Drugs that effect Bone mineral Haemostasis

Sources:

- **Bertram G. katzung Basic & Clinical Pharmacology 15th Edition**
- **Goodman and Gilman's The Pharmacological Basis of Therapeutics 13th edition.**

Sequence Of Lecture

Core Subject

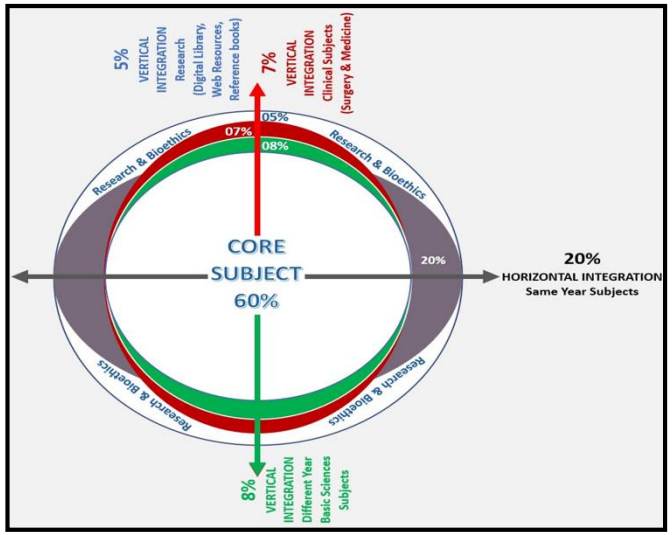
Spiral Integration

Horizontal Integration

Vertical integration

EOLA(End of lecture assessment)

Digital Library References



(Research, Bioethics, Artificial Intelligence, Family Medicine)

