

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

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Answer These Questions

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





Assessment Question

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/m²

You'll need to do whatever you can to attain a BMI <25 kg/m²

I'm not sure



Assessment Question

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

I'm not sure



Assessment Question

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

I'm not sure



Assessment Question

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

I'm not sure

Now is the Time

*Intensifying Treatment to Minimize
the Risks Associated With
Comorbidities, Including T2DM*

PeerView
Live

2022 Fast Facts on Diabetes in the United States^{1,2}

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

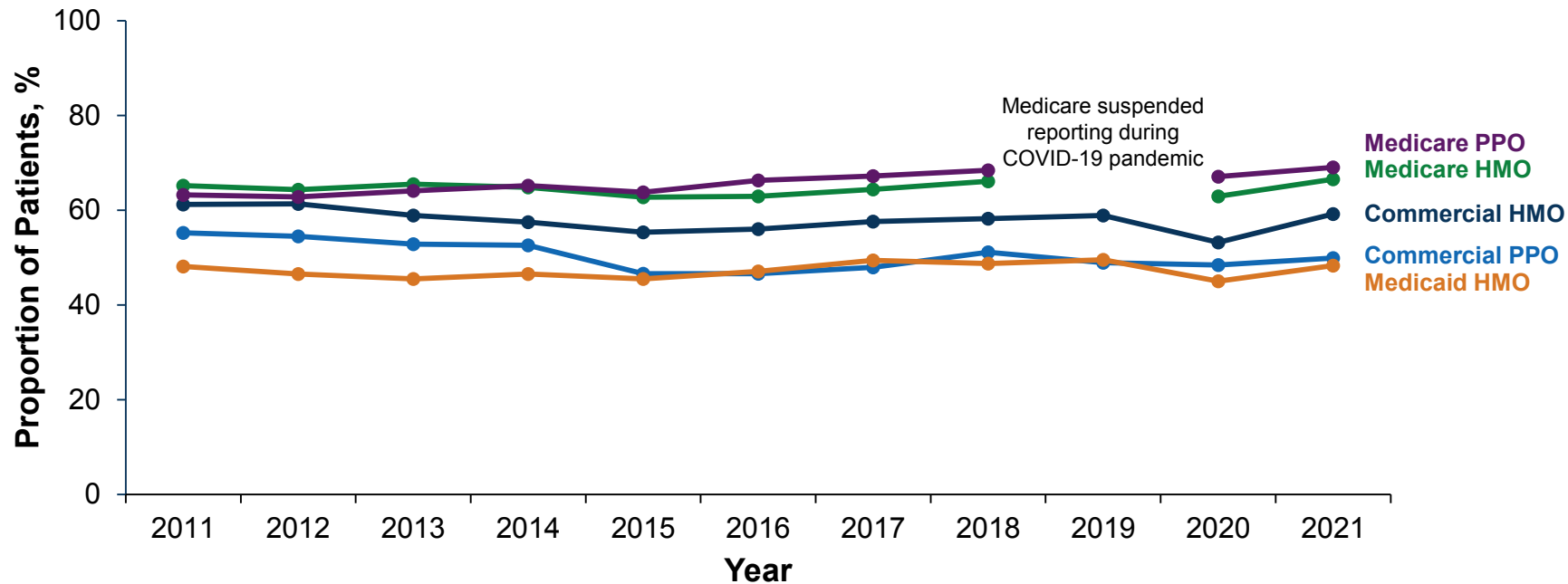
ADA Standards: Recommended Screening Methods and Classification^{1,2}

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
- Repeat testing every 3 years if results are normal

Trends in A1C Management (<8%) by Insurance Type: 2022-2021 National Averages¹

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 Complications¹

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

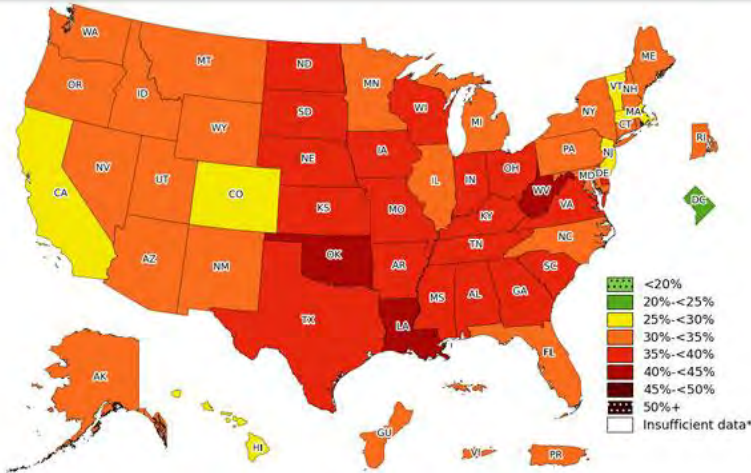
Prevalence: 29% to 61%

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

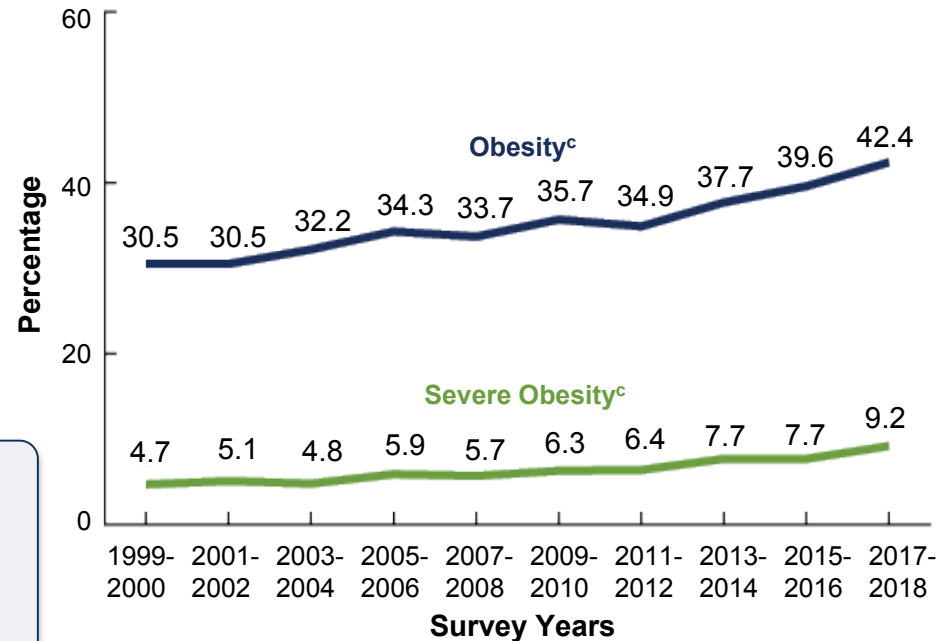
2021^{1,a}



In a cohort of over 18 million US patients with overweight/obesity ...³

- Annual probability of $\geq 5\%$ weight loss was 10%
- Reducing BMI to healthy weight was less likely especially if BMI ≥ 45 kg/m²

