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Endocrine and Exocrine Disorders in the Older Adult

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Meet the Speaker

Haley Phillippe is an Associate Clinical Professor of Pharmacy Practice with Auburn University Harrison College of Pharmacy and Clinical Associate Professor of Family Medicine with the University of Alabama School of Medicine, Huntsville Campus. Dr. Phillippe's professional interests include geriatrics, diabetes, dyslipidemia, drugs of abuse, and hypertension. She currently practices in a large outpatient family medicine clinic where she focuses on the management of chronic disease states and medications in older adults. Dr. Phillippe has 12 years of practice experience in LTCs/SNFs.

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Disclosure

- Haley Phillippe does not have relevant financial relationships with ineligible companies.
- None of the planners for this activity have relevant financial relationships to disclose with ineligible companies.

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Learning Objectives

1. Determine therapeutic options for diabetes, hypothyroidism, and osteoporosis in the older adult.
2. Interpret endocrine and exocrine clinical findings and incorporate functional status into therapeutic decision-making.
3. Resolve and/or prevent endocrine and exocrine medication-related problems.
4. Apply endocrine and exocrine therapy recommendations and person-specific goals to older adult patient cases.

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Type 2 Diabetes

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Diabetes and the Older Adult

- ~30% of people > 65 years old have diabetes
- ~50% of people > 65 years old have prediabetes
- Increased rates of premature death, functional disability, accelerated muscle loss, and coexisting illnesses
- Increased risk of geriatric syndromes
  - Polypharmacy
  - Cognitive Impairment
  - Depression
  - Urinary Incontinence
  - Falls and Pain

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Centers for Disease Control and Prevention. National Diabetes Statistics Report [Internet], 2021. Available from https://www.cdc.gov/diabetes/php/data-research/index.html . Accessed 18 January 2025. ADA Standards of Care. Diabetes Care. 2025;48(S1):S1-S282.

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Diagnosis of Diabetes

ADA Diagnostic Criteria
1. A1C ≥ 6.5%[a]
OR
2. 8-hour FPG ≥ 126 mg/dL (7 mmol/L)
OR
3. 2-hr plasma glucose ≥ 200 mg/dL (11.1 mmol/L) during OGTT
OR
4. Random plasma glucose ≥ 200 mg/dL (11.1 mmol/L) with classic symptoms of hyperglycemia

[a]less reliable in increased red blood cell turnover such as sickle cell disease, hemodialysis, recent blood loss/transfusion, erythropoietin therapy, some HIV drugs, and iron-deficient anemia

A1C Correlation to Average Glucose

A1C (%)	Mean plasma glucose mg/dL	mmol/L
5	97	5.4
6	126	7.0
7	154	8.6
8	183	10.2
9	212	11.8
10	240	13.4
11	269	14.9
12	298	16.5

Caveats: RBC turnover, ethnicity

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OGTT, oral glucose tolerant test

ADA Standards of Care. Diabetes Care. 2025;48(S1):S1-S282.

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Glycemic Goals in Older Adults (ADA)

Patient Characteristics/ Health Status	Rationale	Reasonable A1C goal	Pre-meal glucose mg/dL (mmol/L)	Bedtime glucose mg/dL (mmol/L)
Healthy (few chronic illnesses, intact cognitive/functional status)	• Longer life expectancy	<7.0 - 7.5%	80-130 (5-7.2)	80-180 (5-8.3)
Complex/intermediate (multiple chronic illnesses or 2+ instrumental ADL impairments or mild-moderate cognitive impairment)	• Intermediate life expectancy • > Treatment burden • > Hypoglycemia and fall risk	< 8.0%	90-150 (5-8.3)	100-180 (5.6-10)
Very complex/poor health (long-term care or end-stage chronic illness or mod-severe cognitive impairment or 2+ ADL dependencies)	• Limited life expectancy	Avoid hypoglycemia & symptomatic hyperglycemia	100-180 (5.6-10)	110-200 (6.1-12.2)
End of Life	• Goal is comfort	Avoid hypoglycemia and symptomatic hyperglycemia		

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Diabetes Treatment Burden: Intensive Glucose Control

- Lifetime DM treatment, ↓A1C 1% QALY gained:
  - 45-year-old: ~1 QALY
  - 65-year-old: ~0.3 QALY
  - 75-year-old: ~0.1 QALY
- ↑ burden negates benefit especially for those ≥ 65 years
  - Common reported burden of insulin eliminates benefit

QALY, net quality-adjusted life-years—incorporates both the quantity and quality of life related to all the potential benefits and harms of therapy

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ADA. Diabetes Care. 2025;48(S1):S1-S308.; ACCE/ACE Guidelines available at: https://www.aace.com/publications/guidelines. Accessed 1/4/25

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Patient Case: John

- 72-year-old African-American male
- PMH of Type 2 DM (10 years), CABG (6 years ago), HTN, dyslipidemia, kidney disease, and COPD
- He lives alone. His daughter assists with cooking and maintaining his home.
- Denies alcohol use; quit smoking 2 years ago
- He has mild cognitive impairment (MMSE 21/30)

PMH, past medical history; DM, diabetes; CABG, coronary artery bypass graft; HTN, hypertension; COPD, chronic obstructive pulmonary disease; MMSE, mini-mental state examination

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Self-Assessment Question #1

According to the 2025 ADA Guidelines, which of the following is the most appropriate A1C goal for John?

A. A1C should not be a goal for managing John's diabetes
B. < 7%
C. < 8%
D. < 8.5%

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Blood Glucose Monitoring

- **Basal insulin or oral agents**
  - Insufficient evidence
  - Varies by patient, but consider: suspected or frequent hypoglycemia, prior to exercise or critical tasks
- **Intensive insulin**
  - Fasting, prior to meals/snacks, bedtime, occasionally post-prandial, hypoglycemia suspected; also consider prior to exercise or other critical tasks
  - At least 3 times daily, may require 6-10 times per day

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Continuous Glucose Monitoring (CGM)

- Most likely to benefit from CGM
  - On an intensive insulin regimen
  - Discordant A1C and self-monitoring blood glucose (SMBG)
  - History of severe hypoglycemia or hypoglycemia unawareness
  - Unclear pattern/labile blood glucose
- Medicare covers Dexcom G6 and FreeStyle Libre 3 for T1D/T2D
  - Prescribed insulin ≥ 1 times daily

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Medication Therapy in Older Adults

- Medication classes with a low risk of hypoglycemia are preferred
- Avoid overtreatment of diabetes
  - Common in older adults
- Simplify complex regimens
  - Match the complexity of the treatment regimen to the patient's self-management ability
  - Decrease pill burden
- Independent living, assisted living, or long-term care

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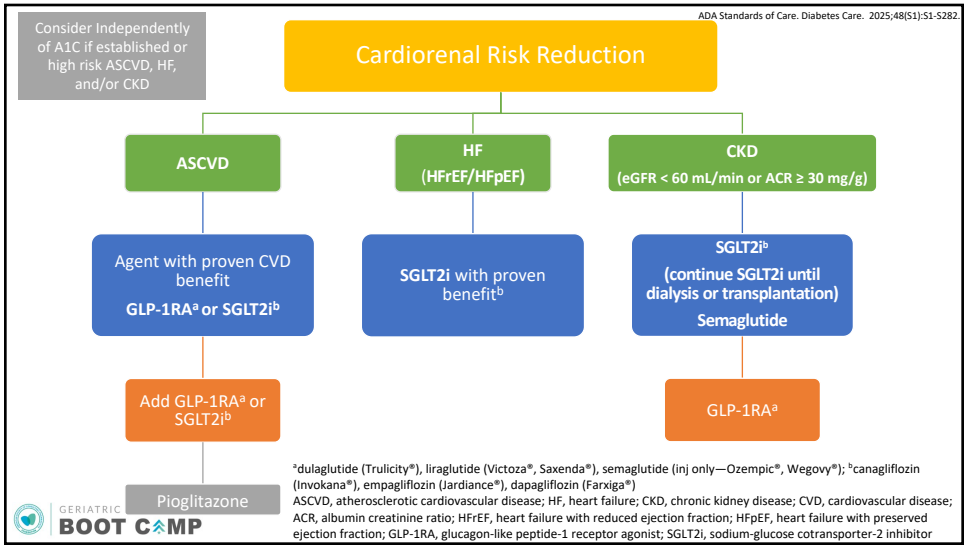
ADA Standards of Care. Diabetes Care. 2025;48(S1):S1-S282.
Consider Independently of A1C if established or high risk ASCVD, HF, and/or CKD
Cardiorenal Risk Reduction
ASCVD
HF (HFrEF/HFpEF)
CKD (eGFR < 60 mL/min or ACR ≥ 30 mg/g)
Agent with proven CVD benefit
GLP-1RA[a] or SGLT2i[b]
SGLT2i with proven benefit[b]
SGLT2i[b] (continue SGLT2i until dialysis or transplantation)
Semaglutide
Add GLP-1RA[a] or SGLT2i[b]
GLP-1RA[a]
Pioglitazone
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[a]dulaglutide (Trulicity®), liraglutide (Victoza®, Saxenda®), semaglutide (inj only—Ozempic®, Wegovy®); [b]canagliflozin (Invokana®), empagliflozin (Jardiance®), dapagliflozin (Farxiga®)
ASCVD, atherosclerotic cardiovascular disease; HF, heart failure; CKD, chronic kidney disease; CVD, cardiovascular disease; ACR, albumin creatinine ratio; HFrEF, heart failure with reduced ejection fraction; HFpEF, heart failure with preserved ejection fraction; GLP-1RA, glucagon-like peptide-1 receptor agonist; SGLT2i, sodium-glucose cotransporter-2 inhibitor

