# Cases in the Community Optimizing Treatment and Considering Weight Management as a Primary Goal in People With T2DM

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# Support

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Answer These Questions Please take a moment to scan this QR code to answer four assessment questions before we begin.







A patient with T2DM, obesity, and hypertension asks you how much they need to reduce their weight to lower their risk of a heart attack. What will you tell them?

You'll need to lose about 5% of your weight

You'll need to lose about 10% of your weight

You'll need to lose about 15% of your weight

You'll need to do whatever you can to attain a BMI <30 kg/m<sup>2</sup>

You'll need to do whatever you can to attain a BMI <25 kg/m<sup>2</sup>

I'm not sure



Marilyn is a woman with a 4-year history of T2DM currently treated with metformin 2,000 mg/d, an A1C of 8.8%, and overweight. She begs you to let her try once more to reach an A1C of <7% and a 10% weight loss with lifestyle modifications in the next 6 months. What will you tell her?

That's exactly what I would have recommended

I'm glad you're willing to give diet and exercise another try

I have some concerns about that approach





You suggest that Marilyn from the previous question replace her metformin with a daily metformin/empagliflozin combination tablet. She is somewhat hesitant to initiate this new medication. How will you increase her comfort with intensifying therapy?

Describe how she might feel after initiating the medication

Explain how the medication works

Inform her that this is what current guidelines recommend in her situation

Reassure her that it's just a pill





When you see Marilyn at a follow-up visit 6 months after initiating metformin/empagliflozin, she has lost 2% of her weight (her goal was 10%), and her A1C is 7.8% (her goal is 7%). What is your next step?

Add dulaglutide

Add tirzepatide

Switch metformin/empagliflozin to metformin and dulaglutide

Switch metformin/empagliflozin to metformin and tirzepatide





Now is the Time Intensifying Treatment to Minimize the Risks Associated With Comorbidities, Including T2DM



#### **2022** Fast Facts on Diabetes in the United States<sup>1,2</sup>

#### Diabetes

 Total: 37.3 million people (11.3%) have diabetes in the United States

Diagnosed: 28.7 million people, including 28.5 million adults Undiagnosed: 8.5 million people (23% of adults)

#### **Prediabetes**

- Total: 96 million people aged 18 years or older (38% of adults)
- 65 years or older: 26.4 million people (48.8% of older adults)

Currently, at least 1 out of 3 people will develop the disease in their lifetime

Projected prevalence of diabetes is 55 million individuals by 2060

1. https://www.cdc.gov/diabetes/data/statistics-report/index.html. 2. Mohebi R et al. J Am Coll Cardiol. 2022;80:565-578.



# ADA Standards: Recommended Screening Methods and Classification<sup>1,2</sup>

Glycemic Status	Fasting Glucose, mg/dL	2-h Glucose, mg/dL	A1C, %
Normal	<100	<140	<5.7
Prediabetes	100-125	140-199	5.7-6.4
Diabetes	≥126	≥200	≥6.5

- Screen if the patient is aged 35 to 70 years and has overweight or obesity
- Screen at younger ages in patients from populations at disproportionate risk

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Repeat testing every 3 years if results are normal

1. USPSTF. JAMA. 2021;326:736-743. 2. American Diabetes Association Professional Practice Committee. Diabetes Care. 2024;47(suppl 1):S20-S42.

### **Trends in A1C Management (<8%) by Insurance Type:** 2022-2021 National Averages<sup>1</sup>



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Adults Aged 18-75 Years With T1DM and T2DM With A1C <8%

1. https://www.ncqa.org/hedis/measures/comprehensive-diabetes-care/.

# T2DM Is Strongly Associated With Several Macrovascular and Microvascular Complications<sup>1</sup>

#### Coronary heart disease

Prevalence: 14% to 21% Most frequently reported form of CVD and most lethal one Risk of death from CHD is higher in women than in men; HR = 1.81 (95% CI, 1.27-2.59) vs HR = 1.48 (95% CI, 1.10-1.99)

#### Heart failure

Prevalence: 19% to 26% Second most common initial manifestation of CVD in T2DM Risk of HF is up to 2-fold in men and 5-fold in women

#### Peripheral artery disease

Prevalence: 16% to 29% Most common initial manifestation of CVD in T2DM Prevalence is 1.8-fold higher in women compared with men

#### Stroke

Prevalence: 8% to 12% Second most frequent cause of death in patients with T2DM after CHD Prevalence is similar in men and women



#### Retinopathy

Prevalence: 34%

Most common microvascular complication of diabetes; responsible for 2.6% of all cases of blindness worldwide Prevalence rates are higher in T1DM compared with T2DM (77.3% vs 25.2%)

#### Neuropathy

Cardiac autonomic neuropathy Prevalence: 31% to 73% in people with T2DM No difference in prevalence across sexes

#### Nephropathy

Prevalence: 29% to 61%

Leading cause of end-stage renal disease in the adult population worldwide

Female sex is a risk factor for nephropathy in T2DM



# The Mean BMI Is Increasing in the United States



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<sup>a</sup> Prevalence of self-reported obesity (BMI ≥30 kg/m<sup>2</sup>) among US adults by state and territory, BRFSS. <sup>b</sup> Adults aged ≥20 y, NHANES. <sup>c</sup> Significant linear trend. 1. https://www.cdc.gov/obesity/data/prevalence-maps.html. 2. https://www.cdc.gov/nchs/products/databriefs/db360.htm. 3. Kompaniyets L et al. *JAMA Network Open.* 2023;6(8):e2327358.