Trends, 1999-2018^{2,b}



^a Prevalence of self-reported obesity (BMI ≥ 30 kg/m²) among US adults by state and territory, BRFSS. ^b Adults aged ≥ 20 y, NHANES. ^c 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 Gain¹⁻³

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

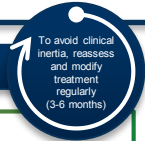
- Mirtazapine
- Amitriptyline
- Nortriptyline
- Doxepin
- Paroxetine
- Imipramine
- Lithium

Antiseizure agents

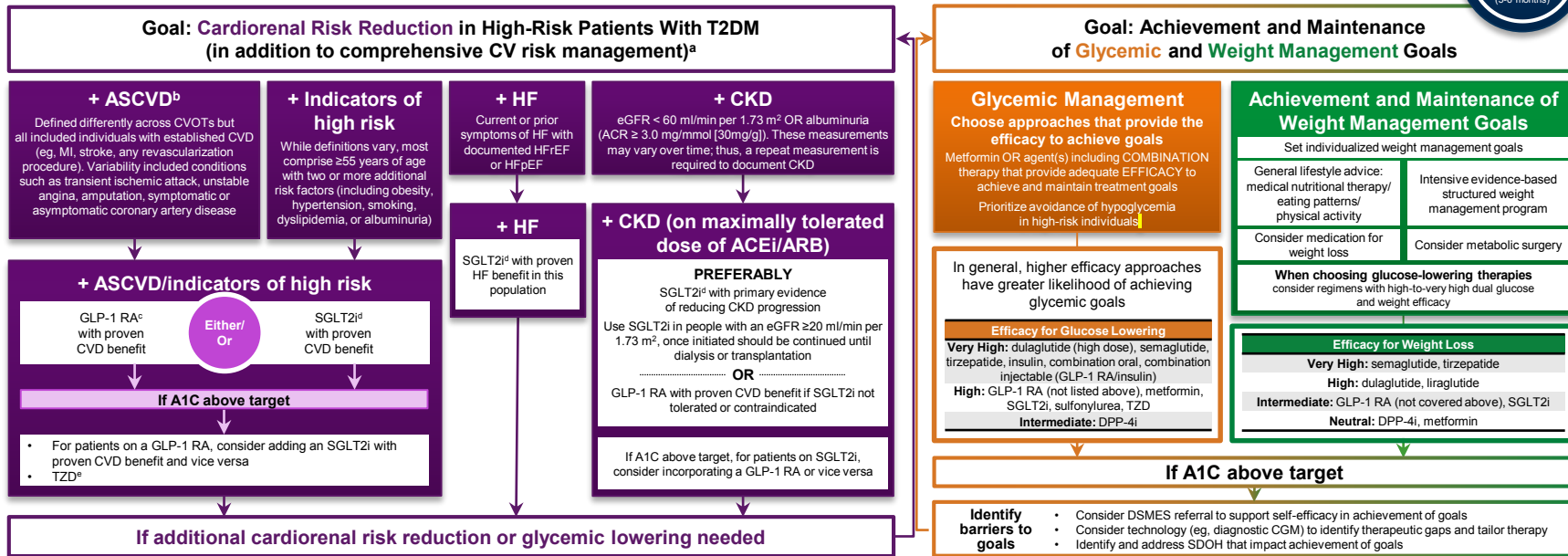
- Carbamazepine
- Valproate
- Gabapentin

**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 Medications¹



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



^a 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. ^b 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. ^c 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. ^d For SGLT2i, CV/renal outcomes trials demonstrate their efficacy in reducing the risk of composite MACE, CV death, all-cause mortality, MI, HF, and renal outcomes in individuals with T2DM with established/high risk of CVD. ^e Low-dose TZD may be better tolerated and similarly effective.

ADA Standards for the Management of T2DM: Use of Glucose-Lowering Medications¹

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



Goal: **Cardiorenal Risk Reduction in High-Risk Patients With T2DM**

Goal: **Achievement and Maintenance of Glycemic and Weight Management Goals**

“I want to help to protect your organs”

Goal: **Cardiorenal Risk Reduction in High-Risk Patients with T2DM (in addition to comprehensive CV risk management)^a**

“I want to help you to achieve your **blood sugar** and **weight** goals to reduce risk of complications”

Goal: **Achievement and Maintenance of Glycemic and Weight Management Goals**

^a 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 Interventions¹

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

1. <https://www.therapeuticinertia.diabetes.org/about-therapeutic-inertia>.

Simplified Management of Glucose-Lowering Medications in T2DM: DCRM Multispecialty Practice Recommendations¹



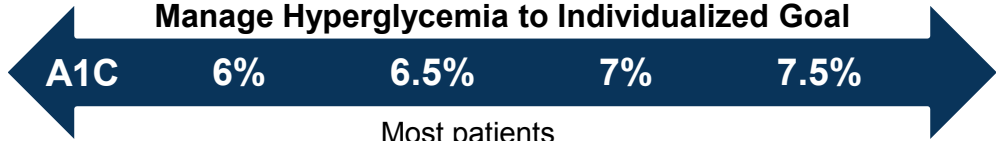
Lifestyle therapy

Reduce ASCVD and Kidney Risks Based on Comorbidities

CAD	HFrEF/HFpEF	CKD	Stroke/TIA
LA GLP-1 RA	SGLT2i	SGLT2i	LA GLP-1 RA
SGLT2i		LA GLP-1 RA	Pioglitazone
Pioglitazone			

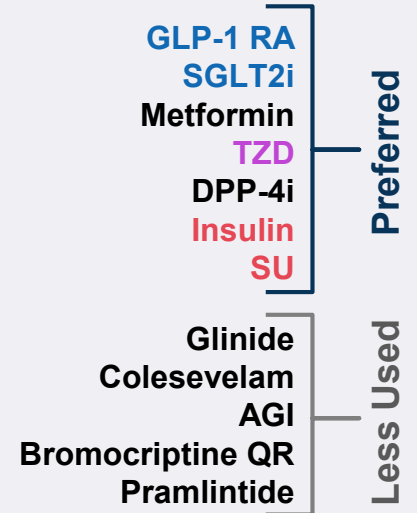
Manage Hyperglycemia to Individualized Goal

Younger, healthier, at lower CV risk



Older, complex, at higher CV risk

Recommended Hierarchy



- Use initial combination therapy for patients with A1C >1%-2% above goal
- Assess glucose management with A1C (3 m), CGM or SMBG, glycated albumin or fructosamine (3 wk)
- Add agents with complementary MOA to maintain glucose control at goal^a
- Choose agents according to recommended hierarchy based on patient's risks, benefits, preferences, and access to therapies
- Insulin is necessary for patients with diabetes symptoms

- Proven benefits in CVOTs
- Hypoglycemia and/or HF risk
- Both

^a Do not combine GLP-1 RA and DPP-4i. Use caution when combining insulin + SU or insulin + TZD.
 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^{1,a}

Many patients want to know *how the medication will affect them* more than *how it works*

Knowing what AEs to expect

How to take it

How it reduces long-term risks

Benefits/risks of different meds

How it fits needs/lifestyle

Primary care physicians need to be comfortable with the medication, and have a team to help them

Shared care model/clinical team

CDE or others to teach injection medication use

EHR alerts for PwT2DM who need intervention/follow-up

Time-saving strategies (even just a few minutes!)

