Cases in the Community

Optimizing Treatment and Considering Weight Management as a Primary Goal in People With T2DM

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PeerView
Live

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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.

PeerView Live

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/m^2
- You'll need to do whatever you can to attain a BMI <25 kg/m^2
- I'm not sure

PQ 1

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

PQ 2

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

PQ 3

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

PQ 4

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

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

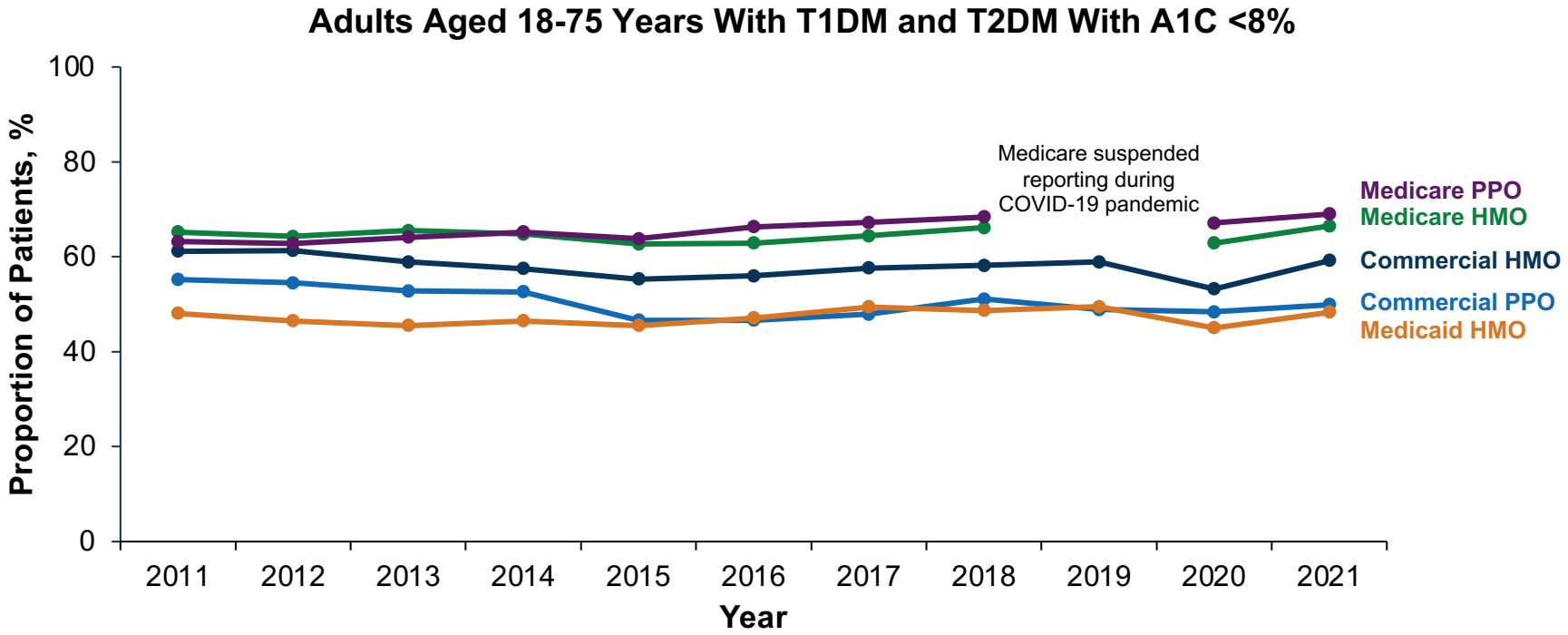
ADA Standards: Recommended Screening Methods and Classification[1,2]

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

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[1]



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

T2DM Is Strongly Associated With Several Macrovascular and Microvascular Complications[1]

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%

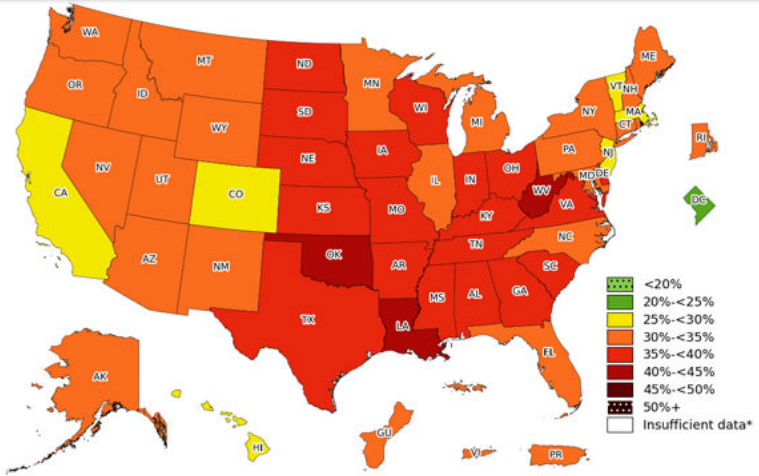
Leading cause of end-stage renal disease in the adult population worldwide

Female sex is a risk factor for nephropathy in T2DM

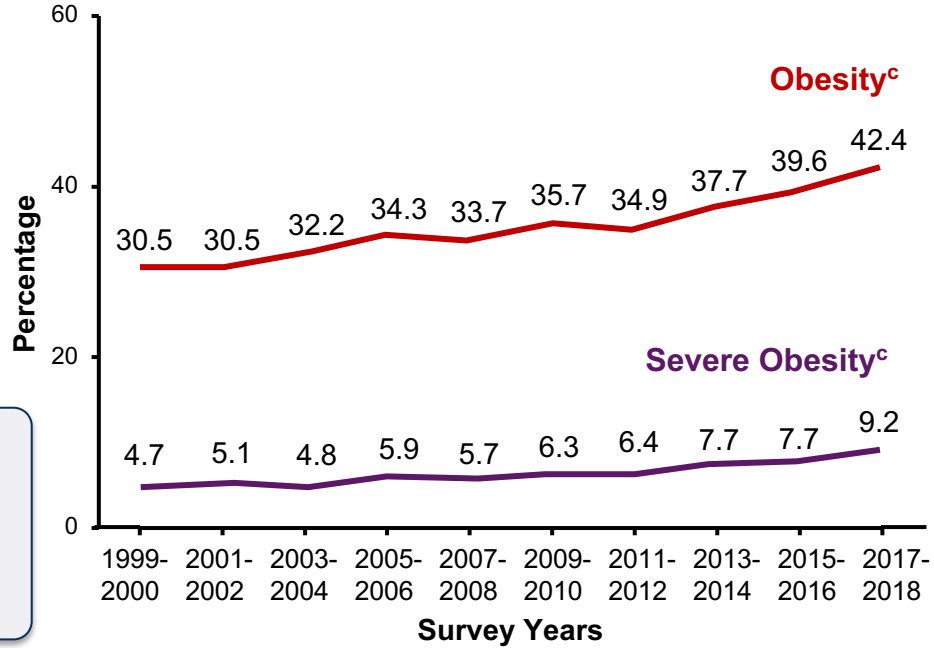
1. Dal Canto E et al. *Eur J Prev Cardiol*. 2019;26(suppl 2):25-32.

