Vitamin D in Orthopaedic Practice

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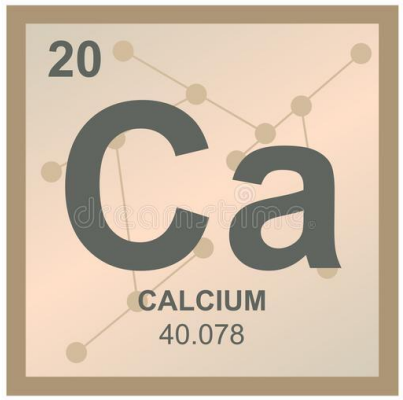
29.08.2020 (MMA)

Calcium and Vitamin D

- Calcium and vitamin D are essential to building strong, dense bones when you're young and to keeping them strong and healthy as you age



What is Calcium and What Does it Do?

- Calcium is a mineral that is necessary for life
- In addition to building bones and keeping them healthy, calcium enables our blood to clot, our muscles to contract, and our heart to beat
- About 99% of the calcium in our bodies is in our bones and teeth

A calcium-rich diet (including dairy, nuts, leafy greens and fish) helps to build and protect your bones.

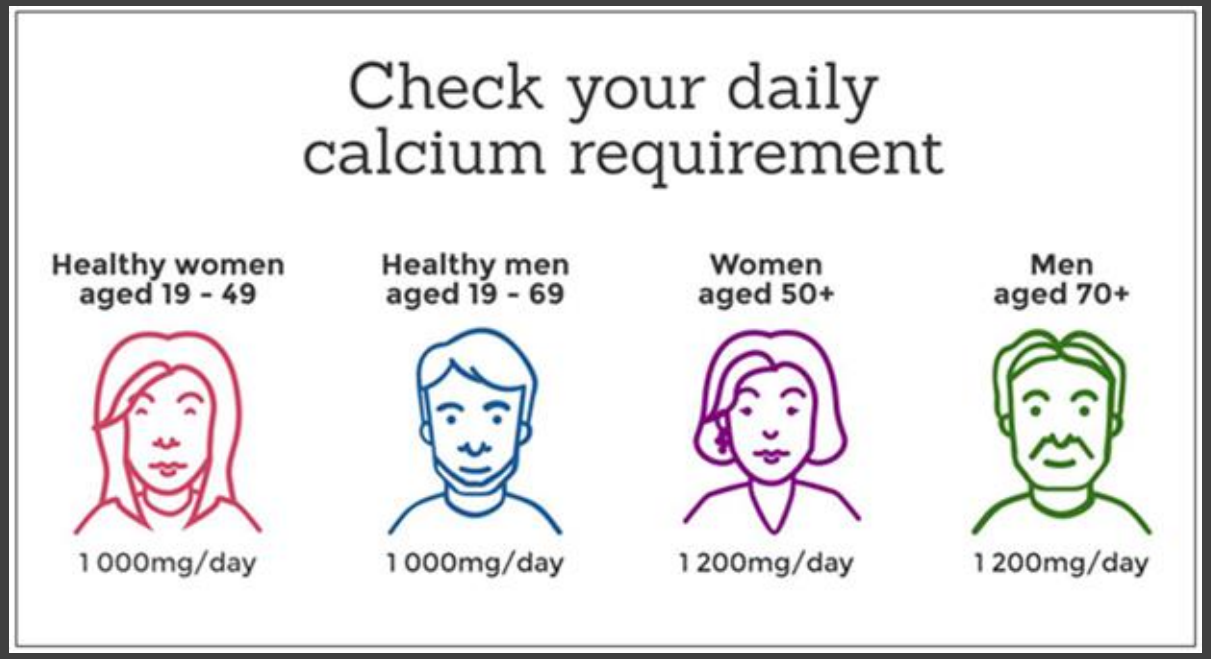
How Much Calcium Do You Need?