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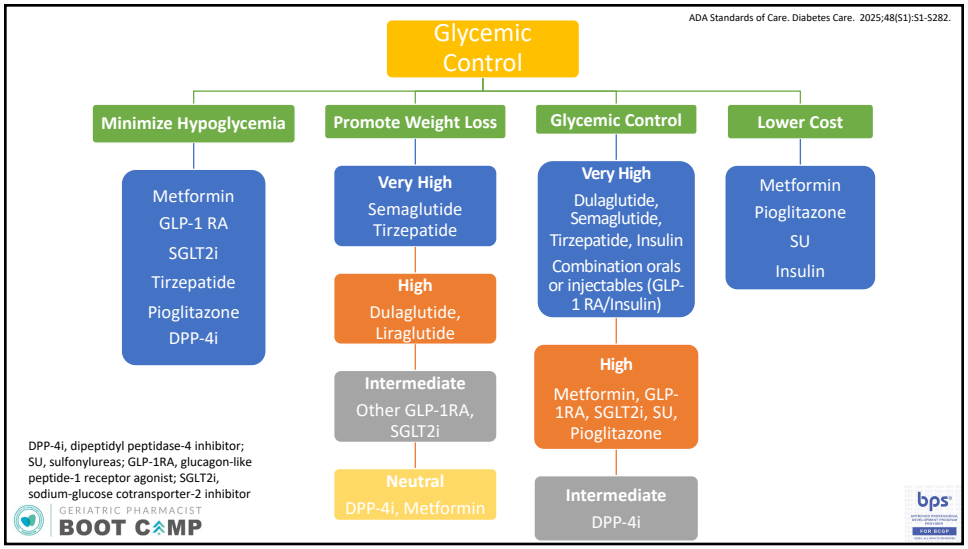
ADA Standards of Care. Diabetes Care. 2025;48(S1):S1-S282.
Glycemic Control
Minimize Hypoglycemia
Promote Weight Loss
Glycemic Control
Lower Cost
Metformin
GLP-1 RA
SGLT2i
Tirzepatide
Pioglitazone
DPP-4i
Very High
Semaglutide
Tirzepatide
High
Dulaglutide, Liraglutide
Intermediate
Other GLP-1RA, SGLT2i
Neutral
DPP-4i, Metformin
Very High
Dulaglutide, Semaglutide, Tirzepatide, Insulin
Combination orals or injectables (GLP-1 RA/Insulin)
High
Metformin, GLP-1RA, SGLT2i, SU, Pioglitazone
Intermediate
DPP-4i
Metformin
Pioglitazone
SU
Insulin
DPP-4i, dipeptidyl peptidase-4 inhibitor; SU, sulfonylureas; GLP-1RA, glucagon-like peptide-1 receptor agonist; SGLT2i, sodium-glucose cotransporter-2 inhibitor
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Combination Therapy

- Most therapies can be combined
- Combinations to avoid
  - GLP-1 RAs with DPP4-I or tirzepatide
    - Similar mechanism of action
  - SUs with insulin
    - Increased risk of hypoglycemia

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Metformin

Efficacy	Hypo-glycemia	Weight Change	CV Effects		Renal Effects		Additional Considerations
			MACE	HF	Progression of DKD	Dosing/Use Considerations	

High	No	Neutral	**Potential Benefit**	Neutral	Neutral	• CI when eGFR < 30
						• Caution and dose reduction when eGFR 30 - 45
							• GI SE common (N/D)
							  • Take with food
							  • Slow dose titration
							  • ER formulation
							• Possible weight loss
							• Potential for B12 Deficiency

MACE, major adverse cardiovascular events; DKD, diabetic kidney disease; NR, not recommended; CI, contraindicated; HF, heart failure; SE, side effect
DKD is a clinical diagnosis marked by reduced eGFR, the presence of albuminuria, or both.

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Adapted Table 1 from Davies MJ, Aroda VR, Collins BS, et al. Management of Hyperglycemia in Type 2 Diabetes, 2022. A Consensus Report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). ADA Standards of Care. Diabetes Care. 2025;48(S1):S1-S282

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GLP-1 RAs

Efficacy	Hypo-glycemia	Weight Change	CV Effects		Renal Effects	
			MACE	HF	Progression of DKD	Dosing/Use Considerations
High to Very High	No	Loss	Neutral: lixisenatide, semaglutide (PO)	Neutral	**Benefit: semaglutide* (SQ) dulaglutide, liraglutide**	• Exenatide: NR eGFR < 30 • Lixisenatide: c aution when eGFR < 30 • Increased risk of SE in patients with renal impairment
			Benefit: dulaglutide†, liraglutide†, semaglutide† (SQ)		Driven by albuminuria outcomes **Semaglutide benefit for progression of CKD**	

†FDA approved for CVD benefit. ; *FDA approved for DKD benefit; MACE, major adverse cardiovascular events; DKD, diabetic kidney disease; NR, not recommended; CI, contraindicated; dulaglutide (Trulicity®), liraglutide (Victoza®), semaglutide (inj—Ozempic®)

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Adapted Table 1 from Davies MJ, Aroda VR, Collins BS, et al. Management of Hyperglycemia in Type 2 Diabetes, 2022. A Consensus Report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). ADA. Diabetes Care. 2025;48(S1):S1-S308

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Comparison of GLP-1 Agonists

Agent	Dosing Schedule	Dosing
~~Exenatide (Byetta®)~~	Discontinued in US	
~~Exenatide ER (Bydureon®)~~	Discontinued in US	
Liraglutide (Victoza®)	Daily (Inj)	0.6 mg, 1.2 mg, 1.8 mg
Dulaglutide (Trulicity®)	Weekly (Inj)	0.75 mg, 1.5 mg, 3 mg, 4.5 mg
Lixisenatide (Adlyxin®)	Daily (Inj)	10 mcg, 20 mcg
Semaglutide (Ozempic®)	Weekly (Inj)	0.25 mg, 0.5 mg, 1 mg, 2 mg
Semaglutide (Rybelsus®)	Daily (PO)	3mg , 7mg, 14 mg

Inj, injection; PO, by mouth

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Rybelsus [package insert]. Bagsvaerd, Denmark: Novo Nordisk; 2024. Ozempic [package insert]. Bagsvaerd, Denmark: Novo Nordisk; 2024. Adlyxin [package insert]. Bridgewater, NJ: Sanofi; 2024. Trulicity [package insert]. Indianapolis, IN: Eli Lilly; 2024. Victoza [package insert]. Bagsvaerd, Denmark: Novo Nordisk; 2024. Bydureon [package insert]. Wilmington, DE: AstraZeneca; 2024. Byetta [package insert]. Wilmington, DE: AstraZeneca; 2024.

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Dual GIP and GLP-1 RA (Tirzepatide—Mounjaro®)

Efficacy	Hypo-glycemia	Weight Change	CV Effects		Renal Effects	
			MACE	HF	Progression of DKD	Dosing/Use Considerations
Very High	No	Loss (very high)	Under investigation		Under investigation	• No dose adjustment • Increased risk of SE in patients with renal impairment

MACE, major adverse cardiovascular events; DKD, diabetic kidney disease; HF, heart failure; GIP, glucose-dependent insulinotropic polypeptide; GLP-1RA, glucagon-like peptide-1 receptor agonist; SE, side effects

Dosing: 2.5 mg once weekly for 4 weeks, then 5 mg once weekly for 4 weeks, then increase in 2.5 mg/week increments every 4 weeks. Max weekly dose 15mg/week.

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Adapted Table 1 from Davies MJ, Aroda VR, Collins BS, et al. Management of Hyperglycemia in Type 2 Diabetes, 2022. A Consensus Report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). ADA. Diabetes Care. 2025;48(S1):S1-S308.

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Clinical Considerations: GLP-1 RAs and Dual GIP and GLP-1RA

- Boxed Warning: Risk of thyroid C-cell tumors
  - Avoid use if personal or primary relative history
- GI SE (N/V/D)
  - Dietary modifications: reduce meal size, decrease intake of high-fat or spicy food
  - Slow titration
- Gallbladder disease
  - Avoid use if high risk for cholelithiasis or cholecystitis
- Acute pancreatitis
  - Do not initiate if high risk for pancreatitis
  - Discontinue if suspected, do not restart
- Avoid if diagnosed with gastroparesis
- Potential for ileus (semaglutide)
  - Discontinue prior to surgical procedure
- Diabetic Retinopathy
  - Close monitoring if older adult and/or diabetes ≥ 10 years
- Affects drug absorption of other medications, especially during dose titrations
  - May decrease birth control absorption

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ADA Standards of Care. Diabetes Care. 2025;48(S1):S1-S282.

