Bone Health in patients with severe brain injury

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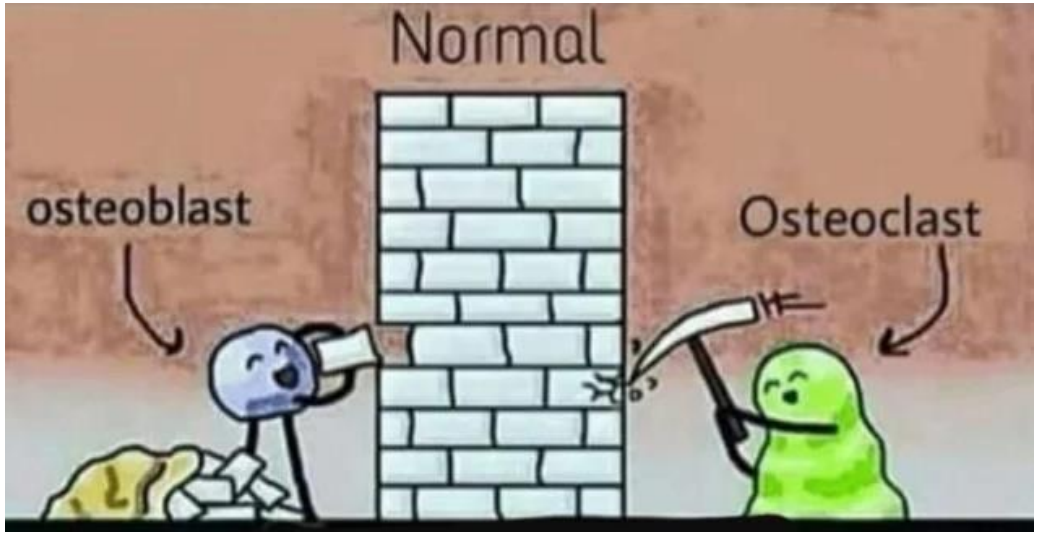
Normal bone health; what do you need to build your house?

The house needs constant work; osteoblasts and osteoclasts

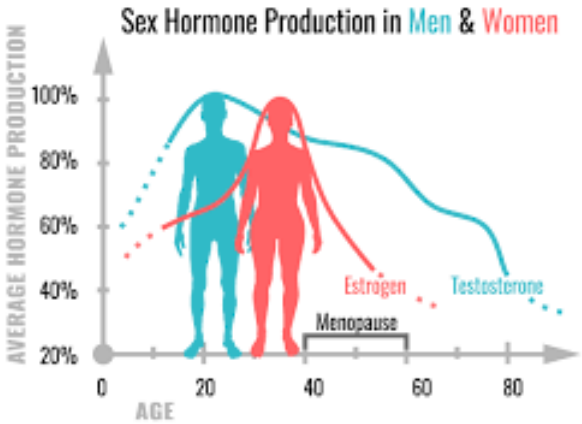


Building materials

- Calcium

- Vitamin D

- Hormones



Physical stress; gravity

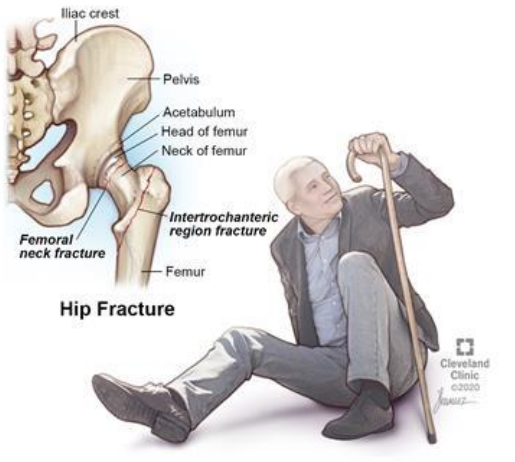
- Need weight through bones in order to retain structure and strength

If we send healthy adults into space, they lose bone (and muscle) very rapidly without constant load bearing exercise; ~1 - 2% BMD per month.

