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A comprehensive analysis of "Environmental and lifestyle risk factors influencing osteoporosis incidence and fracture outcomes: a systematic review of global and Indian populations.

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Background: Osteoporosis is a chronic metabolic bone disorder characterized by reduced bone mineral density (BMD) and deterioration of bone microarchitecture, leading to skeletal fragility and an increased risk of low-trauma fractures. These fragility fractures predominantly affect the spine, hip, and wrist, often resulting from minor mechanical stress that would not typically cause bone failure in healthy individuals. The disease arises from an imbalance between bone resorption and formation, driven by age-related hormonal changes, genetic predisposition, and modifiable risk factors such as nutritional deficiencies or sedentary lifestyles. Diagnosis relies on dual-energy X-ray absorptiometry (DXA), which quantifies BMD at critical skeletal sites, or clinical identification of fragility fractures in the absence of significant trauma.

Preventive and therapeutic strategies emphasize a multimodal approach. Non-pharmacological interventions include optimizing dietary calcium and vitamin D intake, weight-bearing and resistance exercises to enhance bone strength and muscle mass, and fall-prevention measures to mitigate injury risks. Pharmacotherapy targets bone remodelling pathways, employing antiresorptive agents (e.g., bisphosphonates, denosumab) to inhibit excessive osteoclast activity or anabolic drugs (e.g., teriparatide, romosozumab) to stimulate osteoblast-mediated bone formation. Regular monitoring of treatment efficacy and fracture risk stratification are essential for personalized management. Emerging therapies continue to explore novel mechanisms to restore bone homeostasis, underscoring the importance of early detection and proactive intervention in high-risk populations.

Keywords: Osteoporosis, Bone mineral density (BMD), Fragility fractures, Dual-energy X-ray absorptiometry (DXA), Pharmacotherapy.

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Pathophysiology of Osteoporosis and Fragility Fractures

Bone Remodelling and Regulatory Mechanisms

Bone homeostasis is maintained through a dynamic equilibrium between formation and resorption, orchestrated by osteoblasts (bone-forming cells) and osteoclasts (bone-resorbing cells). Osteoblasts synthesize the organic bone matrix and facilitate its mineralization, while osteoclasts degrade mineralized bone through acidification and enzymatic digestion. This process is tightly regulated by systemic hormones, including parathyroid hormone (PTH), calcitonin, estrogen, and vitamin D, as well as local mediators such as cytokines (e.g., interleukin-6, tumor necrosis factor-alpha) and prostaglandins. Estrogen deficiency, a hallmark of postmenopausal osteoporosis, disrupts this balance by upregulating osteoclast activity and prolonging their survival, accelerating bone loss.

Peak Bone Mass and Age-Related Bone Loss

Peak bone mass, the maximum skeletal density achieved by early adulthood (around age 30), is influenced by genetic, nutritional, and lifestyle factors. Men typically attain higher peak bone mass than women, though earlier assertions regarding elevated bone mass in individuals of African ancestry are under scrutiny. Following peak attainment, bone mass remains stable for approximately a decade, with formation and resorption rates in equilibrium. In women, the onset of menopause triggers a rapid decline in estrogen levels, leading to a 2% annual reduction in bone mineral density (BMD) for about 10 years, after which the rate of loss slows.[1] Age-related declines in renal vitamin D synthesis, reduced calcium absorption, and diminished osteoblast function further exacerbate bone loss in both sexes.

Cortical and Trabecular Bone Degradation

Osteoporotic bone loss impacts both cortical (compact) and trabecular (spongy) bone. Cortical bone undergoes thinning due to increased porosity from resorption cavities, while trabecular bone experiences a reduction in the number, size, and connectivity of trabeculae. These structural compromises diminish bone strength and load-bearing capacity. Trabecular bone, with its higher surface area and metabolic activity, is more susceptible to rapid resorption, particularly in regions like the vertebral bodies and femoral neck. The combined loss of cortical and trabecular integrity heightens fracture risk, even under minimal mechanical stress.

Fragility Fractures: Definition and Clinical Significance

Fragility fractures result from low-energy trauma, such as falls from standing height or less, and are diagnostic of osteoporosis in the absence of other pathologies. These fractures predominantly occur at skeletal sites with high trabecular bone content:

i)Vertebral Compression Fractures: Most common in the thoracic and lumbar spine, often presenting with height loss or kyphosis.

ii)Proximal Femur Fractures: Include femoral neck and intertrochanteric fractures, associated with significant morbidity and mortality.

iii)Distal Radius Fractures: Typically follow a fall onto an outstretched hand (Colles fracture).

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iv)Proximal Humerus and Pelvic Fractures: Less frequent but indicative of severe bone fragility.

v)Fractures of the ribs, clavicle, patella, or metatarsals are generally not attributed to osteoporosis, as they often result from direct trauma rather than skeletal insufficiency.

Mechanisms of Skeletal Fragility

The pathogenesis of fragility fractures involves both quantitative and qualitative bone deterioration. Reduced BMD directly correlates with fracture risk, but micro architectural defects-such as trabecular perforation and cortical thinning-compromise biomechanical resilience.[2] Vertebral bodies, composed of 90–95% trabecular bone, are particularly vulnerable to compressive forces, while hip fractures often result from combined axial and torsional stresses. Additionally, age-related declines in muscle mass (sarcopenia) and impaired balance increase fall propensity, synergizing with bone fragility to elevate fracture risk.[3]

Clinical and Therapeutic Implications

Understanding these pathophysiological mechanisms underscores the importance of early intervention. Pharmacotherapies like bisphosphonates and RANKL inhibitors (e.g., denosumab) target excessive osteoclast activity, while anabolic agents (e.g., teriparatide) stimulate osteoblast function. Non-pharmacological strategies, including resistance training and dietary optimization, aim to preserve bone mass and prevent falls. Advanced imaging techniques, such as high-resolution peripheral quantitative CT (HR-pQCT),[4] now enable detailed assessment of micro architectural deterioration, refining risk stratification and treatment monitoring.

Classification of Osteoporosis

Osteoporosis is categorized into primary (idiopathic or age-related) and secondary (disease- or medication-induced) forms, both manifesting similar fracture patterns but differing in etiology.

a) Primary Osteoporosis

Accounting for >95% of cases in women and ~80% in men, primary osteoporosis lacks a definitive underlying cause. It predominantly affects postmenopausal women (due to estrogen deficiency) and older men (linked to age-related testosterone decline). Key contributors include gonadal insufficiency, inadequate calcium/vitamin D intake, hyperparathyroidism, and prolonged use of glucocorticoids or proton pump inhibitors. Suboptimal calcium intake during adolescence may also impair peak bone mass attainment.

Risk Factors for Primary Osteoporosis

Family members with osteoporosis
A diet that is low in calcium and vitamin D
Sedentary lifestyle
Thin build
Early menopause
Cigarette smoking
Excessive alcohol consumption

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Osteoporosis risk is influenced by several key factors. Mechanical stress—such as regular weight-bearing activity—is essential for bone growth, so prolonged inactivity or immobilization leads to bone loss. Individuals with a low body mass index are at greater risk due to decreased bone mass. Insufficient intake of calcium, phosphorus, magnesium, and vitamin D, as well as chronic acidosis, can also contribute to weakened bones. Substance use, specifically tobacco and excessive alcohol, decreases bone mass. Genetic predisposition plays a role, as a family history of osteoporosis or hip fracture increases one's risk. Experiencing a previous fragility fracture further raises the likelihood of future fractures. Though traditionally certain populations, such as non-Hispanic White and Asian women, were considered at higher risk, these differences are now understood to be complex, largely affected by social determinants of health. Current recommendations favour using population-specific risk calculators rather than relying solely on race or ethnicity.

Pathophysiological mechanisms involved:

Enhanced osteoclast activity: Driven by upregulated cytokines (e.g., RANKL), promoting osteoclast differentiation and bone resorption.

Impaired osteoblast function: Age-related reductions in osteoblast numbers and activity, exacerbated by sclerostin-mediated inhibition of Wnt/β-catenin signaling.

Hormonal dysregulation: Elevated PTH and vitamin D deficiency amplify resorption.

b) **Idiopathic osteoporosis,** a rare subtype, occurs in premenopausal women, men <50 years, or adolescents with normal gonadal function and no secondary causes, often presenting with low bone mass (Z-score ≤−2.0 on DXA).

c) Secondary Osteoporosis: Responsible for <5% of cases in women and ~20% in men, secondary osteoporosis arises from specific conditions or therapies. Common causes include:

Endocrine disorders: Hyperthyroidism, Cushing syndrome, hypogonadism.
Chronic diseases: Rheumatoid arthritis, malabsorption syndromes, multiple myeloma.
Medications: Glucocorticoids, anticonvulsants, anticoagulants.
Chronic kidney disease (CKD): Complex mechanisms like secondary hyperparathyroidism, hyperphosphatemia, calcitriol deficiency, and adynamic bone disease disrupt remodelling.
In CKD, mineral-bone disorders exacerbate skeletal fragility through altered calcium-phosphate homeostasis and osteomalacia. Secondary causes often coexist with primary osteoporosis, accelerating bone loss and fracture risk.

