Preventing Fractures to Retain Quality of Life with Aging: Vitamin D, Calcium, Osteoporosis and Sarcopenia

“Bone Attacks and Their Prevention”

Neil Binkley, MD

April 29, 2014
Disclosure

Much of this is my opinion

Noted as such by orange font

“Bone Attack” is not (yet) a widely accepted concept
Summary

◆ Fractures (bone attacks) are NOT OK
◆ Get your bone density measured
◆ Aim for a calcium intake of ~1,000-1,200 mg/day
  ● This **can** be obtained from diet
◆ Take at least 1,000 IU of vitamin D₃ daily
  ● This **cannot** be obtained from diet
◆ You are going to hear more about sarcopenia
◆ Our protein intake is too low
◆ We need to exercise more
◆ The current osteoporosis drugs work
  ● They are not poisons
~80% of Americans Who Break Their Hip Receive NO Treatment to Reduce Their Risk for Future Fracture (and it’s getting worse)

Broken Bones (Osteoporotic Fractures) Should be Thought of as “Bone Attacks”
We Need to Improve Understanding That Fractures Indicate Disease (Just Like Heart Attacks Indicate Disease)

“I had a heart attack climbing stairs. I have high cholesterol and blockages in the arteries to my heart.”

“I broke my _____ falling down the stairs. It was an accident; anyone would have fractured if they fell like I did.”
“So I fell and broke a bone; what’s the big deal?”
Aunt Edna: Having Fractures is Not OK...

In her 50’s

In her 70’s
Bone Attacks Reduce Quantity and Quality of Life

**Why should you be concerned?**

The consequences of a fracture due to osteoporosis can be extremely serious:

- Chronic pain, immobility, and long-term disability – often leading to loss of independence and reduced quality of life.

Twenty to twenty-four per cent of people who have had a hip fracture will die in the first year following the fracture, and many other fracture types are also associated with an increased risk of death.

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Hip fracture survivors often experience loss of function and independence, with 40% unable to walk independently and 60% requiring assistance a year later. In the year following a hip fracture, 33% are in a nursing home or totally dependent, placing a significant burden on family members who may have to become caregivers for their loved ones.

www.share.iofbonehealth.org/WOD/2012
Fractures Cause Dependency
Independence is a Big Deal!

Telephone survey of ~800 older adults in 2007

- What do you fear most?
  - Loss of independence: 26%
  - Moving out of home into nursing home: 13%
  - Giving up driving: 11%
  - Loss of family/friends: 11%
  - Death: 3%

Consequences of Bone Attacks

◆ Dependency
  ● Reduced ability to perform activities of daily living
  ● Only ~40-50% are able to live independently after a hip fracture
◆ Pain; acute and/or chronic
◆ Change in body habitus
◆ Respiratory compromise
◆ Depression/anxiety/fear of falling
◆ Cost ~$13 billion annually
◆ Death; ~20% one year mortality following hip fracture
If You Have Had a Bone Attack, Ask Why Did I Have This? and What Should Be Done?

The Occurrence of a Fracture Identifies the Person as Being at Risk For Another (IT’S NOT JUST “I FELL”)

Bone Attacks Require Evaluation and Often Need Measures to Reduce the Risk For Another
One is Enough
(It’s actually one too many.....)

Every year
There are 2 million bone breaks
That are no accident.

Stop at one
Make your first break your last

www.2million2many.org/

Fractures are warning signs
Almost half of the patients who are treated in hospital for a hip fracture have had a previous fracture of some kind.

That first fracture was a warning sign! It should have resulted in immediate screening and, if indicated, management and treatment for osteoporosis.

Sadly, the reality is that most hospitals and clinics fail to ‘capture’ that first fracture – leaving patients open to a future of suffering and debility. Over 80% of fracture patients are never offered screening and/or treatment for osteoporosis, despite the fact that there are effective medications that can reduce fracture risk by as much as 30–70%.

www.share.iofbonehealth.org/WOD/2012
2/3 of Spine Bone Attacks are “Silent”
Spine Imaging is Needed for Those With Height Loss of ≥ 1.5

“VFA”
“Why don’t we get bone attacks when we are younger?”

