OSTEOPOROSIS
TO TREAT OR NOT TO TREAT

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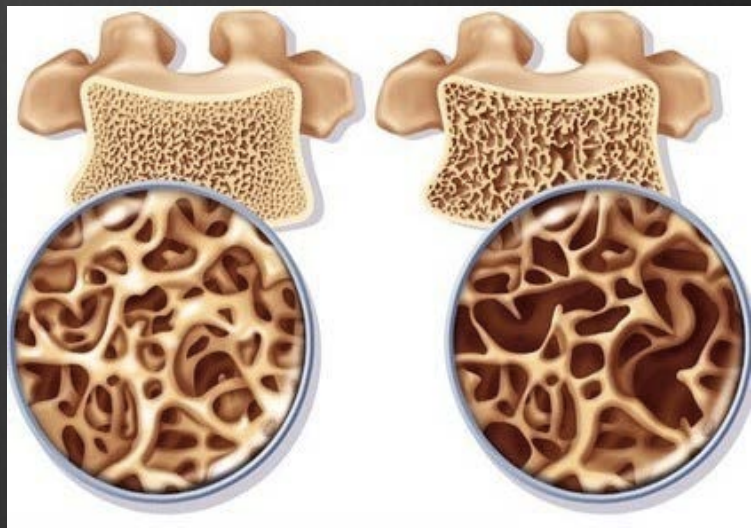
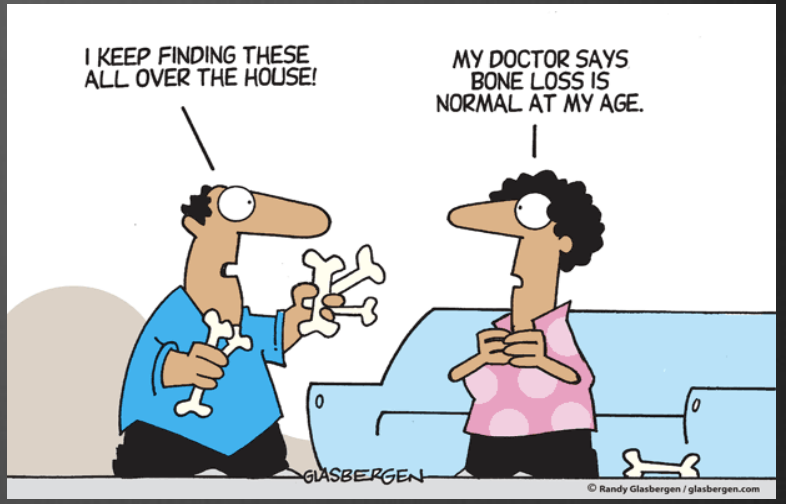


- Introduction
- Whom to test for osteoporosis
- Tests for osteoporosis
  - DEXA scan
  - Other tests
- Treatment
  - Available options (Pros and cons)
  - Whom? how long for? Drug holiday
  - Osteonecrosis of the jaw
- Role of
  - Calcium
  - Vitamin D
  - Exercise