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SGLT-2 Inhibitors

Efficacy	Hypo-glycemia	Weight Change	CV Effects		Renal Effects
			MACE	HF	Progression of DKD
Intermediate to High	No	Loss	**Benefit:** **empagliflozin†** **canagliflozin†**	**Benefit:** **dapagliflozin‡** **empagliflozin‡** **canagliflozin** **ertugliflozin**	**Benefit:** **canagliflozin§** **dapagliflozin§** **empagliflozin** Glucose lowering effect is minimal if eGFR < 45 mL/min

†FDA approved for CVD benefit. ‡FDA approved for HF indication. § FDA approved for DKD indication.
MACE, major adverse cardiovascular events; DKD, diabetic kidney disease; NR, not recommended; canagliflozin (Invokana®), empagliflozin (Jardiance®), dapagliflozin (Farxiga®), ertugliflozin (Steglatro®)

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Adapted Table 1 from Davies MJ, Aroda VR, Collins BS, et al. Management of Hyperglycemia in Type 2 Diabetes, 2022. A Consensus Report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). ADA. Diabetes Care. 2025;48(S1):S1-S308

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Clinical Considerations: SGLT-2 Inhibitors

- DKA risk
  - Discontinue before any scheduled surgery, during prolonged fasting, or during critical illness to avoid potential risk for diabetic ketoacidosis (DKA)
- Genitourinary infections
  - Avoid if recurrent infections
- Risk of volume depletion, hypotension
  - Increased risk if illness or fasting
  - May require reduction of other volume-contracting agents
- Risk of Fournier's gangrene (rare)
- Beers Criteria
  - Increased risk of urogenital infections
  - Higher risk of euglycemic diabetic ketoacidosis

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Comparison of SGLT-2 Inhibitors

Agent	Dosing	Renal Dosing
Canagliflozin (Invokana®)	100-300 mg daily	• eGFR 30-59 mL/min: 100 mg daily • eGFR <30 mL/min with urinary albumin >300 mg/day: do not initiate, may continue 100 mg daily • CI in dialysis
Dapagliflozin (Farxiga®)	5-10 mg daily HF: 10 mg daily	• eGFR <25 mL/min: do not initiate, may continue 10 mg daily • CI in dialysis
Empagliflozin (Jardiance®)	10-25 mg daily	• eGFR 20-30 mL/min: do not initiate, may continue 10 mg daily • CI in dialysis
Ertugliflozin (Steglatro®)	5-15 mg daily	• eGFR < 45 mL/min: NR
Bexagliflozin (Brenzavvy®)	20 mg daily	• eGFR < 30 mL/min: NR

CI, contraindicated; NR, not recommended

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ADA. Diabetes Care. 2024;47(S1):S1-S308. ACCE/ACE Guidelines available at: https://pro.aace.com/clinical-guidance/2023-aace-consensus-statement-comprehensive-type-2-diabetes-management-algorithm. Accessed 1/10/24

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Dual SGLT-1 and SGLT-2 Inhibitor

- Sotagliflozin (Inpefa®)
  - Not FDA approved for treating diabetes
    - Lowers glucose via delayed glucose absorption in the gut via inhibition of the cotransporter SGLT-1 in addition to increasing urinary glucose excretion.
  - FDA approved for reducing risk of cardiovascular death, hospitalization for heart failure, and urgent heart failure in people with heart failure or T2D, CKD, and other cardiovascular risk factors
  - No dose adjustments in kidney disease

SGLT-1, sodium-glucose cotransporter-1; SGLT2i, sodium-glucose cotransporter-2 inhibitor

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Sotagliflozin [package insert]. Woodlands, TX: Lexicon Pharmaceuticals; 2023.

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Pioglitazone (TZD)

Efficacy	Hypo-glycemia	Weight Change	CV Effects		Renal Effects		Additional Considerations
			MACE	HF	Progression of DKD	Dosing/Use Considerations	
High	No	Gain	**Potential Benefit**	**Increased Risk**	Neutral	• No dose adjustment needed • Potential for fluid retention especially with HF and/or renal impairment	• **Boxed Warning: HF** • Risk of bone fractures • Fluid retention • Do not use if history of bladder cancer • Benefit in NASH/NAFLD • Benefit secondary stroke prevention

MACE, major adverse cardiovascular events; DKD, diabetic kidney disease; HF, heart failure; NASH, nonalcoholic steatohepatitis; NAFLD, nonalcoholic fatty liver disease

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Adapted Table 1 from Davies MJ, Aroda VR, Collins BS, et al. Management of Hyperglycemia in Type 2 Diabetes, 2022. A Consensus Report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). ADA. Diabetes Care. 2025;48(S1):S1-S308

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DPP-4 Inhibitors

Efficacy	Hypo-glycemia	Weight Change	CV Effects		Renal Effects		Additional Considerations
			MACE	HF	Progression of DKD	Dosing/Use Considerations	
Intermediate	No	Neutral	Neutral	**Potential Risk: saxagliptin**	Neutral	• Renal dose adjustment required for all except linagliptin	• Potential risk of acute pancreatitis • Joint pain • Bullous pemphigoid

DKD, diabetic kidney disease; HF, heart failure

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Adapted Table 1 from Davies MJ, Aroda VR, Collins BS, et al. Management of Hyperglycemia in Type 2 Diabetes, 2022. A Consensus Report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). ADA. Diabetes Care. 2025;48(S1):S1-S308

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Comparison of DPP-4 Inhibitors

Agent	Dosing	Renal Dosing
Alogliptin (Nesina®)	25 mg daily	• eGFR 30-60 mL/min: 12.5 mg daily • eGFR <30 mL/min: 6.25 mg daily
Linagliptin (Tradjenta®)	5 mg daily	• No dose adjustment
Sitagliptin (Januvia®)	100 mg daily	• eGFR 30-45 mL/min: 50 mg daily • eGFR <30 mL/min: 25 mg daily
Saxagliptin (Onglyza®)	2.5 - 5 mg daily	• eGFR <45 mL/min: 2.5 mg daily

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Adapted Table 1 from Davies MJ, Aroda VR, Collins BS, et al. Management of Hyperglycemia in Type 2 Diabetes, 2022. A Consensus Report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). ADA. Diabetes Care. 2025;48(S1):S1-S308

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Sulfonylureas (SU)

Efficacy	Hypo-glycemia	Weight Change	CV Effects		Renal Effects		Additional Considerations
			MACE	HF	Progression of DKD	Dosing/Use Considerations	
High	**Yes**	Gain	Neutral	Neutral	Neutral	• Glyburide NR • Glipizide and glimepiride[a]	• **Hypoglycemia increased in older adults** • Weight gain • Glyburide/glimepiride longer half life, increased hypoglycemia (Beers Criteria) • Glipizide is preferred SU

[a]Initiate conservatively to avoid hypoglycemia; MACE, major adverse cardiovascular events; DKD, diabetic kidney disease; NR, not recommended; CI, contraindicated; HF, heart failure

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Self-Assessment Question #2

Which of the following would be the best drug therapy for a patient with T2DM and ASCVD?

A. Glyburide
B. Saxagliptin
C. Empagliflozin
D. Lixisenatide

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When To Use Injectable Therapy

Immediate start Basal insulin is recommended for patients with severe hyperglycemia

Above A1C target despite appropriate oral therapy	• GLP-1 RA or dual GIP/GLP-1 RA
Above A1C target despite oral therapy + GLP-1 Ra or dual GIP/GLP-1 RA therapy	• Add Basal insulin or bedtime NPH
Above A1C or TIR target despite basal/NPH titration	• Add prandial insulin

TIR, time in therapeutic range

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ADA. Diabetes Care. 2025;48(S1):S1-S308.; ACCE/ACE Guidelines available at: https://www.aace.com/publications/guidelines. Accessed 1/4/24

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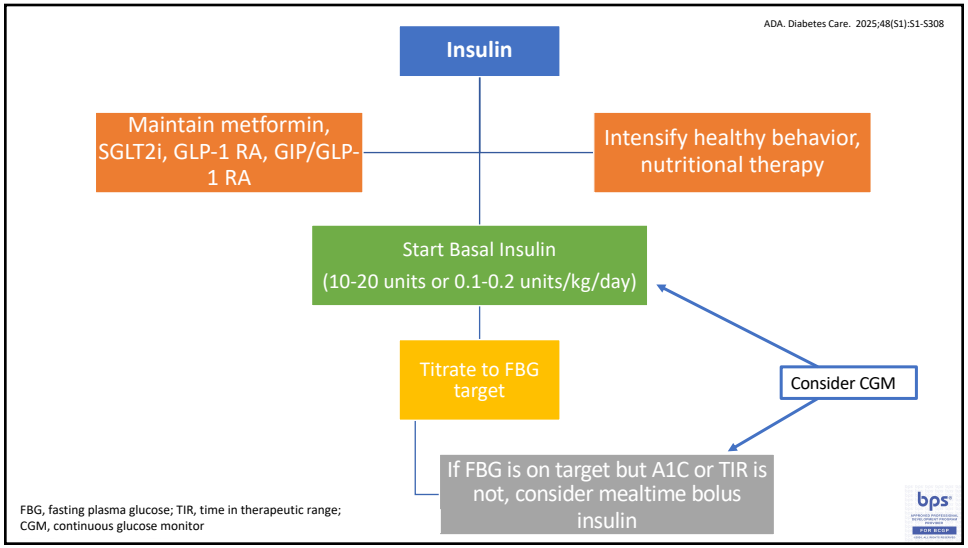

