Prevention and Treatment of osteoporosis and common side effects of treatments.

LECTURE 8

Why Worry about Osteoporosis and Bone Loss?

Osteoporosis is a disease of the bone that makes a person's bones weak and more likely to break.

Approximately 10 million Americans have osteoporosis and another 44 million have low bone density, placing them at increased risk.

One in two women and up to one in four men will break a bone in their lifetime due to osteoporosis**.**

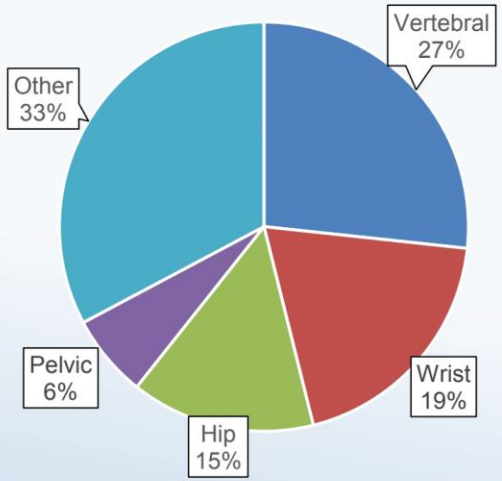
half of all adults age 50 and older, are at risk of breaking a bone and should be concerned about bone health.

For women, the incidence is greater than that of heart attack, stroke and breast cancer combined.

2 Million Fractures Per Year

Osteoporosis is responsible for 2 million fractures per year (since 2005)

- **300,000 hip fractures**
- **550,000 vertebral fractures**
- **400,000 wrist fractures**
- **135,000 pelvic fractures**
- **675,000 fractures at other sites**



Estimated to increase to 3 million/year by 2025

SOURCE: www.asbmr.org/ItineraryBuilder/PresentationDetail.aspx?pid=5dba18cd-e365-4eaa-bc16-af1dabf235de&ptag=SessionsList

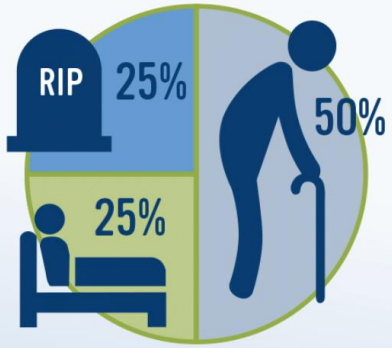
National Osteoporosis Foundation

Osteoporosis is serious, even deadly.[2]

EACH YEAR IN THE U.S., APPROXIMATELY 300,000 HIP FRACTURES OCCUR

Approximately **75,000** Americans who experience a hip fracture die in the year following the fracture.

Another **75,000** Americans move from the hosipital to a nursing home and never return "home."



The remaining **150,000** Americans never regain their previous function. Six months after a hip fracture, only 15 percent of patients can walk across a room unaided.

[2]Singer A, et al. Mayo Clin Proc. 2015;90:53-62

Plenty of Vitamin D and Calcium

National Osteoporosis Foundation (**NOF**) recommends that adults under age 50 get 400-800 International Units (IU) of **vitamin D** every day, and that adults age 50 and older get 800-1,000 IU of **vitamin D** every day. Some people need more **vitamin D**.

NOF recommends that women age 50 and younger get 1,000 mg of **calcium** from all sources daily and that women age 51 and older get 1,200 mg. For men, **NOF** recommends 1,000 mg of **calcium** daily for those age 70 and younger and 1,200 mg for men age 71 and older.

Supplements

Calcium: An essential element for life

Calcium is crucial to maintain life. Just about every cell in the body, including those in the heart, nerves and muscles, relies on calcium to function properly and bones require calcium to maintain their strength. The main goal of good calcium nutrition is to maintain an adequate supply so that our bodies do not have to dip into our only calcium reservoir - our bones.

Vitamin D: A key factor in good calcium absorption

The body makes vitamin D when exposed to sunlight. Since most people don't always get enough sun exposure and it may be difficult to obtain necessary amounts of vitamin D through diet alone, supplements are generally a good idea. Vitamin D3 increases calcium absorption by as much as 30 percent. BHOF recommends that Americans aged 19 to 50, including pregnant or lactating women, receive 400 - 1000 international units (IU) of vitamin D3 per day. Adults over 50 should receive 800-1000 IU daily.