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Category	Specific Causes/Examples
Malignancy	Multiple myeloma, other cancers
Pulmonary Disease	COPD (due to disease, corticosteroid therapy, tobacco use, decreased physical activity)
Renal Disease	Chronic kidney disease
Medications	Chronic corticosteroid use, antiepileptic drugs, medroxyprogesterone, aromatase inhibitors, Thiazolidinediones (rosiglitazone, pioglitazone), thyroid replacement, heparin, ethanol, tobacco, proton pump inhibitors, H2 blockers
Endocrine Disorders	Glucocorticoid excess, hyperparathyroidism, hyperthyroidism, hypogonadism, hyperprolactinemia, diabetes
Metabolic Disorders	Hypercalciuria, hypophosphatemia, chronic hypophosphatemia, hypovitaminosis D
Physical Inactivity	Immobilization, prolonged weightlessness (space flight)
Liver Disease	Chronic liver disease
Malabsorption	Malabsorption syndromes (e.g., celiac disease, inflammatory bowel disease)

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Category	Specific Causes/Examples
Rheumatologic Disease	Rheumatoid arthritis

Table1: Enumerate causes of Secondary Osteoporosis

Osteoporosis is a multifactorial disease influenced by both intrinsic and extrinsic risk factors that compromise bone strength and increase susceptibility to fractures. Mechanical loading is a critical determinant of bone remodelling; thus, prolonged immobilization or extended periods of physical inactivity result in accelerated bone resorption and decreased bone mineral density (BMD). Individuals with a low body mass index (BMI) are at heightened risk due to reduced mechanical stress on the skeleton and lower reserves of bone-forming substrates.

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Nutritional deficiencies play a significant role in osteoporosis pathogenesis. Inadequate dietary intake of calcium, phosphorus, magnesium, and vitamin D impairs bone mineralization and disrupts calcium-phosphate homeostasis, leading to increased bone turnover and net bone loss. Chronic endogenous acidosis, as seen in renal tubular acidosis or high-protein diets, further promotes bone demineralization by enhancing calcium mobilization from bone stores.

Lifestyle factors such as tobacco use and excessive alcohol consumption have deleterious effects on bone health. Nicotine and other tobacco constituents inhibit osteoblast function, while alcohol impairs calcium absorption and disrupts hormonal regulation of bone remodelling.[5]

A positive family history of osteoporosis, especially a parental history of hip fracture, is a well-established non-modifiable risk factor, reflecting the contribution of genetic determinants to peak bone mass and bone quality. Importantly, individuals with a prior fragility fracture are at significantly increased risk for subsequent clinical and subclinical vertebral fractures, indicating underlying skeletal fragility.

Historically, ethnic background has been considered a risk factor, with individuals of White and Asian ancestry thought to be at greater risk. However, recent research highlights the limitations of population-based categorizations, as genetic diversity and environmental factors complicate risk stratification based on ethnicity alone.

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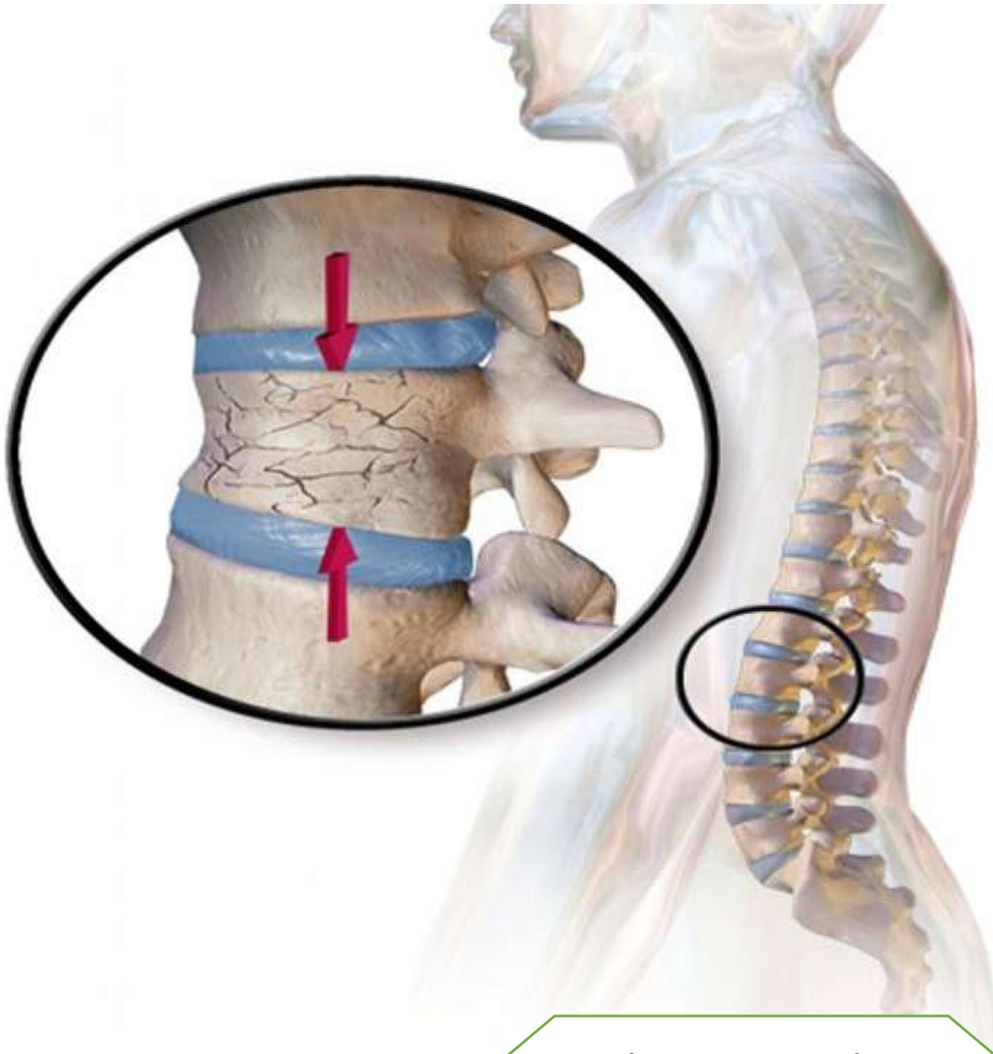

Fig 1: Compression fracture of the spine due to osteoporosis

People who have had one osteoporosis- having more of these fracture.[6]

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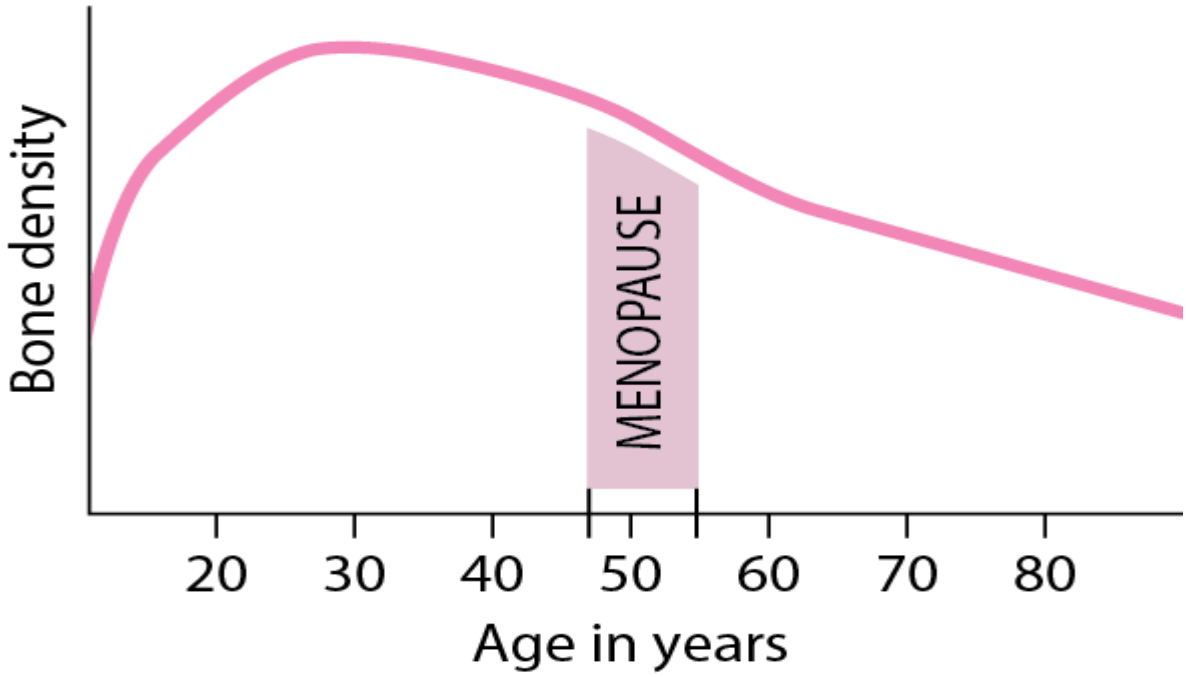

Fig2: Depicting Loss of Bone Density in Women

In women, bone density (or mass) progressively increases until about age 30, at which time bones are at their strongest. After that, bone density gradually decreases.[7] The decrease in bone density accelerates after menopause, which occurs on average around the age of 51 years. [8]

Symptoms of Osteoporosis

At first, osteoporosis causes no symptoms. Bone density loss occurs very gradually. Some people never develop symptoms. However, when osteoporosis causes bones to break (fracture), people may have pain depending on the location of the fracture.[9] Fractures tend to heal slowly in people who have osteoporosis and may lead to deformities such as curvature of the spine.