The Mean BMI Is Increasing in the United States

2022[1,a]



Trends, 1999-2018[2,b]



In a cohort of over 18 million US patients with overweight/obesity …[3]

- Annual probability of ≥5% weight loss was 10%
- Reducing BMI to healthy weight was less likely especially if BMI ≥45 kg/m^2

[a] Prevalence of self-reported obesity (BMI ≥30 kg/m^2) 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 Gain[1-3]

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

Antidepressants/ mood stabilizers

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

Antihypertensive agents

- Atenolol
- Metoprolol
- Nadolol
- Propranolol

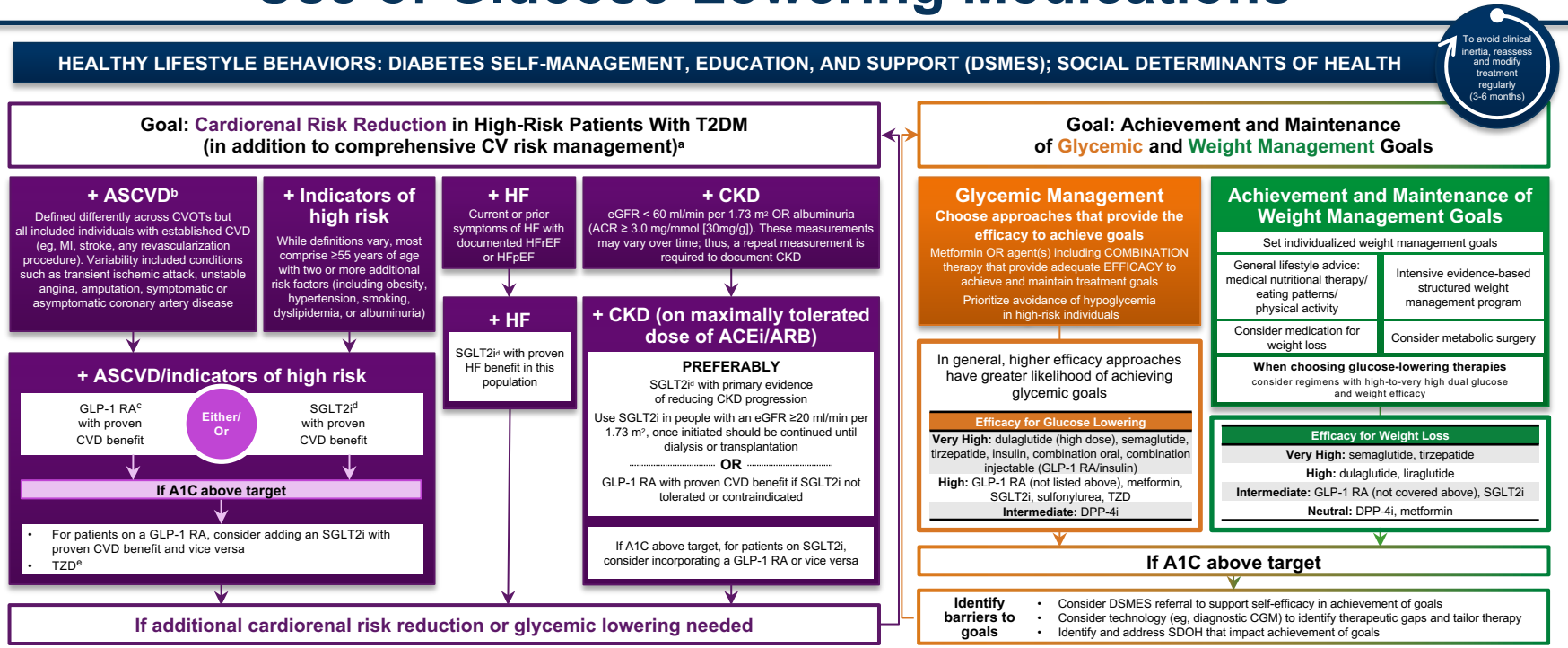
Antiseizure agents

- Carbamazepine
- Valproate
- Gabapentin

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

1. Ahmed NJ et al. *Pharmazie*. 2022;77:299-301. 2. https://www.accessdata.fda.gov/scripts/cder/daf/. 3. Christensen SM et al. *Obesity Pillars*. 2022;4:100041.

