Cases in Diabetes

Cecilia C. Low Wang, MD, FACP, FACE
Professor of Medicine
University of Colorado Anschutz Department of Medicine
Division of Endocrinology, Metabolism, and Diabetes
Aurora, CO

Carol H. Wysham, MD
Clinical Professor of Medicine
University of Washington School of Medicine
Clinical Endocrinologist
Spokane, WA

CONTINUING EDUCATION COMPANY

1

Disclosures

Cecilia Low Wang, MD

Consultant: Genentech/Roche

Independent Data Monitoring Committee: Genentech/Roche

Carol Wysham, MD

Advisory Board: Abbott; Eli Lilly; MannKind; Novo Nordisk

Consultant: Eli Lilly; Novo Nordisk

Research Grant: AbbVie; Bayer Pharmaceuticals; Eli Lilly; Novo Nordisk

Speaker's Bureau: Abbott; Eli Lilly; MannKind; Novo Nordisk

CONTINUING EDUCATION COMPANY

2

Case Study #1

Cecilia Low Wang, MD

38-year-old Female with Hypothyroidism and Obesity, A1c 5.9%

CONTINUING EDUCATION COMPANY

3

Case 1

- 38-year-old female returns to clinic to follow up on routine labs which showed abnormal results. She is concerned and wants to know what they mean.
- She reports some fatigue but has no polyuria, increased thirst, blurry vision, or unexplained weight loss.
- PMHx: Hashimoto's disease-causing hypothyroidism. s/p tonsillectomy.
- Mother: hypothyroidism and diabetes. Father: B12 deficiency. Sister: type 1 diabetes.
- Meds: levothyroxine, multivitamin

CONTINUING EDUCATION COMPANY

4

Case 1 (Continued)

- Exam: BP 138/72. HR 69. Ht 5’4”, Wt 175 lb (BMI 30). Obese F in NAD. Mildly enlarged thyroid. Otherwise, unremarkable, no edema.
- Labs:
  - BMP glucose 112 mg/dL
  - TSH 2.7 mU/L
  - CBC WNL.
  - Point of care (POC) A1c 5.9%

Case 1, Question 1

Which of the Following Labs Is the Best Next Step?

A. Fasting glucose
B. A1c
C. Lipid panel
D. Anti-GAD antibody
E. Islet autoantibody panel

Classification of Prediabetes: *Beyond Type 2 Diabetes*

A common assumption: Prediabetes or dysglycemia = metabolic syndrome, with progression to type 2 diabetes

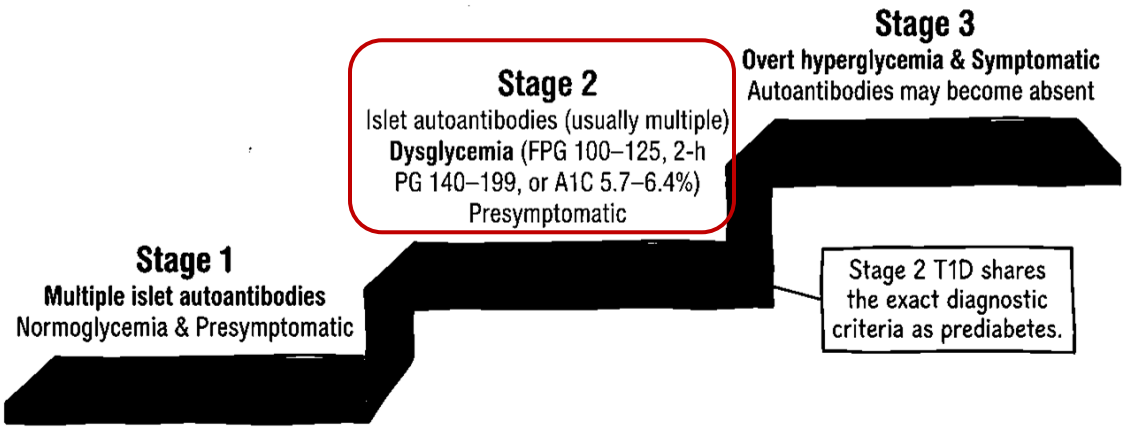
However, up to 40% of adults with new-onset type 1 diabetes are misclassified as having type 2 diabetes

Prediabetes is not always non-autoimmune progressive loss of beta-cell function. It can also represent progression of autoimmune beta cell destruction

ADA PPC. 2. Diagnosis and Classification of Diabetes: Standards of Care in Diabetes - 2026. *Diabetes Care* 2026;49(Suppl. 1):S27-S49.

7

Type 1 Diabetes Has Stages Too, Including Prediabetes



ADA PPC. 2. Diagnosis and Classification of Diabetes: Standards of Care in Diabetes - 2026. *Diabetes Care* 2026;49(Suppl. 1):S27-S49.

8

Why Detecting Stage 2 T1D Matters

Progression to Stage 3 (Overt T1D) is rapid.

~60% progress within 2 years.

~75% progress within 5 years.

1. **Prompt Referral:** Send to a specialized center for metabolic staging. Do not wait for overt hyperglycemia.
2. **Prevent DKA:** Educate the patient immediately on symptoms of DKA, avoiding life-threatening emergency presentations (which occur in 25-50% of undiagnosed cases).
3. **Preserve Beta Cells:** Evaluate for approved preventative treatments (e.g., teplizumab) or clinical trial enrollment to delay clinical onset.

ADA PPC. *Diabetes Care* 2026;49(Suppl. 1):S27-S60.

9

When to Suspect Type 1 Diabetes

Age
Younger age at diagnosis (< age 35 yr)

Autoimmunity
Personal or FHx of autoimmune disease or polyglandular autoimmune syndromes

Body Habitus
BMI <25 kg/m^2

Background
Family history of type 1 diabetes

Control
Inability to achieve glycemic control on noninsulin therapies

Comorbidities
Treatment with immune checkpoint inhibitors for cancer

ADA PPC. 2. Diagnosis and Classification of Diabetes: Standards of Care in Diabetes - 2026. *Diabetes Care* 2026;49(Suppl. 1):S27-S49.

10

A New Paradigm for Prediabetes and Diabetes Classification in Primary Care

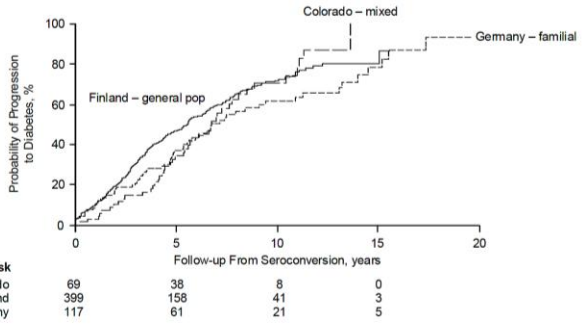
- ✓ Verify prediabetes/diabetes precisely using 2026 ADA criteria (confirmatory tests required).
- ✓ Do not assume all adult-onset dysglycemia is Type 2 Diabetes.
- ✓ Actively look for the AABBCC clinical flags (Age, Autoimmunity, BMI <25, Background, Control, Comorbidities).
- ✓ Screen with the Autoantibody Toolkit (GAD, IA-2, ZnT8, IA) to catch Stage 2 Type 1 Diabetes early.

Refer and intervene to preserve beta-cell function and prevent DKA before Stage 3 overt diabetes occurs, and to detect T1D

ADA PPC. 2. Diagnosis and Classification of Diabetes: Standards of Care in Diabetes - 2026. *Diabetes Care* 2026;49(Suppl. 1):S27-S49.