Vico et al. *Bone Miner. Res.* **32**, 2010–2021 (2017)

Absence of anything trying to prevent building or actively damaging the building

- Drugs
- Illnesses



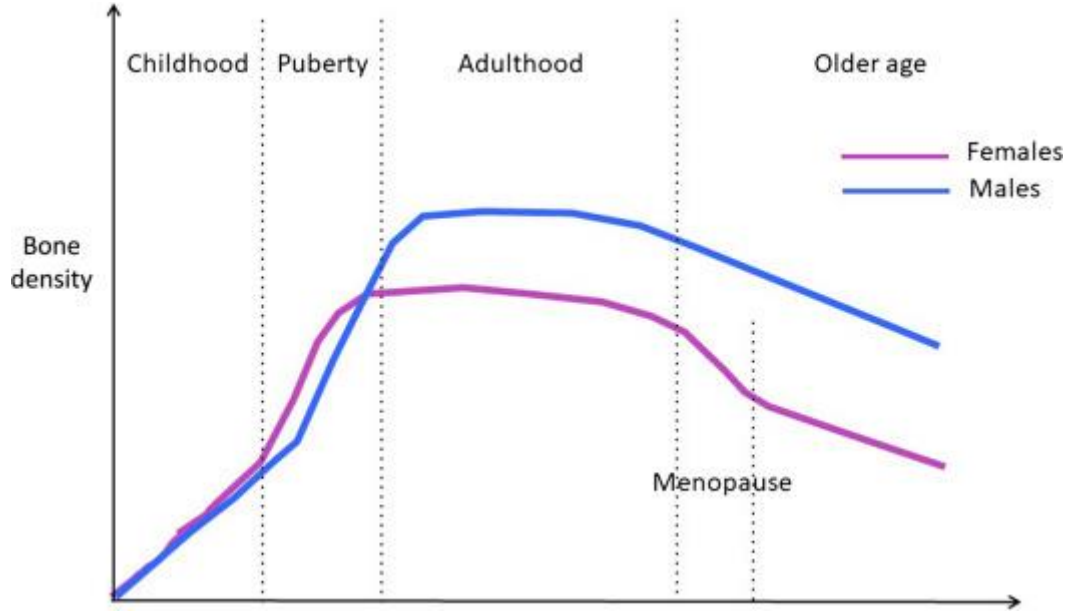
- Family history

- Smoking

- Alcohol

Peak bone mass

- Reached in early 30s
- Gradual decline after this
- Downhill more rapidly for women after the menopause



So what happens in the context of severe brain injury?

- 2 clinical scenarios:

- Adult with severe brain injury
  - Already has a fully formed skeleton

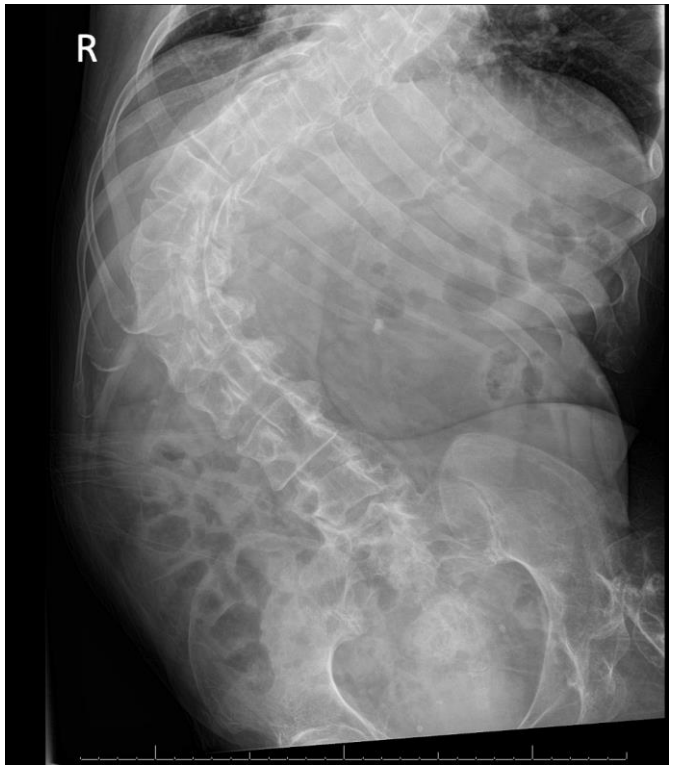
- Child with severe brain injury
- Might be birth injury or genetic abnormality
  - Haven't yet ossified their skeleton
  - Bony development is impaired

