), and sleep apnea. His diabetes has been well-controlled on metformin and empagliflozin for 5 years, but he has struggled with his diet for the past 2 years due to his frequent travels to assist his aging parents. He averages 12,000 steps per day, yet his hemoglobin A1c has been around 8.5% for the past 12 months. He knows he can probably make dietary changes but is realistic about his family's circumstances, so he asks you about the possibility of adding another medication.

*Figures/algorithms and tables are extremely helpful for busy clinicians and should be included when appropriate. Additionally, preventing and treating diabetic complications will be thoroughly covered in Section 4, so please minimize discussion in this section and refer readers to Section 4 when appropriate.*

### Key Questions to Consider:

#### Noninsulin Pharmacologic Treatment

- How should physicians approach individualized glycemic goals for patients with T2D? Please review variations in recommendations/guidelines from the American Diabetes Association (ADA), American College of Physicians (ACP), etc., and provide a summary of evidence from landmark trials (ACCORD, ADVANCE, UKPDS 33 and 34, VADT, etc.).
- When is metformin considered first-line oral treatment for T2D?
- Based on individual patient risks and comorbidities (ie, cardiovascular disease, chronic kidney disease, obesity), when are sodium-glucose cotransporter-2 inhibitors and glucagon-like peptide-1 receptor agonists (GLP-1RA) indicated? How effective are these newer medications in treating diabetes? When should GLP-1RA be used instead of insulin? How should family physicians titrate the doses of these medications? What are common adverse events and contraindications to their use? Please provide tables of different pharmacological agents divided by class, and hemoglobin A1c reduction by each.
- When are dipeptidyl peptidase-4 inhibitors, sulfonylureas, thiazolidinediones, alpha-glucosidase inhibitors, and meglitinides indicated? How effective are these medications in treating diabetes? How should family physicians titrate the doses of these medications? What are common adverse events and contraindications to their use? Please provide table of different pharmacological agents divided by class, and hemoglobin A1c reduction by each.

#### Insulin Therapy

- When should insulin be considered in the outpatient treatment of T2D? How effective is insulin in treating T2D? What are common adverse events and how should they be managed?
- When is basal (long-acting) vs bolus (short-acting) insulin indicated? When should basal insulin be split into 2 times/day dosing instead of once daily? What types of basal insulins are there (ultra-long-acting, long-acting/intermediate-acting insulin)? What types of bolus insulins are there (rapid-acting, short-acting)? When would premixed insulin (basal + bolus) be used? Please provide a table summarizing insulin types,

concentrations, brand names, onset, peak, and duration. An accompanying figure comparing the onset, peak, and duration profiles across insulin types would also be helpful.

- Which patients should self-monitor blood glucose? What are the recommended fasting, premeal, and postprandial blood glucose targets? How often should regimens be adjusted? Aside from self-monitored blood glucose testing, when should continuous glucose monitoring be considered? *Note: continuous glucose monitoring is thoroughly covered in Section 2.*
- When should concentrated insulins (eg U-200, U-300, U-500) be prescribed?
- If space allows, include practical guidance on initiating and adjusting insulin therapy, including total daily dose calculation, use of insulin-to-carbohydrate ratios, correction factors, when to start insulin pump.
- Should oral diabetic medications be continued when the patient is on insulin therapy? Which ones could be held or discontinued? When should insulin therapy be discontinued? How should insulin be adjusted when adding GLP-1RA therapy?
- Which factors affect individualized goals of insulin therapy (eg, age, life expectancy, comorbid conditions, duration of diabetes, risk of hypoglycemia, cost, patient motivation and preferences, quality of life)?

