

Endocrinology and Diabetes Cases

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Disclosure

Consultant: Aqua; AstraZeneca; Bayer; BDI, Inc.;
Boehringer Ingelheim; Fractyl; Lilly; Novo Nordisk;
Roche; Sparrow; Vertex; vTV Therapeutics; Zealand
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Stock Options: BDI, Inc.

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Patient Case 1: 73-year-old Woman with T2D, Obesity and HFpEF

- She has a history of intolerable GI side effects (primarily diarrhea) with tirzepatide treatment
- Developed euglycemic DKA on canagliflozin

CURRENT DIABETES MEDS:

- metformin 1000 mg twice a day
- sitagliptin 100 mg once daily

LABS:

- Hemoglobin A1c is 8.7%



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Patient Case 1, Question 1 What Would You Do Next?

- A. Add basal insulin
- B. Add different SGLT2 inhibitor
- C. Add sulfonylurea
- D. Try a different GLP-1RA



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Patient Case 1: 73-year-old Woman with T2D, Obesity and HFpEF

Changes to Regimen:

- Added Lantus 10 units once daily at bedtime
- Continued metformin
- Continued sitagliptin

3 Month Follow Up:

A1c 8.7% => 7.6%

Glucose Meter:

Range: 72 - 220s

Fasting 110 -140

Predinner: 72 -180

Bedtime: 110-220

No hypoglycemia



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Patient Case 1, Question 2 What Would You Do Next?

- A. Add basal insulin
- ~~B. Add different SGLTi~~
- C. Add sulfonylurea
- D. Try a different GLP-1RA



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Good Candidates for Insulin Therapy

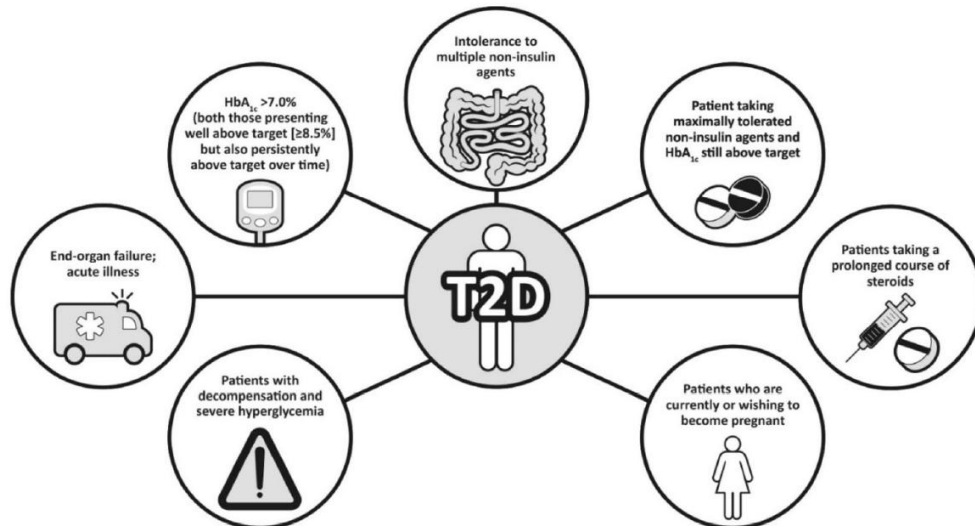


Figure 1. People with type 2 diabetes who are candidates for basal insulin. HbA_{1c} : glycated hemoglobin; T2D: type 2 diabetes.

Ann Med . 2021 Dec;53(1):998-1009

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Patient Case 1



What else might you consider?

- A. Add basal insulin
- ~~B. Add different SGLTi~~
- C. Add sulfonylurea
- D. Try a different GLP-1RA 

CURRENT DIABETES MEDS:

- metformin 1000 mg twice a day 
- sitagliptin 100 mg once daily

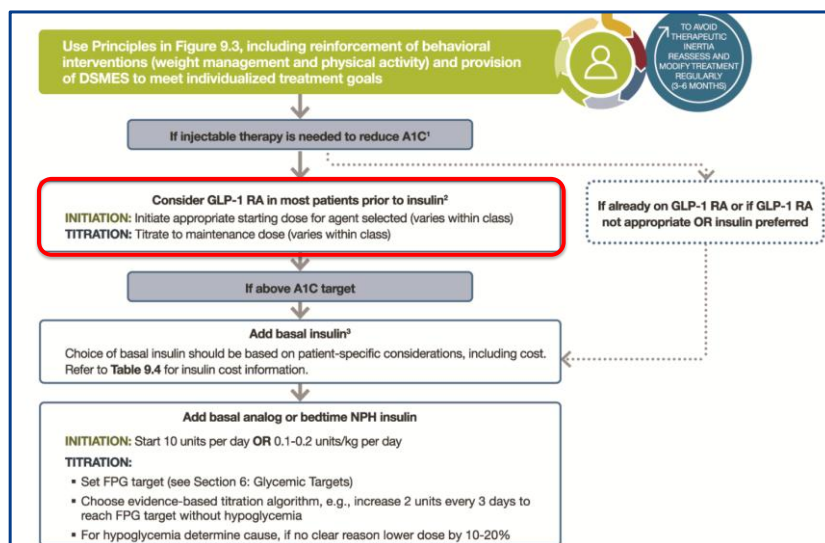
Consider re-trial of GLP-1RA along with reduced dose of metformin in patients who have diarrhea on the combination

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PHARMACOLOGIC APPROACHES TO GLYCEMIC TREATMENT



Intensifying to injectable therapies (1 of 2)



Pharmacologic Approaches to Glycemic Management: *Standards of Medical Care in Diabetes - 2022. Diabetes Care* 2022;45(Suppl. 1):S125-S143

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Patient Case 1



73-year-old woman with obesity, T2D and HFpEF

- She has a history of intolerable GI side effects (primarily diarrhea) with tirzepatide treatment
- Developed euglycemic DKA on canagliflozin

CURRENT DIABETES MEDS:

- metformin 1000 mg twice a day
- sitagliptin 100 mg once daily
- Insulin glargine 10 units daily

What about her HFpEF?