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Long-acting Insulins

Insulin	PK Properties[a]	Administration	Initial Dose/Titration
Glargine U-100	Onset: 3-4 hrs Duration: 24 hrs	Once daily or twice daily	Initial dose: 10-20 units or 0.1-0.2 units/kg a day Titration: increase 2 units every 3 days; slower titration for degludec
Glargine U-300	Onset: 6 hrs Duration: 24 hrs		
Detemir (discontinuing 2024)	Onset: 1-2 hrs Duration: 14-24 hrs		
Degludec	Onset: 1-2 hrs Duration: >40 hrs	Once daily	

[a]Long-acting insulins have no peak; PK, pharmacokinetic; min, minutes; hrs, hours

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Trujiloo J, Haines S. Diabetes mellitis. In: DiPiro JT, Yee GC, Posey LM, et al. Pharmacotherapy: A Pathophysiologic Approach. 11ed. McGraw-Hill; 2021: chap 91. Accessed September 24, 2025. https://accesspharmacy.mhmedical.com.; Insulin glargine. Lexi-Drugs. Waltham, MA: UpToDate, 2024. http://online.lexi.com/. Updated September 16, 2022. Accessed September 24, 2025.; Insulin detemir. Lexi-Drugs. Waltham, MA: UpToDate, 2025. http://online.lexi.com/. Updated September 16, 2023. Accessed September 24, 2025.; Insulin degludec. Lexi-Drugs. Waltham, MA: UpToDate, 2024. http://online.lexi.com/. Updated September 16, 2021. Accessed September 24, 2025.

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Short-acting and Intermediate-acting Insulins

Insulin	PK Properties	Administration	Initial Dose/Titration
Short-acting			
Regular	Onset: 30-60 min Peak: 2-4 hrs Duration: 6-8 hrs	30 min before meal	Initial: 4 units or 10% of the basal insulin dose Titration: 1-2 units or 10-15 % of dose twice weekly
Intermediate-acting			
NPH	Onset: ~2 hrs Peak: 4-12 hrs Duration: 18-26 hrs	Once daily at bedtime or twice daily	0.1 to 0.2 units/kg/day or 10 units/day Titration: increase 2 units every 3 days or switch to twice daily

PK, pharmacokinetic; min, minutes; hrs, hours

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Trujiloo J, Haines S. Diabetes mellitis. In: DiPiro JT, Yee GC, Posey LM, et al. Pharmacotherapy: A Pathophysiologic Approach. 12ed. McGraw-Hill; 2023: chap 91. Accessed September 24, 2025. https://accesspharmacy.mhmedical.com.; Insulin regular. Lexi-Drugs. Waltham, MA: UpToDate, 2024. http://online.lexi.com/. Updated September 16, 2022. Accessed September 24, 2025.; 10. Insulin NPH. Lexi-Drugs. Waltham, MA: UpToDate, 2024. http://online.lexi.com/. Updated September 16, 2021. Accessed September 24, 2025.

35

Rapid-acting Insulins

Insulin	PK Properties	Administration	Initial Dose/Titration
Lispro	Onset: 5-15 min Peak: 45-75 min Duration: 3-5 hrs	15 min before or immediately after meal	Initial: 4 units **or** 10% of the basal insulin dose Titration: 1-2 units **or** 10-15 % of dose twice weekly
Lispro-aabc		At start of or within 20 min after starting meal	
Glulisine		15 min before or within 20 min after starting meal	
Aspart		5-10 min before meal	
Aspart ("faster acting")		At start of or within 20 min after starting meal	
Inhaled Insulin	Onset: <15 min Peak: 50 min Duration: 2-3 hrs	At start of meal[a]	Initial: 4 units Titration: 4 units twice weekly

[a]Inhaler and cartridges must be at room temperature for 10 minutes before administration; PK, pharmacokinetic; min, minutes; hrs, hours

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Trujiloo J, Haines S. Diabetes mellitis. In: DiPiro JT, Yee GC, Posey LM, et al. Pharmacotherapy: A Pathophysiologic Approach. 11ed. McGraw-Hill; 2021: chap 91. Accessed September 24, 2024. https://accesspharmacy.mhmedical.com.; Insulin lispro. Lexi-Drugs. Waltham, MA: UpToDate, 2021. http://online.lexi.com/. Updated September 16, 2021. Accessed September 24, 2024.; Insulin aspart. Lexi-Drugs. Waltham, MA: UpToDate, 2021. http://online.lexi.com/. Updated September 16, 2021. Accessed September 24, 2024.; Insulin glulisine. Lexi-Drugs. Waltham, MA: UpToDate, 2021. http://online.lexi.com/. Updated September 16, 2021. Accessed September 24, 2024.; Insulin (oral inhalation). Lexi-Drugs. Waltham, MA: UpToDate, 2021. http://online.lexi.com/. Updated September 16, 2021. Accessed September 24, 2024.

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Short-acting and Intermediate-acting Concentrated

Insulin	PK Properties	Administration	Initial Dose/Titration
U-500 regular	Onset: 30 min Peak: 4-8 hrs Duration: 13-24 hrs	Two times daily (60% before breakfast and 40% before supper) Or Three times daily (40% before breakfast, 30% before lunch and supper)	**Discontinue all other insulins** Initial dose: 80% of the TDD of previous insulin regimen (round down to nearest 5 units) Titration: 5-15% rounded to nearest 5 units

PK, pharmacokinetic; min, minutes; hrs, hours; TDD, total daily dose

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Trujiloo J, Haines S. Diabetes mellitis. In: DiPiro JT, Yee GC, Posey LM, et al. Pharmacotherapy: A Pathophysiologic Approach. 12ed. McGraw-Hill; 2023: chap 91. Accessed January 24, 2025. https://accesspharmacy.mhmedical.com

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Premixed Insulins

Insulin	PK Properties[a]	Administration	Initial Dose/Titration
NPH/regular 70/30	Onset: 30-60 min Duration: 10-16 hrs	Twice daily 30-45 min before breakfast and supper	Insulin naïve: 0.3 units/kg/day or 10 units/day in divided doses Converting from other insulin therapy: Current TDD in divided doses Titration: individualized
Lispro 50/50	Onset: 15-30 min Duration: 14-24 hrs	Twice daily 15 min before breakfast and supper	
Lispro 75/25	Onset: 5-15 min Duration: 10-16 hrs		
Aspart 70/30	Onset: 10-20 min Duration: 18-24 hrs	Twice daily 15 min before or after breakfast and supper	

[a]Premixed insulin has dual peaks; PK, pharmacokinetic; min, minutes; hrs, hours; TDD, total daily dose

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Trujiloo J, Haines S. Diabetes mellitis. In: DiPiro JT, Yee GC, Posey LM, et al. Pharmacotherapy: A Pathophysiologic Approach. 11ed. McGraw-Hill, 2021: chap 91. Accessed September 24, 2024. https://accesspharmacy.mhmedical.com; Insulin NPH and insulin regular. Lexi-Drugs. Waltham, MA: UpToDate, 2021. http://online.lexi.com/. Updated September 16, 2021. Accessed September 24, 2024.; Insulin lispro protamine and insulin lispro. Lexi-Drugs. Waltham, MA: UpToDate, 2021. http://online.lexi.com/. Updated September 16, 2021. Accessed September 24, 2024.; Insulin aspart protamine and insulin aspart. Lexi-Drugs. Waltham, MA: UpToDate, 2021. http://online.lexi.com/. Updated September 16, 2021. Accessed September 24, 2024.

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Premixed Insulin/GLP-1 RA Combinations

Insulin	PK Properties	Administration	Initial Dose/Titration
Glargine/lixisenatide Soliqua®	Refer to individual agents	Once daily within 60 min of breakfast	Insulin naïve or current basal insulin dose < 30 units: 15 units Current basal insulin dose ≥ 30 units: 30 units Titration: 2-4 units once weekly Max dose: 60 units
Degludec/liraglutide Xultophy®		Once daily with or without food	Insulin naïve or GLP-1 RA naive: 10 units Currently taking basal insulin or GLP-1 RA: 16 units Titration: increase 2 units twice weekly Max dose: 50 units

Trujiloo J, Haines S. Diabetes mellitis. In: DiPiro JT, Yee GC, Posey LM, et al. Pharmacotherapy: A Pathophysiologic Approach. 12ed. McGraw-Hill; 2023: chap 91. Accessed January 24, 2025. https://accesspharmacy.mhmedical.com; Insulin glargine and lixisenatide. Lexi-Drugs. Waltham, MA: UpToDate, 2023. http://online.lexi.com/. Updated September 16, 2021. Accessed January 24, 2025.; Insulin degludec and liraglutide. Lexi-Drugs. Waltham, MA: UpToDate, 2023. http://online.lexi.com/. Updated September 16, 2021. Accessed January 24, 2025.