WOMEN

- Age 50 & younger 1,000 mg daily
- Age 51 & older 1,200 mg daily

MEN

- Age 70 & younger 1,000 mg daily
- Age 71 & older 1,200 mg daily

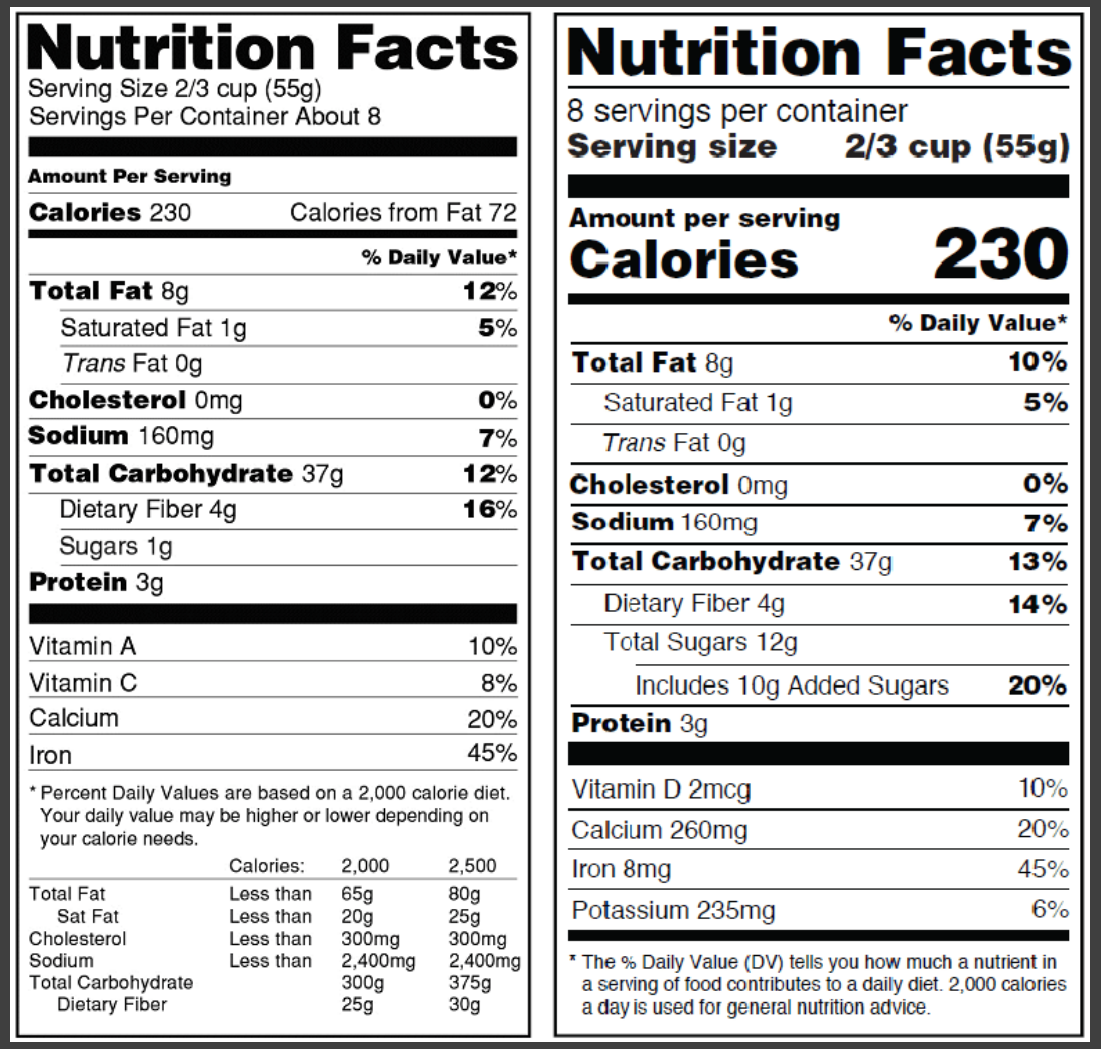


Sources of Calcium

- Calcium-Rich Food Sources
  - Dairy products, such as milk, yogurt, and cheese are high in calcium
  - Certain green vegetables
  - Some juices, breakfast foods, soymilk, cereals, snacks, breads
  - If you drink soymilk or another liquid that is fortified with calcium, be sure to shake the container well as calcium can settle to the bottom

Reading Food Labels – How Much Calcium Am I Getting?

- Check the nutrition facts panel for the daily value (DV)
  - 30% DV of calcium equals 300 mg of calcium
  - 20% DV of calcium equals 200 mg of calcium
  - 15% DV of calcium equals 150 mg of calcium



Nutrition Facts

Serving Size 2/3 cup (55g)
Servings Per Container About 8

Amount Per Serving

Calories 230	Calories from Fat 72
	% Daily Value*
Total Fat 8g	**12%**
Saturated Fat 1g	**5%**
Trans Fat 0g	
Cholesterol 0mg	**0%**
Sodium 160mg	**7%**
Total Carbohydrate 37g	**12%**
Dietary Fiber 4g	**16%**
Sugars 1g	
Protein 3g	
Vitamin A	10%
Vitamin C	8%
Calcium	20%
Iron	45%

* Percent Daily Values are based on a 2,000 calorie diet. Your daily value may be higher or lower depending on your calorie needs.

	Calories:	2,000	2,500
Total Fat	Less than	65g	80g
Sat Fat	Less than	20g	25g
Cholesterol	Less than	300mg	300mg
Sodium	Less than	2,400mg	2,400mg
Total Carbohydrate		300g	375g
Dietary Fiber		25g	30g

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Total Carbohydrate 37g	**13%**
Dietary Fiber 4g	**14%**
Total Sugars 12g	
Includes 10g Added Sugars	**20%**
Protein 3g	
Vitamin D 2mcg	10%
Calcium 260mg	20%
Iron 8mg	45%
Potassium 235mg	6%

* The % Daily Value (DV) tells you how much a nutrient in a serving of food contributes to a daily diet. 2,000 calories a day is used for general nutrition advice.