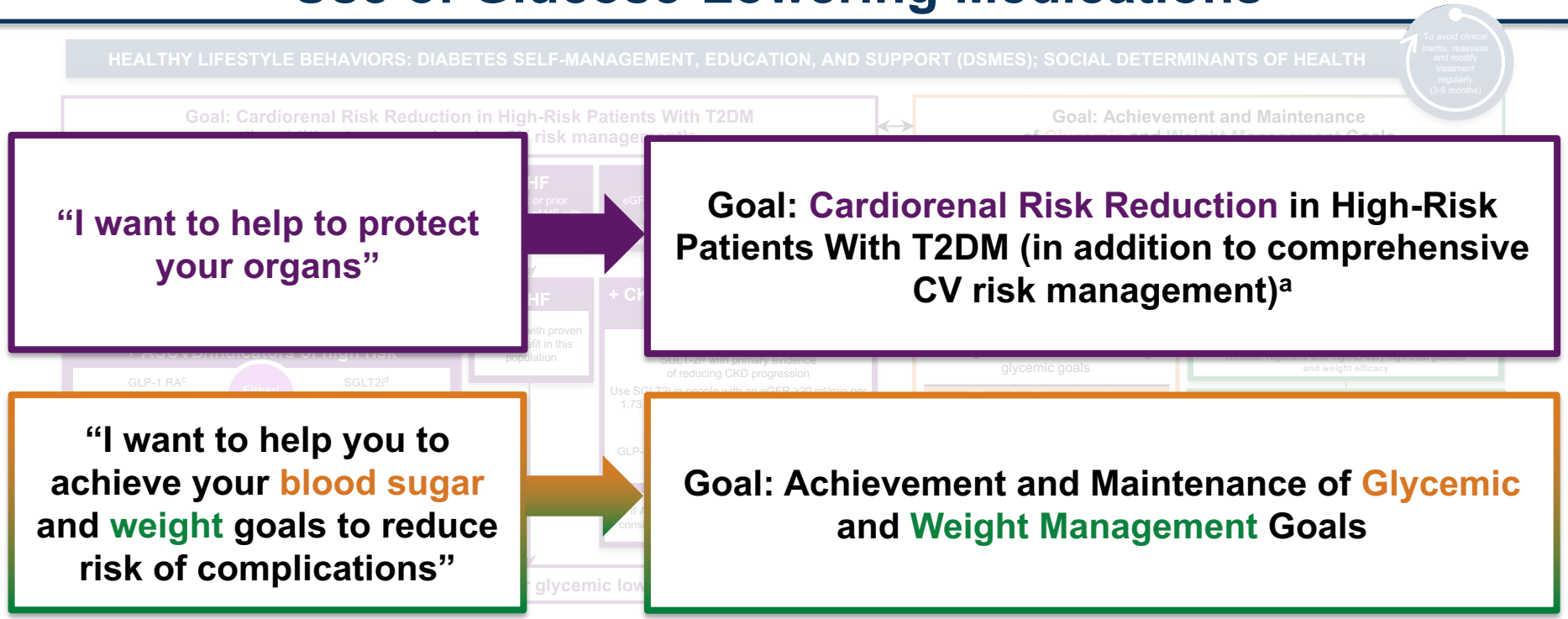
ADA Standards for the Management of T2DM: Use of Glucose-Lowering Medications[1]



[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, HHF, and renal outcomes in individuals with T2DM with established/high risk of CVD. [e] 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.

ADA Standards for the Management of T2DM: Use of Glucose-Lowering Medications[1]



[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 Interventions[1]

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.

Glucose-Lowering Therapy in T2DM: DCRM 2.0 Practice Recommendations for Hyperglycemia[1]

Lifestyle Therapy: Hyperglycemia Track

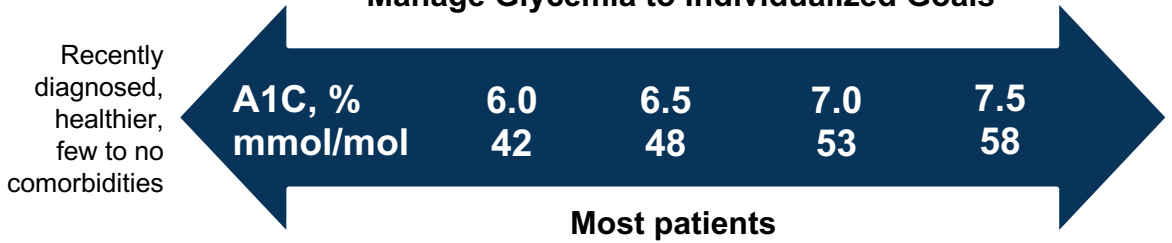
Glucose Hierarchy

Preferred
- GLP-1 RA[a]
- Metformin
- SGLT2i[b]
- TZD
- DPP-4i
- Insulin
- SU

Less Used
- Glinide
- Colesevelam
- AGI
- Bromocriptine QR
- Pramlintide

Proven benefits in CVOTs
Hypoglycemia and/or HF risk
Both

Manage Glycemia to Individualized Goals



- **Generally, use initial combination therapy for patients with A1C >1%-2% above goal**
- Lower A1C goals can be achieved safely provided there is no hypoglycemia
- Assess glucose control with A1C plus CGM or SMBG and intensify therapy until goal achieved[c]
- Add agents with complementary MOA to maintain glucose control at goal[d]
- Choose agents according to recommended hierarchy based on patient's risks, benefits, preferences, and access to therapies
- Consider initial insulin therapy in severe hyperglycemia/metabolic decompensation

[a] GLP-1 RA or GIP/GLP-1 RA. [b] If CKD, efficacy may be lower; consider using SGLT2i later in glucose hierarchy. [c] Glycated albumin or fructosamine may also be considered for evaluation of glycemic control. [d] Do not combine incretin classes (GLP-1 RA, GIP/GLP-1 RA, DPP4i; use caution when combining insulin + SU, insulin + SGLT2i, or insulin + TZD.

1. Handelsman Y et al. *Metabolism*. 2024 Jun 4 [Epub ahead of print].

Glucose-Lowering Therapy in T2DM: DCRM 2.0 Practice Recommendations for Cardiorenal Event Prevention[1]

Lifestyle Therapy: Cardiorenal Track

Prevent ASCVD/HF/CKD Events Independent of Glycemic Status

ASCVD	HFpEF	HFrEF/HFmrEF	CKD	Stroke/TIA
GLP-1 RA[a,b]	SGLT2i[b]	SGLT2i[b]	SGLT2i[b]	GLP-1 RA[a]
SGLT2i[b]	GLP-1 RA[a,b]		GLP-1 RA[a,b]	Pioglitazone
Pioglitazone				

Proven benefits in CVOTs

Hypoglycemia and/or HF risk

Both

[a] GLP-1 RA with proven benefit. [b] Combining GLP-1 RA and SGLT2i is encouraged to improve outcomes.

