Osteoporosis:
Understanding Your Risk Factors

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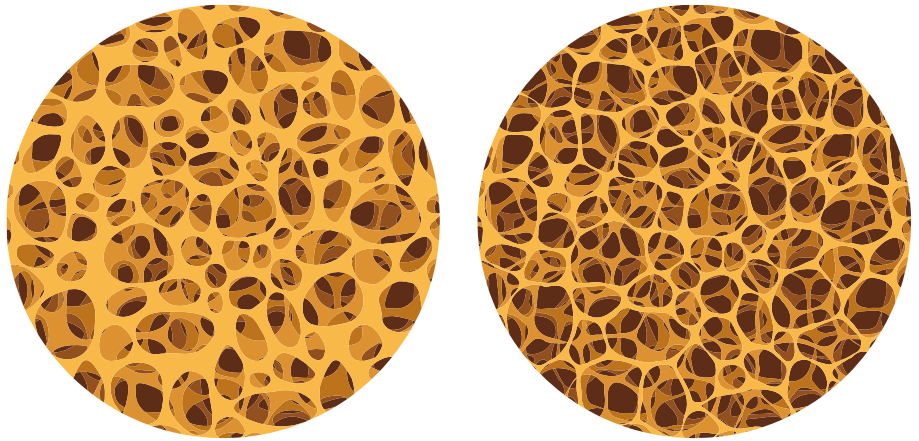
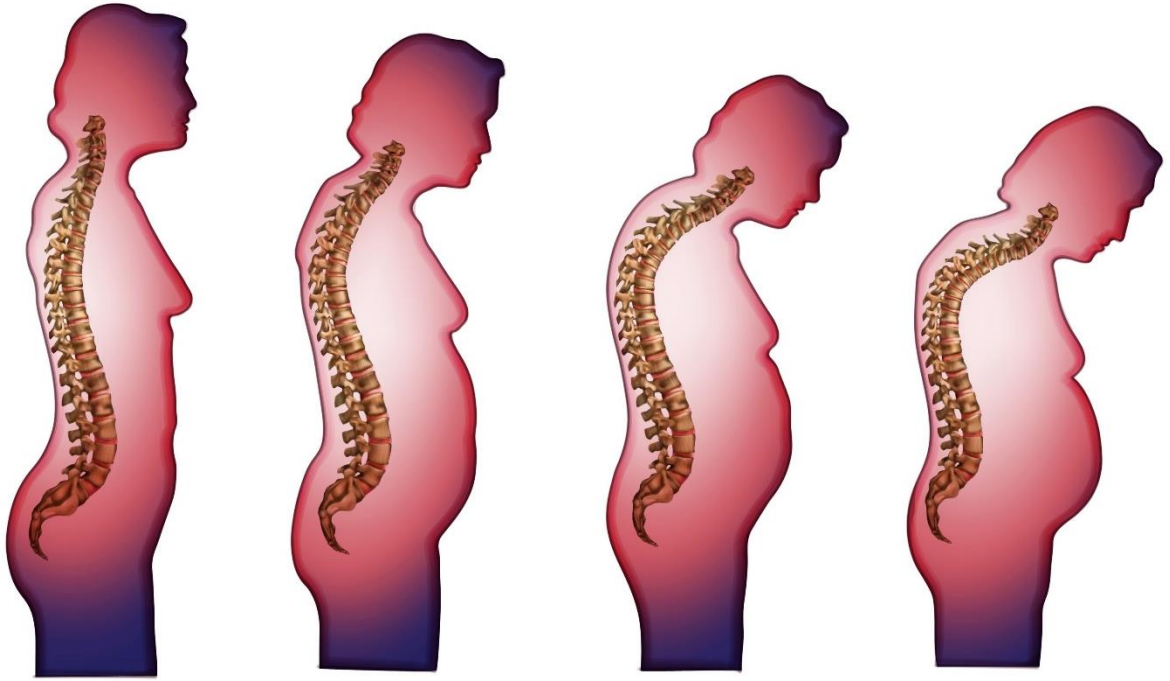
The Development of Osteoporosis



Young Normal **Osteoporotic**



Characterized by low bone mass and microarchitectural deterioration of bone tissue, leading to enhanced bone fragility and increased risk of fractures

Consensus Development Conference. Am J Med. 1993; 94:646-650.

Osteoporosis Is a Serious Public Health Problem

Fracture Prevalence and Incidence

- At 50 yr of age, **lifetime risk** of fracture is[1]:
  - **1 in 2 in women**
  - 1 in 4 in men
- Affects 10.2 million Americans aged ≥ 50 yr[2]
  - 8.2 million women
  - 2.0 million men
- 2 million fractures yearly[3]

Fracture Morbidity and Mortality

- Hospitalization
  - US **hospitalization** rates **exceed** those for heart attack, stroke, and breast cancer[4]
- Increased **morbidity** and **mortality** after fracture[5]

1. National Osteoporosis Foundation. General facts. 2. Wright. J Bone Miner Res. 2014;29:2520. 3. Burge. J Bone Miner Res. 2007;22:465. 4. Singer. Mayo Clin Proc. 2015;90:53. 5. Nazrun. Ther Clin Risk Manag. 2014;10:937.