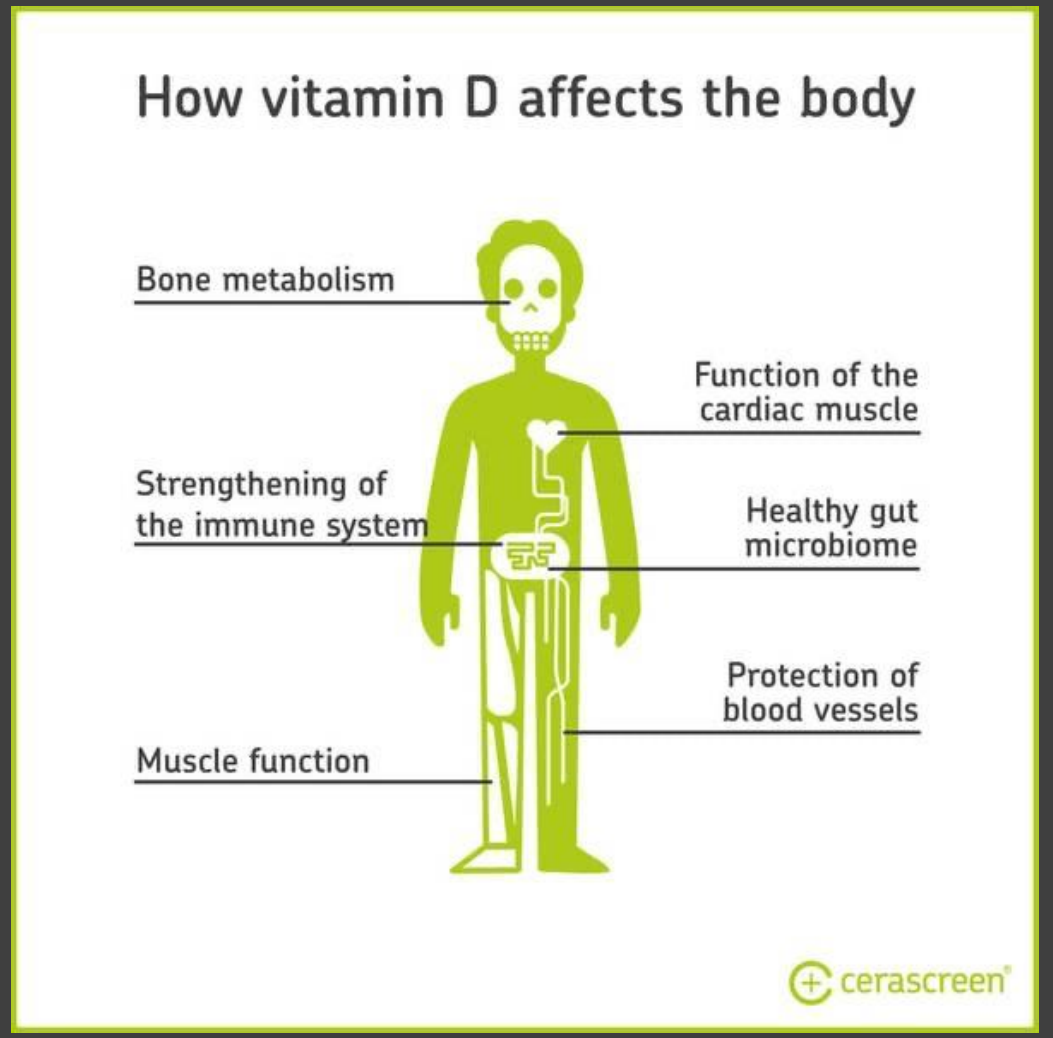
Calcium Supplements

- The amount of calcium we need from a supplement depends on how much we get from food
- When choosing a supplement, keep the following in mind
  - Choose brand-name supplements with proven reliability
  - Read the product label carefully to determine the amount of elemental calcium
  - Calcium is absorbed best when taken in amounts of 500 – 600 mg or less
  - Take (most) calcium supplements with food
  - When starting a new calcium supplement, start with a smaller amount to better tolerate it
  - Side effects from calcium supplements, such as gas or constipation may occur

What is Vitamin D and What Does it Do?

- Vitamin D plays an important role in protecting your bones, both by helping your body absorb calcium and by supporting muscles needed to avoid falls

- If you don't get enough vitamin D, and you're more likely to break bones as you age

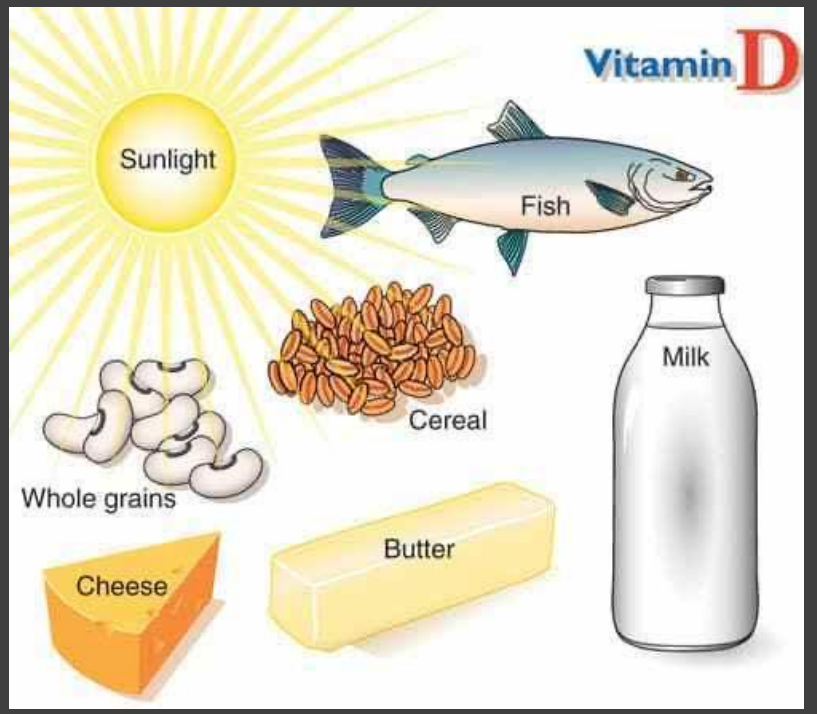


How Much Vitamin D Do You Need?