Introduction

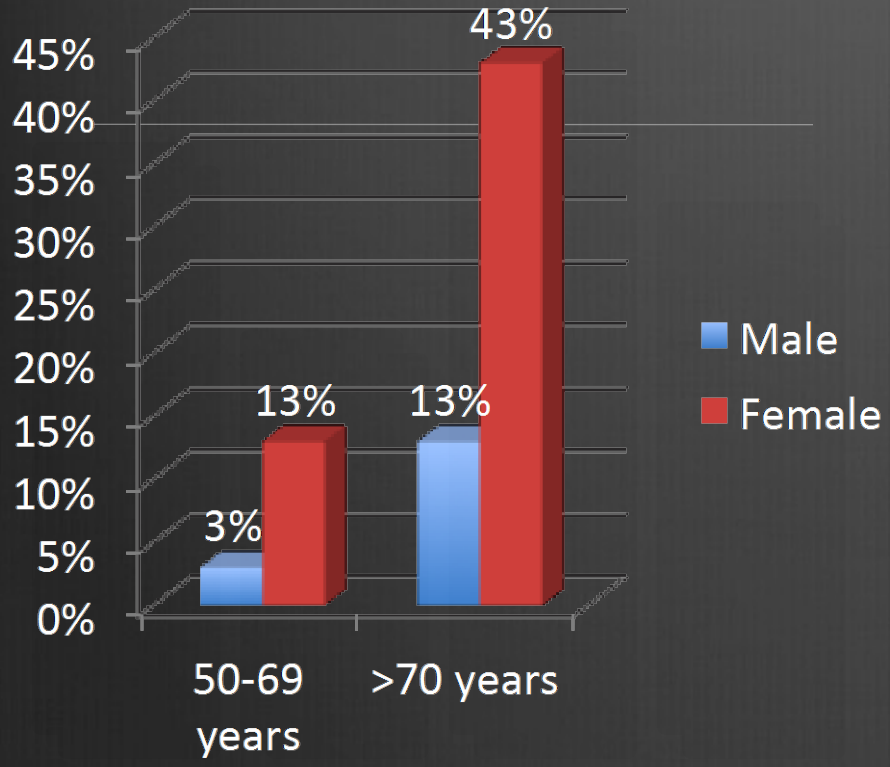


- Characterised by reduced bone mass and deterioration of bone strength
- Australian data:
  - Affects 2.2 million Australians
  - 2/3 women and 1/3 men over the age of 60 suffer from a fracture in lifetime.
- Minimal trauma fracture: (fall from standing height)
- Common sites of fracture- wrist, arm, legs, ribs, hips and spine

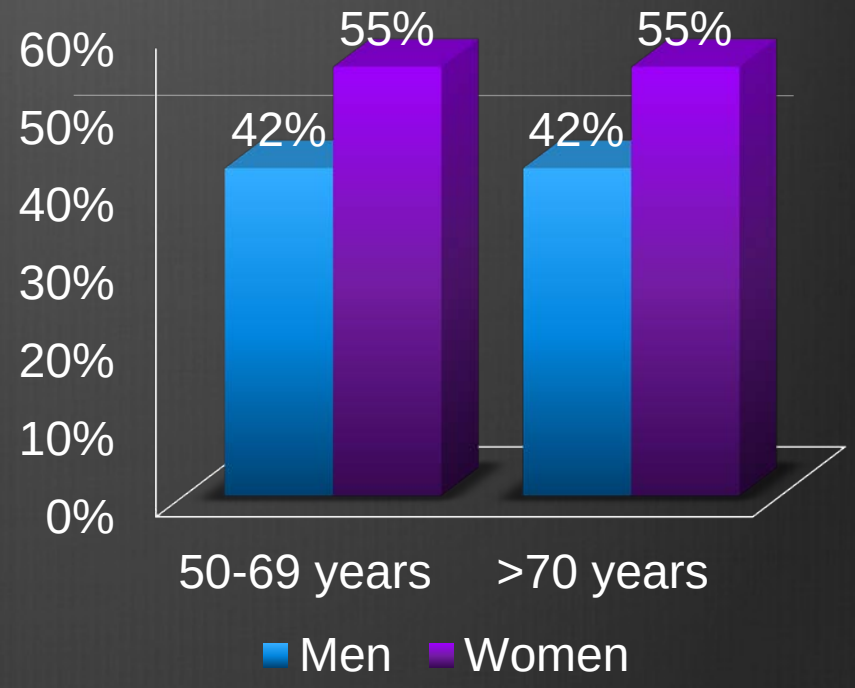
Non hip, non vertebral fractures are more common in age 50-69 years

- "Silent thief"
  - www.garvan.org.au/research/diseases-we-research/osteoporosis

Osteoporosis



Osteopenia



Watts JJ, Abimanyi-Ochom J, Sanders K. Osteoporosis costing all Australians: A new burden of disease analysis – 2012 to 2022.Glebe, NSW: Osteoporosis Australia, 2013 ■

Risk factors

- Major
  - H/o minimal trauma fracture
  - Loss height >= 3 cm
  - Female
  - Age >70
  - Previous fractures
  - Parental h/o hip fracture
  - H/o falls
  - Premature menopause or hypogonadism
  - Corticosteroids (pred >7.5 mg/day for > 3 months)
  - Certain drugs
  - Certain medical conditions
  - Body weight < 58 kg
  - Low muscle mass / strength
  - Poor balance
- Other
  - Smoking
  - Excessive alcohol
  - Calcium, energy or protein under nutrition
  - Vit D Deficiency