Osteoporosis Guideline Recommendations for Screening

AACE Guidelines[1]

- Evaluate all postmenopausal women aged ≥50 yr for osteoporosis risk
- Obtain a detailed history, physical exam, and clinical fracture risk assessment with FRAX® or other tool
- Consider BMD testing based on clinical fracture risk profile
- When BMD is measured, axial DXA measurement of the lumbar spine and hip should be used, with **1/3 radius**

IOF-ESCEO Guidelines[2]

- Use country-specific FRAX® in postmenopausal women at risk for fracture
- In intermediate-risk individuals, include DXA BMD measurement if available in FRAX® calculation
- **Trabecular bone score may be used as an adjunct to BMD and FRAX®**
- Vertebral fracture assessment should be considered if ≥4 cm height loss, kyphosis, recent or current long-term oral steroid therapy, or BMD T-score ≤-2.5

NAMS Guidelines[3]

- Measure bone density in postmenopausal women with risk factors for low bone density
  - Women ≥65 yr
  - Women ≥50 yr with additional risk factors
  - History of fracture since menopause
  - Known medical causes of bone loss or fracture

1. Camacho. Endocr Pract. 2020;26(suppl 1):1. 2.. Kanis. Osteoporos Int. 2019;30:3. 3. NAMS. Menopause. 2021;28:937.

Osteoporosis: Modifiable and Non-Modifiable Risk Factors

Understanding these categories is critical for effective prevention and

management strategies, especially for healthcare professionals and patients at high risk.

Modifiable Risk Factors

- Diet and Nutritional Status
- Physical Activity/Sedentary Lifestyle
- Smoking and Alcohol Intake
- Underlying Chronic Diseases (e.g., Diabetes, RA)

Non-Modifiable Risk Factors

- Age (Advanced)
- Genetics and Family History
- Gender (Female)
- Certain Medication Exposures

Zhu J, March L. Treating osteoporosis: risks and management. Aust Prescr. 2022

The Crucial Role of Diet in Bone Health

A healthy, nutrient-rich diet is a key modifiable factor that can significantly lessen the impact of chronic diseases like osteoporosis.