In long bones, such as the bones of the arms and legs, the fracture usually occurs at the ends of the bones rather than in the middle. Long bone fractures typically are painful.

The bones of the spine (vertebrae) are particularly at risk of fracture due to osteoporosis. These fractures are the most common osteoporosis-related fracture. They usually occur in the middle to lower back.[10] Typically, the drum-shaped body of one or more vertebrae collapses into itself and becomes compressed into a wedge shape. These vertebral compression fractures may occur in people who have any type of osteoporosis, including those on medications that cause bone density loss and increased risk of fracture. The weakened vertebrae may collapse spontaneously or after a slight injury, such as with coughing or with a fall from a standing height.[11]

Most of these vertebral compression fractures do not cause pain. However, pain can develop, usually starting suddenly, staying in a particular area of the back, and worsening when a person stands or walks.[12] The area may be tender. Usually the pain and tenderness begin to go away gradually after 1 week. However, lingering pain may last for months or be constant. If several

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vertebrae break, an abnormal curvature of the spine may develop, causing muscle strain and soreness as well as deformity.

Fragility fractures are fractures that result from a relatively minor strain or fall, such as a fall from a standing height or less, including a fall out of bed, that normally would not cause a fracture in a healthy bone.[13] Fragility fractures commonly occur in the wrist, hip, and spine (vertebral compression fractures). Other bones include the upper arm bone (humerus) and the pelvis.

Hip fracture, one of the most serious fractures, is a major cause of disability and loss of independence in older adults, and is associated with reduced survival.

Wrist fractures occur often, especially in people with postmenopausal osteoporosis.

People who have had one fracture in which osteoporosis had been a factor are at much higher risk of having more such fractures. Fractures of the nose, ribs, collarbone, knee cap, and bones in the feet are not considered osteoporosis-related fractures.

Osteoporosis is typically asymptomatic until a fracture takes place. Nonvertebral fractures usually present with clear symptoms, but about two-thirds of vertebral compression fractures are clinically silent, although some patients may experience chronic back pain due to other underlying causes such as osteoarthritis.[14] When symptomatic, vertebral compression fractures present with acute, localized back pain that does not radiate and is exacerbated by weight-bearing. There may also be spinal point tenderness. This pain generally begins to subside within a week, but residual discomfort can persist for months or become constant.[15] Persistent pain may indicate additional vertebral fractures or other spinal disorders, including malignancy or infection.[16]

Multiple thoracic compression fractures can lead to dorsal kyphosis, resulting in an exaggerated cervical lordosis known as a "dowager hump."[17] Associated biomechanical stress on the spinal musculature and ligaments may cause chronic, dull, aching pain, especially in the lower back. Progressive spinal deformity can compromise thoracic volume, leading to shortness of breath, and compress the abdominal cavity, causing early satiety due to displacement of abdominal organs. These complications highlight the importance of early detection and management of osteoporotic fractures to maintain function and quality of life.[18]

Diagnosis of Osteoporosis

i)Dual-energy x-ray absorptiometry (DXA)

ii) Presence of a fragility fracture

Although low bone mineral density (and the associated increased risk of fracture) can be suggested by radiographic findings, it must be confirmed by a bone mineral density measurement. Typically, DXA is used; quantitative CT scanning can produce similar bone mineral density measurements but is not widely available. Alternatively, osteoporosis can also be diagnosed based on the occurrence of a fragility fracture, regardless of the bone mineral density score. This diagnostic criterion is particularly relevant for fractures of the spine, hip, humerus, or distal radius.

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Dual-energy x-ray absorptiometry (DXA)[19]

Bone mineral density should be measured using a DXA scan to screen people at risk, provide a quantitative measure of bone loss, help predict the risk of fracture, and monitor those undergoing treatment. In a DXA scan, the target areas, typically the spine and one or both hips, are imaged using x-rays of high and low energy (hence the term "dual energy"). The difference in attenuation between high and low energy beams is a reflection of bone mineral content. The bone mineral content divided by area of bone (also measured in the DXA scan) is the bone mineral density in g/cm2. The presence of significant osteoarthritis in the target areas may increase the reported bone density.

If the spine or a hip is unsuitable for accurate assessment by DXA (eg, because of hardware from prior total hip arthroplasty or spinal fusion surgery), the distal radius can be scanned (called "1/3 radius" on the DXA scan report). The distal radius should also be scanned in a patient with hyperparathyroidism because this is the most common site of bone loss in hyperparathyroidism.

DXA results are reported as T-scores and Z-scores.

The T-score corresponds to the number of standard deviations that the patient's bone mineral density differs from the peak bone mass of a healthy, young person of the same sex and race/ethnicity. The World Health Organization establishes cutoff values for T-scores that define osteopenia and osteoporosis (2). A T-score < -1.0 and > -2.5 defines osteopenia. A T-score ≤ -2.5 defines osteoporosis.

The Z-score corresponds to the number of standard deviations that the patient's bone mineral density differs from that of a person of the same age and sex and should be used for children, premenopausal women, or men < 50 years. If the Z-score is ≤ -2.0, bone mineral density is low for the patient's age and secondary causes of bone loss should be considered.

A DXA scan is recommended for the following patients:

i)All women ≥ 65 years

ii)Women between menopause and age 65 who have risk factors, including a family history of osteoporosis, a low body mass index, cigarette smoking, use of excess alcohol (eg, >3 or more standard drinks per day is used in the FRAX score) and/or use of medications with a high risk of bone loss (eg, glucocorticoids, aromatase inhibitors)

iii)Patients (men and women) of any age who have had 1 or more fragility fractures

iv)Patients with evidence on imaging studies of decreased bone mineral density or asymptomatic vertebral compression fractures incidentally noted on imaging studies

v)Patients at risk of secondary osteoporosis

DXA scans can also assess vertebral deformities in the lower thoracic and lumbar spine, a procedure termed vertebral fracture assessment (VFA), which can be performed during bone mineral density testing with DXA (4). Vertebral compression deformities in the absence of

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trauma, even those clinically silent, are diagnostic of osteoporosis and are predictive of an increased risk of future fractures. VFA is more likely to be useful in patients with height loss ≥ 3 cm. If the VFA results reveal suspected abnormalities, radiographs should be performed to confirm the diagnosis.

The need for pharmacologic therapy is based on the probability of future fractures, which is related to DXA results as well as other factors. The fracture risk assessment (FRAX) score (see Fracture Risk Assessment Tool) predicts the 10-year probability of a major osteoporotic (hip, spine, forearm, or humerus) fracture in untreated patients. The score accounts for several significant risk factors for bone loss and fracture, including bone mineral density, multiple clinical features, and country of origin of the patient (to account for observed population differences). If the FRAX score is above certain thresholds (in the United States, a ≥ 20% probability of major osteoporotic fracture or 3% probability of hip fracture), pharmacologic therapy should generally be recommended (5). There are limitations to the use of the FRAX score because it does not account for several factors, including history of falls or increased fall risk, the patient's bone mineral density at the lumbar spine, or family history of vertebral fractures.

Radiographs

Osteoporotic bones typically show decreased radio density and loss of trabecular structure but are inadequate for diagnostic purposes. However, radiographs are important for documenting fractures resulting from bone loss.[20] Loss of vertebral body height and increased biconcavity characterize vertebral compression fractures. Thoracic vertebral fractures may cause anterior wedging of the bone. Vertebral fractures most commonly occur at the mid-thoracic level when due to osteoporosis. Vertebral fractures above the mid-thoracic region should raise consideration for malignancy or trauma as the etiology. Radiographs of the spine to look for asymptomatic vertebral fragility fractures should be considered in older patients with severe back pain and localized vertebral spinous tenderness and in patients who report > 3 cm height loss.[21] Corticosteroid-related osteoporosis, also called glucocorticoid-induced osteoporosis (GIOP), is most likely to cause vertebral compression fractures but may also cause fractures at other sites where osteoporotic fractures are common. Hyperparathyroidism can be differentiated when it causes sub periosteal resorption or cystic bone lesions (rarely). Osteomalacia may cause abnormalities on imaging tests similar to those of osteoporosis.[22]

Differentiating Osteoporosis and Osteomalacia

Two metabolic bone diseases decrease bone mass: osteoporosis and osteomalacia.