11

Once a Person Has 2 or More T1D Autoantibodies, the Risk of Progression Is High Whether or Not T1D Is in the Family



Ziegler AG, et al. *JAMA*. 2013;309(23):2473-2479.

The risk of Stage 3 T1D with 2 or more T1D-associated autoantibodies is:

44% in 5 years
70% in 10 years
~100% lifetime risk

INDIANA UNIVERSITY SCHOOL OF MEDICINE

Riley Children's Health Indiana University Health

Slide by Linda DiMeglio, AACE 2026 Annual Meeting

12

Case 1: What Were the Clues

- 38-year-old female returns to clinic to follow up on routine labs which showed abnormal results. She is concerned and wants to know what they mean.
- She reports some fatigue but has no polyuria, increased thirst, blurry vision, or unexplained weight loss.
- PMHx: **Hashimoto's disease** causing hypothyroidism. s/p tonsillectomy.
- Mother: **hypothyroidism** and diabetes. Father: **B12 deficiency**. Sister: **type 1 diabetes**.
- Meds: levothyroxine, multivitamin
- Exam: BP 138/72. HR 69. Ht 5'4", Wt 175 lb (BMI 30). Obese F in NAD. Mildly enlarged thyroid. Otherwise unremarkable, no edema.
- Labs: BMP glucose 112, TSH 2.7, CBC WNL. POC A1c 5.9%

Case 1, Question 2

Which of the Following Labs Is the Best Next Step?

A. Fasting glucose
B. A1c
C. Lipid panel
D. Anti-GAD antibody
E. Islet autoantibody panel

Case 1 Question:
38 yo F with Hypothyroidism and Obesity, A1c 5.9%

- Which of the following labs is the best next step?
  - A. Fasting glucose – *Can be ordered to confirm prediabetes*
  - B. A1c – *Can be ordered to confirm prediabetes*
  - C. Lipid panel – *Can be ordered to determine CKM stage*
  - D. Anti-GAD antibody – *Can be ordered as a first step*
  - E. Islet autoantibody panel – *Optimal next step to classify prediabetes*

15

Case 1: Follow-Up (Scenario A)

- T1D autoantibody panel was negative for all 4 antibodies (GAD65, IA-2, ZnT8, IAA)
- She enrolled in a CDC Diabetes Prevention Program class
  - Learned about healthy lifestyle changes and behavior change strategies
  - Lost 25 lb (BMI 30 → BMI 25.7 kg/m^2)
  - A1c 5.9% → 5.4%
- You continue annual monitoring of her A1c

16

Case 1: Follow-Up (Scenario B)

- T1D autoantibody panel was positive (GAD65, IA-2)
- You continued Q6 month A1c monitoring
- She enrolled in a CDC Diabetes Prevention Program class
  - Learned about healthy lifestyle changes and behavior change strategies,
  - Lost 25 lb (BMI 30 → BMI 25.7 kg/m^2)
  - A1c 5.9% → 5.4%
- 4 years later, her A1c increased to 6.2%

17

Case 1: Follow-Up (Scenario B)

Diabetologia (2024) 67:1731–1759
https://doi.org/10.1007/s00125-024-06205-5

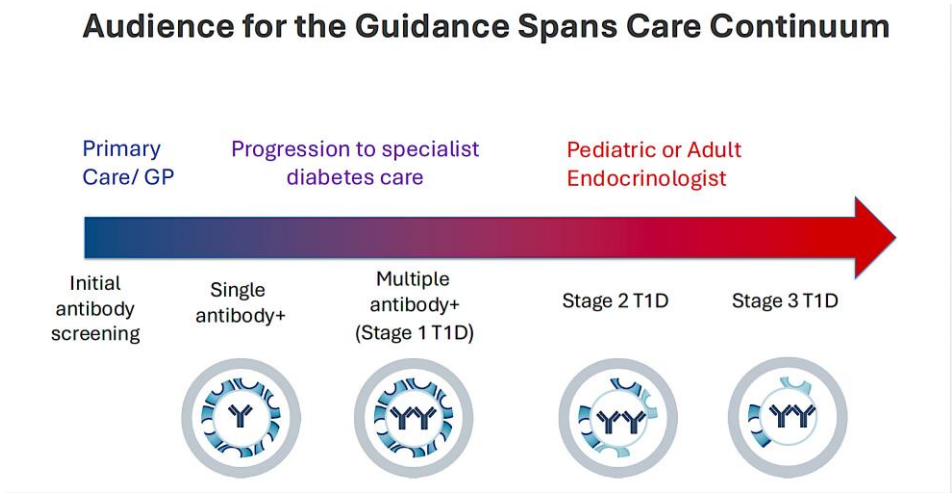
CONSENSUS REPORT

Consensus guidance for monitoring individuals with islet autoantibody-positive pre-stage 3 type 1 diabetes

- Purpose of monitoring:
  - Prevent DKA at the onset of Stage 3 T1D
  - Gives time to plan and prepare
  - Referral to clinical research studies
  - Potential intervention to delay onset of Stage 3 T1D if available

18

Case 1: Follow-Up (Scenario B)



Slide by Linda DiMeglio, AACE 2026 Annual Meeting. Phillip M, et al. *Diabetologia* 2024;67:1731-1759.

19

Case Study #2

Carol Wysham, MD

Diagnosis and Management of MASLD in Diabetes

CONTINUING EDUCATION COMPANY

20

Case 2

57-year-old male with 7 year of type 2 diabetes, diagnosed after an episode of severe pancreatitis. Diabetes complicated by proteinuria, obesity, hypertension, hyperlipidemia

Currently taking metformin 1000 mg BID, empagliflozin 25 mg QD, rosuvastatin 20 mg QD, Losartan 100 mg QD. His glycemic control has been excellent from the time of diagnosis.

Examination: BP-124/72, Weight – 240 lbs, BMI- 31.4 kg/$m^{2.}$ He has marked central adiposity

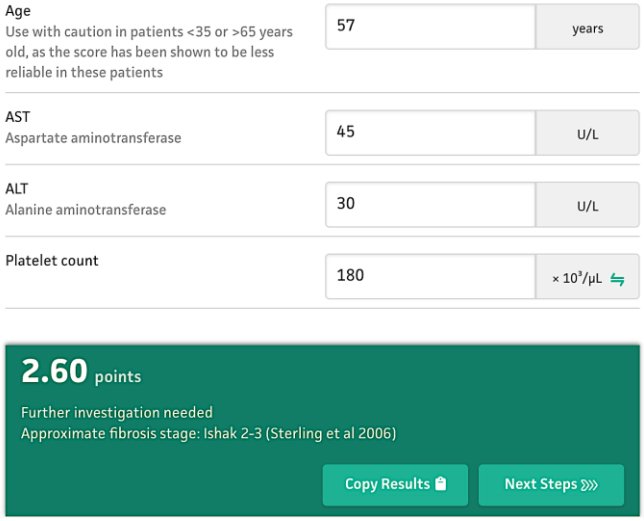
Current labs: A1c 6.7%, eGFR – 63, UACR – 33 mg/gr Cr, LDL-C – 82 mg/dl, TG – 269 mg/dl, ALT – 30 U/L, AST – 45 U/L , Plt – 180 K/mcL

Case 2, Question 1

Should He Be Screened for At Risk MASH?