# Many Medications May Cause Weight Gain<sup>1-3</sup>

Most frequently reported as causing weight gain in FAERS

- Risperidone
- Adalimumab
- Pregabalin
- Aripiprazole
- Etanercept
- Prednisone
- Levothyroxine sodium
- Olanzapine
- Infliximab
- Tocilizumab

#### **Psychotropic agents**

- Olanzapine
- Quetiapine
- Clozapine
- Risperidone

#### Antihypertensive agents

- Atenolol
- Metoprolol
- Nadolol
- Propranolol

#### Antidepressants/ mood stabilizers

- Mirtazapine
- Amitriptyline
- Nortriptyline
- Doxepin
- Paroxetine
- Imipramine

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Lithium

#### Antiseizure agents

- Carbamazepine
- Valproate
- Gabapentin

#### Review medications for weight-promoting agents; replace with weight-sparing agents for the same indication

# ADA Standards for the Management of T2DM: Use of Glucose-Lowering Medications<sup>1</sup>

HEALTHY LIFESTYLE BEHAVIORS: DIABETES SELF-MANAGEMENT, EDUCATION, AND SUPPORT (DSMES); SOCIAL DETERMINANTS OF HEALTH



<sup>a</sup> In people with HF, CKD, established CVD, or multiple risk factors for CVD, the decision to use a GLP-1 RA or SGLT2i with proven benefit should be independent of background use of metformin. <sup>b</sup> A strong recommendation is warranted for people with CVD and a weaker recommendation for those with indicators of high CV risk. Moreover, a higher absolute risk reduction and thus lower numbers needed to treat are seen at higher levels of baseline risk and should be factored into the shared decision-making process. <sup>c</sup> For GLP-1 RA, CVOTs demonstrate their efficacy in reducing composite MACE, CV death, all-cause mortality, MI, stroke, and renal endpoints in individuals with T2DM with established/high risk of CVD. <sup>d</sup> For SGLT2i, CV/renal outcomes trials demonstrate their efficacy in reducing the risk of composite MACE, CV death, all-cause mortality, MI, HHF, and renal outcomes in individuals with T2DM with established/high risk of CVD. <sup>d</sup> For SGLT2i, CV/renal outcomes trials demonstrate their efficacy in reducing the risk of composite MACE, CV death, all-cause mortality, MI, HHF, and renal outcomes in individuals with T2DM with established/high risk of CVD. <sup>d</sup> For SGLT2i, CV/renal outcomes trials demonstrate their efficacy in reducing the risk of composite MACE, CV death, all-cause mortality, MI, HHF, and renal outcomes in individuals with T2DM with established/high risk of CVD. <sup>e</sup> Low-dose TZD may be better tolerated and similarly effective.

1. American Diabetes Association Professional Practice Committee. Diabetes Care. 2024;47(suppl 1):S158-S178.

#### PeerView.com

o avoid clinical ertia. reassess

and modify

# ADA Standards for the Management of T2DM: Use of Glucose-Lowering Medications<sup>1</sup>

EALTHY LIFESTYLE BEHAVIORS: DIABETES SELF-MANAGEMENT, EDUCATION, AND SUPPORT (DSMES); SOCIAL DETERMINANTS OF HEALTH

![](_page_17_Figure_2.jpeg)

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<sup>a</sup> In people with HF, CKD, established CVD, or multiple risk factors for CVD, the decision to use a GLP-1 RA or SGLT2i with proven benefit should be independent of background use of metformin.

1. American Diabetes Association Professional Practice Committee. Diabetes Care. 2024;47(suppl 1):S158-S178.

# ADA Recommendations for Overcoming Therapeutic Inertia in T2DM: Clinician/Practice-Level Interventions<sup>1</sup>

# Understand Impact of Treatment Inertia

- Schedule "diabetes only" visits where you and your patients can focus solely on diabetes
- Ask office staff to remind patients to bring their glucose logs, list of medications, and monitoring devices
- Aim to adjust therapy any time a patient's A1C or other targets are not at goal
- Consider making changes between A1C tests based on monitoring results

#### Recognize Treatment Inertia

- Check for barriers
  - Diabetes distress
  - Depression
  - Low health literacy
  - Social determinants of health
- Schedule follow ups based on A1C
  - Every 6-8 weeks for those at 9% or higher
  - Every 2-3 months for those at 7% to 8.9%
  - Every 3-6 months for those less than 7% or at their personal target

#### **Plan With Patients**

- Develop a diabetes care plan that includes a personal A1C target
- Take into account patient needs, concerns, and wishes
- Review and update regularly
- Refer all patients for diabetes self-management education when diagnosed or if they have not been before

# Simplified Management of Glucose-Lowering Medications in **T2DM: DCRM Multispecialty Practice Recommendations**<sup>1</sup>

![](_page_19_Figure_1.jpeg)

1. Handelsman Y et al. J Diabetes Complications. 2022:36:108101.

# Helpful Tactics for Increasing Patient Comfort With Intensifying T2DM Treatment When Needed: The Top 5<sup>1,a</sup>

![](_page_20_Figure_1.jpeg)

<sup>a</sup> MOTION study of a geographically representative survey of 300 PwT2DM and 100 primary care HCPs; Canada, 2020. 1. Wrzal PK et al. *Can J Diabetes*. 2022;46:P337-P345.E2.