Consequences of severe brain injury; immobility and lack of weight bearing

- Immobility in adults causes immediate and progressive reduction in BMD (bone mineral density)
- This seems to be potentially reversible within the first 6 months
- BMD will plateau as body readjusts to new normal, and will remain low

Minaire. *Clin Rheumatol* 1989 Jun;8 Suppl 2:95-103. doi: 10.1007/BF02207242

Consequences of birth brain injury; abnormal skeletal development



- Never weight bearing
- Bones never achieve their peak density
- Spasticity and posture can cause abnormalities in joint and spine

- Weight bearing can improve BMD; cerebral palsy children with programmed standing >2 hours/day showed increased BMD compared to those doing 20 minutes/day

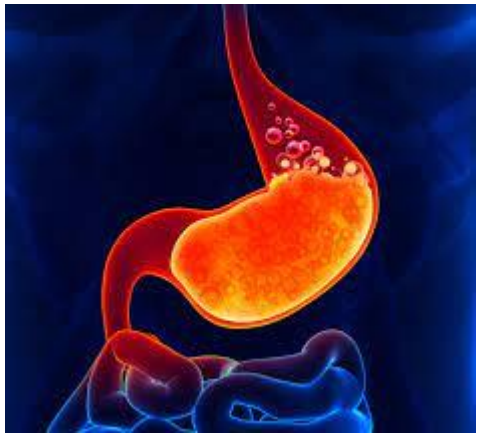
Young et al. *Medicine*: March 2017 - Volume 96 - Issue 10 - p e5896

Common co-existing conditions in brain injury that cause problems with bone health; **epilepsy**

- Epilepsy is really common in any cause of brain injury
- Majority of patients are on lifelong anti convulsants, often complex regimens
- Dose and duration of Rx alters impact on bones
- Some anti convulsants contribute to poor bone health; enzyme inducing drugs seem to have more effect
  - Carbemazepine
  - Phenytoin
  - Phenobarbitone
  - Topiramate
  - Primidone
  - Valproate (not enzyme inducing)

Miziak et al. Expert Opinion on Drug Safety. 2014, Vol 7 p 935-946

Common coexisting problems; GORD



- PPIs are associated with osteoporosis
- Large Canadian population based study showed an independent association with osteoporotic fracture and PPI
- Often prescribed for patients with swallowing difficulties/no swallow reflex
- Many patients are temporarily or permanently ng/PEG/JEJ fed

- H2 antagonists are no longer an alternative option.

Fraser et al. *Osteoporosis International* volume 24, pages1161–1168 (2013)

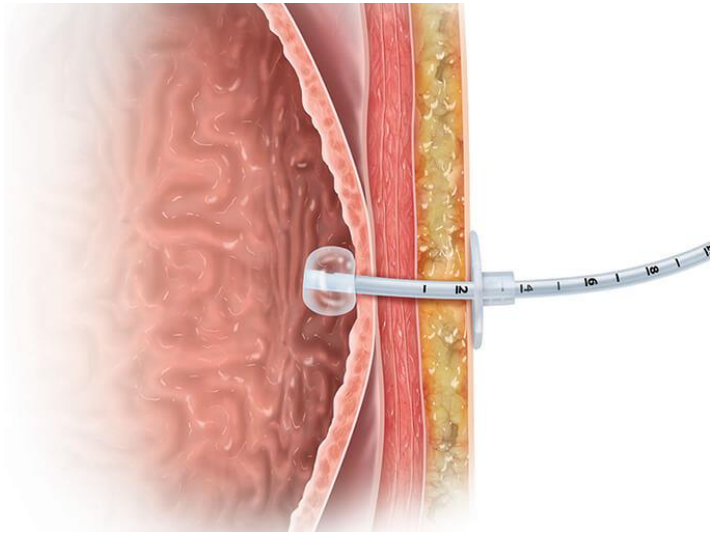
Common coexisting problems; depression

- SSRIs cause accelerated bone loss
- Ideally should be avoided in treating depression in patients at risk of osteoporosis or with poor bone health
- SSRIs are commonest anti depressants prescribed
  - Fluoxetine
  - Citalopram
  - Escitalopram
  - Sertraline
  - Paroxetine

Other medications which can cause accelerated bone loss

- Low molecular weight heparin
  - Particularly an issue for adults with long hospital stays
- Steroids
  - Dose dependent
- Aromatase inhibitors
  - Breast cancer
- Thiazolidinediones
  - Type 2 diabetes
- Calcineurin inhibitors
  - To prevent rejection after transplants

