

ABRIDGED ARGENTINE GUIDELINES FOR THE DIAGNOSIS, PREVENTION, AND TREATMENT OF OSTEOPOROSIS 2007

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Consensus of the Argentine Society for Osteoporosis (SAO) and the Argentine Association of Osteology and Mineral Metabolism (AAOMM).

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INTRODUCTION

In order to review and update the Guidelines prepared in 2004¹, the Argentine Association of Osteology and Mineral Metabolism and the Argentine Society for Osteoporosis have incorporated the latest advances in diagnosis, prevention, and treatment of osteoporosis.

All aspects of osteoporosis care and fracture prevention were reviewed and outlined as a series of recommendations.

We present an abridged English version of the Guidelines published in 2007 simultaneously in both societies' official journals: *Actualizaciones en Osteología* and *Revista Argentina de Osteología*.*

EPIDEMIOLOGY

It is necessary to establish guidelines for the diagnosis, prevention and treatment of osteoporosis, hoping to minimize the medical, social, and financial burden imposed by this disease on the public health system²⁻⁴.

Several studies carried out in Argentina using axial densitometry in two anatomical sites (lumbar spine, and proximal femur), reveal that out of four women aged 50 or above, one is normal, two have osteopenia, and one has osteoporosis in at least one skeletal region.

In our country there are six epidemiological studies of hip fracture incidence: three have been published in full⁵⁻⁷, while the remaining have been partially presented at medical meetings⁸⁻¹⁰. In average, there are 320 hip fractures per year per 100,000 women of more than 50 years of age, and 125 fractures per 100,000 men of the same age; the female/male ratio is 2.56.

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DEFINITION

Osteoporosis is a metabolic bone disease characterized by low bone mass and microarchitectural deterioration, leading to higher bone fragility and increased risk of fractures. The World Health Organization (WHO) defines osteoporotic fracture (or fragility fracture) as that caused by an injury representing a force or torsion exerted upon the bone, which would not suffice to fracture a normal bone.

Bone density is expressed in grams of mineral per area or volume, and is determined by the peak bone mass attained and the balance between gains and losses occurring later in life.

The diagnosis of osteoporosis continues to be based on a low bone mineral density (BMD). In a consensus meeting organized by the WHO, held in Geneva in 1994, a classification was made based on the comparison of the BMD value found in a given patient with the mean BMD of the normal young adult population of the same sex and ethnicity – postmenopausal caucasian women¹¹; see **Table 1**.

Table 1. Classification of BMD values, according to a Committee of Experts of the WHO.

Normal: > -1.0

Osteopenia : $< -1.0 / -2.5$

Osteoporosis: < -2.5

Severe osteoporosis: < -2.5 plus the presence of fracture

This classification is based on the *T*-score, which is the number of standard deviations above or below the mean BMD of the normal young adult population of the same sex studied with central DXA technique.

- In men older than 50 years the *T*-score is also considered, and the preceding WHO classification is applicable^{12,13}.
- In premenopausal women and in men younger than 50 years the *Z*-score is considered (relative to normal subjects of the same age and sex). Normal, > -2.0 ^{12,13}.
- In children both bone mineral content (BMC) and BMD are evaluated, considering the *Z*-score at the lumbar spine and whole body (the hip should not be measured except in situations when the two other areas cannot be evaluated). Normal, > -2.0 ^{12,13}.

These cut-off values do not have a biological significance; they were created to allow comparisons of osteoporosis prevalence in different countries and populations, and should not be taken as the sole criterion for taking therapeutic decisions.

TECHNIQUES FOR MEASURING BMD

For the time being there is no method that allows the measurement of bone resistance clinically. BMD is frequently used as a substitute measurement, since it can account for approximately 70% of bone resistance¹⁴.

Equipments used to measure BMD are classified according to a) the technique employed, or b) the anatomical region of the skeleton that can be evaluated¹⁵. There is central or peripheral DXA (*Dual energy X-ray Absorptiometry*), axial

QCT (*Quantitative Computerized Tomography*) or peripheral QCT (*pQCT*), ultrasound densitometry (*QUS*, *Quantitative Ultrasound*) of the tibia, the calcaneum, or the phalanges.