Weighing the Options for Glucose Management and Weight Loss

# **ADA Standards: Holistic Person-Centered Approach** to T2DM Management<sup>1,2</sup>

![](_page_22_Figure_1.jpeg)

2. American Diabetes Association Professional Practice Committee. Diabetes Care. 2024;47(suppl 1):S158-S178.

#### Glycemic Efficacy: Change in A1C From Baseline Among Drugs Approved for Glycemic Control and Obesity Management in PwT2DM<sup>1</sup>

Approved for <u>T2DM</u>					
A1C -0.4% to -0.8%	A1C -0.81% to -0.99%		-1.0% to -1.9%	A1C - 2.0% to -2.5%	
AGIs <sup>12</sup>	Dapaglifi	Dapaglifiozin <sup>12</sup> Ba		Tirzepatide <sup>11</sup>	
DPP-4 inhibitors <sup>10</sup>	Empaglif	fozin <sup>12</sup> Di	ulaglutide <sup>13</sup>		
Meglitinides <sup>12</sup>	Exenatid	Exenatide ER <sup>12</sup> Premixed insulin <sup>12</sup>			
Rosiglitazone <sup>8</sup>	Metforr	nin <sup>12</sup> Liraglutide 1.8 mg SC <sup>6</sup>			
SGLT2 inhibitors <sup>10</sup>	Pioglitaz	zone <sup>7</sup> Semaglutide 2 mg SC <sup>9</sup>			
	Sulphonyl	ureas <sup>12</sup> Semaglutide 14 mg <sup>16</sup>			
Approved for Obesity Management					
A1C +1.0% to 1.5	A1C 0 to -0.3	A1C -0.4% to -0.8%	A1C -1.0% to -1.9%	TBD	
Phentermine <sup>3</sup>	Orlistat <sup>5</sup>	Naltrexone/ bupropion <sup>1</sup>	Liraglutide 3.0 mg SC <sup>14</sup>	Hydrogel <sup>4a</sup>	
		Phentermine/ topiramate <sup>2</sup>	Semaglutide 2.4 mg SC <sup>15</sup>		

<sup>a</sup> Patients with an A1C <8.5% were included in the study, which found no significant change in A1C.

1. https://contravehcp.com/wp-content/uploads/Contrave\_PI.pdf. 2. https://www.accessdata.fda.gov/drugsatfda\_docs/label/2022/022580s021lbl.pdf. 3. Elhag W et al. *Annals Med Surg*. 2019;45:75-81. 4. Greenway FL et al. *Obesity (Silver Spring)*. 2019;27:205-216. 5. https://www.accessdata.fda.gov/drugsatfda\_docs/label/2022/020766s038lbl.pdf. 6. https://www.accessdata.fda.gov/drugsatfda\_docs/label/2011/021073s043s044lbl.pdf. 8. https://www.accessdata.fda.gov/drugsatfda\_docs/label/2007/021071s031lbl.pdf. 9. https://www.accessdata.fda.gov/drugsatfda\_docs/label/2017/209637lbl.pdf. 10. Scheen AJ. *Diabetes Metab*. 2020;46:186-196. 11. Frías JP et al. *N Engl J Med*. 2021;385:503-515. 12. Tsapas A et al. *Annals Int Med*. 2020;173:278-286. 14. https://www.accessdata.fda.gov/drugsatfda\_docs/label/2023/213051s012lbl.pdf. 16. https://www.accessdata.fda.gov/drugsatfda\_docs/label/2023/213051s012lbl.pdf.

#### Weight-Loss Efficacy of Treatments for T2DM<sup>1</sup>

![](_page_24_Figure_1.jpeg)

High to Moderate Certainty Evidence	
Among the most effective	
Among the intermediate effective	
Not convincingly different from standard treatment	
Among the intermediate harmful	
Among the most harmful	

Low to Very Low Certainty Evidence
Possibly among the most effective
Possibly among the intermediate effective
Possibly not convincingly different from standard treatment
Possibly among the intermediate harmful
Possibly among the most harmful

# Setting Realistic Expectations for Weight Loss in People With T2DM Across Treatment Options<sup>1-7,a,b</sup>

![](_page_25_Figure_1.jpeg)

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<sup>a</sup> Patients managed with antidiabetic medications plus diet or lifestyle modification. <sup>b</sup> Patients had A1C of 7%-10% with diet and exercise alone and were naïve to injectable diabetes therapy.