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Diabetes: Clinical Pearls

- Patient-specific goals and therapy are CRITICAL
- ASCVD, HF, and renal
- Caution with sulfonylureas (hypoglycemia)
- Simplification and deprescribing are important!

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Hypothyroidism

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Risk Factors and Etiologies

- Age-related
- Females > Males
- Iodine deficiency (most common cause worldwide but not in U.S.)
- Autoimmune thyroiditis (most common cause in U.S.)
  - Hashimoto's thyroiditis or chronic autoimmune thyroiditis
    - More common in older adults
  - Autoimmune thyroid disease (AITDs)
  - More common in people with other autoimmune diseases such as T1D, Addison's Disease, Down's Syndrome, Turner's Syndrome, celiac disease, rheumatoid arthritis, lupus

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Symptoms

- Common in older adults
  - Fatigue, dyspnea, changes in taste/hearing or ataxia
- Less common in older adults
  - Cold intolerance, constipation, weight gain, paresthesia, muscle cramps
- Confounded by comorbidity
  - Bradycardia, diastolic hypertension, pallor, dry skin, coarse hair, hoarseness, voice changes, delayed tendon reflexes, depression and mental status changes
- **Thyroid should always be on differential for cognitive changes**

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Complications

- Depression
- Operative complications
- Myxedema coma
  - Endocrine emergency
    - Multisystem failure and possible coma
    - Mortality rate ~40%

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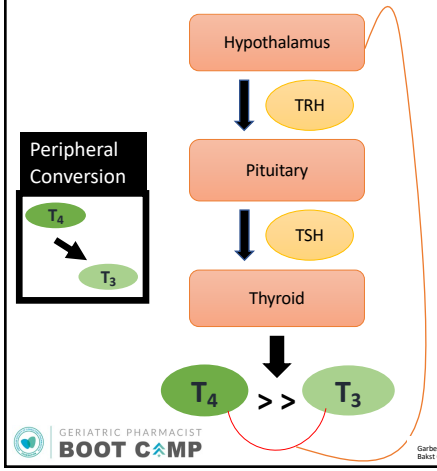
Thyroid Hormone Relationships

TRH, thyroid releasing hormone;
TSH, thyroid stimulating hormone



- Thyroid hormone secretion regulated by hypothalamus (TRH) and pituitary (TSH)
- Thyroid releases 100% of T_4, but only 20% of T_3
- T_4 is converted to active T_3 in peripheral tissues
- T_3 is primarily responsible for action
- T3 and T4 presence acts as a negative feedback loop to "turn off" production
- High plasma binding ($T_4 > T_3$) predicts half life and interactions

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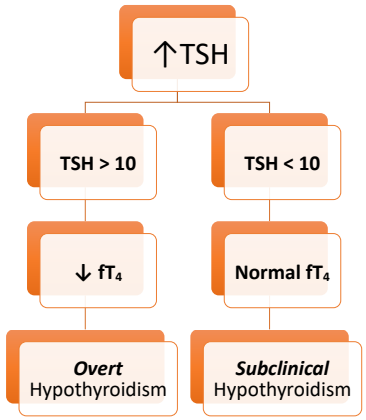
Hypothyroidism: Overt vs Subclinical



Normal Levels
TSH: 0.1 – 4 mIU/L
fT_4: 0.7 – 1.9 ng/dL

Subclinical Hypothyroidism

- Some patients will normalize without treatment
- May progress to overt
  - Increased risk if anti-thyroid peroxidase antibodies
- Sometimes symptomatic
- Treatment is provisional

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Medication Options

T_3

- Peaks 2-4 hrs
- T ½ < 1 day
- Higher risk of thyrotoxicosis

T_4

- Peaks 2-4 hrs
- T ½ ~ 7 days
- Requires conversion of T_4 to T_3
- Missed doses have less clinical impact

Agent	Equivalent Dosing	Pearls
Liothyronine (T_3)	25 mcg	• Rapid acting ($t_{1/2}$ ~1 day) • Multiple daily dosing • Peaks/troughs • Avoid in older adults
Desiccated *porcine* thyroid (T_3>T_4)	1 grain/60 mg	• Mixed $t_{1/2}$ • Inexpensive • Thyrotoxicosis risk • Avoid in older adults
Levothyroxine (T_4)	100 mcg	• Long acting ($t_{1/2}$ ~7 days) • Stable

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Drug Interactions

Other Considerations:

- Some AEDs and rifampin may increase clearance
- Amiodarone therapy and selenium deficiency may block peripheral conversion

Protein binding changes → metabolic activity	
↑ Protein or Binding (↓ free concentration/activity)	• Estrogen, estrogen agonist/antagonist, methadone, 5-FU • Liver disease, HIV
↓ Protein or Binding (↑ free concentration/activity)	• Corticosteroids, androgens, furosemide, salicylates, AEDs (i.e., phenytoin) • Acute illness

Absorption → administration, impaired absorption	
Conditions	Celiac disease, chronic diarrhea, GI bypass surgery
Interactions	Minerals, BAS, fiber supplements, acid suppression therapy, foods (empty stomach preferred)

T ½, half life; 5-FU, fluorouracil; AEDs, antiepileptic drug; BAS, bile acid sequestrants

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Hypothyroidism: Management

Overt:
Treat!
And treat to therapeutic TSH

Subclinical:
To treat or not to treat?
Symptom resolution?

- Typical adult requirement: Levothyroxine 50-100 mcg/day (0.8 mcg/lb)
- Reduce starting dose in older adults?
  - Levothyroxine 25-50 mcg/day
  - Titrate 12.5-25 mcg every 4-6 weeks
- Alternative regimens
  - Once to twice weekly
- Reassess TSH in 4-6 weeks after initiation or dose adjustments

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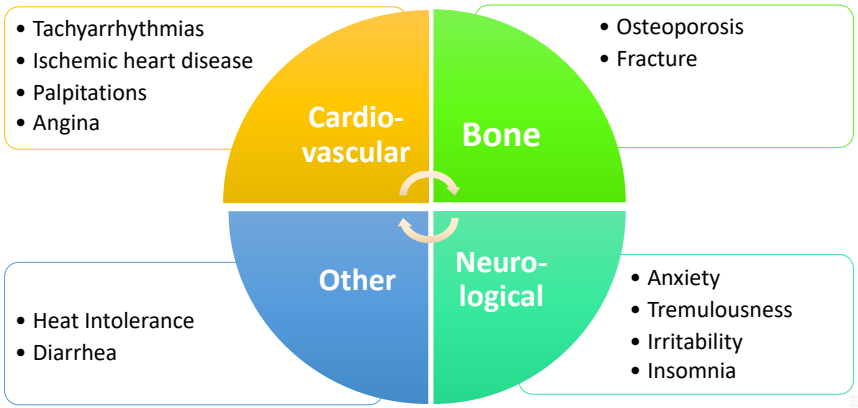
Risks of Over-Treatment



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Self-Assessment Case: Louise

- 71-year-old female
- Complains of fatigue, depressed mood and tiring easily
- TSH: 5.1
- fT4: 1.5

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Self-Assessment Question #3

Which of the following interventions is most appropriate for this patient?

A. Levothyroxine 50 mcg once daily for overt hypothyroidism
B. Desiccated thyroid 60 mg daily for subclinical hypothyroidism
C. Levothyroxine 25 mcg once daily for subclinical hypothyroidism
D. Liothyronine 5 mcg twice daily for overt hypothyroidism

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Hypothyroidism: Clinical Pearls

- Keep your radar up!
- Patient-specific decision to treat subclinical symptoms
- Levothyroxine preferred!
- MULTIPLE drug-drug and drug-disease interactions
- Monitor signs/symptoms of hypothyroidism and over-treatment

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Osteoporosis

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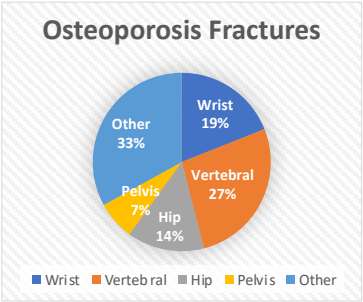
Osteoporosis Importance

- Preventable and treatable!
- Underdiagnosed and undertreated
- 35% women ≥ 80 years of age
  - White/Hispanic > Native American > African American > Asian
- 11% men ≥ 80 years of age
- Fragility wrist and vertebral fractures throughout adulthood
- Hip fractures more common in older adults



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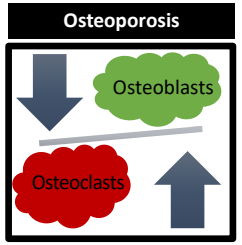
Bone Remodeling

- "Outer shell" cortical bone is more common (80% of bone)
  - Long bones (e.g., forearm and hip)
- "Spongy" trabecular bone is most susceptible
  - Vertebrae and ends of long bones
- Bone formation
  - Osteoblasts
- Bone resorption
  - Osteoclasts, low serum Ca, low vitamin D
  - RANKL = Receptor activator of nuclear factor kappa-B ligand = responsible for osteoclast development, activation, lifespan