With advancing age we are more likely to have both osteoporosis and sarcopenia

“What is osteoporosis?
Osteoporosis: A systemic skeletal disease characterized by low bone mass and microarchitectural deterioration of bone tissue, resulting in increased bone fragility and susceptibility to fracture.
What Causes Osteoporosis?
Usually it is Not Just One Thing

- Low bone mass at skeletal maturity (~ age 30)
- Advanced age
- Low calcium and/or vitamin D intake
- Use of prednisone (corticosteroids)
- Smoking/High alcohol consumption
- Lower body weight
- Low physical activity
- Loss of estrogen/testosterone

These ultimately lead to bone remodeling imbalance
Due to Remodeling Imbalance, Bone Density Declines with Advancing Age

This decline contributes to the increased risk for bone attacks, most commonly of the spine/hip/wrist.
How Common Are Bone Attacks (Osteoporosis-related Fractures?)

Women ~40%

Men ~25%
How can I know if I have osteoporosis?”
Get a Bone Density Test

- Risk factors do not work to guess bone density
  - Advanced age
  - Female gender
  - Caucasian race
  - Thin
  - Family history of osteoporosis
  - Etc, etc.

Radiation Exposure:
- DXA ~ 3 uSV
- Daily Background ~8-10 uSV
You Want to Know Your T-score

WHO Diagnostic Classification

Normal

Osteopenia

Osteoporosis

Severe Osteoporosis

-2.5

IF you have osteoporosis some routine laboratory testing is needed
“Osteoporosis” Clinicians Have Historically Focused on the Bone

Focus on the Individual’s Fracture Risk
FRAX®: The WHO Fracture Risk Assessment Tool

www.shef.ac.uk/frax
Please answer the questions below to calculate the ten year probability of fracture with BMD.

**Questionnaire:**

1. Age (between 40-90 years) or Date of birth
   - Age: 72
   - Date of birth: Y: [ ] M: [ ] D: [ ]

2. Sex
   - Male
   - Female

3. Weight (kg) 65.77
4. Height (cm) 165.1

5. Previous fracture
   - No
   - Yes

6. Parent fractured hip
   - No
   - Yes

7. Current smoking
   - No
   - Yes

8. Glucocorticoids
   - No
   - Yes

9. Rheumatoid arthritis
   - No
   - Yes

10. Secondary osteoporosis
    - No
    - Yes

11. Alcohol 3 or more units per day
    - No
    - Yes

12. Femoral neck BMD (g/cm²)
    - T-Score: -2.2

**BMI 24.1**

The ten year probability of fracture (%)

- Major osteoporotic: 22
- Hip fracture: 9.2

**Weight Conversion**

- Pounds: 145
- Kgs: [Convert]

**Height Conversion**

- Inches: 65
- Cms: [Convert]
How can I know if I have sarcopenia?”

Sarc for flesh (muscle), penia for deficiency

Term coined in 1989; recently defined as: “The age-associated loss of skeletal muscle mass and function… a complex syndrome associated with muscle mass loss alone or in conjunction with increased fat mass.”

Fielding, et. al, J Am Med Dir Assoc 2011; 12: 249-256
Sarcopenia Increases Risk of Falling

- Falls become common with advancing age
  - ~1/3rd of adults age 65 and >40% over age 75 fall each year

- Many osteoporosis-related fractures due to falls
  - Over 90% of hip fractures due to falls
  - ~6% of US medical expenditures for older adults due to fall-related injury

Guideline for falls prevention; AGS/BGS, JAGS 49:664-672, 2001
Bone Attacks Occur Due to:
Loss of Bone Mass/Strength AND
Loss of Muscle Mass/Strength as We Age

As a Result, We Fall Down on Weak Bones and They Break
“How can I reduce my risk of bone attacks?”
Exercise Works

- Improves muscle strength
- Preferably resistance training
  - This works; strength gains of 30% to >100% rapidly
- Injuries not common but do occur
- May require supervision (PT)

