Diabetes Management

Biguanide: Metformin	
Mechanism	Decrease gluconeogenesis and increase insulin sensitivity
Effect	A1C: 1.5-2% Fasting > Prandial
Dosing	Titration for gastrointestinal adverse effects Renal Dosing: CrCl <45 mL/min → don't start or reduce dose, CrCl <30 mL/min-avoid!
Considerations in Older Adults	• Low hypoglycemia risk • GI and weight loss • To reduce GI side effects (N/D): take with food, slow dose titration, ER formulation • B12 deficiency/insufficiency
Sulfonylureas: Glyburide, glipizide, glimepiride	
Mechanism	Increase beta-cell secretion (diabetes duration-burnt out?)
Effect	A1C: 1.5% Fasting > Prandial
Dosing	Renal Dosing: Risk for accumulation greatest for glyburide
Considerations in Older Adults	• Hypoglycemia, hypoglycemia, hypoglycemia • Weight gain • Glyburide and glimepiride have longer half-life, increased hypoglycemia • Glipizide is preferred
Thiazolidinediones: Piolgitazone, ~~rosiglitazone~~	
Mechanism	Enhance insulin sensitivity > decrease gluconeogenesis
Effect	A1C: 0.5-1.5% Prandial > Fasting
Dosing	Once daily Delayed onset (targets nuclear receptor)
Considerations in Older Adults	• Avoid in CHF or high risk • Contraindicated in Class III-IV HF • Avoid if history of bladder cancer • Weight gain • Fracture risk • Fluid retention • Benefits in NASH/NAFLD • Some benefit secondary stroke prevention
SGLT 2 Inhibitors: Canagliflozin, dapagliflozin, empagliflozin, ertugliflozin, bexagliflozin	
Mechanism	Prevents reabsorption of 90% filtered glucose from urine
Effect	A1C: 0.5-1% Fasting

Dosing	Once daily

Considerations in Older Adults	• ASCVD benefit: empagliflozin, canagliflozin, dapagliflozin
	• CHF benedfit: dapagliflozin, empagliflozin, canagliflozin, ertugliflozin, bexagliflozin
	• CKD benefit: canagliflozin, empagliflozin, dapagliflozin
	• Weight loss
	• BP reductions (4/2 mmHg)
	• 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
	• Beers Criteria
	  • Increased risk of urogenital infections
	  • Higher risk of euglycemic diabetic ketoacidosis
	• Incontinence
	• Risk of Fournier's gangrene (rare)
	• Possible increased fracture risk: canagliflozin

DPP-IV Inhibitors: Alogliptin, linagliptin, sitalgiptin, saxagliptin	
Mechanism	Prevents degredation of endogenous "inceretins" GLP-1 and GIP: increase glucose-mediated insulin secretion, decrease glucagon
Effect	A1C: 0.5-1% Prandial > Fasting
Dosing	Once daily Renal dose adjustments, no renal dose adjustment for linagliptin
Considerations in Older Adults	• Pancreatitis • Weight neutral • Low hypoglycemia risk • Joint pain • Saxagliptin: increased CHF hospitalization risk
GLP-1 Agonists: Dulaglutide, exenatide, liraglutide, lixisenatide, semaglutide	
Mechanism	Provides exogenous source of GLP-1: increase glucose-mediated insulin secretion, decrease glucagon
Effect	A1C: 0.5-1.5% Prandial > Fasting
Dosing	Injectable Semaglutide: injectable and oral Exenatide: not recommended eGFR < 30 Lixisenatide: caution when eGFR < 30

Considerations in Older Adults	• Weight loss
	• ASCVD benefit: liraglutide, semaglutide (inj), dulaglutide
	• Renal benefit: liraglutide, semaglutide
	• Low hypoglycemia risk
	• 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

GIP and GLP-1 Agonists: tirzepatide	
Mechanism	Glucose-dependent insulinotropic polypeptide (GIP) receptor and glucagon-like peptide-1 (GLP-1) receptor agonist that increases glucose-dependent insulin section, decreases inappropriate glucagon section, and slows gastric emptying
Effect	A1C: 1.5 – 2.3%
Dosing	Initial: 2.5 mg once weekly for 4 weeks then increase to 5 mg once weekly May increase dose in 2.5 mg/week increments every 4 weeks Max dose: 15mg/week

Considerations in Older Adults	• Weight loss
	• Low hypoglycemic risk
	• ASCVD benefit: Under investigation
	• Renal benefit: Under investigation
	• 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
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	• Potential for ileus (semaglutide)
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	  • Close monitoring if older adult and/or diabetes ≥ 10 years
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Agent	Equivalent Dosing	Pearls
Liothyronine (T_3)	25 mcg	Rapid acting ($t_{1/2}$ ~1 day); multiple daily dosing; peaks/troughs
Dessicated *porcine* thyroid (T_3>T_4)	1 grain/60 mg	Mixed $t_{1/2}$; inexpensive; thyrotoxicosis risk
Levothyroxine (T_4)	100 mcg	Long acting ($t_{1/2}$ ~7 days), stable

