Bone Health: Beyond Calcium
Robert Kress, RPh

Home Study Webcast
2 slides per page
Bone Health: Beyond Calcium

ACTIVITY DESCRIPTION
Along with an aging society, cases of osteopenia and osteoporosis are on the rise. Due to various reasons, from side-effects of conventional therapy to a greater interest in preventative wellness, practitioners and patients alike are looking for alternatives and complements to conventional drug treatment for healthy bones.

TARGET AUDIENCE
The target audience for this activity is pharmacists, pharmacy technicians, and nurses in hospital, community, and retail pharmacy settings.

LEARNING OBJECTIVES
After completing this activity, the pharmacist will be able to:
- Briefly review prescription drug classes used to prevent and treat osteoporosis
- Describe the primary nutrients, in addition to calcium, which play a significant role in supporting bone health
- Identify which medication classes deplete bone healthy nutrients
- Explain lifestyle factors such as diet, exercise, and stress management that are supportive to bone health

After completing this activity, the pharmacy technician will be able to:
- List prescription drug classes used to prevent and treat osteoporosis
- List primary nutrients in addition to calcium, that play a significant role in supporting bone health

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ACTIVITY TYPE
Knowledge-Based Home Study Webcast

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ABOUT THE AUTHOR
Robert Kress, RPh, graduated from Temple University School of Pharmacy in Philadelphia PA in 1994. After becoming disenchanted with chemical dominant based medical system, Robert took his passion for nutrition and became board certified in clinical nutrition through the Clinical Nutrition Certification Board, as well as trained as a compounding pharmacist through the Professional Compounding Centers of America. During this time, with his wife Amy, opened their own compounding and nutritional clinic, which blossomed into a complete anti-aging clinic housing other integrative practitioners. Robert became certified in Quantum Reflex Analysis, a practice of kinesiology, as well as have trained and certified in other modalities such as Reiki and auricular acupuncture.

Currently, Robert consults with both with patients to enhance their health through lifestyle medicine as well other practitioners to help integrate, promote and implement natural medicine in their practices. Robert also provides regular educational Wellness Workshops and writes regularly on the topic of lifestyle medicine and integrative care.

Robert believes as pharmacists, we are offered the perfect opportunity to integrate natural medicine into our practices, as its core to the history of pharmacy. Patients are looking for natural solutions for their health, while practitioners are looking towards integrative care to help solve their clients problems and enhance their practices.

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Objectives

• Briefly review prescription drug classes used to prevent and treat osteoporosis
• Describe the primary nutrients, in addition to calcium, which play a significant role in supporting bone health.
• Identify which medication classes deplete bone healthy nutrients
• Explain lifestyle factors such as diet, exercise, and stress management that are supportive to bone health.
Bone Metabolism

• Healthy bone metabolism is a lifelong process where mature bone tissue is removed from the skeleton through a process called bone resorption, and new bone tissue is formed.

• In the case of thinning and porous bone (osteopenia and osteoporosis) bone tissue is resorbed faster than new bone is made. This leads to loss of minerals within the bone, strength, mass and structure, leading to an increase risk of fractures.

Bone metabolism definitions

• Osteopenia- Reduced bone density
• Osteoporosis- Porous bone with increased risk of fractures
• Calcitonin- Lowers the levels of calcium and phosphate in the blood and promotes the formation of bone.
• Osteocalcin- Binds with calcium for healthy bone mineralization.
• Osteoclasts- Cells that break down old bone tissue
• Osteoblasts- Cells that replace old bone tissue with new material.
Bone Health: The Pharmacists Role

- Educate on preventative & complementary options for osteopenia and osteoporosis.
- Assess current medications for issues that can lead to weakening of bones, or increase risk of falls and fractures. (opioids, benzodiazepines, anticholinergics)
- Identify disease states that increase risk of falls such as visual problems, postural hypotension, vertigo, structural problems, etc.
- Identify side-effects or possible contraindications of medication therapy for osteoporosis.
- Offer options and alternatives to both patients and physicians.
- Identify medications that deplete bone supporting nutrients.