1. Garvey WT et al. Diabetes Care. 2014;37:3309-3316. 2. Davies M et al. Lancet. 2021;397:971-984. 3. Davies M et al. JAMA. 2015;314:687-699.

4. Hollander P et al. Diabetes Care. 2013;36:4022-4029. 5. Berne C. Diabet Med. 2005;22:612-618. 6. Rosenstock J et al. Lancet. 2021;398:143-155.

7. Garvey WT et al. Lancet. 2023; 402:613-626.

# ADA Standards: Holistic Person-Centered Approach to T2DM Management<sup>1-3</sup>

![](_page_26_Figure_1.jpeg)

1. Davies MJ et al. *Diabetes Care*. 2022;45:2753-2786. 2. American Diabetes Association Professional Practice Committee. *Diabetes Care*. 2024;47(suppl 1):S158-S178. 3. Pop-Busui et al. *Diabetes Care*. 2022;45:1670-1690.

# ADA Standards: Holistic Person-Centered Approach to T2DM Management<sup>1,2</sup>

![](_page_27_Figure_1.jpeg)

# GLP-1 and GIP/GLP-1 Discovery, Clinical Development, and Future Directions<sup>1</sup>

![](_page_28_Figure_1.jpeg)

PeerView.com

1. Drucker DJ, Holst JJ. Diabetologia. 2023;66:1765-1779. 2. Kosiborod MN, et al. N Engl J Med. 2023;389:1069-1084. 3. Nicholls SJ et al. Am Heart J. 2024;267:1-11.

4. Rossing P et al. Nephrol Dial Transplant. 2023;38:2041-2051. 5. Gragnano F et al. Eur Heart J Cardiovasc Pharmacother. 2024;10:7-9.

6. https://clinicaltrials.gov/study/NCT04822181. 7. https://clinicaltrials.gov/study/NCT03648554 8. https://clinicaltrials.gov/study/NCT04777396.

# Case Discussion 1: Andrew, a White Man Aged 43 Years

#### Andrew

- Medical history: T2DM (2 years), HTN, dyslipidemia, former smoker (quit ~5 y ago)
- **Family history**: father has T2DM (15 years) and heart disease; mother is recently deceased
- BMI: 30.8 kg/m<sup>2</sup>; height: 70 inches (178 cm); weight: 215 lb (97.4 kg)
- A1C: 8.3%; BP: 174/88 mmHg
- TC: 180 mg/dL; HDL-C: 40 mg/dL; LDL-C: 123 mg/dL; TG: 85 mg/dL
- eGFR: >90 mL/min/1.73 m<sup>2</sup>; UACR: 11 mg/g
- ALT: 38; AST: 29
- Current medications
  - Insulin glargine 10 units daily, sitagliptin 100 mg/d, atorvastatin 40 mg/d, losartan/HCTZ 100 mg/12.5 mg daily

#### **Visit Notes**

- Architect; works with his father in a small family firm
- Still upset over recent loss of his mother to lung cancer
- Married with 2 children
- Does not exercise regularly; participates in recreational softball league

![](_page_29_Picture_16.jpeg)

### **Let's Pause to Discuss Andrew**

#### Andrew

- Medical history: T2DM (2 years), HTN, dyslipidemia, former smoker (quit ~5 y ago)
- **Family history**: father has T2DM (15 years) and heart disease; mother is recently deceased
- BMI: 30.8 kg/m<sup>2</sup>; height: 70 inches (178 cm); weight: 215 lb (97.4 kg)
- A1C: 8.3%; BP: 174/88 mmHg
- TC: 180 mg/dL; HDL-C: 40 mg/dL; LDL-C: 123 mg/dL; TG: 85 mg/dL
- eGFR: >90 mL/min/1.73 m<sup>2</sup>; UACR: 11 mg/g
- ALT: 38; AST: 29
- Current medications
  - Insulin glargine 10 units daily, sitagliptin 100 mg/d, atorvastatin 40 mg/d, losartan/HCTZ 100 mg/12.5 mg daily

![](_page_30_Picture_11.jpeg)

- 1. What changes would you recommend to Andrew's basal insulin therapy?
- 2. What A1C goal would you set for Andrew?

![](_page_30_Picture_14.jpeg)

# Intensifying Basal Insulin Therapy With Insulin/GLP-1 RA Coformulation or Continuing Basal Insulin: LixiLan-L<sup>1</sup>

![](_page_31_Figure_1.jpeg)

1. Aroda V et al. Diabetes Care. 2016;39:1972-1980.

# Intensifying Basal Insulin Therapy With Prandial Insulin or Tirzepatide: SURPASS-6<sup>1</sup>

![](_page_32_Figure_1.jpeg)

1. Rosenstock J et al. JAMA. 2023;330:1631-1640.

Encouraging Personal Success Through Individualized, Shared Decision-Making

![](_page_33_Picture_1.jpeg)

# Shared Decision-Making: What It Is and Why We Use It<sup>1</sup>

Use shared decision-making to identify appropriate and individualized glycemic targets and reach agreement on treatment changes

![](_page_34_Picture_2.jpeg)

Employ SDM to collaborate with patients on individualized diabetes plans

![](_page_34_Picture_4.jpeg)

