# OSTEOPOROSIS

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## Abstract

Osteoporosis is the most frequent metabolic bone disease. It is characterized by decreased bone strength and bone fractures and consequently decreased quality of life with increased morbidity and mortality. It affects the population of postmenopausal women and older people of both gender, but also patients with other primary diseases. Modern diagnostic procedures such as bone mineral density measurement, trabecular bone score (TBS) measurement, and fracture assessment risk score (FRAX) enable early diagnosis and treatment in high-risk patients. The complex etiology and pathophysiology of osteoporosis require secondary causes to be differentiated from primary osteoporosis before the most optimal treatment is initiated. The treatment should be personalized. Two methods of treatment are antiresorptive treatment aimed toward the inhibition of bone degradation and anabolic treatment with stimulation of new bone formation. Ideally, the prevention of fractures should be the treatment of choice, otherwise, prevention of new fractures and improvement of life is the therapeutic goal. Bisphosphonates are the first line antiresorptive treatment together with denosumab, a monoclonal human antibody against RANK ligand (receptor activator of nuclear factor kappa B). Teriparatide, an N-terminal parathormone fragment, is the dominant anabolic drug. Vitamin D deficiency is a widespread problem and contributes to bone mass decrement and increased risk for fractures. With further advancements in understanding the biology of bone tissue, new therapeutic agents are expected in the treatment of patients with osteoporosis.

**Keywords:** osteoporosis, osteoporosis management, bone mineral density, fracture risk

## Introduction

Osteoporosis is a chronic metabolic bone disorder characterized by a progressive reduction in bone mass, and changes in bone structure and quality, which lead to decreased bone strength and the development of pathological fractures, as the main cause of reduced quality of life and increased morbidity and mortality[1, 2]. Due to the aging of the human population, this disease is becoming epidemic and primarily affects postmenopausal women and older individuals of both sexes[3].

The World Health Organization (WHO) has established arbitrary criteria to define osteoporosis based on bone mineral density measurements using the T-score. The T-score represents the difference in bone mass between the patient and a young adult reference population, expressed in standard deviations (SD), where a negative sign indicates that the bone mass is, that many SD below the average bone mass of a young adult woman[4, 5]. The threshold for osteoporosis is a T-score below -2.5 SD. The Z-score is used in premenopausal women and represents the difference in bone mass between the patient and individuals of the same age (table 1).

There are numerous risk factors (table 2) that can lead to the development of osteoporosis. The presence of these factors in patients indicates the need for conducting skeletal densitometry. Some of these factors can be improved through appropriate therapeutic procedures, while others cannot be influenced[4].

In every patient with a fracture after minimal trauma or with densitometrically confirmed osteoporosis, it is necessary to conduct a clinical investigation to exclude possible secondary causes of osteoporosis (table 3). Osteoporosis can be part of the clinical picture of various underlying diseases, which in that case represent the main cause of reduced bone mass, and then we refer to it as secondary osteoporosis[4]. Only when these diseases are excluded, we are dealing with primary osteoporosis, also known as involutional osteoporosis, which is further classified into two subtypes (table 4).

## Epidemiology of osteoporosis

The incidence of osteoporosis increases with age due to progressive loss of bone tissue over the years. In women, during the menopausal period (typically around the age of 50), when ovarian function ceases, there is an acceleration of bone loss as the protective effect of ovarian hormones diminishes[1, 2, 5, 6]. If a woman has reached her peak bone mass at that time, it is expected that she will meet the criteria for osteoporosis between the ages of 70-80 (Type 2 senile


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**Table 1.** According to the World Health Organization (WHO) and the assessment of bone mineral density (BMD)

| THE DEFINITIONS ACCORDING TO THE WORLD HEALTH ORGANIZATION (WHO) BASED ON DENSITOMETRY | | |
|---|---|---|
| CLASSIFICATION | T SCORE | BONE MINERAL DENSITY (BMD) |
| Normal BMD | T score > -1 | BMD up to 1 SD of reference values for young adults |
| Osteopenia (small BMD) | T score -1 to -2.5 | A decrease in BMD between 1 and 2.5 SD compared to young adults |
| Osteoporosis | T score ≤ -2.5 | A decrease in BMD equal to or greater than 2.5 SD compared to young adults |
| Severe-advanced osteoporosis | T score ≤ -2.5 | A decrease in BMD equal to or greater than 2.5 SD with regard to young adults with the presence of one or more fractures |