Osteoporosis & Bone Fractures

- 2/3 of those with osteoporosis women, 1/3 men.
- 1 in 3 women and 1 in 5 men over the age of 50 will experience osteoporotic fractures. Primary fractures are vertebral, hip, wrist, forearm.
- A 10% loss of bone mass in the vertebrae can double the risk of vertebral fractures, while a 10% loss of bone mass in the hip can result in a 2 ½ times risk of hip fracture.
- Worldwide there are 8.9 million fractures annually, with 1.2 million in the U.S. at a cost of $38 million dollars daily (hospital and nursing home care)

International Osteoporosis Foundation https://www.iofbonehealth.org/facts-statistics
Surgeon General Bone Health & Osteoporosis Report
Hip Fractures

- Of the 8.9 million fractures, 1.6 million are hip fractures with great implications and costs as well as a negative prognosis after fracture.
- 1 in 3 women and 1 in 9 men older than 80 years of age.
- Approximately 20% of hip fracture patients will be dead one year after the hip fracture.
- Nearly 70% of those who survive the acute post-op stage are discharged to a nursing home.
- Only 25% of hip fracture victims ever regain their former level of independence.


Total cost in care per month per patient 6 months after hip fracture compared to 6 months prior to hip fracture, excluding cost of initial hospitalization
Surgeon General Bone Health & Osteoporosis Report

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<td>Informal care</td>
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<tr>
<td>Total per month</td>
<td>1739</td>
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</table>
Better Outcome With Better Health

3 factors give 90% prediction of successful recovery and regaining ones independence
1. Those with the best pre-fracture mobility are likely to survive and do well.
2. The ability to walk within 2 weeks of surgery
3. Living with another person who will provide critical social support.

Patients who met any 2 of these conditions have an 80% chance of returning home, patients who meet 1, have a 50%, patients meeting none, have a 12% chance of returning home.


Bone Mass as we age

• 18 to 20 years old - 90% of peak bone mass is acquired by age 18 in girls and age 20 in boys.
• 30 to 35 - Peak bone mass has been reached and bone mass begins breaking down.
• Age of menopause and andropause (approx. 50 for men and women), begin loss become more rapid (hormone modulated).
• 50 to 80 - Bone mass declines about 30%.

https://www.niams.nih.gov/Health_Info/Bone/osteoporosis/bone_mass.asp
http://my.clevelandclinic.org/health/articles/menopause-and-osteoporosis
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1472881/
Risk Factors to Bone Loss

- Age
- Family history
- Eating disorders, metabolism and digestive problems leading to decreased absorption of vitamins and minerals
- Chemotherapy and radiation
- Long term treatments of medications including steroids and anticonvulsants
- Hormonal imbalance/Menopause/Andropause
- Oophorectomy (removal of ovaries)

Risk Factors to Bone Loss

- Thin framed
- White or Asian ethnicity
- Limited physical activity/sedentary
- Diets of high sugar and soda pop
- Diets low in calcium
- Excessive alcohol consumption
- Cigarette smoking
- Low vitamin D

https://nihseniorhealth.gov/osteoporosis/riskfactors/01.html
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1589320/
http://my.clevelandclinic.org/health/articles/menopause-and-osteoporosis
Why Lifestyle Medicine for Bone Health?

• Provides preventative measures to maintain healthy bones.
• Possible side-effects, contraindications, and costs of drug based osteoporosis therapy.
• Often provides complementary benefits in other areas of health.
• Growing patient desire and interest.
• The Surgeon General recommends.

U.S. Surgeon General Bone Health Pyramid

Source: Surgeon General Bone Health & Osteoporosis Report
Pharmacotherapy

Hormonal Therapy

Bisphosphonates

SERM’s

Monoclonal Antibodies

Hormonal Therapy

• Estrogen and Progestin FDA approved for prevention but not treatment of osteoporosis.
• Estrogen and Progestin increase risk of breast cancer, heart attack, stroke, and pulmonary embolism.
• Natural sex hormones estrogen, progesterone and testosterone all have in-vivo roles in healthy bone metabolism.
Hormonal Therapy

Calcitonin (Fortical ® or Miacalcin ®)

- FDA approved to treat women with osteoporosis and shown to prevent fractures of spine, but not hip and wrist.
- Calcitonin is a hormone produced by the thyroid gland that lowers the levels of calcium and phosphate in the blood and promotes the formation of bone.
- Has fallen out of preference due to new drugs being backed by better evidence.
- Increase risk of malignancies

Teriparatide (Forteo)