WOMEN AND MEN

- Under age 50 — 400-800 IU daily
- Age 50 and older — 800-1,000 IU daily

Sources of Vitamin D



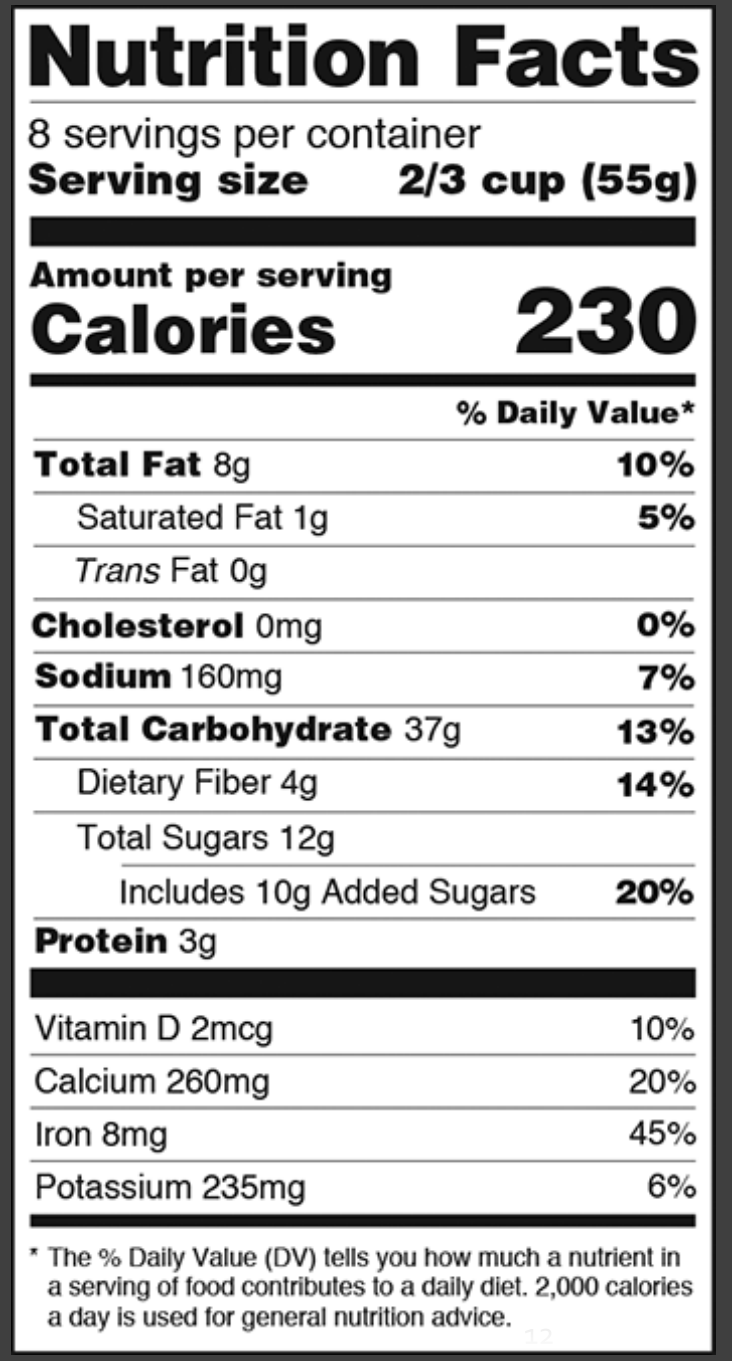
- Sunlight
  - Just 10 to 15 minutes of sunlight without sunscreen couple of times a week usually gives you enough vitamin D
- Food
  - mackerel, salmon, tuna, cheese, egg yolk & vitamin-fortified milk
  - Check the food label - one eight-ounce serving of milk usually has 25% of the daily value (DV) of vitamin D
- Supplements
  - vitamin D2 (ergocalciferol) and vitamin D3 (cholecalciferol), both types are good for bone health

Vitamin D Deficiency: Are You at Risk?

- People who spend little time in the sun or those who regularly cover up when outdoors
- People living in nursing homes or other institutions or who are homebound
- People with certain medical conditions such as Celiac disease and inflammatory bowel disease
- People taking medicines that affect vitamin D levels such as certain anti-seizure medicines
- People with very dark skin
- Obese or very overweight people
- Older adults with certain risk factors

How Much Vitamin D Should You Supplement?

- Subtract the total amount of vitamin D you get each day from the recommended total daily amount for your age



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High-Dose Vitamin D: No Help for Bone Health

High-Dose Vitamin D

- Vitamin D might not be much help for strengthening bones among healthy adults without osteoporosis
  - Clinical trial assessing three levels of daily vitamin D supplementation -- 400 IU, 4,000 IU, and 10,000 IU
  - Radial volumetric bone mineral density (BMD) was significantly lower among those (ages 55-70) taking higher doses for 3 years

Ref: Burt LA, et al "Effect of high-dose vitamin D supplementation on volumetric bone density and bone strength" JAMA 2019; DOI: 10.1001/jama.2019.11889.

High-dose vitamin D for bone health: May do more harm than good

- High-dose vitamin D supplementation provides no benefit for maintaining bone quality in healthy older adults without osteoporosis

- Rather than a hypothesized increase in volumetric bone mineral density (BMD) with doses well above the recommended dietary allowance, a negative dose-response relationship was observed

Ref: Lauren A. Burt, PhD <https://bonelab.ucalgary.ca/people/investigators/lauren-burt> , of the McCaig Institute for Bone and Joint Health at the University of Calgary (Alta.)

High-Dose Vitamin D for bone health

- High-dose vitamin D increases fall risk
- Large, intermittent vitamin D doses may increase fracture, fall risk in elderly
- Hypercalcemia and hypercalciuria had significant dose-response effects

Ref: Burt LA, et al "Effect of high-dose vitamin D supplementation on volumetric bone density and bone strength" JAMA 2019; DOI: 10.1001/jama.2019.11889.

High-Dose Vitamin D for bone health

- Vitamin D is considered beneficial for preventing and treating osteoporosis in individuals with 25(OH)D levels less than 30 nmol/L
- Recent meta-analyses did not find a major treatment benefit for osteoporosis or for preventing falls and fractures

Ref: Burt LA, et al "Effect of high-dose vitamin D supplementation on volumetric bone density and bone strength" JAMA 2019; DOI: 10.1001/jama.2019.11889.

High-Dose Vitamin D for bone health

- No dose of vitamin D supplementation was able to prevent bone loss
- Each dose saw a drop in the percentage of radial volumetric BMD over 3 years
  - 400 IU: -1.2%
  - 4,000 IU: -2.4%
  - 10,000 IU: -3.5%

Ref: Burt LA, et al "Effect of high-dose vitamin D supplementation on volumetric bone density and bone strength" JAMA 2019; DOI: 10.1001/jama.2019.11889.

