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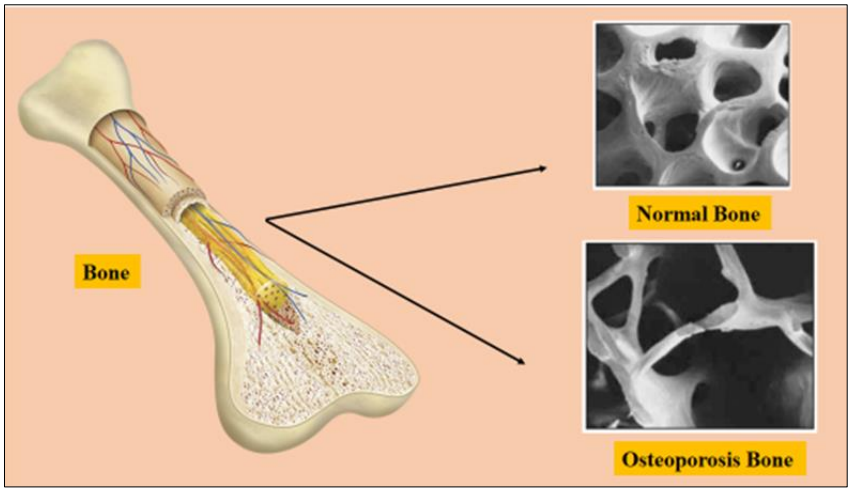
Nutritional interventions of osteoporosis

Riya Mehta

Abstract
Osteoporosis is a prevalent chronic condition marked by a loss of bone mineral density, decreased bone strength, and a higher risk of fragility fractures. Fragility fractures are linked to a high rate of morbidity, death, and disability, and are a serious public health concern across the world. Nutritional variables can have a considerable impact on the development and course of this illness, however this is still unknown. Bone metabolism equilibrium is thought to be dependent on calcium intake and vitamin D levels. The proper consumption of calcium, vitamins, protein, fruits, vegetables, and other nutrients is also important and expert consensus and clinical practice guidelines have set recommendations. Although some dietary patterns appear to be advantageous, further research is required to completely understand the exact impact of nutrition on bone fragility. As the rate of incident fragility fractures climbs with age, so does the rate of osteoporosis. This narrative review discusses the physiological mechanisms involved in bone homeostasis and how they relate to management and therapy. Traditional osteoporosis pathophysiology theories centered on endocrine pathways including oestrogen and vitamin D insufficiency, as well as secondary hyperparathyroidism. However, recent research has revealed fascinating new insights into the processes that contribute to the start of osteoporosis that go well beyond this. This review examines a number of pathways, including interactions between bone and the immune system, the gut microbiota, and cellular senescence.

Keywords: Osteoporosis, pathogenesis, osteoimmunology, gut microbiota, osteoporosis therapy, and dietary patterns

1. Introduction
Osteoporosis is a disorder of the skeletal which reduces bone mass, skeleton micro architecture and stamina and raises the problem of fractures. The subsequent loss of the ability of move often causes a major reduce in health related quality of life (HRQoL). The World Health Organization (WHO, Geneva) stated that osteoporosis is a serious health cause and increase in death rate in elderly patient (Weng *et al*., 2020) [92]. Patient with suffer with either osteoporosis or depression are prone to develop other disease and require more medical resources than do the normal population (Chai *et al*., 2020) [10]. Osteoporosis is prevalent among women between the age of 40- 60, and the evidence that it increasing with the salt consumption with the disease. Osteoporosis is related with the lifestyle factor such as inadequate consumption of good diet and active in physically. However, it needs to consider that how lifestyle related factor can affect the problem of osteoporosis (Kim *et al*., 2017) [36].



The present study highlighted that no qualitative and quantitative differences in the intake of adequate food group to distributing the calcium consumption in woman with and without osteoporosis. The nutritional education and nutrition intervention with promote middle aged improve their life style, enhance nutritional status and improve the effect of conventional therapy for osteoporosis. However older person are characterized by great diversity and extended convexity which may not necessarily be accompanied by good health. On the other side many people enjoy healthy aging in a good pattern as physically as well as mentally into and beyond their 80s, number of older person face external factors such as limited access to appropriate and fair health care facilities and poor lifestyle throughout the life. Since a growing number of people will getting to older with age, the challenge is increasing but no less necessary to ensure that older person live with a great health and with limited rates of aged related disabilities (Ghosh *et al*., 2021) [34] and Osteoporosis represents a widespread public health problem.

Many different nutrients are essential for bone and mineral utilization specially calcium. A well balanced nutrition Mediterranean diet good physical exercise, proper health care proved to be beneficial for several chronic disease. Osteopathic surgeons prefer calcium powder, medicine and supplement for various causes like fracture, osteoporosis, chronic musculoskeletal pain, yet there is no proper evidence to support benefit of taking them regularly. The minimum requirements for calcium intake are 500-1000 mg/day for a good and good lifestyle but this amount of calcium is not fully gain by diet. Despite this, the serum calcium level remains unaltered due to well controlled absorption and excretion of the calcium by human body (Sheth *et al*., 2021) [72].

The physiology of osteoporosis is characterized by the reduction in the mass also the quality of bone decreased and increased the risk factor of fragility. Skeletal homeostasis can be maintained through the balanced activities of osteoblasts and osteoclasts. Osteoporosis is considered to be a disorder that is caused by an imbalance between bone formation and resorption. Whereas osteoblasts and osteoclasts have been the first target for elucidating the cell-based mechanism underlying the pathophysiology of osteoporosis much less attention has been paid to the role of osteocytes. As osteocytes are the skeletal agings and cell embedding in the matrix and become the osteocytes. Another factor is the transcription factor; a gene responsible for tricho dento osseous syndrome has also been reported to be expressed in osteocytes. The osteoblast is different from osteocytes the cell becomes deeply embedded in the bone matrix, where oxygen and nutrients supplies are considered to be limited. According to the national institute of arthritis and musculoskeletal and skin disease osteoporosis is a disease marked by decreased bone strength that may create an increased risk of broken bones or fractures. Inadequate dietary consumption is the key factor of osteoporosis also women in middle age with low body mass index are at increased risk of osteoporosis. Many times osteoporosis can be cured by the healthcare financing system due to osteoporosis incidence in the country can be decreased.