Advantages of peripheral equipments: lower cost, portability, lower dose of ionizing radiation (QUS does not irradiate the patient). Peripheral BMD is useful for evaluating the risk of fracture; it can be used to identify patients who should be further evaluated.

Limitations of peripheral equipments: lack of uniform criteria for the diagnosis of osteoporosis. A low value in a peripheral study must be confirmed with an axial BMD. Peripheral densitometry must not be used to monitor the response to treatment, since the peripheral skeleton generally responds with small increments in BMD, which overlap with the precision error of the equipments¹⁵.

INDICATIONS FOR BMD

Bone densitometry should be carried out in:

- Women over 65 years¹⁶, and women aged below 65 who present at least one risk factor (see **Table 2**)
- Adults with a fragility fracture, adults with diseases or conditions associated to low bone mass or rapid bone loss
- Men aged over 70 years
- In all patients who need to be treated; also it is convenient in the follow-up of treated patients to monitor results, with periodic measurements depending of the case^{13,17}.

It should be noted that several studies demonstrate the presence of osteopenia (up to 50%) and osteoporosis (up to 30%) among patients without any risk factor.¹⁸⁻²³

Sites for DXA studies:

Antero-posterior (AP) spine and femur, in all patients²⁴⁻²⁶.

Measurement of the non-dominant forearm is indicated whenever AP spine and femur cannot be either studied or interpreted, in patients with primary hiperparathyroidism and in very obese subjects.

Regions of interest recommended for vertebral evaluation are L1-L4 in the AP spine, measuring all vertebrae, excluding only those affected by structural changes or artifacts²⁷. In our midst, and given the variations observed in the measurement of L1, this committee recommends measuring L2-L4.

The measurement of the lateral spine should not be used for diagnosis or follow-up²⁷.

In the proximal femur the regions of interest are the femoral neck, the trochanter or total hip; Ward's triangle should not be used for diagnosis^{12,28}.

BMD can be measured in both femurs, but there are not enough data to use the average *T*-score for diagnosis. Several recent studies, some of which were performed in Argentina, found a high percentage of subjects having up to 10% difference in BMD between sides, and for this reason it is advisable to include both proximal femurs in the initial evaluation. For diagnosis and follow-up the femur with the lower value should be chosen^{29,30}. The WHO classification for

the diagnosis of osteopenia and osteoporosis should not be used in peripheral measurements, except for 33% radius (also called radius 1/3). When there are measurements of more than one anatomical site, diagnosis should be based on the area with the lowest value.

Table 2. Risk factors to be considered for the indication of densitometry^{3,23,31-33}.

Personal history of fractures
Family history of fractures (1st degree relatives)
Associated diseases (see Table 3)
Early menopause (< 40 years) or surgical menopause (< 45 years)
Estrogen deficiency in the premenopause
Low body weight (Body Mass Index, in kg/m² < 20), or past history of eating disorders
Glucocorticoid use, or use of other drugs (see Table 4)
Smoking (> 10 cigarettes daily)
Organ transplantation
Primary or secondary amenorrhea
Prolonged immobilization
Low calcium intake

PREVENTION OF OSTEOPOROSIS

Low BMD does not cause specific symptoms. Only a full clinical history, directed to the identification of risk factors for low bone mass, may lead to the diagnosis of osteopenia or osteoporosis.

RISK FACTORS FOR OSTEOPOROSIS

Risk factors are shown in **Table 2**; the most important ones are described below:

Low body weight: Extreme thinness should cause suspicion of osteopenia. It is considered as a risk factor when BMI is 20 kg/m² or below. Past history of eating disorders is extremely important, since they usually have accompanying hypoenestrogenism and malabsorption of nutrients, capable of affecting bone health.