Common coexisting problems; feeding



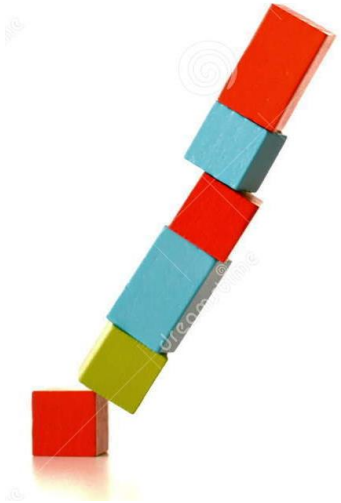
- Many patients will be on nasogastric or parental feeding regimens
- All contain calcium and vitamin D
- Variable amounts of calcium and vitamin D depending on the product

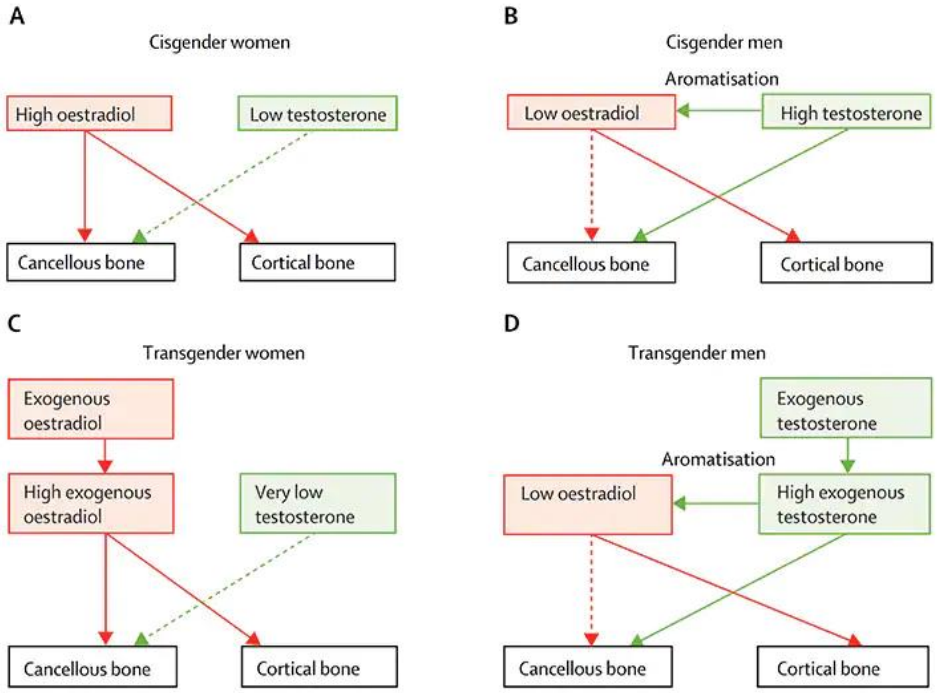
- If a patient can eat, brain injury may alter decision making in dietary choices, that result in low intake of calcium
- High caffeine intake is detrimental
- Should limit caffeinated drinks

Weight

- Heavier people have higher bone density than lighter people
- This can be an issue in children with genetic or acquired brain injury

Hormones





- **Men**
- Testosterone; is it present?
- Should be replaced if low

- **Women**
- Regular menstruation is essential
- ?Age menarche
- Women need to maintain their weight to keep menstruating; anorexia is a major risk factor
- Progesterone only contraception accelerates osteoporosis
- Implant and depo are particularly poor for bone
- May used for convenience and comfort in menstruating women; should be avoided in immobile patients
- HRT/combined OCP does not improve BMD in pre-menopausal amenorrhoeic woman
- Premature menopause should always be treated to maintain optimum bone health, consider transdermal oestrogen

- **Transgender patients**
- Issues entirely dependent on what regimen of medication they have had, and at what age it commenced