A. Yes, all people with T2D should be screened. Screen with Fib-4
B. Yes, all people with T2D should be screened with VCTETM
C. No, his transaminase levels and platelet count are normal.

FIB-4 Index



Med+ Calc

23

Limitations of FIB-4 for Screening in MASLD

- Large numbers report in the indeterminate range → requires second-line testing
- Age-related misclassification: false positives in older adults; reduced sensitivity in < 35
- Does not screen for early fibrosis
- Susceptible to confounders: AST/ALT (alcohol, muscle), platelets (inflammation)
- Not disease-specific: cannot distinguish MASLD from other liver diseases
- Unreliable in acute illness due to lab variability

Clinical Implication: AASLD recommends FIB-4 as a first-line triage tool, not stand-alone screening; requires confirmatory testing (e.g., elastography, ELF)

AASLD Practice Guidance (2023–2024); EASL Guidelines (2021–2024); Sterling et al. Hepatology 2006; McPherson et al. Gut 2017; Castera et al. J Hepatol 2019

24

Case 2, Question 2

What Would You Suggest for Confirmatory Testing for At Risk MASH?

A. Ultrasound
B. Vibration controlled transient elastography (VCTE)
C. ELF testing

CONTINUING EDUCATION COMPANY

25

Limitations of VCTE for Screening At-Risk MASH

- Reduced accuracy in obesity: higher failure rates; XL probe only partially mitigates.
- Operator and technique dependence: variability in acquisition and reproducibility
- Confounding factors elevate stiffness: inflammation, congestion, cholestasis, food intake
- Reduced reliability in early disease (F0–F1)
- For F2 - Sensitivity: ~70–85%, Specificity: ~65–80%; F3 Sensitivity: ~80–90%, Specificity: ~75–90%
- Failure/uninterpretable rates up to ~5–20%

AASLD Practice Guidance (2023–2024); EASL Guidelines (2021–2024); Castera et al. J Hepatol 2019; Siddiqui et al. Hepatology 2019; Tapper & Lok Gastroenterology 2017

26

ELF Cutoffs and Prognostic Value

Common thresholds:

A. <7.8 → low risk

- 7.8–9.8 → indeterminate
- ≥9.8 → high risk (≥F3)
- ≥11.3 → predicts liver-related events

Strong predictor of:

- Cirrhosis progression
- Hepatic decompensation
- Liver-related mortality

AASLD 2023–2024; EASL 2021–2024; Newsome PN J Hepatol 2020; Vali Y BMJ 2020; Day JW Hepatology 2021

27

Role of ELF in Clinical Algorithms

Guideline-based approach (AASLD/EASL):

- Step 1: FIB-4 (rule-out)
- Step 2: ELF or VCTE (risk stratification)

Best use cases:

- Indeterminate FIB-4
- Failed or unreliable VCTE
- Longitudinal monitoring

AASLD 2023–2024; EASL 2021–2024; Newsome PN J Hepatol 2020; Vali Y BMJ 2020; Day JW Hepatology 2021

28

Case 2, Question 3

His VCTE – 8.4 kPa Indicating F2 Fibrosis. What Is the Next Step?

A. Order an ELF test
B. Order a Magnetic Resonance Elastography
C. Order secondary work up to rule out secondary causes
D. Refer to Gastroenterology
E. Rule out secondary causes of liver disease

29

Testing to Rule Out Other Causes of Liver Disease

Viral Hepatitis Panels: Hepatitis B surface antigen (HBsAg) and Hepatitis C antibody (anti-HCV)

Alcohol History & Testing: Iron Studies: Serum iron, total iron-binding capacity (TIBC), and ferritin are used to rule out hereditary hemochromatosis.

Autoimmune Markers: Antinuclear antibodies (ANA), anti-smooth muscle antibodies (ASMA), and sometimes anti-liver kidney microsome (LKM) antibodies for autoimmune hepatitis.

Metabolic & Genetic Screen: Ceruloplasmin (for Wilson's disease, especially in younger patients)

Thyroid Function Tests: Thyroid-stimulating hormone (TSH) to rule out hypothyroidism

30

Case 2, Question 4

All of His Testing for Secondary Causes Was Negative. What Do You Recommend?

A. Start Resmetirom 100 mg QD
B. Refer for education for lifestyle modification and follow up 6 months
C. Start Semaglutide 0.25 mg QW

Start Semaglutide 0.25 mg Weekly

- Rationale:
  - He has diabetes, obesity, MASH and CKD, treatment with semaglutide would be a good first choice to treat his multiple comorbidities

Follow-Up of At-Risk MASH on Semaglutide

Monitoring :
Clinical (q3–6 mo): weight, BP, adherence | Target ≥10% weight loss
Laboratory (q3–6 mo): AST/ALT, platelets, HbA1c, lipids
⚠ ALT normalization ≠ fibrosis regression

Fibrosis Surveillance:
- FIB-4 (q6–12 mo): rising value should trigger escalation
- Elastography (q1–2 yr): track liver stiffness trend
→ Fibrosis trend > single measurement

Escalation:
- Rising fibrosis markers, weight loss <5–7%, persistent metabolic risk
- Intensify therapy, consider combination

Advanced Disease (≥F3):
- Referral to gastroenterology for HCC surveillance q6 mo (US ± AFP)

Management success = fibrosis stability

33

Case Study #3

Cecilia Low Wang, MD

52-year-old Male with T2D, HTN, High TG, Obesity, CKD Stage 3, BP 134/82, A1c 6.9%, LDL-c 92, UACR 44

CONTINUING EDUCATION COMPANY

34

Case 3

- A 52-year-old male with T2D x 10 years, HTN, high triglycerides, obesity, and CKD stage 3 presents to your clinic to establish care.
- He and his family moved to the area 3 months ago due to a job change.
- He denies any current symptoms including chest pressure with exertion, paroxysmal nocturnal dyspnea, orthopnea, or GI symptoms. He denies ever smoking.
- Family history of T2D in his father and a sister.
- Medications: HCTZ 25 mg, glipizide 10 mg BID, sitagliptin 100 mg QD, lisinopril 40 mg QD, atorvastatin 20 mg QD.

Case 3 (Continued)

- Exam: BP 134/82. Ht 5'8", Wt 210 lb (BMI 32).
- CV – RRR no murmurs, PULM – clear lung fields, ABDOM – NABS, nontender, EXTREM – no edema, NEURO – lack of ankle reflexes, pinprick sensation present throughout. FEET – no edema, no ulcers/lesions.
- Bloodwork from 4 months ago: A1c 6.9%. Hgb 13 g/dL. Creatinine 1.5 mg/dL, eGFR 56 mL/min/1.73 m^2. UACR 44 mg/g. TChol 167 mg/dL. LDL-C 97 mg/dL. HDL-C 32 mg/dL. TG 188 mg/dL.

Case 3, Question 1

Which of the Following Is the Best Next Step for His Medication Regimen?