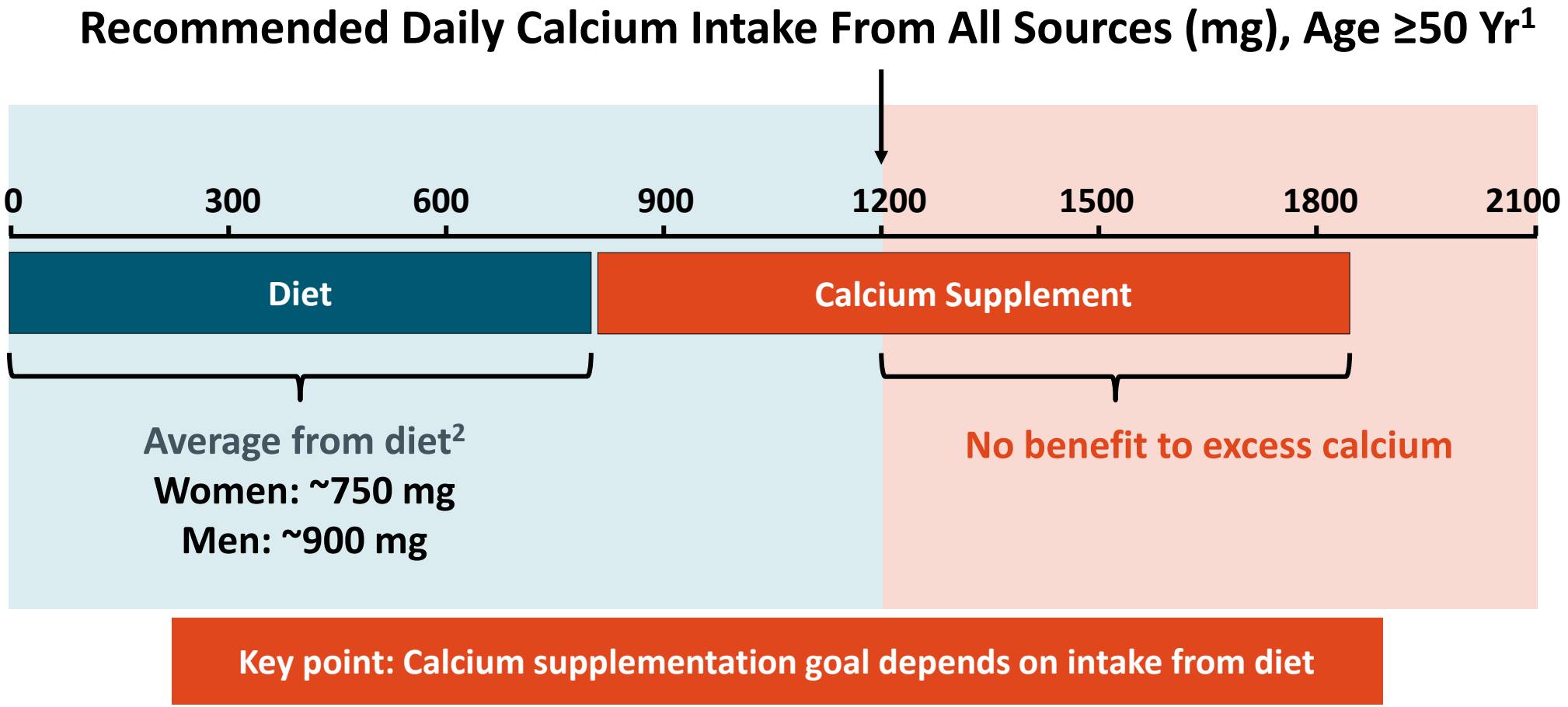
Positive Dietary Patterns

- High intake of dairy products, fruits, and whole grains
- Adequate intake of dietary protein, calcium, and vitamin D
- A mother's diet can influence the bone mass established in their highlighting the lifelong impact of nutrition.

> A good general nutritional status with adequate dietary protein, calcium, vitamin D, fruits, and vegetables has a positive influence on bone health influence on bone health

Alyafei A, Daley SF. The Role of Dietary Lifestyle Modification in Chronic Disease Prevention and Management. 2025

Reducing Risk: Calcium Intake



Key point: Calcium supplementation goal depends on intake from diet

1. Camacho. Endocr Pract. 2020;26(suppl 1):1. 2. Bailey. J Nutr. 2010;140:817.

Are Calcium Supplements Bad for the Heart?

Evidence of Harm[1,2]

- Post hoc studies/meta-analyses
- Mostly women
- CV events usually not primary endpoints
- CV events usually not adjudicated

No Evidence of Harm[3-6]

- Prospective studies
- Both men and women
- CV events often primary endpoints
- CV events often adjudicated

**The concern is not about calcium supplements;
it's about OVERDOING IT with calcium supplements.**

**I have no concern using calcium supplements
to achieve total intake ~1200 mg/day**

1. Bolland. BMJ. 2010;341:c3691. 2. Bolland. BMJ. 2011;342:d2040. 3. Lewis. J Bone Miner Res. 2011;26:35.
4. Samelson. Am J Clin Nutr. 2012;96:1274. 5. Prentice. Osteoporos Int. 2013;24:567. 6. Khan. J Bone Miner Res. 2015;30:1758.

Vitamin D Supplementation

Goal

- Adequate 25-hydroxyvitamin D level: ≥30 ng/mL[1-3]
- Desirable range: 30-50 ng/mL[2,3]
  - Toxicity unlikely with levels up to 100 ng/mL[4]

Supplements

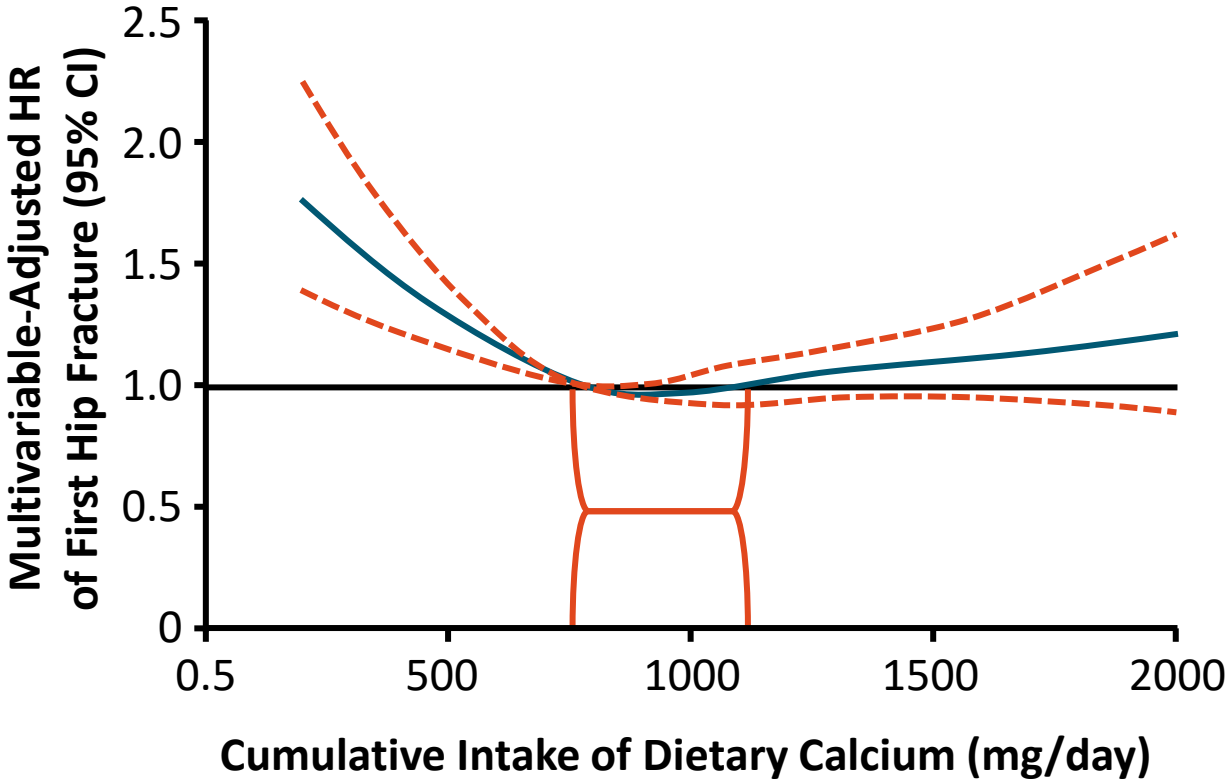
- Most patients require vitamin D3 at 1000-2000 IU/day to achieve this[2]
- Supplements are available (1000 IU, 2000 IU, 50,000 IU…)
- "Safe upper limit" is 4000 IU/day[1]