2. Osteoporosis pathophysiology

Osteoporosis is a classic example of degenerative disease. Genetic, intrinsic, external and life factors all have a role in illness. A person's personal style is influenced by variety of things. The diseases risk Endocrine processes, such as oestrogen insufficiency, were widely stresses in traditional pathophysiologic models. Hyperparathyroidism is the elderly as well as secondary hyperparathyroidism reduced dietary intake owing to oestrogen insufficiency (Clarke and khosla., 2010) [42] identified low calcium intake and widespread vitamin D insufficiency as significant predictors of postmenopausal osteoporosis (Clarke and khosla). It has become obvious, however in the pathophysiological factors leading to the beginning of osteoporosis have been discovered in recent years to go much beyond this.

2.1 Fracture and Osteoporosis

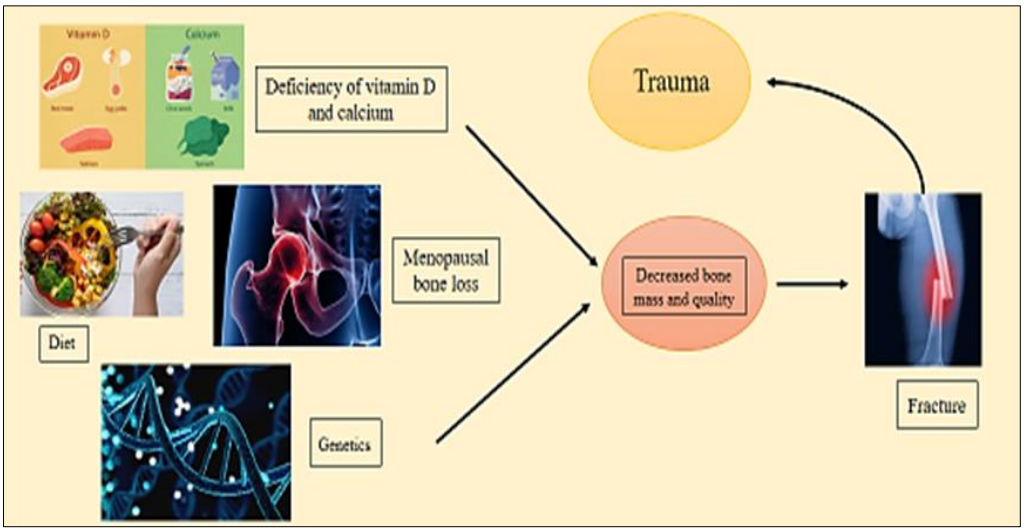
Osteoporosis affects bones to become brittle and inflexible, making them more susceptible to fractures from even minor stresses like bending over or coughing. Osteoporosis-related fractures most commonly occur in the hip, wrist, and spine. Bone is a living tissue that is constantly trying to break down and replacing itself. Whenever the generation of new bone does not keep up with the loss of old bone, osteoporosis develops. The major causes of fractures that create trauma include vitamin D and calcium insufficiency, menopausal bone loss, nutrition, ageing, and other variables that induce a decline in bone density and integrity.

2.2 Gut micro biome and osteoporosis

The effect of the gut microbiome (GM) on a person's health is a new and fast growing topic that offers intriguing new insights into the interaction between the homeostasis of bone metabolism and the intestinal flora (Behera *et al*., 2020; Ding *et al*., 2020; Pacifici., 2018) [3, 22, 60]. It is now well known that the Gut microbiome, which includes all microorganisms found in the human digestive system, has an impact on the development and homeostasis of GI tract tissues as well as tissues in extra-GI locations (e.g nutrient production and absorption, host growth, immune homeostasis).

Furthermore, alterations in the composition of the GM have been associated to complicated disorders including as type 1 and 2 diabetes, transient ischemia stroke, and rheumatoid arthritis (Behera *et al*., 2020) [3].

Observed that germ-free mice have more bone mass, which was the first connection between bone homeostasis and the GM. Experiments showing that using probiotics or antibiotics to modulate the GM affects bone health (Guess *et al*., 2019, Li *et al*., 2016, Ohlsson *et al*., 2014, Parvaneh *et al*., 2015, Rozenberg *et al*., 2016) [32, 44, 59, 61, 65] contribute to this interaction. A study that found germ-free mice are protected from trabecular bone loss caused by sex steroid deprivation provides important evidence for the GM's role in estrogen-driven bone deterioration (Li *et al*., 2016) [44].



Various mechanisms, including the impact of the GM on host metabolism, have been hypothesized to modify this intimate "microbiota-skeletal" axis. The GM has been found to alter bone mineral density through influencing the absorption of nutrients essential for skeletal growth, such as calcium (Rodrigues *et al*., 2012) [66]. Intestinal pH levels, which vary depending on GM composition, may alter nutrient absorption. Microbial fermentation of dietary fibres to short chain fatty acids (SCFAs) appears to play a part in this process as well. Consumption of various prebiotic diets that can be fermented to SCFAs was linked to enhanced calcium desorption in adults (Whisner *et al*., 2014, 2016) [94, 95].

Mice fed SCFAs or a high-fiber diet, for example, showed an increase in bone density. Furthermore, both postmenopausal and inflammation-induced bone loss were reduced, and the protective effect was linked to a reduction in osteoclast development and bone desorption (Lucas *et al*., 2018) [47]. SCFAs are a kind of microbial metabolite that is produced in the gut and then circulated throughout the body. These chemicals can thus govern organs that are anatomically distant, such as the skeletal system (Zaiss *et al*., 2019) [100].

The GM's ability to alter immunological activities is well-known. As a result, the GM's effects on intestinal and systemic immune responses, which influence bone homeostasis, constitute another crucial connection between the GM and the skeletal system. The most plausible mechanisms mediating this GM-immune-bone axis are bone active cytokines generated by immune cells in the gut or immune cells activated in the gut and then circulating to the bone (Pacifici, 2018) [60]. Th17 cells and Treg cells are expected to play a key role in this interaction among immune system cells. In particular, gut macrobiotics have been demonstrated to affect the balance of Th17/Treg cells (Dar *et al*., 2018a, b) [23, 26], with SCFAs playing a significant role in supporting Treg cell development and proliferation (Arpaia *et al*., 2013; Furusawa *et al*., 2013; Smith *et al*., 2013; Zaiss *et al*., 2019) [1, 28, 79, 100].