- HCTZ 25 mg
- Glipizide 10 mg BID
- Lisinopril 40 mg QD
- Sitagliptin 100 mg QD
- Atorvastatin 20 mg QD

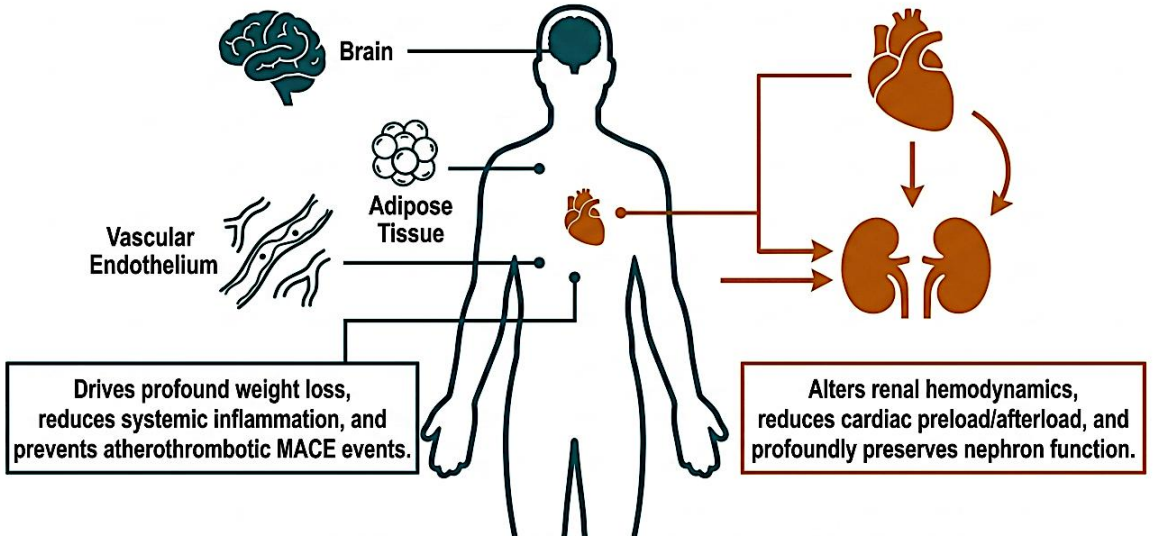
A. No change. His A1c is at goal, <7%.
B. Add a GLP1RA
C. Add an SGLT2i
D. Stop glipizide and start a GLP1RA
E. Stop glipizide and start an SGLT2i
F. Stop glipizide and sitagliptin and start a GLP1RA

CONTINUING EDUCATION COMPANY

37

GLP-1 RAs & Dual GIP/GLP-1 RAs
The Metabolic & Systemic Protectors

SGLT2 Inhibitors
The Hemodynamic & Renal Protectors



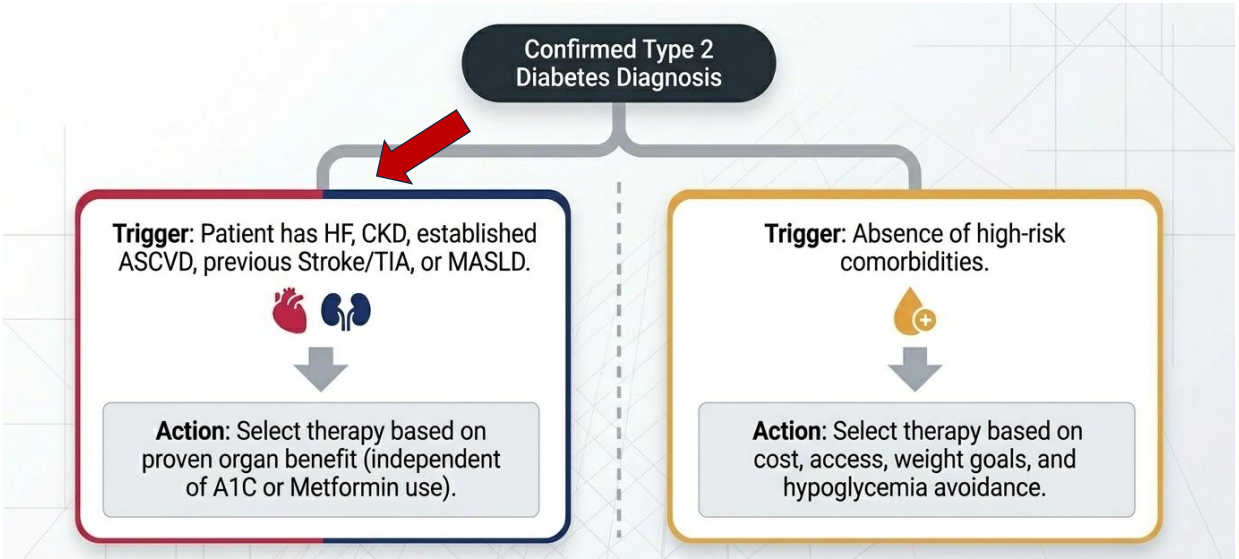
38

SGLT2i vs GLP1RA

	SGLT2i	GLP-1RA
Heart Failure (HFrEF)	+++ Foundational ✓	Neutral ○
Heart Failure (HFpEF + Obesity)	+++	++
Chronic Kidney Disease	+++ Foundational ✓	++ Albuminuria/FLOW trial
Atherosclerotic CVD (MACE)	+	+++ First Line
Severe Obesity	+ Modest	+++ Profound
Liver Health (MASH)	Neutral ○	++ Reverses Steatohepatitis
Primary Risks	⚠ Genital mycotic, DKA	⚠ GI intolerance, Muscle loss
Administration	Daily Oral	Weekly SubQ / Daily Oral

39

The First Decision Point



Samson SL, et al. *Endocr Pract* 2026;32:473-518.

40

#1: Does the patient have heart failure? No

Primary Pathway: SGLT2i

The Rule: First-line foundational therapy (Class 1 guideline recommendation) regardless of baseline A1C.

The Impact: Reduces heart failure hospitalizations by 20–25% and improves clinical stability across HFrEF and HFpEF.

Emerging Pathway: GLP-1 RAs

The HFpEF + Obesity Phenotype: Demonstrated by the STEP-HFpEF DM trial data.

The Impact: Semaglutide 2.4mg yields a 13.7-point improvement in KCCQ-CSS symptoms, significant 6-minute walk distance gains, and 9.8% weight loss over 1 year.

41

#2: Does the Patient Have CKD (eGFR, UACR)? Yes

Kidney Function Slider

eGFR: 90 60 45 30 20 15

SGLT2i Zone

Reduces CKD progression composite outcomes by ~38%.

Operational Insight:
While glycemic efficacy drops at eGFR <45, the profound **cardiorenal protective benefits remain highly robust** down to an eGFR of 20 mL/min/1.73m^2

GLP-1 RA Zone

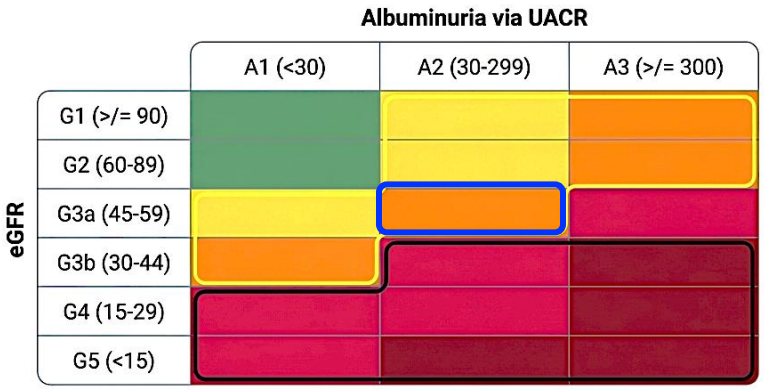
The FLOW Trial Impact: Semaglutide injection reduced the risk of major kidney disease events by 24%.