To convert ng/mL to nmol/L, multiply by 2.5.
To convert IU to mcg, divide by 40.

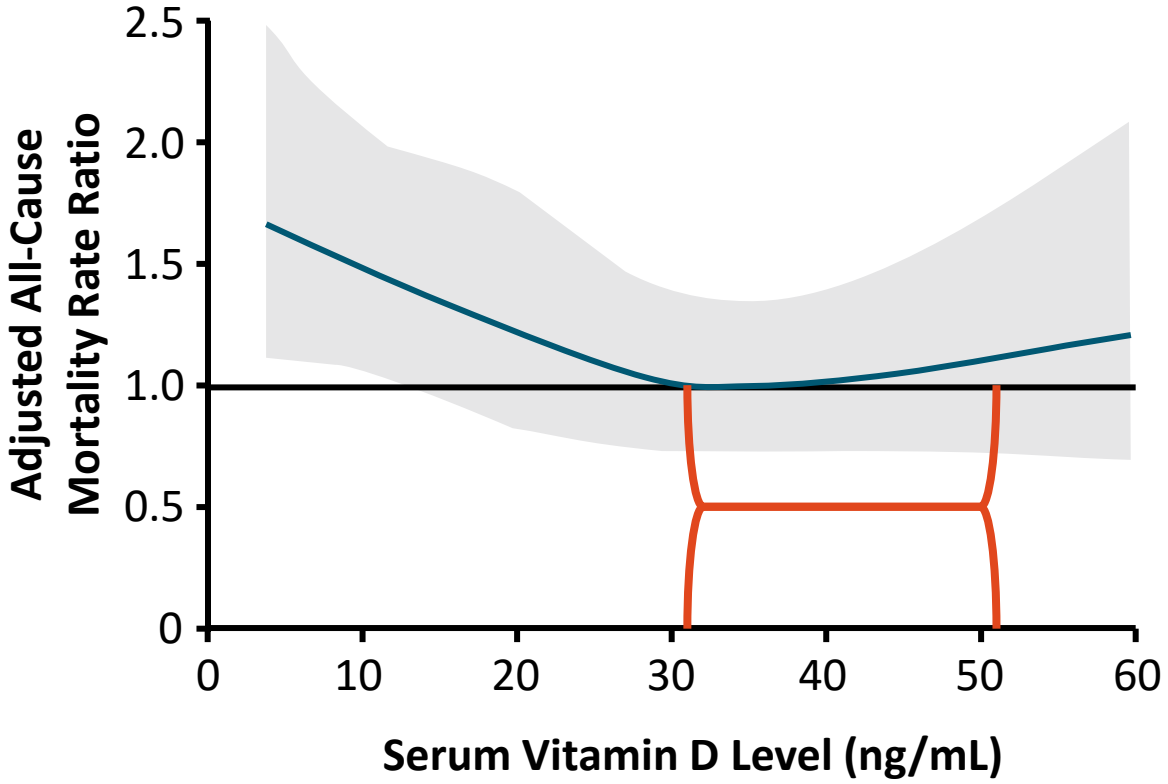
1. Cosman. Osteoporosis Int. 2014;25:2359. 2. Camacho. Endocr Pract. 2020;26(suppl1):1.
3. Ross. J Clin Endocrinol Metab. 2011;96:53. 4. Dudenkov. Mayo Clin Proc. 2015;90:577.