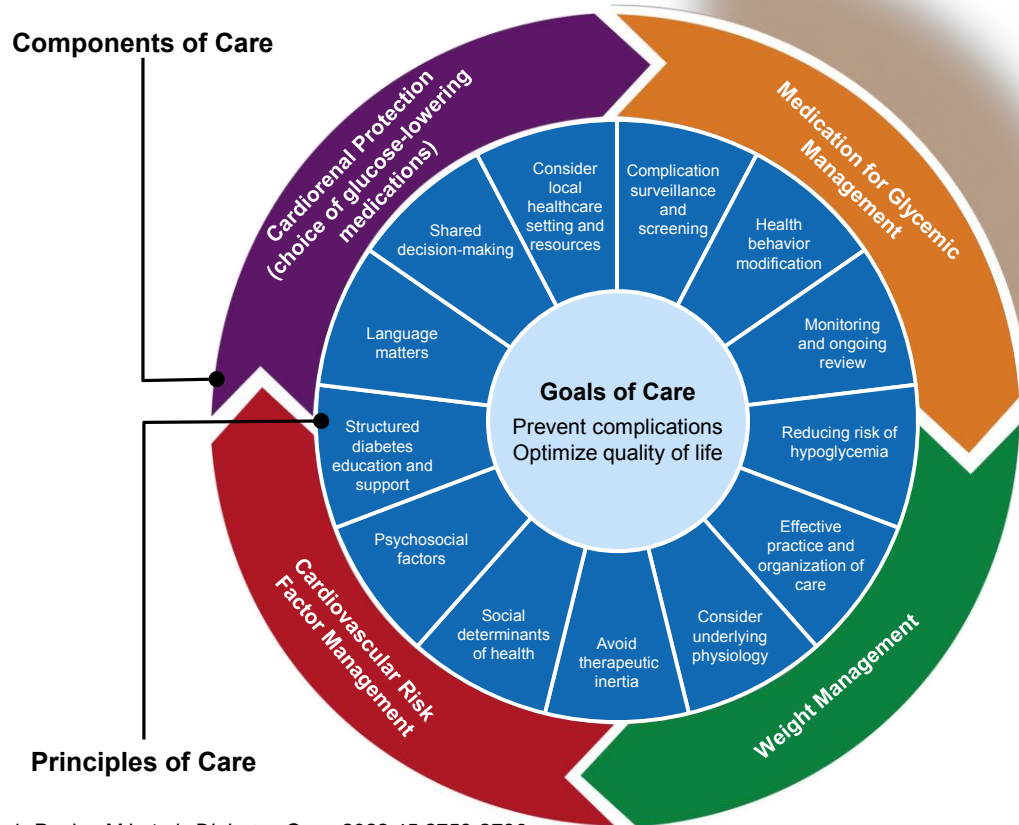
Assessing TIR with CGM

^a 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^{1,2}



Glycemic Management

Choose approaches that provide the efficacy to achieve goals

- Metformin OR agent(s) including COMBINATION therapy that provide adequate EFFICACY to achieve and maintain treatment goals
- Prioritize avoidance of hypoglycemia in high-risk individuals
- In general, higher efficacy approaches have greater likelihood of achieving glycemic goals

Efficacy For Glucose Lowering	
Very High	Dulaglutide (high dose), semaglutide, tirzepatide, insulin, combination oral, combination injectable (GLP-1 RA/insulin)
High	GLP-1 RA (not listed above), metformin, SGLT2i, sulfonylurea, TZD
Intermediate	DPP-4i

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.

Glycemic Efficacy: Change in A1C From Baseline Among Drugs Approved for Glycemic Control and Obesity Management in PwT2DM

Approved for T2DM^a

A1C -0.4% to -0.8%

AGIs¹
DPP-4 inhibitors²
Meglitinides¹
Rosiglitazone³
SGLT2 inhibitors²

A1C -0.81% to -0.99%

Dapagliflozin¹
Empagliflozin¹
Exenatide ER¹
Metformin¹
Pioglitazone⁴
Sulphonylureas¹

A1C -1.0% to -1.9%

Basal insulin¹
Dulaglutide⁵
Premixed insulin¹
Liraglutide 1.8 mg SC⁶
Semaglutide 14 mg⁷

A1C -2.0% to -2.5%

Semaglutide 2 mg SC^{8,9}
Tirzepatide¹⁰

Approved for Obesity Management^a

A1C +1.0% to 1.5

Phentermine¹¹

A1C 0 to -0.3

Orlistat¹²

A1C -0.4% to -0.8%

Naltrexone/
bupropion¹³
Phentermine/
topiramate¹⁴

A1C -1.0% to -1.9%

Liraglutide
3.0 mg SC¹⁵
Semaglutide
2.4 mg SC¹⁶

A1C -2.0% to -2.5%

Tirzepatide¹⁷

^aDoses shown are for agents that are approved at different doses in T2DM and obesity.

1. Tsapas A et al. *Annals Int Med.* 2020;173:278-286. 2. Scheen AJ. *Diabetes Metab.* 2020;46:186-196. 3. https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/021071s052lbl.pdf.

4. https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/021073s049lbl.pdf. 5. Chang KC et al. *Cardiovas Diabetol.* 2020;19:172. <https://doi.org/10.1186/s12933-020-01148-8>.