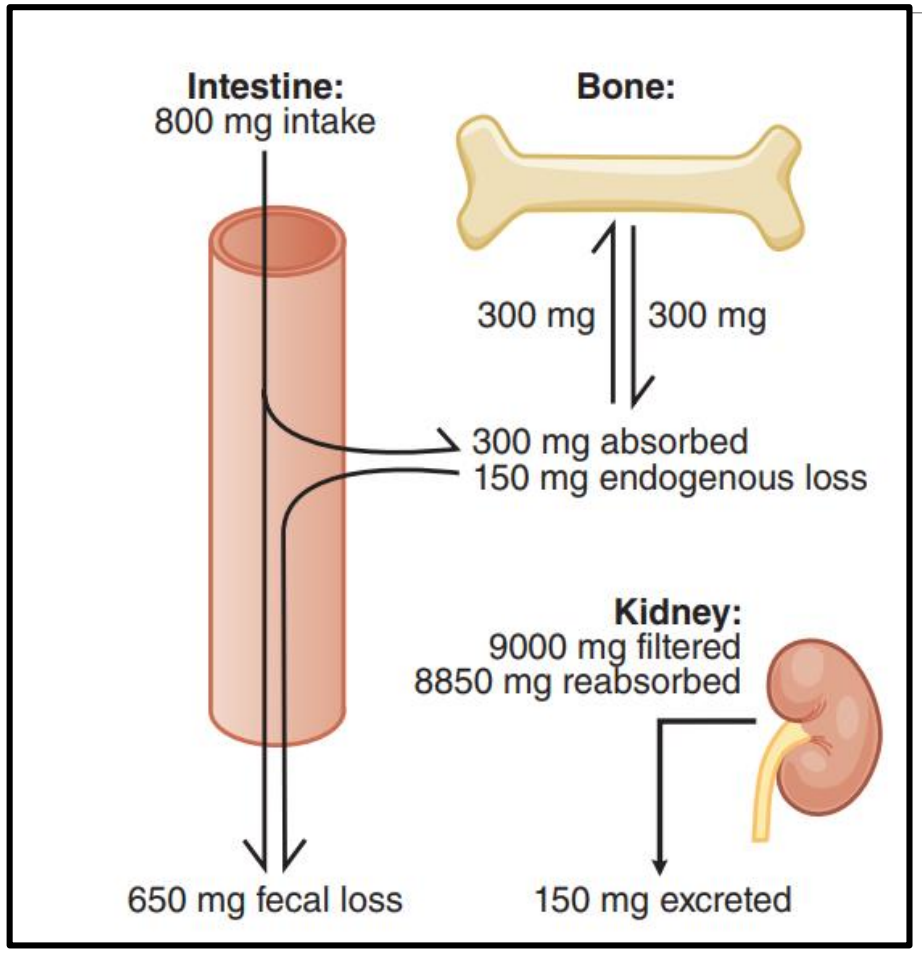
Learning Outcomes

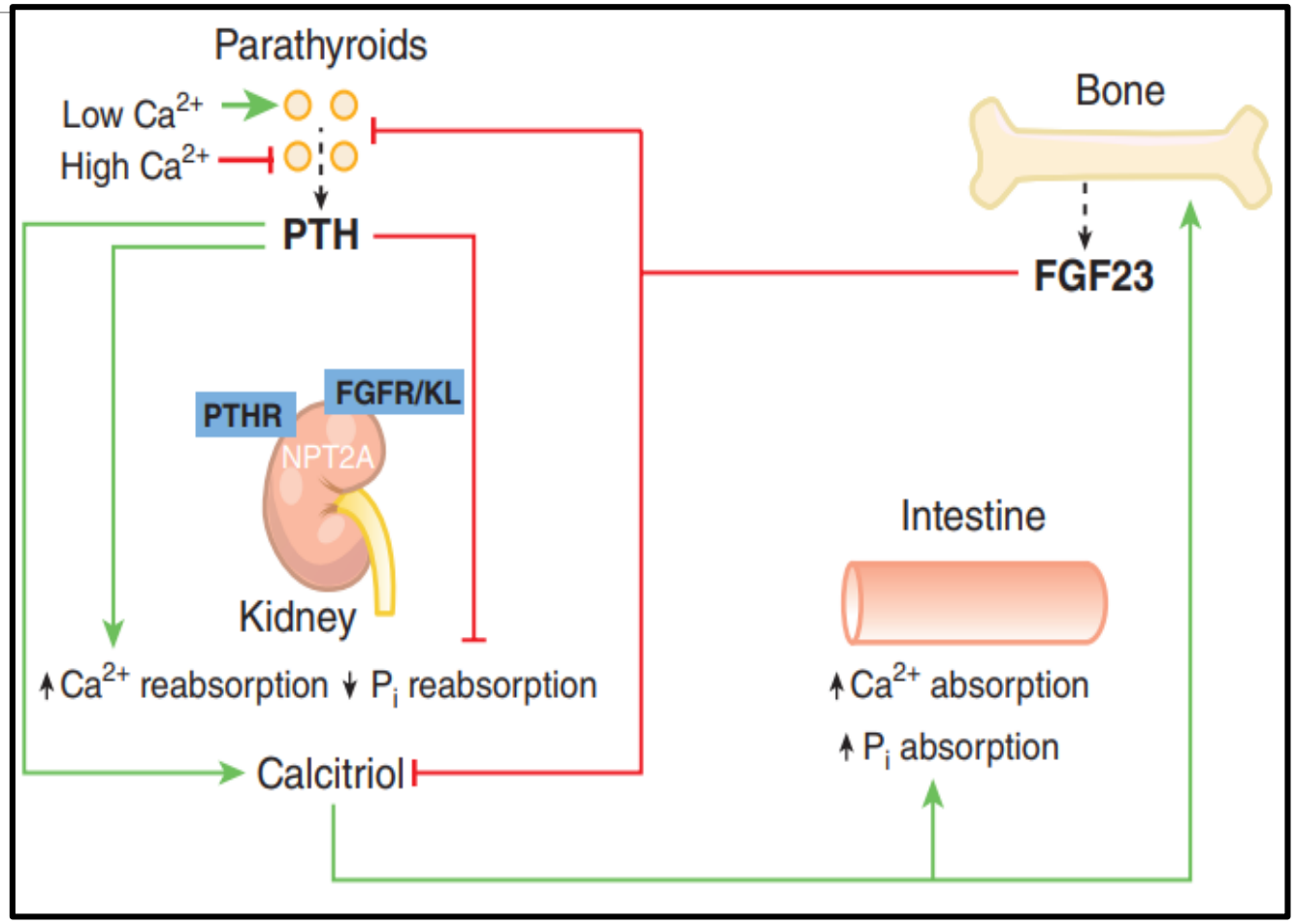
- Pathophysiology of different bone mineral diseases
- Role of PTH, Calcium, Vit.D & FGF23
- Salient features of Drugs
- Newer approaches for Osteoporosis