Calcium and Vitamin D: A Happy Medium

Dietary Calcium and Fractures[1]



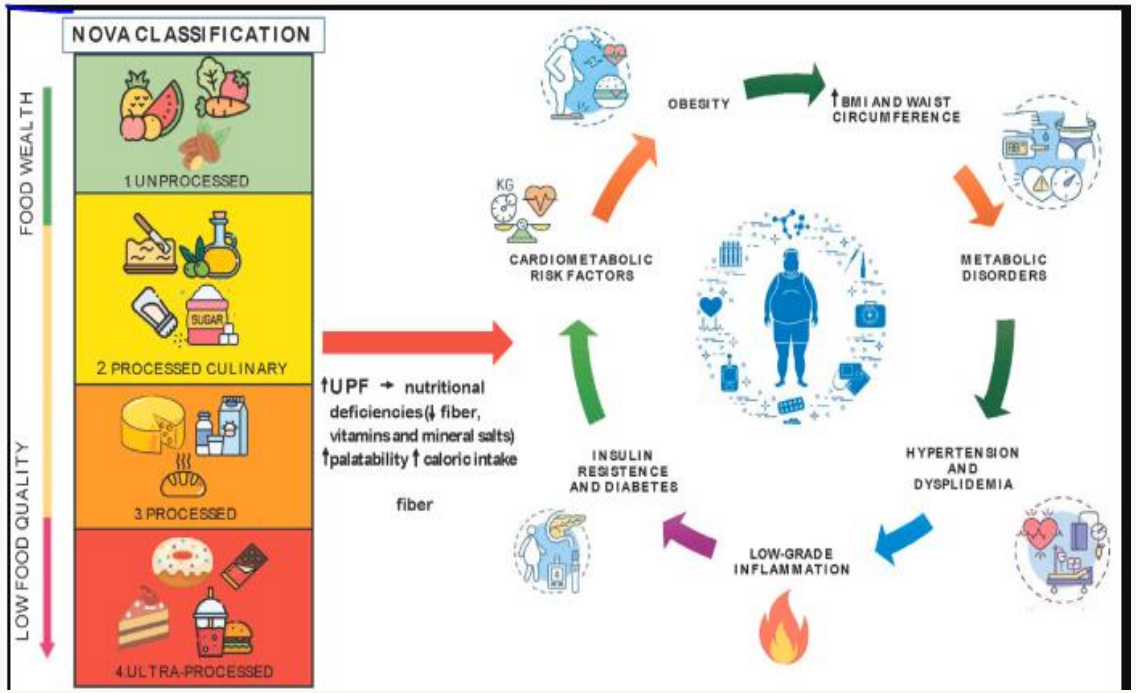
Vitamin D and Mortality[2]



1. Warensjö. BMJ. 2011;342:d1473. 2. Melamed. Arch Intern Med. 2008;168:1629.

The Crucial Role of Diet in Bone Health

Consumption of "junk food" and a sedentary lifestyle directly undermine bone integrity.



Nutritional Deficiencies & Risk

Vitamin K2 Absence: Junk food often lacks Vitamin K2, which is crucial for calcium removal from soft tissues and proper bone mineralization

Vitamin D Deficiency: which is vital for calcium absorption and bone bone remodeling.

> **High-caloric diets and heavy alcohol** consumption have been associated with lower higher rates of fracture.

Alyafei A, Daley SF. The Role of Dietary Lifestyle Modification in Chronic Disease Prevention and Management.2025

Alcohol Consumption: A Nonlinear Association with Fracture Risk

The relationship between alcohol intake and bone health is complex and non-linear, presenting conflicting evidence that requires careful clinical requires careful clinical interpretation and patient counseling.

Low-to-Moderate Intake

Some studies, (OSTPRE-FPS), suggest that low-to-moderate alcohol consumption may exert protective effects on bone health in elderly women.

The Inverse Association

Meta-analyses confirm that light alcohol consumption is significantly associated reduced (inverse) risk of hip fracture.

Heavy Consumption

Conversely, heavy or excessive alcohol consumption is linked to an elevated risk of hip of hip fracture and detrimental impacts on bone on bone mineral density (BMD) in both cortical cortical and trabecular compartments in men men and women.

Osteoporotic patients must be consistently counseled on minimizing alcohol intake, avoiding heavy consumption, and integrating cigarette cessation and estrogen status monitoring.

Alcohol: A Simple Nutrient with Complex Actions on Bone in the Adult Skeleton. Alcohol Clin Exp Res. 2016

Smoking: A Significant Contributor to Bone Loss

Cigarette smoking is an established and powerful risk factor for osteoporosis, directly leading to a loss of bone mass and an increased an increased susceptibility to osteoporotic fractures.

1

Decreased BMD

Reduced BMD in smokers, particularly at the radius, neck, and whole body.

2

Hormonal Imbalances

Smoking disrupts critical calcium-calcium-regulating hormones: PTH increase, while active form of of Vitamin D decrease by approximately 10%.

3

Impact on Sex Hormones

Smoking increases FSH and LH, decrease in estrogen levels, leading to a rapid acceleration of bone loss.

Key Takeaway

Smoking affects calcium homeostasis and bone metabolism by altering the levels of PTH and vitamin D vitamin D metabolites, creating an environment highly conducive to bone deterioration.

The Effect of Tobacco Smoking on Bone Mass: An Overview of Pathophysiologic Mechanisms.
J Osteoporos. 2018 Dec 2;2018

Genetic Determinants of Bone Mineral Density

The genetics of osteoporosis is one of the most active research areas in bone biology.

It is well-established that a substantial variation in BMD is genetically determined, influencing individual susceptibility to the disease.