LABS:

Hemoglobin A1c is 7.6%

eGFR is 47 ml/min/1.73m²

Urine albumin/creatinine (UACr) 150 mg/g

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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)

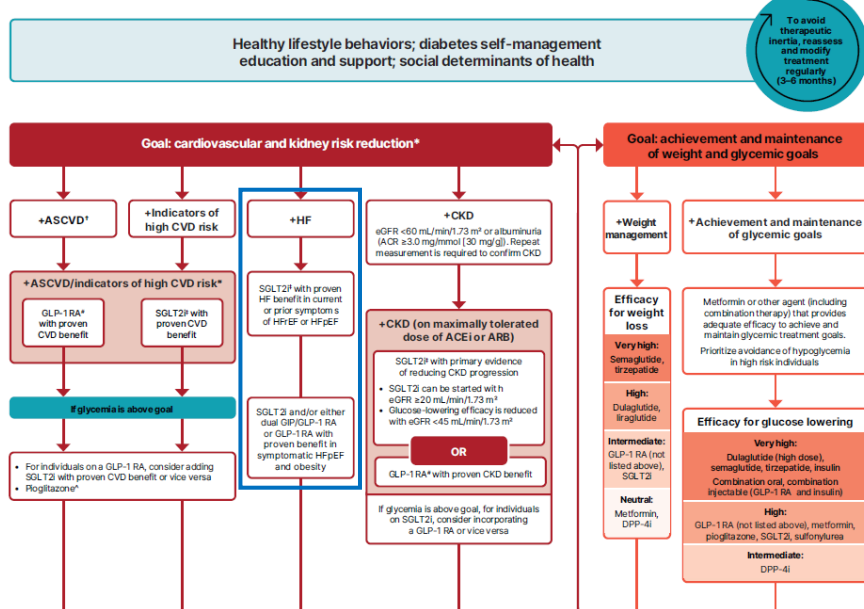
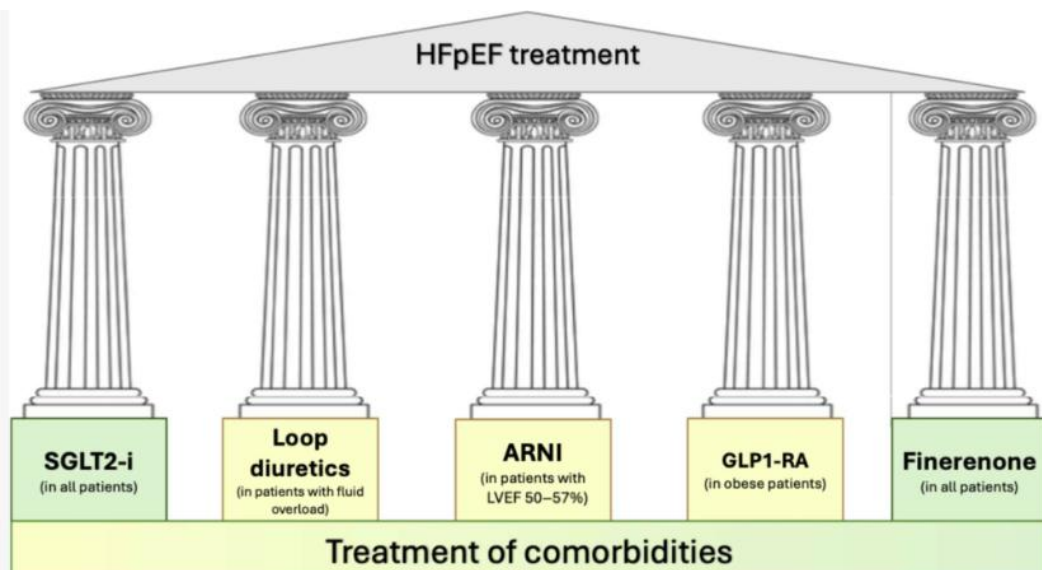


Figure 9.4 Pharmacologic Approaches to Glycemic Treatment: Standards of Care in Diabetes - 2026. Diabetes Care 2026;49(Suppl. 1):S183-215



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HFpEF Treatment Approach



J. Clin. Med. 2025, 14(15), 5406; <https://doi.org/10.3390/jcm14155406>

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Patient Case 1



73-year-old Woman with Obesity, T2D and HFpEF

Options to improve outcomes:

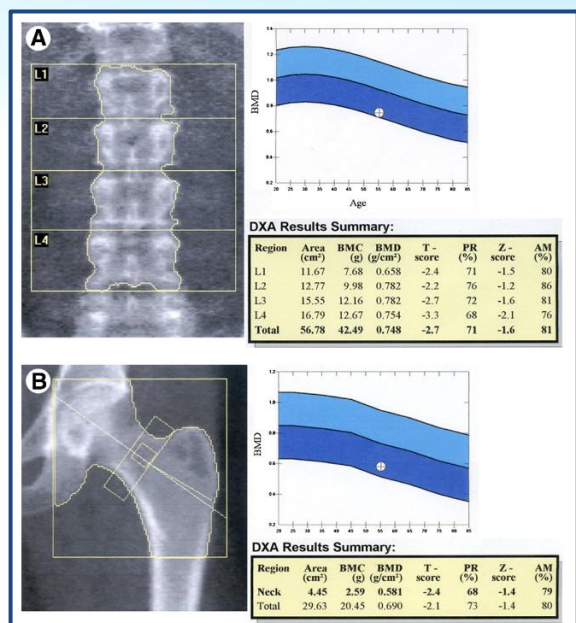
- Probably cannot take SGLT2i again given euglycemic DKA
- Consider retrial of GLP-1 or dual GLP-1/GIP RA
 - *semaglutide or tirzepatide*
- Finerenone treatment
- ARNI
- Loop diuretics if needed for congestion/fluid overload

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Patient Case 2

A 68-year-old woman was previously treated with zoledronic acid for 3 years after she was found to have vertebral osteoporosis on routine DXA.

She has now been on a drug holiday for four years. She continues to take calcium and vitamin D supplementation.

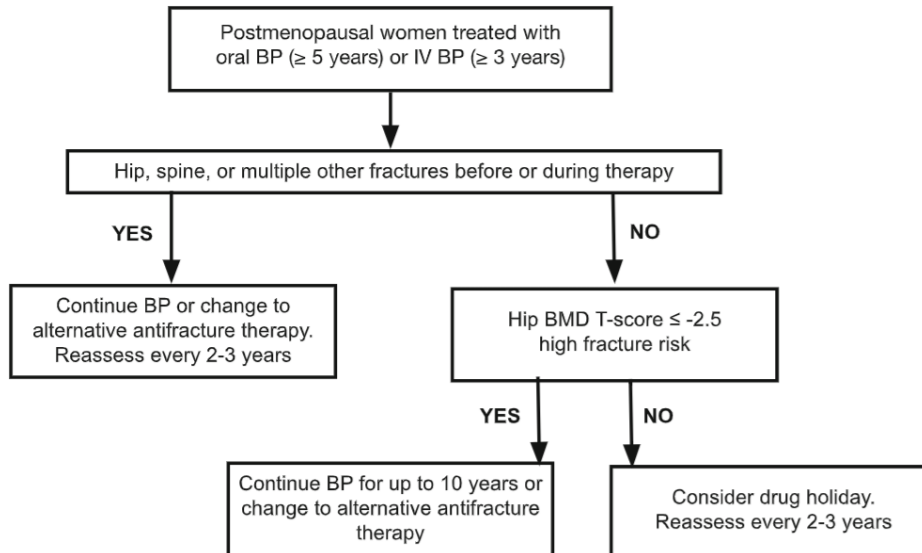


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Semin Nucl Med 40:62-73 2010

