How much of our BMD is under our control (vs. genetics)?

Genetic effects on bone loss: longitudinal twin study (Makovey, 2007)

- Peak BMD is under genetic regulation.
- Is bone loss also under genetic regulation?
- Yes to some extent (~40%) for BMD in...
  - Lumbar spine
  - Total forearm
  - Whole body
- Not for BMD in the hip (any location)

Who should get a bone mineral density test?

Osteoporosis Self-Assessment Tool in ruling out low BMD (Rud, 2007)

- (self-reported wt. in kg – age in yrs) x 0.2
  - OST ≤ -4 = high risk → get BMD
  - OST between -3 to 1 = moderate risk → get BMD
  - OST > 2 = low risk

- Systematic review of 36 studies
  - Performed moderately in r/o out femoral neck T-score ≤ -2.5
  - Performed poorly in r/o lumbar spine T-score ≤ -2.5

- Who should get a BMD test?
  - OST <2, age 64+ w/ risk factor to ↓ number falsely classified as needing BMD
How should we define osteoporosis?

Disease Definitions: Osteoporosis (Herndon, 2007)
- Traditionally, a disease was something a pt experienced directly: e.g., hip fracture
  - Conditions historically considered risk factors now disease: e.g., osteoporosis.
- WHO: T-score < -2.5 = osteoporosis
- National Osteoporosis Foundation: Treat...
  - all women w/ BMD < -2.0
  - women w/ 1+ risk factor & BMD < -1.5

Comparison of prevalence of osteoporosis at different definitions, with 10-yr risk of hip fracture, for women 50+

Implications of expanding definitions of osteoporosis...
- ↑ number of people with the diagnosis
- New identified patients are at lower risk
- Potential benefit from treatment is smaller
- Risk of treatment is relatively constant

Perceived risk of osteoporosis (Reventlow, 2007)
- In-depth interviews of women in their 60s.
  - Women who perceive a current risk tend to reduce their physical activity to reduce risk of bone damage.
  - Knowledge of reduced BMD reinforced uncertainty about what bones could endure.
  - Experiences with physical activity without injury increased activity.
  - Recommendation: With BMD results, encourage weight-bearing physical activity.
Does low BMD = fx?

Low BMD & fx burden
(Cranney, 2007)

- 16,505 postmenopausal women 50+
- 756 fractures
- Fx rates higher among women 65+
- Fx rates higher among women w/ osteoporosis but most fx occurred in women w/o osteoporosis

Does current/former smoking = fx?

Smoking status as a predictor of hip fx risk (Jenkins, 2008)

- 190 women 50+ with osteoporotic hip fx, 298 unmatched controls
- Compared to non-smokers...
  - Former smokers ↑ risk 2.27 times
  - Current smokers ↑ risk 3.72 times
- Detrimental effects of smoking appears to persist beyond quitting

Can we predict hip fx in the next 5 years?

Factors associated with 5-yr risk of hip fx (Robbins, 2007)

- 93,676 women in the longitudinal Women’s Health Initiative → predictive algorithm
  - Algorithm validated by 68,132 women
  - Algorithm tested in 10,750 women w/ DXA
- 11 factors predicted 80% of the fx w/in 5-yrs
  - History of fracture after age 54 yrs
  - Parental hip fracture
  - Current smoking
  - Current corticosteroid use
  - Treated diabetes
  - Age
  - Self-reported health
  - Weight
  - Height
  - Race/ethnicity
  - Self-reported physical activity
What are the most current evidence-based recommendations for prevention & treatment of osteoporosis?


- Evidence-based recommendations
- Utilizes absolute fracture risk & 10-yr fx risk
- Enhance tx decisions for a specific patient.
- Adapted WHO algorithm estimates likelihood of a person to break a bone due to low bone mass or osteoporosis over a period of 10 years.
  - Cost effectiveness analysis
  - Includes BMD @ hip & 9 clinical risk factors


- Risk factors in the WHO Fracture Risk Assessment Model
  - Current age
  - Gender
  - Personal hx of fx
  - Femoral neck BMD
  - Low BMI (kg/m²)
  - Oral glucocorticoid use
  - 2nd osteoporosis (e.g., RA)
  - Parental hx of hip fx
  - Current smoking
  - Alcohol intake 3+/day


- Universal recommendations:
  - Get daily recommended amounts of calcium (1200mg) and vitamin D₃ (800-1000 IU).
  - Engage in regular weight-bearing & muscle-strengthening exercise.
  - Fall prevention
  - Avoid smoking & excessive alcohol.


- Women with low-energy fracture should be screened (Löfman, 2007)
  - 303 women 55+ with recent low-energy fx
  - Questionnaire on previous fx & risk factors
  - BMD measured at hip, L-spine, & forearm
  - Vertebral fx strongest marker of low BMD
  - As # of previous fx ↑, BMD ↓
  - Recommendation:
    - Any women 55+ with a low-energy fx should get BMD measured with highest priority to those with vertebral, hip, or multiple fxs.
High-trauma fx & low BMD
(Mackey, 2007)

- 8022 women followed 9 yrs (3475 fx) & 5995 men followed for 5 years (440 fx).
- Outcome measures:
  - Hip & spine BMD
  - Non-spine fx confirmed by radiograph report
  - Trauma classified at high or low
- Similar to low-trauma non-spine fx, high-trauma non-spine fx are associated with low BMD & ↑ risk of subsequent fx in older adults.
- Recommendation – Don’t limit screening to people following low trauma fx

If we have to wait a year (or 2) before repeating BMD testing to check the efficacy of treatment, is there a short-term method?