**Table 2.** Risk factors that lead to osteoporosis and fractures

| FACTORS THAT CANNOT BE MODIFIED | FACTORS THAT CAN BE MODIFIED |
|---|---|
| Personal history of fractures in adulthood | Estrogen deficiency<br>- early natural or artificial (bilateral ovariectomy) menopause (before age 45)<br>- longer periods of amenorrhea (> 1 year) |
| Family history of fractures in first-degree relatives | Malnutrition and poor nutrition (especially reduced intake of calcium and vitamin D) |
| Female gender | Alcoholism |
| Older age | Frequent falls |
| White race | Inadequate physical activity |
| Dementia | Decreased muscle mass |

osteoporosis). If the peak bone mass was low, bone mass decreases immediately after menopause and osteoporosis occurs (type 1 postmenopausal osteoporosis). In developed countries, bone fractures are more common in women. from breast cancer and higher than her risk of dying from endometrial cancer[4, 7].

**Table 3.** The causes of secondary generalized osteoporosis

| CANCER AND HEMATOLOGICAL DISORDERS | ENDOCRINOLOGICAL DISORDERS AND HYPOGONADISM | |
|---|---|---|
| - Multiple myeloma (in people over 60 years of age)<br>- Cancer with PTHrP production<br>- Lymphomas and leukemia<br>- Mastocytosis<br>- Thalassemia | - Cushing's syndrome<br>- Primary and secondary hyperparathyroidism<br>- Thyrotoxicosis<br>- Adrenal insufficiency (Addison's disease)<br>- *Diabetes mellitus* type 1 and 2 | - Acromegaly<br>- Hyperprolactinemia<br>- *Anorexia nervosa*<br>- Hypothalamic amenorrhea<br>- Turner and Klinefelter syndrome |
| GASTROINTESTINAL AND NUTRITIONAL DISORDERS | HEREDITARY DISEASES | |
| - Malabsorption syndromes<br>- Gastrectomy<br>- Long-term parenteral malnutrition<br>- Chronic liver diseases (biliary cirrhosis) | - Glycogenosis<br>- Marfan syndrome<br>- *Osteogenesis imperfect*<br>- Hypophosphatasia<br>- Ehlers-Danlos syndrome<br>- Homocystinuria | |
| RHEUMATOLOGICAL DISORDERS | OTHER DISORDERS | |
| - Rheumatoid arthritis | - Long-term immobilization<br>- Pregnancy and lactation<br>- Sarcoidosis<br>- Chronic obstructive pulmonary disease<br>- Multiple sclerosis | |

**Table 4.** Types of primary osteoporosis

| SUBTYPES OF INVOLUTIONAL OSTEOPOROSIS | CLINICAL CHARACTERISTICS OF SUBTYPES |
|---|---|
| Type 1 (Postmenopausal osteoporosis) | - typically in postmenopausal women for the first 5-10 years after menopause<br>- affects predominantly trabecular (spongy) bone-vertebrae |
| Type 2 (Senile osteoporosis) | - typically in persons of both sexes after 70 years of age<br>- affects both cortical and trabecular bone |

Every second woman and every eighth man over the age of 50 will experience a fracture, particularly of the vertebrae. One in five women will experience a new fracture within the first year after the initial fracture[6]. The risk for a 50-year-old woman to die from a hip fracture is equal to her risk of dying

## Pathogenesis of osteoporosis and disease development

Bone strength is the result of the interaction between bone mineral density (BMD) and bone quality (micro-

architecture, bone geometry, bone turnover rate, accumulation of microscopic damage, degree of mineralization, and collagen properties)[4]. Bone is a dynamic tissue that undergoes continuous changes throughout life due to the presence of two processes: bone formation (ossification), controlled by bone cells called osteoblasts (derived from mesenchymal cells), and bone resorption, carried out by osteoclasts (cells derived from hematopoietic stem cells). Macroscopically, bone can be divided into an outer layer called cortical or compact bone, which constitutes 80% of the total skeleton, and an inner part called trabecular or spongy bone[4]. This structure, with an cortical bone and inner trabecular lattice, enables optimal mechanical functioning of the bone. The trabecular bone is oriented in the direction of external mechanical forces. In addition to its mechanical function, bone serves as a reservoir or "ion bank" for essential ions such as calcium, magnesium, phosphorus, sodium, and other ions necessary for various physiological processes[4].

