OSTEOPOROSIS
TO TREAT OR NOT TO TREAT

Dr. Amee Sonigra
Rheumatologist and General Physician
Arthritis Care
Princess Alexandra Hospital
Logan Hospital
QUT
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
In the 50-69 years age group, 13% of men and 3% of women have osteoporosis. In the >70 years age group, 43% of men and 13% of women have osteoporosis. For osteopenia, 55% of women aged 50-69 and 42% of women aged >70 have the condition. Additionally, 42% of men aged 50-69 and 55% of men aged >70 have osteopenia.

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

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

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 2 yearly (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


Osteoporosis prevention, diagnosis and management in postmenopausal women and men over 50 years of age 2nd edition
Around 50% first minimal trauma fracture occurs in patients with normal or osteopenic range.

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

<table>
<thead>
<tr>
<th>Classification</th>
<th>T-score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>−1.0 or higher</td>
</tr>
<tr>
<td>Osteopenia</td>
<td>Between −1.0 and −2.5</td>
</tr>
<tr>
<td>Osteoporosis</td>
<td>−2.5 or lower</td>
</tr>
</tbody>
</table>

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

Mechanism of Action of Available Osteoporosis Therapies

- Estrogen therapy
- Selective estrogen receptor modulators
- Teriparatide
  - PTH analog
- Bisphosphonates
  - Binds to bone; inhibits osteoclasts
- Denosumab
  - RANK Ligand inhibitor

Osteoblast

Osteoclast

Osteoclast Precursors

Multinucleated Osteoclast

RANKL

RANK

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 (5 mg 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 antiangiogenic therapy 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


Vahtsevanos et al, 2009 JCO
Khosla et al, 2007 JBMR
Atypical Femoral fractures

- 5 fractures/10,000 patient years
- Diaphyseal region
- Transverse fracture ± short oblique medial extension
- Lateral cortical thickening, especially at fracture site
- Flaring of lateral cortex
- More common in those of Asian ethnicity

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 at least 12 months of anti-resorptive therapy or when other anti-resorptive 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 malignancy, metabolic bone disease or pre-existing hypercalcemia
- Dizziness, nausea, leg cramps, headaches, inj site reactions (<5%)
- Transient hypercalcemia 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

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
Vitamin D

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

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
Thanks