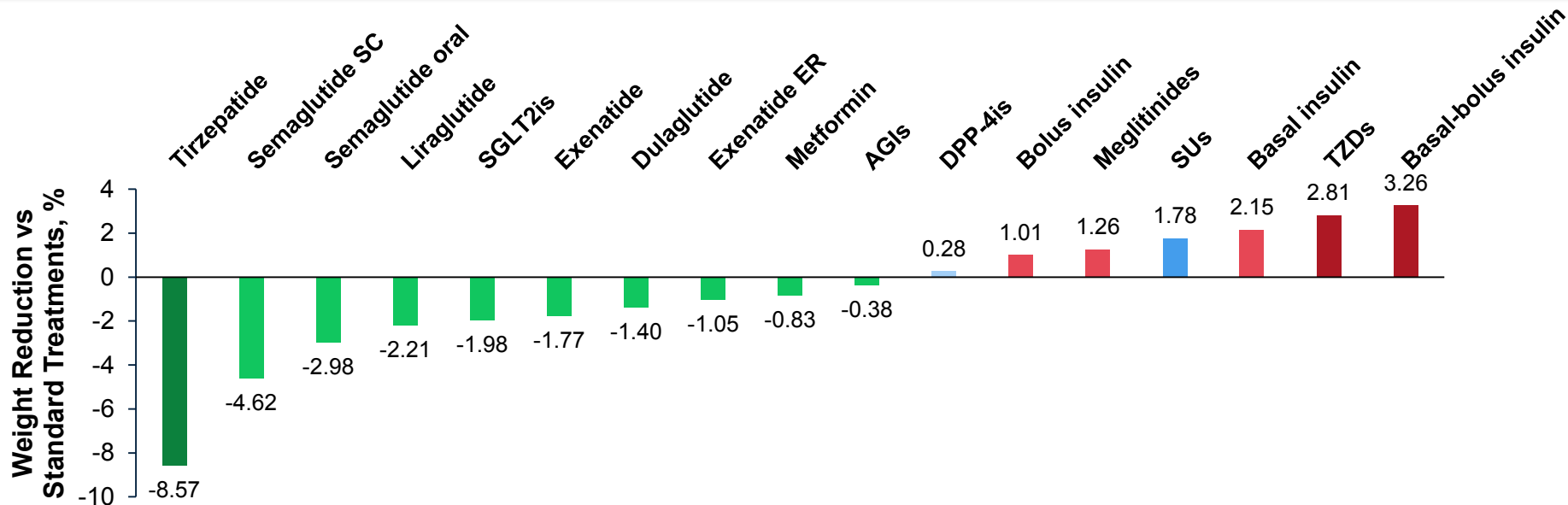
6. https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/022341s039lbl.pdf. 7. https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/213051s018lbl.pdf.

8. https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/209637s020s021lbl.pdf. 9. Frias JP et al. *Lancet Diabetes Endocrinol.* 2021;9:563-574. 10. Frias JP et al. *N Engl J Med.* 2021;385:503-515. 11. Elhag W et al. *Annals Med Surg.* 2019;45:75-81. 12. https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/020766s038lbl.pdf. 13. https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/200063s021lbl.pdf.

14. https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/022580s023lbl.pdf. 15. https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/206321s016lbl.pdf.

16. https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/215256s011lbl.pdf. 17. Garvey WT et al. *Lancet.* 2023;402:613-626.

Weight-Loss Efficacy of Treatments for T2DM¹

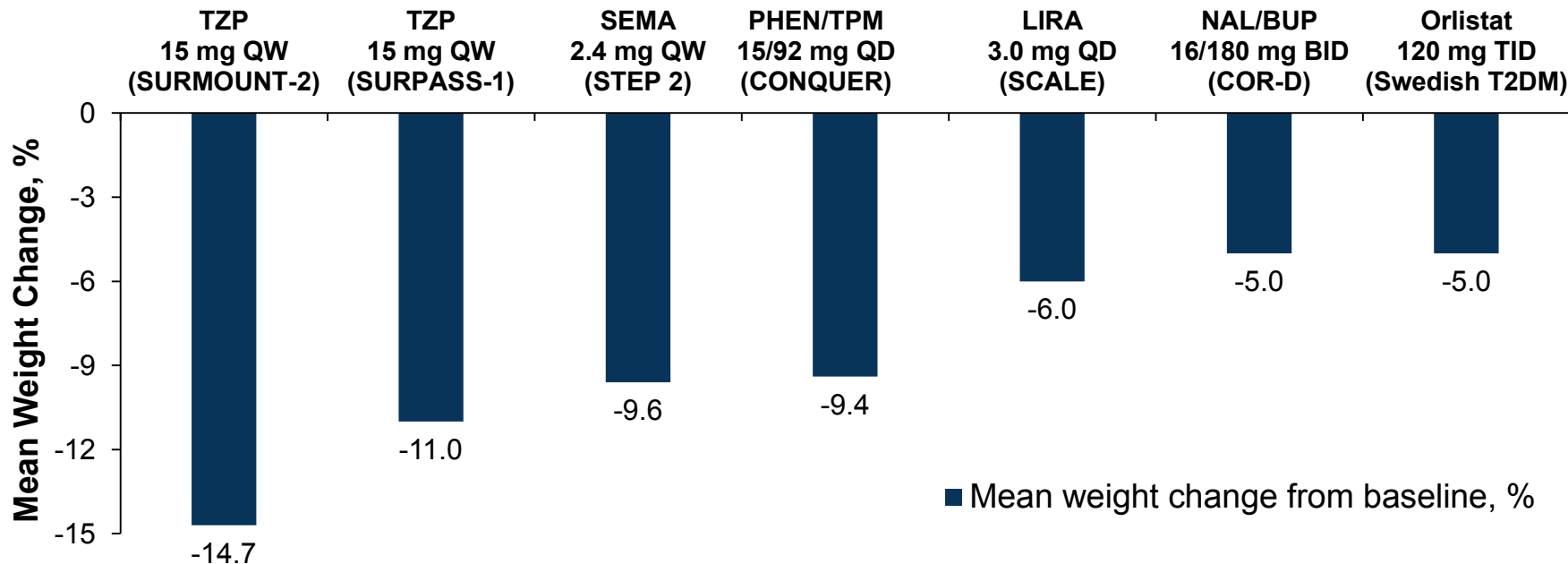


High to Moderate Certainty Evidence
Among the most effective
Among the intermediate effective
Not convincingly different from standard treatment
Among the intermediate harmful
Among the most harmful

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

1. Shi Q et al. *BMJ*. 2023;381:e074068.

Setting Realistic Expectations for Weight Loss in People With T2DM Across Treatment Options^{1-7,a,b}