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When to Consider a Bisphosphonate Holiday

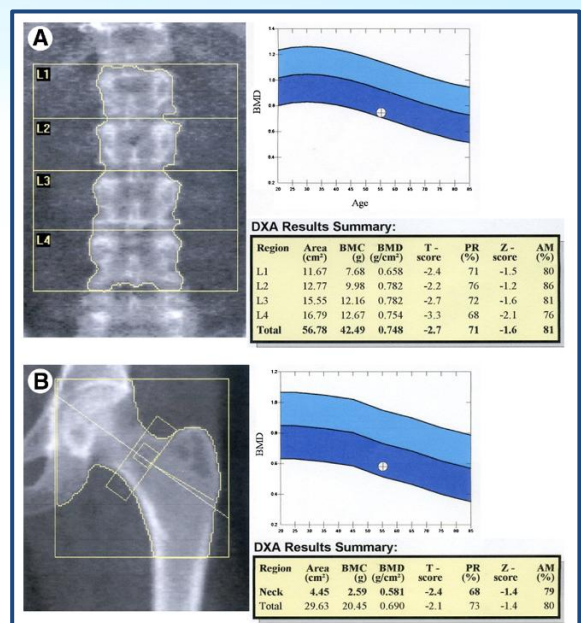


Osteoporos Int (2022) 33:2049–2102

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Patient Case 2

Her daughter reports that the patient has experienced several recent falls, but she has had no fractures. A recent DXA shows stability of bone density in the spine and hip.



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Patient Case 2, Question 1

What Do You Recommend at This Time?

- A. Continued observation, with repeat DXA in 2 years
- B. Re-calculate her FRAX score to see if she warrants re-treatment for osteoporosis
- C. Enrollment in a yoga class for seniors to improve her balance
- D. Resume bisphosphonate therapy



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Patient Case 2

Bisphosphonate	FPPS Inhibitory Potency [12,51]	Binding Affinity to Hydroxyapatite [12,52]	Accumulation and Saturation Potential [12,52]	Current Recommended Drug Holiday Duration [17]
Alendronate	Low	High	High	2–3 years
Risedronate	High	Low	Low	1–2 years
Zoledronate	High	High	Low	2–3 years

- Protective effect of zoledronic acid is likely 2-3 years beyond last dose given
- FRAX calculator not validated for patients on drug holiday
- Even though her DXA is stable, her risk for fractures is increasing
 - Advancing age (now > 65 years)
 - Frequent falls (address those risks separately)

J. Clin. Med. 2021, 10(5), 1140; <https://doi.org/10.3390/jcm10051140>

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Patient Case 3



A 24-year-old woman with a history of treated hypothyroidism calls you as she has had a positive urine pregnancy test.

This is her first pregnancy; her last menstrual period began 6-7 weeks ago. She feels well and has continued to take her usual 88 mcg dose of levothyroxine daily.

Laboratory values (2 months ago):

TSH 0.7 mIU/L (normal 0.5 to 5.0 mIU/L)

Free T4 1.6 ng/dL (normal 0.7 to 1.9 ng/dL)



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Patient Case 3, Question 1

What Do You Recommend Now?

- A. Repeat thyroid hormone levels now
- B. Repeat thyroid hormone levels early in her second trimester
- C. Increase levothyroxine dose to two tablets daily on two days per week
- D. Increase levothyroxine dose to two tablets every day
- E. Refer to endocrinology



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Hypothyroidism and Pregnancy

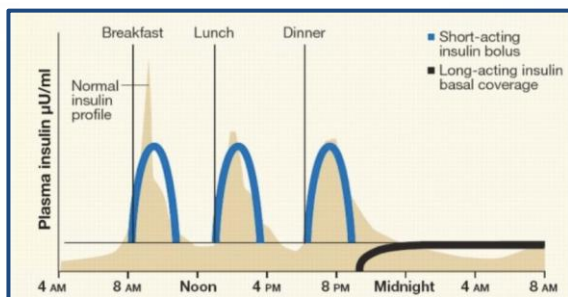


- Women with hypothyroidism before pregnancy **will require an increased replacement dose of levothyroxine** early in the first trimester
- At the time of a positive pregnancy test, patients should **double their daily dose of thyroid hormone on two days each week**
 - Provides a 28% increase in total dose, which approximates the increased requirements in pregnancy
- Test TSH every 4 weeks through 20 weeks' gestation, and once at 30 weeks' gestation
 - **Target is TSH < 2.5 mU/L**, or lower half of trimester-specific reference range

JAMA June 15, 2021 Vol 325, No 23.
Thyroid Vol 31 No 5, 2021

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Patient Case 4 Poor Control on High-Dose Insulin

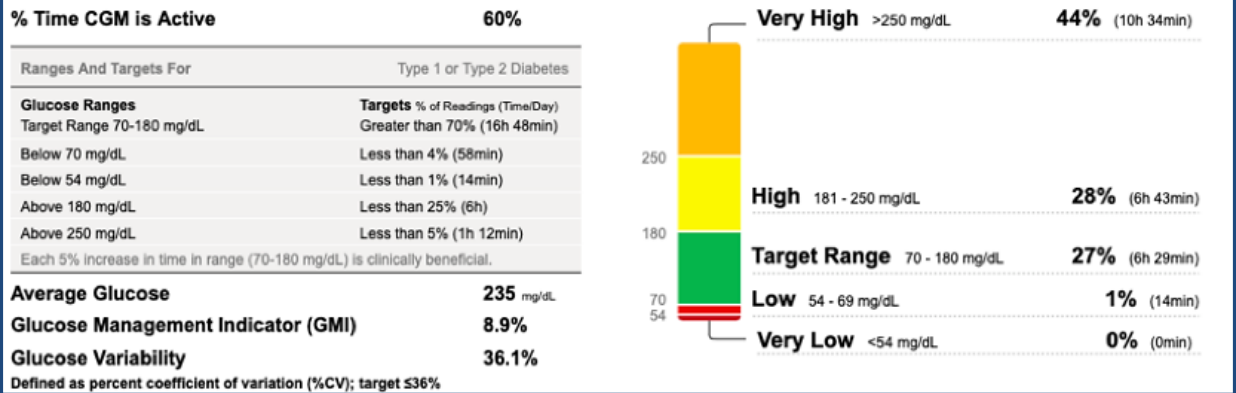


- 78-year-old woman with T2DM and CKD. She recently lost her husband and is living alone.
- Insulin doses have been steadily increased over time
- Glargine insulin 60 units daily, and aspart 30 units with meals.
- On lisinopril and empagliflozin given CKD
- Weight 80 kg
- POC glucose 65, A1c 9.3%
- eGFR 30, UACR 328 mg/g