Preferred for advanced CKD (eGFR <30) due to lower hypoglycemia risk and combined MACE reduction

42

Using the KDIGO Risk Matrix

52 yo male,
creatinine 1.5 mg/dL
eGFR 56 mL/min/1.73 m^2
UACR 44 mg/g



Moderate-to-High Risk CKD
→ Triggers CKM Stage 2

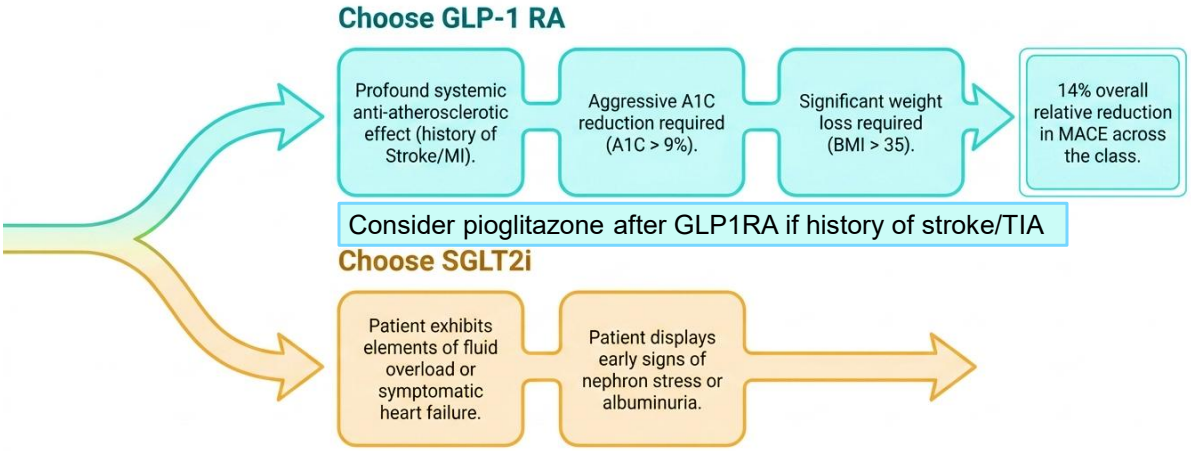
Very High-Risk CKD
→ Triggers CKM Stage 3
(Risk Equivalent to Subclinical CVD)

Clinical Imperative: Routine eGFR testing is insufficient. Annual Urine Albumin-Creatinine Ratio (UACR) measurement is mandatory for all Stage 2+ adults to accurately predict HF risk and kidney failure.

Ndumele CE, et al. *Circ* 2023;148:1606-1635

43

#3: Does the Patient Have ASCVD or Are They at High Risk? Have They Had a Stroke or TIA? No



44

Case 3, Question 2

52-year-old Male with T2D, HTN, High TG, Obesity, CKD Stage 3, 134/82, A1c 6.9%, LDL-c 92, UACR 44

Which of the Following Is the Best Next Step for His Medication Regimen?

- HCTZ 25 mg
- Glipizide 10 mg BID
- Lisinopril 40 mg QD
- Sitagliptin 100 mg QD
- Atorvastatin 20 mg QD

A. No change. His A1c is at goal, <7%.
B. Add a GLP1RA
C. Add an SGLT2i
D. Stop glipizide and start a GLP1RA
E. Stop glipizide and start an SGLT2i
F. Stop glipizide and sitagliptin and start a GLP1RA

Case 3: 52-year-old Male with T2D, HTN, High TG, Obesity, CKD Stage 3, 134/82, A1c 6.9%, LDL-c 92, UACR 44

New Regimen

- Semaglutide 0.25 mg SQ Qwk
- HCTZ 25 mg
- Lisinopril 40 mg QD
- Atorvastatin 20 mg QD

- You discuss the rationale for SGLT2i vs GLP1RA explaining the focus on CKD. You go over the potential side effects.
- He wants to focus on losing weight to mitigate his CKM risks.
- Therefore, you stop the glipizide and sitagliptin, start the lowest dose of semaglutide, and counsel him regarding potential side effects, and lifestyle changes.

Case 3, Question 3

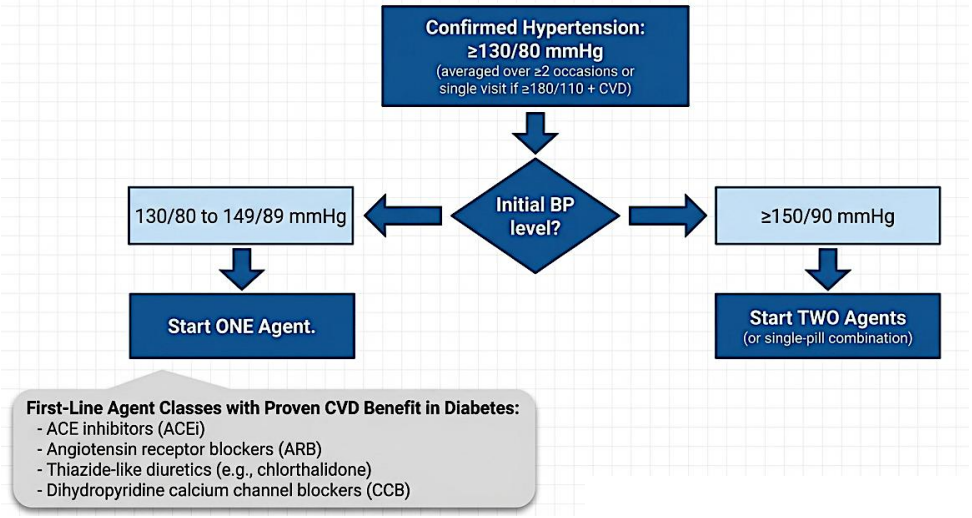
What Is the Best Next Step for His Cardiovascular Risk?

New Regimen

- Semaglutide 0.25 mg SQ Qwk
- HCTZ 25 mg
- Lisinopril 40 mg QD
- Atorvastatin 20 mg QD

A. No change. His blood pressure and LDL-c will improve with weight loss on the GLP1RA
B. Add losartan
C. Add amlodipine
D. Increase the atorvastatin

Starting Antihypertensive Therapies



ADA PPC. 10. Cardiovascular Disease and Risk Management - Standards of Care in Diabetes - 2026. *Diabetes Care* 2026;49(Suppl. 1):S216-S245.

Standard vs Intensive BP Goals

<130/80 mmHg

Patient Profile: Standard risk, older adults with polypharmacy, individuals prone to orthostatic hypotension.

Clinical Rationale: Reduces cardiovascular events and microvascular complications safely for the majority.

<120 mmHg SBP

Patient Profile: High cardiovascular or kidney risk (e.g., established CVD, two or more risk factors, CKD).

Clinical Rationale: BPROAD and ESPRIT trials demonstrated a 12-21% additional reduction in major adverse cardiovascular events (MACE).

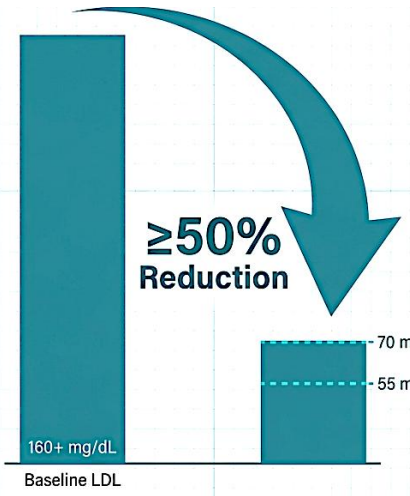
Monitoring Alert: Requires close monitoring for symptomatic hypotension, syncope, acute kidney injury (AKI), and hyperkalemia.