Vitamin D Receptor (VDR) Gene

Involved in calcium uptake and bone formation

Estrogen Receptor-α (ERα) Gene

Affecting osteoblast and osteoclast activity

Collagen Type I α1 (COLIA1) Gene

This gene can affect collagen structure and quantity

An insight into the paradigms of osteoporosis: From genetics to biomechanics. Bone Rep. 2021

Glucocorticoid-Induced Osteoporosis

Most common secondary cause of **osteoporosis**

Rapid Initial Bone Loss

Bone loss occurs rapidly in the first 3 months of therapy.

Annual Bone Loss

A slower but steady phase of annual bone loss follows the initial phase.

initial phase.

Mechanisms of Glucocorticoid Action on Bone

Increased Resorption: Glucocorticoids increase RANKL (Receptor Activator for Nuclear Factor κ-B Ligand) expression and decrease

leading to elevated osteoclast-mediated bone resorption.

Inhibited Formation: They inhibit osteoblast differentiation by increasing Dickkopf (an inhibitor of Wnt signaling) and suppressing IGF-I gene transcription, which

gene transcription, which is essential for bone formation and Type I collagen synthesis.

The molecular etiology and treatment of glucocorticoid-induced osteoporosis. Tzu Chi Med J. 2021

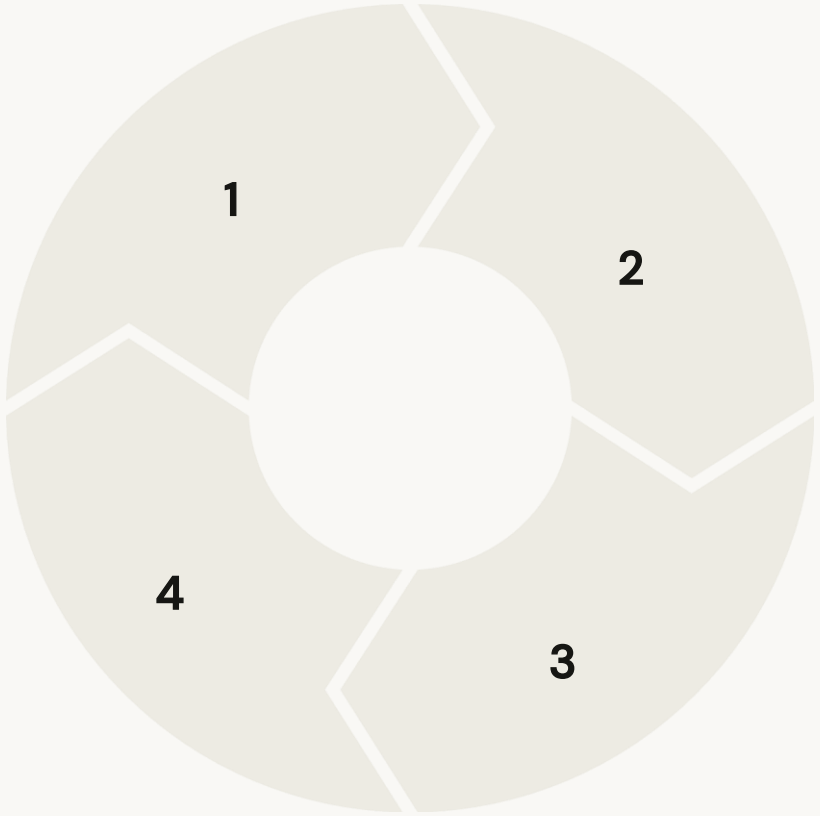
Endocrine Factors: Primary Hyperparathyroidism (PHPT)

Excessive PTH Secretion

PHPT causes uncontrolled secretion of Parathyroid Parathyroid Hormone,

Renal & Vitamin D Effects

PTH acts on the kidney to increase calcium reabsorption and stimulate the conversion of hydroxy vitamin D to its active form,



Elevated Bone Resorption

Elevated bone turnover, releasing calcium stores into the bloodstream.

Increased Fracture Risk

High fracture risk, particularly of the forearms and and vertebrae, in PHPT patients due to decreased decreased BMD.

Epidemiology, Pathophysiology, and Genetics of Primary Hyperparathyroidism. J Bone Miner Res. 2022

Rheumatoid Arthritis and Systemic Inflammation

Rheumatoid Arthritis (RA) is a systemic inflammatory disease strongly associated with secondary osteoporosis due to active inflammation, the frequent use of glucocorticoid therapy.

Dual Forms of Bone Loss in RA

Generalized Bone Loss

Periarticular (Localized) Bone Loss

Molecular Mechanisms: Cytokines & Signaling

An abundance of bone-resorbing cytokines within the synovial tissues, tissues, including:

- ✓ IL-1α and IL-1β, IL-6, IL-11, and IL-17
- ✓ Tumor Necrosis Factor (TNF)-α
- ✓ RANKL/OPG System Disruption

Systemic Manifestations and Complications in Patients with Rheumatoid Arthritis. J Clin Med. 2020

Diabetes Mellitus: A Complex Risk to Skeletal Health

Impact of Diabetes Type on Bone Density

Type 1 Diabetes Mellitus

Typically associated with a reduction in BMD, leading to increased fracture risk risk primarily due to poor bone quality and high falling risk.