- Derivative of human parathyroid hormone, which is primary regulator of calcium and phosphate metabolism.
- Shown to stimulate new bone formation and prevent spine, hip, wrist, and other bone fractures in people with osteoporosis.
- Daily injection
- Side-effects may include nausea, leg cramps, high calcium levels.
- Black box warning for osteosarcoma
Bisphosphonates

• FDA approved for the prevention and treatment of osteoporosis.
• Decrease bone resorption and slow down bone loss.
• 2012 FDA expressed concerns on safety of use beyond 3 to 5 years based on information that women who received continuous bisphosphonate treatment for 6 or more years had increased fracture rate.
• Reports and incidences of patients on bisphosphonates with unusual breaks, such as femur, and bone taking longer to heal.

http://www.fda.gov/Drugs/DrugSafety/ucm101551.htm

Bisphosphonates

• Incidences of jaw remodeling as well as necrosis of jaw.
• Side-effects can cause severe heartburn, ulcers, damage to stomach and esophagus, joint, and muscle pain.

Examples of bisphosphonates

<table>
<thead>
<tr>
<th>Brand Name</th>
<th>Generic Name</th>
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<tbody>
<tr>
<td>Actonel</td>
<td>risedronate</td>
</tr>
<tr>
<td>Boniva</td>
<td>ibandronate</td>
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<tr>
<td>Fosamax</td>
<td>alendronate</td>
</tr>
<tr>
<td>Reclast</td>
<td>zoledronic acid</td>
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http://www.fda.gov/Drugs/DrugSafety/ucm263320.htm
http://www.fda.gov/Drugs/DrugSafety/ucm101551.htm
Selective Estrogen Receptor Modulators (SERMs)

- Estrogen like activity on certain tissues (ex- bone tissue) and anti-estrogen effect on other tissues. (ex- breast and sometime uterus)
- Raloxifene (Evista) approved to prevent and treat osteoporosis.
- Reduce risk of spine fractures, but not hip fractures.
- Increase risk of blood clots, hot flashes, nausea, and leg cramps.


Raloxifene (Evista)

Black box warnings:

- Venous Thromboembolism Risk- contraindicated in women with active or past history of venous thromboembolism.
- Fatal Stroke Risk- increased risk of death from stroke in postmenopausal women with documented CHD or risk factors for major coronary events.

Monoclonal antibodies

Denosumab (Prolia)

• Inactivates the natural bone breakdown mechanism.
• Shown to be effective in reducing fractures and preventing bone loss.

http://pi.amgen.com/~/media/amgen/repositorysites/pi-amgen-com/prolia/prolia_pi.ashx

Denosumab (Prolia)

• Can suppress the immune system through a similar mechanism where it inactivates breakdown of bone, possibly leading to serious infections of skin, lower stomach area (abdomen), bladder, or ear.
• Inflammation of the inner lining of the heart (endocarditis).
• Osteonecrosis of the jaw, unusual thigh bone fractures.

https://www.prolia.com/important-safety-information/
Poll Starting

Poll Ending
Diet

An alkaline based diet supports bone health.

- A Western-type diet has been reported to be associated with osteoporosis and urinary calcium loss.
- Urinary calcium has been found to be increased with acid-forming foods, such as meat, fish, eggs, and cereal, and negatively associated with plant foods and is likely determined by the acid-base status of the total diet.
- Bone loss may be attributable, in part, to the mobilization of skeletal salts to balance the endogenous acid generated from acid-forming foods.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3195546/
Diet

• Studies have found inverse relationships between vegetable and fruit intake and risk of osteoporosis.
• Nutritional Density- along with calcium; vegetables, leafy greens, fruits, nuts, beans, and whole grains contain a variety of antioxidants, minerals, vitamins, and other phytonutrients which play a role in facilitating bone remodeling.
• Adequate protein diets are actually associated with greater bone mass and fewer fractures when calcium intake is adequate.


Diet

Bone helpful advice:

• Eat an alkalizing diet such as fruits, vegetables, nuts, and seeds.
• Avoid forming foods such as large amounts of animal protein, processed foods, salt, caffeine, unhealthy fats, refined sugars.