Whom to test

Woman or man age (years)	Risk factor profile for which a diagnostic assessment is recommended
< 50 years	• Minimal trauma fracture as individual case decision • Disease or condition associated with bone loss
50-60 years	• Vertebral fracture (where there is no history of major trauma) • Peripheral minimal trauma fracture as individual case decision • Disease or condition associated with bone loss • Medications increasing bone loss
60-70 years	• Vertebral fracture (where there is no history of major trauma) • Peripheral minimal trauma fracture • Hip fracture in a parent • Underweight • Multiple falls • Immobility • Disease or condition associated with bone loss • Medications increasing bone loss

1. The International Society for Clinical Densitometry. 2015 ISCD official positions – Adult. Middletown, CT: ISCD, 2015. Available at www.iscd.org/official-positions/2015-iscd-official-positions-adult [Accessed 31 January 2017].
2. Cosman F, de Beur SJ, LeBoff MS, et al. Clinician's guide to prevention and treatment of osteoporosis. Washington, DC: National Osteoporosis Foundation, 2014.
3. Watts NB, Bilezikian JP, Camacho PM, et al. American Association of Clinical Endocrinologists medical guidelines for clinical practice for the diagnosis and treatment of postmenopausal osteoporosis. Endocr Pract 2010;16 Suppl 3:1–37.

DEXA scan

- For confirmation of osteoporosis
- At risk individuals
- 2 sites: Lumbar spinal and femoral (except Radial in patients with AS or hip prosthesis)
- Repeat BMD not generally required unless:
  - Medication change
  - Treatment interruption
  - Minimal trauma fracture on treatment
- Minimum 2yearly (reliably measure change in BMD)
- Low risk patients-5-15 years, particularly if normal or Osteopenic BMD, T> -1.5)
- High risk-might need annual

- Leslie WD, Majumdar SR, Morin SN, Lix LM. Change in bone mineral density is an indicator of treatment-related antifracture effectin routine clinical practice: A registry-based cohort study. Ann Intern Med 2016;165(7):465–72. doi:10.7326/M15-2937.
- Austin M, Yang YC, Vittinghoff E, et al. Relationship between bone mineral density changes with denosumab treatment and riskreduction for vertebral and nonvertebral fractures. J Bone Miner Res 2012;27(3):687–93.
- Osteoporosis prevention, diagnosis and management in postmenopausal women and men over 50 years of age2nd edition

Table 1 – WHO classification for diagnosis of osteoporosis using BMD measurements

Classification	T-score
Normal	−1.0 or higher
Osteopenia	Between −1.0 and −2.5
Osteoporosis	−2.5 or lower

WHO, World Health Organization; BMD, bone mineral density.

Around 50% first minimal trauma fracture occurs in patients with normal or osteopenic range.

Whom to treat?