Good-for-Your-Bones Foods

National Osteoporosis Foundation Recommendations

Dairy products such as low-fat and non-fat milk, yogurt and cheese	Calcium. Some dairy products are fortified with Vitamin D.
Canned sardines and salmon (with bones)	Calcium
Fatty varieties such as salmon, mackerel, tuna and sardines	Vitamin D

Collard greens, turnip greens, kale, okra, Chinese cabbage, dandelion greens, mustard greens and broccoli.	**Calcium**
Spinach, beet greens, okra, tomato products, artichokes, plantains, potatoes, sweet potatoes, collard greens and raisins.	Magnesium
Tomato products, raisins, potatoes, spinach, sweet potatoes, papaya, oranges, orange juice, bananas, plantains and prunes.	Potassium
Red peppers, green peppers, oranges, grapefruits, broccoli, strawberries, brussels sprouts, papaya and pineapples.	Vitamin C
Dark green leafy vegetables such as kale, collard greens, spinach, mustard greens, turnip greens and brussel sprouts.	Vitamin K

Recent research has found that:
Olive oil,
Soybeans,
Blueberries
Foods rich in omega-3s,
Fish oil
Flaxseed oil

May also have bone boosting benefits. While additional research is needed before the link between these foods and bone health can definitively be made, the many overall health benefits of these foods make them excellent choices to add to your diet..

Pharmaceutical Interventions

MEDICATION

The goal of osteoporosis therapy is to try to restore the balance of resorption and formation. It can be done by slowing resorption through the use of antiresorptive medication or by promoting bone formation using anabolic medication. By doing so, these therapies lower the risk for fractures, which is the goal of treatment.

All of these drugs reduce the risk of fractures. They come in a range of formulations, from daily tablets to yearly intravenous infusions. There is no best medication for everyone. Factors that influence choice of therapy include baseline level of risk, comorbid medical conditions, goals of therapy, and patient preference.

There are many medications available to treat osteoporosis and reduce the risk of fracture. They fall into two basic categories: antiresorptives and anabolics. Antiresorptive drugs include bisphosphonates (alendronate, ibandronate, risedronate, zoledronic acid), denosumab, calcitonin, estrogen/estrogen-progestin, an estrogen agonist/antagonist (raloxifene), and a tissue specific estrogen complex (estrogen/bazedoxifene). Antiresorptive drugs work by slowing the resorption or breakdown part of the remodeling cycle. Anabolics work by stimulating the formation part of the remodeling process. More bone is formed than is taken away. The result is stronger bone that is less likely to break. Teriparatide, a parathyroid hormone analog, abaloparatide, a parathyroid hormone-related protein analog, and romosozumab-aqqg, a sclerostin inhibitor, are the FDA-approved anabolic medicines available at this time.

Antiresorptive Agents

Bisphosphonates

Alendronate	Fosamax®, Fosamax Plus D™	Oral (tablet, solution)	Daily/Weekly	Women & Men
Alendronate	Binosto®	Oral (effervescent tablet)	Weekly	Women & Men
Ibandronate	Boniva®	Oral (tablet)	Monthly	Women
Ibandronate	Boniva®	Intravenous (IV) injection	Every 3 months	Women
Risedronate	Actonel®	Oral (tablet)	Daily/Weekly/Twice Monthly/Monthly	Women & Men
Risedronate	Atelvia™	Oral (tablet)	Weekly	Women
Zoledronic Acid	Reclast®	Intravenous (IV) infusion	One Time per Year/Once every two years	Women & Men

RANK ligand (RANKL) inhibitor

Denosumab	Prolia™	Injection	Every 6 Months	Women & Men

Estrogen* (Hormone Therapy)

Estrogen	Multiple Brands	Oral (tablet)	Daily	Women
Estrogen	Multiple Brands	Transdermal (skin patch)	Twice Weekly/Weekly	Women

Estrogen Agonists/Antagonists also called selective estrogen receptor modulators (SERMs)				
Raloxifene	Evista®	Oral (tablet)	Daily	Women
Tissue Specific Estrogen Complex (TSEC)				
Estrogen/Bazodoxifene	Duavee®	Oral (tablet)	Daily	Women
Anabolic Agents				
Sclerostin Inhibitor				
Romosozumab-aqqg	Evenity	Injection	2 injections once monthly for 12 months	Women
Parathyroid Hormone (PTH) Analog				
Teriparatide	Forteo®	Injection	Daily	Women & Men
Parathyroid Hormone-Related Protein (PTHrp) Analog				
Abaloparatide	Tymlos	Injection	Daily	Women

*Estrogen is also available in other preparations including a vaginal ring, cream, by injection and as an oral tablet taken sublingually (under the tongue). The vaginal preparations do not provide significant bone protection.