In osteoporosis, bone mass decreases, but the ratio of bone mineral to bone matrix is normal.

In osteomalacia, the ratio of bone mineral to bone matrix is low.

Osteoporosis results from a combination of low peak bone mass, increased bone resorption, and impaired bone formation. Osteomalacia is due to impaired mineralization, usually because of severe prolonged vitamin D deficiency or abnormal vitamin D metabolism (see Vitamin D). Osteomalacia can be caused by disorders that interfere with vitamin D absorption (eg, celiac disease) and by certain medications (eg, antiseizure medications). Osteoporosis is much more common than osteomalacia in the United States. The two disorders may coexist, and their clinical expression is similar; moreover, patients with osteoporosis may have mild to moderate vitamin D deficiency.

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Osteomalacia should be suspected if the patient has bone pain, recurrent rib or other unusual fractures, and the vitamin D level is consistently very low. To definitively differentiate between the two disorders, clinicians can perform a tetracycline-labelled bone biopsy, but this is rarely warranted.[23]

Tests which can be used in addition to those mentioned above:

An evaluation for secondary causes of bone loss should be considered in a patient with a Z-score ≤ -2.0. Laboratory testing should usually include the following:

-Serum calcium, magnesium, and phosphorus
-25-Hydroxy vitamin D level
-Liver function tests, including testing for a low alkaline phosphatase
-Intact PTH level (hyperparathyroidism)
-Serum testosterone in men (hypogonadism)
-24-hour urine for calcium and creatinine (hypercalciuria)
Other tests such as thyroid-stimulating hormone or free thyroxine to evaluate for hyperthyroidism, measurements of 24-hour urinary free cortisol to evaluate for Cushing syndrome, and blood counts and other tests to exclude cancer, especially myeloma (eg, serum protein electrophoresis, serum free light chains, urine protein electrophoresis), should be considered depending on the clinical presentation.

Patients with weight loss should be screened for gastrointestinal disorders (eg, malabsorption, celiac disease, inflammatory bowel disease) as well as cancer. Bone biopsy is reserved for unusual cases (eg, young patients with fragility fractures and no apparent cause, patients with chronic kidney disease who may have other bone disorders, patients with persistently very low vitamin D levels suspected of having osteomalacia).

Levels of fasting serum C-telopeptide cross-links (CTX) or urine N-telopeptide cross-links (NTX) reflect increased bone resorption. However, the reliability of the assays varies, which complicates their utility for routine clinical care. These tests should be performed as fasting labs obtained first thing in the morning. Studies suggest that elevated levels of CTX and NTX may be helpful in predicting fracture risk in an untreated patient.[24] These bone turnover markers may help with monitoring response to antiresorptive therapy, and determine the timing and duration of a drug holiday (8). In patients on antiresorptive therapy, levels should be markedly suppressed. If not, abnormal absorption or poor adherence to treatment regimen should be suspected.

Treatment of Osteoporosis

Risk factor modification

Calcium and vitamin D adequacy by dietary intake or with use of supplements

Antiresorptive medications (eg, bisphosphonates, hormone replacement therapy, a selective estrogen receptor modulator, receptor activator of nuclear factor kappa-B ligand [RANKL] inhibitor [denosumab])[25]

Anabolic agents (eg, parathyroid hormone (PTH) analogues such as teriparatide and abaloparatide)

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Romosozumab, a monoclonal antibody against sclerostin with both antiresorptive and anabolic effects

The goals of treatment of osteoporosis are to preserve bone mass, prevent fractures, decrease pain, and maintain function.

The rate of bone loss can be slowed with pharmacotherapy, but adequate calcium and vitamin D ingestion and physical activity are critical to maintaining optimal bone mineral density. Modifiable risk factors should also be addressed.

Risk factor modification

Risk factor modifications aim to reduce risk of osteoporosis and risk of fractures. Measures include:

Weight-bearing exercise

Moderation of alcohol intake

Smoking cessation

Fall prevention measures

Weight-bearing exercise can help increase bone mineral density. The optimal amount of weight-bearing exercise is not established, but an average of 30 minutes a day is recommended. However, excessive exercise without adequate dietary caloric intake in premenopausal women may lead to weight loss and amenorrhea, and subsequent bone loss. If alcohol is consumed, intake should be no more than 1 drink a day for women and 2 drinks a day for men.

Clinicians should routinely ask about recent falls and otherwise assess fall risk. Many older patients are at risk of falls because of poor coordination and balance, poor vision, muscle weakness, confusion, and use of medications that cause postural hypotension or alter the sensorium. Physical therapists can evaluate a patient's gait and fall risk and help create safe individualized programs of core-strengthening exercises to help increase stability and decrease risk of falls. Educating patients about the risks of falls and fractures, instructing how to safely perform daily activities, and modifying the home environment for safety also are important for preventing fractures.

Calcium and vitamin D

All men and women should consume at least 1000 mg of elemental calcium daily. An intake of 1200 mg a day (including dietary consumption) is recommended for postmenopausal women and older men and for periods of increased requirements, such as pubertal growth, pregnancy, and lactation. Calcium intake should ideally be from dietary sources, with the addition of supplements if dietary intake is insufficient. Calcium supplements are taken most commonly as calcium carbonate or calcium citrate. Calcium citrate is better absorbed in patients with achlorhydria, but both are well absorbed when taken with meals. Patients taking gastric acid suppressants (eg, proton pump inhibitors, H2 blockers) or those who have had gastric bypass surgery should take calcium citrate to maximize absorption. Calcium should be taken in divided doses, usually 500 to 600 mg 2 times a day.

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Vitamin D supplementation with 600 to 800 international units a day is recommended. Patients with vitamin D deficiency may need even higher doses. Supplemental vitamin D is usually given as cholecalciferol, the natural form of vitamin D, although ergocalciferol, the synthetic plant-derived form, is also acceptable. The 25-hydroxy vitamin D level should be ≥ 30 ng/mL.

Antiresorptive medications

Bisphosphonates are first-line therapy. By inhibiting bone resorption, bisphosphonates preserve bone mass and can decrease vertebral and hip fractures by up to 50%.[26] Bone turnover is reduced after 3 months of bisphosphonate therapy and fracture risk reduction is evident as early as 1 year after beginning therapy. Bisphosphonates can be given orally or IV. Evidence supports a treatment duration with oral bisphosphonates (eg, alendronate or risedronate) for 5 years or with IV zoledronic acid for 3 years; however, a longer treatment duration may be warranted in some patients at particularly high fracture risk.

Oral bisphosphonates must be taken on an empty stomach with a full (8-oz, 250 mL) glass of water. After administration, the patient must remain upright for at least 30 minutes (60 minutes for ibandronate) and not take anything else by mouth during this time period, because food decreases bioavailability. These medications are safe to use in patients with a creatinine clearance > 35 mL/minute. Oral bisphosphonates can cause esophageal irritation. Esophageal disorders that delay transit time and symptoms of upper gastrointestinal disorders are relative contraindications to oral bisphosphonates. IV bisphosphonates are indicated if a patient is unable to tolerate or is nonadherent with oral bisphosphonates.

Osteonecrosis of the jaw (ONJ) and atypical femoral fractures have been rarely reported in patients receiving antiresorptive therapy with bisphosphonates, and also with use of romosozumab, or denosumab. Risk factors for ONJ include invasive dental procedures, IV bisphosphonate use, and radiation to the head and neck to treat cancer. The benefits of reduction of osteoporosis-related fractures far outweigh this small risk. Although some dentists ask a patient to discontinue a bisphosphonate for several weeks or months before an invasive dental procedure, it is not clear that doing so decreases the risk of osteonecrosis of the jaw.[27]

Long-term bisphosphonate use may increase the risk of atypical femoral fractures. These fractures occur in the mid-shaft of the femur with minimal or no trauma and may be preceded by weeks or months of thigh pain. The fractures may be bilateral even if symptoms are only unilateral.

To minimize atypical fracture incidence, consideration should be given to stopping bisphosphonates after approximately:

3 to 5 years of use in patients with osteoporosis (by DXA scan) but few or no other risk factors for bone loss (3 years for IV zoledronic acid and 5 years for oral bisphosphonates)

5 to 10 years of use in patients with osteoporosis (by DXA scan) and fractures or additional significant ongoing risk factors for bone loss and future osteoporotic fractures.

Intermittent cessation of bisphosphonate treatment (drug holiday), as well as initiation and duration of therapy, depend on patient risk factors such as age, comorbidities, prior fracture history, DXA scan results, and fall risk. The drug holiday is 1 year or longer. Patients on a

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bisphosphonate holiday should be closely monitored for a new fracture or accelerated bone loss evident on a DXA scan, especially after being off therapy for 2 years or more.