SDM can help improve decisions, patient knowledge, and patient risk perception

![](_page_34_Picture_6.jpeg)

SDM helps to acknowledge and address emotional needs of PwT2DM

![](_page_34_Picture_8.jpeg)

SDM has been linked to better self-care (eg, improved diet, foot care)

![](_page_34_Picture_10.jpeg)

# The SDM-Q-9 Tool Ensures That the Patient Is Included in Decision-Making<sup>1</sup>

My doctor made clear that a decision needs to be made

My doctor wanted to know exactly how I wanted to be involved in making the decision My doctor told me that there are different options for treating my medical condition

My doctor asked me which treatment option I prefer

My doctor helped me understand all the information My doctor precisely explained the advantages and disadvantages of the treatment options

My doctor and I thoroughly weighed the different treatment options

My doctor and I selected a treatment option together

My doctor and I reached an agreement on how to proceed

# Stigmatization, Racial Bias, and Poor Communication Among HCPs and Marginalized Populations

People of color (POC) report feeling dismissed, disregarded, devalued, and excluded from decision-making<sup>1</sup>

- Symptoms/complaints are not taken seriously by HCPs
- · Viewed as uneducated, unreliable, and less desirable patients
- Inadequate treatment has been reported across multiple types of healthcare
- This results in higher unmet needs, loss of trust in healthcare, and delay in seeking care

![](_page_36_Picture_6.jpeg)

# **Communicating Within the Patient Encounter<sup>1</sup>**

Is now a good time for us to discuss how your weight and health may be affecting each other and how we can work together on it?

#### **Questions to Ask the Patient**

- What concerns you most about your weight?
- What is the most important outcome you hope to achieve with weight loss?
- What would stand in the way of achieving that outcome?
- Is there a first step that you are ready to take?
- What impact will the changes we have discussed have on your life?
- Obesity is a chronic problem; what frequency and type of follow-up would be most helpful?

#### **Response From PCP**

- Acknowledge concerns
- Link obesity to comorbidities

• Provide resources

Yes

Schedule follow-up or referral

#### **Response From PCP**

No

"I understand you may not be ready to discuss your weight. However, I am concerned about the impact of your weight on your health. There may be some things we can do together in the future. Please make a follow-up appointment when you are ready for another discussion."

![](_page_37_Picture_16.jpeg)

# ADA Standards: Weight Management Assessment Recommendations<sup>1</sup>

![](_page_38_Figure_1.jpeg)

1. American Diabetes Association Professional Practice Committee. *Diabetes Care*. 2024;47(suppl 1):S158-S178. 2. Albury C et al. *Lancet Diabetes Endocrinol*. 2020;8:447-455.

# Life's Essential 8: Healthy Living Is for Everyone American Heart Association Guidelines<sup>1,2</sup>

![](_page_39_Picture_1.jpeg)

# Upstream Weight-Centric Approach to T2DM Management Has Wide-Ranging Benefits<sup>1</sup>

![](_page_40_Figure_1.jpeg)

Weight-centric approach Upstream intervention

Glucocentric approach Downstream intervention

![](_page_40_Picture_4.jpeg)

![](_page_40_Picture_5.jpeg)

# How Much Weight Loss Is Needed to Improve T2DM?

•	Measures of glycemia <sup>1</sup>	20/	
•	Triglycerides <sup>1</sup>	-3 /0	
•	HDL-C <sup>1</sup>		
•	Systolic and diastolic blood pressure		
•	Hepatic steatosis measured by MRS <sup>2</sup>		
•	Measures of feeling and function <ul> <li>Symptoms of urinary stress incontinence<sup>3</sup></li> <li>Measures of sexual function<sup>4,5</sup></li> <li>Quality of life measures (IWQOL)<sup>6</sup></li> </ul>	-5%	
•	NASH Activity Score measured on biopsy <sup>7</sup>	400/	
•	Apnea-Hypopnea Index <sup>8</sup>	-10%	
•	Reduction in CV events, mortality, remission of T2DM <sup>9-11</sup>	-15%	
1. Wing RR et al. <i>Diabet</i> 4. Wing RR et al. <i>Diabet</i> 7. Promrat K et al. <i>Hepa</i>	es Care. 2011;34:1481-1486. 2. Lazo M et al. <i>Diabetes Care</i> . 2010;33:2156-2163. 3. Phelan S et al. <i>J Urol</i> . 2012;187:9 es Care. 2013;36:2937-2944. 5. Wing RR et al. <i>J Sex Med</i> . 2010;7:156-165. 6. Engel SG et al. <i>Obes Res</i> . 2003;11:120 tology. 2010:51:121-129. 8. Foster GD et al. <i>Arch Intern Med</i> . 2009:169:1619-1626. 9. Després JP et al. <i>BMJ</i> . 2001:322	39-944. 7-1213. 2:716-720.	