- But, we don’t exercise….
  - Only 32% of 23,153 adults age 35-65 years exercise for ≥ 3.5 hours per week  
    Ford, et. al., Arch Intern Med, 169;1355-1362, 2009
  - ~12% of people age 65-74 and 10% of those ≥ 75 perform strength training exercise two or more days/week  
    MMWR, 53;25-28, 2004
**Watching TV is THE Leisure Activity of Adults Age 55+**

Table 28b. Average number of hours and percentage of total leisure time that people age 55 and over spent doing selected leisure activities on an average day, by age group, 2010

<table>
<thead>
<tr>
<th>Selected leisure activities</th>
<th>55–64</th>
<th>65–74</th>
<th>75 and over</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Average hours per day</td>
<td>Percent of leisure time</td>
<td>Average hours per day</td>
</tr>
<tr>
<td>Socializing and communicating</td>
<td>0.6</td>
<td>11.3</td>
<td>0.7</td>
</tr>
<tr>
<td>Watching TV</td>
<td>3.0</td>
<td>57.8</td>
<td>3.8</td>
</tr>
<tr>
<td>Participation in sports, exercise, and recreation</td>
<td>0.3</td>
<td>4.9</td>
<td>0.3</td>
</tr>
<tr>
<td>Relaxing and thinking</td>
<td>0.3</td>
<td>5.2</td>
<td>0.5</td>
</tr>
<tr>
<td>Reading</td>
<td>0.4</td>
<td>7.1</td>
<td>0.6</td>
</tr>
<tr>
<td>Other leisure activities</td>
<td>0.7</td>
<td>13.7</td>
<td>0.8</td>
</tr>
</tbody>
</table>

http://www.agingstats.gov/agingstatsdotnet/Main_Site/Data/2012_Documents/Docs/EntireChartbook.pdf#page=140

**Need Cultural Change Towards Exercise**
LIFE: Lifestyle-integrated Functional Exercise Program

“LIFE; a new approach – turning everyday activities into opportunities to improve your balance and strength and prevent falls”

“As well as preventing falls, other benefits of improving your balance and strength are:”

- Your walking will improve
- You will feel better
- You will have more energy
- You will find it easier to do the household chores
- You will stay independent”

LIFE: Lifestyle-integrated Functional Exercise Program (Examples)

Activity - Tandem stand (Balance)

Instructions:
- The heel of one foot is directly in front of the toe of the other
- Swap the foot that is in the front
- Use support from your hands as needed
- To be safe make sure that you have support readily available
- To make it more challenging use less support from your hands.

Correct foot placement for tandem stand

Ideas for including Tandem Stand into your daily activities
- At the kitchen bench while waiting for the kettle to boil
- At the bathroom sink while cleaning your teeth
- While on the telephone.

Activity – One leg stand (Balance)

Instructions:
- Stand on one leg
- The position of the other leg can be varied
- Support can be from hands, finger tips, trunk or the other foot
- Support can vary depending on what you are doing
- Use support as needed from:
  - Hands,
  - Tummy or hips
  - Knees.

Ideas for Including One Leg Stand into your daily activities
- While making your lunch
- While heating food in the microwave
- When you clean your teeth
- In the queue at the supermarket.

To be safe make sure that you have support readily available.
To make it more challenging use less support from your hands.

Mark Twain Had It Wrong.....

“Whenever I get the urge to exercise, I lie down until the feeling passes away.”

DO SOMETHING.....
Should I take calcium and/or vitamin D supplements (or other supplements) to reduce my risk for fractures?

People Are Supposed to Eat Food
It is Reasonable to Consider the Ancestral Human (Paleolithic) Diet

Frassetto, et. al., Eur J Clin Nutr 2009: 63; 947-955
Paleolithic period ~2.5 million to ~10,000 years ago
  - Humans began to cultivate plants and domesticate animals

Hunter-gatherer diet consisted of:
  - Animal source foods
    - Lean meats, organs, bone marrow
  - Uncultivated plants
    - Fruits, nongrains, vegetables, nuts
  - “Paleo” diet for this study included honey, eggs, pineapple, lettuce, celery, tomatoes, almonds, tuna, turkey, pork, chicken, oranges

Average “Paleo” calcium intake 800 mg/day ± 400 mg/day

Frassetto, et. al., Eur J Clin Nutr 2009: 63; 947-955
Calcium supplements may boost heart attack risk