ADA PPC. 10. Cardiovascular Disease and Risk Management - Standards of Care in Diabetes - 2026. *Diabetes Care* 2026;49(Suppl. 1):S216-S245.

49

LDL-c Reduction Consists of Two Targets: Relative Reduction AND Absolute Level

Modern lipid management requires achieving BOTH a specific absolute threshold AND a massive relative drop from baseline.
High-intensity statins are the bridge across this chasm.



Rule 1: The Relative Drop

A ≥50% reduction in LDL cholesterol is mandated for all patients at higher cardiovascular risk or with established ASCVD.

Rule 2: The Absolute Floor

Primary Prevention (High Risk): <70 mg/dL

Secondary Prevention (ASCVD): <55 mg/dL

(1) Samson SL, et al. *Endocr Pract* 2026;32:473-518. (2) ADA PPC. 10. Cardiovascular Disease and Risk Management - Standards of Care in Diabetes - 2026. *Diabetes Care* 2026;49(Suppl. 1):S216-S245.

50

Type 2 Diabetes Lipid Management for Primary Prevention

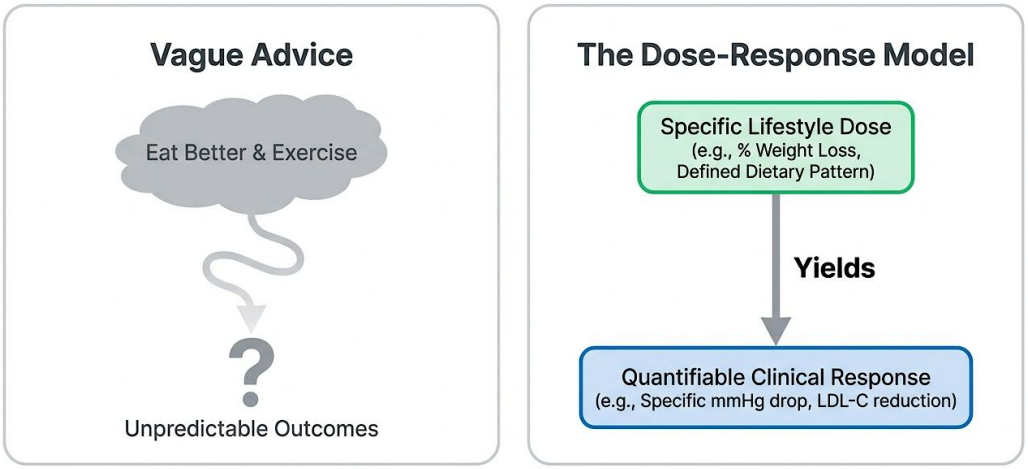
Age 20–39	**Condition:** + Additional ASCVD risk factors.	**Action:** Consider Moderate-Intensity Statin.
Age 40–75 (The Core Cohort)	- **Standard Risk:** Moderate-Intensity Statin. - **High Risk (≥1 ASCVD Risk Factor):** High-Intensity Statin. Target: <70 mg/dL and ≥50% reduction. - **Very High Risk** (Multiple factors + LDL ≥70): Add Ezetimibe or PCSK9i.	
Age >75	**Condition:** Already on statin -> Continue.	**Not on statin ->** Initiate moderate-intensity after risk/benefit discussion.

ASCVD risk factors: age, HTN, dyslipidemia, smoking, CKD, obesity

(1) Samson SL, et al. *Endocr Pract* 2026;32:473-518. (2) ADA PPC. 10. Cardiovascular Disease and Risk Management - Standards of Care in Diabetes - 2026. *Diabetes Care* 2026;49(Suppl. 1):S216-S245.

51

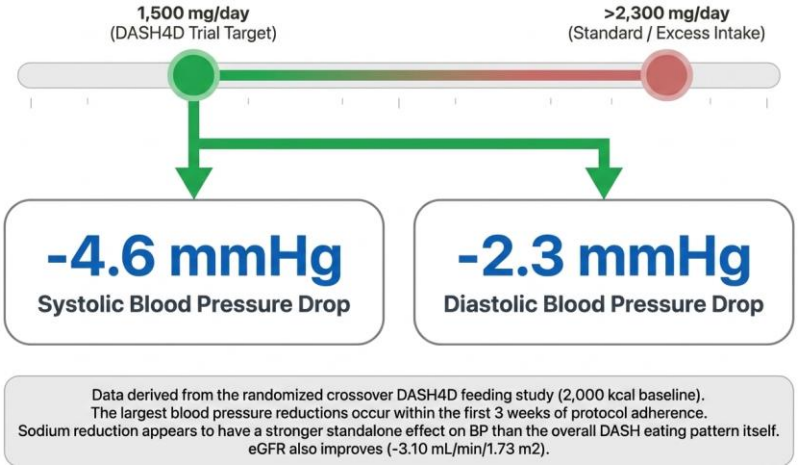
Specific Recommendations Are Needed to Increase Success



(1) Samson SL, et al. *Endocr Pract* 2026;32:473-518. (2) ADA PPC. 5. Facilitating Positive Health Behaviors and Well-being to Improve Health Outcomes- Standards of Care in Diabetes - 2026. *Diabetes Care* 2026;49(Suppl. 1):S89-S131.

52

BP Lowering with the DASH 1500 mg Sodium/Day Eating Pattern



(1) Samson SL, et al. *Endocr Pract* 2026;32:473-518. (2) ADA PPC. 5. Facilitating Positive Health Behaviors and Well-being to Improve Health Outcomes- Standards of Care in Diabetes - 2026. *Diabetes Care* 2026;49(Suppl. 1):S89-S131.

53

Case 3, Question 3

What Is the Best Next Step for His Cardiovascular Risk?

New Regimen

- Semaglutide 0.25 mg SQ Qwk
- HCTZ 25 mg
- Lisinopril 40 mg QD
- Atorvastatin 20 mg QD

A. No change. His blood pressure and LDL-c will improve with weight loss on the GLP1RA
B. Add losartan
C. Add amlodipine
D. Increase the atorvastatin

Take Home Points from Cases 1 and 3

- Even in patients with overweight or obesity, consider whether type 1 diabetes should be evaluated using the AABBCC method or the new AACE algorithm for classification. Also consider for prediabetes.
- Specific GLP1RA and GIP/GLP1RA have strong evidence for ASCVD risk reduction and are more potent for weight loss, while SGLT2i are first-line for HF and/or CKD. Semaglutide has been demonstrated to reduce CV **and** CKD risk. Shared decision-making is needed to balance all of the benefits, risks, and priorities.
  - Remember that other diabetes med(s) may need to be de-escalated
- BP is more amenable to improvement with weight loss than LDL-cholesterol. Dietary pattern matters for both BP and LDL-c.
- Avoid using ACEi with ARB, and target LDL-c <70 mg/dL for primary prevention when multiple risk factors are present.

55

Case Study #4

Carol Wysham, MD

Management of Obesity in Diabetes

CONTINUING EDUCATION COMPANY

56

Case 4
ML: 55-year-old Woman with New History of Type 2 Diabetes Presents as New Patient

Long history of increased weight. Previous diagnosis of prediabetes. Prescribed calorie restricted diet and exercise per DPP guidelines. With this, she lost 10 pounds (X%), but regained all back.