Osteoporosis Management

Calcium: 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) Calcium citrate preferred in lower pH (older adults, PPI therapy)
Considerations	↑ elemental Ca = ↑Constipation Kidney stones Dietary sources preferred, QS dietary intake
Vitamin D: Cholecalciferol (D3), Ergocalciferol (D2)	
Effect	Enhance calcium absorption Fracture & fall prevention
Dosing & Formulations	Vitamin D level ≥ 30 mg/dL: Vitamin D3 800-1000 (20-25 mcg) International Units (IU) PO daily Vitamin D level ≤ 29 mg/dL: <u>First 8-12 weeks</u> • Vitamin D2 50,000 IU (1,250 mcg) PO weekly **Or** • Vitamin D3 5,000 IU (12-175 mcg) PO daily <u>Maintenance</u> • Vitamin D3 1,000-2,000 IU (25-50 mcg) PO daily
Considerations	Ergocalciferol (D3)—derived from animal Ergocalciferol (D2)—derived from plants Correct deficiencies and insufficiencies Maintain sufficiency Obesity, malabsorption, AEDs, and darker skin tones may require higher doses
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
Dosing & Formulations	Caution in renal impairment, at risk of dehydration, on diuretics or nephrotoxic drugs NR if CrCl < 35 mL/min
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, GI malabsorption (e.g., celiac, Crohn's, gastric bypass)** Difficulty swallowing—effervescent tablet, solution or IV agent Rare risk of ONJ and atypical femur fracture
RANK-L inhibitor: Denosumab	
Indications	Treatment of postmenopausal women Treatment in men
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**
Considerations	**Boxed warning for severe hypocalcemia if on dialysis** **Drug of choice in renal dysfunction** Topical reactions Possible risk for ONJ or atypical femur fracture
PTH Analogs: Abaloparatide, Teriparatide	
Indications	Treatment of postmenopausal women Teriparatide: Treatment of men, steroid-induced
Effect	FRR for vertebral and nonvertebral only
Dosing & Formulations	Teriparatide 20 mcg : daily SQ injection to abdomen, monitor first dose Abaloparatide 80 mcg: daily SQ injection
Considerations	Anabolic agents Use should be followed by anti-resorptive (bisphosphonate, denosumab) Use should not follow anti-resorptive therapy—lower BMD increases Must correct Ca and Vit D before initiation Nausea, orthostatic hypotension, leg cramps, hypercalcemia Teriparatide can be used for longer than 2 year duration Black Box: osteosarcoma—avoid if prior radiation to bone or bone metastasis Falsely elevated Ca levels—must check 16 hours after administration Expensive
Sclerostin Inhibitor: Romosozumab	
Indications	Treatment of postmenopausal women at high risk for fracture
Effect	FRR 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**
Considerations	Anabolic effects Considered a "rescue drug" for very high fracture risk Use can be followed by anti-resorptive therapy (bisphosphonate, denosumab) or can follow bisphosphonate therapy Must correct hypocalcemia prior to use, supplement Ca and Vit D **BBW—increased risk of MI, stroke, and CV death** If dose missed, administer ASAP, subsequent dose 1 month later Useful in renal dysfunction Possible risk for ONJ or atypical fracture
Raloxifene, bazedoxifene +/- conjugated estrogens—Not Recommended	
Indications	Post menopausal prevention; treatment (raloxifene only)
Effect	FRR for vertebral only
Dosing & Formulations	Raloxifene 60 mg daily
Considerations	**Raloxifene: ↓ breast cancer** Cardiovascular: No effect on CV outcomes **↑ VTE** **Stroke risk in women 70+: not recommended** Hot flashes & leg cramps
Calcitonin—Not Recommended	
Indications	Treatment in women >5 years past menopause
Effect	FRR for vertebral only
Dosing & Formulations	200 units (1 spray) intranasally daily (alternate) 100 units SQ daily
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
Estrogens—Not Recommended	
Indications	Prevention in post menopausal women (USPSTF recommends against preventative use)
Effect	Dose-dependent increased in spine, hip, and total body Best effect with early replacement

Dosing & Formulations	Esterified estrogens: 0.3 mg/d Conjugated equine: 0.625 mg/d Ethinyl estradiol: 5 mcg/d Transdermal: 50 mcg/d
Considerations	↓colon cancer risk **↑fatal and nonfatal MI , stroke, VTE, breast cancer**