Only lately has another unexpected relationship been discovered between SCFAs, the immune system, and bone metabolism. The impact of intermittent parathyroid hormone (PTH) therapy on bone formation is dependent on SCFAs, particularly butyrate, generated by the microbiota. They also showed that butyrate, in combination with PTH, can cause CD4+ T cells to develop into Treg cells, which then activate CD8+ T cells to generate Wnt10b. Wnt10b is a major Wnt signalling activator found in stromal cells and osteoblasts that promotes bone formation by enhancing osteoblast proliferation, differentiation, and survival (Monroe *et al*., 2012) [24].

T cell activation has also been linked to PTH-induced bone loss (Gao, *et al*., 2008; Tawfeek *et al*., 2010) [98, 82], however it is unclear whether these T-cells originate in the bone marrow or the gut. Yu *et al*. 2020 [99] have demonstrated that bone loss caused by PTH is dependent on the activation of intestinal TNF+ and Th17 T cells in response to the gut micro biota, as well as their migration to the bone marrow (Yu *et al*., 2020) [99]. Taken together, mounting data suggests that the microbiome and its metabolites, particularly SCFAs, play a vital regulatory role in bone homeostasis. Probiotics and therapies that target the GM and its metabolites might thus be a potential future preventative and treatment method of osteoporosis.

2.3 Osteoporosis and cellular senescence

Senescent cells produce an overabundance of proinflammatory cytokines, chemokines, and extracellular matrix-degrading proteins, a condition known as senescence-associated secretory phenotype (SASP) (Tchkonia *et al*., 2013) [88]. During the ageing process, the number of senescent cells rises (Tchkonia *et al*., 2010) [87], which has been shown to have a crucial role in age-related tissue dysfunction and the development of numerous age-related disorders such as diabetes, hypertension, atherosclerosis, and osteoporosis (Khosla *et al*., 2020) [42].

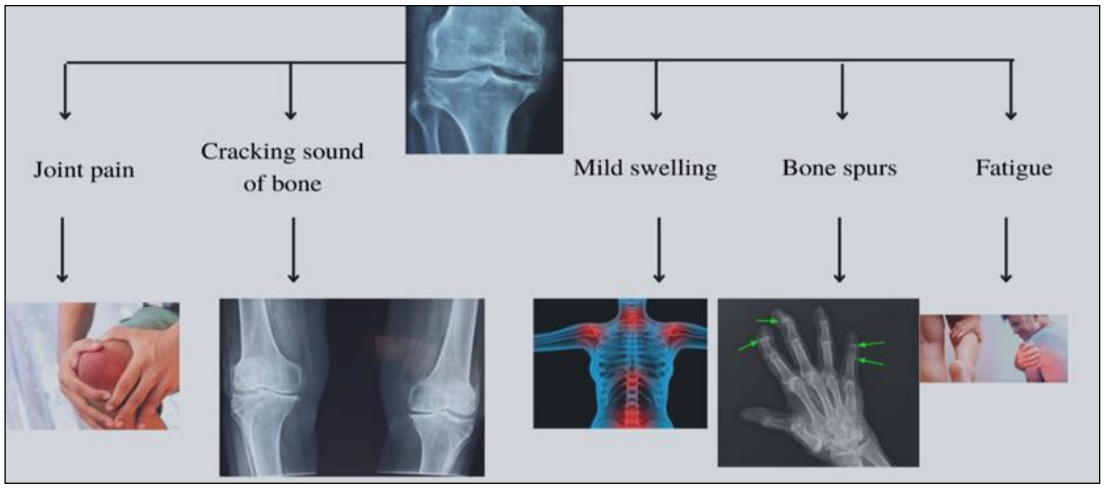
(Farr *et al*., 2016) [30] made a significant addition to our knowledge of the function of senescence in the development of osteoporosis only a few years ago. They discovered that B and T cells, myeloid cells, osteoprogenitors, osteoblasts, and osteocytes are among the categories of cells in the bone microenvironment that become senescent with age, and that senescent myeloid cells and osteocytes produce more important SASP factors than younger cells. Furthermore, they found evidence of senescent cell accumulation in bone biopsy samples from older postmenopausal women compared to younger premenopausal women (Farr *et al*., 2016) [30].

(Farr) established a causal relationship between cellular senescence and age-related bone loss in a more recent investigation. They found that removing senescent cells or inhibiting their SASP reduced age-related bone loss in mice by reducing trabecular and cortical bone resorption and

enhancing or preserving bone formation on endocortical and trabecular surfaces (Farr *et al*., 2017) [30]. Furthermore, the observed bone sparing effect was mediated in part by the eradication of senescent osteocytes, which is consistent with the discovery of an elevated SASP specifically in osteocytes (Farr *et al*., 2016; Piemontese *et al*., 2017) [29, 63]. (Farr *et al*., 2017) [30] To summarise, significant progress has been achieved in understanding the role of senescence and its processes in age-related bone loss. Targeting cellular senescence with senolytics and senostatics has emerged as a potentially effective therapeutic method for the treatment of age-related osteoporosis, based on these novel discoveries.