“A balanced diet with ample fruit and vegetables and adequate protein appears to be important to bone mineral density.”

http://ajcn.nutrition.org/content/87/5/1567S.full
http://ajcn.nutrition.org/content/76/1/245.short
Supplements

Calcium • Major component of the bone mineral matrix.
• About 99% of body calcium in bones and teeth, 1% in cells, soft tissue and body fluid.
• Calcium supplements alone are minimally effective in treatment or prevention of osteoporosis. A broad range of nutrients is best.
Drugs That Deplete Calcium

• Aspirin & Salicylates
• Corticosteroids
• Proton Pump Inhibitors
• H2 receptor blockers
• Aluminum & magnesium antacids
• Antibiotics (tetracycline, Aminoglycosides)
• Bile acid sequestrants
• Loop diuretics
• Thiazide diuretics
• Potassium sparing diuretics
• Oral estrogen therapy
• Bisphosphonates
• Anticonvulsants

Calcium RDA and Limits

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<tr>
<th></th>
<th>Daily RDA</th>
<th>Daily Upper Limit</th>
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<tbody>
<tr>
<td>Men</td>
<td></td>
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<tr>
<td>19-50 Years old</td>
<td>1,000 mg</td>
<td>2,500 mg</td>
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<tr>
<td>51-70 Years old</td>
<td>1,000 mg</td>
<td>2,000 mg</td>
</tr>
<tr>
<td>71 and older</td>
<td>1,200 mg</td>
<td>2,000 mg</td>
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<tr>
<td>Women</td>
<td></td>
<td></td>
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<tr>
<td>19-50 Years old</td>
<td>1,000 mg</td>
<td>2,500 mg</td>
</tr>
<tr>
<td>51 and older</td>
<td>1,200 mg</td>
<td>2,000 mg</td>
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</tbody>
</table>
Magnesium

- Essential bone matrix mineral.
- Only 1% of magnesium is distributed in the blood.
- Essential for absorption and metabolism of calcium.
- Supports healthy bone mineral density.
- Necessary for the conversion of vitamin D to its active form.
- RDA (400-420 mg/day for men and 310-320 mg/day for women)
- Some estimates- only 25% of Americans get the RDA, up to 80% of Americans are deficient in it.

https://ods.od.nih.gov/factsheets/Magnesium-HealthProfessional/

Drugs That Deplete Magnesium

- Corticosteroids
- Proton pump inhibitors
- Aluminum & magnesium antacids
- Antibiotics (Tetracyclines, aminoglycosides)
- Cholestyramine
- Cardiac glycosides
- Loop diuretics

- Thiazide diuretics
- Oral estrogen therapy

Vitamin D

- Promotes intestinal calcium and phosphorous absorption, reduces urinary calcium loss.
- Enhances healthy bone composition.
- Studies of Vitamin D along with calcium, have shown to support bone composition of the femur, promote healthy hip bones, promote calcium utilization and maintain healthy bones in post-menopausal women.
- RDA 600 IU’s / Day
- Optimal blood levels of testing 25-OH D between 40 and 60 ng/dl which often requires dosages much higher than the RDA.

https://www.vitamindcouncil.org/health-conditions/vitamin-d-and-osteoporosis/

Drugs That Deplete Vitamin D

- Corticosteroids
- H2 blockers
- Aluminum & magnesium Antacids
- Cholestyramine
- Anticonvulsants

Vitamin K

- Vitamin K enhances bone formation through carboxylation of osteocalcin, which in turn binds with calcium for healthy bone mineralization.
- Helps maintain healthy calcium concentration and levels in vascular tissues.
- Provides synergistic support for bone health with vitamin D.

Vitamin K1 & K2

- Phylloquinone (K1) is found in plants and green leafy vegetables.
- Menaquinone (K2) is created by intestinal bacteria and can also be derived from vitamin K1.
- Food sources of Vitamin K2 are less common, limited to foods such as egg yolks, butter, and fermented soy.
Vitamin K1 & K2

- Vitamin K1 is historically the form of Vitamin K that is used for its role in the prevention and support of individuals with osteoporosis.
- Vitamin K2 has been known for its heart and vascular health benefits. Vitamin K2 is attributed to promoting healthy vascular calcium balance and cardiac function through healthy arterial blood flow and vascular elasticity; preventing normal age-related progression of arterial wall stiffening.
- Vitamin K2 has also proven to be a powerful single entity for bone health as well.

http://umm.edu/health/medical/altmed/supplement/vitamin-k
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4566462/

Drugs That Deplete Vitamin K

- Numerous antibiotics (cephalosporin's, fluoroquinolone's, macrolides, penicillin's, sulfonamides, tetracyclines)
- Cholestyramine
- HMG-CoA reductase inhibitors (statins)
- Anticonvulsants

https://www.ncbi.nlm.nih.gov/pubmed/25655639
Balance of Calcium, Magnesium, D, K

• Excessive calcium not counterbalanced by magnesium can lead to cardiovascular issues. Calcium causes muscles to contract, and if you don’t have enough magnesium, you lack the muscle and nerve function it promotes, and muscles go into spasm.