Vascular events in healthy older women receiving calcium supplementation: randomised controlled trial

Mark J Bolland, research fellow, P Alan Barber, senior lecturer, Robert N Doughty, associate professor, Barbara Mason, research officer, Anne Home, research fellow, Ruth Ames, research officer, Gregory D Gamble, research fellow, Andrew Grey, associate professor, Ian R Reid, professor

The following lessons have come from this review: True placebo-controlled randomization in a trial of a single, readily available nutrient such as calcium is often difficult to achieve. Compliance with study parameters must be maintained, probably to levels well above 80% to provide confidence in a verifiable outcome, and it is important to monitor the intake of other dietary nutrients that might alter calcium effects. Clear, definable adjudicated endpoints must be utilized. The most appropriate and stringent methods of statistical analysis must be applied. Based on these criteria, the weight of evidence is insufficient to conclude that calcium supplements cause adverse cardiovascular events; however, the debate continues.
“Never go to excess, but let moderation be your guide.”

Aim For ~1,000 mg/day

Marcus Cicero
(Roman philosopher and Statesman; 106-43 BC)
Calcium Summary

◆ Aim for 1000-1200 mg/day
  ● Close to the “Paleo” diet
  ● It is possible to get too much of anything; the jury is still out regarding vascular events
  ● One “serving” is ~250 mg

◆ There is no “best” calcium supplement
  ● Don’t spend $$$$ 

◆ If supplements are needed they should be taken with a meal
How much vitamin D do I need?
Vitamin D Historically Came From Sun Exposure

UVB (~280-315 nm) Produces Vitamin D

Vitamin D3

7-DHC

Pre D3

UVB

Holick, Ann NY Acad Sci, 435:1-13, 1985
Human D-volution?

Because we no longer live outside, vitamin D inadequacy is common

Vieth, AJCN, 2000
No Skin Production of Vitamin D in Wisconsin from November Through February

There is essentially zero skin synthesis in Boston (lat 42.3° N) from Nov thru Feb

Chen, 1998
Vitamin D is Rare in Foods; as a Result, Mean US Intake is Low At All Ages

**Food** | **IU**
--- | ---
Cod Liver Oil, 1 Tbs | 1360
Salmon, 3.5 oz | 360
Mackerel, 3.5 oz | 345
Milk, 1 cup | 100
Fortified cereal, 3/4 cup | 50
Liver, 3.5 oz | 30
Egg, one whole | 25

Data from NHANES III mean D intake from food + supplements

Moore, J Am Diet Assoc, 2004
Due to Little Sun Exposure and Low Amounts in Food, Many People Do Not Have Adequate Vitamin D

“I’m so confused by all of the stuff that I see in the news about vitamin D.”

April 25, 2014: 1551 vitamin D related papers in the medical literature (over 12/day)
<table>
<thead>
<tr>
<th>Respected Groups Have Differing Daily Intake Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Ministry of Health</strong></td>
</tr>
<tr>
<td>Nutrient Reference Values for Australia and New Zealand</td>
</tr>
<tr>
<td><strong>200-600 IU</strong></td>
</tr>
<tr>
<td><strong>CPME</strong></td>
</tr>
<tr>
<td>Comité Permanent des Médecins Européens Standing Committee of European Doctors</td>
</tr>
<tr>
<td><strong>600-800 IU</strong></td>
</tr>
<tr>
<td><strong>INSTITUTE OF MEDICINE</strong></td>
</tr>
<tr>
<td>Of the National Academies</td>
</tr>
<tr>
<td>Food and Nutrition Board</td>
</tr>
<tr>
<td><strong>600-800 IU</strong></td>
</tr>
<tr>
<td><strong>International Osteoporosis Foundation</strong></td>
</tr>
<tr>
<td><strong>800-1,000 IU</strong></td>
</tr>
<tr>
<td><strong>The Endocrine Society®</strong></td>
</tr>
<tr>
<td><strong>1,500-2,000 IU</strong></td>
</tr>
</tbody>
</table>
The USPSTF recommends exercise or physical therapy and vitamin D supplementation to prevent falls in community-dwelling adults aged 65 years or older who are at increased risk for falls.