Bone is formed during fetal life, youth, and puberty, and this process is controlled by numerous genes and influenced by various hormones and cytokines. Once the bone is formed, its shape and structure continuously change through two processes: modeling and remodeling[4]. Modeling primarily occurs during the growth period when new bone is created at sites that are not associated with areas where the bone is being resorbed, resulting in bone shaping and adaptation to mechanical conditions and forces. Modeling is the main process that increases bone mass or volume throughout life. Remodeling is the primary process in adults, where bone resorption and formation are closely and inseparably linked in both time and space, leading to changes in bone shape. This continuous bone metabolism predominantly occurs in trabecular bone, which represents 80% of bone metabolism, even though it constitutes only 20% of the total skeleton.

The key molecular mediator of bone remodeling is a system consisting of three components: RANK, RANK ligand (RANKL), and osteoprotegerin (OPG)[8, 9]. This system is the main regulator of osteoclast formation and, consequently, bone resorption. Dysregulation of this system exists not only in osteoporosis but also in bone loss caused by glucocorticoid hormones, multiple myeloma, and rheumatoid arthritis. Parathyroid hormone (PTH) receptors are present only on osteoblasts and not on osteoclasts, although PTH acts by activating osteoclasts and stimulating bone resorption. However, it does so indirectly through this system. The binding of PTH to membrane receptors on osteoblasts leads to the expression of RANK ligands on the osteoblast membranes. Subsequently, RANKL binds to RANK receptors on osteoclast precursor cells, activating and multiplying them, ultimately leading to the formation of mature osteoclasts that initiate bone resorption[8, 9]. Osteoprotegerin is a false receptor that is also produced by osteoblasts. It binds to excess RANKL molecules, preventing their excessive binding to RANK and the overactivation of osteoclasts. In this way, osteoblasts, in a sense, control their involvement in osteoclast activation. Essentially, all hormones that affect calcium metabolism and bone metabolism act through this molecular system. During menopause, when estrogen levels in women fall below a critical level, there is increased activation of osteoclasts that were tonically inhibited or suppressed by estrogen during a woman's reproductive life. This effect primarily occurs through this system[4].

Most of the bone tissue is formed during puberty, especially during the period of accelerated growth. Around the transition from the second to the third decade of life, the processes of bone formation and resorption become balanced (as much bone tissue is resorbed, an equal amount is formed). Then, after the fourth and fifth decades of life, bone resorption starts to outweigh formation, leading to a gradual decrease in bone mass. The timing of when bone mass will decrease to a critical level where fractures occur easily depends on the "peak bone mass". If an individual has formed a low amount of bone mass during their youth for various reasons, when the loss of bone mass becomes dominant, osteoporosis can develop rapidly. Therefore, the best prevention of osteoporosis is to maximize the formation of bone tissue during the growth period.

Postmenopausal women, on average, experience a loss of 1-2% of bone mass per year, while in men, the loss is around 0.2-0.5% per year. The main cause of bone loss in women is estrogen deficiency. The pathogenesis of osteoporosis in men is not fully understood, although a deficit in androgens may play a role. Men experience a slower but progressive loss of bone tissue, which manifests as fractures in later years, most commonly in the seventh and eighth decades of life.

## Clinical presentation of osteoporosis

Osteoporosis is initially asymptomatic, making it a silent and insidious disease, and patients without symptoms are unaware that they have it unless individuals with risk factors are specifically referred for bone densitometry, which reveals reduced bone mass[4]. Unfortunately, osteoporosis is far more commonly discovered only when complications arise, such as fractures occurring after minimal trauma ("pathological fractures"). More often, in patients experiencing pain in the musculoskeletal system, the cause of pain can be artrotic changes, which sometimes serve as an indication for measuring the bone mass. After a fracture occurs, the dominant symptom is pain, accompanied by the appearance of deformity and impaired or restricted mobility. In patients with hip fractures, there is an increased mortality rate (20% of patients with hip fractures die within the first year after the fracture), 40% are unable to walk independently, and 80% are unable to perform at least one basic daily activity independently[10]. Fractures of the vertebral bodies can cause numerous consequences, including chronic back pain, progressive kyphosis (abnormal curvature of the spine), loss of height, reduced ability to perform daily activities (including

personal hygiene tasks), loss of self-esteem, fear of new fractures, social isolation, depression, and an increased frequency of doctor visits[4]. Fractures in the *lumbar vertebrae* can reduce the space between the ribs and pelvis, disrupting the anatomy of the abdomen and the arrangement of organs within it, leading to gastrointestinal symptoms such as decreased appetite, early satiety, abdominal pain, bloating, constipation, and more. Fractures in the *thoracic vertebrae* can result in restrictive respiratory impairments and the development of *dyspnea* (shortness of breath)[4].