1. Handelsman Y et al. *Metabolism*. 2024 Jun 4 [Epub ahead of print].

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

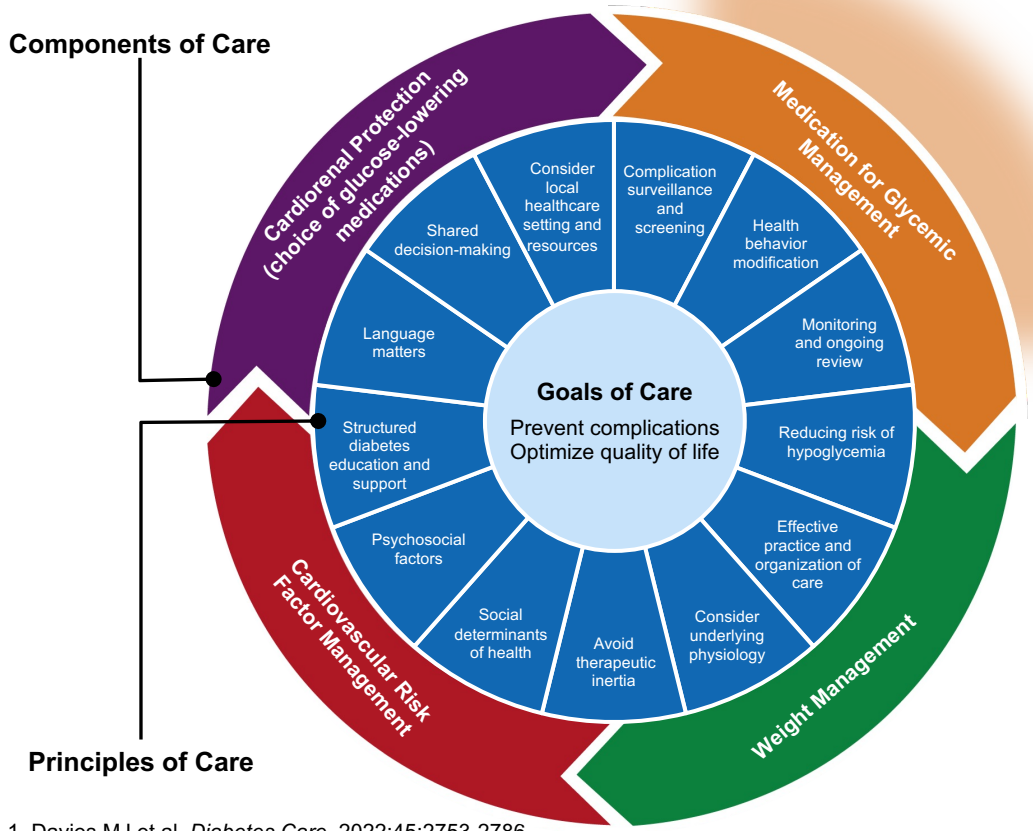
- Shared care model/clinical team
- CDE or others to teach injection medication use
- EHR alerts for PwT2DM who need intervention/follow-up
- Time-saving strategies (even just a few minutes!)
- Assessing TIR with CGM

[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%	A1C -0.81% to -0.99%	A1C -1.0% to -1.9%	A1C -2.0% to -2.5%
AGIs[1]	Dapaglifiozin[1]	Basal insulin[1]	Semaglutide 2 mg SC[8,9]
DPP-4 inhibitors[2]	Empaglifozin[1]	Dulaglutide[5]	Tirzepatide[10]
Meglitinides[1]	Exenatide ER[1]	Premixed insulin[1]	
Rosiglitazone[3]	Metformin[1]	Liraglutide 1.8 mg SC[6]	
SGLT2 inhibitors[2]	Pioglitazone[4]	Semaglutide 14 mg[7]	
	Sulphonylureas[1]		

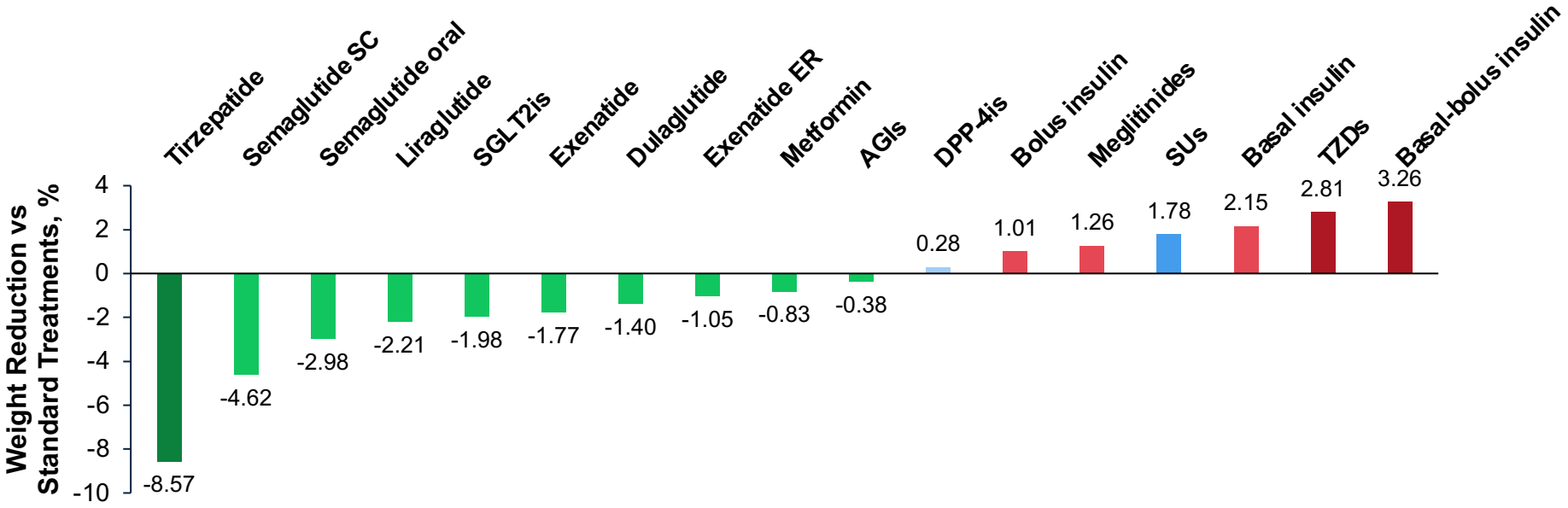
Approved for Obesity Management[a]