Alcohol and smoking

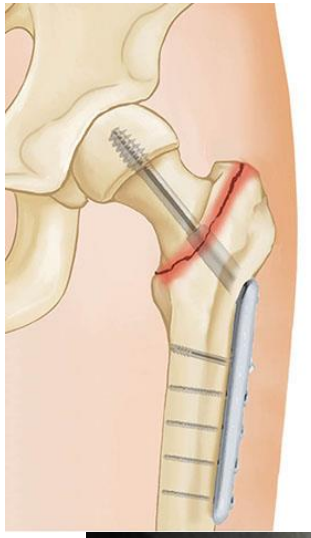
- Usually an issue before the injury

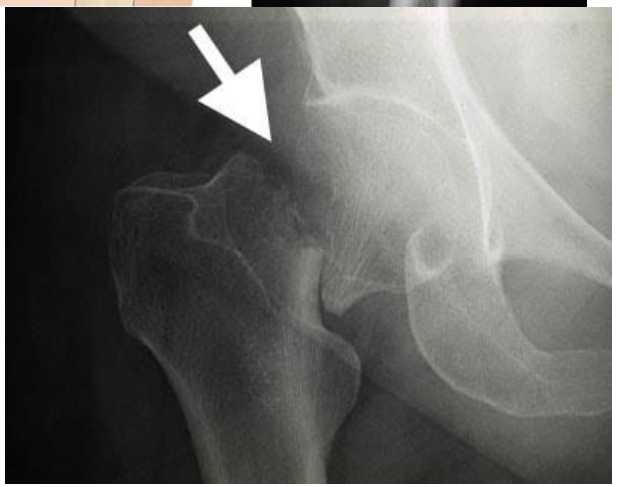
- Alcohol
- Not uncommon to have been a factor in a severe adult brain injury
- 3 units/day is counted as at risk in terms of bone health
- Dose dependent

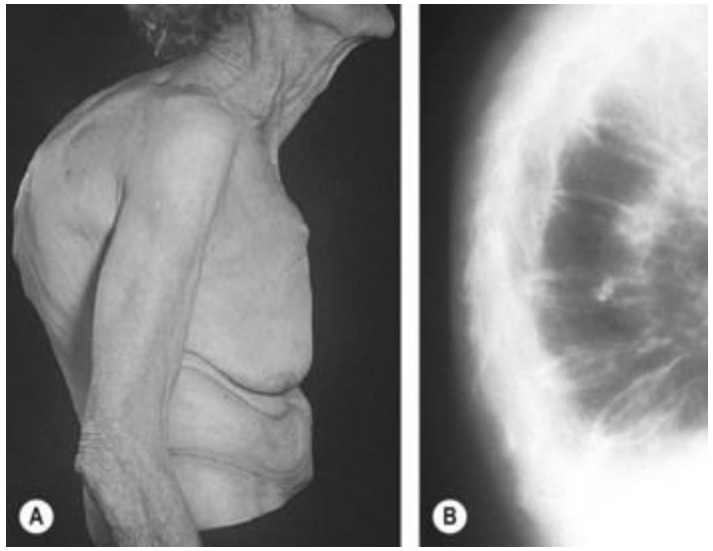
- Smoking contributes to osteoporosis
- Dose dependent

Family history; significant risk

- Maternal or paternal low trauma hip fracture
- Particularly before the age of 70
- Other classically osteoporotic fractures
  - Colles
  - Vertebral







Other associated illnesses

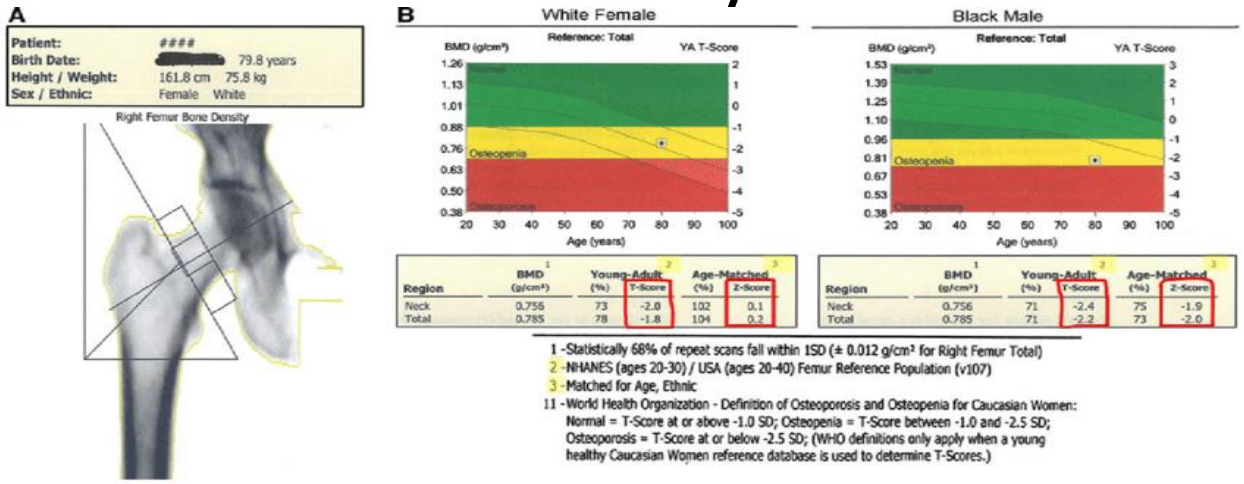
- Coeliac disease
- Any illness/surgery that causes malabsorption
- Inflammatory arthritis, particularly rheumatoid arthritis
- Hyperthyroidism
- Diabetes
- Hyperparathyroidism