## Diagnosis of osteoporosis

It is necessary to perform basic laboratory tests[1, 2, 4] which include: routine biochemical analyses with total and ionized calcium, phosphorus, and protein electrophoresis (to exclude the presence of paraproteins i.e. multiple myeloma), thyroxine, and thyroid stimulating hormone (TSH) to exclude thyrotoxicosis, vitamin D in the blood, gonadotropins, and testosterone in younger men, as well as specific markers of bone formation (i.e. osteoblast function) and bone resorption (i.e. osteoclast function) (table 5). These markers can indicate the rate of bone metabolism[6], which can affect the choice of treatment (i.e. "slow" and "fast" bone metabolism).

Radiography of the skeleton has its place in the diagnosis of osteoporosis, especially when there is suspicion of fractures after the onset of skeletal pain (particularly in the spine)[4]. Radiographically, there are three types of vertebral body fractures: compressive (crush) fracture, where the entire height of the vertebral body is lost (height reduced by more than 20% compared to the surrounding *vertebrae*), wedge fracture, where the anterior height of the vertebral body is lost and the remaining vertebra resembles a wedge, and a fish-tail fracture, where the height of the vertebra is reduced in the middle portion.

## Bone mass measurement

There are several non-invasive techniques for measuring bone mineral density, or bone mass. These include the DEXA technique (Dual-Energy X-ray Absorptiometry), SXA (Single X-ray absorptiometry), quantitative CT (Computerized Tomography), and ultrasound technique[4, 6]. Although measurements can be taken at different sites of the skeleton, it is common to measure the hip and lumbar spine. The technique of choice is DEXA, which uses two X-ray beams to determine the mineralized tissue area, and the obtained mineral content is divided by the bone area. In osteoarthritis, bony osteophytes and calcium deposited in other periarticular structures around the joints can falsely improve the findings. There are also software additions to the DEXA technique, such as VFA (Vertebral Fracture Assessment), which examines fractures, and TBS, which allows the assessment of trabecular bone microarchitecture[4]. Quantitative CT scanning is generally not used due to increased radiation exposure and higher cost compared to DEXA. The ultrasonic technique is imprecise but suitable for its device mobility and more favorable cost, and it is used as a screening procedure[4].

## Algorithm of risk assessment for the occurrence of fractures and prognosis

The main consequence of osteoporosis is fracture, as mentioned earlier[4]. Computer algorithms (FRAX) have been developed to calculate the probability of major fractures occurring in individuals with multiple risk factors included in the algorithm[5]. These risk factors include the patient's age, gender, previous fractures (clinical or asymptomatic), bone density in the neck of the femur, low body weight (body mass index less than 21 kg/m$^2$), use of glucocorticoids for more than three months (at a prednisone-equivalent dose of $\geq$ 5 mg/day), presence of rheumatoid arthritis, family history of fractures, current or past smoking, excessive alcohol intake (more than three alcoholic drinks per day), and secondary causes of osteoporosis. By inputting these data into the algorithm, it calculates the ten-year risk of major fractures (spine, hip, forearm, or shoulder) and assesses the need for treatment. The algorithm is available online and is straightforward to use and interpret[11]. Several countries have also developed variations of the algorithm.

Just like with most other diseases, prevention is of utmost importance in osteoporosis. Once diagnosed with osteoporosis, the amount of bone loss will never return to normal. However, with treatment, it is necessary to reduce the risk of new fractures[3, 4].