3. Causes, signs and symptoms of osteoporosis

3.1 Causes of osteoporosis



Chronic dieting, significant deficiencies, a calcium-deficient diet, and vitamin D deficiency all accelerate bone loss and osteoporosis. Women are more prone to develop osteoporosis than males because they have smaller bones, hormonal changes, and a lower peak bone mass than men. Men, on the other hand, are still vulnerable, particularly after the age of 70. People with weak bone structures and low body weight are more likely to develop osteoporosis. Age causes bone to lose its acceleration and new bone to develop slowly. The bones may degrade over time, raising the risk of osteoporosis. An overactive thyroid gland is the hormonal cause of bone loss. Furthermore, age-related drops in oestrogen and testosterone levels in both women and men add to the concern. Family history: If one of the parents has had osteoporosis or many fractures, the chances of developing osteoporosis and fractures are increased. Medical condition: Several hormonal and endocrine disorders induce osteoporosis. Diabetes and hyperthyroidism are two prevalent endocrine diseases. Hormones crucial for healthy bone growth and development are disrupted in such situations. Long periods of inactivity or immobility, high alcohol use (> 4 drinks per day for men; > 2 drinks per day for women), smoking and cigarette consumption, caffeine consumption (> 2.5 units [e.g., cups of coffee] per day), and other variables all contribute to the syndrome's development. Rheumatoid arthritis (RA) causes inflammation to spread throughout the body, notably in the joints. They may extend and contract as needed. This can lead to bone deterioration surrounding RA-affected joints, such as the joints in the hands. In the human body, new bone is continually replacing old bone. RA inflammation interrupts the cycle. It accelerates bone deterioration and delays bone growth. When the bones become weak, osteoporosis occurs. Inflammation can also make it more difficult for the body to absorb important minerals for bone health, such as calcium and vitamin D. Corticosteroids induce osteoporosis and fractures in a substantial percentage of people who use them. There is a dosage-dependent impact that is difficult to characterize due to the varying durations at each dose. The favorable benefits of steroids on the underlying condition May somewhat offset their harmful effects on bone. Because the effects of long-term steroid therapy are so varied and can be clinically severe, patients should have their bone density assessed and actions taken to attempt to retain bone. Hyperthyroidism: The thyroid gland ceases generating thyroid hormones, resulting in hypothyroidism. The thyroid hormone has an effect on how quickly your bones are rebuilt throughout time. As a result, excessive or low thyroid hormone levels might be detrimental to bone health (Emily and Elizabeth. 2003) [78].

4. Treatments of osteoporosis

(A) Non-pharmacological alternatives

4.1. A Recognized the importance

In the first step, basic interventions such as prescribing exerci se, weight-bearing physical activity, and smoking cessation, avoiding excessive alcohol use, optimizing calcium dietary intake, and eating a balanced diet rich in fruits and vegetables with a slant toward higher protein intake are modifiable variables that contribute to osteoporosis prevention (Berg *et al*., 2008, and Movossagh *et al*., 2017) [4, 48]. Acute decompensation and development of the frailty syndrome can be minimized by lowering the risk of falls and subsequent fractures through enhanced bone mineral density (Bauer *et al*., 2013 and Woolford *et al*., 2020) [5, 97].

4.2. A Medication at its most basic level

Vitamin D levels of 800 international units (IU) per day, along with calcium intake of 700 to 1200 mg per day, can reduce the risk of hip and non-vertebral fractures (preferable by dietary intake). This vitamin D dose, which reduces the risk of falls, is recommended for women and men over 50, and can be increased in individuals who are at a higher risk of fractures. Taking large amounts of vitamin D (> 100.000 IU) on a daily basis, on the other hand, has been associated to an

increased risk of fractures and falls (Sanders *et al*., 2010) [45]. In patients receiving bone-specific therapy, a combination and vitamin D is required to get the full benefits seen in the intervention studies and to avoid subsequent hyperparathyroidism, hypomagnesemia and bone metabolism abnormalities (Bolland *et al*., 2015; Compston *et al*., 2017) [8, 12]. Vitamin D is a fat soluble so it's vital to get it with your meal for the best absorption.

4.3. A Drug that is specific

According to clinical algorithms specified in guidelines, certain medicine must be supplied to patients with a high risk of fractures or patients who have a fragility fracture (Kanis *et al*., 2019; Qaseem *et al*., 2017) [37, 64].

There hasn't been a research with enough power to show that different treatment strategies reduce fracture risk differently (Kanis *et al*., 2019; Qaseem *et al*., 2017) [37, 64]. However, osteoanabolic drugs reduce the risk of vertebral and nonvertebral fractures more quickly than antiresorptive drugs, and they should be considered first-line therapy in patients who have had previous fragility fractures, multiple fractures during the clinical course (Cosman, 2020) [21], or have a very low bone mineral density (t-score below–3). Treatment selections are made based on clinical judgement, which considers potential side effects, the influence on specific skeletal components, and costs (Cosman, 2020) [21].

After an overnight fast and 30 minutes before breakfast (and the intake of other drugs) or drinks (other than water), alendronate must be administered once weekly, 70 mg by mouth or 10 mg daily. Among the medical indications are the prevention of postmenopausal osteoporosis and glucocorticoid-induced osteoporosis (at a lower dosage of 5 mg daily), as well as the treatment of postmenopausal osteoporosis, osteoporosis in males, and glucocorticoid-induced osteoporosis. Found that alendronate can help prevent hip and vertebral fractures. The patient should remain upright for 30 minutes after taking the drug to lessen the risk of upper gastrointestinal side effects.

Risedronate is a multiple sclerosis medication that has been approved by the FDA. Postmenopausal osteoporosis, men with osteoporosis and a high risk of fractures, and males with osteoporosis and a high risk of fractures, as well as to prevent fractures in children Males and postmenopausal women both take glucocorticoids. Take 5 mg of the preparations every day and 35 mg once a week in the mouth have been shown to reduce the incidence of vertebral and hip fractures, and they should be treated at the same time. Similar to how alendronate works (Kanis *et al*., 2013) [38].

(B) Pharmacological alternatives

4.1. B Vitamin D and Calcium -Vitamin D deficiency is widespread in older individuals, not just because of physiological changes in the skin's capacity to synthesize vitamin D, but also because of malnutrition, chronic renal illness, institutionalization, or being housebound. National recommendations call for 1000 mg of calcium and 400 international units (IU) of vitamin D per day. Elderly persons who are housebound or in a nursing home should take 800 IU of vitamin D every day. Calcium and vitamin D supplementation decreased the risk of hip fracture by 30% and overall fracture risk by 15%, according to a meta-analysis (Weaver *et al*., 2016) [96].

Calcium supplementation has been linked to an increased risk of cardiovascular illness, including myocardial infarction (Harvey *et al*., 2017 & Lewis *et al*., 2015) [19, 46]. Other studies, on the other hand, revealed no link between calcium supplementation and cardiovascular disease risk (Chung *et al*., 2016) [13].