• Insufficient magnesium can lead to impaired conversion to active vitamin D, leading to unhealthy bone mineral composition.

Balance of Calcium, Magnesium, D, K

• Vitamin K keeps calcium in its place (in the bones.) If not enough vitamin K, calcium can accumulate in the wrong places, like soft tissue.

• Vitamin D promotes intestinal calcium absorption, and reduces urinary calcium loss.

• Large doses of vitamin D without sufficient amounts of K and magnesium can lead to magnesium deficiency and improper distribution of calcium.
Poll Starting

Poll Ending
Drug Induced Nutrient Depletion’s of 4 Core Bone Healthy Nutrients

<table>
<thead>
<tr>
<th></th>
<th>Calcium</th>
<th>Magnesium</th>
<th>Vitamin D</th>
<th>Vitamin K</th>
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<td>Bile acid sequestrants</td>
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<tr>
<td>Statins</td>
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Trace Minerals

Boron
- Supports calcium, phosphorus, magnesium, and vitamin D metabolism.
- Plays a role in reducing urinary calcium and magnesium excretion.
- Plays a role in the synthesis of estrogen, vitamin D, and other steroidal hormones.
- Strengthens connective tissue in the bone matrix.
- Average dose: 1 to 3 mg daily
Trace Minerals

Strontium
- Supports healthy osteoblast differentiation, osteoblast collagen formation, and balanced osteoclast activity.
- Studies have shown strontium to support healthy vertebrae integrity and composition, as well as promoted healthy hip bones.
- Strontium is absorbed via calcium transport mechanisms, thus should not be taken at the same time as calcium to avoid competitive inhibition.

Zinc, manganese, copper have shown to support healthy bone metabolism

Exercise

- Regular exercise generates stronger bone.
- Our bones respond to the demands we place on them.
- Especially weight bearing, such as resistance and impact, as well as stretching and cardiovascular training supports strong bones healthy living.
- Balance training to reduce the risk of falling.
- For those prone or with osteoporosis, refer to local better bones class or those specializing in exercise in such cases.

Source: Surgeon General Bone Health & Osteoporosis Report
General Recommendation for Physical Activity in Adults
Source: Surgeon General Bone Health & Osteoporosis Report

Balance training

Strength training
2 to 3 times per week

Weight bearing exercises such as walking

30 minutes or more of moderate physical activity on most, preferable all, days of the week

Weight-Bearing Exercises
Source: Surgeon General Bone Health & Osteoporosis Report

<table>
<thead>
<tr>
<th>High Impact</th>
<th>Low Impact</th>
<th>Non-Weight-Bearing</th>
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<tbody>
<tr>
<td>Hiking</td>
<td>Walking</td>
<td>Lap swimming</td>
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<tr>
<td>Dancing</td>
<td>Treadmill walking</td>
<td>Indoor cycling</td>
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<tr>
<td>Jogging</td>
<td>Cross-country ski-machines</td>
<td>Stretching or flexibility exercises</td>
</tr>
<tr>
<td>Downhill &amp; Cross country skiing</td>
<td>Stair-step machines</td>
<td>Yoga</td>
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<tr>
<td>Aerobic dancing</td>
<td>Water aerobics</td>
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<td>Weight lifting or resistance</td>
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<tr>
<td>Jumping rope</td>
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</table>
Stress Management

• Stress is a natural occurrence, and an adaptive energy needed to get stronger and grow.
• When it becomes chronic, not managed, it is a detriment to our health and wellbeing.