Biochemical markers to assess risk & tx efficacy (Abe, 2008)

- Biochemical markers for assessing level of bone resorption
  - Does urinary or serum NTX show better efficacy for assessing osteoporosis tx effects during the early phase of tx?
- 40 post menopausal women completed RPCT (tx was Actonel)
- There was a significant ↓ in urinary NTX @ 4 wks; serum NTX didn't show ↓ until 16 wks.

Biochemical markers to assess risk & tx efficacy (Abe, 2008)

- Implications:
  - If women know the treatment is working then it may improve persistence.
- Problems:
  - We still don't know the relationship between marker changes & BMD with therapy in order to determine the magnitude of decrease of a biochemical marker necessary to prevent bone loss or, more importantly, fracture.
  - We don't know if biochemical markers are useful for exercise interventions.

Chocolate consumption & bone density (Hodgson, 2008)

- 1001 randomly selected women age 70-85.
- Older women who consumed chocolate on a daily basis had lower BMD
- The estimated effect size is similar or greater in magnitude compared with other dietary factors such as calcium, protein, and tea.
- Mechanism is unclear but both coco & sugar stimulate urinary calcium excretion.

With regard to osteoporosis, are we what we eat?
Soy isoflavone intake & BMD in the spine (Ma, 2007)

- Meta-analysis of 10 studies with a total of 608 subjects.
- The spine BMD in subjects who consumed isoflavones significantly in comparison to that in subjects who did not.
- These favorable effects become greater when more than 90 mg/day of isoflavones are consumed.
- Soy isoflavone consumption for 6 months can be enough to exert beneficial effects on bone in menopausal women.
- Long term effects unknown.

Vitamin D

- Perez-Lopez (2007) Vitamin D for musculoskeletal health
- Holick (2007) Vitamin D deficiency
- Conflict in the literature
  - Vitamin D2 is just as good as D3
  - Vitamin D2 supplements can be harmful, because they suppress the immune system so that the body cannot fight disease & infection effectively

Vitamin D3 sources

- Cod liver oil, 1 Tsp = 1360 IU/serving
- Salmon, 3.5 oz = 360 IU/serving
- Mackerel, 3.5 oz = 345 IU/serving
- Tuna fish canned in oil, 3 oz = 200 IU/serving
- Sardines, drained, 1.75 oz = 250 IU/serving
- Fortified milk, 1 cup = 98 IU/serving
- Fortified ready-to-eat cereals, 1 c = 40 IU/serving
- 1 whole egg = 20 IU/serving

Anything new regarding drugs to manage osteoporosis?

- Once-yearly zoledronic acid (Black, 2007)
  - Double-blind, placebo-controlled trial
  - Infusion at baseline, at 12 months, and at 24 months with follow up at 36 months.
    - 3889 patients were randomly assigned to receive a single 15-minute infusion of zoledronic acid (5 mg)
    - 3876 were assigned to receive placebo
  - Outcome measures:
    - new vertebral fracture & hip fracture
    - BMD, bone turnover markers, and safety outcomes
Once-yearly zoledronic acid (Black, 2007)
- Reduced the risk of vertebral fracture by 70% during 3-year period, as compared with placebo
- Reduced the risk of hip fracture by 41%
- Zoledronic acid was also associated with a significant improvement in BMD and bone metabolism markers.
- Adverse events, including change in renal function, were similar in the 2 study groups.
- Serious atrial fibrillation occurred more frequently in the zoledronic acid group (in 50 vs. 20 patients, P<0.001).

Effect of weighted exercises on BMD (Zehnacker, 2007)
- Systematic review of 20 articles
- Evidence to support use of weighted exercise to ↑ BMD in post menopausal women to prevent or reduce osteoporosis effects.
- Therapeutic exercise should be...
  - Site-specific for hip, spine, & wrist
  - Intensity 75%-80% 1RM, w/ 8-12 reps,
  - Frequency 3 to 5 times/week
  - Duration of at least 45 minutes

What you need to know when you ask your patient about their last BMD?

Self-report of DXA (Cadarette, 2007)
- 871 Women age 65-90 years
  - 510 Women reporting having had a DXA were eligible and asked to report the results of their most recent test.
  - Participant responses were compared against DXA reports obtained from physicians.
- 81% of women who reported having had a DXA had one by physician records.
- Of these, the positive predictive value for self-report of having had a DXA was 93%.

Overall, the agreement between self-report & actual DXA results was poor.
  - 84% of those with normal bone reported this
  - 29% of those with osteopenia reported their results correctly
  - 62% of those with osteoporosis reported their results correctly.
  - Self-report of a clinical diagnosis of osteoporosis was better among those with a low trauma fracture, yet underestimated osteoporosis prevalence by 24%.
  - There is minimal measurement error in self-report of having had a DXA test. However self-report of DXA results is not a good proxy for clinical diagnosis.
So on what do we need to focus?

Shifting focus from osteoporosis to falls (Järvinen, 2008)

- Falling, not osteoporosis, is the strongest single risk factor for fxs in older adults
- BMD is a poor predictor of fx risk
- Drug tx is expensive & will not prevent most fractures in older adults
- RCTs show that falls can be reduced by 50%
- Assess fall risk

Thank you for listening