Overall, there is insufficient data to suggest that the risks of supplementing exceed the benefits, and current recommendations encourage supplementation for people at high risk of insufficiency and those getting osteoporosis therapies. Supplementing with calcium and vitamin D has also been demonstrated to improve muscular health and lower the chance of falling (Bischoff *et al*., 2009) [9].

Dose of calcium	Dose of vitamin D	Gender (50- <70 years)	Administration
1000 mg/d	600 IU/d= 180 mg	Female	Take with food
1000-1200 mg/d	800 IU/d= 240 mg	Male	Take with food

4.2. B Bisphosphonates

Bisphosphonates bind to hydroxyapatite tightly, inhibiting osteoclast-mediated bone resorption while also increasing bone mineral density. They have been linked to reduced fracture risk in patients of all ages, including those who are fragile (Sanderson *et al*., 2016, Vandenbroucke *et al*., 2017 and Zullo *et al*., 2019) [80, 91, 101].

10 mg of alendronate taken daily for 10 years raised bone mineral density by 13.7 percent at the lumbar spine, 10.3 percent at the trochanter, 5.4 percent at the femoral neck, and 6.7 percent at the whole proximal femur, according to evidence. Importantly, when started as a secondary preventative intervention after a fracture, both oral and intravenous bisphosphonate medications have been found to lower the risk of death (Vandenbroucke *et al*., 2017, Zullo *et al*., 2019, Beaupre *et al*., 2011 and Sambrook *et al*., 2011) [91, 101, 7, 73].

For postmenopausal women and men over 50 years of age with verified osteoporosis on DXA, UK NICE advice (NICE 2020) recommends Alendronate 10 mg once day or 70 mg once weekly; or Risedronate 5 mg once daily or 35 mg once weekly. BMD is normally assessed every three to five years. If the patient is at risk of fracture or has begun corticosteroid medication, treatment will be maintained. A medication holiday may be indicated if the T-score is greater than 2.5, pending further examination of BMD and fracture risk. However, discontinuing bisphosphonates at this time in postmenopausal women may be linked to a 40% increased risk of new clinical fractures compared to those who continue to take bisphosphonates (Mignot *et al*., 2017) [54].

GI problems, bone/joint pain, oesophageal ulcers, and, in rare cases, osteonecrosis of the jaw are all side effects of oral bisphosphonates (the highest risk is in patients with cancer). Atypical femoral fractures can develop at a rate of 1:1000 per year following 5 years of bisphosphonate therapy. Oral bisphosphonates should be taken with a glass of water on an empty stomach in an upright position (Tella *et al*., 2014) [83]. Because of the complicated dose regimen, adherence to bisphosphonates can be difficult in older adults, which can be exacerbated by polypharmacy, decreased cognition, and physical care demands. Bisphosphonates are also not stable enough to be stored in compliance aids.

Alternative formulations, such as intravenous (IV) annual Zoledronic acid or bisphosphonate alternatives, may be utilised in elderly persons with severe gastro-oesophageal reflux, dysphagia, or cognitive impairment (Kanis *et al*., 2013) [38]. Bisphosphonates are eliminated via the kidneys and should be avoided if you have kidney disease. GFR thresholds (estimated glomerular filtration rates) are used to guide treatment decisions. When creatinine clearance is less than 35 mL/min/1.73 m2 and 30 mL/min/1.73 m2, for example, alendronate and risedronate should be avoided. However, in elderly adults, especially those with frailty Table and sarcopenia, eGFR may not be accurate. In these instances, the Cockcroft and Gault GFR calculation is suitable to utilise, especially when IV Zoledronic is being investigated.

4.3. B Denosumab

Denosumab is a completely humanised antiresorptive drug that targets the receptor activator of nuclear factor kappa B ligand (RANKL). RANKL is a significant stimulator of osteoclastic bone resorption generated by osteoblasts that resembles the activity of osteoprotegerin (OPG) (Cutris *et al*., 2018 and Cairoli *et al*., 2018) [14]. It is given as a subcutaneous injection once every six months and has been shown to be effective in individuals with renal illness, albeit in severe renal impairment, underlying renal bone disease should be addressed. Denosumab administration increases BMD and lowers the risk of vertebral, non-vertebral, and hip fractures (Cummings *et al*., 2009) [15]. Skin infections, particularly cellulitis, are rare side effects. This is uncommon at the injection site and is likely to be due to the drug's immunomodulatory properties. When there is simultaneous renal impairment, hypocalcaemia is a danger, especially if the patient is vitamin D deficient.

4.4. B Teriparatide

The first fully anabolic (bone-forming) agent was teriparatide (recombinant human 1–34 parathyroid hormone peptide). It is given in daily dosages of 20 g via subcutaneous injection. When compared to placebo, it promotes bone formation and provides considerable gains in BMD, resulting in a 70% reduction in the frequency of new moderate or severe vertebral fractures over 18 months of therapy, as well as reductions in non-vertebral fractures (Neer *et al*., 2001, and Moreira *et al*., 2017) [57, 55].

In comparison to oral risedronate, superiority in terms of BMD increase and fracture reduction has recently been proven (Kendler *et al*., 2018) [39]. Nausea, headaches, and dizziness are the most common side effects, however temporary hypercalcaemia and hypercalciuria can also occur. Combination therapies such as teriparatide plus denosumab or teriparatide plus zoledronic acid may provide synergistic effects as compared to using these medicines alone (Tsai *et al*., 2013) [84], while such techniques are not yet extensively utilised or licenced.

4.5. B Abaloparatide

Abaloparatide is a 34-amino-acid synthetic peptide with structural similarities to parathyroid hormonerelated peptide (Miller *et al*., 2016) [49]. It stimulates the PTH-1 receptor in the same way as teriparatide does, but with a higher affinity for the RG receptor configuration. After 18 months, abaloparatide causes significant increases in BMD and a decrease in both vertebral (86 percent relative reduction) and non-vertebral fractures (43 percent relative reduction). Abaloparatide appeared to have a greater effect on reducing major osteoporotic fracture risk than teriparatide. Similar to teriparatide, there is a higher risk of hypercalcaemia when compared to placebo, and both are now utilised in the same therapeutic context in the United States (abaloparatide is not accessible in Europe).