- **Osteoblasts**—bone forming cells
- **Osteoclasts**—bone resorbing cells
- **Osteocytes**—bone communication cells

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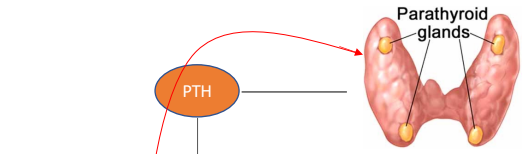
Regulation of Remodeling

Bone Remodeling mediated by:
1. Serum Ca
2. Vitamin D



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Osteoporosis and Fracture Risk Factor

Previously Discussed
- Female
- **Age**
- Race

Lifestyle
- Prior osteoporotic fractures
- Current Smoking
- Excess alcohol (≥ 2-3 per day)
- History of falls
- Low calcium/vitamin D intake
- Immobilization/low physical activity
- Low body weight
- Family history

Conditions
- Menopause (premature)
- Malabsorption disorders
- Hyperparathyroidism
- RA and Lupus or other autoimmune conditions
- Fall risk conditions
- Cognitive impairment
- Height loss of 1.5" or more
- **Low bone mineral density (BMD)**

RA, rheumatoid arthritis

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Risk Factors: Medications

- Aluminum-containing antacids
- Anti-androgen therapy
- Anticoagulants
- Anticonvulsants
- Aromatase inhibitors
- Barbiturates
- Canagliflozin
- Chemotherapy
- Cyclosporine, tacrolimus
- Depo-medroxyprogesterone
- Glucocorticoids ***5mg+ prednisone equivalent for 3+ months**
- Gonadotropin-releasing hormone (GnRH) agonists/antagonists
- Loop diuretics
- Methotrexate
- Nucleoside Reverse Transcriptase Inhibitors (NRTIs)
- Proton Pump Inhibitors (PPI)
- Selective serotonin reuptake inhibitors (SSRIs)
- Tacrolimus
- Thiazolidinediones (TZDs)
- Excessive thyroid therapy

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Screening & Assessment

- Who to screen?
  - All women by age 65
  - All men over age 70
  - All post-menopausal (PM) women ≥ 50 years
  - Men and women age ≥ 50 years with risk factors
  - Perimenopausal with increased risk of bone loss/fracture
- Central DXA X-ray gold standard
  - Peripheral devices used for screening only
  - Lumbar spine and hip (femoral neck, total hip)
  - Reported as standard deviations (SD) from either:
    - Matched population: Z-score
    - "Normal", young population: T-score
    - Each SD = 10% ↓ bone mass, 1.5-2.5 x ↑ fracture risk

PM, post-menopausal; DXA = dual-energy x-ray absorptiometry

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Risk Prediction: FRAX®

Used to predict fracture risk:
1. Limited DXA access
2. Determine DXA need
3. Treatment naive

Country: US (Caucasian) Name/ID:

Questionnaire:

1. Age (between 40 and 90 years) or Date of Birth
   Age: 60 Date of Birth: Y: M: D:
2. Sex: Male / Female
3. Weight (kg): 75
4. Height (cm): 160
5. Previous Fracture: No / Yes
6. Parent Fractured Hip: No / Yes
7. Current Smoking: No / Yes
8. Glucocorticoids: No / Yes
9. Rheumatoid arthritis: No / Yes
10. Secondary osteoporosis: No / Yes
11. Alcohol 3 or more units/day: No / Yes
12. Femoral neck BMD (g/cm^2)

Select BMD | Clear | Calculate

BMI: 29.3
The ten year probability of fracture (%)
without BMD

Major osteoporotic	6.8
Hip Fracture	0.5

Underestimates future fracture risk

FRAX® = Fracture Risk Assessment Tool

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Centre for Metabolic Bone Diseases. Calculation Tool. FRAX Fracture Risk Assessment Tool Website. https://www.sheffield.ac.uk/FRAX/tool.aspx?country=9. Accessed 1/24/2025.

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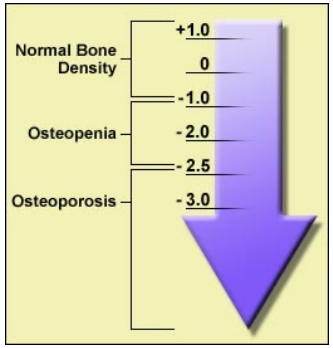
Diagnostic Criteria

- **Osteopenia (low bone mass)**
  - T-score: -1 to -2.4
- **Osteoporosis**
  - T-score: -2.5 or less (lumbar spine, femoral neck, or total hip)
  - Severe or established: ≤ -2.5 with one or more fractures



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Who Should Receive Treatment?

- T-score ≤-2.5 (lumbar spine, femoral neck, or total hip)
- T-score -1 to -2.5 + previous hip or spine fracture
- T-score -1 to -2.5 with a FRAX®:
  - 10-year hip fracture risk of ≥ 3%
  - 10-year major osteoporotic fracture of ≥ 20%
- Consider treatment for low-trauma or fragility fractures

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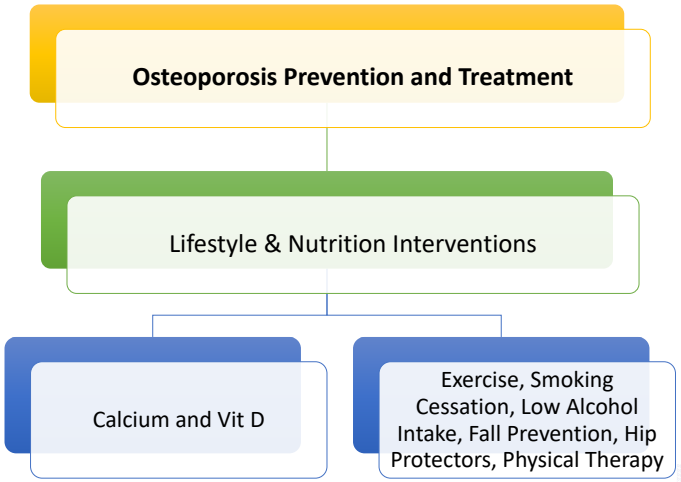
Treatment Algorithm



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Calcium Supplementation

Carbonate (40% elemental), Citrate (21% elemental), Gluconate (9% elemental)

Effect	Increase BMD (mostly with vitamin D)
Dosing & Formulations	Women 19-50 years old, men 19-70 years old: 1,000 mg/day Women ≥ 51 years old, men ≥ 71 years old: 1,200 mg/day < 600 elemental per dose (500 – 600 mg twice daily)
Considerations	↑ elemental Ca = ↑ Constipation Kidney stones Dietary sources preferred QS dietary intake (average 600 mg/day) OP patients are high bone risk—Ca benefit outweighs CV risk

QS, quantum satis; OP, osteoporosis

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Camacho PM, Petak SM, Binkley N, et al. American Association of Clinical Endocrinologists and American College of Endocrinology Clinical Practice Guidelines for the Diagnosis and Treatment of Postmenopausal Osteoporosis. Endocr Pract. 2020;26(S1):1-46.

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Calcium Supplements

- Calcium carbonate
  - Acid dependent—must take with food
    - Not good if taking PPI/H2-blocker
  - More GI upset—constipation
  - Least expensive and smallest number of tablets
- Calcium citrate
  - Acid independent—with or without food
    - Good if taking PPI/H2-blocker
    - Good for older adults (decreased acid production)
  - Less GI upset
  - More expensive and higher pill burden (larger pill and increased quantity)

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Camacho PM, Petak SM, Binkley N, et al. American Association of Clinical Endocrinologists and American College of Endocrinology Clinical Practice Guidelines for the Diagnosis and Treatment of Postmenopausal Osteoporosis. Endocr Pract. 2020;26(S1):1-46.

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Notes on Supplementation…

Women's 50+ Healthy Advantage

Directions: Adults: One tablet daily, with food.

Supplement Facts
Serving Size: One tablet

	Amount Per Serving	% Daily Value
Vitamin A (20% as beta-carotene)	3500 IU	70%
Vitamin C	120 mg	200%
Vitamin D (as Vitamin D_3)	1000 IU	250%
Vitamin E	30 IU	100%
Vitamin K	20 mcg	25%
Thiamin (B_1)	4.5 mg	300%
Riboflavin (B_2)	3.4 mg	200%
Niacin	20 mg	100%
Vitamin B_6	6 mg	300%
Folic Acid	400 mcg	100%
Vitamin B_{12}	25 mcg	417%
Biotin	30 mcg	10%
Pantothenic Acid	15 mg	150%
Calcium (elemental)	300 mg	30%

DIRECTIONS: For adults, take two (2) softgels daily, preferably with a meal.