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Patient Case 4

CGM Report



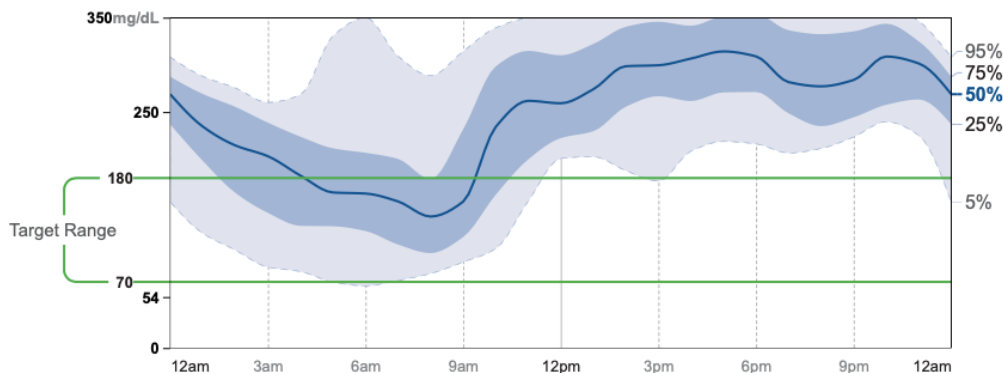
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Patient Case 4

AMBULATORY GLUCOSE PROFILE (AGP)

AGP is a summary of glucose values from the report period, with median (50%) and other percentiles shown as if occurring in a single day.



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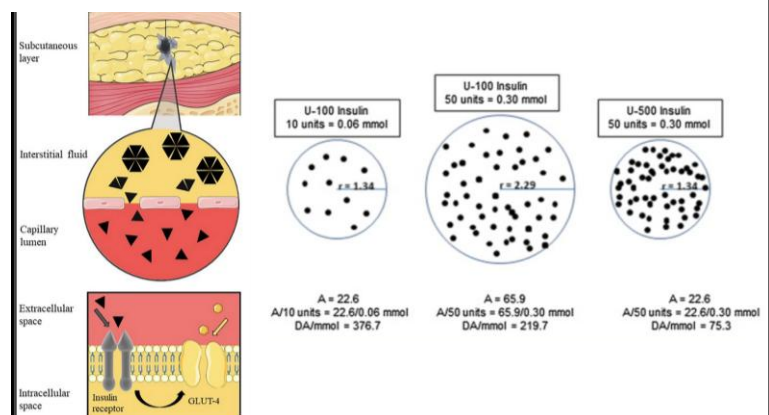
Patient Case 4, Question 1

What Would You Suggest Next?

- A. Increase doses of mealtime (aspart) insulin
- B. Change to concentrated, U500 insulin
- C. Encourage adherence to all prescribed insulin injections
- D. Do something else

Insulin Absorption Issues

- Smaller volume will have a larger surface-to-volume ratio which increases the diffusion area of the injection depot
- Larger injection volume may also depress the local microcirculation, further delaying absorption



Concentrated U-500 Regular Insulin



- **5 X more concentrated than standard U-100 insulin.**
- With 500 units per mL, the **total volume** per dose is 1/5th that of a U-100 dose, permitting better absorption
 - Onset: 15-30 minutes
 - Peak: 4-8 hours
 - Duration of activity: 13-24 hours (mean 21 hours)
- Delivery
 - KwikPen is the safest and preferred delivery device. Package size = 2 x 3 mL pens
 - Each pen contains 1500 units, dials by 5 unit increments; may deliver a single dose up to 300 units
 - Dose should be entered as **exact units** -- historically used with U-100 and tuberculin syringes prior to the advent of U-500 syringes, **should NOT be utilized**

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U-500 Dosing Considerations



- 1st dose of U-500 should be administered 12-16 hours after the last dose of prior basal insulin
- Doses of U-500 should be administered 30 minutes before meals
- Initial total daily dose (TDD) when transitioning from a U-100 insulin regimen:
 - If A1c $\leq$ 8% or 7-day average glucose $<$ 183 mg/dL: 80% of prior TDD
 - If A1c $>$ 8% or 7-day average glucose $>$ 183 mg/dL: 100% of prior TDD
- Dose proportions and titration
 - BID: 60% - 40% before breakfast and supper
 - TID: 40% - 30% - 30% before breakfast, lunch, and supper
 - Up-titration: +5-15% per dose
 - Down-titration: -10% per dose

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U-500 Dosing Considerations



- Dose reduction for hypoglycemia more important than dose increase for hyperglycemia
- Allow at least 1 week between dose titrations
- Do not give correction dosing
- Do not give with other types of insulin



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Patient Case 4



But first.....

- In discussing her insulin use, the patient notes that due to hypoglycemia she only takes her insulin if her glucose is over 200-250.
- This has gotten worse since her husband died and she is not eating regularly or only eating food people prepare for her.
- **Solution(s):**
 - Weight-based insulin (TDD = 0.3-0.5 units/kg/day)
 - Consider basal insulin + non-insulin medications
 - Consider split/mixed (e.g. 70/30) insulin

The best regimen is the one the patient will take.

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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)

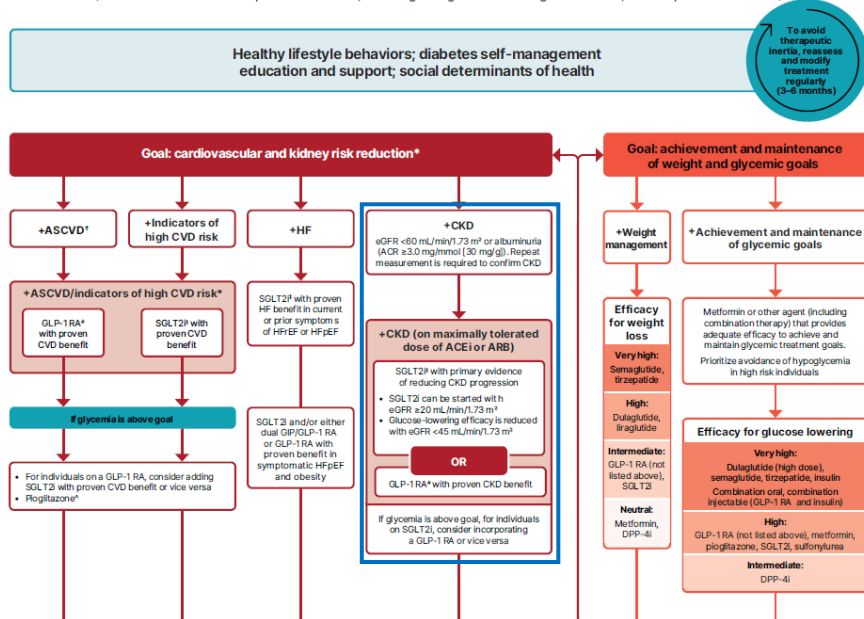


Figure 9.4 Pharmacologic Approaches to Glycemic Treatment: Standards of Care in Diabetes - 2026. Diabetes Care 2026;49(Suppl. 1):S183-215