Vitamin D for bone health

- In a clinical trial of 311 adults, free of osteoporosis, ages 55-70
- Baseline serum 25-hydroxyvitamin D levels between 12-50 ng/mL (30-125 nmol/L)
- Baseline serum calcium levels between 8.4-10.2 mg/dL (2.10-2.55 mmol/L)
- Take no more than 200 IU of additional vitamin D each day
- Recommended level of calcium (1,200 mg/day) were provided calcium citrate tablets

Vitamin D for bone health

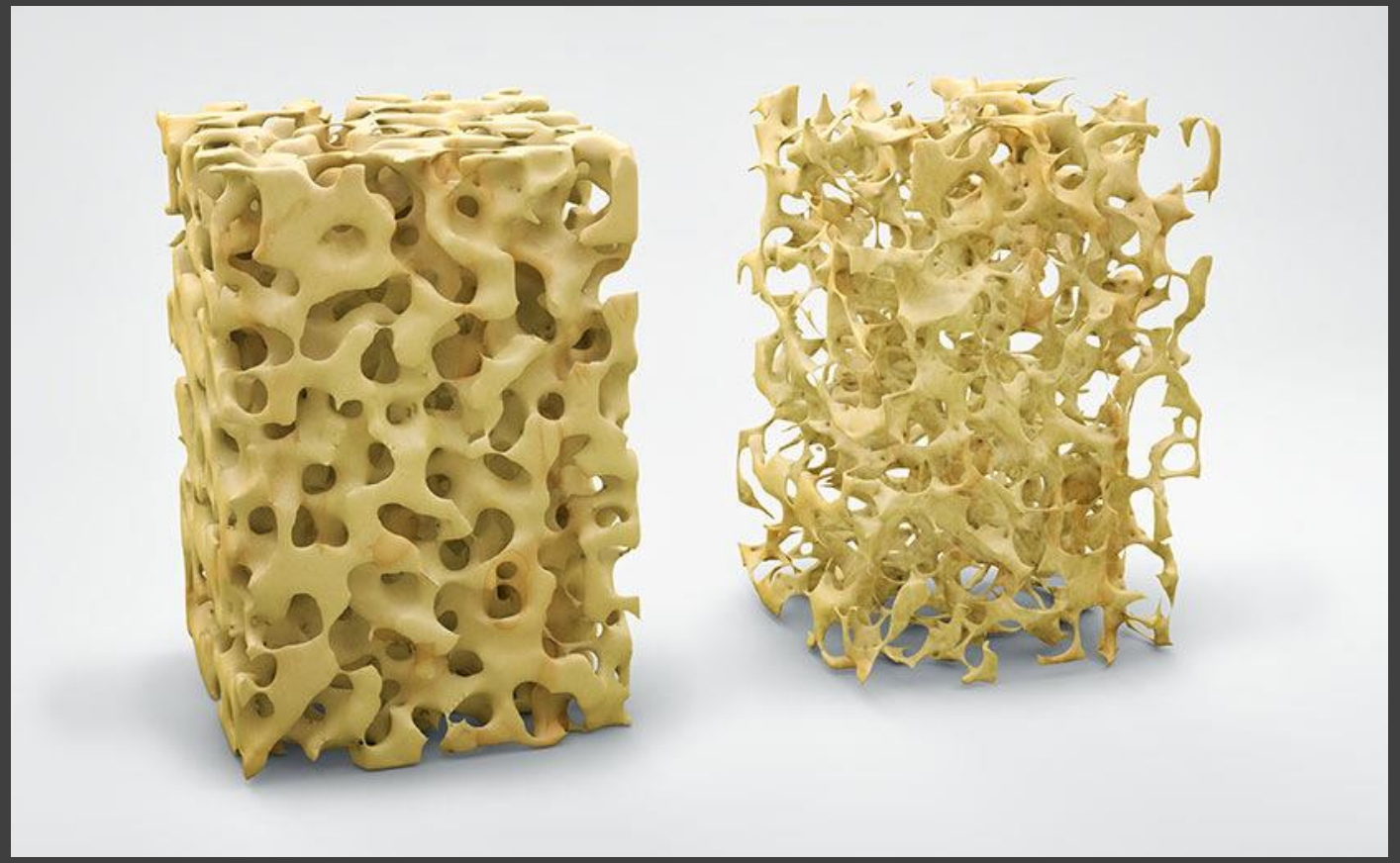
- Volumetric BMD was measured with high-resolution peripheral quantitative CT and DXA scans
- BMD showed no changes over time

Ref: Burt LA, et al "Effect of high-dose vitamin D supplementation on volumetric bone density and bone strength" JAMA 2019; DOI: 10.1001/jama.2019.11889

Vitamin D and Osteoporosis

- Osteoporosis represents a significant health challenge worldwide
- Approximately 9 million fractures occur globally every year
- By the year 2050, hip fractures are expected to increase 240% over the number in 1990

- Osteoporosis is a disease characterized by low bone mass and the weakening of bone tissue that is typically seen in elderly women. This is dangerous as it leads to an increased risk of bone fractures. Adequate calcium and vitamin D intake are safe ways to reduce the risk of osteoporosis related fractures



Vitamin D and Osteoporosis

- Having a prior fracture, increases the risk of a new fracture 2- and 4-fold
- Osteoporosis is one of the main conditions that affect older people, and as life expectancy is going up, there is a real need to focus on prevention
- Recommend adequate calcium (Ca) and vitamin D intake, avoiding smoking and heavy drinking, and also exercising regularly

Vitamin D and Osteoporosis

- Vitamin D is necessary for building strong bones
- Vitamin D deficiency is significant all over the world
- Taking vitamin D supplements addition to calcium may help reduce the risk of hip and other bone fractures in older people