Single most important consideration; have they had a fracture?

- **Presence of a low trauma fracture strongly predicts another**

- Has the patient ever had a low trauma fracture?
- Defined as a fracture after a fall from standing height
- Use common sense and a careful history

Measurement of bone mineral density



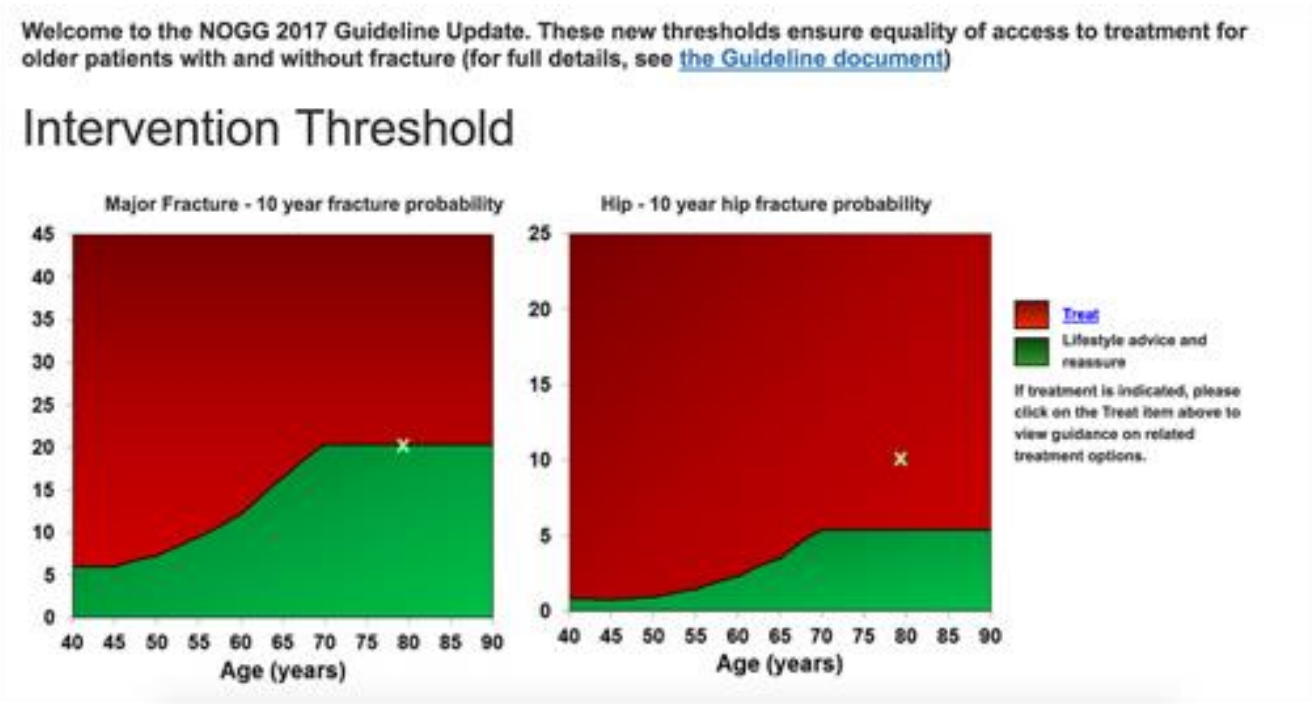
- DEXA

- Validated for >40 years
- <u>Not validated for children</u>
- T score at femoral neck is most important measure