10. Lean ME et al. Lancet. 2018;391:541-551. 11. Lean ME et al. Lancet Diabetes Endocrinol. 2019;7:344-355.

# Essential Patient Counseling When Prescribing a GLP-1-Based Therapy<sup>1-4</sup>

- Small servings, eat slowly, stop eating when no longer hungry
- Caution with alcohol, high fat, spicy foods
- Adverse effects of weight loss, independent of therapy: loss of muscle mass, fluid and electrolyte deficits, cold intolerance, constipation, gallbladder events<sup>1</sup>
  - >1 g/kg/d of high-quality protein intake, drink plenty of water, consider higher sodium intake (tomato juice, soups), eat vegetables and other sources of fiber

- Exercise, preferably at least 5 days per week, and do not forget strength training
- Take a jacket with you everywhere
- Sense of well-being and the enjoyment of food improves once rapid weight loss slows
- Communicate common AEs associated with GLP-1-based therapies (ie, transient GI symptoms) and share when patients should notify their HCP
  - Severe abdominal pain
  - Intestinal blockage

1. Pi-Sunyer FX. Ann Int Med. 1993;119:722-726. 2. Wharton S et al. Postgrad Med. 2022;134:14-19. 3. Sodhi M et al. JAMA. 2023;330:1795-1797. 4. https://www.accessdata.fda.gov/scripts/cder/daf/.

![](_page_42_Picture_12.jpeg)

# Factors Affecting the Adherence To and Persistence With GLP-1-Based Therapies in People With T2DM<sup>1,2</sup>

Reasons for Treatment Discontinuation	Factors Associated With Higher Adherence and Persistence		
Inadequate blood glucose control	Initiating treatment with low dose		
Gastrointestinal side effects	Ease of use of injection device		
Preference for oral medication over injection	Weekly dosing rather than daily or twice daily dosing		
Injection-related concerns (including pain and fear)	Early (within 6 months) A1C level reduction		
High cost	Early (within 6 months) weight loss		
Injection site reaction			
Inadequate body weight reduction	Since this study was performed,		
Inconvenience of injection schedule	an oral GLP-1 RA has become available		

## Case Discussion 2: Ella, a Black Woman Aged 56 Years

Ella

- **Medical history**: T2DM (8 y), hyperlipidemia (12 y), HTN (6 y), angina, GERD, sleep apnea
- **Family history**: father had T2DM, died after a stroke at age 66; mother is 81 years of age with HTN and CVD
- BMI: 39.3 kg/m<sup>2</sup>; weight: 229 lb (103.7 kg); height: 64" (163 cm)
- A1C: 7.4%; BP: 142/90 mmHg, P 78
- Postmenopausal
- TC: 248 mg/dL; HDL-C: 36 mg/dL; LDL-C: 172 mg/dL; TG: 480 mg/dL
- eGFR: 54 mL/min/1.73 m<sup>2</sup>; BUN: 28; Cr: 1.4; UACR: 68 mg/g
- ALT: 48; AST: 40; CBC: normal; platelets: 148; electrolytes: normal
- **ROS**: fatigue, poor sleep, some knee pain, some swelling in legs
- Current medications
  - Metformin HCL 500 mg QD, glipizide 15 mg QD, pravastatin 10 mg QD, lisinopril 20 mg QD

#### Visit Notes

- Attorney with an unpredictable schedule
- Divorced with 3 teen-to-adult–aged children
- Typically eats 2 meals/d
- Used to walk in park during midday, but knee pain makes that difficult
- She feels her body got significantly worse after menopause and she "wants to find a better way to get it all in control!"

#### Let's Pause to Discuss Ella

#### Ella

- **Medical history**: T2DM (8 y), hyperlipidemia (12 y), HTN (6 y), angina, GERD, sleep apnea
- **Family history**: father had T2DM, died after a stroke at age 66; mother is 81 years of age with HTN and CVD
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- **ROS**: fatigue, poor sleep, some knee pain, some swelling in legs
- Current medications
  - Metformin HCL 500 mg QD, glipizide 15 mg QD, pravastatin 10 mg QD, lisinopril 20 mg QD

![](_page_45_Picture_13.jpeg)

- 1. What is the highest treatment priority for Ella?
- 2. How would you intensify Ella's treatment consistent with current guidelines and evidence?

### SURPASS-3: MRI Substudy<sup>1</sup>

#### Man aged 59 years on metformin and an SGLT2i randomized to tirzepatide 5 mg QW

Baseline

![](_page_46_Figure_3.jpeg)

BMI: 44.8 kg/m<sup>2</sup>; body weight: 134.2 kg; WC: 139.7 cm; A1C: 78.1 mmol/mol (9.3%); FSG: 10.3 mmol/L (186 mg/dL)

BMI: 36.2 kg/m<sup>2</sup>; body weight: 108.4 kg; WC: 124.4 cm; A1C: 43.2 mmol/mol (6.1%); FSG: 5.9 mmol/L (107 mg/dL)

![](_page_46_Picture_6.jpeg)