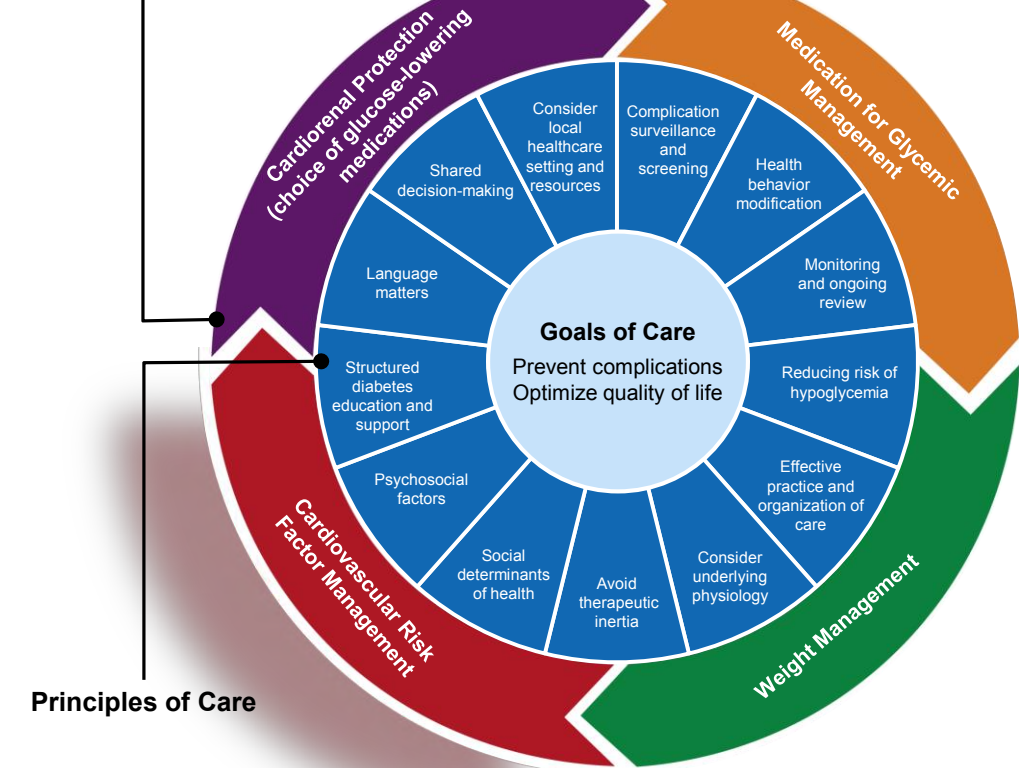
Δ A1C, %	-2.1	-2.1	-1.6	-1.6	-1.3	-0.6	-1.1
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^a Patients managed with antidiabetic medications plus diet or lifestyle modification. ^b Patients had A1C of 7%-10% with diet and exercise alone and were naïve to injectable diabetes therapy.

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 Management¹⁻³

Components of Care



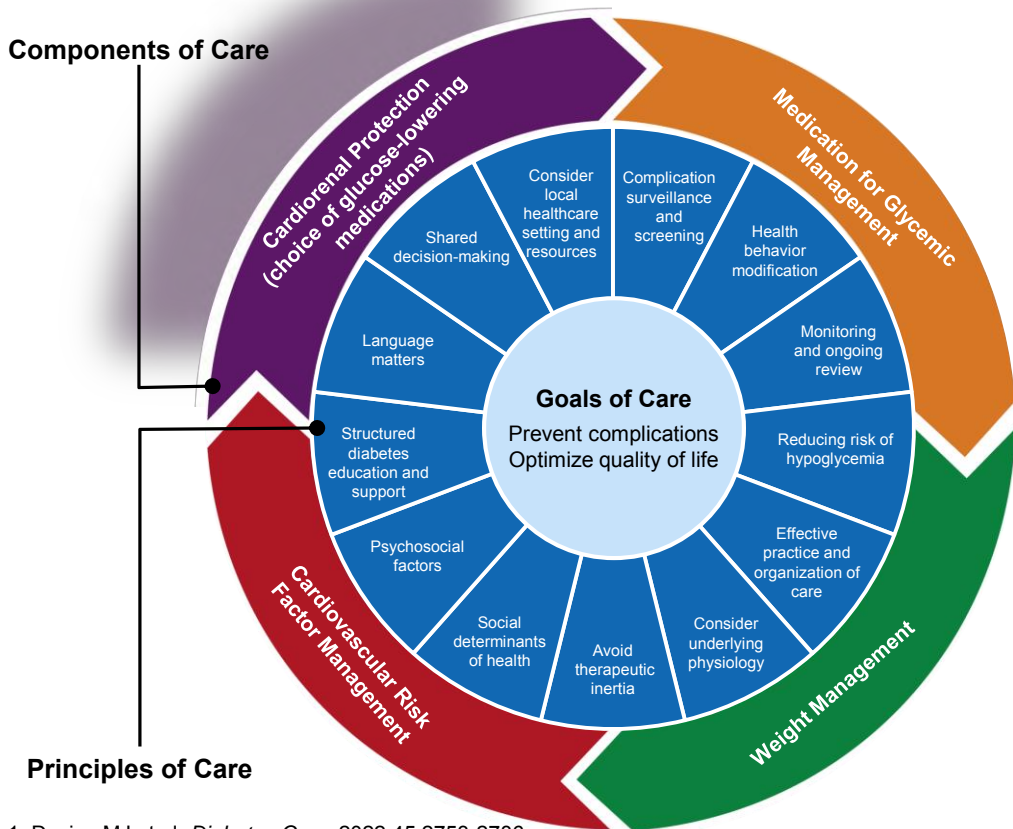
Principles of Care

Ensure Strategies Are in Place to Detect and Optimize Management of CV Risk Factors

CV risk factor screening and surveillance	history, physical, and ECG NT-proBNP, BNP, or hs-cTn
BP lowering	target <130/80 mmHg
Lipid lowering	statins
Antithrombotic agent	indicated for secondary prevention
Smoking cessation	for all

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^{1,2}



+CKD
(on maximally tolerated dose of ACEi/ARB)

Preferably
SGLT2i with primary evidence of reducing CKD progression
Use SGLT2i in people with an eGFR ≥ 20 mL/min per 1.73 m²; once initiated should be continued until initiation of dialysis or transplantation

----- OR -----

GLP-1 RA with proven CVD benefit if SGLT2i not tolerated or contraindicated

If additional cardiorenal risk reduction or glycemic management needed, consider combination SGLT2i/GLP-1 RA