Tried ketogenic diet, upon which she lost 12 pounds over 2 months, but was too hard to adhere to and regained all of her lost weight.

Joined weight watchers 6 months ago and has lost 13 pounds.

She is very frustrated that despite her attempts at weight loss that she was unable to prevent progression to diabetes. She denies any symptoms

Case 4: ML

Other medical history: Gestational diabetes at age 35, Coronary artery disease, hypertension, obstructive sleep apnea (on CPAP), osteoarthritis, depression.

Current medications: Irbesartan 150 mg QD, Rosuvastatin 40 mg QD, citalopram 20 mg QD, calcium citrate 1200 mg QD., acetaminophen 1000 mg BID

Physical exam: Weight – 220 lbs, BMI – 35.5 BP-125/70 mmHg, acanthosis nigricans around the neck

Laboratory studies: A1c – 8.1%. LDL-C – 64 mg/dl, TG – 159 mg/dl, eGFR 58 ml/min/1.73 m^2, UACR – 37 mg/grCr, AST – 45, ALT – 45 U/L, plt – 179K

Case 4, Question 1

Should Obesity Be a Major Point of Discussion at This Visit?

A. Yes, because it underlies most of her medical conditions.
B. Yes, because patients has expressed concern about her weight.
C. No, because her elevated A1c is the most pressing issue.
D. A & B

CONTINUING EDUCATION COMPANY

59

Addressing Patient Weight Concern: A High-Leverage Clinical Intervention

Why It Matters
60–80% of patients concerned
<50% report clinician engagement
Missed opportunity at peak motivation

Clinical Impact
↑ engagement & adherence
~2–5% greater weight loss
Improved A1c, BP, lipids

If Ignored
↓ trust and follow-up
Therapeutic inertia
Goal discordance

Mechanism
Aligns with patient priorities
Drives engagement
Improves persistence

Guidelines
ADA: person-centered care
Endocrine Society: shared decision-making
OMA: proactive discussion

Addressing weight concern improves adherence, amplifies weight loss (~2–5%), and improves outcomes.

Kaplan et al. *Obesity* 2018 (ACTION Study), Rubino et al. *Diabetes Obes Metab* 2020, Wadden et al. *Obesity* 2011, Look AHEAD trial – *NEJM* 2013 & *Lancet Diabetes Endocrinol* 2014, Publ & Heuer, *Obesity* 2009; Publ et al, *Obesity Reviews* 2020, Kushner & Kahan, *JAMA* 2018

60

Case 4, Question 2

Which of the Following Is Least Appropriate as First Step in Her Treatment Plan?

A. Start metformin 500 mg BID.
B. Start metformin 500 mg BID and SGLT-2 inhibitor.
C. Increase irbesartan to 300 mg QD and start GLP-1RA or GLP-1RA/GIP.
D. Increase irbesartan to 300 mg QD and start SGLT-2 inhibitor.

CONTINUING EDUCATION COMPANY

61

Pharmacologic Approaches to Glycemic Treatment in T2D

Use of glucose-lowering medications in the management of type 2 diabetes
(For recommendations for specific conditions, including non-glucose-lowering medications, refer to pertinent sections)

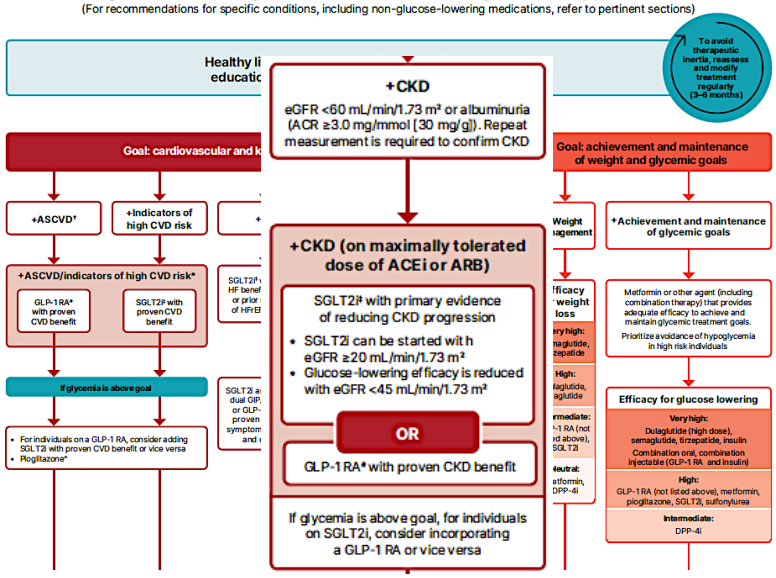


Figure 9.4
Pharmacologic Approaches to Glycemic Treatment:
Standards of Care in Diabetes - 2026. Diabetes Care 2026;49(Suppl. 1):S183-215

62

62

Case 4, Question 3

For Those of You Who Chose GLP-1RA or GLP-1RA/GIP, Which One Would You Choose and Why?

A. GLP-1RA/GIP because of greater weight loss and that is all that matters in management of diabetes associated with obesity
B. GLP-1RA/GIP because of indication for treatment of obstructive sleep apnea
C. GLP-1RA (semaglutide) because of indication for cardiovascular disease, chronic kidney disease and MASH

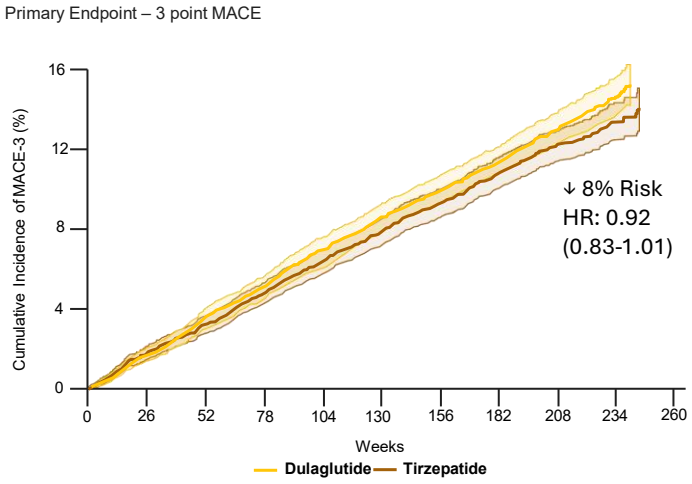
63

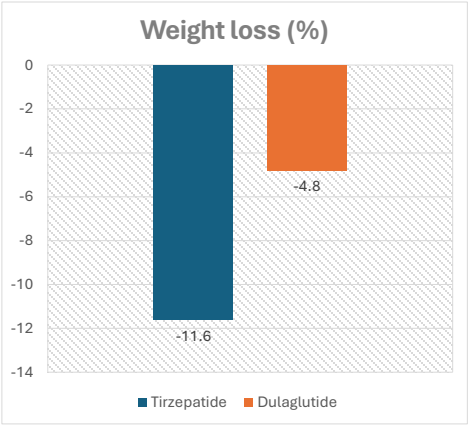
Current Landscape of FDA Approved Indication for Incretin Therapies

Obesity	Type 2 Diabetes	ASCVD risk reduction (without DM)	OSA	MASH	DKD
Liraglutide Semaglutide Tirzepatide Orforglipron	Liraglutide Dulaglutide Semaglutide Tirzepatide	Semaglutide (SC and PO)	Tirzepatide	Semaglutide	Semaglutide

64

Why Not Tirzepatide for This Patient? Results of SURPASS-CVOT Showed Noninferiority of Tirzepatide vs Dulaglutide, Despite Greater Weight Loss.