# Addressing Recent Safety Concerns About GLP-1–Based Therapies

The Concern	The Evidence
Intestinal obstruction	<b>No difference in the risk of intestinal obstruction</b> was found for GLP-1 RAs or DPP-4 is vs SGLT2 is in real-world study of new users (N = $190,321$ ) <sup>1</sup>
Pancreatic cancer	<b>No increased risk of pancreatic cancer</b> for GLP-1 RA-ever users vs GLP-1 RA-never users, basal insulin ever-users, or basal insulin never-users in population study (N = 543,595) <sup>2</sup>
Suicidality	<ul> <li>Post-marketing studies from US, Canada, UK, EU have suggested increased risks<sup>3</sup></li> <li>Bariatric surgery, phentermine/topiramate, and bupropion are associated with increased risk<sup>3</sup></li> <li>Semaglutide was associated with 73% <i>lower</i> risk of incident suicidal ideation and 56% <i>lower</i> risk of recurrent suicidal ideation in a real-world study of people with obesity or T2DM (N = 240,618)<sup>4</sup></li> <li>Monitor for mood changes in all new users of GLP-1–based agents, regardless of history of depression<sup>3</sup></li> </ul>
Immunogenicity	<ul> <li>Anti-drug antibodies can limit efficacy or increase hypersensitivity reactions<sup>5</sup></li> <li>~50% of people using tirzepatide develop anti-drug antibodies in a meta-analysis of 7 RCTs (N = 7,342)<sup>5</sup></li> <li>Immunogenicity did not affect tirzepatide pharmacokinetics or efficacy<sup>5</sup></li> <li>Most hypersensitivity and ISRs in antibody-positive PwT2DM were mild to moderate in severity<sup>5</sup></li> </ul>

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3. Lau D, Gamble JM. Diabetes Obes Metab. 2024 Jan 16. Online ahead of print. 4. Wang W et al. Nat Med. 2024;30:168-176.

5. Mullins GR et al. J Clin Endocrinol Metab. 2024;109:361-369.

<sup>1.</sup> Ueda P et al. Clin Gastroenterol Hepatol. 2023 Sep 15. Online ahead of print. 2. Dankner R et al. JAMA Netw Open. 2024;7:e2350408.

# Severe Hypoglycemia Rates Are Similar for All Combinations of Sulfonylureas and DPP-4is<sup>1</sup>

Exposure <sup>a</sup>	Events, n	Person- Years, n	Incidence Rates (95% CI) <sup>ь</sup>	Crude HR (95% CI)	Adjusted HR (95% Cl) <sup>c</sup>
Long-acting SUs with DPP-4i	48	8,098	5.93 (4.37-7.86)	0.85 (0.64-1.14)	0.87 (0.65-1.16)
Short-acting SUs with DPP-4i	770	111,174	6.93 (6.44-7.43)	1.00 (reference)	1.00 (reference)
SUs with peptidomimetic DPP-4i	76	12,122	6.27 (4.94-7.85)	0.95 (0.75-1.20)	0.96 (0.76-1.22)
SUs with non- peptidomimetic DPP-4i	738	107,226	6.88 (6.40-7.40)	1.00 (reference)	1.00 (reference)

<sup>a</sup> All exposure categories are considered in this model, but not presented in this table, as there was not interest in drawing inferences regarding the "other combinations" category. <sup>b</sup> Per 1,000 person-years. <sup>c</sup> Adjusted for calendar year, age, sex, BMI, smoking status, alcohol-related disorders, arterial hypertension, hyperlipidemia, CHF, CKD, cognitive impairment, acute infection, diabetes duration, A1C, number of non-SU antidiabetic drugs, microvascular diabetic complications, macrovascular diabetic complications, history of severe hypoglycemia, quinolone use, tramadol use, and prior number of hospitalizations. 1. Dimakos J et al. *Clin Pharmacol Ther.* 2023;114:712-720.

![](_page_48_Picture_3.jpeg)

**Answer These Questions** Please take a moment to scan this QR code to reconsider your answers to the four assessment questions before we conclude.

![](_page_49_Picture_1.jpeg)

![](_page_49_Picture_2.jpeg)

![](_page_50_Picture_0.jpeg)

A patient with T2DM, obesity, and hypertension asks you how much they need to reduce their weight to lower their risk of a heart attack. What will you *now* tell them?

You'll need to lose about 5% of your weight

You'll need to lose about 10% of your weight

You'll need to lose about 15% of your weight

You'll need to do whatever you can to attain a BMI <30 kg/m<sup>2</sup>

You'll need to do whatever you can to attain a BMI <25 kg/m<sup>2</sup>

I'm not sure

![](_page_51_Picture_0.jpeg)

Marilyn is a woman with a 4-year history of T2DM currently treated with metformin 2,000 mg/d, an A1C of 8.8%, and overweight. She begs you to let her try once more to reach an A1C of <7% and a 10% weight loss with lifestyle modifications in the next 6 months. What will you *now* tell her?

That's exactly what I would have recommended

I'm glad you're willing to give diet and exercise another try

I have some concerns about that approach

![](_page_51_Picture_7.jpeg)

![](_page_51_Picture_8.jpeg)

![](_page_52_Picture_0.jpeg)

You suggest that Marilyn from the previous question replace her metformin with a daily metformin/empagliflozin combination tablet. She is somewhat hesitant to initiate this new medication. How will you *now* increase her comfort with intensifying therapy?