4.6. B Romosozumab

Sclerostin, an osteocyte-derived glycoprotein that regulates osteoblast bone production, is predominantly controlled by mechanical stress, with higher load lowering sclerostin secretion. Sclerostin suppresses bone formation by binding to LRP5/6 and thereby blocking the canonical Wnt signaling pathway. Romosozumab is a humanised antibody that has a high affinity for sclerostin and causes significant improvements in bone density. Romosozumab 210 mg monthly for 12 months decreased the risk of vertebral fracture by 73% in a phase 3 fracture endpoint study including 7180 women with postmenopausal osteoporosis (Cosman *et al*., 2016) [17]. This effect was most noticeable between months 7–12 of treatment. All patients received open label denosumab treatment during the study's second year.

All patients received open label denosumab therapy during the study's second year. By the conclusion of the year, participants who had received romosozumab throughout year one had a 75 percent lower risk of vertebral fracture than those who had received placebo followed by denosumab.

After 12 months, clinical fracture risk was reduced by 36% when compared to placebo. The rate of non-vertebral fractures was reduced by 25%, however the reduction was not statistically significant. In a study of individuals with a higher risk of fracture, efficacy was proven versus alendronic acid as a comparison (Saag *et al*., 2017) [72]. However, there was a little disparity in cardiovascular events here (greater with romosozumab). The US Food and Drug Administration and the European Medicines Agency are both considering romosozumab at the time of writing.

5. Nutritional requirements for osteoporosis

5.1. Calcium, dairy products and vitamin- D

Calcium and vitamin D are needed for bone strength and are found in the mineral matrix of the bone as calcium phosphate. Adherence to a healthy diet is the greatest approach to ensure enough calcium intakes. However, when dietary calcium sources are inadequate or poorly tolerated, pharmaceutical calcium supplementation may be beneficial. The majority of clinical practice recommendations suggest this Some experts, however, are sceptical of this suggestion because of its limited effectiveness and the risk of side effects (Chiodini *et al*., 2018, Kanis *et al*., 2017, Compston *et al*., 2017[19] and Bolland *et al*., 2015) [18, 40, 19, 8]. Dairy products (milk, yoghurt, and cheese), fish (especially sardines with bones), lentils, and a few vegetables and fruits are the most significant sources of calcium in the diet (particularly nuts and seeds). Vitamin D is primarily responsible for calcium homeostasis. Vitamin D is derived in two ways: 80–90% through cutaneous synthesis following exposure to sunshine, and 10–20% from a small number of foods, such as fatty fish, mushrooms, and certain fortified dairy products. Despite this, no diet can supply enough vitamin D to fulfil daily needs. The fortification of many foods may have a role in increasing vitamin D consumption. Vitamin D deficiency may be prevented and

corrected with adequate sunshine exposure. Vitamin D shortage has negative health repercussions, and this vitamin is critical for bone health maintenance. Vitamin D deficiency can exacerbate osteoporosis in the elderly or postmenopausal women. Additionally, appropriate 25-hydroxyvitamin D concentrations are required to maximise the effectiveness of anti-osteoporotic medicines

Dairy products are the main food sources providing bone-beneficial nutrients, such as calcium, phosphorus and magnesium and these elements have a morphological role in bone healthy structure. Dairy products are also a source of protein, vitamin B-12, zinc, potassium and riboflavin. If fortified with vitamin D, dairy products might be a fantastic source of the vitamin. Yogurt and cheese have greater vitamin D concentrations by weight than milk, but serving amounts are often less in these items than in milk. As a result, consuming plain dairy products or those supplemented with calcium and/or vitamin D on a daily basis may help to improve total body bone mineral content (BMC). This relationship, however, differs by ethnicity (Tai *et al*., 2015) [85].

5.2. Minerals for other type

Other minerals, such as potassium and magnesium, have a role in bone health as well. Potassium in the diet may help to minimize acid load and, as a result, calcium depletion in the bones. Potassium, in addition to assisting in the maintenance of an alkaline condition in the body, may also aid in the buildup of calcium. A buildup of calcium in the kidneys the greatest potassium consumption was found in a country wide Korean population research. In males over 50, having a higher lumbar, total hip, and femur neck BMD was linked to having a higher lumbar, total hip, and femur neck BMD (Kong *et al*., 2017) [43].

Magnesium is required for calcium metabolism as well (Erem *et al*., 2019) [27]. With a concentration of 10–30 mM in the human body, magnesium is the second most prevalent intracellular action after potassium. Magnesium may be found in a variety of foods, including green leafy vegetables, legumes, and nuts. The daily magnesium limits for women and males are 310–360 mg and 400–420 mg, respectively. Individual needs differ based on age, gender, and past nutritional status.

Magnesium is required for neuronal activity and muscular contractions, as well as the exchange of calcium and potassium ions across cell membranes. The bone stores around 50–60% of the total magnesium content of the body. Magnesium ions attach to the surface of hydroxyapatite crystals in the bone structure, improving the solubility of phosphorous and calcium hydroxyapatite and, as a result, influencing crystal size and formation. Magnesium also promotes osteoblast development; therefore a lack of it is linked to a reduction in bone formation. Magnesium is also required for the activation of vitamin D, as it is required by the majority of enzymes involved in vitamin D metabolism (Uwitonze *et al*., 2018) [89].

Magnesium levels are lower in populations who consume more processed foods (refined grains, sweets, and fats), as is the case in the United States (Rosanoff *et al*., 2012) [67]. The soil used for agriculture is becoming more lacking in important elements such as magnesium, which is posing a big challenge. Although there are no randomised researches examining the influence of magnesium on bone disease, small-scale investigations have linked low serum magnesium levels to osteoporosis (okyay *et al*., 2013) [58]. Low magnesium intake in elderly people promotes excessive calcium release from the bones, worsening bone fragility and increasing the risk of fractures and falls (Veronese *et al*., 2017) [90].