## Treatment of osteoporosis

The most optimal solution would be for each country to initiate a national project for the prevention of osteoporosis. It would be necessary to eliminate or improve all modifiable risk factors, especially during puberty when the attainment of peak bone mass and mineral density is expected[4]. Sufficient vitamin D intake and calcium supplementation should be ensured during this period of growth, possibly through food fortification programs. These preventive measures are

**Table 5.** Laboratory markers for bone metabolism

| BONE FORMATION MARKERS (OSTEOBLAST FUNCTIONS) | BONE DEGRADATION MARKERS (OSTEOCLAST FUNCTIONS) |
|---|---|
| - bone alkaline phosphatase isoenzyme<br>- osteocalcin<br>- Procollagen I Carboxyterminal Propeptide (PICP)<br>- Procollagen I N-terminal Peptide (PINP) | - tartrate-resistant acid phosphatase<br>- serum and urine C and N telopeptide (CTx and NTx)<br>- cross-links<br>- pyridinoline and deoxypyridinoline |

possible in economically developed countries. Unfortunately, in Serbia, there are currently no preventive programs in place to prevent the occurrence of osteoporosis.

The goals of treatment are to reduce the risk of fractures by improving bone mass, bone architecture, and bone strength, as well as limiting the frequency of falls and injuries[12]. Each form of primary and secondary osteoporosis requires the selection of specific treatment approaches, making the treatment approach individualized. Non-pharmacological treatment involves adequate intake of calcium and vitamin D through diet, weight-bearing exercises, smoking cessation, limiting alcohol/coffee intake, and implementing various fall prevention techniques. Since a daily diet may not provide sufficient calcium and vitamin D intake, and sun exposure in regions with moderate latitude may not be enough to ensure adequate vitamin D production in the skin, it is necessary to supplement with calcium and vitamin D supplements.

It is advised to have a daily intake of 2,000-3,000 International Units (IU) of vitamin D in the form of cholecalciferol (vitamin D3) in Europe, which is significantly higher, compared to previous recommendations (800 IU). If certain types of food were fortified with vitamin D, the percentage of our population with vitamin D deficiency would likely be significantly lower. It is assumed that nearly 90% of the population in Serbia has a vitamin D deficiency, although there are no epidemiological studies to assess and confirm this. Calcium should be taken in the form of supplements in amounts of 1,000-1,500 mg per day since it is not achievable through food alone. This calcium dosage is completely safe and does not increase the risk of renal calculosis.

Conceptually, there are two forms of pharmacological therapy: antiresorptive treatment, aimed at inhibiting the breakdown and loss of previously formed bone tissue, and anabolic treatment, which aims to stimulate the production of new bone tissue (table 6). Ideally, treatment should be preventive with the aim of preventing the onset of fractures, and if fractures do occur, the goal of treatment is to prevent new fractures and to enable the patient to lead a better quality of life[12, 13].

Antiresorptive medications do not directly lead to an increase in bone mass but rather achieve it indirectly by inhibiting bone resorption. They cannot repair the microarchitecture of the bone or normalize bone mineral density[12, 13]. There are numerous therapeutic guidelines proposed by various international and national osteoporosis associations[13-15]. In most guidelines, antiresorptive agents are still considered the first-line treatment due to their effectiveness and significantly lower cost, especially in the case of bisphosphonates.

**Table 6.** Forms of pharmacological treatment of osteoporosis

| ANTI-RESORPTIVE TREATMENT | ANABOLIC TREATMENT |
|---|---|
| Bisphosphonates | Teriparatide and parathyroid hormone |
| Denosumab | Abaloparatide |
| Estrogen-gestagen preparations | Romosozumab |
| SERM (Selective Estrogen Receptor Modulator) | |

Bisphosphonates are synthetic analogs of calcium pyrophosphate that are absorbed onto the surface of bone trabeculae and can remain there for years until they are activated within the osteon, where they are located. They are phagocytosed by osteoclasts, blocking their enzymatic machinery in the cytoplasm and inducing their apoptosis, or programmed cell death. This reduces bone resorption by decreasing the number of osteoclasts and resorption *lacunae*. Due to the inseparable connection and communication between osteoclasts and osteoblasts, bisphosphonates significantly reduce the activity of osteoblasts, although they continue to produce bone tissue to some extent. The most potent bisphosphonates are amino bisphosphonates (alendronate, risedronate, ibandronate, and zoledronate), and the choice of medication depends on the anti-fracture efficacy of each agent in different parts of the skeleton, safety profile, cost, and convenience of administration. Their anti-fracture efficacy is presented in table 7. Another advantage of bisphosphonates is that discontinuation of treatment does not lead to a recurrence of bone loss, which is the case with non-bisphosphonate drugs where discontinuation can result in rebound bone loss[13, 14].