- Used in FRAX to assess fracture risk

- Much more useful in an ambulatory population
- Less useful in an immobile population

FRAX
www.sheffield.ac.uk/FRAX



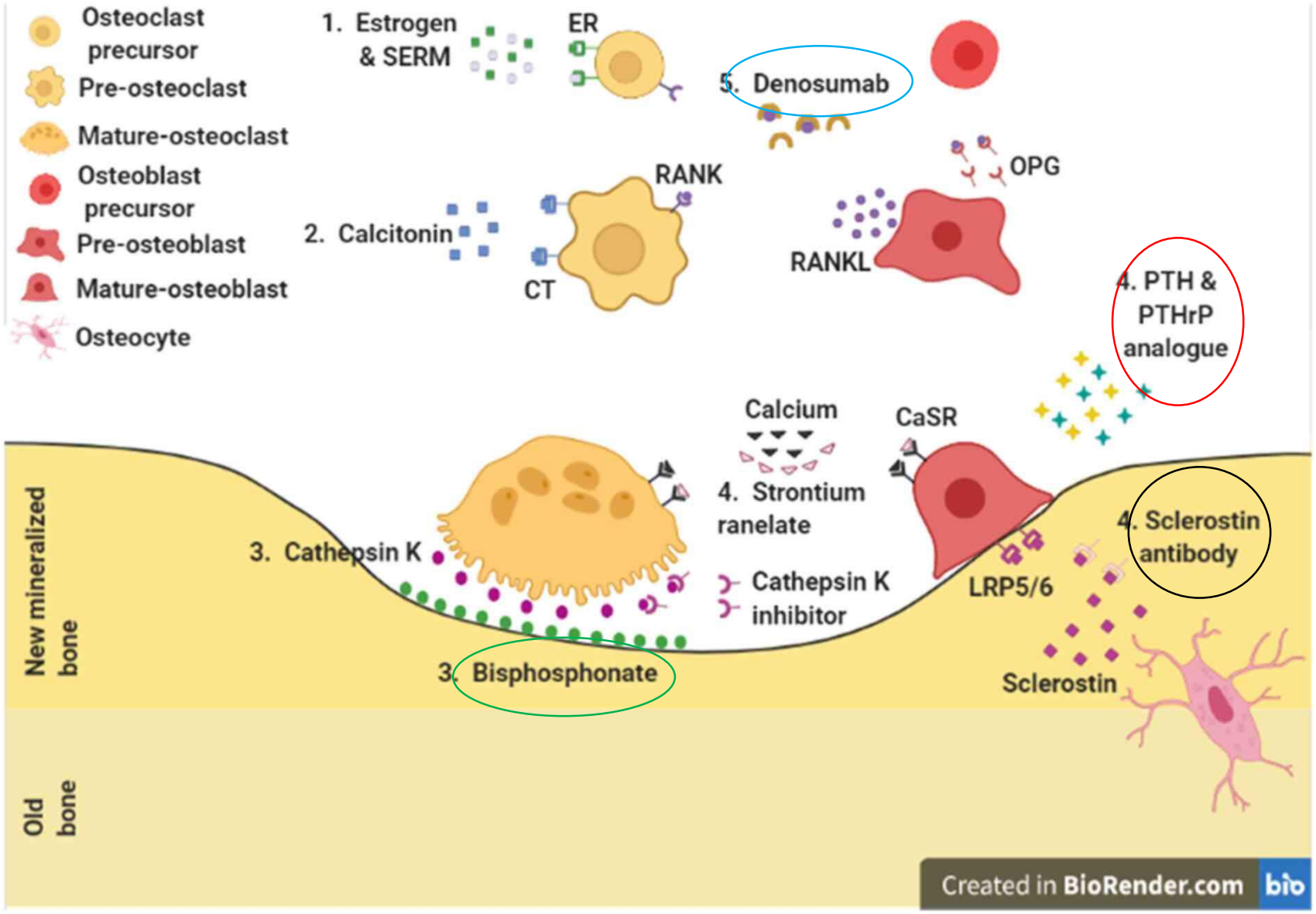
Treatment

- Control all the variables that you can

- Review medication
- Ensure adequate calcium and vitamin D
- Ensure as much load bearing/weight bearing as possible depending on the individual
- Consider hormones
- Consider other risk factors such as FHx or pre-injury life style factors