Type 2 Diabetes Mellitus

Increased BMD (likely due to obesity),
yet paradoxically, higher risk of overall and hip fx.

Women with T1DM face up to 12-fold higher risk of hip fracture, emphasizing that high that high fracture risk in DM is often due to increased risk of falling (due to neuropathy, neuropathy, retinopathy, etc.) rather than just decreased BMD.

Molecular Mechanisms of Damage

- ✓ Advanced Glycation End Products (AGEs)
- ✓ Conversely, high glucose inhibits osteoblast growth and mineralization.
- ✓ Adipogenesis vs. Osteogenesis

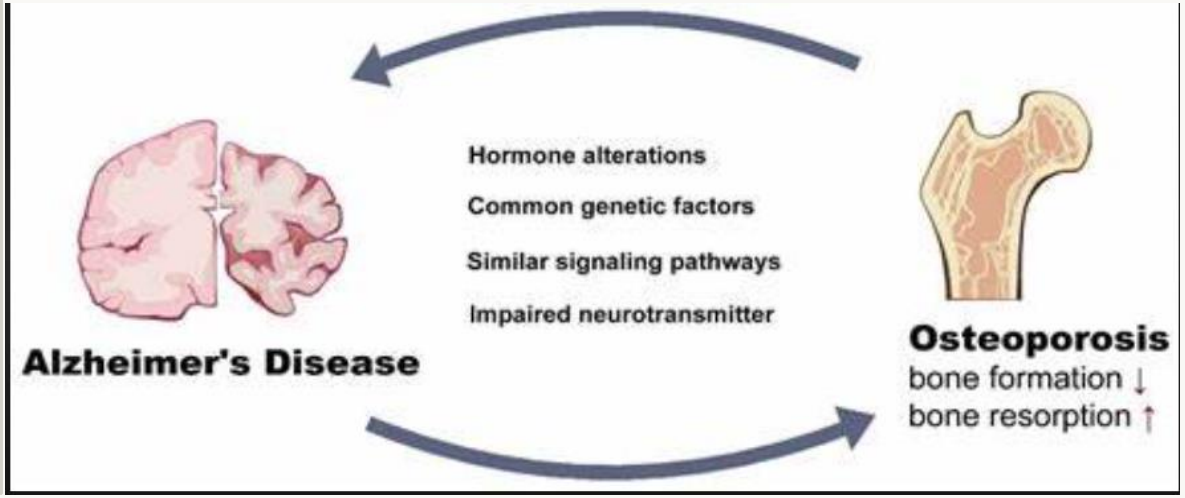
Bone Health in Patients With Type 2 Diabetes. J Endocr Soc. 2024

Comorbidities: Dementia and Cancer

Osteoporosis and Alzheimer's Disease (AD) common non-modifiable risk factors: body mass loss, vitamin D deficiencies, and physical activity.

The incidence of hip fracture is significantly higher in AD higher in AD

Pathological Link: Amyloid beta (Aβ) peptides associated with AD may increase

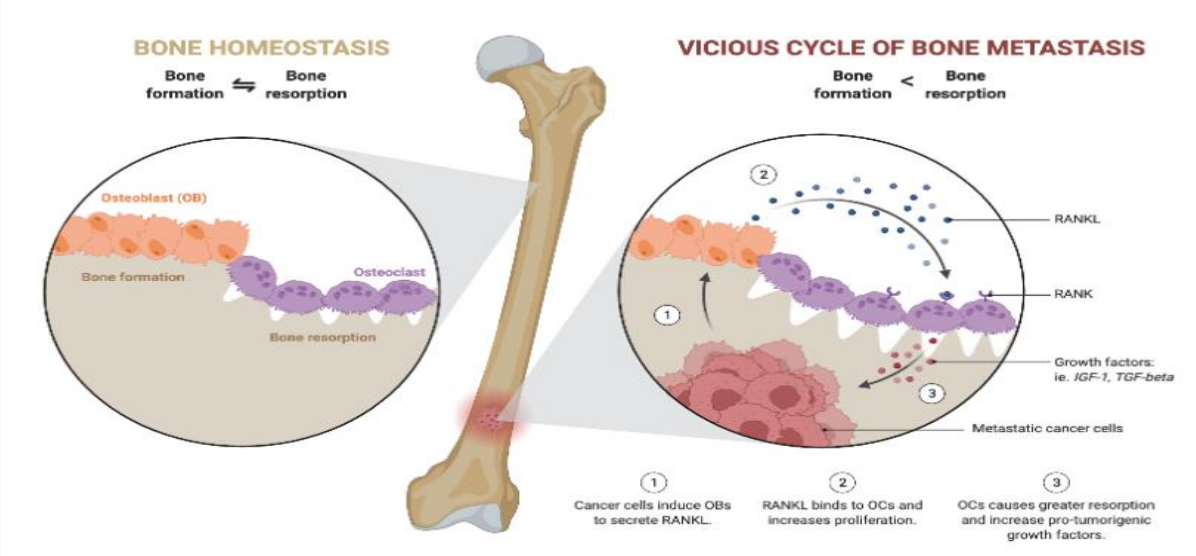


Modifiable risk factors for bone health & fragility fractures, Best Practice & Research Clinical Rheumatology,2022