5.3. Protein consumption

Protein is also necessary for bone health. Proteins make up nearly half of bone volume and a third of bone bulk. When mineralization occurs, they are incorporated into the organic matrix of bone as part of the collagen structure. Insulin-like growth factor I (IGF-I), an orthotropic hormone necessary for bone production, is similarly affected by dietary proteins. The IGF-I hormone enhances the rate of phosphate reabsorption from the kidney and promotes calcium and phosphorus absorption in the gut. It is also involved in the creation of calcitriol. As a result, maintaining bone health need a sufficient amount of dietary protein. Dietary protein intake of 1.0–1.2 g/kg body weight/day is recommended by the Europea Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis (ESCEO), with at least 20–25 g of high-quality protein at each main meal (Rizzoli *et al*., 2014) [70].

Meat, fish, poultry, eggs, and dairy products are the major sources of protein in a balanced diet. Protein is required for the creation and maintenance of the bone matrix. However, based on the "nutritional acid load theory," it was previously thought that a high protein diet might cause a negative calcium balance. This idea links increased acid production and bone resorption (particularly that of animal origin, which contains more sulphur amino acids) to the development of harmful hypercalciuria and bone loss, leading to osteoporosis and an increased risk of fragility fractures (Bonjour *et al*., 2013) [6].

Recent meta-analyses have found that consuming more protein—more than 0.8 g/kg body weight/day, which is greater than the conventional dietary recommendations—is linked to a higher BMD, a decreased risk of hip fracture, and a slower rate of bone loss. It is especially crucial in elderly persons with osteoporosis, and it must always be supplemented with enough dietary calcium (Rizzoli *et al*., 2018) [69].

It's also crucial to consider the anabolic impact of protein consumption, which, together with physical exercise, is a major driver of muscle protein synthesis. Muscle mass and strength improve with exercise, and a combination of appropriate protein intake and exercise causes more muscle protein accretion than either intervention alone. Similarly, a well-balanced dietary protein intake combined with resistance training is a significant factor in maintaining bone strength. Higher protein consumption has been shown to have no negative impact on bone health.

They are also helpful in preventing age-related bone loss and lowering the risk of hip fracture in older people (Groenendijk *et al*., 2019) [33]. Within the confines of a balanced diet, no significant variations in hip fracture outcomes have been discovered between animal and vegetable protein consumption. All of these favorable results, however, are contingent on appropriate calcium consumption, as previously stated. Dairy products are likely to be beneficial since they include both proteins and calcium, with 1 L of milk containing 32 g of protein and 1200 mg of calcium.

Furthermore, yoghurts are fortified with milk powder in some countries, resulting in a 50 percent higher amount of essential nutrients than yoghurt made from plain milk. Calciotropic hormones benefit from the mix of protein and calcium found in dairy products. They resulted in a decrease in circulating PTH, a rise in IGF-I, and a reduction in bone resorption indicators, as well as an improvement in BMD (Rizzoli *et al*., 2018) [69]. As a result, diets with little protein cause far more serious issues than those with too much. Fruit and vegetables are high in the minerals needed for healthy bone health, such as potassium and magnesium, as well as vitamin C, vitamin K, folate, and carotenoids (New *et al*., 2003 and Ahmadieh *et al*., 2011) [56, 2].

5.4 K and C vitamins

Vitamin K aids in the development of the bone matrix during mineralization. It regulates other vitamin K-dependent proteins by acting as a cofactor for the microsomal -carboxylase, which accelerates the post-translational conversion of glutamyl to -carboxyglutamyl residues in osteocalcin. Osteocalcin is a calcium-binding protein in bone that aids in the mineralization process when it is -carboxylated. Vitamin K is made up of several distinct molecular forms: vitamin K1 is a single form produced by plants, whereas vitamin K2 is made up of several forms produced mostly by bacteria. The most common kind of vitamin K found in human diets is vitamin K1. The presence of vitamin K2 in cheese is a unique trait. A recent meta-analysis done in 2019 (Mott *et al*., 2019) [50] included over 11,000 individuals and was mostly focused on postmenopausal or osteoporotic patients.

Vitamin K supplementation appeared to have minimal clinically meaningful influence on BMD and vertebral fracture outcomes for these individuals, according to the study, which was partly due to the heterogeneity of the trials considered, particularly in terms of treatment regimens. Clinical fractures were less common in the vitamin K-supplemented group in postmenopausal women and osteoporotic patients; although the impact appeared to be lower when the analysis was limited to low-risk-of-bias trials. Because there are so few trials available, it's difficult to extrapolate insights from this meta-analysis to other populations. Another comprehensive analysis indicated that the use of oral vitamin K antagonists as part of anticoagulant medication was not connected to nor lowered BMD, nor was it linked to an increased risk of fracture (Veronese *et al*., 2015) [90], confirming earlier findings that vitamin K had no clinically relevant effect on BMD.

Because of its antioxidant characteristics, vitamin C can help with bone health. It has the ability to inhibit osteoclast activity (Finck *et al*., 2014) [31]. It also contributes in collagen synthesis and functions as a cofactor for osteoblast differentiation.

Vitamin C is a sign of a balanced diet rich in fruits and vegetables. Although there was significant between-study variability at the femoral neck, a systematic review and meta-analysis of observational studies revealed that higher dietary vitamin C consumption was positively linked with BMD at the femoral neck and lumbar spine. Differences in research design, gender, and age contributed to the variability. A higher dietary vitamin C intake was linked to a lower risk of hip fracture and osteoporosis, as well as a higher BMD, at both the femoral neck and lumbar spine sites (Malmir *et al*., 2018) [51]; a more recent meta-analysis backs up the idea that increasing dietary vitamin C intake can reduce the risk of hip fractures in both men and women (Sun *et al*., 2018) [75]. Despite these impressive bone advantages, there is little information in clinical practice guidelines about vitamin C dietary recommendations, which should be taken into mind.

6. Combination of calcium

Calcium plus vitamin D and vitamin K was the most popular combination in our survey. Calcium supplements are frequently sold in conjunction with vitamins D, K, zinc and magnesium. Zinc is a key component of many metalloenzymes in the body, however increased calcium consumption reduces zinc absorption, which can be counteracted by supplementation. Magnesium is required for several enzyme processes. The amount of magnesium absorbed and excreted is determined by the amount of magnesium consumed. Calcium consumption calcium shortage can be exacerbated by a high calcium intake, thus it's critical to keep the calcium to magnesium ratio balanced. For best heath the ratio should be less than 2.8. (Rosanoff *et al*., 2016) [71].