Ref: Bárbara DN, Alejandra B, Marina G, et al. Impact of vitamin D3, calcium and exercise in the management of osteoporosis. *MOJ Women's Health.* 2020;9(2):38–40. DOI: 10.15406/mojwh.2020.09.00266

How calcium and vitamin D can help osteoporosis

Calcium and Vitamin D

- Calcium alone and vitamin D alone have weak results on fracture, with the impossibility of reducing fractures or increasing BMD
- The effects of vitamin D on bone mineral density showed a small benefit only at the femoral neck
- No effect at any other site

Ref: Bárbara DN, Alejandra B, Marina G, et al. Impact of vitamin D3, calcium and exercise in the management of osteoporosis. *MOJ Women's Health.* 2020;9(2):38–40. DOI: 10.15406/mojwh.2020.09.00266

Calcium and vitamin D

- Both calcium from dietary sources and supplements produces small non progressive increases in BMD what are improbable to lead to a significant reduction in risk of fracture

Ref: Tai V, Leung W, Grey A, et al. Calcium intake and bone mineral density: systematic review and meta-analysis. *BMJ*.2015;351:h4183

Calcium and vitamin D

- When Ca is added to vitamin D supplementation, a slightly lower risk of total and hip fractures has been demonstrated in fragile elderly women

Ref: Black DM, Rosen CJ. Clinical Practice. Postmenopausal Osteoporosis. *N Engl J Med*. 2016;374(3):254–262

Calcium and vitamin D

- Meta-analysis from the National Osteoporosis Foundation (NOF)
  - calcium plus vitamin D supplementation produced a statistically significant 15% reduced risk of total fractures and a 30% reduced risk of hip fractures

Ref: Cano A, Chedraui P, Goulis DG, et al. Calcium in the prevention of postmenopausal osteoporosis: EMAS clinical guide. *Maturitas*. 2018;107:7–12

Treatment of osteoporosis

- Treatment options include pharmacological treatments (includes bisphosphonates, estrogen agonist/antagonist, parathyroid hormones, etc.), and physical therapy (following a fracture)

- Lifelong adequate calcium and vitamin D intake are necessary for an individual to reach peak bone mass, as skeletal bones contain approximately 99% of the calcium within the body and vitamin D aids in the absorption of calcium

Calcium and vitamin D in the treatment of osteoporosis

- Most drugs used in osteoporosis are almost always supplemented with calcium and vitamin D

Ref: Cano A, Chedraui P, Goulis DG, Lopes P, Mishra G, Mueck A, et al. Calcium in the prevention of postmenopausal osteoporosis: EMAS clinical guide. Maturitas. 2018;107:7-12.

Drug	Study (Author)	Supplement calcium	Supplement vitamin D	Percentage supplemented
Alendronate	FIT (Black et al.)[28]	500 mg	250 IU	82%
Risedronate	VERT (Harris et al.)[29]	500 mg	500 IU	100%
Ibandronate	BONE (Delmas et al.)[30]	500 mg	400 IU	100%
Zoledronate	HORIZON (Black et al.)[31]	1,000 mg	400 – 1,000 IU	100%
Raloxifene	MORE (Ettinger et al.)[32]	500 mg	400 – 600 IU	100%
Bazedoxifene	(Silverman et al.)[33]	<1,200 mg	400 – 800 IU	100%
Teriparatide	Fracture Prevention Trial (Neer et al.)[34]	1,000 mg	400 – 1,200 IU	100%
Denosumab	FREEDOM (Cummings et al.)[35]	>1,000 mg	400 – 800 IU	100%
Romosozumab	FRAME (Cosman et al.)[36]	500 –1,000 mg	600 – 800 IU	100%

* EMA: European Medicines Agency; FDA: Food and Drugs Administration.

Ref: Cano A, Chedraui P, Goulis DG, Lopes P, Mishra G, Mueck A, et al. Calcium in the prevention of postmenopausal osteoporosis: EMAS clinical guide. Maturitas. 2018;107:7-12.

Treatment of osteoporosis

- Regarding vitamin D, determining the plasma levels of vitamin D is recommended
- Insufficient levels of vitamin D have been described associated with an inadequate response of osteoporosis drugs
- Maintained levels of vitamin D ≥33 ng/ml presented a probability 4, 5 times greater than presenting a favorable response to antiresorptive treatment

Ref: Carmel AS, Shieh A, Bang H, Bockman RS. The 25(OH)D level needed to maintain a favorable bisphosphonate response is ≥33 ng/ml. Osteoporos Int. 2012;23:2479-87.

Treatment of osteoporosis

- Correcting the levels of calcium and vitamin D is recommended, diet or the use of supplements, in patients with osteoporosis who are going to receive an antiresorptive or osteoforming drug

- The correction of vitamin D levels can be associated with a decrease in the risk of falls, and therefore with a lower risk of osteoporotic fracture

Ref: Martinez-Laguna D, Rev Osteoporos Metab Miner. 2019; 11 (Supl 1): S13-17

Exercise

- Exercise not only increases muscle mass and strength, but also improves balance

Exercise

- Walking is unlikely to stimulate an adequate osteogenic response to increase BMD and prevent osteoporosis
- Resistance exercise proved to be effective in developing muscle mass and increasing strength even in people who are fragile or have a prior fracture
- Non-weight bearing progressive resistance strength training for the neck of femur (Cochrane Collaborative Study)
- Exercise training reduced overall fracture number by 51% and vertebral fracture number by 44%
- As for falls, reduced the risk of fall-related fractures by 40% in adults aged ≥50years