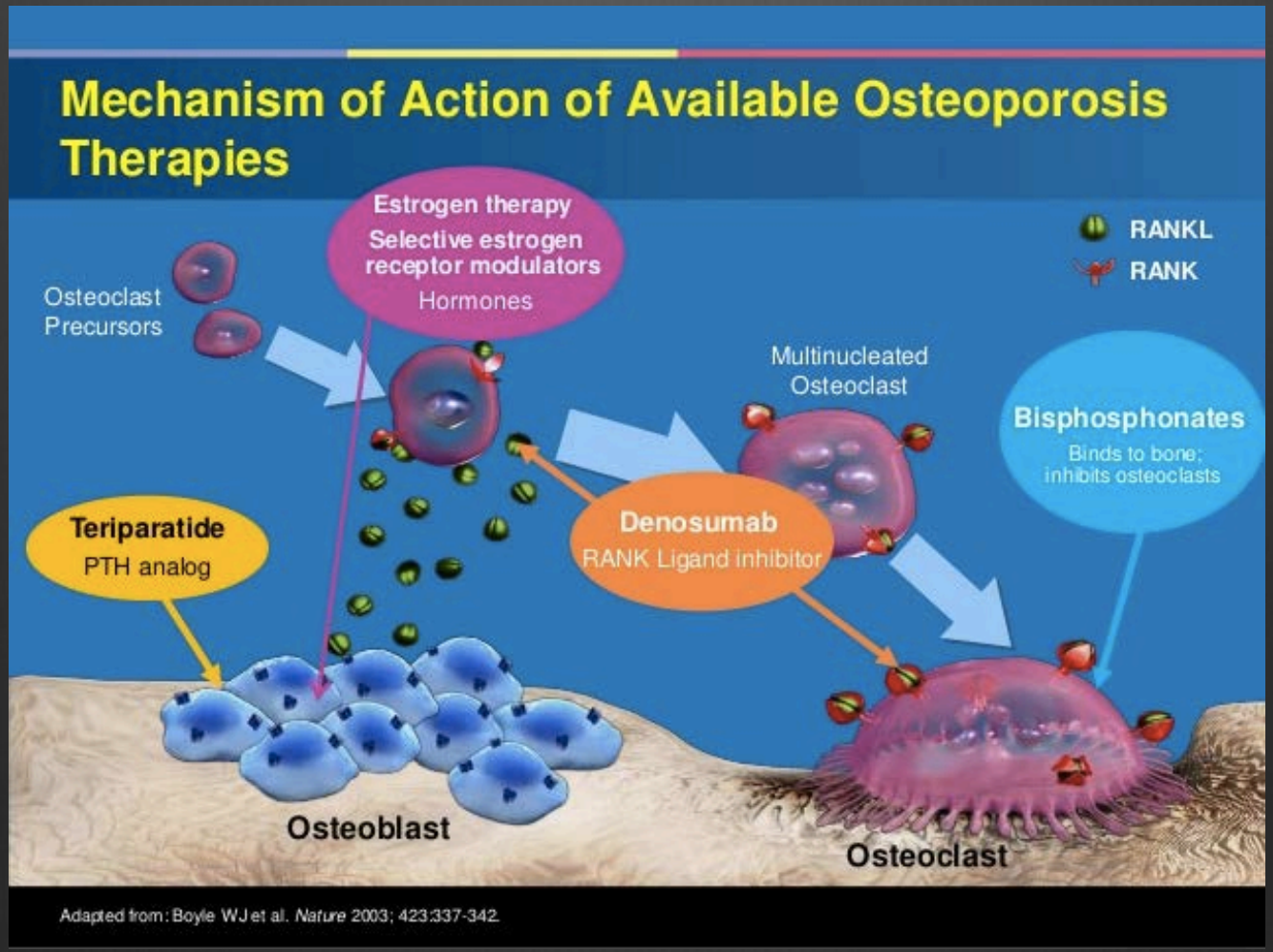
- Minimal trauma fracture
- >=70 years age , T score -3.0 or less
- On prolonged corticosteroids (prednisolone >= 7.5 mg/day for more than 3 months and T score -1.5 and less)
- ? Osteopenia in high risk individuals

- http://www.racgp.org.au/guidelines/musculoskeletaldiseases/osteoporosis

Fracture risk assessment

- Absolute fracture risk algorithms
  - the GarvanFracture Risk Calculator available at www.garvan.org.au/bone-fracture-risk
  - Fracture Risk Assessment Tool [FRAX] available at www.shef.ac.uk/FRAX
- more accurately determine individual fracture risk
- assisting the patient in making a treatment decision.

Treatment options (PBS listed)



Bisphosphonates

- Bisphosphonates are potent inhibitors of bone-resorbing cells (osteoclasts). They inhibit bone resorption by interfering with normal osteoclast function and inducing osteoclast apoptosis.

