Frequently Asked Questions (FAQs) about Osteoporosis

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Objectives:

• Address FAQs about osteoporosis

• Explain a Fracture Risk Assessment and Bone Mineral Density (BMD) test

• Understand the benefits and risks of osteoporosis medications, treatment duration and concept of drug holiday

• Understand the role of calcium, vitamin D and exercise in promoting bone health and preventing fractures
Osteoporosis
“porous bone”

- Skeletal disorder of comprised bone strength
  - Low bone density (quantity)
  - Deterioration of bone microarchitecture (quality)

- Consequence is fragility fracture
Contributors to Bone Strength

- Bone Density
- Bone Architecture
- Bone Mineral
- Bone Turnover

The diagram shows the relationships between bone density, bone architecture, bone mineral, and bone turnover as contributors to bone strength.
What is a Fragility Fracture?

- A fracture that occurs spontaneously or after minor trauma (such as a fall from standing height or less)
- **Excludes**: craniofacial, hand, ankle, and foot
QUESTION:
Why do we put so much emphasis on fractures?
Consequences of Fracture

In women with hip fracture:

- Fracture begets future fracture
- Reduced quality of life
- Long-term care admission
- Mortality

- 40% had prior fracture\(^1\)
- 40% need assistance walking\(^2\)
- 18% enter LTC\(^3\)
- 23% die within 1 year\(^4\)

Lifetime risk of hip fracture in women >50 years old is 12.1\(^5\)

QUESTION:

What are the indications for bone mineral density testing?
Bone Mineral Density (BMD)

- Osteoporosis: T-score ≤ -2.5
- Strongly correlates with fracture risk
- Screening BMD: men & women ≥ 65
- Earlier BMD if have risk factors
- But does not directly reflect bone microarchitecture
- Must incorporate into a fracture risk assessment tool (FRAX or CAROC)
QUESTION:

What is a Fracture Risk Assessment?
OC 2010 Guidelines: Fracture Risk Assessment

10-year Fracture Risk Assessment

CAROC

FRAX Canada

- Age and Sex
- BMD (femoral neck)
- Fragility Fracture
- Steroids

- BMI (weight, height)
- Parental hip fracture
- Smoking, Alcohol
- Rheumatoid Arthritis
- Other secondary causes

Papaioannou A, et al. CMAJ 2010
Who Needs Medications?

- **LOW risk (<10%)**: NO Medication
- **MODERATE (10-20%)**: Depends - other Risk factors
- **HIGH risk (>20%)**: YES – Medication

QUESTION:
What if I am at moderate risk of fracture?
Decision for Moderate risk patients:

Factors that warrant consideration for medications

**Fracture**
- Finding of unknown spine fracture on xray
- Wrist fracture in those either > 65yrs or with T-score ≤-2.5

**BMD**
- Spine T-score much lower than femoral neck T-score
- Rapid bone loss

**Medications**
- Long-term or repeated systemic glucocorticoid use not meeting conventional criteria* for prolonged use
- Other medications associated with bone loss or osteoporosis (eg. aromatase-inhibitors)

**Other**
- High risk for falls (≥ 2 falls in the past 12 months)
- Disorders strongly associated with osteoporosis, rapid bone loss or fractures

Repeat BMD in 1-3 years and reassess risk

No

Yes

Consider treatment
Always consider patient preference

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QUESTION:
How effective are osteoporosis medications?
What about side effects?
RANK Ligand

Denosumab
RANK Ligand Inhibitor

Raloxifene
Estrogen
Reduce RANK Ligand

Bisphosphonates
bind to bone
inhibit osteoclasts

Teriparatide
PTH Analog

Pre-Osteoclasts → Active Osteoclasts → Mononuclear Cells → Pre-Osteoblasts → Osteoblasts → Osteocytes

Resting Bone Surface → Resorption → Reversal → Bone Formation → Mineralization
## Osteoporosis Medication Options

<table>
<thead>
<tr>
<th><strong>Anti-Resorptive (Inhibits Bone Loss)</strong></th>
<th><strong>Anabolic Agent (Bone Forming)</strong></th>
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</thead>
<tbody>
<tr>
<td>Bisphosphonates</td>
<td>Teriparatide (FORTEO)</td>
</tr>
<tr>
<td>- Alendronate (Fosamax)</td>
<td></td>
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<tr>
<td>- Risedronate (Actonel)</td>
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<tr>
<td>- Zoledronic Acid (Aclasta)</td>
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<tr>
<td>Denosumab (Prolia)</td>
<td></td>
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<tr>
<td>Raloxifene (Evista)</td>
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<tr>
<td>Hormone Therapy (Estrogen)</td>
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</table>

What are the BENEFITS of Medications?

- Reduce risk of fracture by about 50%
- Improve or stabilize bone density
- HIGH risk patients benefit the most
What are the RISKS of Medications?