History of previous fracture after minimal trauma: Past history of fractures in the vertebrae or long bones practically doubles the risk of sustaining a new fracture.^{32,34}

Family History: Patients whose first-degree relatives have had fractures, have an increased risk of presenting osteoporosis.

Corticosteroids: The relative risk (RR) of a vertebral fracture is 5.2 with doses above 7.5 mg prednisone per day or its equivalent, whereas with lesser doses RR is < 5. However, daily doses as low as 2.5 mg prednisone increase the RR when treated subjects are compared to an untreated population. The increase in RR is independent of the dose and the duration of treatment, and progressively diminishes after the discontinuation of the glucocorticoid^{31,35-39}.

If the patient has any of the diseases shown in **Table 3**, or takes any of the medications listed in **Table 4**, he or she must be studied to rule out secondary osteoporosis. In these cases it is necessary to treat the primary disease.

Table 3. Diseases causing decreased bone mineral density^{31,33,40,41}.

Eating disorders
Osteomalacia
Hyperparathyroidism
Hyperthyroidism
Hypogonadism
Cushing's syndrome
Hyperprolactinemia with altered menstrual cycles
Chronic renal failure
Nephrolithiasis
Hypercalciuria
Chronic liver diseases (primary biliary cirrhosis, chronic hepatitis)
Malabsorption syndrome
Celiac disease
Gastrectomy; Bariatric surgery
Chronic inflammatory arthropathies
Multiple myeloma
Chronic hematological disorders
Hematological neoplasias
Diabetes mellitus, type 1
Osteogenesis imperfecta
Smoking; Alcohol abuse
Prolonged immobilization (more than 3 months)
Cancer
AIDS

Table 4. Drugs causing decreased bone mineral density.

Glucocorticoids at any dose
Thyroid hormone at TSH-suppressive doses
GnRH analogues
Antiandrogens
Aromatase inhibitors
Anticonvulsants
Anticoagulants
Furosemide
Thiazolidindiones⁴²
Proton pump inhibitors: ranitidine, omeprazole and similar drugs⁴³
Lithium⁴⁴

DIAGNOSTIC METHODS IN OSTEOPOROSIS

Radiology: AP and lateral radiographs of the dorsal and lumbar spine are an indispensable tool to diagnose vertebral deformities and other pathologies.

Densitometry: Skeletal areas to be evaluated are the lumbar spine (AP) and the proximal femur.

Laboratory: General and specific biochemical tests that will help in the differential diagnosis between primary and secondary osteoporosis.

Laboratory of mineral metabolism. It should include the following determinations: Serum calcium, phosphate, creatinine, magnesium, PTH, and 25-hydroxyvitamin D; tubular reabsorption of phosphate; urine calcium and magnesium.

Laboratory of bone remodeling. It indicates the dynamics of bone turnover^{45,46}. See **Table 5**.

Table 5. Laboratory studies in osteoporosis.

General tests:

Complete blood count; Sedimentation rate;
Blood urea nitrogen; Glycemia;
Serum protein electrophoresis;
Liver function tests; Urinalysis.

Specific tests*: Serum testosterone (total and/or bioavailable) in men;
Serum TSH; Serum and/or urine cortisol.

Laboratory of mineral metabolism:

Serum calcium; Serum phosphate; Serum creatinine; Serum magnesium;
Tubular reabsorption of phosphate;
Urine calcium; Urine creatinine; Urine magnesium;
Serum PTH*; Serum 25-hydroxyvitamin D*

Laboratory of bone remodeling**:

Bone formation: Alkaline phosphatase or its bone isoenzyme; Osteocalcin; PINP.

Bone resorption: Deoxypyridinoline; Collagen telopeptides (NTX, CTX)

Notes:

*According to clinical criteria, to aid in the differential diagnosis between primary and secondary osteoporosis.

** Generally, one formation marker and one resorption marker are requested.

RISK FACTORS FOR FRACTURES

There is agreement about the undisputable usefulness of BMD measurement in order to determine future risk of fracture^{47,48}.