Bone Mineral Haemostasis

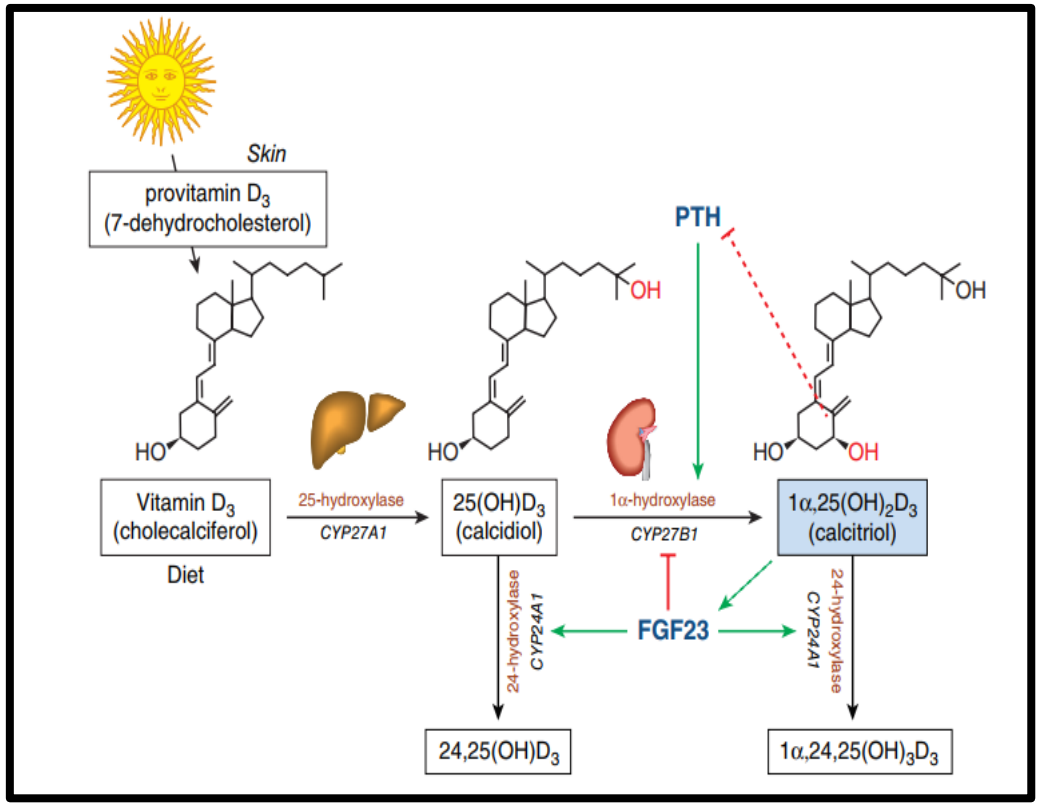
- Calcium
- Vitamin D
- PTH
- Calcitonin
- FGF23
- RANKL