- **HAVE THEY HAD A FRACTURE?**

Treatments for osteoporosis



Patient with a low trauma fracture or pre-existing osteoporosis

- If all correctable causes have been addressed and vitamin D is replete
- Consider **bisphosphonate**
- Initially give for 5 years then re-consider
- Alendronate can be given in liquid form down a PEG/JEJ
- Iv zoledronate should be considered if:
  - Unable to tolerate oral bisphosphonate
  - Unable to absorb oral bisphosphonate
  - Child
- Side effects
  - Osteonecrosis of the jaw
    - 1/30 000 to 1/50 000 with oral, 1/5000 to 1/10 000 with iv
    - Dental check mandatory prior to iv
  - GI irritation
  - Arthralgia and myalgia
  - Hypocalcaemia with iv; vitamin D must be >50

Other treatments

- Denosumab; RANK ligand inhibitor
  - 6 monthly subcutaneous injection
  - 20% risk of multiple rebound vertebral fractures within 3-6 months if stopped
  - Risk ONJ
  - Increased risk skin and urine infections
  - Hypocalcaemia (Vitamin D must be >50)
- Teriparatide; parathyroid hormone analogue
  - Strict NICE guidance around prescribing
  - One 18-24 month course/lifetime; daily injection
  - 2 Fractures plus T score of -3.5, 1 fracture plus T score of -4
  - Anti-resorptive agents to be prescribed afterwards
- Romosozumab; sclerostin inhibitor
  - Just been approved by NICE
  - Yet to establish local guidelines for which patients will be eligible
  - Likely to be similar to teriparatide
  - 2 injections/month for 1 year only

Other treatments

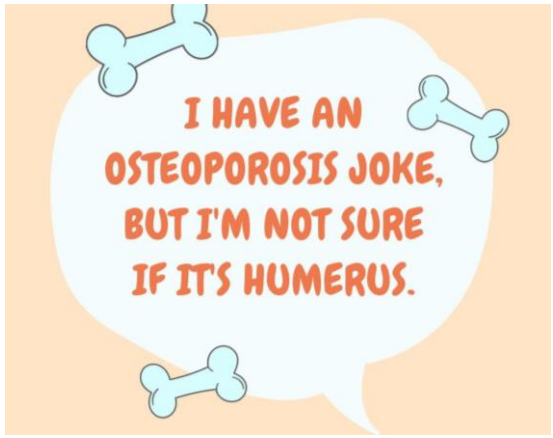
- Strontium
  - Increases risk of MI/CVA/DVT/PE
  - Unlikely to be an option in this group
- Raloxifene
  - Poor efficacy

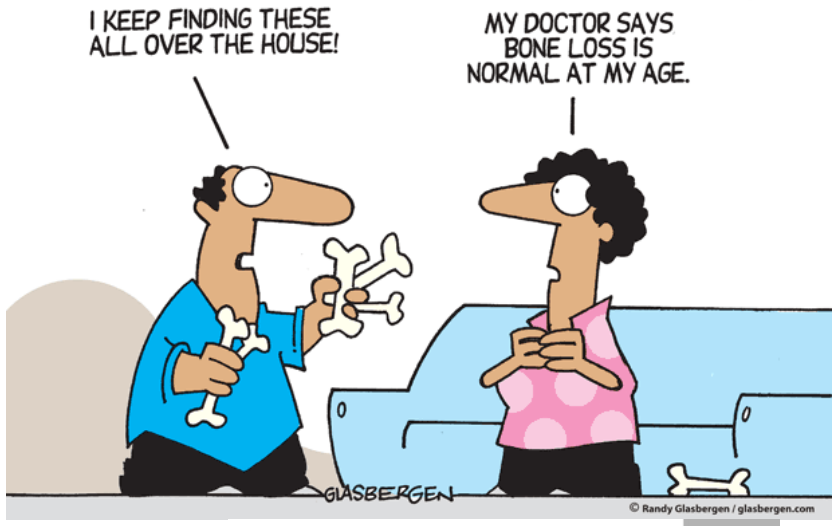
How do I decide what to do?

- Careful history
- Adjust all adjustables
- Look at their fractures – this trumps everything else
- Treat pragmatically

Any questions?

I think you need more calcium in your diet!





"You're taking too much of that clamshell calcium, Margaret."