Supplement Facts
Serving size 2 Softgels
Servings Per Container 110

Amount Per Serving		% Daily Value
Calories	15	
Total Fat	1 g	1%***
Vitamin D (as D3 Cholecalciferol)	25 mcg (1,000 IU)	125%
Calcium (as Calcium Carbonate)	1,200 mg (1.2 g)	92%

***Percent Daily Values are based on a 2,000 calorie diet.

200 mg elemental calcium

Drug Facts

Active ingredient (in each tablet)	Purpose
Calcium carbonate USP 500mg	Antacid

Uses relieves
- heartburn
- sour stomach
- acid indigestion
- upset stomach associated with these symptoms

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Vitamin D

25(OH)-Vitamin D Assessment
Deficient: < 20 ng/mL
Insufficient: < 30 ng/mL
No level? Supplement

Vitamin D: Cholecalciferol (D_3) , Ergocalciferol (D_2)

Effect	Enhance calcium absorption Helps osteoporosis drugs work better
Considerations	Correct deficiencies and insufficiencies Maintain sufficiency Obesity, malabsorption, AEDs, darker skin tones may require higher doses Long-term doses > 4,000 IU can lead to Vit D toxicity

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Vitamin D Supplements

- Cholecalciferol (D3)
  - Preferred—derived by animal (same as produced in humans)
- Ergocalciferol (D2)
  - Produced from plants—good if following vegan or vegetarian diet

Dosing	
Vitamin D level ≥ 30 mg/dL	Vitamin D3 800-1000 (20-25 mcg) International Units (IU) PO daily
Vitamin D level ≤ 29 mg/dL	First 8-12 weeks • Vitamin D2 50,000 IU (1,250 mcg) PO weekly **Or** • Vitamin D3 5,000 IU (12-175 mcg) PO daily Maintenance • Vitamin D3 1,000-2,000 IU (25-50 mcg) PO daily

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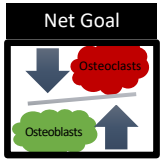
Drug Therapy

- **Osteoblasts**—bone forming cells
- **Osteoclasts**—bone resorbing cells
- **Osteocytes**—bone communication cells
- **RANKL**—activates receptor responsible for osteoclast development, activation, lifespan



Antiresorptive

- Either promote osteoclast apoptosis or decrease osteoclast activity
- Bisphosphonates
- Receptor Activator of Nuclear Factor Kappa-β Ligand (RANKL) inhibitors
- Estrogen and estrogen agonist/antagonist
- Calcitonin

Anabolic

- Activates osteoblasts or increases osteoblast activity
- Parathyroid Hormone (PTH) analogs
- Sclerostin inhibitor

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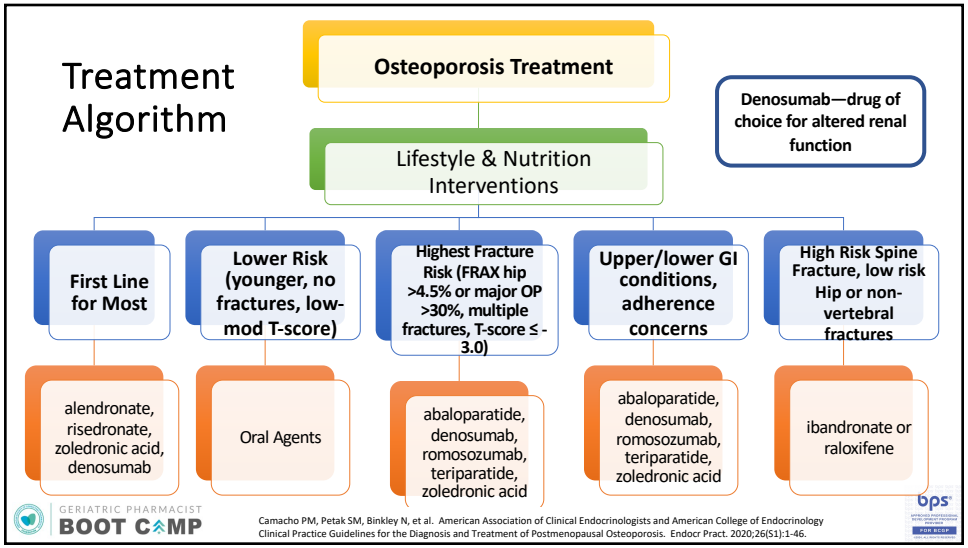

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But First…

- Treatment goal
  - Success = stable or increasing BMD + no NEW fractures
    - Stable BMD = not worsened by more than ~4% in spine or ~6% in hip
  - Prevent falls
  - 1 fracture DOES NOT = therapy failure
    - Suggest fracture risk is high
    - May change treatment selection and/or duration
- Recheck BMD every 1-2 years after starting therapy and then every 2 years

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Bisphosphonates—Dosing

Drug	Prevention	Treatment
Alendronate (Fosamax®, generic)	5 mg PO daily 35 mg PO weekly	10 mg PO daily 70 mg PO weekly (tablet and liquid) 70 mg + D weekly (70 mg alendronate/2,800 IU or 5,600 IU Vit D)
Ibandronate (Boniva®, generic)	2.5 mg PO daily 150 mg PO monthly	2.5 mg PO daily 150 mg PO monthly 3 mg IV every 3 months
Risedronate (Actonel®, Atelvia®, generic)	5 mg PO daily 35 mg PO weekly 150 mg PO monthly	5 mg PO daily 35 mg PO weekly 150 mg PO monthly
Zoledronic acid (Reclast®, generic)	5 mg IV every 2nd year	5 mg IV once yearly

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Camacho PM, Petak SM, Binkley N, et al. American Association of Clinical Endocrinologists and American College of Endocrinology Clinical Practice Guidelines for the Diagnosis and Treatment of Postmenopausal Osteoporosis. Endocr Pract. 2020;26(S1):1-46. O'Connell MB, Borchert JS. Osteoporosis and Osteomalacia. In: Dipiro JT, Yee GC, Posey LM, et al eds. Pharmacotherapy: A Pathophysiologic Approach. 12th ed. New York, NY: McGraw-Hill; 2023.

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Bisphosphonates: alendronate, risedronate, ibandronate, zoledronic acid (ZA)

Indications	Post-menopausal prevention/treatment: ALL Steroid-induced prevention: risedronate, ZA Steroid-induced treatment: alendronate, risedronate, ZA Treatment of men: alendronate, risedronate, ZA
Effect	Alendronate, ZA, and risedronate: FRR for vertebral, nonvertebral, and hip Ibandronate: FRR for vertebral fracture only Fracture data available for PO daily and annual IV only Fractures reduced by 6-12 months, plateau 2-5 years FRR, fracture risk reduction
Dosing & Formulations	Caution in renal impairment, at risk of dehydration, on diuretics or nephrotoxic drugs Not recommended if eGFR/CrCl < 35 mL/min (alendronate, zoledronic acid) or eGFR/CrCl < 30 (ibandronate, risedronate)
Considerations	Administration instructions (empty stomach, water, upright position, no other drugs) Calcium and Vit D must be WNL before initiation ZA and acute phase reaction (fever, flu-like) **Oral formulations: caution if esophageal disease (e.g., strictures) or abnormalities (anatomic or functional), GI malabsorption (e.g., celiac, Crohn's, gastric bypass), inability to remain upright** Difficulty swallowing—effervescent tablet, solution or IV agent Oral tablets must be swallowed whole with 6-8 ounces of water

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Camacho PM, Petak SM, Binkley N, et al. American Association of Clinical Endocrinologists and American College of Endocrinology Clinical Practice Guidelines for the Diagnosis and Treatment of Postmenopausal Osteoporosis. Endocr Pract. 2020;26(S1):1-46. O'Connell MB, Borchert JS. Osteoporosis and Osteomalacia. In: Dipiro JT, Yee GC, Posey LM, et al eds. Pharmacotherapy: A Pathophysiologic Approach. 12th ed. New York, NY: McGraw-Hill; 2023.

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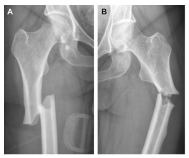
Bisphosphonate "Risks"



http://www.jrheum.org/content/38/12/2686

- Bone, joint, muscle pain
  - Resolves upon discontinuation
- Osteonecrosis of the jaw (ONJ)
  - Rare (1:100K)
  - Cancer, higher dose IV, concomitant glucocorticoid therapy, mandibular bone surgery, poor oral hygiene
- Atypical subtrochanteric (femur) fracture
  - Rare
  - Longer duration use increases risk
  - 1.78 per 100K at 2 years vs. 100 per 100K at 8 years

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Continuum of Bisphosphonates

Moderate Risk: Holiday after 3 years (ZA) or 5 years (oral agents)
Higher Risk: Continue for 6 years (ZA) or 10 years (oral agents)

	Initial Therapy	
3-5 Year Evaluation	**Higher** *(hip **T score ≤ -2.5**, prior fracture, ↑ FRAX, new fx, ↑ fall risk)*	**Moderate Risk**
Duration	3-5 More Years	Start Holiday
2-3 Year Holiday	Consider Alternate Therapy (anabolic agent, raloxifene)	No Therapy During Holiday
	End holiday if fracture, significant BMD loss	

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RANK-Ligand Inhibitor

RANK-L inhibitor: Denosumab (Prolia®, Xgeva®)

Indications	Treatment of postmenopausal women Treatment in men Steroid-induced osteoporosis
Effect	FRR for vertebral, nonvertebral, and hip
Dosing & Formulations	60 mg SQ in upper arm, thigh, abdomen every 6 months by a healthcare provider **No drug holiday recommended**—rapid bone loss if discontinued
Considerations	Must correct Ca and Vit D before initiation **Drug of choice in renal impairment** **Boxed warning for severe hypocalcemia if on dialysis** Topical reactions Possible risk for ONJ or atypical femur fracture

ONJ = Osteonecrosis of the jaw; FRR = fracture risk reduction

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Camacho PM, Petak SM, Binkley N, et al. American Association of Clinical Endocrinologists and American College of Endocrinology Clinical Practice Guidelines for the Diagnosis and Treatment of Postmenopausal Osteoporosis. Endocr Pract. 2020;26(S1):1-46.