Excess calcium can accumulate in the artery wall and vitamin K is a key component in preventing this problem. Vitamin K2 is a kind of vitamin k. (Since it does not need to be activated in the liver) has a significant role to play. Matrix GLA protein (MGP), which is a key protein in the matrix, plays a function in its activation. Vascular smooth muscle cells generate a calcification inhibitor. MGP inhibits the buildup of calcium in the vascular system (Maresz *et al*., 2015) [52]. Vitamin K is also thought to lower the risk of fractures, as well as increasing bone density when used in conjunction with both vitamin D and calcium have a beneficial influence on bone density (Peter weber., 2001).

6.1 Calcium and the risk of osteoporosis

Osteoporosis is the most prevalent bone disease, which is marked by a loss of bone density and a high risk of fracture (Shea *et al*., 2002) [76]. In their study of 9961 adults (4958 women and 5003 men), Ferrari discovered that high-dose calcium supplementation improves BMD in women only when vitamin D levels are low (50 nM), while there is no link between calcium consumption and BMD in males at any level of vitamin D. The Auckland calcium research was a randomized controlled trial of a 1g/day calcium supplement for 5 years, followed by a 5-year follow-up when the calcium was stopped. The author found that there was no reduction in total fracture but a substantial reduction in forearm and vertebral fracture after 5 years, but that the favorable effects of calcium on BMD did not last once the calcium supplement was stopped (Meeta *et al*., 2013) [53]. Calcium supplements have little or no effect on BMD according to the majority of research. The Indian menopausal society recommends screening for osteoporosis diagnosis. Patients with high risk variables, such as age have a lower chance of surviving. BMI, previous fragile fracture history, parenteral history of hip fracture and alcohol and glucocorticoid users are also factors to consider screened. They also suggest that physical examinations and tests be used. A complete blood count and serum analysis are part of a standard blood test. Creatinine, vitamin D, PTH, ALP, calcium and phosphorous levels measuring of levels. According to the IMS a dexa scan should be performed in women who have been menopausal for more

than 5 years, as well as women who have been menopausal for less than 5 years. With risk factors, less than 5 years postmenopausal (Eastell *et al*., 2019). The second is X – rays and quantitative ultrasonography are among the tests that are advised as well as bone markers. The Indian Menopausal society recommends screening for osteoporosis diagnosis. Patients with high risk variables, such as age, have a lower chance of surviving. The Endocrine Society also recommends bone markers (ES) (Qaseem *et al*., 2017) [64].

Bisphosphonates are the first-line therapy for osteoporosis. The American College of Physicians (APC), the International Medical Council (IMC), and the European Society of Osteoporosis (ES) has all issued statements on osteoporosis. The IMC strongly advises hormone treatment, although ACP advises against it. Hormone Replacement is not a first-line treatment for ES osteoporosis. Terriparatide and Denosumab are recommended as first-line drugs for osteoporosis by ACP and ES, whereas Terriparatide but not Denosumab is recommended by IMC. IMS's recommendation Calcium osteoporosis preventive vitamins for postmenopausal women ladies who don't have any danger factors Calcium and Vitamin D aren't the same thing. IMC considers it the first-line therapy for osteoporosis. APC or ES are two options. It's APC and ES both propose a 5-year treatment period for osteoporosis (Qaseem *et al*., 2017 and Tseng *et al*., 2005) [64, 86].

6.2 Fracture and calcium

Calcium supplementation, according to 64 percent of those who responded to our study, helps to avoid fractures. According to (Zhao *et al*., 2017) [102], calcium and vitamin D supplementation reduces hip fractures in postmenopausal women by 43%. (Bolland *et al*., 2015) [8]. Shown that such a huge influence exists due to the widespread osteomalacia caused by vitamin D deficiency among the older ladies who have been chosen. According to (Sullivan *et al*., 2017) [77], there is no evidence that supplementing with vitamin D reduces the incidence of fracture. Calcium, Vitamin D, or a mix of the two fracture prevention through calcium supplementation is not suggested at this time (Kong *et al*., 2017 [43] and Sullivan *et al*., 2017) [77]. In their analysis of fracture healing and posttraumatic bone turnover, Fischer found that calcium and vitamin D supplementation reduces posttraumatic bone loss caused by mineral mobilization. From a source other than the fracture this postoperative bone loss may be a cause of subsequent fracture in osteoporotic individuals. Calcium and vitamin D supplements aid in the prevention of osteoporosis. Finally, calcium supplementation is beneficial. Vitamin D and calcium can help to avoid fractures. Fracture healing and postoperative bone loss can both be improved with this combination.

7. Conclusion

Osteoporosis is a disease that worsens with age and is becoming more common as the world's population ages. Osteoporosis and sarcopenia frequently coexist and are associated with significant morbidity and death in older adults. Both are frequently misdiagnosed and untreated. In both basic and secondary care, routine bone and muscle health assessments should be part of a holistic multidisciplinary driven, tailored complete geriatric evaluation. Nutrition, physical activity, exercise, gait and balance therapies have all been found to improve bone and muscle health as well as decrease the number of falls. As part of an older person's treatment approach, these should be implemented with other lifestyle changes. Regardless of dietary preferences, enough calcium consumption appears to be recommended for bone health. Overall, following a balanced dietary pattern that includes fruits, vegetables, whole grains, chicken, fish, nuts and legumes, low-fat dairy products, and avoiding processed foods can improve bone health and reduce the risk of osteoporosis and fractures. In ordinary practise, orthopaedic surgeons routinely prescribe calcium supplements; nevertheless, the justification for prescription differs per surgeon. Even among surgeons, the dose, duration, preferred calcium salt, and calcium combination vary. Calcium supplementation is of limited value, and the evidence for prescription calcium for fracture prevention or osteoporosis is equivocal. There has never been a countrywide survey of the Indian population to provide calcium supplement guidelines.

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