The USPSTF recommends against daily supplementation with 400 IU or less of vitamin D₃ and 1,000 mg or less of calcium for the primary prevention of fractures in non-institutionalized postmenopausal women.

http://www.uspreventiveservicestaskforce.org/uspstf/uspsfalls.htm
http://www.uspreventiveservicestaskforce.org/uspstf/uspsvitd.htm
How Can People NOT be Confused...
Remember the Obvious:
We Are Not All The Same....
# The 2011 Report on Dietary Reference Intakes for Calcium and Vitamin D from the Institute of Medicine: What Clinicians Need to Know

A. Catharine Ross, JoAnn E. Manson, Steven A. Abrams, John F. Aloia, Patsy M. Brannon, Steven K. Clinton, Ramon A. Durazo-Arvizu, J. Christopher Gallagher, Richard L. Gallo, Glenville Jones, Christopher S. Kovacs, Susan T. Mayne, Clifford J. Rosen, and Sue A. Shapses

## TABLE 1. Calcium and vitamin D dietary reference intakes by life stage

<table>
<thead>
<tr>
<th>Life-stage group (age and gender)</th>
<th>Calcium RDA (mg/d) (intake that covers needs of ≥97.5% of population)</th>
<th>UL (mg/d)</th>
<th>Vitamin D RDA (IU/d) (intake that covers needs of ≥97.5% of population)</th>
<th>Serum 25OHD level (ng/ml) (corresponding to the RDA)</th>
<th>UL (IU/d)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1–3 yr (M+F)</td>
<td>700</td>
<td>2500</td>
<td>600</td>
<td>20</td>
<td>2500</td>
</tr>
<tr>
<td>4–8 yr (M+F)</td>
<td>1000</td>
<td>2500</td>
<td>600</td>
<td>20</td>
<td>3000</td>
</tr>
<tr>
<td>9–13 yr (M+F)</td>
<td>1300</td>
<td>3000</td>
<td>600</td>
<td>20</td>
<td>4000</td>
</tr>
<tr>
<td>14–18 yr (M+F)</td>
<td>1300</td>
<td>3000</td>
<td>600</td>
<td>20</td>
<td>4000</td>
</tr>
<tr>
<td>19–30 yr (M+F)</td>
<td>1000</td>
<td>2500</td>
<td>600</td>
<td>20</td>
<td>4000</td>
</tr>
<tr>
<td>31–50 yr (M+F)</td>
<td>1000</td>
<td>2500</td>
<td>600</td>
<td>20</td>
<td>4000</td>
</tr>
<tr>
<td>51–70 yr (M)</td>
<td>1000</td>
<td>2000</td>
<td>600</td>
<td>20</td>
<td>4000</td>
</tr>
<tr>
<td>51–70 yr (F)</td>
<td>1200</td>
<td>2000</td>
<td>600</td>
<td>20</td>
<td>4000</td>
</tr>
<tr>
<td>71+ yr (M+F)</td>
<td>1200</td>
<td>2000</td>
<td>800</td>
<td>20</td>
<td>4000</td>
</tr>
<tr>
<td>Pregnant or lactating (F)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>14–18 yr</td>
<td>1300</td>
<td>3000</td>
<td>600</td>
<td>20</td>
<td>4000</td>
</tr>
<tr>
<td>19–50 yr</td>
<td>1000</td>
<td>2500</td>
<td>600</td>
<td>20</td>
<td>4000</td>
</tr>
<tr>
<td>Infants</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0–6 months (M+F)</td>
<td>200</td>
<td>1000</td>
<td>400</td>
<td>20</td>
<td>1000</td>
</tr>
<tr>
<td>6–12 months (M+F)</td>
<td>260</td>
<td>1500</td>
<td>400</td>
<td>20</td>
<td>1500</td>
</tr>
</tbody>
</table>
“...as Lombardi began his junior year at Fordham, (1935)... Leading scholars feared that universities were deteriorating into incoherence, with an emphasis on uninterpreted fact instead of fundamental principle...”
Fundamental Principle Regarding Vitamin D

“I suggest that the 25(OH)D levels in the lifeguards are normal.”