### **Initial References to Consider**

- Vaughan EM, Santiago-Delgado ZM. Management of Type 2 Diabetes Mellitus With Noninsulin Pharmacotherapy. *Am Fam Physician*. 2024;109(4):333-342.
- Howard-Thompson A, Khan M, Jones M, George CM. Type 2 Diabetes Mellitus: Outpatient Insulin Management. *Am Fam Physician*. 2018;97(1):29-37.
- Kalyani RR, Neumiller JJ, Maruthur NM, Wexler DJ. Diagnosis and Treatment of Type 2 Diabetes in Adults: A Review. *JAMA*. 2025;334(11):984-1002.
- Samson SL, Vellanki P, Blonde L, et al. American Association of Clinical Endocrinology Consensus Statement: Comprehensive Type 2 Diabetes Management Algorithm - 2023 Update. *Endocr Pract*. 2023;29(5):305-340.
- Davies MJ, Aroda VR, Collins BS, et al. Management of Hyperglycemia in Type 2 Diabetes, 2022. A Consensus Report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). *Diabetes Care*. 2022;45(11):2753-2786.
- American Diabetes Association Professional Practice Committee. 6. Glycemic Goals and Hypoglycemia: Standards of Care in Diabetes-2025. *Diabetes Care*. 2025;48(1)(Suppl 1):S128-S145.
- Qaseem A, Wilt TJ, Kansagara D, et al.; Clinical Guidelines Committee of the American College of Physicians. Hemoglobin A1c Targets for Glycemic Control With Pharmacologic Therapy for Nonpregnant Adults With Type 2 Diabetes Mellitus: A Guidance Statement Update From the American College of Physicians. *Ann Intern Med*. 2018;168(8):569-576.
- Castelli G, Barlett SJ. Should Metformin Continue as First-Line Pharmacotherapy for Patients With Type 2 Diabetes? Yes: Metformin Is Still the Best Choice. *Am Fam Physician*. 2024;109(3):200-201.

- Barry HC, Shaughnessy AF. Should Metformin Continue as First-Line Pharmacotherapy for Patients With Type 2 Diabetes? No: Other Drugs Have Stronger Evidence of Benefit. *Am Fam Physician*. 2024;109(3):202-203.
- Shi Q, Nong K, Vandvik PO, et al. Benefits and harms of drug treatment for type 2 diabetes: systematic review and network meta-analysis of randomised controlled trials. *BMJ*. 2023;381:e074068.
- Lee CG, Heckman-Stoddard B, Dabelea D, et al. Diabetes Prevention Program Research Group. Effect of metformin and lifestyle interventions on mortality in the Diabetes Prevention Program and Diabetes Prevention Program Outcomes Study. *Diabetes Care*. 2021;44(12):2775-2782.
- Goldberg RB, Orchard TJ, Crandall JP, et al. Diabetes Prevention Program Research Group. Effects of long-term metformin and lifestyle interventions on cardiovascular events in the Diabetes Prevention Program and its outcome study. *Circulation*. 2022;145(22):1632-1641.
- Qaseem A, Obley AJ, Shamliyan T, et al.; Clinical Guidelines Committee of the American College of Physicians. Newer Pharmacologic Treatments in Adults With Type 2 Diabetes: A Clinical Guideline From the American College of Physicians. *Ann Intern Med*. 2024;177(5):658-666.
- Agarwal A, Mustafa R, Manja V, et al. Cardiovascular, kidney related, and weight loss effects of therapeutics for type 2 diabetes: a living clinical practice guideline. *BMJ*. 2025;390:e082071.
- Nong K, Jeppesen BT, Shi Q, et al. Medications for adults with type 2 diabetes: a living systematic review and network meta-analysis. *BMJ*. 2025;390:e083039.
- American Diabetes Association Professional Practice Committee. 9. Pharmacologic Approaches to Glycemic Treatment: Standards of Care in Diabetes-2025. *Diabetes Care*. 2025;48(1)(Suppl 1):S181-S206.

## Section 4: Preventing and Managing Retinopathy, Nephropathy, and Neuropathy

### Example Case

JS is a 63-year-old with uncontrolled type 2 diabetes (T2D), hypertension, dyslipidemia, stable angina, stage 2 chronic kidney disease, and neuropathy, who has been fearful of needles all her life. Despite a healthy diet, regular exercise, and multiple oral diabetic medications (metformin, acarbose, glipizide, empagliflozin), her hemoglobin A1c has ranged from 8.7% to 9.5% and she remains averse to the thought of insulin and semaglutide injections. You refer her to your clinical pharmacist who suggested trying oral semaglutide to improve her glycemic control and for its added mortality benefits.

*Figures/algorithms and tables are extremely helpful for busy clinicians and should be included when appropriate. Additionally, preventing onset of T2D among patients with prediabetes will be thoroughly covered in Section 1, so please minimize discussion in this section and refer readers to Section 1 when appropriate.*

### Key Questions to Consider

#### Overview, Screening

- What is the prevalence of microvascular complications (ie, retinopathy, nephropathy, neuropathy) in patients with T2D? How are they diagnosed and classified relative to quality metrics?
- What are the recommended screening intervals for retinopathy, nephropathy, and neuropathy? And when present, how frequently should these patients be seen?