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Patient Case 5

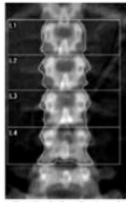
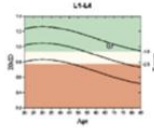
A 66-year-old otherwise healthy woman has been recently diagnosed with breast cancer and will soon begin aromatase inhibitor therapy. She went through menopause around age 52 and has no personal or family history of fractures. She does not have problems with gait instability or falls. She does not smoke.

On examination, she is alert and in no distress. Vital signs are stable and her BMI is 22. She has had no loss of height and has no kyphosis or bony tenderness on palpation.

She has a normal eGFR and calcium level, and her vitamin D level is 35

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Patient Case 5

DAP: 2.2 cGy*cm²

Scan Type: x Lumbar Spine

Her DXA scan shows osteopenia of the hips:

T score L femoral neck is -1.6

T score R femoral neck is -1.1

Results:

	BMD (g/cm ²)	T-score	PR (%)	Z-score	AM (%)
Left Hip (Neck)	0.668	-1.6	79	0.0	100
Left Hip (Total)	0.816	-1.0	87	0.3	105
Right Hip (Neck)	0.725	-1.1	85	0.5	109
Right Hip (Total)	0.834	-0.9	89	0.5	108
Spine (Total)	1.016	-0.3	97	1.7	122

Total BMD CV 1%

Summary:

	Classification
Left Hip BMD (Neck)	Osteopenia
Left Hip BMD (Total)	Normal
Right Hip BMD (Neck)	Osteopenia
Right Hip BMD (Total)	Normal
Spine BMD (Total)	Normal

A spine fracture indicates 5X risk for subsequent spine fracture and 2X risk for subsequent hip fracture.

World Health Organization criteria for BMD impression classify patients as Normal (T-score at or above -1.0), Osteopenia (T-score between -1.0 and -2.5), or Osteoporosis (T-score at or below -2.5).

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Patient Case 5, Question 1

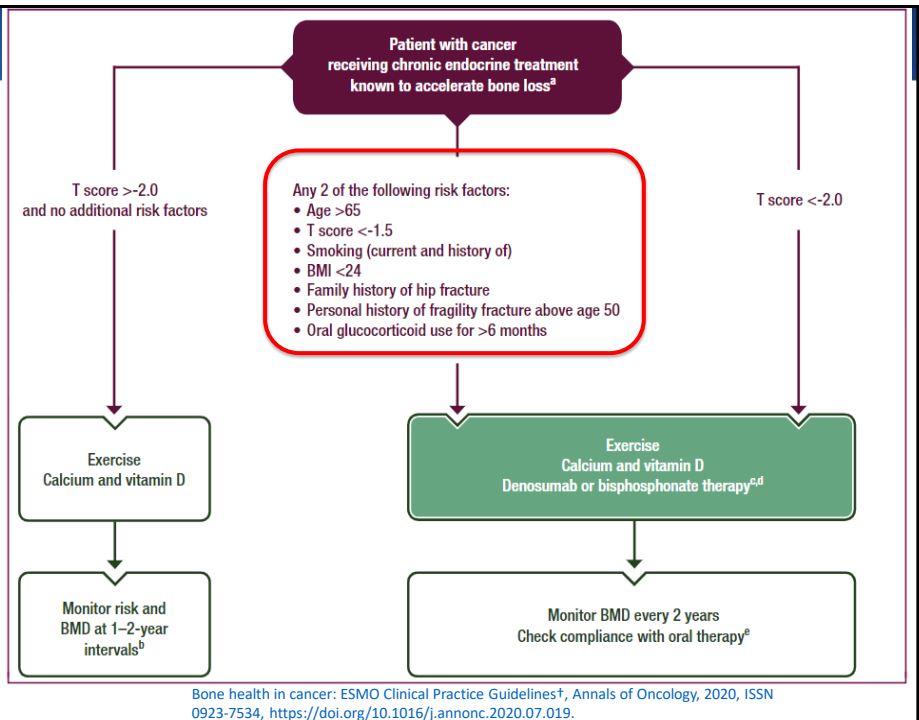
What Do You Recommend Now?

- Follow up DXA scan in one year
- Check bone turnover markers in 6 months
- Begin denosumab (Prolia) 60 mg SC every 6 months
- Begin teriparatide (Forteo) 20 mcg SC daily
- Begin raloxifene (Evista) 60 mg daily

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Algorithm for Managing Bone Health During Cancer Treatment

ADT, androgen deprivation therapy; AI, aromatase inhibitor; BMD, bone mineral density; BMI, body mass index; DXA, dual X-ray absorptiometry; ONJ, osteonecrosis of the jaw.



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Patient Case 6

A 57-year-old man presents for evaluation of a lump on the right side of his neck. It is not painful and he has had no difficulty swallowing or breathing. He otherwise feels well.



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Patient Case 6

- He has no symptoms suggestive of hypo or hyperthyroidism.
- He has no personal or family history of thyroid cancer and has not had head or neck irradiation.
- His medical history includes HTN and hyperlipidemia. He is a non-smoker.
- On examination, there is a palpable prominence in the mid right thyroid lobe. There is no pain on palpation, and the gland moves easily with swallowing. There is no palpable neck adenopathy.