Comorbidities: Dementia and Cancer

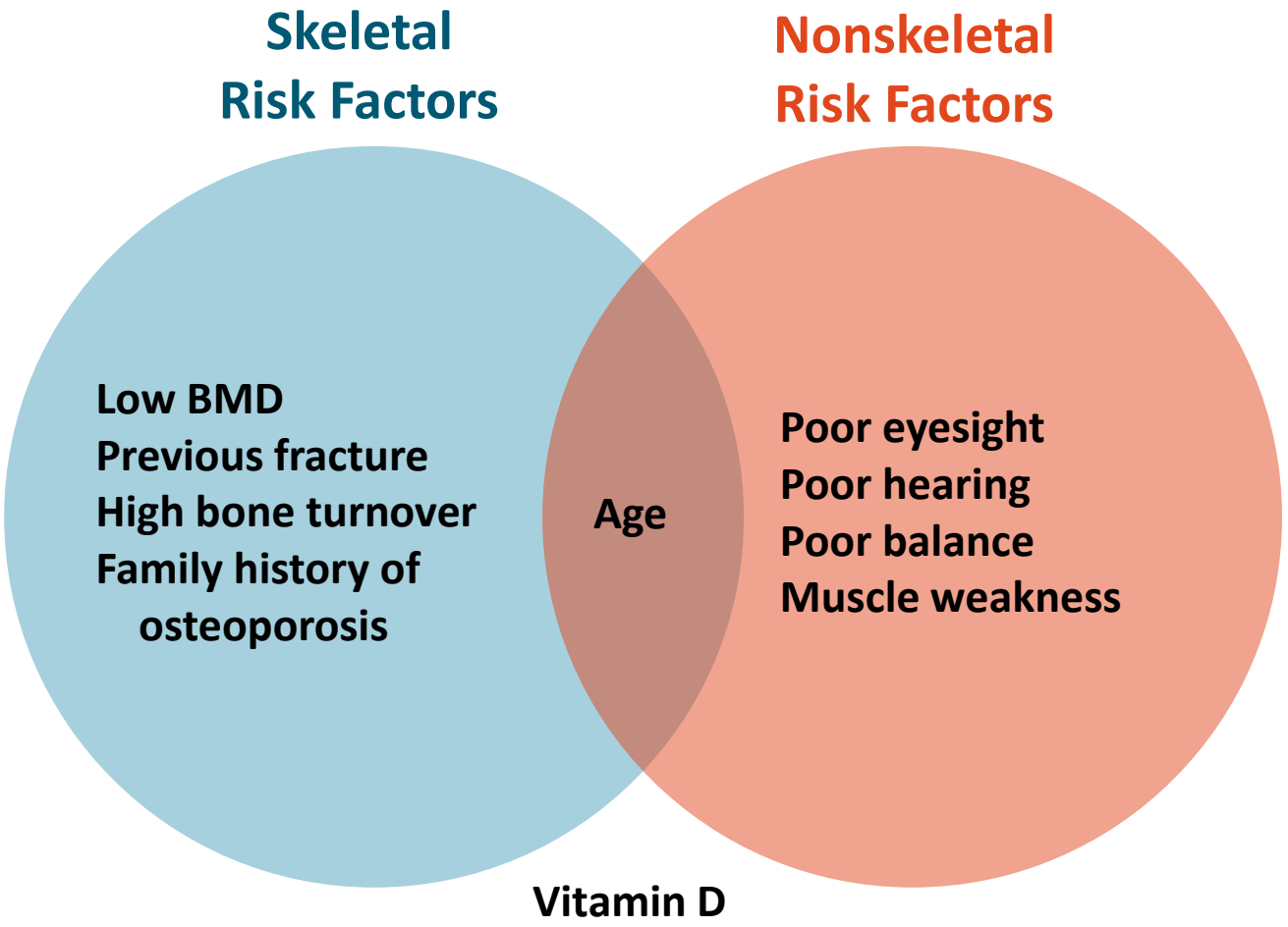
Cancer and Bone Disease

- ✓ Cancer-induced bone disease is severe
- ✓ Primary malignancy
- ✓ Its treatments
- ✓ Bone metastases particularly in breast and prostate.



Modifiable risk factors for bone health & fragility fractures,
Best Practice & Research Clinical Rheumatology,2022

Components of Fracture Risk



Camacho. Endocr Pract. 2020;26(suppl 1):1.

Patient Education to Reduce Risk

- High intake of dairy products, fruits, and whole grains contributes positively to overall bone density.
- Adequate intake calcium, and vitamin D is essential for maintaining robust bone structure.
- Consistently counseled on minimizing alcohol intake, avoiding heavy consumption, and integrating these guidelines with cigarette