Hollis, J Nutr, 135:317-325, 2005

IF we use highly sun exposed people to define a goal 25(OH)D concentration what is our target?
“We studied two traditional tribes. Both live 2-4° south of the equator in Tanzania, have skin type VI and neither uses sunscreen.”

Practically Every Human Disease Has Been Associated with Low Vitamin D

- Osteomalacia/Osteoporosis
- Muscle function and falls
- Cancer
- Multiple sclerosis
- Hypertension
- Diabetes mellitus
- Inflammatory bowel disease
- Rheumatoid arthritis
- TB
- Macular degeneration
- Cognitive impairment
- Cardiovascular events

- Peripheral vascular disease
- Polymyalgia rheumatica
- Chronic pain
- Autism
- Infection
- Athletic performance
- Depression
- Seasonal affective disorder
- Obesity
- Incontinence
- Aging
- Overall mortality
When Something Sounds Too Good to be True, it IS too Good to Be True...

Can Vitamin D Help Prevent Swine Flu and Other Diseases?
April 29, 2009 in Cold & Flu Prevention, Diabetes, Did You Know?, Educational, Empowering,

Vitamin D 'may help slow ageing'
A vitamin made when sunlight hits the skin could help slow down the ageing of cells and tissues, say researchers.
A King's College London study of more than 2,000 women found those with higher vitamin D levels showed fewer ageing-related changes in their DNA.
Vitamin D and Chronic Disease
Chicken or Egg?
Vitamin D Summary: April 2014

◆ Vitamin D inadequacy is common
  - Contributes to bone and muscle loss with age
◆ Fixing this is cheap and virtually side effect free
  - A “one size fits all” dosing approach does not work
◆ 1000 IU of vitamin D₃ daily is a reasonable starting point
  ● Humans make D₃ (not D₂) in our skin
◆ A 25(OH)D blood test is required to know what your vitamin D level is
  - 25(OH)D test if osteoporosis, falls history or prior bone attack
◆ Vitamin D is NOT the fountain of youth
“What about other supplements?”

- All-New
- All-Natural
- Non-Prescription
- Non-Drug Bone-Health Breakthrough

“XXX is not a drug. XXX is a dietary supplement and is not intended to be used as a substitute for any disease treatment, including drugs used for the treatment of osteoporosis.”

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Recommendation to restrict the use of Protelos / Osseor (strontium ranelate)

Press release

26/04/2013

Recommendation to restrict the use of Protelos / Osseor (strontium ranelate)

CHMP confirms recommendation from the PRAC

The European Medicines Agency’s (EMA’s) Committee for Medicinal Products for Human Use (CHMP) has recommended a restriction in the use of the osteoporosis medicine Protelos / Osseor, following an assessment of data showing an increased risk of serious heart problems. The CHMP recommended that Protelos / Osseor should only be used to treat severe osteoporosis in postmenopausal women at high risk of fracture and severe osteoporosis in men at increased risk of fracture. Additional measures, including restrictions in patients with heart or circulatory problems, were also recommended to minimise the heart risks of these medicines.
We Need More Protein To Preserve Muscle Mass and Function

1.2 grams/kg = ~54 grams/100 pounds
190 # = ~100 grams…
What Does This Look Like?
Protein Content of Some Foods

- Chicken breast; 3.5 oz = 30 g
- Chicken drumstick = 11 g
- Fish; 3.5 oz = 22 g
- Tuna; 6 oz can = 40 g
- Ham; 3 oz = 19 g
- Egg; large = 6 g
- Milk; 1 cup = 8 g
- Tofu; 1/2 cup = 20 g
- Beans; 1/2 cup = ~7-10 g
- Nuts; 1/4 cup = ~5-9 g
- Cottage cheese; ½ cup = 13 g
Potential Medical Approaches to Treat Sarcopenia and Thereby Improve Muscle Mass and Function are Coming

- Anabolic steroids
- Selective androgen receptor agonists
- Myostatin antagonists
- Others…. 

[Red circle with line through muscle image]
Should Men With Osteoporosis Receive Testosterone Therapy?? No

- ADAM Questionnaire (Androgen Deficiency in the Aging Male)
  - Do you have a decrease in libido?
  - Do you have a lack of energy?
  - Do you have a decrease in strength and/or endurance?
  - Are you falling asleep after dinner?
  - Are you grumpy?