- No medication is absolutely safe
- All drugs have side effects
- Safe means that benefits of drug therapy outweigh the risks for a person
- Rare concerning risks:
  - Osteonecrosis of the Jaw (ONJ)
  - Atypical Femur Fracture (AFF)
# Bisphosphonates – Side Effects:

<table>
<thead>
<tr>
<th>Category</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Gastrointestinal:</strong></td>
<td>- Only with ORAL bisphosphonates</td>
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<tr>
<td></td>
<td>- local irritation to the mucosa</td>
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<tr>
<td></td>
<td>- occurs on the day the dose is taken</td>
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<td></td>
<td>- monitor for heartburn</td>
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<tr>
<td><strong>MSK</strong></td>
<td>- muscle, bone, joint aches/pains</td>
</tr>
<tr>
<td><strong>Acute-Phase reaction</strong></td>
<td>- IV bisphosphonates</td>
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<tr>
<td></td>
<td>- for ~3-4 days</td>
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<tr>
<td></td>
<td>- fever, muscle/joint aches, tiredness</td>
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</tbody>
</table>
Denosumab (Prolia): Side Effects

MSK
- Muscle, joint/bone aches & pain
- ~ for up to 3-4 days after dose

Skin
-itching, redness, dryness, eczema
- Infection (cellulitis)

Hypocalcemia
- If inadequate vitamin D or calcium level
Osteonecrosis of the Jaw (ONJ)

• Exposed bone in jaw area for 8 weeks or longer in absence of radiation therapy
• >90% cases in cancer patients on high dose iv bisphosphonates or high dose denosumab
• Very rare: 1-90 per 100,000 patient-years exposure
• Mechanism unclear
• Accumulative dose effect
• Associated with invasive dental surgeries, poor dental hygiene and dental infection

Atypical Femur Fracture (AFF)

- Unusual fracture of femur shaft below hip joint
- No trauma or minimal trauma
- Complete or incomplete
- Rare: 1 to 78 cases in 100,000 patient-years exposure
- Long duration bisphosphonate
- Reports with denosumab
- Unclear mechanism
- Prodromal thigh pain
- Up to 60% occur both femurs

Shane E et al, JBMR 2014; 29: 1-23
Figure 1. Risks of major osteoporotic fracture and other rare events

- Bis-ONJ*: 1.03
- Bis-AFF (8 y): 78
- Bis-AFF (2 y): 2
- Death by murder*: 1.62
- Fatal MVA*: 8.4
- Major osteoporotic fracture in low-risk women: 650
- Major osteoporotic fracture in moderate-risk women: 1600
- Major osteoporotic fracture in high-risk women: 3100


Data from Khan et al* (Canadian data).
Data from Dell et al** (American data).
Data from Statistics Canada*** (Canadian data).
Data from Transport Canada**** (Canadian data).
QUESTION:

What are the factors associated with non-adherence to osteoporosis medications?
Non-Adherence to Medications:

“Drugs don’t work… if you don’t take them”

FACTORS:
- Side effects, fear
- Inconvenience of regimen
- Self-perceived risk
- Relationship with healthcare provider & communication style
Effect of Adherence on Fracture Rate

<50% marginal benefit

>75%

Rare Risks & Media Concerns

- creates patient fear, anxiety, doubt, mistrust, confusion

“Perspective, not Panic”
Neil Andrews
managing Editor, IBMS BoneKEy
Resources:

• Osteoporosis Canada: www.osteoporosis.ca
  – NEWS: Position Statements
• National Osteoporosis Foundation (NOF): www.nof.org
• International Osteoporosis Foundation (IOF): www.iofbonehealth.org
• ASBMR Task Force Publications: ONJ, AFF
• Health Canada Drug Advisory Notices
QUESTION:

What is the optimal duration of treatment on OP medications?

What is a drug holiday?
Bisphosphonate
How long to treat?

• Proven anti-fracture efficacy
  ▪ Therapy for 3-5 yrs in large trials reduced vertebral, non-vertebral and hip fractures

• Unclear optimal duration beyond 5 years
  ▪ Long retention of drug in bones after stopping
  ▪ Safety concerns with long-term use with rare but concerning risks (ONJ, AFF)
Drug Holiday Concept

- Interruption of bisphosphonate therapy (drug hiatus)
  - May minimize prolonged drug exposure and reduce risk of adverse events while still maintaining some degree of anti-fracture benefit from residual anti-resorptive effect of retained drug

- Unique to bisphosphonates

- Data to support concept is from extension trials (bisphosphonate treatment extended for 10 years)

- Does NOT apply to denosumab, SERMS, estrogen
Approach to Duration of Bisphosphonate Treatment

• Low risk → can stop treatment
• Moderate risk → consider drug holiday after 3-5 years
• High risk → likely to benefit from continued treatment especially if high risk fracture (spine/hip #) or multiple #s
  » Continue bisphosphonate
  » Switch to another class of agents

Individualize decision based on multiple risk factors, benefit to risk ratio and patient preference

How about Denosumab (Prolia)?