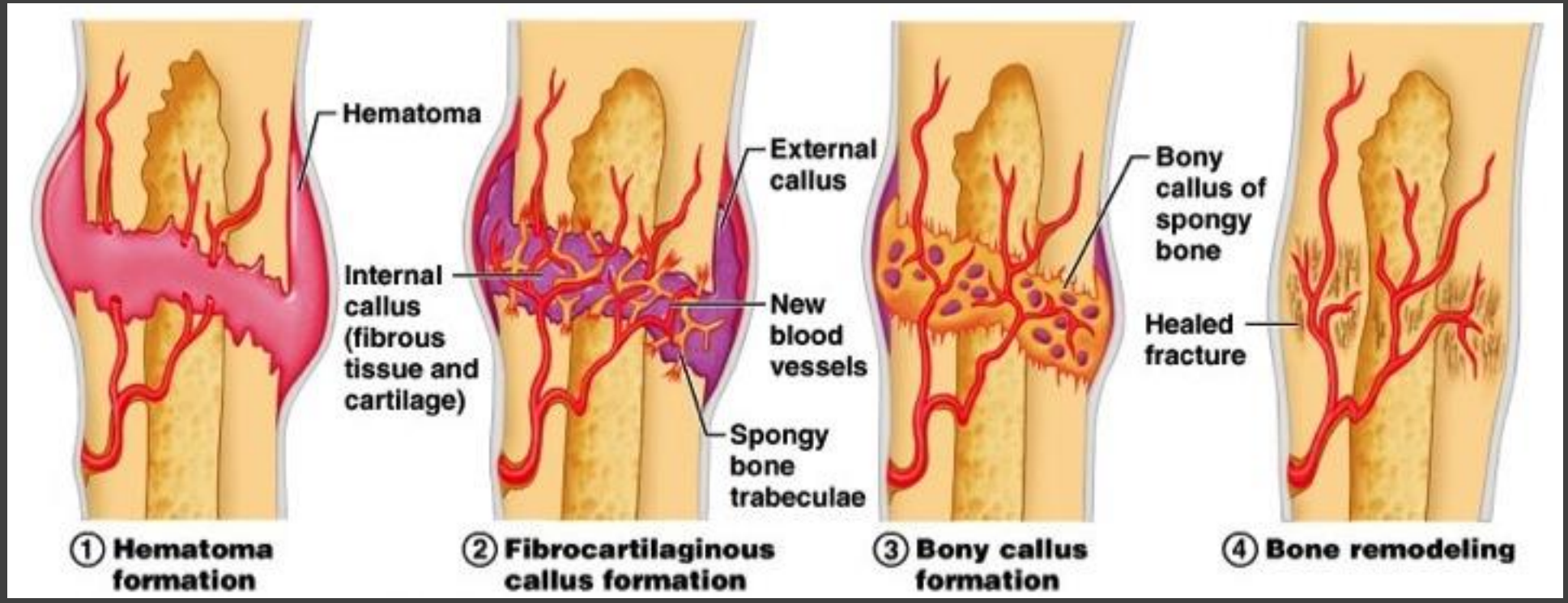
Ref : Zhao R, Feng F, Wang X. Exercise interventions and prevention of fall- related fractures in older people: a meta-analysis of randomized controlled trials. *Int J Epidemiol*. 2017;46(1):149–161.

Fall Prevention and Vitamin D

- Statistically significant reduction in falls with vitamin D supplementation
- Supplementation with 1000 IU of vitamin D3 per day significantly reduced the number of falls
- Impact of vitamin D on fall frequency appears to be dose-dependent, higher dose (700 to 1000 IU/day) showed a risk reduction, whereas lower dose (200 to 600IU/day) did not

Ref: https://journals.lww.com/menopausejournal/toc/2016/03000

Vitamin D and Fracture Healing



Vitamin D and Fracture Healing: An Ongoing Puzzle

- **QUESTION:** Whether vitamin D is of potential relevance in preventing future fractures, and especially in the impacting the healing process of current fractures.

Vitamin D and Fracture Healing

- Vitamin D has no clinically meaningful effect on the maintenance of bone mineral density and has no bearing on bone health or on fracture healing

Ref: Bolland MJ, Grey A, Avenell A. Effects of vitamin D supplementation on musculoskeletal health: a systematic review, meta-analysis, and trial sequential analysis. Lancet Diabetes Endocrinol 2018; 6(11): 847-858. [PMID: 30293909] [DOI:10.1016/S2213-8587(18)30265-1]

Vitamin D and Fracture Healing

- Vitamin D and calcium supplements may not lower fracture risk and did not protect against fracture
- Recommendations for calcium supplementation on elderly, nursing- home bound women with vitamin defficiencies and low bone density, for whom calcium and vitamin D supplements did significantly reduce fracture risk.
- People with or at risk for low bone density (perimenopausal and postmenopausal women, people diagnosed with other skeletal disorders, or who take certain medications), should discuss whether they need supplements and to have blood levels of vitamin D monitored.

Ref: https://www.health.harvard.edu/blog/calcium-vitamin-d-fractures-oh-20180212132247

Vitamin D and Fracture Healing

- No conclusive evidence regarding the routine use of vitamin D as a supplement in cases with bone fractures and their prevention
- More research regarding a role for vitamin D in bone fracture healing and prevention is warranted

Ref: Marks Ray. Vitamin D and Fracture Healing: An Ongoing Puzzle. International Journal of Orthopaedics 2019; **6(2)**: 1050-1060
Available from: URL: http://www.ghrnet.org/index.php/ijo/article/view/2569