A1C +1.0% to 1.5	A1C 0 to -0.3	A1C -0.4% to -0.8%	A1C -1.0% to -1.9%	A1C -2.0% to -2.5%
Phentermine[11]	Orlistat[12]	Naltrexone/ bupropion[13]	Liraglutide 3.0 mg SC[15]	Tirzepatide[17]
		Phentermine/ topiramate[14]	Semaglutide 2.4 mg SC[16]	

[a] Doses 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. Frías JP et al. *Lancet Diabetes Endocrinol*. 2021;9:563-574. 10. Frías 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 T2DM[1]

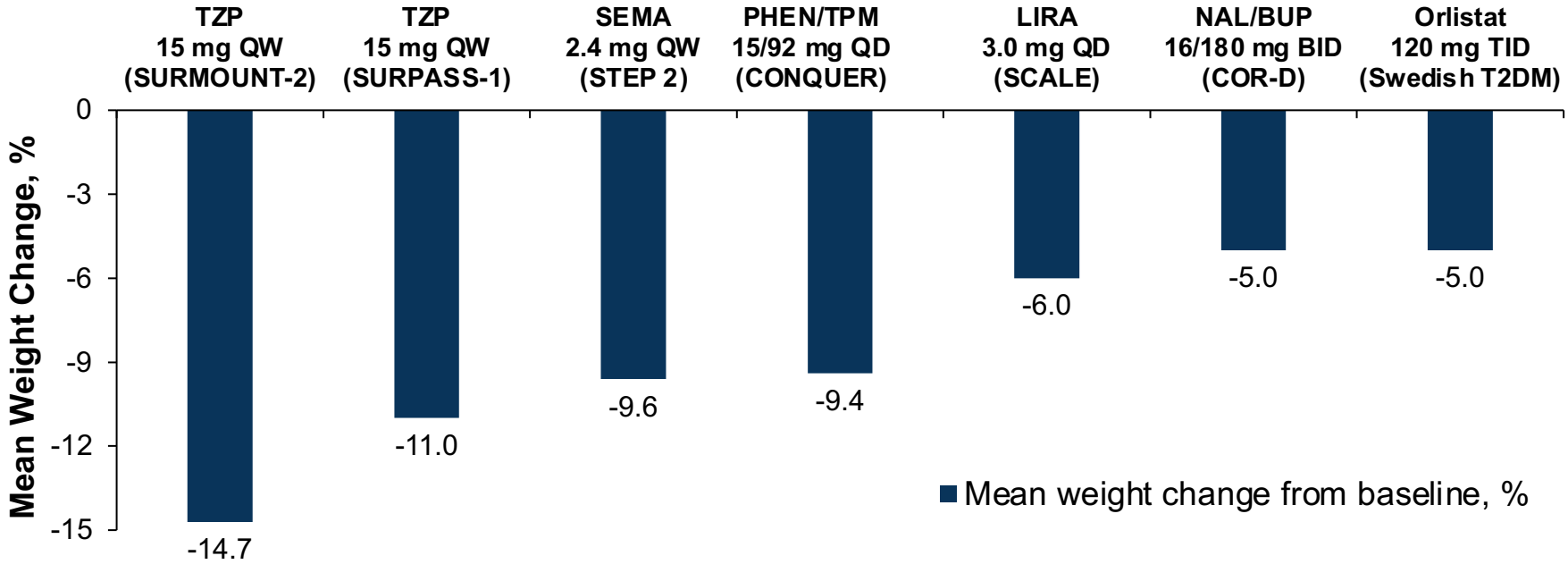


High to Moderate Certainty Evidence
Among the most effective
Among the intermediate effective
Not convincingly different from standard treatment
Among the intermediate harmful
Among the most harmful

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]

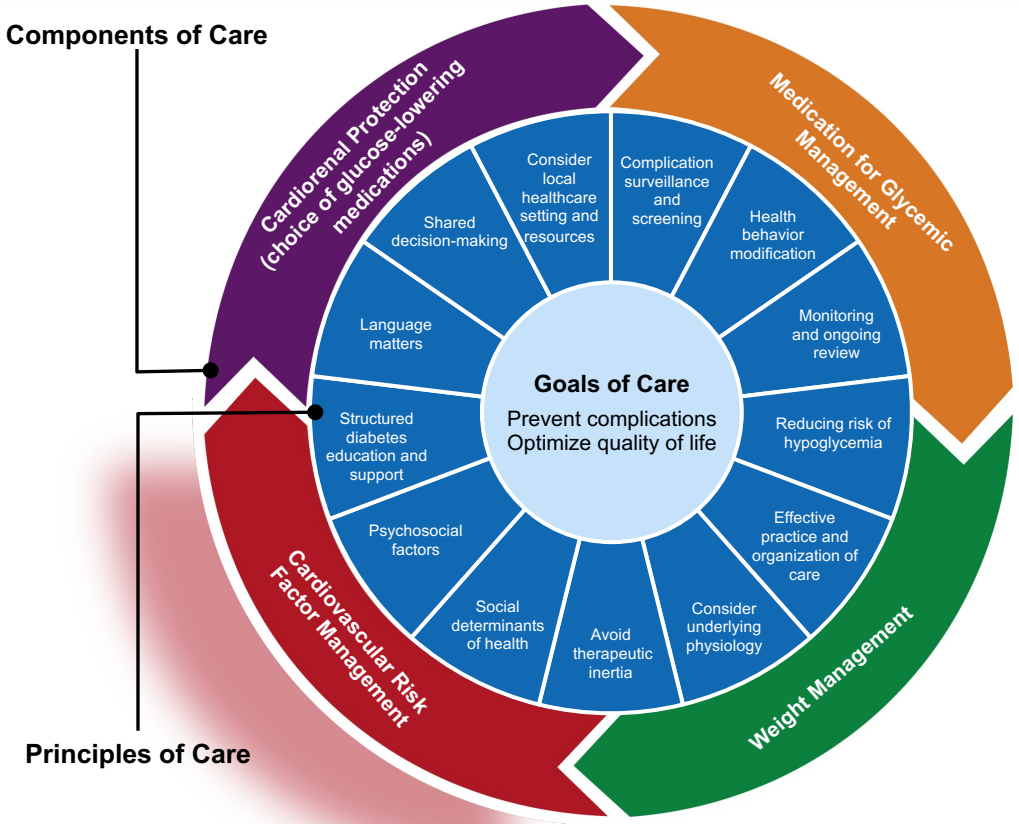


ΔA1C, %	-2.1	-2.1	-1.6	-1.6	-1.3	-0.6	-1.1

[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 Management[1-3]