During therapy with an antiresorptive medication such as a bisphosphonate, bone turnover is suppressed, as evidenced by low serum or urinary levels of (fasting) N-telopeptide cross-links (NTX) or C-telopeptide cross-links (CTX). Thus, measures of bone turnover markers can help determine adherence to therapy, as well as sufficient absorption, which are particularly useful for monitoring in patients taking oral bisphosphonates. These markers may remain low for ≥ 2 years off therapy. In untreated patients, an increase in levels of bone turnover markers, particularly with higher levels, indicates an increased risk of fracture. However, it is not clear whether levels of bone turnover markers should be used as criteria for when to start or end a drug holiday.[28]

The immediate initiation of a bisphosphonate after an osteoporotic fracture has been controversial because of a theoretical concern that these agents may impede bone healing; although this has not been borne out in the clinical literature. Most experts recommend starting a bisphosphonate during the hospitalization for the fracture. There is no reason to delay therapy in order to obtain a DXA scan because a hip or vertebral fragility fracture establishes the presence of osteoporosis.

Denosumab is a monoclonal antibody against the receptor activator of nuclear factor Kappa-B ligand (RANKL) and reduces bone resorption by inhibiting osteoclast differentiation and formation. Denosumab may be helpful in patients intolerant of or unresponsive to other therapies or in patients with impaired renal function. This medication has been found to have a good safety profile at 10 years of therapy. Denosumab is contraindicated in patients with hypocalcemia because it can cause calcium shifts that result in profound hypocalcemia and adverse effects such as tetany. Osteonecrosis of the jaw and atypical femoral fractures have been rarely reported in patients taking denosumab.

Patients taking denosumab should not undergo a drug holiday because discontinuation may cause a rapid loss in bone mineral density and, importantly, increase the risk of fractures, particularly vertebral fractures, often multiple. If and when denosumab is discontinued, patients should be transitioned to a bisphosphonate such as IV zoledronic acid for at least a year, longer if there is ongoing risk of fracture or evidence of loss of bone mineral density after only a single IV zoledronic acid infusion.

Raloxifene is a selective estrogen receptor modulator (SERM) that may be appropriate for treatment of osteoporosis in women who cannot take bisphosphonates or denosumab. It is given orally once daily and reduces vertebral fractures by approximately 50% but has not been shown to reduce hip fractures. Raloxifene does not stimulate the uterus and antagonizes estrogen effects in the breast. It reduces the risk of invasive breast cancer. Raloxifene may increase risk of thromboembolism.

Estrogen therapy preserves bone mineral density and decreases the risk of fractures. However, because of the availability of other more effective treatments and the potential risks associated with continued therapy, estrogen is not typically used as first-line therapy for the sole indication of treating osteoporosis. The use of estrogen increases the risk of thromboembolism and endometrial cancer and is also associated with additional risks (eg, breast cancer, endometrial

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cancer, coronary artery disease, stroke, and gallbladder disease), some of which vary depending on the use of estrogen-alone versus estrogen combined with a progestin. Thus, the potential harms of estrogen treatment for osteoporosis outweigh its potential benefits for most women.

Intranasal salmon calcitonin should not regularly be used for treating osteoporosis. Salmon calcitonin may provide short-term analgesia after an acute fracture, such as a painful vertebral fracture, due to an endorphin effect. It has not been shown to reduce future fractures.

Anabolic agents

Anabolic agents include teriparatide (synthetic PTH [PTH1-34]) and abaloparatide (a human PTH analog that binds to PTH type 1 receptor). They are given daily by subcutaneous injection and increase bone mass, stimulate new bone formation, and reduce the risk of fractures. Patients taking a PTH analog should have a creatinine clearance > 35 mL/minute. Romosozumab, the monoclonal antibody against sclerostin, has both anabolic and antiresorptive effects.

These three anabolic agents (teriparatide, abaloparatide, and romosozumab) are generally indicated for patients who have the following characteristics:

-Cannot tolerate antiresorptive medications or have contraindications to their use

-Fail to respond (ie, develop new fractures or lose bone mineral density) to antiresorptive medication, as well as calcium, vitamin D, and weight bearing exercise possibly have severe osteoporosis (eg, T-score < -3.0) or multiple vertebral fragility fractures have glucocorticoid-induced osteoporosis (teriparatide only) Any of these three anabolic agents can be considered for use during a bisphosphonate when not used on a particular day.

The use of anabolic agents to treat osteoporosis had been limited to 2 years based on a boxed warning because of concern of increased risk of developing osteosarcoma in initial 2-year clinical trials, but the restriction of 2 years of therapy is no longer required. Consequently, although 2 years of treatment with an anabolic agent remains a reasonable course of therapy, giving a second 2-year course of therapy can now be considered. However, after completion of a treatment course with an anabolic agent, the bone mineral density gains are quickly lost if a patient is not promptly transitioned to an antiresorptive agent such as a bisphosphonate. Anabolic agents should ideally be used before antiresorptive agents. Gains in bone mineral density are greater if an anabolic agent is used prior to an antiresorptive agent (ie, considering an "anabolic window"), and bone mineral density gains are attenuated if an anabolic agent is administered following an antiresorptive medication.

Anabolic agents are safe to initiate at any time after a fracture. It is not clear whether early post-fracture use of anabolic agents accelerates bone healing.

Other medications for osteoporosis

Romosozumab is a monoclonal antibody against sclerostin (a small protein made by osteocytes that inhibits new bone formation by osteoblasts). It has both antiresorptive and anabolic effects and has been shown to increase bone mineral density in the hip and lumbar spine and reduce fracture risk in postmenopausal women. Romosozumab is indicated for patients with severe

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osteoporosis, particularly in older adults, those who are frail, and those with an increased risk of falling. It should also be considered in patients who fracture despite adequate antiresorptive therapy. It is given via monthly subcutaneous injection for 1 year.

Romosozumab treatment for 1 year followed by alendronate for 1 year is more efficacious than treatment with alendronate for 2 years (28), and romosozumab for 1 year followed by denosumab for 2 years decreases fracture risk and increases bone mineral density. As with denosumab, when romosozumab is discontinued, antiresorptive therapy should be given to prevent rapid bone loss. Romosozumab carries a boxed warning due to increased risk for cardiovascular events, including myocardial infarction, stroke, and cardiovascular death. Romosozumab should not be initiated within 12 months of a patient having had a myocardial infarction or stroke.

Monitoring response to treatment

Monitoring for ongoing bone loss or the response to treatment with serial DXA scans should be performed using the same DXA machine, and the comparison should use actual bone mineral density (g/cm2) rather than T-score. In patients with osteopenia, DXA should be repeated periodically to determine whether there is ongoing bone loss or development of frank osteoporosis requiring treatment. The frequency for follow-up DXA scanning varies from patient to patient, but some reasonable guidelines are as follows:

Patients being treated with oral bisphosphonates: Repeat DXA scan usually after 2 to 3 years of therapy. DXA scan may be repeated more frequently if clinically warranted, for example in a patient taking glucocorticoids.

Patients treated with IV bisphosphonates: Repeat DXA scan for monitoring after 3 years of therapy to help determine if treatment has been adequate or a longer therapy course is warranted.

Patients treated with anabolic therapy: Repeat DXA scan upon completion of therapy (18 to 24 months of teriparatide or abaloparatide, 1 year of romosozumab) to document improvement in bone mineral density with anabolic therapy and to establish a new baseline.

Results may help identify patients at higher risk of fractures due to a suboptimal response to osteoporosis treatment. Patients who have a significantly lower bone mineral density despite treatment, or those who sustain a fracture while on treatment, should be evaluated for secondary causes of bone loss, poor medication absorption (if taking an oral bisphosphonate), and (except for patients treated with IV bisphosphonates or parenteral medications given in the office) medication adherence.

Treating pain and maintaining function

Acute back pain resulting from a vertebral compression fracture can be treated with short-term orthopaedic bracing as needed, analgesics, and, when muscle spasm is prominent, moist heat and massage. Core-strengthening exercises are helpful for patients who have back pain and a prior healed vertebral fracture. Chronic backache may be relieved by exercises to strengthen paravertebral muscles. Avoiding heavy lifting can help. Bed rest should be minimized, and consistent, carefully designed weight-bearing exercise should be encouraged.

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In some patients, vertebroplasty or kyphoplasty can be used to relieve severe pain due to a new vertebral fragility fracture; however, the evidence for efficacy is inconclusive (30, 31). In vertebroplasty, methyl methacrylate is injected into the vertebral body. In kyphoplasty, the vertebral body is first expanded with a balloon then injected with methyl methacrylate. These procedures may reduce deformity in the injected vertebrae but do not reduce and may even increase the risk of fractures in adjacent vertebrae. Other adverse effects include rib fractures, cement leakage, pulmonary embolism, and myocardial infarction. Further study to determine indications for these procedures is warranted.