GENERAL MEASURES FOR THE PREVENTION OF OSTEOPOROSIS AND FRACTURES

Dairy intake: From age 50 on, daily calcium intake should be 1,200 mg^{49,50}.

It is important to insure a good protein intake (1 g/kg.day), and adequate intake of other nutrients.

Physical activity: Exercise, through muscular activity, has a strong relationship with the risk of fracture⁵¹. It constitutes the mechanical stimulus for the optimal adaptation of mass, architecture, and skeletal structure to meet biomechanical requirements; besides, it reduces the risk of falls which can lead to fracture –approximately 5% of falls–⁵².

Sun exposure: Vitamin D is synthesized in the skin upon exposure to ultraviolet rays. Short exposures are indicated (around 15-20 minutes), avoiding the hours of peak sunlight. The “safe” serum level of 25-hydroxyvitamin D is 30 ng/ml or above⁵³.

PREVENTION OF FALLS

The propensity to fall is more related to non-vertebral fractures; it is usually associated to modifiable or correctable causes, such as those mentioned below^{54,55}.

- a) Sedatives, hypotensives, hypoglycemic agents
- b) Visual impairment
- c) Domestic obstacles for deambulation

d) Pets

Simple exercises can be taught to the elderly to improve equilibrium, and strength in the lower limbs.

Hip protectors: Hip protectors are external devices placed on the hip area, which can absorb the impact of falls and reduce the risk of fractures of the proximal femur⁵⁶⁻⁶³.

RECOMMENDATIONS FOR OSTEOPOROSIS TREATMENT AND THE PREVENTION OF FRACTURES

General considerations

The main goal of osteoporosis treatment is to reduce the incidence of fragility fractures. The assessment of the probability of these fractures is based on the evaluation of several risk factors identified in case-control and prospective epidemiological studies. Some of the risk factors are strongly related with biomechanical properties of the skeleton (i. e., BMD and structure), while others are related to the propensity to fall. Four of these factors, although inter-related, have independent predictive capacity, are applicable to the general population and to different types of fracture: age, personal history of fracture (vertebral or extravertebral), BMD, and hip fracture in a first-degree relative. The majority of the remaining factors are more related to the risk of hip fracture^{64,65}.

Recommendations for decision making before the indication of pharmacological treatment

Osteoporosis and its consequence –fracture– are multifactorial. Risk factors for osteoporotic fracture must not be considered independently, and they relate differently to different types of fracture⁶⁶. Medical interventions have been proven effective in fracture prevention.

Regarding BMD, *there is no evidence* of an absolute value of Z-score or T-score that indicates the need of treatment in individual cases; data that guide decisions of pharmacological intervention are based on population studies. The information provided by BMD must be combined with related risk factors, and also with knowledge about the effectiveness, inconveniences, side effects, and costs of the treatment that is being considered⁶⁷.

The following recommendations are based on the review of the main prospective trials specifically designed for evaluating the efficacy of different treatments to reduce the incidence of osteoporotic fractures. The evidences gathered from such trials are a necessary argument before choosing an intervention in daily clinical practice.

Therapeutic decisions are based on a balance between benefits and risks, which must be carefully considered in each particular case both by the physician and the patient.

Treatment should be started in:

- Postmenopausal women with prevalent osteoporotic fractures
- Postmenopausal women without previous fracture, with one or more risk factors (besides menopause), who have a T-score of -2.0 or below by DXA of an axial site (spine or hip)
- Postmenopausal women without previous fracture, without risk factors, who have a T-score of -2.5 or below by DXA of an axial site
- Men and premenopausal women with osteoporosis
- Patients receiving chronic corticosteroid therapy. Administration of 5 mg prednisone daily (or its equivalent) during more than three months should prompt densitometric evaluation. These patients must receive antiosteoporotic treatment at higher BMD values than those with postmenopausal osteoporosis. Treatment should be started with a T-score of -1.0 or below³⁹
- In subjects older than 80 years, some experts recommend starting treatment with Z-scores below -1.5

Pharmacological treatment options

Medications for the treatment of osteoporosis can be classified in three groups: a) anti-catabolic or anti-resorptive drugs⁶⁸, b) anabolic or bone-forming drugs⁶⁸, c) drugs with complex mechanisms.