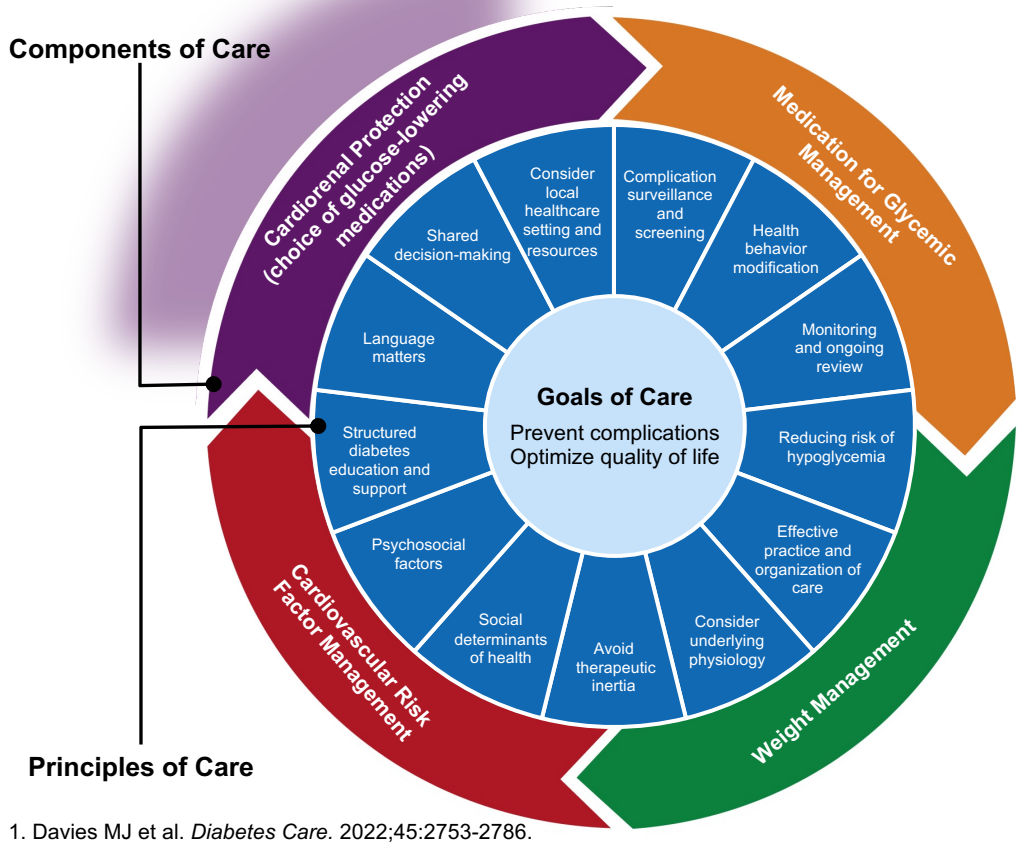


Ensure Strategies Are in Place to Detect and Optimize Management of CV Risk Factors

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 m^2; 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 Directions[1]

1987
GLP-1 is an incretin hormone

1993
DPP-4 inactivates GLP-1

1996
GLP-1 inhibits food intake

2005
First GLP-1 RA approved for T2DM

2006
First DPP-4 approved for T2DM

2012
First 1x/wk GLP-1 RA approved for T2DM

2014
First GLP-1 RA approved for obesity

2016
First positive GLP-1 RA CVOT

2019
First oral GLP-1 RA approved for T2DM

2022
First GIP/GLP-1 R co-agonist approved for T2DM

Under Investigation

HFpEF
STEP-HFpEF[2]
STEP-HFpEF DM[3]

PAD
SURPASS-CVOT[4]
STRIDE[5]

DKD
FLOW[6]

NASH
ESSENCE[7]
REALIST[8]

Neurodegenerative disorders
EVOKE/EVOKE Plus[9,10]

1. Drucker DJ, Holst JJ. *Diabetologia*. 2023;66:1765-1779. 2. Kosiborod MN et al. *N Engl J Med*. 2023;389:1069-1084. 3. Kosiborod MN et al. *N Engl J Med*. 2024;390:1394-1407.
4. Nicholls SJ et al. *Am Heart J*. 2024;267:1-11. 5. https://clinicaltrials.gov/study/NCT04560998. 6. Perkovic V et al. *N Engl J Med*. 2024 May 24 [Epub ahead of print].
7. https://clinicaltrials.gov/study/NCT04822181. 8. https://clinicaltrials.gov/study/NCT03648554. 9. https://clinicaltrials.gov/study/NCT04777396.
10. https://clinicaltrials.gov/study/NCT04777409

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^2; **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^2; **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

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^2; **height**: 70 inches (178 cm); **weight**: 215 lb (97.4 kg)
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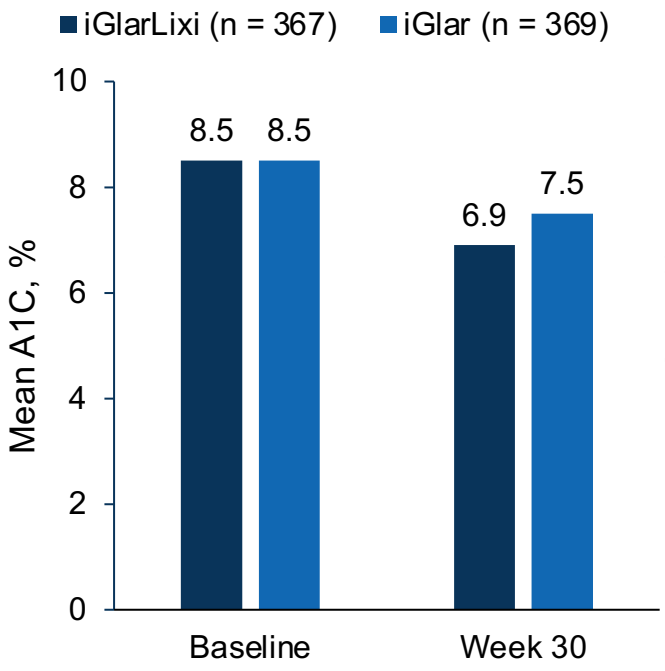
- **ALT**: 38; **AST**: 29
- **Current medications**
  - Insulin glargine 10 units daily, sitagliptin 100 mg/d, atorvastatin 40 mg/d, losartan/HCTZ 100 mg/12.5 mg daily