- Commonly prescribed:
  - Alendronate (70 mg weekly)
  - Risedronate (5 mg daily, 35 mg weekly or 150 mg monthly
  - Zoledronic acid (5mg iv 12-18/12, 3 infusions within 5 years)

- C/I:
  - Hypocalcemia
  - Uveitis
  - For tablets other than available Alendronate enteric coated , any inability to sit upright for 30 minutes after taking tablets or disorders that delay gastric emptying
  - Severe renal impairment (eGFR < 35 ml/min)

- Other considerations
  - Calcium supplements should be taken 2 hours apart
  - Vitamin D level should be > 50 mmol/lit (minimises risk of hypocalcemia)
  - Dental assessment and dental hygiene , procedures before commencement
  - Headache, myalgia and fever can occur soon after Zoledronic acid infusion

RANK L inhibitor (Denusumab)

- Prevents RANKL binding to its receptor (RANK) on the osteoclast surface. Osteoclast formation,function and survival is disrupted, resulting in decreased bone resorption and increased mass and strength of both cortical and trabecular bone.
- PBS listing for men and women over the age of 70 years with a T-score –2.5 or less, and for men and women with a minimal trauma fracture.
- 60 mg sc every 6/12
- C/I: hypocalcemia
- Practical considerations:
  - Correct hypocalcemia prior to treatment
  - Dental hygiene
- S/E:
  - Cellulitis risk (0.2/100 pt. years)
  - Risk of hypocalcemia in patients with renal insufficiency

Medication Related Osteonecrosis of the jaw (MRONJ)

- Area of exposed bone in the maxillofacial region that has persisted for more than eight weeks, in a patient receiving bisphosphonates, denosumab or antiangiogenictherapy for cancer, and where there is no history of radiation therapy to the jaws or obvious metastatic *disease to the jaws.
- Rare (<1-10 cases/10,000 with oral bisphosphonates, 1.7/10,000 cases for iv Zoledronic acid)
- Reported with high dose iv bisphosphonates + concomitant corticosteroids in cancer treatment
- Very uncommon with osteoporosis treatment (100 times less)
- Related to duration of therapy
- Dental hygiene and dental surgery imp. risk factors (? Reduced risk with oral antibiotics with surgery)
- DM, RA, corticosteroids – risk factors
- More common in Asian community
- ?Heals with withdrawal and wound closure
- Ruggiero SL, Dodson TB, Fantasia J, et al. American Association of Oral and Maxillofacial Surgeons position paper on medicationrelated

*osteonecrosis of the jaw—2014 update. J Oral Maxillofac Surg 2014;72(10):1938–56.

Vahtsevanos et al, 2009 JCO
Khosla et al, 2007 JBMR

Atypical Femoral fractures

- 5 fractures/10,000 patient years
- Diaphyseal regio
- T
- ension
- teral cortical thickening, especially at fracture site
- Flaring of lateral cortex
- More common in those of Asian ethnicity

> 100 typical hip fractures prevented for 1 atypical fracture observed

Dell et al 2012

Kaiser Permanente

JBMR 27:2544-50

Anabolic agents (Teriperatide)

- Synthetic human PTH (1-34)
- PBS subsidized for postmenopausal women or men (hypogonadism or idiopathic causes) with T <-3.0 and 2 or more fractures, on atleast 12 months of anti resorptive therapy or when other antiresoprtive agents are not tolerated or C/I
- 20 microgram daily injection s.c. on thigh or abdomen
- Restricted to 18/12 (reported osteosarcoma in animal studies)
- C/I Paget's disease, previous bony mets or primary bone maligancy, metabolic bone disease or pre existing hyper calcemia
- Dizziness, nausea, leg cramps, headaches, inj site reactions (<5%)
- Transient hyper calcemia and mild increase in uric acid
- Requires informed consent
- Continue antiresorptive treatment after 18/12 as maintenance

Other agents

- **Raloxifene (Selective oestrogen receptor modulator)**
  - Ostrogen like effects on bone and anti oestrogen effect on breast and endometrium
  - Indicated for post menopausal women with minimal trauma fracture
  - May be used as a second line agent in post menopausal women with OP, at risk of breast cancer
  - Risk of thromboembolism
- **Hormone replacement therapy (HRT)**
  - Slows the rate of bone loss in post menopausal women
  - Safe option for osteoporotic women (<60 years), at risk of minimal trauma fracture and require treatment of post menopausal symptoms