#### Prevention

- Among patients with T2D *without* microvascular complications, how well do the following interventions prevent these complications?
  - Sodium-glucose cotransporter-2 inhibitors
  - Glucagon-like peptide-1 receptor agonists, or dual glucose-dependent insulinotropic polypeptide agonists/glucagon-like peptide-1 receptor agonists
  - Blood pressure control: intensive vs standard
  - Glycemic control: intensive vs standard/conventional

#### Retinopathy

- Among patients with T2D and retinopathy, how well do the following interventions improve disease-specific outcomes? How well do they prevent progression or worsening of retinopathy?
  - Laser photocoagulation
  - Intravenous injections of anti-vascular endothelial growth factor
  - Blood pressure control: intensive vs standard
  - Glycemic control: intensive vs standard/conventional

#### Nephropathy

- Among patients with T2D and nephropathy, how well do the following interventions improve disease-specific and global outcomes? How well do they prevent progression or worsening of nephropathy?
  - Blood pressure control: intensive vs standard
  - Glycemic control: intensive vs standard/conventional

- Angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, calcium channel blockers
- Sodium-glucose cotransporter-2 inhibitors
- Glucagon-like peptide-1 receptor agonists, or dual glucose-dependent insulinotropic polypeptide agonists/glucagon-like peptide-1 receptor agonists
- Statins
- Dietary interventions: protein intake, sodium intake
- Among patients with advanced diabetic nephropathy, when should renal replacement therapy vs conservative kidney management be considered? Please briefly differentiate and focus on health outcomes of home hemodialysis, in-center hemodialysis, peritoneal dialysis, and kidney transplantation. Consider a table for this.

### Neuropathy

- Among patients with T2D and neuropathy, how well do the following interventions improve outcomes? How well do they prevent progression or worsening of neuropathy
  - Glycemic control: intensive vs standard/conventional
  - Antidepressants: tricyclic antidepressants, serotonin-norepinephrine reuptake inhibitors
  - Gabapentinoids: gabapentin, pregabalin
  - Sodium channel blockers: lamotrigine, lacosamide, carbamazepine, oxcarbazepine, valproic acid
  - Topical treatments: capsaicin, lidocaine
  - Lifestyle interventions: weight management
  - Opioids, tapentadol, tramadol

### Initial References to Consider

- Agarwal A, Mustafa R, Manja V, et al. Cardiovascular, kidney related, and weight loss effects of therapeutics for type 2 diabetes: a living clinical practice guideline. *BMJ*. 2025;390:e082071.
- Nong K, Jeppesen BT, Shi Q, et al. Medications for adults with type 2 diabetes: a living systematic review and network meta-analysis. *BMJ*. 2025;390:e083039.
- American Diabetes Association Professional Practice Committee. 3. Prevention or Delay of Diabetes and Associated Comorbidities: Standards of Care in Diabetes-2025. *Diabetes Care*. 2025;48(1)(Suppl 1):S50-S58.
- Samson SL, Vellanki P, Blonde L, et al. American Association of Clinical Endocrinology Consensus Statement: Comprehensive Type 2 Diabetes Management Algorithm - 2023 Update. *Endocr Pract*. 2023;29(5):305-340.
- Goldberg RB, Orchard TJ, Crandall JP, et al. Effects of Long-term Metformin and Lifestyle Interventions on Cardiovascular Events in the Diabetes Prevention Program and Its Outcome Study. *Circulation*. 2022;145(22):1632-1641.
- Khan TA, Field D, Chen V, et al. Combination of Multiple Low-Risk Lifestyle Behaviors and Incident Type 2 Diabetes: A Systematic Review and Dose-Response Meta-analysis of Prospective Cohort Studies. *Diabetes Care*. 2023;46(3):643-656.
- Diabetes Prevention Program Research Group. Long-term effects of lifestyle intervention or metformin on diabetes development and microvascular complications over 15-year

follow-up: The Diabetes Prevention Program Outcomes Study. *Lancet Diabetes Endocrinol.* 2015;3(11):866-875.