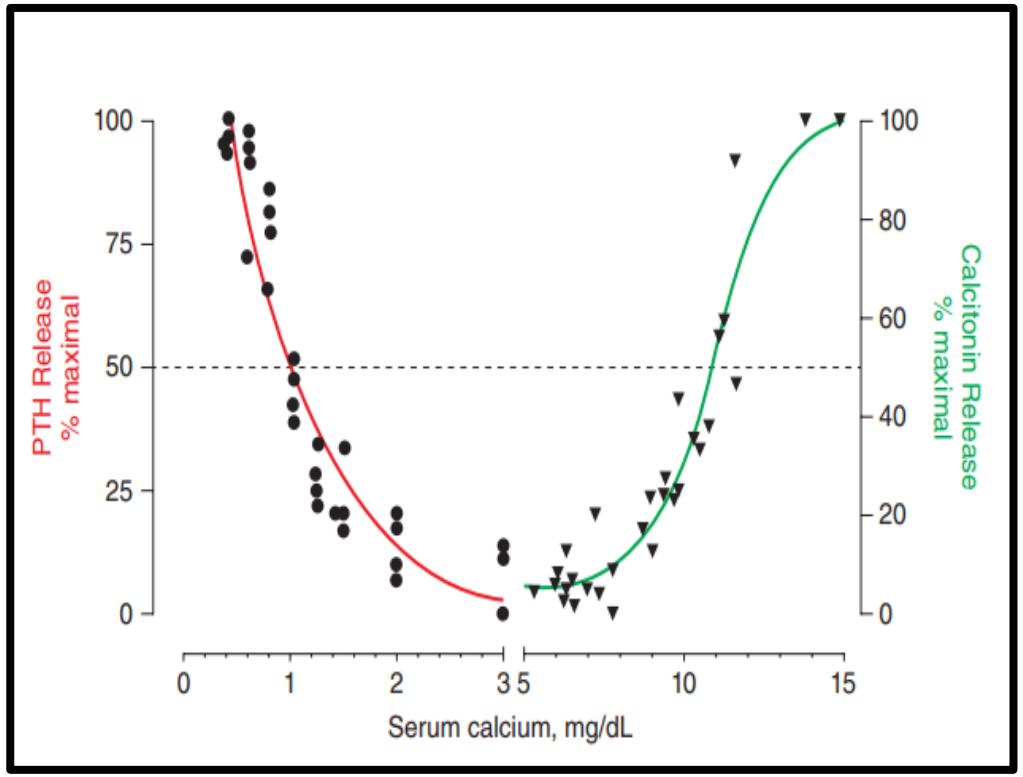
Bone Mineral Haemostasis



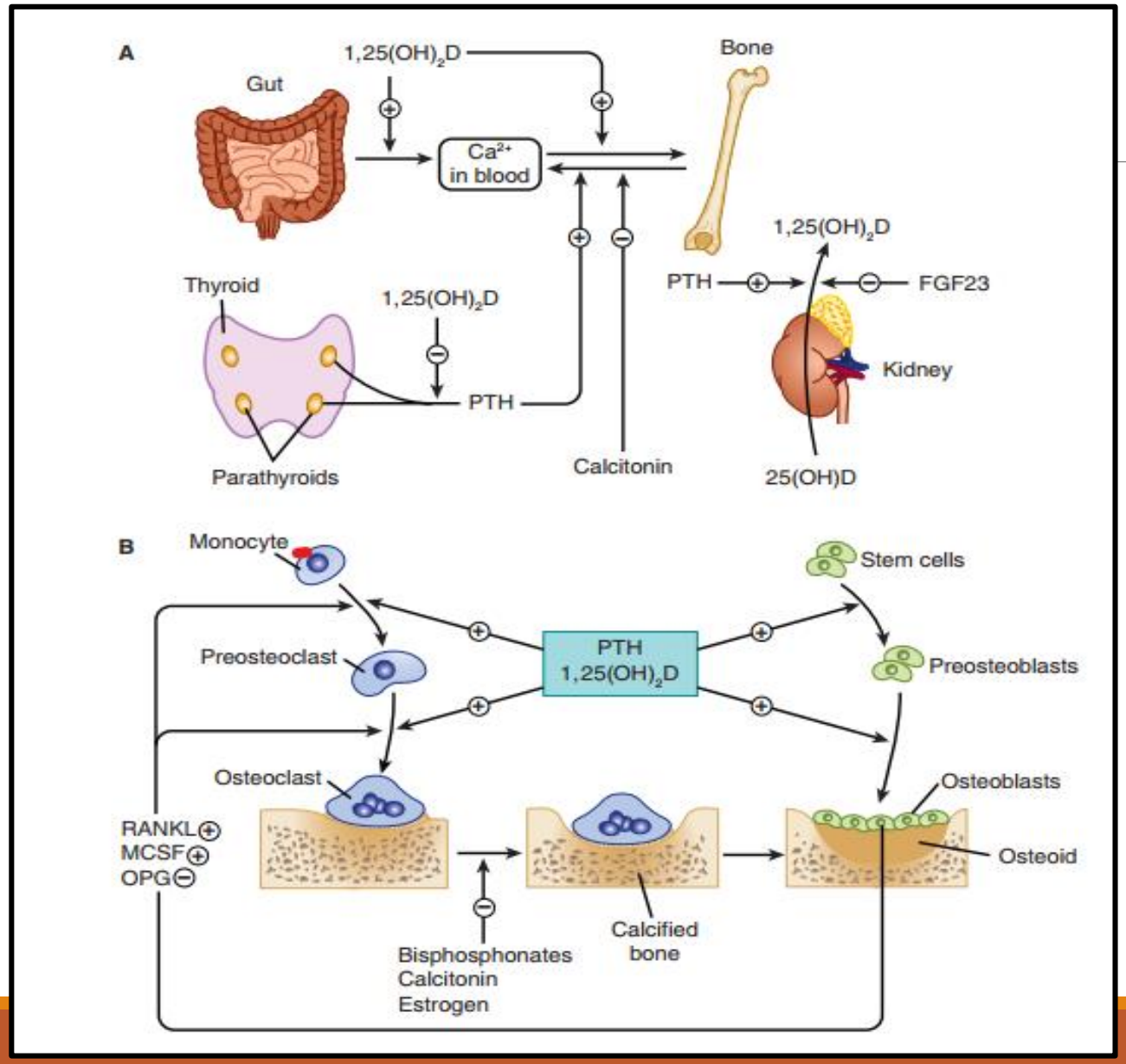


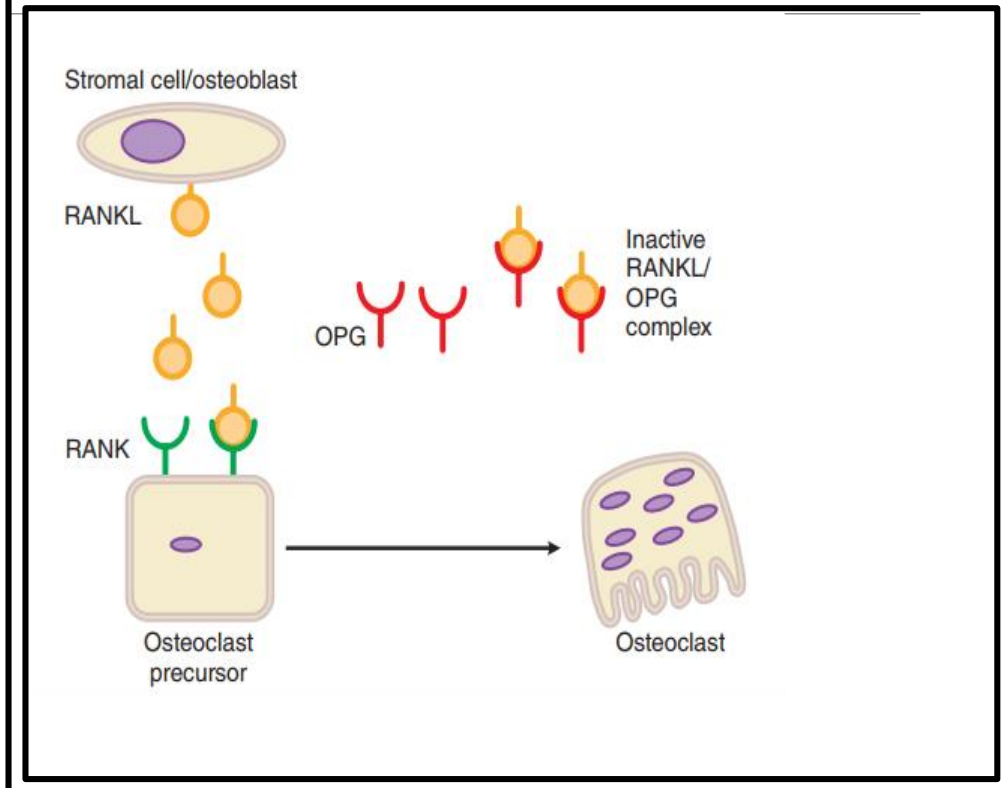
Bone Mineral Haemostasis





Bone Mineral Haemostasis





Bone Mineral Haemostasis

- The net effect of PTH is to raise serum calcium and reduce serum phosphate
- The net effect of FGF23 is to decrease serum phosphate
- The net effect of vitamin D is to raise both

TABLE 42–2 Actions of parathyroid hormone (PTH), vitamin D, and FGF23 on gut, bone, and kidney.

	PTH	Vitamin D	FGF23
Intestine	Increased calcium and phosphate absorption (by increased 1,25[OH]$_2$D production)	Increased calcium and phosphate absorption by 1,25(OH)$_2$D	Decreased calcium and phosphate absorption by decreased 1,25(OH)$_2$ production
Kidney	Decreased calcium excretion, increased phosphate excretion, stimulation of 1,25(OH)$_2$D production	Calcium and phosphate excretion may be decreased by 25(OH)D and 1,25(OH)$_2$D[1]	Increased phosphate excretion, decreased 1,25(OH)$_2$D production
Bone	Calcium and phosphate resorption increased by high doses. Low doses increase bone formation.	Increased calcium and phosphate resorption by 1,25(OH)$_2$D; bone formation may be increased by 1,25(OH)$_2$D	Decreased mineralization due to hypophosphatemia and low 1,25(OH)$_2$D levels.
Net effect on serum levels	Serum calcium increased, serum phosphate decreased	Serum calcium and phosphate both increased	Decreased serum phosphate

[1]Direct effect. Vitamin D also indirectly increases urine calcium owing to increased calcium absorption from the intestine and decreased PTH.