Nicholls SJ. et al. *N Engl J Med.* 2025;393:2409-2420

65

Why Not Tirzepatide for This Patient?

- In post-hoc analysis, effects of semaglutide on CV and renal risks occurred before significant weight loss[1]
- Impact of GIP on atherosclerosis in animal models is variable[2]

1. Data on file Novo Nordisk, Inc; 2. Hammoud R, Drucker D. *Nat Rev Endocrinol* 2023 Apr;19:201-216

66

ML Returns for Follow Up at 4 Months

She is currently taking semaglutide 1.0 mg QW, irbesartan 300 mg QD. Her knees feel better. She is walking 3 times/wk and lifts weights 3 times/wk. Her depression is well-controlled.

Physical exam: Weight – 204 (-7%). BP – 120/68

Laboratory studies: A1c – 6.8%, eGFR – 62 ml/min/1.73m^2, UACR – 28 mg/grcr, LDL- ALT – 38 U/L, LDL – 61 mg/dl

Case 4, Question 5

What Else Would You Recommend at This Time?

A. Nothing, just wait until 3 month follow up of A1c
B. Change citalopram to bupropion
C. Refer to registered dietician for discussion of dietary plan for weight management that incorporates her lifestyle preferences.
D. B & C

Medications Associated with Weight Gain

Class	Medication Examples
Insulin & Secretagogues	Insulin; Sulfonylureas (glipizide, glyburide); Meglitinides
Thiazolidinediones (TZDs)	Pioglitazone, Rosiglitazone
Atypical Antipsychotics	Olanzapine, Clozapine, Quetiapine, Risperidone
Corticosteroids	Prednisone, Dexamethasone
Antidepressants	Mirtazapine, Citalopram, Paroxetine, TCAs
Mood Stabilizers	Lithium, Valproate
Beta Blockers	Propranolol, Metoprolol, Atenolol
Antiepileptics	Valproate, Carbamazepine, Gabapentin, Pregabalin
Antihistamines	Diphenhydramine, Cyproheptadine
Hormonal Therapies	Progestins (medroxyprogesterone), Estrogen combinations

69

She Returns in Another 3 Months

Her weight has stabilized at 200 (-9%). She was hoping she would lose more weight and wonders if there is another option.

Weight – 200 lbs, BMI – 32.3 kg/m^2, BP – 116/68, and otherwise unchanged.

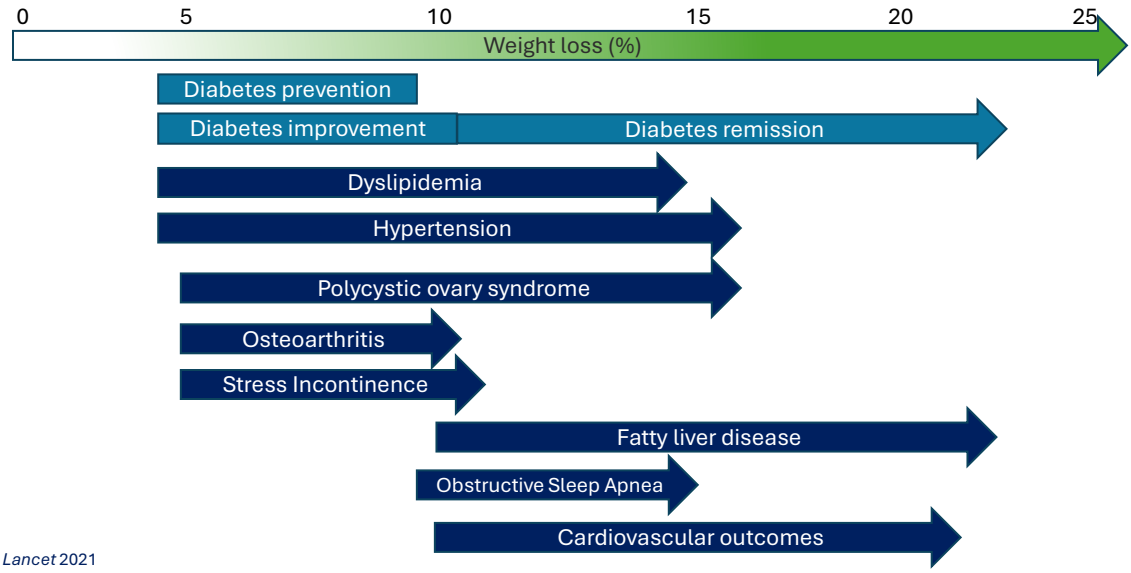
Laboratory testing: A1c – 6.6%, eGFR – 66 ml/min/1.73 m^2, UACR – 22 mg/gr cr, AST – 29 U/L, ALT – 31 U/L , plt – 190K.

Case 4, Question 6

What Is Your Goal for Weight Loss for ML?

A. >10%
B. >15%
C. > 20%

Magnitude of Weight Loss Correlates with Health Benefits



Lingvay *Lancet* 2021

Case 4, Question 7

What Is the Least Appropriate Option for ML, at This Point?

A. Add SLGT-inhibitor
B. Increase semaglutide to 2.0 mg
C. Change semaglutide to tirzepatide
D. Change semaglutide to orforglipron

CONTINUING EDUCATION COMPANY

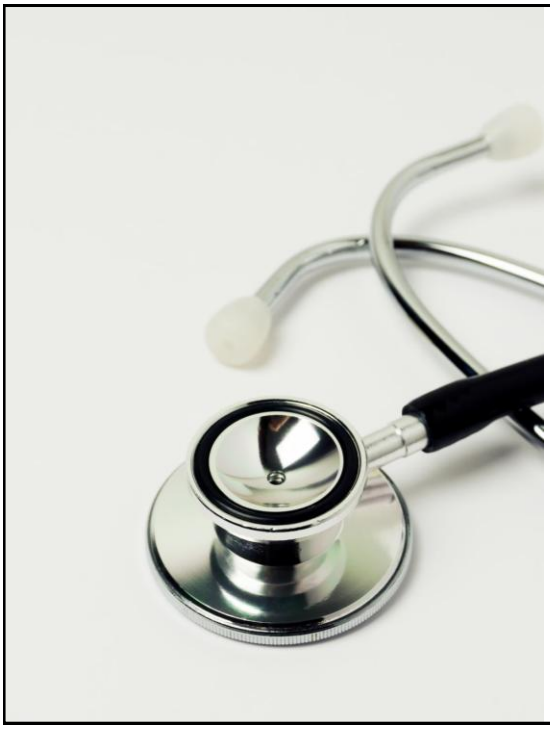
73

Goal–Based Direction for Next Step for ML

- If your goal is 10% - addition of SLGT-2 inhibitor will give you 2 – 4% additional weight loss and potential for additional cardiorenal protection.
- If your goal is 15% - changing to tirzepatide may be appropriate
- If your goal is > 20% - consider bariatric surgery
- Dual/triple agonists are under investigation that might match weight loss seen with bariatric surgery.

- Of course, the patient's preferences need to be considered, but only after understanding the goals of using medications to minimize future cardiorenal risks

74



Summary

- Addressing excess body weight in our patients with T2D has the potential of
  - Treating many of the adiposity related comorbidities
  - Putting diabetes into remission
  - Prevention of progression of long-term complications of diabetes
- Going forward, it will be important to separate out the potential for benefit of these agents beyond weight loss on cardiorenal complications.

75