Table 2. FDA-Approved Treatments for Osteoporosis

Drug (Brand)	Efficacy
Biphosphamates	
Alendronate (Fosamax, Fosamax Plus D, Binosto, generic)	Reduced incidence of spine and hip fractures by 50% and risk of vertebral fractures by approximately 48% over 3 years
Ibandronate (Boniva)	Reduced incidence of vertebral fractures by about 50% over 3 years; reduction in nonvertebral fractures not documented
Risedronate (Actonel, Atelvia, generic)	Reduced incidence of vertebral fractures by about 41%-49% and nonvertebral fractures by about 36% over 3 years
Zoledronic acid (Reclast)	IV infusion. Reduced incidence of vertebral fracture by about 70%, hip fractures by about 41%, and nonvertebral fractures by about 25% over 3 years
Calcitonin (Miacalcin, Fortical)	Intranasal spray or subcutaneous injection. Reduced vertebral fractures by about 30%; has not been shown to reduce the risk of nonvertebral fractures
Hormone Therapy	
Estrogen (Climara, Estrace, Estraderm, Estratab, Ogen, Ortho-Est, Premarin, Vivelle) Hormone (Activella, Femhrt, Premphase, Prempro)	When estrogen and hormone therapies are considered solely for prevention of osteoporosis in women, the FDA recommends that approved non-estrogen treatments should be considered first to reduce the risk of myocardial infarction, stroke, invasive breast cancer, pulmonary emboli, and deep vein thrombosis
Raloxifen (Evista)	Reduced the risk of vertebral fractures by 30%
Teriparatide (Forteo)	Reduced the risk of vertebral fractures by about 65% and non-vertebral fractures by about 53% after about 18 months of therapy.
Denosumab (Prolia)	Reduced the incidence of vertebral fractures by about 68%, hip fractures by about 40%, and nonvertebral fractures by about 20% over 3 years

Based on National Osteoporosis Foundation 2013 Guidelines.[12]

Calcium + vitamin D[23-28]	NS	NS	16-18%	NA	24-32%[b]	29-43%	Constipation, hypercalcemia, renal stones
Oral BP[15,16,41,42,44]	41-62%	23-30%	26-53%	34-44%	NS	NS	Gastrointestinal, musculoskeletal pain, ONJ
IV BP[50,51,56,57]	46-77%	25-27%	41%[50]; NS-30%[51]	60%	25%	NS-22%	Acute phase reaction, potential renal impairment, hypocalcemia, ONJ
PTH[17,77]	65%	53%	NA	65%	NS	NA	Hypercalcemia, dizziness, cramps, gout, urolithiasis, osteosarcoma
SERM[83]	30-50%	NS	NS	NA	NA	NA	VTE, cramps, hot flashes, vaginal bleeding, peripheral edema (but 66% reduction in breast cancer)
HT[82]	32-38%	22-27%[c]	32-36%	NA	NA	NA	Cardiac events, stroke, breast cancer, VTE
Calcitonin[88]	36%	NS	NA	NA	NA	NA	Rhinitis, epistaxis
Denosumab[90]	68%	20%	40%	NA	NA	NA	Eczema, cellulitis, flatulence,




Exercise

PHYSICAL ACTIVITY AND EXERCISE

Physical activity is an important factor in the risk reduction and treatment of osteoporosis. Physical activity places an increased "load" or force on our bones. Bones respond by forming new bone and remodeling the bone to be stronger. Bones need to be stimulated by physical activity -- so it is necessary to be active in different ways in order to "load" or stimulate these bones and maintain their structural competence and strength.

Physical activity also contributes to a sense of well-being and an overall improvement in quality of life as well as improving balance and coordination which, in turn, reduces risk of falling -- falls that can result in fractures. In addition, improved strength, flexibility, and posture can reduce pain and enable people with osteoporosis to do daily tasks more easily.

There are 4 types of exercise and activity integral to the management of low trauma fracture and osteoporosis:

- Strength
- Posture and core stability
- Balance
- Weight-bearing

Specific exercises will be discussed in much more detail later in this workshop.