- Haw JS, Galaviz KI, Straus AN, et al. Long-term sustainability of diabetes prevention approaches: A systematic review and meta-analysis of randomized clinical trials. *JAMA Intern Med.* 2017;177(12):1808-1817.
- Brown TJ, Brainard J, Song F, et al. PUFAH Group. Omega-3, omega-6, and total dietary polyunsaturated fat for prevention and treatment of type 2 diabetes mellitus: Systematic review and meta-analysis of randomised controlled trials. *BMJ.* 2019;366:l4697.
- Thomas DE, Elliott EJ, Naughton GA. Exercise for type 2 diabetes mellitus. *Cochrane Database Syst Rev.* 2006;2006(3):CD002968.
- Look AHEAD Research Group; Wing RR, Bolin P, Brancati FL, et al. Cardiovascular effects of intensive lifestyle intervention in type 2 diabetes. *N Engl J Med.* 2013;369(2):145-154.
- American Diabetes Association Professional Practice Committee. 8. Obesity and Weight Management for the Prevention and Treatment of Type 2 Diabetes: Standards of Care in Diabetes-2025. *Diabetes Care.* 2025;48(1)(Suppl 1):S167-S180.
- Qaseem A, Obley AJ, Shamliyan T, et al.; Clinical Guidelines Committee of the American College of Physicians. Newer Pharmacologic Treatments in Adults With Type 2 Diabetes: A Clinical Guideline From the American College of Physicians. *Ann Intern Med.* 2024;177(5):658-666.
- American Diabetes Association Professional Practice Committee. 10. Cardiovascular Disease and Risk Management: Standards of Care in Diabetes-2025. *Diabetes Care.* 2025;48(1)(Suppl 1):S207-S238.
- Li S, Vandvik PO, Lytvyn L, et al. SGLT-2 inhibitors or GLP-1 receptor agonists for adults with type 2 diabetes: a clinical practice guideline. *BMJ.* 2021;373(1091).
- Kanie T, Mizuno A, Takaoka Y, et al. Dipeptidyl peptidase-4 inhibitors, glucagon-like peptide 1 receptor agonists and sodium-glucose co-transporter-2 inhibitors for people with cardiovascular disease: a network meta-analysis. *Cochrane Database Syst Rev.* 2021;(10):CD013650.
- Usman MS, Bhatt DL, Hameed I, et al. Effect of SGLT2 inhibitors on heart failure outcomes and cardiovascular death across the cardiometabolic disease spectrum: a systematic review and meta-analysis. *Lancet Diabetes Endocrinol.* 2024;12(7):447-461.
- Arnold SV, Bhatt DL, Barsness GW, et al.; American Heart Association Council on Lifestyle and Cardiometabolic Health and Council on Clinical Cardiology. Clinical Management of Stable Coronary Artery Disease in Patients With Type 2 Diabetes Mellitus: A Scientific Statement From the American Heart Association. *Circulation.* 2020;141(19):e779-e806.
- Dunlay SM, Givertz MM, Aguilar D, et al.; American Heart Association Heart Failure and Transplantation Committee of the Council on Clinical Cardiology. Council on Cardiovascular and Stroke Nursing; and the Heart Failure Society of America. Type 2 Diabetes Mellitus and Heart Failure: A Scientific Statement From the American Heart Association and the Heart Failure Society of America: This statement does not represent an update of the 2017 ACC/AHA/HFSA heart failure guideline update. *Circulation.* 2019;140(7):e294-e324.

- American Diabetes Association Professional Practice Committee. 11. Chronic Kidney Disease and Risk Management: Standards of Care in Diabetes-2025. *Diabetes Care*. 2025;48(1)(Suppl 1):S239-S251.
- Natale P, Green SC, Tunnicliffe DJ, et al. Glucagon-like peptide 1 (GLP-1) receptor agonists for people with chronic kidney disease and diabetes. *Cochrane Database Syst Rev*. 2025;2(2):CD015849.
- Agarwal A, Zeng X, Li S, et al. Sodium-glucose cotransporter-2 (SGLT-2) inhibitors for adults with chronic kidney disease: a clinical practice guideline. *BMJ*. 2024;387:e080257.
- Samson SL, Vellanki P, Blonde L, et al. American Association of Clinical Endocrinology Consensus Statement: Comprehensive Type 2 Diabetes Management Algorithm - 2023 Update. *Endocr Pract*. 2023;29(5):305-340.
- Erviti J, Saiz LC, Leache L, et al. Blood pressure targets for hypertension in people with chronic renal disease. *Cochrane Database Syst Rev*. 2024;(10):CD008564.
- Neuen BL, Heerspink HJL, Vart P, et al. Estimated Lifetime Cardiovascular, Kidney, and Mortality Benefits of Combination Treatment With SGLT2 Inhibitors, GLP-1 Receptor Agonists, and Nonsteroidal MRA Compared With Conventional Care in Patients With Type 2 Diabetes and Albuminuria. *Circulation*. 2024;149(6):450-462.
- American Diabetes Association Professional Practice Committee. 12. Retinopathy, Neuropathy, and Foot Care: Standards of Care in Diabetes-2025. *Diabetes Care*. 2025;48(1)(Suppl 1):S252-S265.
- Do DV, Han G, Abariga SA, et al. Blood pressure control for diabetic retinopathy. *Cochrane Database Syst Rev*. 2023;(3):CD006127.