Prevention of Osteoporosis

The goals of prevention are 2-fold: preserve bone mass and prevent fractures. Preventive measures are indicated for the following:

Postmenopausal women
Older men (typically men > 70 years old)
Patients who have osteopenia
Patients who already have osteoporosis (to prevent worsening)
Patients taking high-dose and/or long-term systemic glucocorticoids or aromatase inhibitors
Patients with secondary causes for bone loss
Preventive measures for all of these patients include appropriate calcium and vitamin D intake, weight-bearing exercise, tobacco avoidance, and limiting alcohol ingestion. Patients should also be counselled on measures to reduce the risk of falls. In addition, pharmacologic therapy is indicated for most patients who have osteopenia if they are at increased risk of fracture, such as those with a high FRAX score, and patients taking corticosteroids or aromatase inhibitors. Educating patients and the community about the importance of bone health remains of utmost importance.

Points to highlighted/ Conclusions:

Peak bone mass in men and women occurs around age 30; in women, bone loss accelerates after menopause to approximately 2% a year for approximately 10 years.

Nearly all cases of osteoporosis in men and women are primary, without an identifiable cause.

Suspect osteoporosis in patients who have fractures caused by unexpectedly little force (fragility fractures) of the spine, hip, humerus, or distal radius.

Use DXA to measure bone mineral density in women ≥ 65 years; women between menopause and age 65 who have risk factors (eg, family history of osteoporosis, a low body mass index, and use of tobacco, alcohol, and/or medications with a high risk of bone loss [eg, chronic glucocorticoid use]); men and women of any age who have fragility fractures; evidence on imaging studies of decreased bone mineral density or asymptomatic vertebral compression fractures; and patients at risk of secondary osteoporosis.

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Consider testing patients for causes of secondary bone loss if they have a Z-score ≤ -2.0, a decline in bone mineral density, an unexplained fracture while on treatment for osteoporosis, or a cause of secondary bone loss is clinically suspected.

For treatment and prevention, ensure adequate intake of calcium and vitamin D, using supplements when necessary, and modify risk factors to help preserve bone mass (eg, with weight-bearing exercise and by minimizing use of alcohol and tobacco) and reduce fall risk.

Medications include antiresorptives (eg, bisphosphonates, a receptor activator of nuclear factor Kappa-B ligand [RANKL] inhibitor, a selective estrogen receptor modulator, medications used for hormone replacement therapy) or anabolic agents such as teriparatide, abaloparatide, or romosozumab.

Monitor response to treatment with DXA at appropriate intervals depending upon the specific medication regimen used.

More Information:

Down to the bone: There's growing evidence that breathing polluted air increases the risk of osteoporosis.

Osteoporosis is frequently described as a "silent" disease because it typically remains undetected until a significant fracture occurs. Globally, its impact is extensive: about one-third of women and one-fifth of men over the age of 50 suffer fractures attributable to osteoporosis. In India, the burden is especially notable, with current estimates suggesting that more than 61 million individuals may have osteoporosis. The disease's silent progression and widespread prevalence highlight the importance of proactive bone health assessment and fracture prevention, particularly among aging populations at greatest risk. Osteoporosis is widely known as a "silent" disease, remaining unnoticed until a person experiences a major bone fracture. Yet, it is extremely common: worldwide, roughly one-third of women and one-fifth of men older than 50 will sustain fractures linked to osteoporosis. In India, although precise statistics are limited, the condition is believed to affect over 61 million people. These figures reflect the significant and under recognized burden of osteoporosis, underscoring the need for increased awareness and preventive measures to reduce fracture risk, especially among older adults.

Recent research indicates that environmental exposure—particularly air pollution—also contributes to the risk of developing osteoporosis. Epidemiological studies conducted globally, including in India, demonstrate that populations living in areas with high levels of particulate pollution experience higher rates of bone loss and osteoporosis-related fractures. Pollutants such as fine particulate matter (PM2.5), nitrogen oxides, and ground-level ozone have been linked to reduced bone mineral density, possibly through mechanisms involving increased oxidative stress, inflammation, and impaired vitamin D synthesis.[29] Although the precise biological pathways are still under investigation, there is growing scientific consensus that air pollution is a significant, modifiable risk factor for poor bone health. This emerging evidence underscores the importance of public health initiatives targeting both traditional and environmental risk factors for osteoporosis prevention, especially in regions with severe air quality challenges.

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Recent research is shedding light on how air pollution contributes to bone damage and potentially increases the risk of osteoporosis, especially in countries with high pollution levels like India. One clear mechanism involves ground-level ozone, a pollutant that forms when exhaust and industrial emissions interact with sunlight.[30] Elevated ozone levels can obscure sunlight, specifically ultraviolet (UV) rays, that are essential for the skin's synthesis of vitamin D. Vitamin D is crucial for calcium absorption and bone mineralization, so its deficiency impairs bone growth and maintenance.

Beyond this visible effect, many of air pollution's impacts on bone are cellular. Pollutants—including particulate matter (PM2.5, black carbon), nitrogen oxides, and other chemical compounds—generate unstable molecules known as free radicals once inhaled. These free radicals, or reactive oxygen species (ROS), can damage DNA, proteins, and cell membranes, leading to increased oxidative stress within bone cells (osteoblasts and osteoclasts). Excessive oxidative stress can hinder normal bone remodelling, tipping the balance toward bone resorption (breakdown) and weakened bone structure.

Pollution also induces low-grade systemic inflammation. Exposure to air pollutants activates immune pathways, elevating cytokines such as TNF-alpha, IL-1β, IL-6, and IL-17. These cytokines can disrupt the activity and maturation of bone-forming (osteoblast) and bone-resorbing (osteoclast) cells.[31] Chronic inflammation interferes with the body's ability to replace old bone with new, healthy tissue, accelerating bone loss and increasing fracture risk.

Certain air pollutants can even act as endocrine disruptors, altering hormone signals essential for bone metabolism. For instance, compounds in polluted air may bind to hormone receptors in bone or related tissues, interfering with the hormonal regulation needed for balanced bone turnover. Moreover, air pollution can directly or indirectly lower vitamin D levels, not just by blocking sunlight but also by promoting metabolic changes that degrade vitamin D.

India's air pollution problem is particularly severe and growing. From 1998 to 2021, average annual levels of particulate pollution in India rose by nearly 68%. The rapid urbanization, increased reliance on fossil fuel combustion, open burning of agricultural residues, and household use of biomass fuels such as firewood, dung, and charcoal for cooking contribute substantially to the nation's poor air quality. Millions of families, particularly in rural regions, use traditional stoves indoors, exposing themselves daily to high concentrations of smoke and pollutants for hours at a time.

The health impact of this chronic exposure is substantial. Large-scale epidemiological studies have consistently found links between prolonged exposure to airborne pollutants and lower bone mineral density, as well as higher rates of fractures, especially in older adults. The risk appears to be greatest in individuals over 60, those with higher body mass index, and among men. These effects are dose-dependent and cumulative: the longer and more severe the exposure, the greater the risk of osteoporosis and fracture.

Ultimately, while further research is needed to untangle all the molecular details and population-level confounders, the evidence for air pollution as a modifiable environmental risk factor for osteoporosis is growing stronger. This recognition has vast implications for public health policy in India and other nations battling pollution: improving air quality is likely to