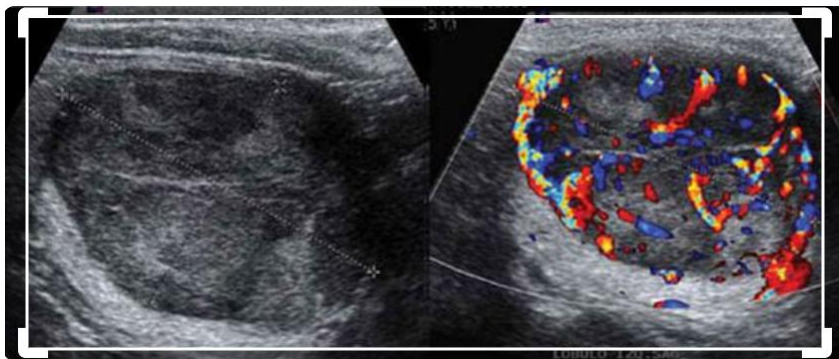


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Patient Case 6

- Thyroid ultrasound shows a 2 cm hypoechoic nodule in the right thyroid lobe. It is a heterogenous, solid nodule with internal vascularity.



TSH = 0.3 mIU/L

(normal 0.5 to 5.0 mIU/L)

Free T4 = 1.2 ng/dL (normal 0.7 to 1.9 ng/dL)

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Patient 6, Question 1

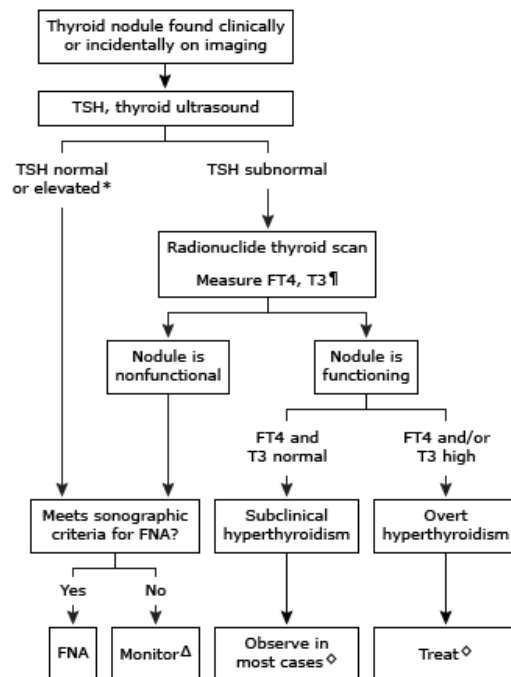
What Is the Next Best Step in the Management of This Thyroid Nodule?

- A. Repeat ultrasound in one year
- B. CT of the neck now
- C. Radioiodine thyroid uptake and scan
- D. Fine needle aspiration biopsy
- E. Ethanol ablation of the nodule

Patient Case 6

- TSH level is key to nodule evaluation
- If TSH is suppressed, thyroid scintigraphy should be performed next
- Autonomous nodules may not produce enough thyroid hormone to significantly suppress TSH

https://www.uptodate.com/contents/diagnostic-approach-to-and-treatment-of-thyroid-nodules?search=thyroid%20nodule&source=search_result&selectedTitle=1~150&usage_type=default&display_rank=1

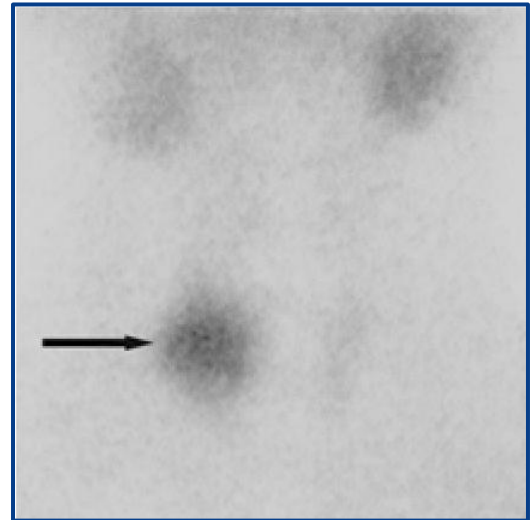


Patient Case 6



Radioiodine thyroid uptake and scan

- Hyperfunctioning nodules are very rarely cancer
- Therefore, a nodule that is hyperfunctioning on radioiodine imaging does not require FNA
- This patient has a slightly suppressed TSH and normal FT4. If FT3 is also normal, only observation is required



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Patient Case 7

58-year-old Man with T2DM and Obesity

- Current medications:
 - metformin 1000 mg BID
 - Insulin glargine 80 units daily
- Weight 250 lbs; BMI = 38
- BP: 145/92
- He reports fasting glucose of 130 -140 mg/dl but glucose is often >250 later in the day
- A1c = 8.0%

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Patient Case 7

AGP Report

Name _____

MRN _____

GLUCOSE STATISTICS AND TARGETS

26 Feb 2019-10 Mar 2019
% Time CGM is Active

13 days
99.9%

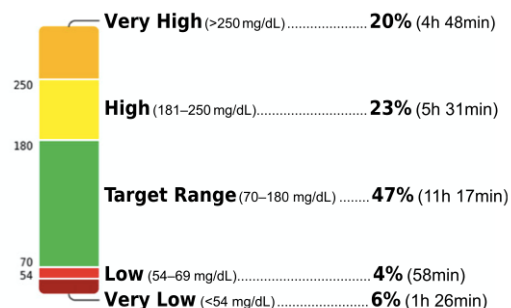
Glucose Ranges **Targets** [% of Readings (Time/Day)]
 Target Range 70–180 mg/dL Greater than 70% (16h 48min)
 Below 70 mg/dL Less than 4% (58min)
 Below 54 mg/dL Less than 1% (14min)
 Above 180 mg/dL Less than 25% (6h)
 Above 250 mg/dL Less than 5% (1h 12min)

Each 5% increase in time in range (70–180 mg/dL) is clinically beneficial.

Average Glucose **173 mg/dL**
Glucose Management Indicator (GMI) **7.6%**
Glucose Variability **49.5%**

Defined as percent coefficient of variation (%CV); target ≤36%

TIME IN RANGES



Diabetes Care 2019;42:1593–1603



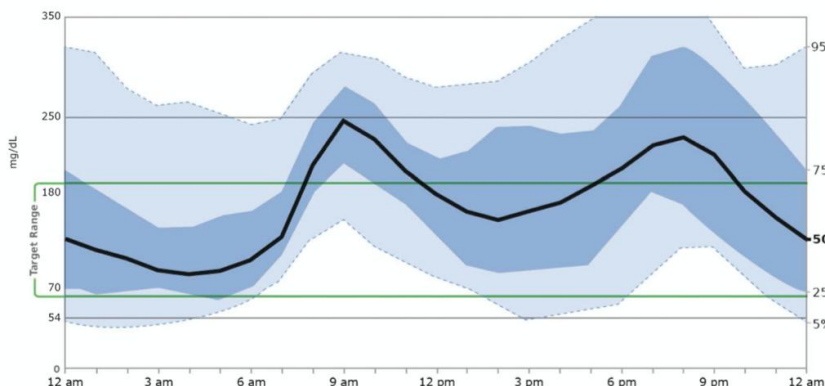
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Patient Case 7

AMBULATORY GLUCOSE PROFILE (AGP)

AGP is a summary of glucose values from the report period, with median (50%) and other percentiles shown as if occurring in a single day.