“Additional large-scale research is needed to provide the data necessary to determine the safety and efficacy of hormone replacement with age and to elucidate what its influence is on functional performance, enhanced health span and longevity.”

Myostatin Antagonists?

- Secreted protein inhibits muscle differentiation & growth
- Animals genetically lacking myostatin (mice, cows and dogs) and humans have been reported to have high muscle mass
- Preliminary human studies report ~5% increase in muscle mass within one month
Medications To Treat Sarcopenia Do Not Exist (Yet)

In Addition to Exercise and Optimization of Nutrition, Osteoporosis Medications Are Often Recommended for People at Risk for Bone Attacks
“But I have heard so much bad about osteoporosis medications....”
Long-term use of osteoporosis drugs linked to hip breaks

Updated 3/10/2010 7:16 PM | Comment | Recommend

present today at the annual conference of American Academy of Orthopedic Surgeons in New Orleans was designed to explore why one in 50 women who got fractures and were on the drugs for more than five years suffered atypical hip fractures of the femur.

“These are healthy active women, not women in nursing homes,” Lane says. “Hip fractures can be life-threatening, so we want to find out what’s causing them in thriving women.”

Fosamax Scare: Those With Osteopenia Gauge Risk

FDA to Look for Link Between Femur Fractures and Bone-Loss Drugs After ABC Reports

Twice doctors have prescribed medications for Jeanette McLearcen with great certainty, only to second-guess the outcomes. After taking hormone replacement for 15 years, the Warren, Mich., retiree was diagnosed with breast cancer. And now, after seven years of taking the controversial drug Fosamax, she is terrified of bone fractures. Just this week, ABC's Dr. Richard Besser reported that Fosamax, one of a class of bisphosphonates used to treat osteoporosis that is

Fosamax Linked to Unusual Femur Fractures

Osteoporosis drug also linked to bone pain and irregular heartbeats in past research
Some of it is the Reporting of Bad News

“Touting rare side effects of medications and bashing pharmaceutical companies has become a popular media pastime that strikes fear and distrust in the hearts of patients, but is not good science and does not contribute to good patient care.”


"Acetaminophen is one of the most commonly used medicines in the United States. When used according to the label directions, it has a well-established record of safety and efficacy."

http://www.fda.gov/Drugs/DrugSafety/SafeUseInitiative/ucm230396.htm
“In seeking truth you have to get both sides of a story.”

Walter Cronkite
“No drug is absolutely safe; all drugs have side effects. Safe in this sense means that the benefits of the drug appear to outweigh the risks.”


Risk vs. Benefit Needs to be Considered
Risk vs. Benefit Needs to be Assessed On An Individual Basis
How do current osteoporosis medications work?

- Anti-resorptive
- Anabolic
- Alter quality
- Extra-skeletal e.g. reduce falls
Current Osteoporosis Medications

- Estrogen
- Raloxifene (Evista)
- Calcitonin (Miacalcin)
- Bisphosphonates
  - Alendronate (Fosamax)
  - Risedronate (Actonel)
  - Ibandronate (Boniva)
  - Zoledronate (Reclast)
- Teriparatide (Forteo)
- Denosumab (Prolia)

These medications work; they cut fracture risk approximately in half.
Osteonecrosis of the Jaw is Exceptionally Rare

An uncommon disease of bare alveolar bone in the absence of local malignancy or radiation therapy

Risk ~1-10/100,000 people
Atypical Femur Fractures, 2014

A type of bisphosphonate drug, Fosamax, was introduced to the U.S. market in 1995. By 2008, the Journal of Orthopedic Trauma had linked Fosamax to a high incidence of low-energy femur fractures. Some people who were taking Fosamax suffered broken femurs while doing nothing more than walking, stepping off a curb or climbing stairs. Research has indicated that Fosamax can increase the likelihood of suffering a broken femur by 125 percent.