Good Stress

• Exercise- physical stress on muscles will make them stronger and grow- when in balance.
• Psychological stress for a test- provides alertness which is good- when in balance.
• Fight for flight- gets us out of danger, preserves us, keeps us alive – when in balance.
Stress Management and Balance

• Our bodies experience not just circadian rhythms (24 hour cycles), but ultradian rhythms.
• An ultradian rhythm is a recurrent period or cycle repeated throughout a 24-hour circadian day which mirror how our body should manage stress.
• We are designed to experience periods of stress, followed by periods of rest and repair during a 24 hour cycle.
• Ex- 90 minutes of focused work or stress, followed by 15 minutes of rest and repair.

Mismanaged stress and health

• In addition to bone health, excessive or mismanaged stress can lead to: chronic fatigue, fibromyalgia, depression, ADHD, anxiety, gastrointestinal disorders, insomnia, hormone imbalances, inflammation, cardiovascular disease, cancer, diabetes, auto-immune diseases, infections disease, allergies, skin conditions, and more.
Types of Stressors

Stress and Bones

• Stress is a bone crusher.
• Mismanaged stress leads to chronically elevated cortisol levels.
• Chronically elevated cortisol levels increased risk for osteoporosis.
• As long as your body remains in a state of chronic stress with elevated cortisol levels, bone formation is disrupted.
Stress Management

**Other ways stress can negatively impact bone health**

- Sugar cravings
- Digestive disorders - constipation or diarrhea can affect nutrient absorption
- Sleep disturbances
- Exhaustion and lack of interest to exercise
- Drug therapy and / or disease states


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**Stress Management Techniques**

- Do not over-commit
- Learn to say no
- Meditation
- Prayer
- Breathing Exercises
- Practice the Art of Silence
- Get out in nature
- Move! Physical activity
- Yoga
- Tai chi
- Adequate sleep
- Mini breaks throughout the day - balance stress & Recovery
- Social support
- Game Play - Tetris
Final thoughts

• Osteopenia and Osteoporosis have numerous risk factors, and through the right choices and components of lifestyle medicine, can be preventable and treatable.

• Prescription therapy is not always a one-stop solution, and can have negative implications such as drug induced nutrient depletions.

• It is critical that we have complementary and alternative offerings in our arsenal to aid our patients.

• Calcium alone is not enough, optimal bone health requires other supplements to work synergistically with calcium.

• In addition to supplements and medications, there are lifestyle strategies including exercise, diet, and stress management for healthy bones.
Exam Questions

1. Which is NOT a known factor for gaining independence after hip surgery?
   a. Having good pre-fracture mobility
   b. Having great insurance
   c. The ability to walk within 2 weeks after surgery
   d. Living with another person who will provide social support

2. At what age have people reached their peak bone mass?
   a. 20 to 25
   b. 30 to 35
   c. 40 to 45
   d. Over 50 years old

3. What is not a risk factor of osteoporosis?
   a. Long term use of anticonvulsant medications or corticosteroids
   b. Playing sports such as soccer, volleyball, or basketball
   c. Deficiency in vitamin d
   d. Cigarette smoking

4. Which type of exercise would provide the best support for building bone mass in a healthy individual?
   a. Indoor cycling
   b. Lap swimming
   c. Weight lifting or resistance training
   d. Treadmill walking
5. Which is not a way that stress can negatively impact bone health?
   a. Sustained elevated cortisol levels disrupts bone formation
   b. Can promote sugar cravings
   c. Makes someone “stress shop” or “retail therapy”
   d. Leads to sleep disturbances

6. Vitamin K enhances bone formation through carboxylation of:
   a. Parathyroid hormone
   b. Osteocalcin
   c. Osteoblasts
   d. Osteoclasts

7. Strontium should not be giving at the same time as which mineral, since they are absorbed via the same transport mechanism?
   a. Magnesium
   b. Calcium
   c. Vitamin D
   d. Vitamin K

8. Boron plays a role in reducing urinary excretion of which two nutrients?
   a. Vitamin D and Vitamin K
   b. Calcium and Magnesium
   c. Strontium and Calcium
   d. Calcium and Vitamin D
9. Which is a healthy food choice for someone looking to prevent osteoporosis?
   a. Soda pop
   b. Caffeine
   c. Green leafy vegetables
   d. Porterhouse steak

10. Side-effects of bisphosphonates include:
    a. Damage to esophagus and stomach
    b. Increased risk of diabetes
    c. Remodeling of the jaw
    d. A and C