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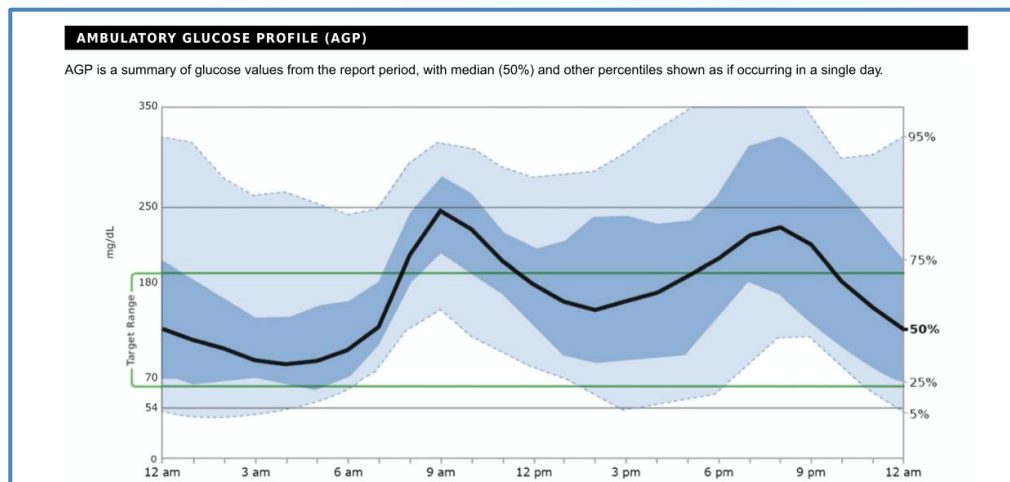
Patient Case 7, Question 1

What Is the Next Best Step?

- A. Add mealtime insulin
- B. Add a sulfonylurea
- C. Add a GLP-1 receptor agonist
- D. Decrease insulin glargine dose

Patient Case 7

Too much basal insulin -> drop in blood sugar overnight

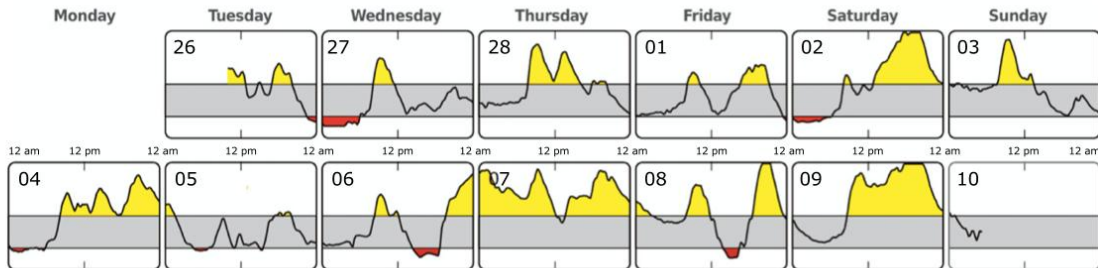


Also having hyperglycemia after meals – but address hypoglycemia first!

Patient Case 7

Overbasalization

DAILY GLUCOSE PROFILES

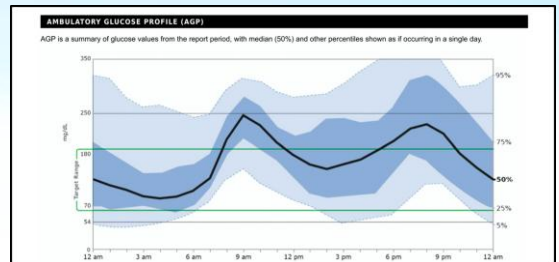


Each daily profile represents a midnight-to-midnight period.

Patient Case 7, Question 2

What Is the Next Best Step?

- A. Add mealtime insulin
- B. Add a sulfonylurea
- C. Add a GLP-1 receptor agonist
- D. Decrease insulin glargine dose



Case Discussion 1

A 66-year-old woman with T2DM, HL and HTN has evidence of chronic kidney disease (eGFR 55, UACr 80). Her HbA1c is 7.3% on metformin and a DPP4i. She is on statin therapy, and BP is controlled on a regimen which includes an ACE inhibitor.

What Would You Recommend at This Time?

- A. No change in treatment
- B. SGLT2 inhibitor
- C. Sulfonylurea
- D. Pioglitazone



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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)

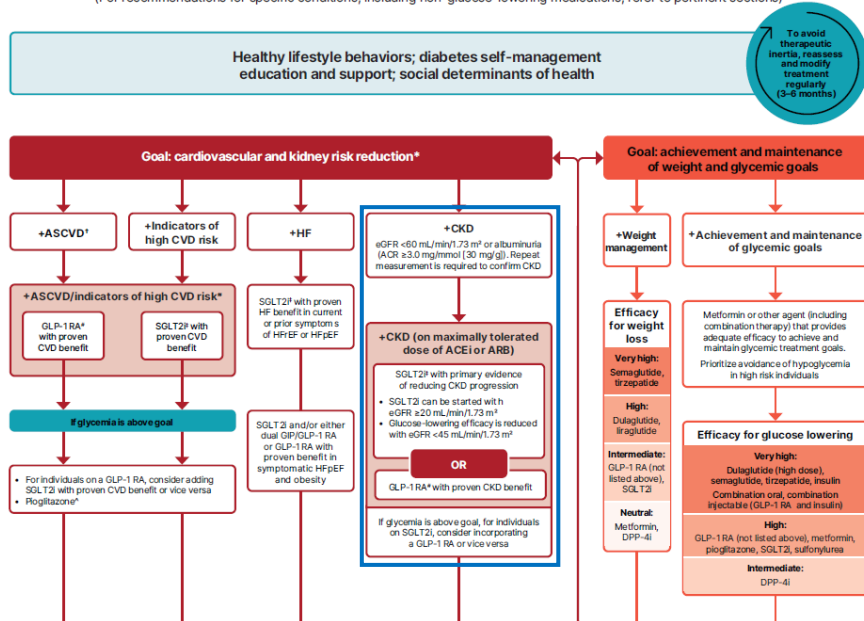
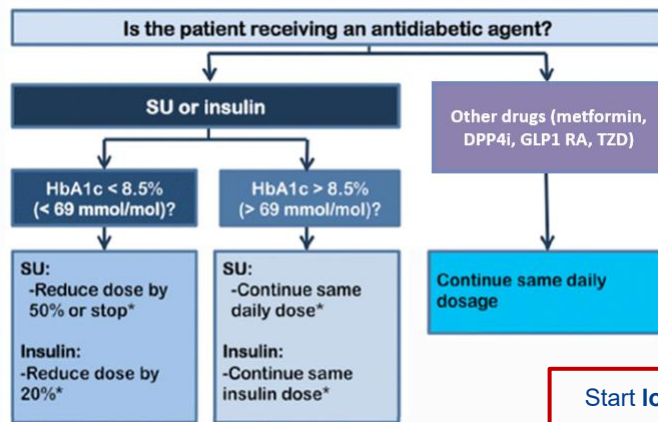