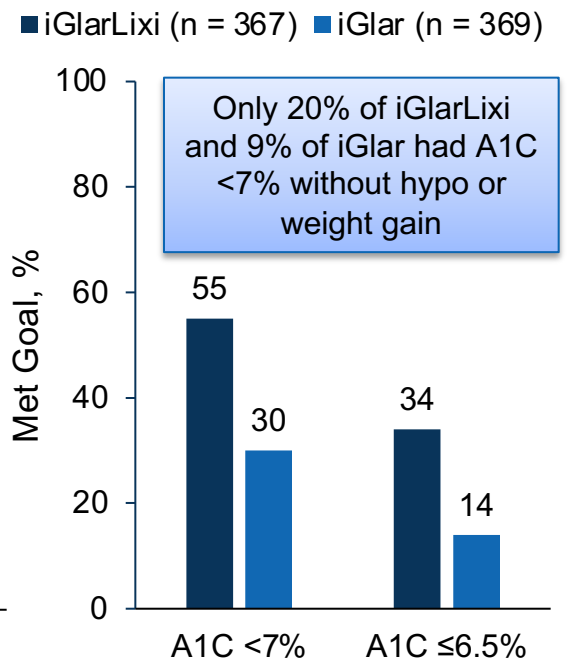
1. **What changes would you recommend to Andrew's basal insulin therapy?**
2. **What A1C goal would you set for Andrew?**

Intensifying Basal Insulin Therapy With Insulin/GLP-1 RA Coformulation or Continuing Basal Insulin: LixiLan-L[1]

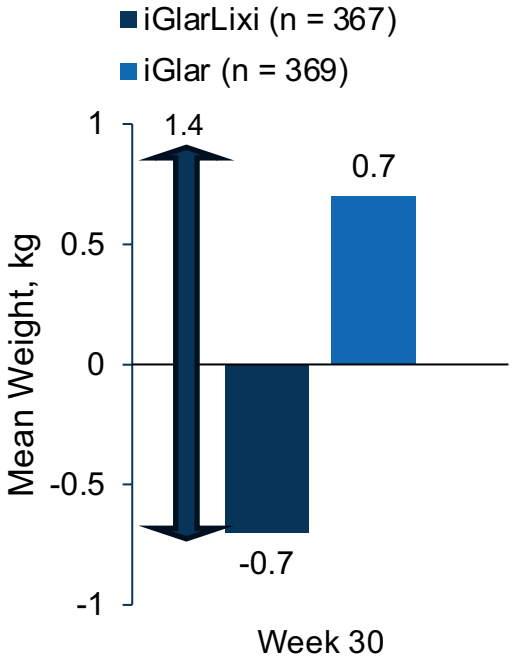
A1C



A1C Goals at 32 Wk

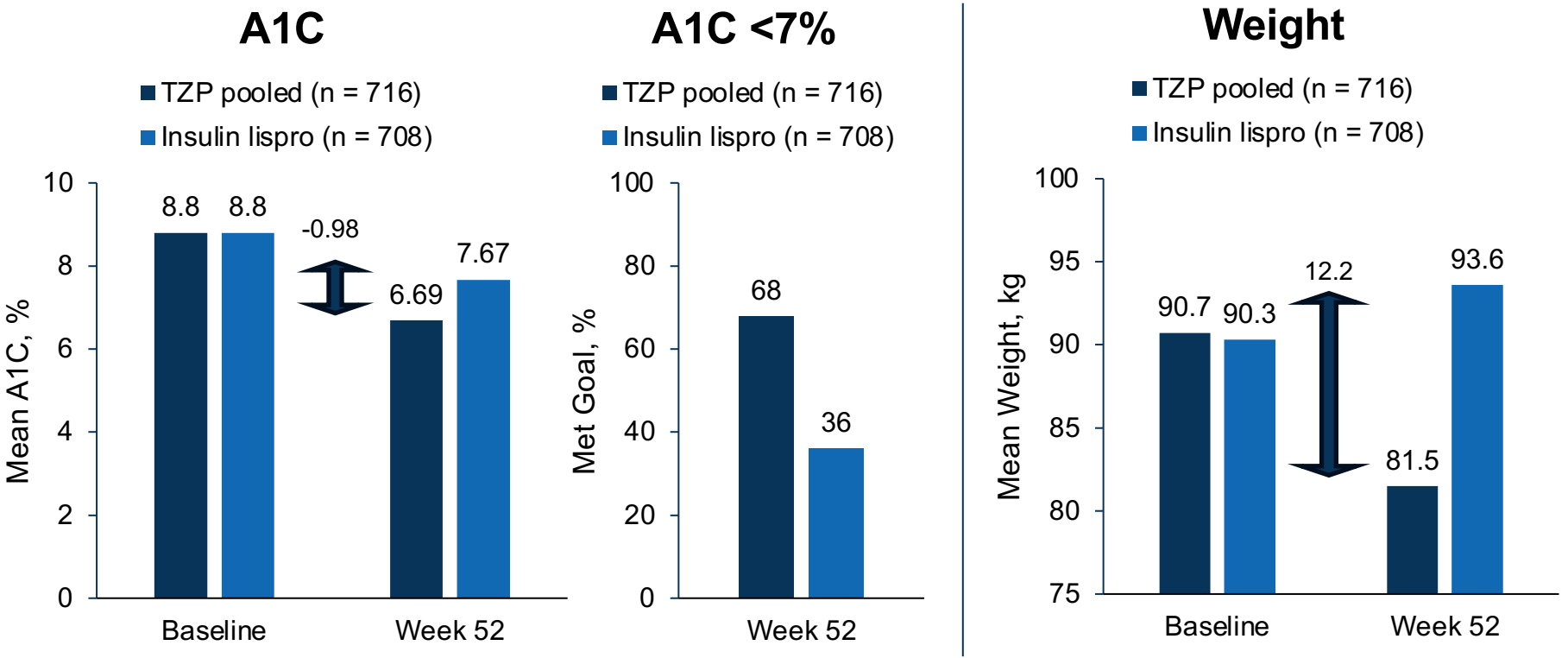


Weight



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

Intensifying Basal Insulin Therapy With Prandial Insulin or Tirzepatide: SURPASS-6[1]