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PTH-Analogs

Camacho PM, Petak SM, Binkley N, et al. American Association of Clinical Endocrinologists and American College of Endocrinology Clinical Practice Guidelines for the Diagnosis and Treatment of Postmenopausal Osteoporosis. Endocr Pract. 2020;26(S1):1-46.

PTH Analogs: Abaloparatide (Tymlos®), Teriparatide (Forteo®, generic)

Indications	Treatment of postmenopausal women Teriparitide: Treatment of men, steroid-induced
Effect	Fracture Risk Reduction for vertebral and nonvertebral only
Dosing & Formulations	Teriparitide: 20 mcg SQ to abdomen daily, monitor first dose Abaloparatide: 80 mcg SQ daily
Considerations	Use should be immediately followed by anti-resorptive therapy (bisphosphonate, denosumab) due to rapid bone loss If follow anti-resorptive therapy—lower BMD increases than if prior to therapy Must correct Ca and Vit D before initiation Nausea, orthostatic hypotension, leg cramps, hypercalcemia Falsely elevated Ca levels—must check 16 hours after administration Teriparatide can be used beyond 2 years of therapy Boxed Warning: osteosarcoma—avoid if prior radiation to bone or bone metastasis Contraindicated in patients with hyperparathyroidism COST!

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Sclerostin Inhibitor

Sclerostin Inhibitor: Romosozumab (Evenity®)

Indications	Treatment of postmenopausal women at high risk for fracture
Effect	Fracture Risk Reduction for vertebral, nonvertebral, and hip
Dosing & Formulations	210 mg once monthly (two consecutive 105 mg injections) in the upper arm, thigh, or abdomen by a healthcare professional **12 month duration—no additional benefit**
Considerations	• Considered a "rescue drug" for very high fracture risk • Must be followed by anti-resorptive therapy (bisphosphonate, denosumab) due to rapid bone loss after discontinuation • Can follow bisphosphonate therapy • Must correct hypocalcemia prior to use, supplement Ca and Vit D • **Boxed Warning—increased risk of MI, stroke, and CV death** • If dose missed, administer ASAP, subsequent dose 1 month later • Useful in renal dysfunction, no dose adjustment with eGFR < 30 mL/min/1.73 m^2 • Possible risk for Osteonecrosis of jaw or atypical fracture

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Camacho PM, Petak SM, Binkley N, et al. American Association of Clinical Endocrinologists and American College of Endocrinology Clinical Practice Guidelines for the Diagnosis and Treatment of Postmenopausal Osteoporosis. Endocr Pract. 2020;26(S1):1-46.

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The WHY: Medication Impact

Medication	↓Vertebral Fracture (%)	↓Non-vertebral Fracture (%)	↓Hip Fracture (%)	↑Spine BMD (%)	↑Hip BMD (%)
Calcitonin	33	---	---	0.7	---
Raloxifene	30-42	---	---	2.6	2.1
Bazedoxifene +/- estrogens	42	---	---	2.2	0.5
Estrogens	33-40	13-27	34	3.5-7	1.7-4.1
Bisphosphonates	41-70	25-39	40-51	4.3-6.7	2.8-6
Denosumab	68	20	40	9.2	6
Teriparitide	65	53	---	8.6	3.5
Abaloparatide	14*	57	---	11.2	4.18
Romosozumab	73	19	38	18	4

*Lower vertebral fracture risk population compared to previous studies

Fracture Site	Alendronate	Ibandronate	Risedronate	Zoledronic Acid
Vertebral	Yes	Yes	Yes	Yes
Non-Vertebral	Yes	No	Yes	Yes
Hip	Yes	No	Yes	Yes

Joseph T. DiPiro, Robert L. Talbert, Gary C. Yee, Gary R. Matzke, Barbara G. Wells, L. Michael Posey• Table 73-5 Fracture and Bone Mineral Density Effects of Osteoporosis Medications from Pivotal Fracture Trials in Postmenopausal Women. Camacho PM, Petak SM, Binkley N, et al. American Association of Clinical Endocrinologists and American College of Endocrinology Clinical Practice Guidelines for the Diagnosis and Treatment of Postmenopausal Osteoporosis. Endocr Pract. 2020;26(S1):1-46.

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What Isn't Used and Why?

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Calcitonin

Calcitonin	
Indications	Treatment in women > 5 years past menopause
Effect	Fracture Risk Reduction (FRR) for vertebral only
Dosing & Formulations	200 IU (1 spray) intranasally daily (alternate) 100 IU SQ/IM daily SQ/IM formulations do not have data for osteoporosis
Considerations	Derived from salmon—contraindicated if fish allergy Hypersensitivity—skin testing prior to initiation Nausea Sweating, facial flushing Increased cancer risk—banned in Canada and Europe

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Estrogens

Estrogens	
Indications	Prevention in post menopausal women Estrogen only—women with a history of hysterectomy Estrogen and progestin—women with intact uterus
Effect	FRR for vertebral, nonvertebral, and hip Best effect with early replacement
Dosing & Formulations	Numerous products include tablets and transdermal patches
Considerations	↓ Colon cancer risk **↑ Fatal and nonfatal MI , stroke, VTE, breast cancer**

FRR,fracture risk reduction

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Camacho PM, Petak SM, Binkley N, et al. American Association of Clinical Endocrinologists and American College of Endocrinology Clinical Practice Guidelines for the Diagnosis and Treatment of Postmenopausal Osteoporosis. Endocr Pract. 2020;26(S1):1-46. O'Connell MB, Borchert JS. Osteoporosis and Osteomalacia. In: Dipiro JT, Yee GC, Posey LM, et al eds. Pharmacotherapy: A Pathophysiologic Approach. 12th ed. New York, NY: McGraw-Hill; 2023.

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Estrogen Agonists/Antagonists (selective estrogen receptor modulators (SERMS))

Raloxifene (Evista®, generic)	
Indications	Post menopausal prevention; treatment
Effect	Fracture Risk Reduction (FRR) for vertebral only
Dosing & Formulations	Raloxifene 60 mg daily
Considerations	**↓ breast cancer** Cardiovascular: **↑ VTE (avoid if other risk factors such as obesity, smoking, hx of VTE)** Leg cramps Hot flashes and menopausal symptoms—due to estrogen antagonist properties

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Camacho PM, Petak SM, Binkley N, et al. American Association of Clinical Endocrinologists and American College of Endocrinology Clinical Practice Guidelines for the Diagnosis and Treatment of Postmenopausal Osteoporosis. Endocr Pract. 2020;26(S1):1-46.

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Tissue-Selective Estrogen Complex

bazedoxifene +/- conjugated estrogens (Duavee®)	
Indications	Post menopausal prevention in women who have not had a hysterectomy
Effect	FRR for vertebral only
Dosing & Formulations	Duavee® 1 tablet PO daily
Considerations	Cardiovascular: ↑ **VTE** **Stroke risk in women 70+: not recommended** Increased risk of endometrial cancer Potential risk for dementia Do not combine with other estrogen products

FRR, fracture risk reduction

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When to Stop Treating?

- When to consider:
  - Prognosis & limited life expectancy
  - Goals of care change
  - Immobility/low fall or fracture risk
  - Administration concerns
- All can be stopped without taper

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Osteoporosis: Clinical Pearls

- Modify risk factors EARLY
- Importance of patient-specific factors in determining the best treatment and duration
- Dietary calcium > supplement
- Vitamin D importance
- Concomitant therapy is not recommended (exception: raloxifene and breast cancer reduction)
- Upon discontinuation of an anabolic agent, therapy with an anti-resorptive agent is recommended
- Switching from bisphosphonate to an anabolic agent can be done
- Switching from denosumab to an anabolic agent is NOT recommended due to attenuation of effect or bone loss

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dc, discontinuation

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Self-Assessment Case: Louise

- 71-year-old female
- PMH of osteopenia, HTN, dyslipidemia, kidney disease, and COPD
- Currently taking calcium and vit D
- DXA: t-score -2.5
- FRAX hip 3.5%; major OP 22%
- SCr 1.2 mg/dL
- eGFR 34 mL/min

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Self-Assessment Question #4

Which of the following is best to manage her bone condition?

A. Ibandronate (Boniva®) for 5 years
B. Zoledronic acid (Reclast®) for 6 years
C. Teriparatide (Forteo®) for 2 years
D. Denosumab (Prolia®) continuously

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