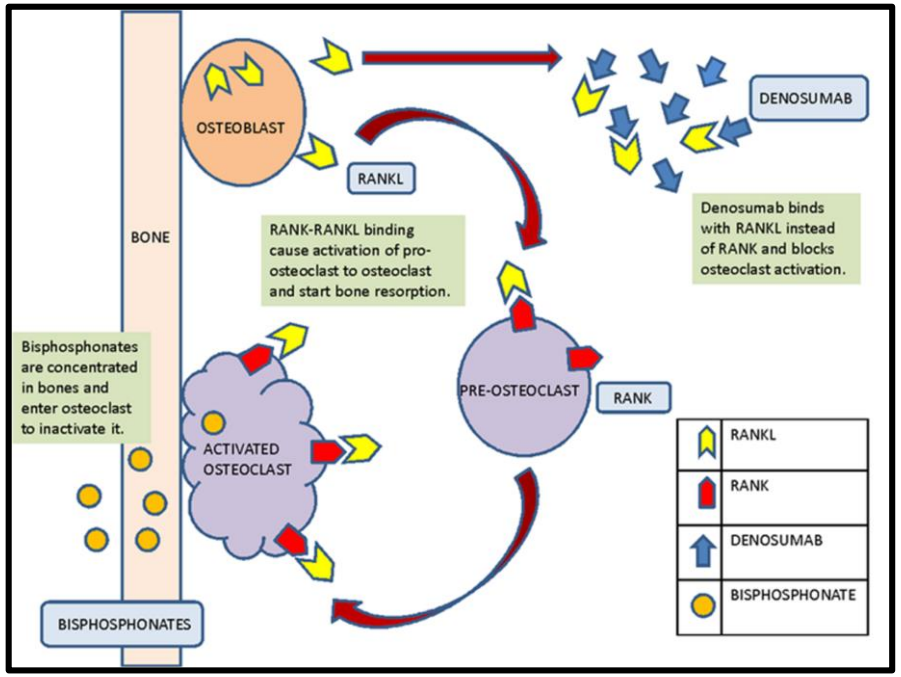
Potential Drugs

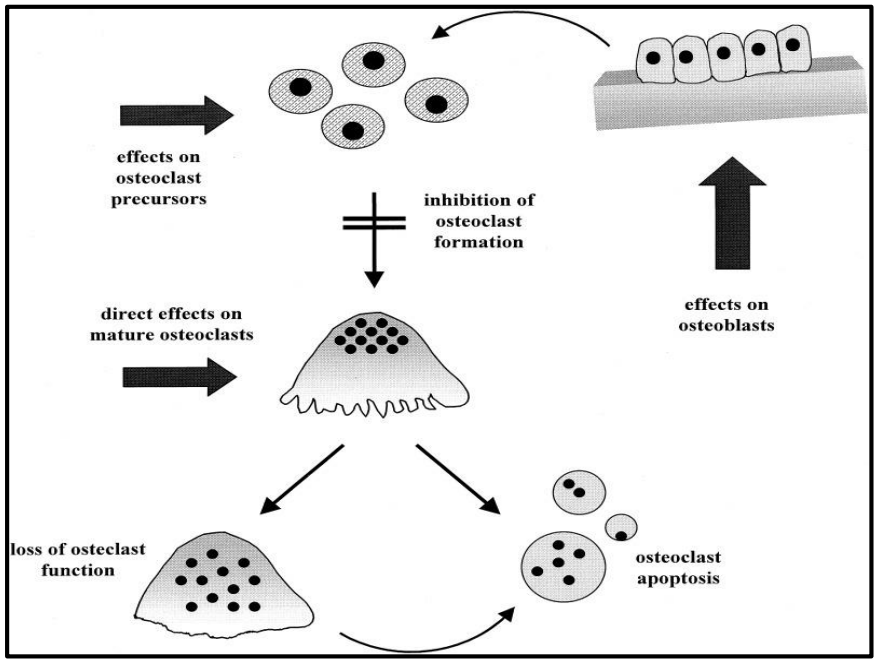
- Vitamin D analogues
- Bisphosphonates
- Hormones
  - PTH(Teriparatide, Abaloparatide,rhPTH1-8..Recombinent)
  - Calcitonin
- SERMs(Raloxifene)
- RANKL Inhibitors(Denosumab)
- Calcium receptor Agonists(Cinacalcet)
- Minerals(Calcium, Phosphate, Strontium)