+ASCVD/Indicators of High Risk

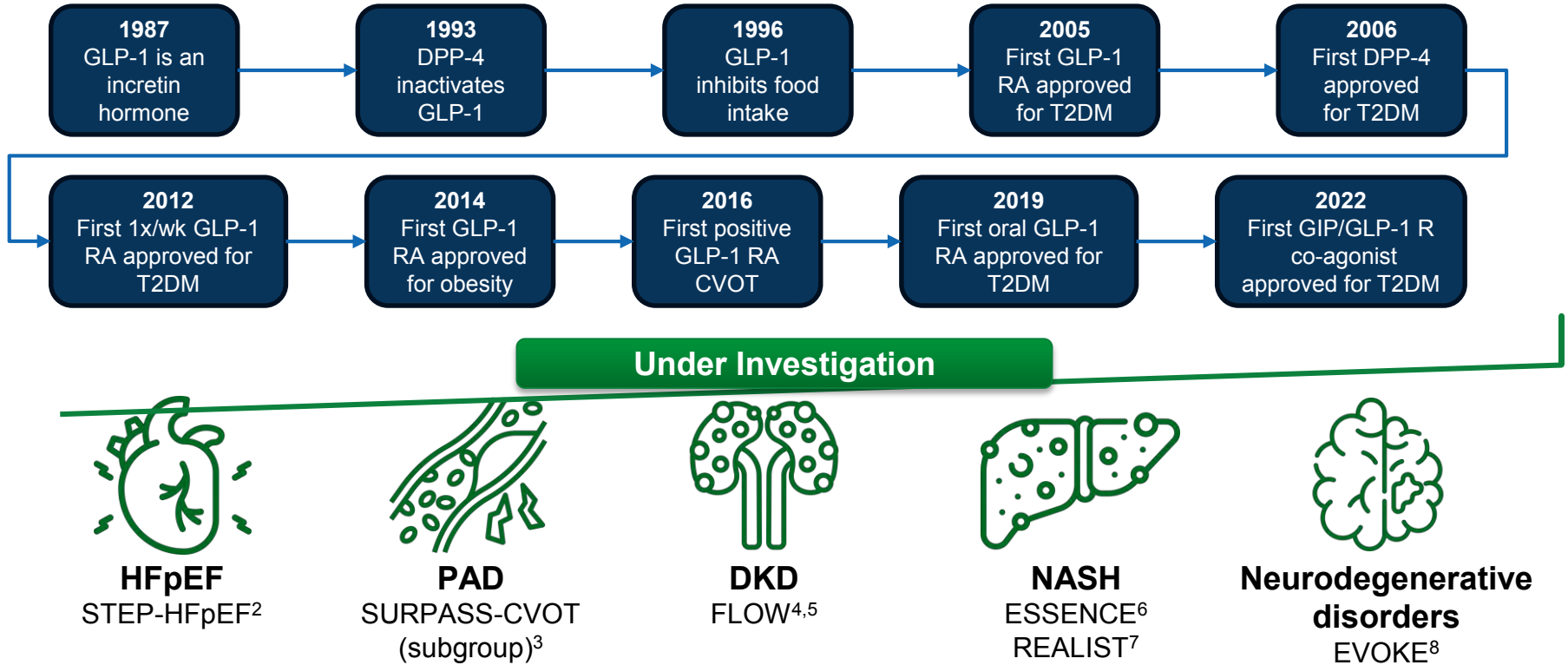
GLP-1 RA with proven CVD benefit **Either/ Or** SGLT2i with proven CVD benefit

If additional cardiorenal risk reduction or glycemic management needed, consider combination SGLT2i/GLP-1 RA

+HF
SGLT2i with proven HF benefit in this population

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.

GLP-1 and GIP/GLP-1 Discovery, Clinical Development, and Future Directions¹



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/m²; **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 m²; **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

Let's Pause to Discuss Andrew

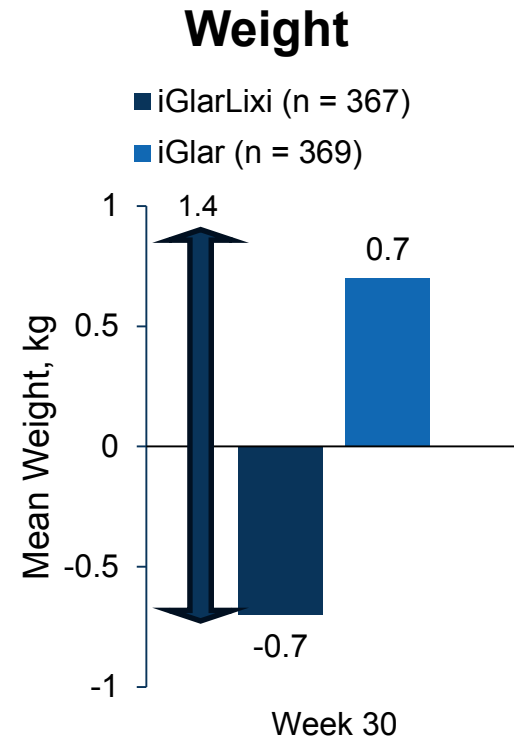
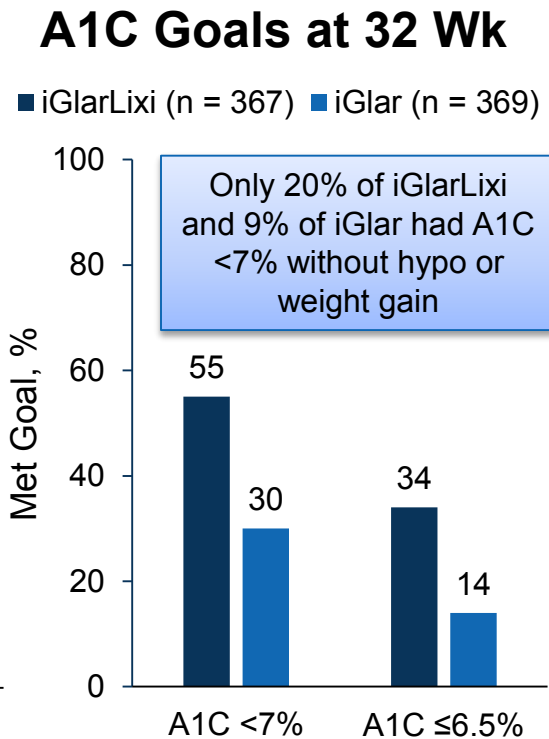
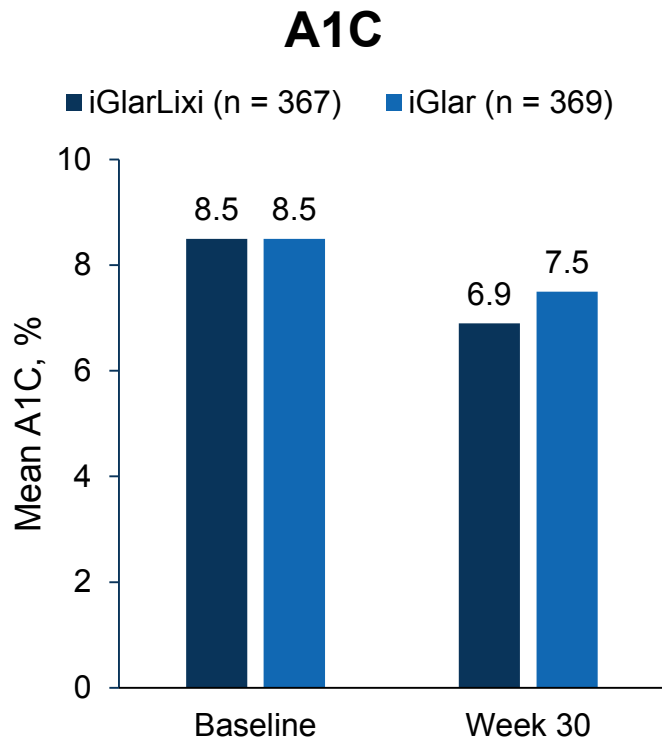
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- **Current medications**
 - Insulin glargine 10 units daily, sitagliptin 100 mg/d, atorvastatin 40 mg/d, losartan/HCTZ 100 mg/12.5 mg daily