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

Encouraging Personal Success Through Individualized, Shared Decision-Making

PeerView
Live

Shared Decision-Making: What It Is and Why We Use It[1]

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)

1. Boeder S et al. *Diabetes Ther.* 2023;14:425-446.

The SDM-Q-9 Tool Ensures That the Patient Is Included in Decision-Making[1]

1. Kriston L et al. *Patient Educ Couns*. 2010;80:94-99.

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[1]

- 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

1. Hamed S et al. *BMC Pub Health*. 2022;22:988.

Communicating Within the Patient Encounter[1]

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

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

No

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."

1. https://stop.publichealth.gwu.edu/Resources.

ADA Standards: Weight Management Assessment Recommendations[1]

- 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 determined[2]
- 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

Be more active

Quit tobacco

Get healthy sleep

Manage cholesterol

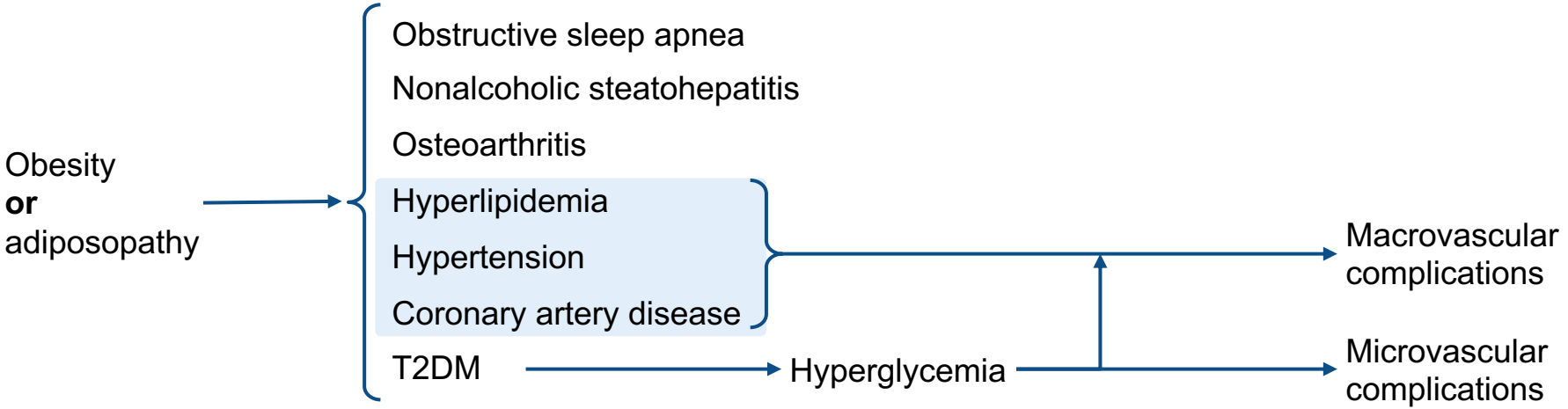
Manage blood pressure

Manage blood sugar

Manage weight

1. https://www.heart.org/-/media/Healthy-Living-Files/LE8-Fact-Sheets/Lifes_Essential_8_Fact_Sheet.pdf. 2. Lloyd-Jones DM et al. *Circulation*. 2022;146:e18-e43.

Upstream Weight-Centric Approach to T2DM Management Has Wide-Ranging Benefits[1]



Weight-centric approach
Upstream intervention

Glucocentric approach
Downstream intervention

1. Lingvay I et al. *Lancet*. 2022;399:394-405.

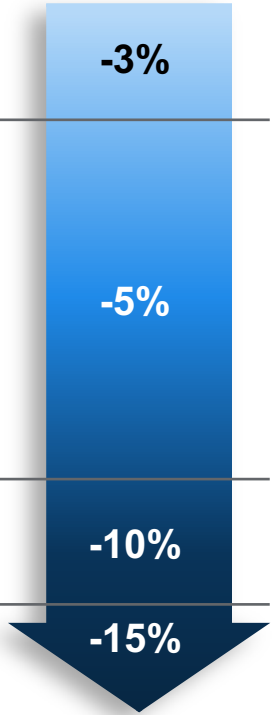
How Much Weight Loss Is Needed to Improve T2DM?

- Measures of glycemia[1]
- Triglycerides[1]

- HDL-C[1]
- Systolic and diastolic blood pressure
- Hepatic steatosis measured by MRS[2]
- Measures of feeling and function
  - Symptoms of urinary stress incontinence[3]
  - Measures of sexual function[4,5]
  - Quality of life measures (IWQOL)[6]

- NASH Activity Score measured on biopsy[7]
- Apnea-Hypopnea Index[8]

- Reduction in CV events, mortality, remission of T2DM[9-11]



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 Therapy[1-4]

- **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 events[1]**
  - >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

1. Lee DSU, Lee H. *Diabetol Metab Syndr.* 2022;14:12. 2. Dougherty T, Heile M. *Am J Manag Care*. 2020;26(16 suppl):S325-S334.

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^2; **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^2; **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
- **BMI**: 39.3 kg/m^2; **weight**: 229 lb (103.7 kg); **height**: 64” (163 cm)
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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

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-4is[1]

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.

PeerView
Live

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/m^2
- You'll need to do whatever you can to attain a BMI <25 kg/m^2
- I'm not sure

PQ 5

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

PQ 6

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

PQ 7

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
HFmrEF: heart failure with mildly reduced ejection fraction
HFpEF: heart failure with preserved ejection fraction
HFrEF: heart failure with reduced 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
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
PPO: preferred provider organization

Abbreviations

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