- More likely to be caused by osteoporosis than by bisphosphonates
  
  “Many more common and equally devastating hip fractures are prevented by bisphosphonates than are potentially caused by the drugs.” Shane, NEJM, 2010

- Risk increases with treatment duration
  
  - Often preceded by leg/groin/hip pain
  - Because of this, many are recommending holidays

Shane, NEJM, 10.1056, 2010
Bakata, ISCD/NOF meeting, 2010
Atypical Femoral Fracture Risk Goes Up With Long Duration Treatment

- 1.8 million Kaiser Permanente enrollees ≥ 45 years of age
- 142 femur fractures met ASBMR criteria for AFF
  - 128 (90%) had previous BP exposure
  - 14 (10%) no prior BP exposure

Adapted from Dell RM, J Bone Miner Res, 2012;27:2544-50
Important to Balance the Risks of No Therapy With the Expected Benefits and Possible Risks of Therapy

**Benefits**
- Decreased fractures
- Decreased mortality
- Maintained QOL

**Risks**
- Atypical femur fractures
- ONJ
- Others very rare

77 year-old woman with two falls in the past year, two fractures since age 50 and a T-score of -2.0

Fracture risk in 5 years
- Any fracture ~41%
- Hip fracture ~25%

Side effect risk in 5 years
- AFF ~1/1000 (0.1%)
- ONJ ~1/20,000 (0.005%)
“There are risks and costs to a program of action. But they are far less than the long-range risks and costs of comfortable inaction.”

John F. Kennedy
(1917-1963)
Treating Osteoporosis is Like Wearing a Seat Belt

MVA Injuries and Deaths

<table>
<thead>
<tr>
<th>No Seat Belt</th>
<th>Seat Belt</th>
<th>Seat Belt Injuries</th>
</tr>
</thead>
<tbody>
<tr>
<td>100</td>
<td>50</td>
<td>50</td>
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</tbody>
</table>

Wearing seat belts reduces the risk of serious crash-related injuries and deaths by about 50%.

Osteoporotic Fractures

<table>
<thead>
<tr>
<th>Fractures Untreated</th>
<th>Fractures Treated</th>
<th>ONJ + AFF</th>
</tr>
</thead>
<tbody>
<tr>
<td>100</td>
<td>50</td>
<td>0</td>
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</tbody>
</table>

Treatment with bisphosphonates reduces the risk of fractures by about 50%.

There are about 2.3 million adults treated in ERs each year for injuries from MVAs and about 2 million osteoporotic fractures each year. The risk of seat belt injuries and serious side effects from osteoporosis treatment is very small in proportion to the benefits. Data from multiple sources.
Osteoporosis Treatment Conclusions 2014
(my opinion…)

- All medications have side effects
- Logical that concerns about side effects causes people to stop or refuse to start medications
  - This is leading to the occurrence of preventable fractures
- For virtually all of those in whom fracture reduction therapy is “indicated” by current guidelines, the risk of fracture far exceeds the risk of adverse effects
  - At least for the first five years
- Tools exist (e.g., FRAX and Garvan) that can help put a number to risk vs. benefits
What is the Future of Bone Attack Prevention?

- Calcium/vitamin D controversy will eventually be solved
  - You will see “vitamin D panels”
  - Controversy will continue regarding other micronutrients

- Critical roles of sarcopenia and EXERCISE in bone attack risk will become widely recognized
  - And potentially treated: ? Myostatin antagonists

- New bone medications will become available soon
  - Odanacatib is likely to be next
  - Antibodies to sclerostin (a protein that inhibits bone formation) are now in phase III trials
Bone Attacks; 2014 Summary

- ~50% of women and 25% of men will sustain an osteoporotic fracture in their lifetime; this is NOT OK…
- All women age > 65 and men > 70 should have their bone density measured
- Aim for 1,000 mg of calcium daily; ideally through diet
- 1,000-2,000 IU vitamin D daily is reasonable
  - Cannot guess your 25(OH)D level; need to measure
  - Vitamin D₃ is more potent than D₂
- Walk and/or do other exercise daily
- Currently available osteoporosis drugs work
  - Consider risks vs. benefits with healthcare provider
- Fractures are not OK
  - Are no more due to “getting old” than are heart attacks
Osteoporotic Fractures Should be Thought of as “Bone Attacks”
Thank You