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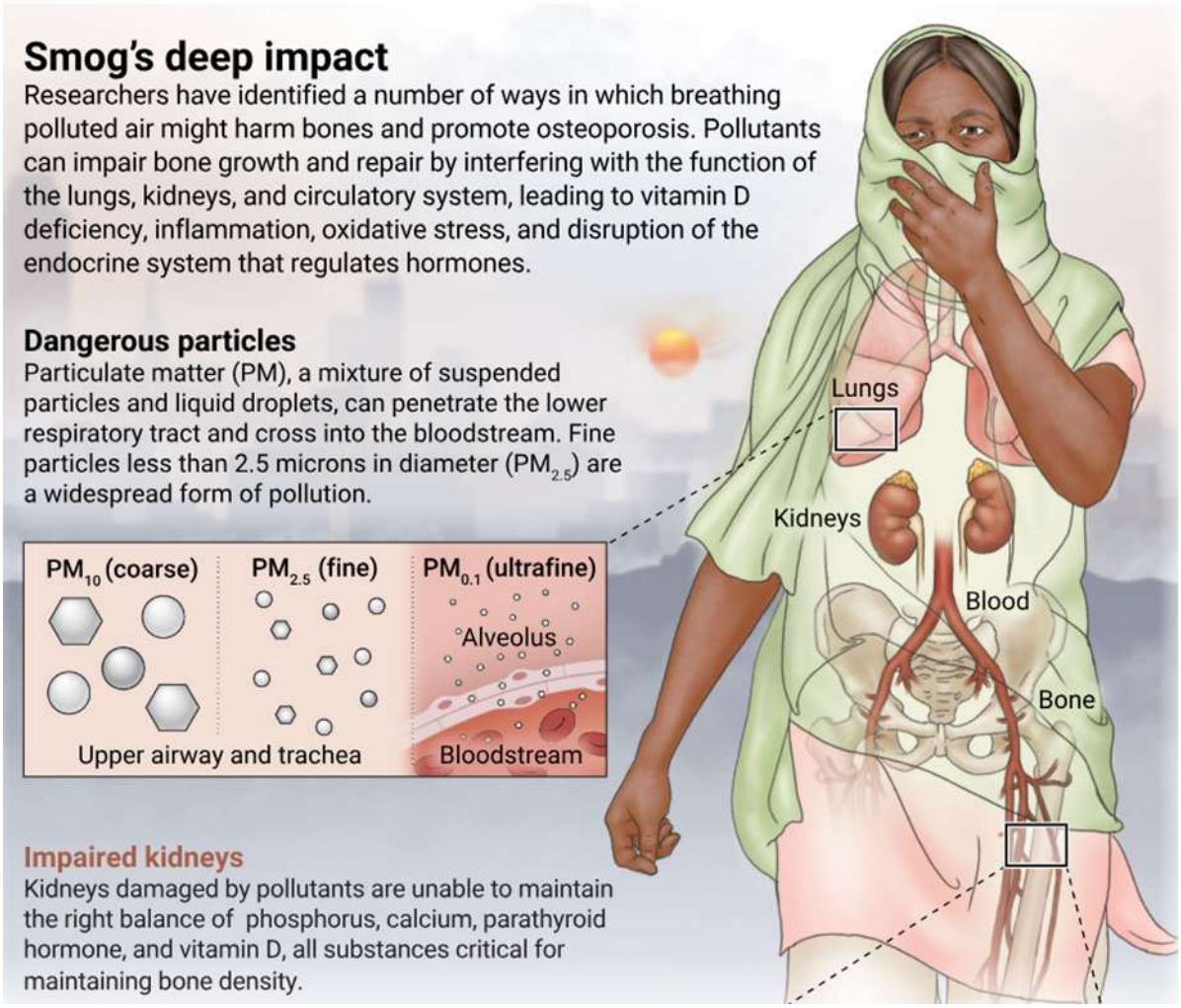
reduce not only respiratory and cardiovascular diseases, but also the burden of osteoporosis and prevent many debilitating fractures as populations continue to age.

Air pollution's established detrimental effects on cardiovascular and respiratory health are now being expanded by growing evidence of its link to osteoporosis, reinforcing calls for comprehensive air quality policies. In India, where pollution levels continue to rise due to urbanization, fossil fuel combustion, agricultural burning, and widespread household use of biomass stoves, these public health implications are particularly urgent.



Epidemiologists and clinicians are emphasizing that reducing air pollution could have a meaningful impact in decreasing the national burden of osteoporosis and related fractures. However, India faces additional obstacles in osteoporosis management. A major challenge is the limited access to diagnostic technology: dual-energy x-ray absorptiometry (DEXA), the gold standard for measuring bone mineral density (BMD), is in short supply. With only about one DEXA scanner for every four million residents—mostly in large urban centers—millions of people, particularly those living in rural or low-income communities, remain undiagnosed and untreated. The high financial cost of DEXA scans adds another barrier, making routine population screening and effective early intervention difficult for many Indians.

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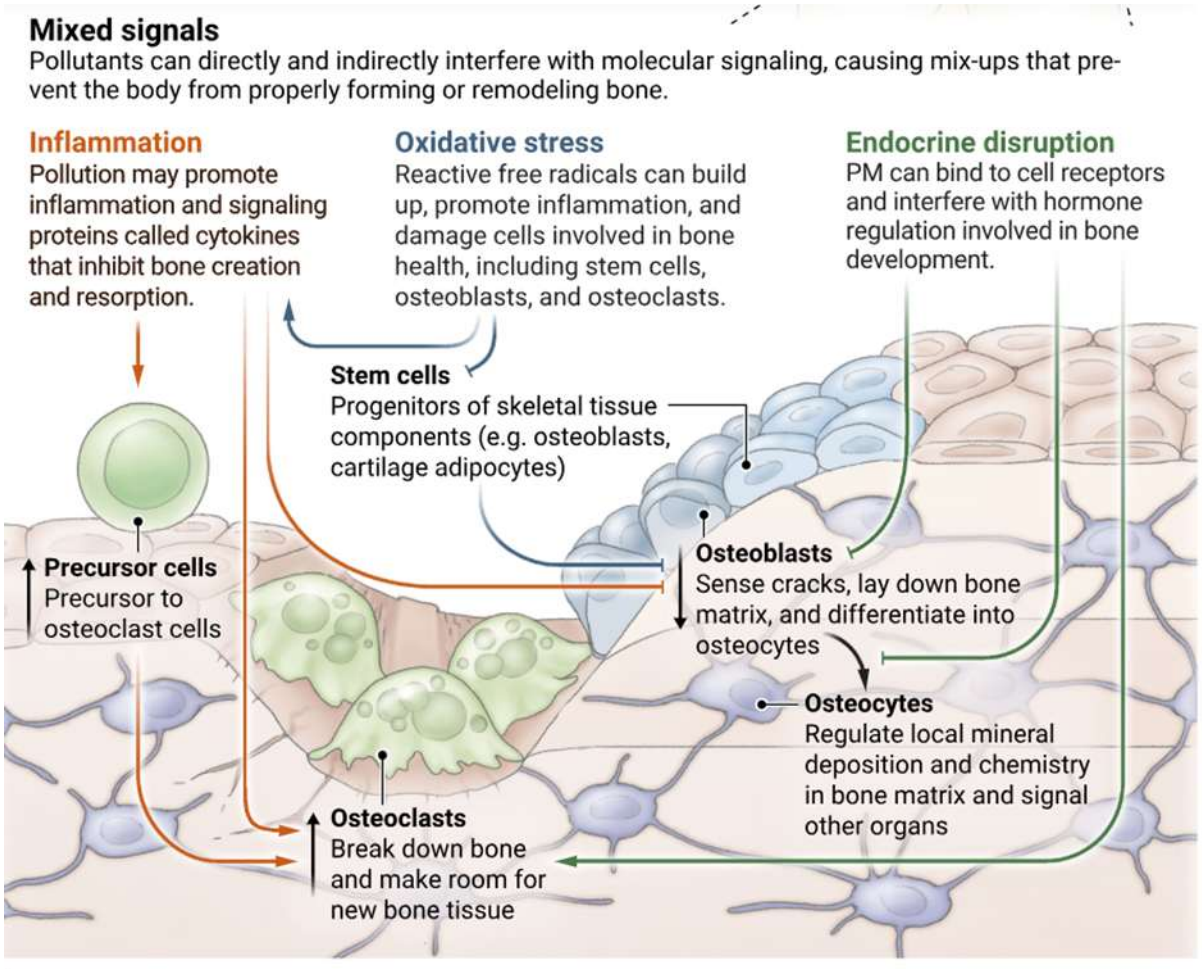
As a result, a substantial proportion of osteoporosis cases in India currently go undetected until a debilitating fracture occurs, representing missed opportunities for prevention and care. These realities highlight the urgent need not just for environmental interventions to reduce air contamination, but also for increased investment in affordable, accessible bone health screening and management across the country. Air pollution is widely recognized for its damaging effects on the cardiovascular and respiratory systems, but new evidence highlights its probable contribution to osteoporosis, underscoring the need for India to prioritize air quality improvement policies. According to experts, such as environmental epidemiologist Otavio Ranzani, reducing air pollution could mitigate not only heart and lung diseases but also bone fragility and fracture risk.



Simultaneously, India faces a critical gap in osteoporosis detection. Dr. Uma Kumar, rheumatology department head at AIIMS, notes that many osteoporosis cases are missed due to a lack of standard diagnostic resources, especially dual-energy x-ray absorptiometry (DEXA) scanners—the gold standard for assessing bone mineral density. India currently has only about one DEXA scanner available for every four million individuals, with most devices located in major cities, making them inaccessible for rural and lower-income populations. Additionally, the high cost of DEXA scans renders routine osteoporosis screening out of reach for many, further complicating early detection and intervention. The combined effect of widespread pollution exposure and inadequate diagnostic infrastructure means that a large

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number of Indians remain undiagnosed until a fracture occurs, emphasizing the urgency of addressing both environmental and healthcare resource challenges.