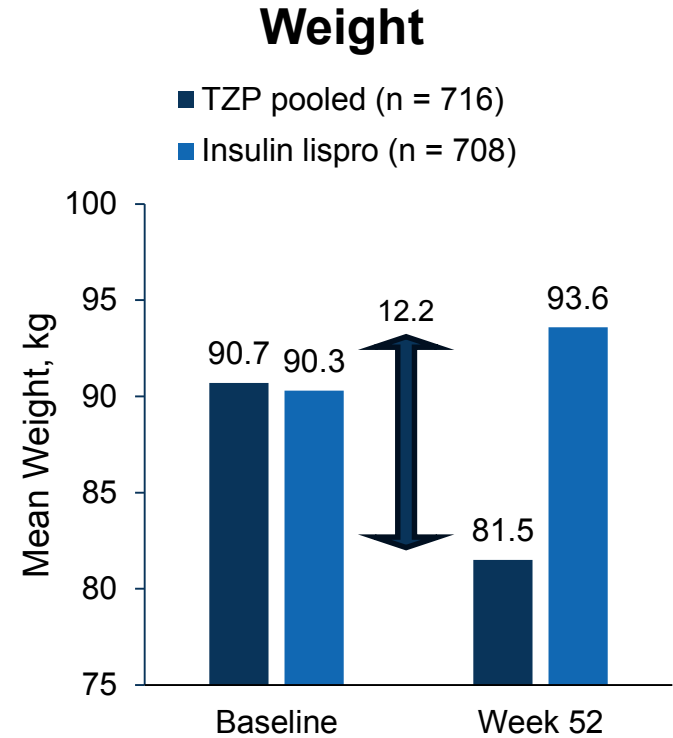
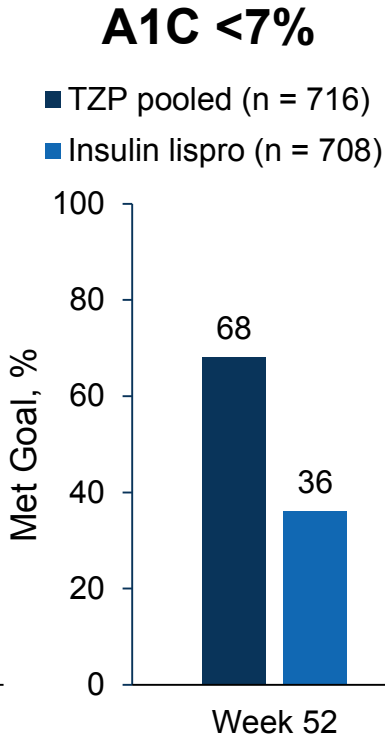
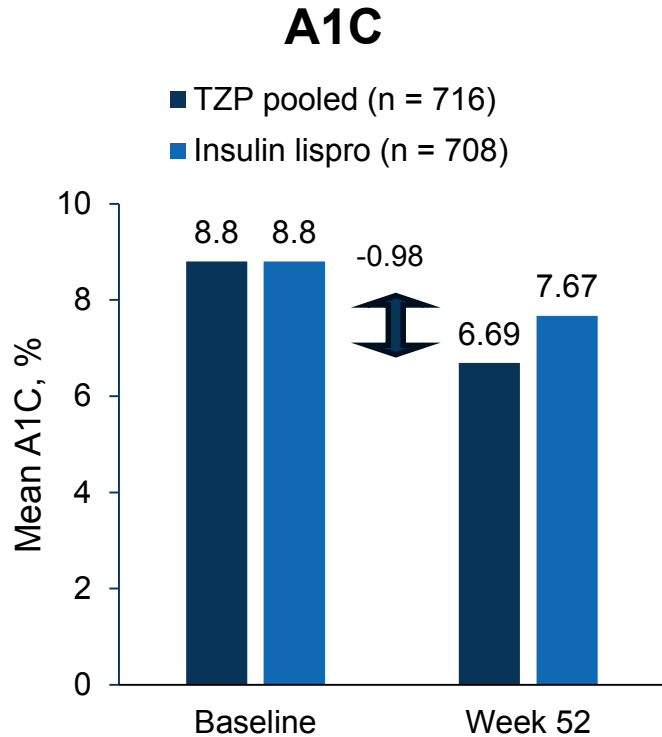
1. What changes would you recommend to Andrew's basal insulin therapy?
2. What A1C goal would you set for Andrew?

Intensifying Basal Insulin Therapy With Insulin/GLP-1 RA Coformulation or Continuing Basal Insulin: LixiLan-L¹



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

Intensifying Basal Insulin Therapy With Prandial Insulin or Tirzepatide: SURPASS-6¹