Figure 9.4 Pharmacologic Approaches to Glycemic Treatment: Standards of Care in Diabetes - 2026. Diabetes Care 2026;49(Suppl. 1):S183-215



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SGLT-2i: Starting with Other Diabetes Medications



*Avoid insulin withdrawal to minimize the risk of euglycemic diabetic ketoacidosis

Start **lowest dose** SGLT2i and assess response, make additional medication adjustments as necessary

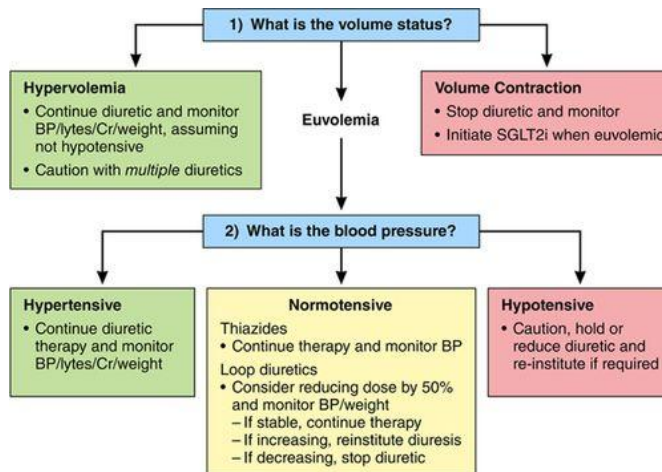
Case Discussion 2

The same patient has been started on an SGLT2 inhibitor. At her follow up appointment, her BP is 108/70 mmHg and she notes occasional lightheadedness when rising from a seated position.

What Would You Recommend at This Time?

- A. Increased intake of fluids
- B. Discontinue HCTZ
- C. Decrease dose of lisinopril
- D. Discontinue SGLT2 inhibitor

SGLT-2i: If Patient on Diuretic Therapy



Case Discussion 3

The 66-year-old woman with T2DM, HL, HTN and CKD is on a medication regimen which includes an SGLT2i. Her lightheadedness has resolved with discontinuation of HCTZ, but she now has a GU infection. Her last prior GU infection was about one year prior to initiation of the SGLT2i.

What Would You Recommend at This Time?

- Fluconazole 150 mg single oral dose
- Fluconazole 150 mg weekly for two months
- Discontinue SGLT2 inhibitor
- Change from SGLT2i to GLP-1 RA therapy

Genital Mycotic Infections (GMIs) with SGLT2 Inhibitors (Pooled 6 Month Data)

More common in

- **Women**
- **Uncircumcised men**
- **GMI history**

Most

- **Only had 1 event**
- **Occur early in therapy**
- **Respond to standard treatment**

Adapted from <http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/EndocrinologicandMetabolicDrugsAdvisoryCommittee/UCM336236.pdf>, www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/EndocrinologicandMetabolicDrugsAdvisoryCommittee/ucm262996.pdf, www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/EndocrinologicandMetabolicDrugsAdvisoryCommittee/UCM378076.pdf and <https://www.fda.gov/Drugs/DrugSafety/ucm617360.htm>. Accessed 21st July, 2015; Nyirjesy P et al. Curr Med Res Opin. 2014;30(6):1109-19; Kim G et al. American Diabetes Association 73rd Scientific Sessions. 21st-25th June 2013. Chicago, IL.

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Case Discussion



How else might care be optimized for this patient with T2DM and chronic kidney disease?

Medications

Metformin 500 mg twice daily

SGLT2i

Atorvastatin 20 mg daily

Lisinopril 20 mg daily

Allergy: Aspirin

Clinical Data

Hemoglobin A_{1c} 7.1%

(4.0%-5.6%) (56 mmol/mol [20-38 mmol/mol])

Estimated GFR 53 mL/min per 1.73 m²

(>60 mL/min per 1.73 m²)

Total Cholesterol 167 mg/dL

Triglycerides 117 mg/dL

HDL Cholesterol 46 mg/dL

LDL Cholesterol 98 mg/dL

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Lipid Management for Primary Prevention of ASCVD

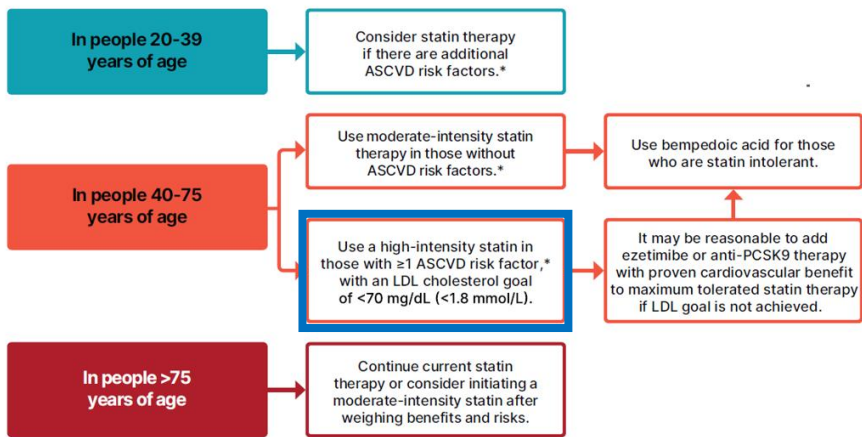


Figure 10.3—Recommendations for primary prevention of atherosclerotic cardiovascular disease (ASCVD) in people with diabetes using cholesterol-lowering therapy. *ASCVD risk factors include older age, hypertension, dyslipidemia, smoking, chronic kidney disease, or obesity. Adapted from "Standards of Care in Diabetes—2024 Abridged for Primary Care Professionals" (315).

Figure 10.3
Cardiovascular Disease and Risk Management:
Standards of Care in Diabetes - 2026 Diabetes Care 2026;49(Suppl. 1):S216-S245