Need a break ? Drug holiday

- 5-10 years after bisphosphonate therapy (BMD >-2.5 and no fracture)
- Lack of evidence to support further increase in BMD after 3-5 years of BMD treatment *
- Individualize decision based on risks
- Repeat BMD after 1 year, assess falls risk , restart or consider Denosumab , if significant decrease in BMD (Lumbar spine >5%) or with additional fracture
- ? Role of bone turnover markers

* www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/DrugSafetyandRiskManagementAdvisoryCommittee/UCM270958.pdf

Calcium

- Adults > 19 + : 1000 mg/day
- Women above 50 or Men above 70 : 1300 mg/day
- Preferably dietary, supplemental Calcium to fill the gaps
- 3-5 serves/day

	Food	Serving Size	Calcium Content (mg)
Coffee	Cappuccino, regular	255ml (small take away cup)	150
	Latte or flat white, low fat	255ml (small take away cup)	174
Skim milk powder	Skim milk powder	¼ cup	313
Egg	Egg, boiled	1 large egg	23
Vegetables	Broccoli, cooked	½ cup	27
	Spinach	1 cup	20
	Silver beet	1 cup	35
Pasta	Wholemeal, cooked	½ cup	19
	White, cooked	½ cup	8
Soy products	Soy beans	100g	76
	Soy milk, unfortified	250ml (1 cup)	33
	Soy milk, fortified	250ml (1 cup)	298
	Soy cheese	40g	180
	Tofu, raw	½ cup	310
Legumes, nuts & seeds	Lentils, dry, cooked, no fat	½ cup	16
	Sesame seeds	30g	19
	Baked beans	130g (small tin)	52
	Tahini	1 tablespoon	66
	Almonds	¼ cup	95
Meat & fish	Rump steak, grilled & trimmed	100g	6
	Lamb chop, grilled & trimmed	100g	11
	Chicken, BBQ with skin	100g	10
	Salmon, red, canned	80g (small can)	180
	Tuna, canned	80g (small can)	10

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	Food	Serving Size	Calcium Content (mg)
Fruit	Apple, red	130g (1 medium)	7
	Banana	100g (1 medium)	5
	Orange	130g (1 medium)	33
	Apricots, dried	¼ cup	23
Bread	White	1 slice	16
	Wholemeal	1 slice	29

Vitamin D

- At least 50mmol/lit at end of Winter
- Usually 10-20 mmol higher at the end of Summer

Skin Type	Season	Skin Exposed	Recommended time of day	Sun Exposure
Moderately Fair	Winter	Arms or equivalent	midday	7 – 30 minutes*
Darker skin	Winter	Arms or equivalent	midday	20 min – 3hrs*

*depends on location within Australia and type of skin

Skin Type	Season	Skin Exposed	Recommended time of day	Sun Exposure
Moderately Fair	Summer	Arms or equivalent	mid morning or mid afternoon	5 – 10 minutes
Darker skin	Summer	Arms or equivalent	mid morning or mid afternoon	15 – 60 minutes*

*depends on location within Australia and type of skin

www.osteoporosis.org.au/vitamin-d

When to measure

- No clear guidelines
- High risk individuals
- ?Consider end of winter and summer in at risk individuals
- After supplementation: 3 months (takes up to 3-5 months to normalize)
- If adequate, no indication for regular monitoring

www.osteoporosis.org.au/vitamin-d

Supplementation

- Vit D3
- In patients with some sun exposure: < 70 years: 600 IU/day, >70 years: 800 IU/day
- Sun avoiders/ at risk individuals/ Mild deficiency: 1000-2000 IU/day
- Mod-severe deficiency: 3000-5000 IU/day, continue 1000-2000 IU/day after level normalises

www.osteoporosis.org.au/vitamin-d

Role of exercise

- Weight bearing (jumping, running, sports etc) and high intensity resistance training (30 min sessions, 2-3/7, 3 sets of 8)
- Short intensive bursts
- Gradual increase in intensity
- Change routine, avoid repetition
- Balance training and falls prevention – major risk of osteoporotic fracture (1/3rd patients > 65, up to 6 % results in fractures)
  - 1hr twice a week for at least 6 months
- www.osteoporosis.org.au/exercise

Important resources

- www.osteoporosis.org.au
- http://www.racgp.org.au/your-practice/guidelines/musculoskeletal/osteoporosis/

Thanks