Encouraging Personal Success Through Individualized, Shared Decision-Making

PeerView
Live

Shared Decision-Making: What It Is and Why We Use It¹

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



Employ SDM to collaborate with patients on individualized diabetes plans



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

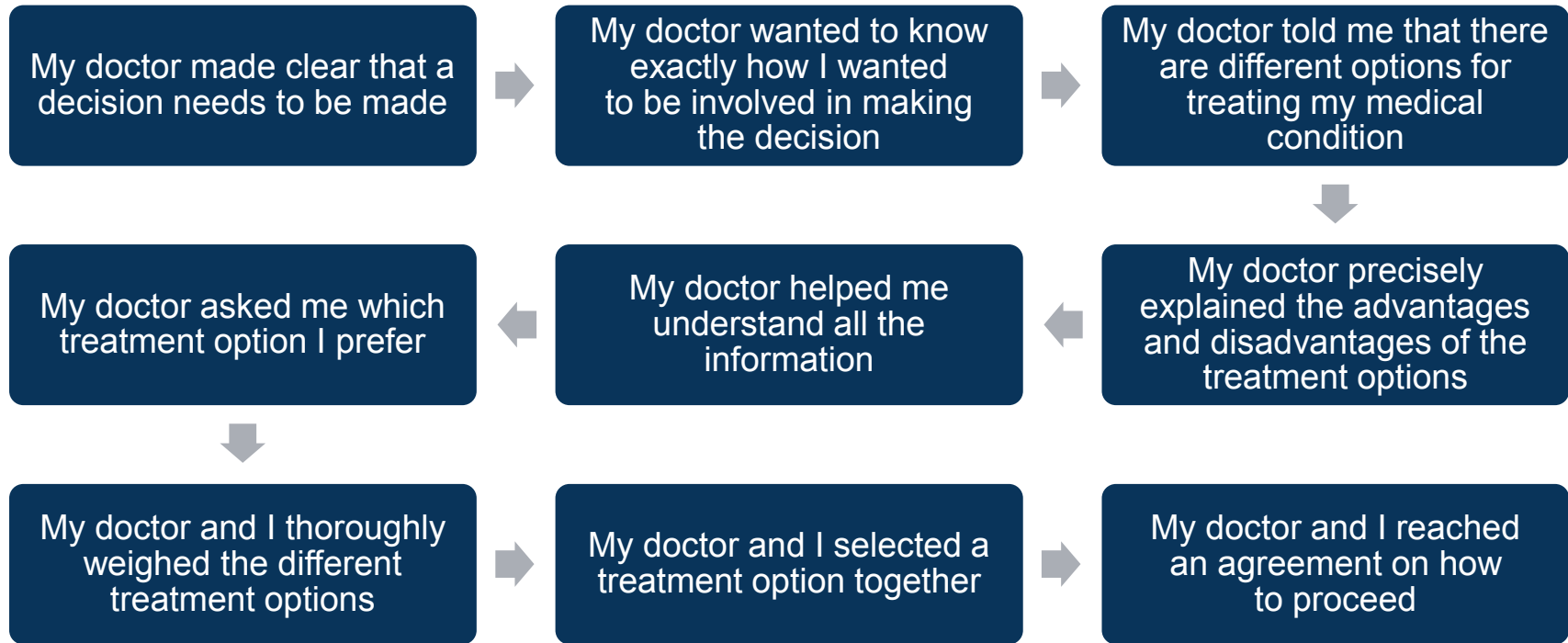


SDM helps to acknowledge and address emotional needs of PwT2DM



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

The SDM-Q-9 Tool Ensures That the Patient Is Included in Decision-Making¹



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

People of color (POC) report feeling dismissed, disregarded, devalued, and excluded from decision-making¹

- 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



Communicating Within the Patient Encounter¹

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?

Yes

No

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
- Schedule follow-up or referral

Response From PCP

“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.”

ADA Standards: Weight Management Assessment Recommendations¹

Use person-centered nonjudgmental language

Measure height/weight and calculate BMI annually; use weight trajectory to inform care

May need to monitor weight more frequently in presence of comorbidities

Ensure privacy during weighing

Be understanding; up to 80% of obesity might be genetically determined²

Modest weight loss can improve glycemia and CV risk factors

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^{1,2}



Eat better



Manage cholesterol



Be more active



Manage blood pressure



Quit tobacco



Manage blood sugar

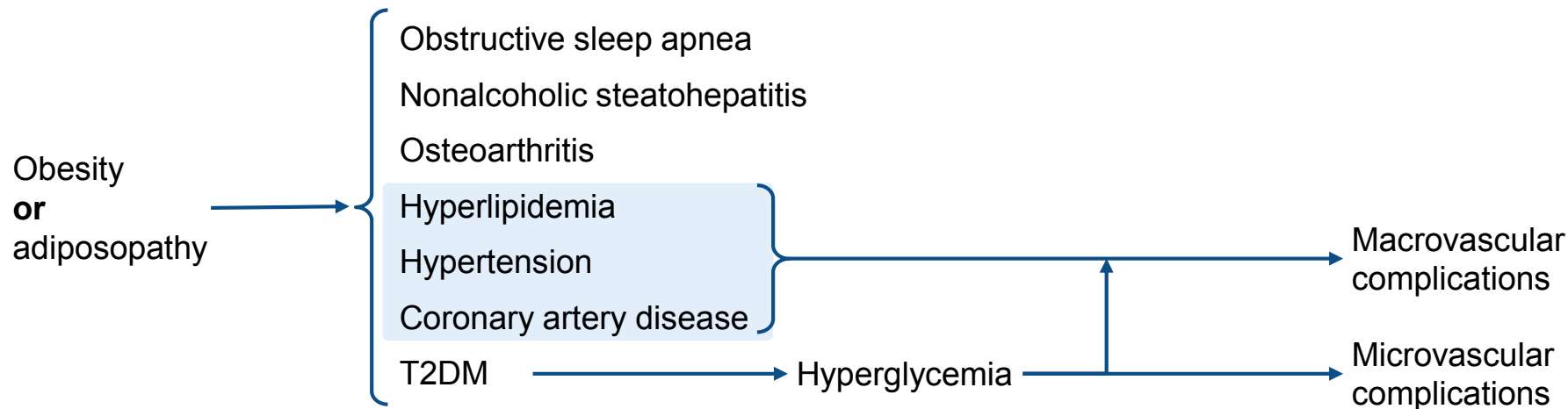


Get healthy sleep



Manage weight

Upstream Weight-Centric Approach to T2DM Management Has Wide-Ranging Benefits¹



Weight-centric approach
Upstream intervention

Glucocentric approach
Downstream intervention

How Much Weight Loss Is Needed to Improve T2DM?

- **Measures of glycemia¹**
- **Triglycerides¹**

- **HDL-C¹**
- **Systolic and diastolic blood pressure**
- **Hepatic steatosis measured by MRS²**
- **Measures of feeling and function**
 - **Symptoms of urinary stress incontinence³**
 - **Measures of sexual function^{4,5}**
 - **Quality of life measures (IWQOL)⁶**

- **NASH Activity Score measured on biopsy⁷**
- **Apnea-Hypopnea Index⁸**

- **Reduction in CV events, mortality, remission of T2DM⁹⁻¹¹**

-3%

-5%

-10%

-15%

1. Wing RR et al. *Diabetes Care*. 2011;34:1481-1486. 2. Lazo M et al. *Diabetes Care*. 2010;33:2156-2163. 3. Phelan S et al. *J Urol*. 2012;187:939-944.
4. Wing RR et al. *Diabetes Care*. 2013;36:2937-2944. 5. Wing RR et al. *J Sex Med*. 2010;7:156-165. 6. Engel SG et al. *Obes Res*. 2003;11:1207-1213.
7. Promrat K et al. *Hepatology*. 2010;51:121-129. 8. Foster GD et al. *Arch Intern Med*. 2009;169:1619-1626. 9. Després JP et al. *BMJ*. 2001;322:716-720.
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 Therapy¹⁻⁴

- **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 events¹**
 - >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/>.

Factors Affecting the Adherence To and Persistence With GLP-1-Based Therapies in People With T2DM^{1,2}

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	
Inconvenience of injection schedule	

Since this study was performed, 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/m²; **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 m²; **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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- **Current medications**
 - Metformin HCL 500 mg QD, glipizide 15 mg QD, pravastatin 10 mg QD, lisinopril 20 mg QD



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

Severe Hypoglycemia Rates Are Similar for All Combinations of Sulfonylureas and DPP-4is¹

Exposure ^a	Events, n	Person-Years, n	Incidence Rates (95% CI) ^b	Crude HR (95% CI)	Adjusted HR (95% CI) ^c
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)

^a 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. ^b Per 1,000 person-years. ^c 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, other 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.



Answer These Questions

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





Assessment Question

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/m²

You'll need to do whatever you can to attain a BMI <25 kg/m²

I'm not sure



Assessment Question

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

I'm not sure



Assessment Question

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

I'm not sure



Assessment Question

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

I'm not sure

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

AE: adverse event

AGI: alpha-glucosidase inhibitors

ALT: alanine transaminase

AMH: 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

ER: 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: 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: 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