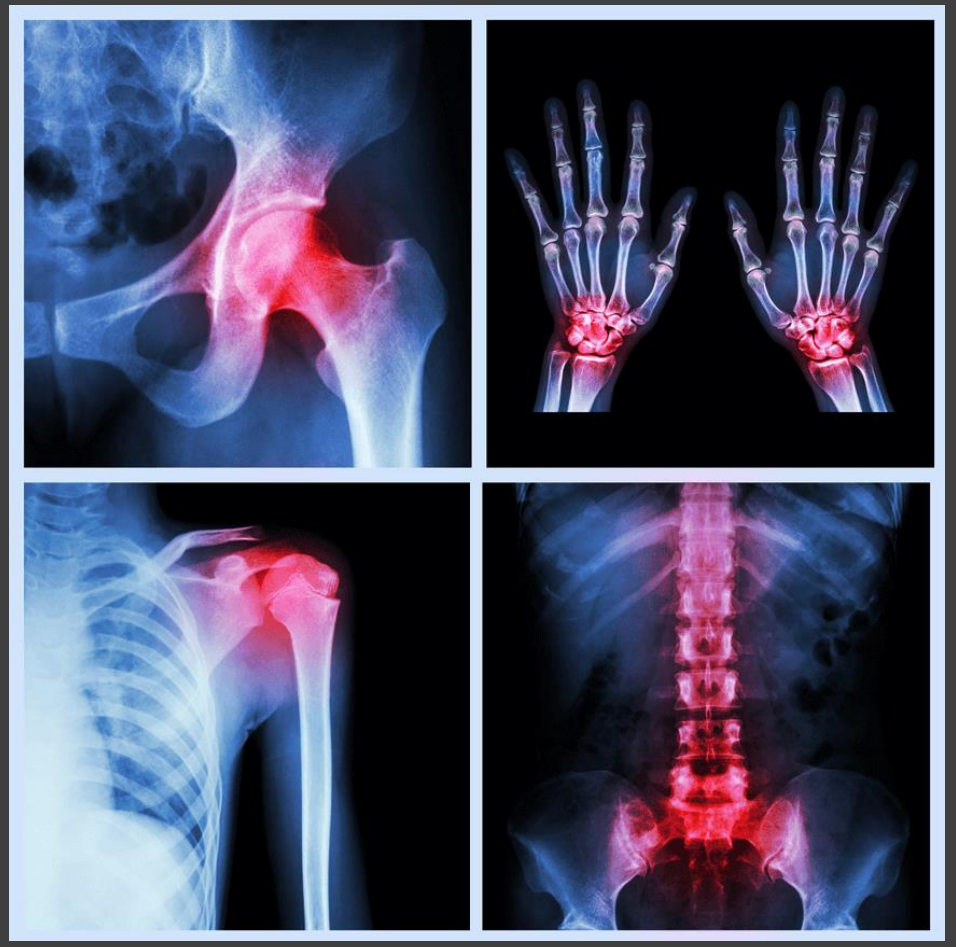
Vitamin D and Fracture Healing

- Experimental animal studies have demonstrated that the concentration of vitamin D metabolites is higher at a fracture callus compared to the uninjured contralateral bone,
- Vitamin D supplementation leads to decreased time to union and increased callus vascularity, and increases mechanical bone strength compared to controls.
- While evidence to confirm that vitamin D supplementation improves fracture healing in clinical studies does not exist, the pre-clinical data are compelling and worthy of further investigation

Ref: Marks R, Department of Health and Behavior Studies, Teachers College, Columbia University, Box 114, 525W, 120th Street, New York, NY 10027, the United States.**Email:** rm226@columbia.edu, Dec 10,2019

Calcium and/or Vitamin D Supplementation for the Prevention of Fragility Fractures: Who Needs It?

- Calcium supplements produce a 1% increase in bone density in the first year of use, without further increases subsequently
- Vitamin D supplements do not improve bone density
- Supplementation with calcium, vitamin D, or their combination does not prevent fractures in community-dwelling adults



Ref: *Nutrients* **2020**, *12*, 1011; doi:10.3390/nu12041011

Prevention of Fragility Fractures

- Correction of severe vitamin D deficiency (<25 nmol/L) is necessary before use of potent anti-resorptive drugs to avoid hypocalcemia
- Calcium supplements cause gastrointestinal side effects, particularly constipation, and increase the risk of kidney stones and, probably, heart attacks by about 20%
- Low-dose vitamin D is safe, but doses >4000 IU/day have been associated with more falls and fractures
- Current evidence does not support use of either calcium or vitamin D supplements in healthy community-dwelling adults.

Ref: *Nutrients* **2020**, *12*, 1011; doi:10.3390/nu12041011

Prevention of Fragility Fractures

- Calcium supplementation, with concomitant vitamin D supplementation, is supported for patients at high risk of calcium and vitamin D insufficiency
- The efficacy and safety of anti-resorptive osteoporosis medications does not require co-administration of supplements, other than for the treatment or prevention of vitamin D deficiency in those with clinical risk factors

Ref: Harvey, N.C.; Biver, E.; Kaufman, J.M.; Bauer, J.; Branco, J.; Brandi, M.L.; Bruyere, O.; Coxam, V.; Cruz-Jentoft, A.; Czerwinski, E.; et al. The role of calcium supplementation in healthy musculoskeletal ageing: An expert consensus meeting of the European Society for Clinical and Economic Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Diseases (ESCEO) and the International Foundation for Osteoporosis (IOF). *Osteoporos Int.* **2017**, *28*, 447–462.

Take Home Message

- High dose vitamin D for bone health may do more harm than good
- No conclusive evidence regarding routine use of vitamin D as a supplement in cases with bone fractures and their prevention
- No consensus that the supplementation of calcium and vitamin D in isolation reduces the rate of osteoporotic fracture

Take Home Message

- To prevent osteoporotic fracture, ensure adequate amount of calcium and vitamin D, regular muscle strengthening exercises, assess personal risk factors for fall, reduce tobacco smoking and alcohol intake

- Correcting the levels of calcium and vitamin D is recommended for patients with osteoporosis who are going to receive an antiresorptive or osteoforming drugs

- Fall prevention is the mainstay of reducing osteoporotic fracture

Thank you

Beware of COVID-19