Romosuzumab… Antibodies against SCLEROSTIN

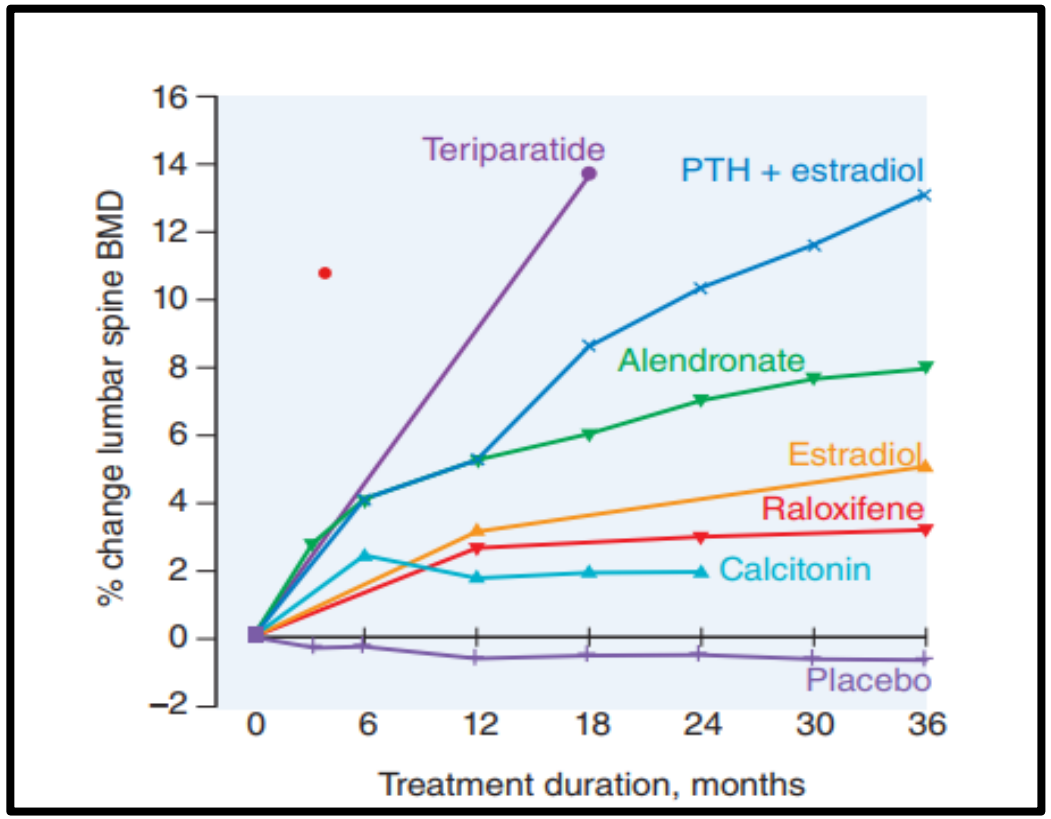
Bisphosphonates

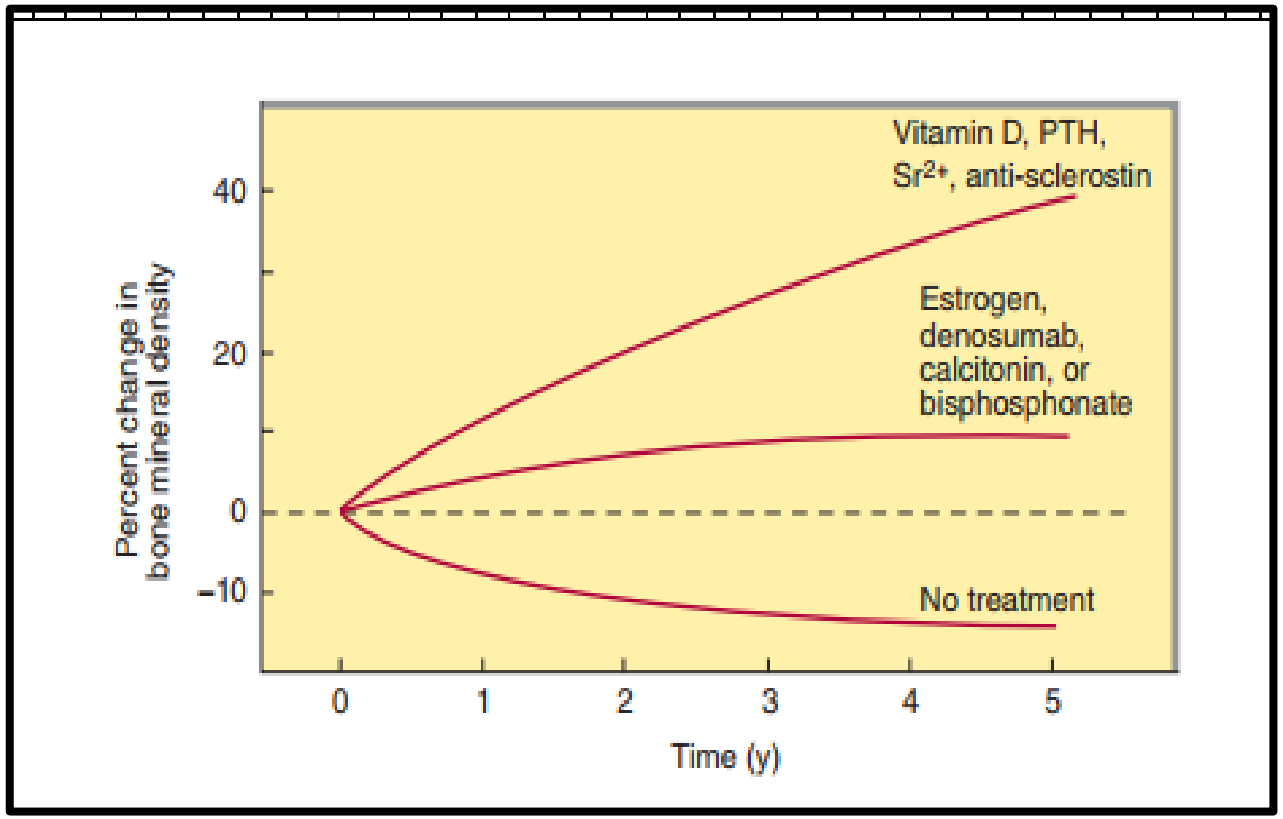
- **Etidronate, Pamidronate, Alendronate, Risedronate, Tiludronate,Ibandronate, & Zoledronate**