- Cannot apply drug holiday
- No skeletal retention once stop therapy:
  - Rapid bone loss
  - Rebound vertebral fractures
- Denosumab should **NOT** be stopped or delayed without considering alternative treatment to prevent rapid bone loss and potential rebound vertebral fractures

Tsourdi E et al, Bone 2017
Cummings S et al, JBMR 2017
QUESTION:
I’m afraid of the side effects of medications. Can I treat my osteoporosis naturally?
A Holistic Approach

Maintaining Healthy Bones

NUTRITION (Calcium & Vit D)

MEDICATION

EXERCISE

FALL PREVENTION
QUESTION:

How much calcium do I need and why is it important to get it from food?
All cells need Calcium to function

• If not enough calcium, the body takes calcium from the bone to meet daily cellular requirements

• Daily Ca requirement: 1000-1200mg for most adults (varies with other factors & comorbidities)

• Benefits of dietary calcium:
  - other nutritional value
  - absorption rate

• Some may need Ca supplements
  - may have side effects (constipation)
  - Interferences with other medications
  - absorption may not be ideal

• If excess calcium intake (by supplements) → increased urine calcium excretion → questioned concerns of vascular risks
All dairy products... cheese, yogurt, milk, ice cream

Dark green leafy vegetables contain calcium, i.e. broccoli, bok choy, kale

Sardines and canned salmon (with bones) provide a good source of calcium

Fortified foods – orange juice, soy, rice beverages
QUESTION:
Does vitamin D help to reduce falls and fractures?
How much vitamin D do I need?
• Vitamin D is needed for optimal Calcium absorption from the gut

• Plays important role in calcium balance, bone mineralization, and muscle function

• Deficiency or Inadequate vitamin D results in poor bone mineralization and bone loss due to rising parathyroid hormone

• Skin makes vitamin D from sun UV rays

• Only few natural dietary sources of vit D

• Vitamin D 800-2000 units daily is recommended for most individuals with osteoporosis or risk factors for fractures

• Neither vitamin D or Calcium *alone* are enough to prevent falls or osteoporotic fractures
Dietary sources of Vitamin D

- Salmon: 3 oz = 794 IU
- Fortified cereal: 1 cup = 40 IU
- Fortified milk: 1 cup = 120 IU
- Egg yolk: 40 IU
QUESTION:

Why is exercise important?
Goal of Exercise in OP

Improve posture
Decrease risk of falls
Minimize future fractures

Improve overall health
# Osteoporosis Exercise Guide

<table>
<thead>
<tr>
<th>Exercise</th>
<th>Frequency</th>
<th>Examples/Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Strength Training</td>
<td>≥ 2x/week</td>
<td>• Exercises for legs, arms, chest, shoulders, back</td>
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<tr>
<td></td>
<td></td>
<td>• Use body weight against gravity, bands, weights*</td>
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<td></td>
<td></td>
<td>• 8-12 repetitions maximum per exercise</td>
</tr>
<tr>
<td>Balance Training</td>
<td>~ 20mins daily</td>
<td>• <em>Standing still</em>: one-leg stand, semi-tandem stance, shift weight between heels and toes while standing</td>
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<tr>
<td></td>
<td></td>
<td>• <em>Dynamic movements</em>: Tai Chi, tandem walking, dancing</td>
</tr>
<tr>
<td>Aerobic physical activity</td>
<td>≥ 5x/week (30min/day)</td>
<td>• Do bouts of 10 min or more</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Accumulate ≥ 30 min per day</td>
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<tr>
<td></td>
<td></td>
<td>• Moderate- or vigorous-intensity*</td>
</tr>
<tr>
<td>Posture/ Back Extensor Training</td>
<td>5-10mins daily</td>
<td>• Lie face up on firm surface, knees bent, feet flat. Use pillow if head doesn’t reach floor. Do this 5-10 min/day</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Progress to supine lying with gentle head press, perform 3-5 seconds “holds”</td>
</tr>
<tr>
<td>Spine Sparing Strategies</td>
<td>During daily activities</td>
<td>• Modify activities that flex (bending forward) or twist the spine</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Teach the “hip hinge” and “step to turn” techniques</td>
</tr>
</tbody>
</table>
Summary

- Osteoporotic fractures are associated with reduced quality of life and risk of mortality
- Fracture risk assessment is important, not just BMD
- High risk patients benefit the most from medications
- Important to consider adherence, side effects, rare risks, duration of medication treatment
- Drug holiday only applies to bisphosphonates, cannot be applied to denosumab
- Holistic approach: nutrition, exercise and fall prevention
Thank you!

More Questions?
Other Questions:

• What about supplementation of other nutrients, especially vitamin K and magnesium?
• Does it matter if the medications are brand name or generic?