Describe how she might feel after initiating the medication

Explain how the medication works

Inform her that this is what current guidelines recommend in her situation

Reassure her that it's just a pill

![](_page_52_Picture_8.jpeg)

![](_page_53_Picture_0.jpeg)

When you see Marilyn at a follow-up visit 6 months after initiating metformin/empagliflozin, she has lost 2% of her weight (her goal was 10%), and her A1C is 7.8% (her goal is 7%). What is your next step *now*?

Add dulaglutide

Add tirzepatide

Switch metformin/empagliflozin to metformin and dulaglutide

Switch metformin/empagliflozin to metformin and tirzepatide

![](_page_53_Picture_8.jpeg)

![](_page_53_Picture_9.jpeg)

# Key Takeaways on Managing Patients With T2DM

- Timely intensification of therapy is needed to prevent or reverse complications of T2DM
- Many medications that regulate glycemia and mood also have significant effects on weight
  - Highly effective glucose-lowering agents that also reduce weight are now available
- GLP-1 RAs and GIP/GLP-1 RAs have beneficial effects on glycemia, weight, and CV risk factors and/or events in PwT2DM
  - Specific benefits and indications vary by agent

- Patients who are especially likely to benefit from a GIP/GLP-1 RA or GLP-1 RA include those who
  - Would benefit from reductions in both weight and A1C
  - Have overweight or obesity
  - Have ASCVD or are at risk of stroke
  - Are far from meeting their glycemic goals

#### **Abbreviations**

ACEi: angiotensin-converting enzyme inhibitors ACR: albumin-to-creatinine ratio ADA: American Diabetes Association AF: adverse event AGI: alpha-glucosidase inhibitors ALT: alanine transaminase AMH<sup>.</sup> anti-Müllerian hormone ARB: angiotensin receptor blocker ASCVD: atherosclerotic cardiovascular disease AST: aspartate aminotransferase BID: twice daily BMI: body mass index BNP: brain natriuretic peptide **BP: blood pressure** BRFSS: Behavioral Risk Factor Surveillance System BUN: blood urea nitrogen **BUP**: buprenorphine C-IMT: carotid intima-media thickness CAI: central adrenal insufficiency CGM: continuous glucose monitor

CHD: congenital heart disease CHF: congestive heart failure CKD: chronic kidney disease Cr. creatinine CV: cardiovascular CVD: cardiovascular disease CVOT: cardiovascular outcome trial DA/NE: dopamine/norepinephrine DKD: diabetic kidney disease DPP-4i: dipeptidyl peptidase 4 inhibitor DSMES: diabetes self-management education and support **DULA:** dulaglutide EASD: European Association for the Study of Diabetes ECG: echocardiogram EE: energy expenditure eAG: estimated average glucose eGFR: estimated glomerular filtration rate EHR: electronic health record FR<sup>-</sup> extended release FAERS: FDA Adverse Event Reporting System

#### **Abbreviations**

FMD: flow-mediated dilation FMP: final menstrual period FPG: fasting plasma glucose FSH: follicle-stimulating hormone GABA-R: gamma-aminobutyric acid receptor GERD: gastroesophageal reflux disease GI: gastrointestinal GIP: glucose-dependent insulinotropic peptide GLP-1: glucagon-like peptide-1 GP/FP: general practitioner/family practitioner GSIS: glucose-stimulated insulin secretion HCP: healthcare professional HCTZ: hydrochlorothiazide HDL: high-density lipoprotein HF<sup>·</sup> heart failure HFpEF: heart failure with preserved ejection fraction HHF: hospitalization for heart failure HMO: health maintenance organization hs-cTn: High-sensitivity cardiac troponin

HTN: hypertension IWQOL: Impact of Weight on Quality of Life LA: long acting LDL: low-density lipoprotein LIRA: liraglutide MACE: major adverse cardiovascular event **MI:** myocardial infarction MOA: mechanism of action MOP-R: mu opioid receptor MRS: magnetic resonance spectroscopy NAL · naloxone NASH: non-alcoholic steatohepatitis NT-proBNP PAD: peripheral arterial disease PCP: primary care provider PHEN: phentermine Pio: pioglitazone PO: by mouth POC: people of color

#### **Abbreviations**

PPO: preferred provider organization PwO: people with obesity PwT2DM: people with type 2 diabetes mellitus PWV: pulse wave velocity PYY: peptide YY QD: every day QOL: quality of life QR: quick release QW: every week RA: receptor agonist ROS: review of systems SC: subcutaneous SDM-Q-9: 9-item shared decision-making questionnaire SDM: shared decision making SDOH<sup>-</sup> social determinants of health SEMA: semaglutide SGLT2i: sodium-glucose cotransporter-2 inhibitor SMBG: self-monitoring blood glucose

SU: sulfonylurea T1DM: type 1 diabetes mellitus T2DM: type 2 diabetes mellitus TC: total cholesterol TG: triglycerides TID: three times a day TIR: time in range TPM: topiramate TZD: thiazolidinedione TZP: tirzepatide UACR: urine albumin-creatinine ratio USPSTF: United States Preventive Services Task Force

![](_page_57_Picture_3.jpeg)