Relative efficacy of different therapeutic interventions on BMD of the lumbar spine





Clinical Pharmacology

- Osteoporosis
  - Bisphophonates
  - SERMs
  - Teriparatide
  - Calcitonin
  - Denosumab
  - Strontium renelate

Clinical Pharmacology

- Hyper Calcemia
  - Saline Diuresis
  - Bisphophonates
  - Calcitonin
  - Phospahate
  - Glucocorticoids

- Hypocalcemia
  - Calcium
  - Vitamin D

Clinical Pharmacology

- Hyper Parathyroidism
- Hypo Parathyroidism
- Rickets
- Idiopathic Hypercalciuria
- Pagets Disease
- Chronic Kidney Disease

EOLA

A 63-year-old woman falls at home and fractures her wrist. She has a 40 pack-year history of smoking. Her doctor recommends a DXA scan, which reveals a very low bone density and prescribes alendronate. How will alendronate help this patient?

a. Enhancing calcium absorption

b. Inhibiting calcium excretion

c. Stimulating osteoclastic activity

d. Inhibiting farnesyl pyrophosphate synthase

e. Stimulating osteoblastic activity

A 65-year-old man is referred to you from his primary care physician (PCP) for evaluation and management of possible osteoporosis. He saw his PCP for evaluation of low back pain. X-rays of the spine showed some degenerative changes in the lumbar spine plus several wedge deformities in the thoracic spine. The patient is a long-time smoker (up to two packs per day) and has two to four glasses of wine with dinner, more on the weekends. He has chronic bronchitis, presumably from smoking, and has been treated on numerous occasions with oral prednisone for exacerbations of bronchitis. He is currently on 10 mg/d prednisone. Examination shows kyphosis of the thoracic spine, with some tenderness to fist percussion over the thoracic spine. The dual-energy x-ray absorptiometry (DEXA) measurement of the lumbar spine is "within the normal limits," but the radiologist noted that the reading may be misleading because of degenerative changes. The hip measurement shows a T score (number of standard deviations by which the patient's measured bone density differs from that of a normal young adult) in the femoral neck of –2.2. What further workup should be considered, and what therapy should be initiated?

There are multiple reasons for this patient's osteoporosis, including a heavy smoking history, possible alcoholism, and chronic inflammatory disease treated with glucocorticoids. High levels of cytokines from the chronic inflammation activate osteoclasts. Glucocorticoids increase urinary losses of calcium, suppress bone formation, and inhibit intestinal calcium absorption as well as decreasing gonadotropin production, leading to hypogonadism. Management should include measurement of serum testosterone, calcium, 25(OH)D, and the 24-hour urine calcium and creatinine levels (to verify completeness of collection), with treatment as appropriate for these secondary causes, plus initiation of bisphosphonate or denosumab therapy as primary treatment.

Digital Library References
Research, Bioethics, Family Medicine, Artificial Intelligence

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- Dimai, H.P., 2023. New horizons: artificial intelligence tools for managing osteoporosis. The Journal of Clinical Endocrinology & Metabolism, 108(4), pp.775-783.
- Singer, A.J., Sharma, A., Deignan, C. and Borgermans, L., 2022. Closing the gap in osteoporosis management: the critical role of primary care in bone health. Current Medical Research and Opinion, (just-accepted), pp.1-20.
- Naik-Panvelkar, P., Norman, S., Elgebaly, Z., Elliott, J., Pollack, A., Thistlethwaite, J., Weston, C. and Seibel, M.J., 2020. Osteoporosis management in Australian general practice: an analysis of current osteoporosis treatment patterns and gaps in practice. *BMC family practice*, *21*(1), pp.1-13.