Estrogen-gestagen preparations, as well as selective estrogen receptor modulators (SERM) such as raloxifene, are not used as independent antiresorptive drugs for osteoporosis due to potential adverse effects associated with long-term use[13, 14]. Denosumab, a monoclonal antibody targeting RANKL (receptor activator of nuclear factor kappa-B ligand) that blocks the activation of osteoclast precursors, is administered as subcutaneous injections every 6 months. It is an effective medication for reducing fracture risk, but it comes with a high cost and has a reversible effect. After discontinuation, there is a rebound loss of bone mass, so

**Table 7.** Antifracture efficacy of certain drugs in osteoporosis

| DRUG | VERTEBRAL FRACTURES | NONVERTEBRAL FRACTURES | HIP FRACTURES |
|---|---|---|---|
| Raloxifene | √ | No evidence | No evidence |
| Alendronate | √ | √ | √ |
| Risedronate | √ | √ | √ |
| Ibandronate | √ | No evidence | No evidence |
| Denosumab | √ | √ | √ |
| Teriparatide | √ | √ | No evidence |


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bisphosphonate must be administered to maintain the achieved effect on bone mass[13, 14].

Teriparatide is a recombinant N-terminal fragment of parathyroid hormone consisting of 34 amino acids. Its use promotes the formation of new bone, improves microarchitecture, and increases bone mass and strength while reducing the incidence of vertebral and non-vertebral fractures. It is administered once daily via subcutaneous injection and improves both cortical and trabecular bone structure after 24 months. However, its use is limited to a two-year treatment period[13, 14]. Intact parathyroid hormone is also used in the treatment of osteoporosis, but it is expensive and unavailable in Serbia. Abaloparatide, a synthetic analog of a human peptide related to PTH, is a more potent agent than teriparatide[16, 17], but it is not available in Serbia. Romosozumab, a monoclonal antibody targeting sclerostin as an inhibitor of osteoblastic activity, is also a powerful anabolic agent but potentially carries adverse effects such as cardiovascular and cerebrovascular events[18, 19].

Finally, there is the option of combined treatment with sequential administration of specific medications[20]. It has been shown that the most effective approach is to start with anabolic agents followed by antiresorptive drugs. Therefore, after treatment with teriparatide, the subsequent use of bisphosphonates is necessary to maintain the achieved gain in bone mass. However, the regulations of the Republic Fund of Health Insurance in Serbia do not currently allow for this treatment approach.

No form of therapy, whether antiresorptive or anabolic, can fully restore bone loss in osteoporosis, and treatment should not be limited by arbitrary periods for which there is no evidence of safety for patients. There have been attempts to introduce the concept of a "drug holiday" (temporary interruption of antiresorptive/bisphosphonate treatment) into modern osteoporosis treatment. However, numerous retrospective and prospective studies have shown that discontinuing treatment increases the risk of new clinical fractures by 20-40%[14]. In other words, the risk of new vertebral fractures is approximately doubled, and the concept of a "drug holiday" has practically been abandoned as a universal category in contemporary guidelines for antiresorptive treatment in osteoporosis patients. After at least 3-5 years of bisphosphonate treatment, the efficacy of treatment and the achieved reduction in fracture risk should be evaluated, but this does not automatically imply treatment discontinuation[14]. There is no significant evidence that decisions regarding a change in treatment should be made before the end of a ten-year treatment period. Treatment for patients with osteoporosis, especially in severe cases, should be lifelong and involve the use of all therapeutic options. Many patients use bisphosphonates for decades, and there is no evidence to suggest that long-term use of these agents has adverse effects[13]. The occurrence of atypical femoral fractures or jaw osteonecrosis is not associated with the duration of bisphosphonate treatment[13, 14]. It is also important to consider the significant non-skeletal benefits of these drugs, particularly their anti-neoplastic effects. One of the recommendations in the latest European guidelines is to initiate treatment for women over the age of 65, even without the need for further evaluation (primarily bone density measurement), if a pathological fracture has occurred[14].

## Conclusion

Osteoporosis has reached epidemic proportions in the modern world, primarily due to the aging of the population. Despite significant advances in understanding the biology of bone tissue and the availability of numerous pharmacological agents, fractures remain the main cause of morbidity and mortality in patients with osteoporosis. It is imperative to introduce new therapeutic agents and allocate significantly greater healthcare resources to the prevention and treatment of this bone disorder.

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