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References:

1. Howe TE, Shea B, Dawson LJ, et al. Exercise for preventing and treating osteoporosis in postmenopausal women. Cochrane Database Syst Rev. (7):CD000333, 2011. Published 2011 Jul 6. doi:10.1002/14651858.CD000333.pub2

2. Brooke-Wavell K, Skelton DA, Barker KL, et al. Strong, steady and straight: UK consensus statement on physical activity and exercise for osteoporosis [published online ahead of print, 2022 May 16]. Br J Sports Med. 56(15):837-846, 2022. doi:10.1136/bjsports-2021-104634

3. Management of osteoporosis in postmenopausal women: the 2021 position statement of The North American Menopause Society. Menopause. 2021;28(9):973-997. doi:10.1097/GME.0000000000001831

4. Shoback D, Rosen CJ, Black DM, et al. Pharmacological Management of Osteoporosis in Postmenopausal Women: An Endocrine Society Guideline Update. J Clin Endocrinol Metab. 2020;105(3):dgaa048. doi:10.1210/clinem/dgaa048

5. ACOG Committee on Clinical Practice Guidelines–Gynecology. Management of Postmenopausal Osteoporosis: ACOG Clinical Practice Guideline No. 2 [published correction appears in Obstet Gynecol. 2022 Jul 01;140(1):138. doi: 10.1097/AOG.0000000000004855.]. Obstet Gynecol. 2022;139(4):698-717. doi:10.1097/AOG.0000000000004730

6. Camacho PM, Petak SM, Binkley N, et al. AMERICAN ASSOCIATION OF CLINICAL ENDOCRINOLOGISTS/AMERICAN COLLEGE OF ENDOCRINOLOGY CLINICAL PRACTICE GUIDELINES FOR THE DIAGNOSIS AND TREATMENT OF POSTMENOPAUSAL OSTEOPOROSIS-2020 UPDATE. Endocr Pract. 2020;26(Suppl 1):1-46. doi:10.4158/GL-2020-0524SUPPL

7. Ayers C, Kansagara D, Lazur B, Fu R, Kwon A, Harrod C. Effectiveness and safety of treatments to prevent fractures in people with low bone mass or primary osteoporosis: a living systematic review and network meta-analysis for the American College of Physicians

[published correction appears in Ann Intern Med 176(6):884, 2023]. Ann Intern Med. 176(2):182-195, 2023. doi:10.7326/M22-0684

8. Black DM, Reid IR, Boonen S, et al. The effect of 3 versus 6 years of zoledronic acid treatment of osteoporosis: A randomized extension to the HORIZON-Pivotal Fracture Trial (PFT). J Bone Miner Res. 27(2): 243–254, 2012. doi: 10.1002/jbmr.1494

9. Khan AA, Morrison A, Hanley DA, et al. Diagnosis and management of osteonecrosis of the jaw: a systematic review and international consensus. J Bone Miner Res. 30(1):3-23, 2015. doi:10.1002/jbmr.2405

10. Black DM, Abrahamsen B, Bouxsein ML, et al. Atypical Femur Fractures: Review of Epidemiology, Relationship to Bisphosphonates, Prevention, and Clinical Management. Endocr Rev. 40(2):333-368, 2019. doi:10.1210/er.2018-00001

11. Black DM, Schwartz AV, Ensrud KE, et al. Effects of continuing or stopping alendronate after 5 years of treatment: the Fracture Intervention Trial Long-term Extension (FLEX): a randomized trial. JAMA. 296(24):2927-2938, 2006. doi:10.1001/jama.296.24.2927

12. Black DM, Reid IR, Boonen S, et al. The effect of 3 versus 6 years of zoledronic acid treatment of osteoporosis: a randomized extension to the HORIZON-Pivotal Fracture Trial (PFT) [published correction appears in J Bone Miner Res. 27(12):2612, 2012]. J Bone Miner Res 27(2):243-254, 2012. doi:10.1002/jbmr.1494

13. Conley RB, Adib G, Adler RA, et al. Secondary Fracture Prevention: Consensus Clinical Recommendations from a Multistakeholder Coalition. J Bone Miner Res. 35(1):36-52, 2020. doi:10.1002/jbmr.3877

14. Cummings SR, San Martin J, McClung MR, et al. Denosumab for prevention of fractures in postmenopausal women with osteoporosis [published correction appears in N Engl J Med 361(19):1914, 2009]. N Engl J Med. 361(8):756-765, 2009. doi:10.1056/NEJMoa0809493

15. Bone HG, Wagman RB, Brandi ML, et al. 10 years of denosumab treatment in postmenopausal women with osteoporosis: results from the phase 3 randomised FREEDOM trial and open-label extension. Lancet Diabetes Endocrinol. 5(7):513-523, 2017. doi:10.1016/S2213-8587(17)30138-9

16. Lyu H, Yoshida K, Zhao SS, et al. Delayed Denosumab Injections and Fracture Risk Among Patients With Osteoporosis : A Population-Based Cohort Study. Ann Intern Med. 173(7):516-526, 2020. doi:10.7326/M20-0882

17. Sølling AS, Harsløf T, Langdahl B. Treatment with zoledronate subsequent to denosumab in osteoporosis: a 2-year randomized study. J Bone Miner Res. 36(7):1245-1254, 2021. doi:10.1002/jbmr.4305

18. Ettinger B, Black DM, Mitlak BH, et al. Reduction of vertebral fracture risk in postmenopausal women with osteoporosis treated with raloxifene: results from a 3-year randomized clinical trial. Multiple Outcomes of Raloxifene Evaluation (MORE) Investigators [published correction appears in JAMA. 282(22):2124, 1999]. JAMA 282(7):637-645, 1999. doi:10.1001/jama.282.7.637

19. Rossouw JE, Anderson GL, Prentice RL, et al. Risks and benefits of estrogen plus progestin in healthy postmenopausal women: principal results From the Women's Health Initiative randomized controlled trial. JAMA. 2002;288(3):321-333. doi:10.1001/jama.288.3.321

20. Anderson GL, Limacher M, Assaf AR, et al. Effects of conjugated equine estrogen in postmenopausal women with hysterectomy: the Women's Health Initiative randomized controlled trial. JAMA. 2004;291(14):1701-1712. doi:10.1001/jama.291.14.1701

21. Manson JE, Chlebowski RT, Stefanick ML, et al. Menopausal hormone therapy and health outcomes during the intervention and extended poststopping phases of the Women's Health Initiative randomized trials. JAMA. 2013;310(13):1353-1368. doi:10.1001/jama.2013.278040

22. Knopp-Sihota JA, Newburn-Cook CV, Homik J, et al. Calcitonin for treating acute and chronic pain of recent and remote osteoporotic vertebral compression fractures: a systematic review and meta-analysis. Osteoporos Int. 23(1):17-38, 2012. doi:10.1007/s00198-011-1676-0

23. Neer RM, Arnaud CD, Zanchetta JR, et al. Effect of parathyroid hormone (1-34) on fractures and bone mineral density in postmenopausal women with osteoporosis. N Engl J Med. 344(19):1434-1441, 2001. doi:10.1056/NEJM200105103441904

ISSN: 0975-3583,0976-2833 VOL 16, ISSUE 10, 2025

24. Miller PD, Hattersley G, Riis BJ, et al. Effect of abaloparatide vs placebo on new Vertebral fractures in postmenopausal women with osteoporosis: a randomized clinical trial [published correction appears in JAMA. 2017 Jan 24;317(4):442]. JAMA. 316(7):722-733, 2016. doi:10.1001/jama.2016.11136

25. Curtis EM, Reginster JY, Al-Daghri N, et al. Management of patients at very high risk of osteoporotic fractures through sequential treatments. Aging Clin Exp Res. 34(4):695-714, 2022. doi:10.1007/s40520-022-02100-4

26. Cosman F, Crittenden DB, Adachi JD, et al. Romosozumab treatment in postmenopausal women with osteoporosis. N Engl J Med. 375(16):1532-1543, 2016. doi: 10.1056/NEJMoa1607948

27. Saag KG, Petersen J, Brandi ML, et al. Romosozumab or alendronate for fracture prevention in women with osteoporosis. N Engl J Med. 377(15):1417-1427, 2017. doi: 10.1056/NEJMoa1708322

28. Lewiecki EM, Dinavahi RV, Lazaretti-Castro M, et al. One year of romosozumab followed by two years of denosumab maintains fracture risk reductions: Results of the FRAME Extension Study. J Bone Miner Res. 34(3):419-428, 2019. doi: 10.1002/jbmr.3622

29. McClung MR, Brown JP, Diez-Perez A, et al. Effects of 24 Months of Treatment With Romosozumab Followed by 12 Months of Denosumab or Placebo in Postmenopausal Women With Low Bone Mineral Density: A Randomized, Double-Blind, Phase 2, Parallel Group Study. J Bone Miner Res. 33(8):1397-1406, 2018. doi:10.1002/jbmr.3452

30. Buchbinder R, Johnston RV, Rischin KJ, et al. Percutaneous vertebroplasty for osteoporotic vertebral compression fracture. Cochrane Database Syst Rev. 4(4):CD006349, 2018. Published 2018 Apr 4. doi:10.1002/14651858.CD006349.pub3

31. Lou S, Shi X, Zhang X, Lyu H, Li Z, Wang Y. Percutaneous vertebroplasty versus non-operative treatment for osteoporotic vertebral compression fractures: a meta-analysis of randomized controlled trials. Osteoporos Int. 30(12):2369-2380, 2019. doi:10.1007/s00198-019-05101-8