Optimal Strain for Maintaining and Building Bone

To maintain bone, low magnitude strains work. To build bone, strains need to be:

- Unusual, novel, not customary in distribution
- High magnitude
- High rates
- (and a bit of good news) Not prolonged!

Exercise Types

‘Any’ is good (On bedrest, bone loss occurs at a rate of ~1% per week and regain at ~1% per month). High impact (jumping) is best yet studied in children and premenopausal women. Exercise preserves bone mass and maximizes bone geometry in adults.

- Weight bearing: meta-analysis showed about a 1% maintenance of bone per year in pre and post-menopausal women
- Progressive resistive/strength training: systematic review and meta-analysis showed about a 1% maintenance of bone

Exercise to Stay Healthy (NOF)

A. Posture exercises

These exercises improve your posture and reduce rounded or “sloping” shoulders. They can help you decrease the risk of breaking a bone, especially in the spine.

B. Hip and back (spine) strengthening exercises

These exercises can help you to strengthen the muscles in your back and hips.

C. Balance exercises

These exercises strengthen your legs and challenge your balance. They can decrease your chance of falling.

D. Functional exercises

These exercises improve how well you move. They can help you in everyday activities and decrease your chance of falling and breaking a bone. For example, if you find it hard to get up from a chair or climb stairs, you should do these activities as exercises (try standing up and sitting down several times until you are tired).

Osteoporosis Exercise Trends

Tai Chi

Yoga/Pilates

Dancing

Doing high-impact aerobics

Hiking

Jogging/running

Jumping Rope

Stair climbing

Tennis

Low-impact weight-bearing exercises

can also help keep bones strong and are a safe alternative if you cannot do high-impact exercises. Examples of low-impact weight-bearing exercises are:

Using elliptical training machines

Doing low-impact aerobics

Using stair-step machines

Fast walking on a treadmill or outside

Muscle-Strengthening Exercises

Lifting weights

Using elastic exercise bands

Using weight machines

Lifting your own body weight

Functional movements, such as standing and rising up on your toes

Cautions

When doing exercise keep in mind your bone density status:

- Someone with major osteoporosis should not be advised to do power lifting.
- Pilates and Yoga may also have compromising positions that could harm patients
- Jumping activities like jumping a rope is a very good impact activity. However, should not been done by anyone at high risk for fracture.
- Don’t let the reports fool you Vibration devices are not proven to be helpful and can cause small micro-fractures.

Tai chi

There are many ways that tai chi helps people with osteoporosis. An excellent study showed tai chi slowed down the loss of bone density approximately three-fold. When people with osteoporosis fall, they are more likely to sustain a fracture. Many studies have shown that tai chi reduces falls.

People with osteoporosis often have arthritis and loss of function due to age and weakness. Tai chi relieves pain from arthritis, improves balance and the ability to do daily activities. Tai chi helps people feel more relaxed and improves mental strength so they can cope better with their conditions.

Yoga

Yoga is a useful addition to your osteoporosis treatment plan. It can help to ease symptoms, improve bone health, and lower your risk of complications. Yoga may also increase bone density after menopause.

Gentle yoga involving weight-bearing poses can build strength, ease pain, and encourage good posture. It also helps improve flexibility, stability, and agility. These benefits make daily movements easier, improve coordination, and reduce your risk of falling.

Yoga Exercises

High plank pose

Downward-facing dog

Tree Pose

Warrior II

Triangle pose

Choose yoga poses that will develop strength without going beyond your limits. Listen to your body and modify poses as necessary.

Out of This World Exercise

https://technology.nasa.gov/patent/MSC-TOPS-59

The ARED is a mechanically simple, but robust device. It employs vacuum cylinders to provide a constant resistance, while flywheel assemblies provide a variable resistance. The variable resistance supplied by the flywheel assemblies is designed to mimic the inertial forces generated when lifting free weights on Earth. It is not dependent on gravity to operate but can operate in Earth gravity as well as microgravity. It was flown to the ISS on Space Shuttle mission STS-126 in November 2008. It is designed to last at least 15 years, with a total life of over 11.2 million cycles. The ARED accommodates a wide range of body types and sizes. There is also a touch screen that makes it easier for an astronaut to follow a personalized prescribed exercise plan. A crewmember may select any exercise from their prescription or choose other available exercises. The crew performs their exercises using either a lift bar or a cable assembly. Resistive load can be adjusted between 0 and 600+ pounds for bar-related exercises and up to 150 pounds for cable-related exercises.