Bisphosphonates

Oral bisphosphonates, especially alendronate, risedronate, and ibandronate are the first line of treatment in postmenopausal women with densitometric osteoporosis, particularly if they have prevalent fractures⁶⁹.

Alendronate and risedronate are indicated for the treatment of glucocorticoid-induced osteoporosis and osteoporosis in men⁷⁰. The use of bisphosphonates for the treatment of osteoporosis in premenopausal women, in the absence of secondary causes, cannot be recommended yet, although it can be considered.

These drugs must be administered with previous knowledge of renal function. There is no consensus on its administration to women of child-bearing age.

Alendronate at a dose of 10 mg daily (or 70 mg weekly), administered for 3 years, reduces the incidence of vertebral, hip, and wrist fractures roughly by 50% in patients with a previous vertebral fracture. Alendronate reduces the incidence of vertebral fractures by 48% along 4 years in patients without prevalent vertebral fractures⁷⁰⁻⁷³.

Risedronate at the dose of 5 mg daily (or 35 mg weekly), administered for 3 years, reduces the incidence of vertebral fractures by 48%, and that of non-vertebral fractures by 33% in patients with a previous vertebral fracture⁷⁴. Although in the elderly population an inverse relationship between BMD and the risk of hip fracture is well established, risedronate did not reduce the incidence of this type of fracture in patients older than 80 years not selected on the basis of their BMD⁷⁵.

Ibandronate p.o. at the dose of 2.5 mg daily (or 20 mg intermittent –every other day up to 12 doses, repeating the cycle every 3 months–) reduced the incidence of vertebral fractures by 62%⁷⁶. Tablets containing 150 mg for monthly administration are available in the market. It is hoped that monthly dosing will improve adherence to treatment⁷⁷⁻⁷⁹.

Intravenous bisphosphonates (pamidronate, ibandronate, and zoledronate) must be considered in patients who are intolerant to oral bisphosphonates, or who cannot receive other medications. The dose of pamidronate is 30-60 mg every 3 months; it is administered diluted in 250 ml of an isotonic solution, which is dripped during 2-3 hours. Ibandronate can be indicated at a dose of 2 mg every 2 months, or 3 mg every 3 months, undiluted, in slow i. v. injection⁸⁰; the effects upon BMD and turnover markers are not inferior to those observed with the daily oral dose of 2.5 mg.

Zoledronate is the most potent of these compounds. It has been approved for the treatment of malignant hypercalcemia and Paget's disease of bone. Recently the results of its use in the treatment of osteoporosis have been published. The dose is 5 mg once a year. After 3 years it decreases the incidence of vertebral fractures by 70%, of hip fractures by 41%, and of non-vertebral fractures by 25%⁸¹. Besides, there is evidence of its efficacy

in the secondary prevention of fractures, when compared to placebo in a numerous group of patients who had recently suffered a hip fracture⁸².

Bisphosphonates accumulate in bone tissue and stay there during a very long time; recent doubts concerning the safety of chronic therapy with these drugs has been expressed. There are reports about cohorts of patients treated with alendronate during 10 years, without loss of its antifracture effect⁸³. On the other hand, the benefit of bisphosphonates is maintained after their interruption following 3-6 years of continued administration⁸⁴. In patients with low or moderate risk of fractures, discontinuation of treatment with a bisphosphonate can be considered after that period^{85,86}.

Calcitonin

Only one trial (PROOF study) has shown that nasal salmon calcitonin, at a daily dose of 200 IU, significantly reduces the rate of vertebral fractures. Nasal or parenteral calcitonin constitutes the first line of treatment of pain associated with acute vertebral collapse. A recent review of the PROOF trial confirmed its usefulness in the population of women aged 70 years or more: there were decreases of 55 and 50% in the RR of vertebral fractures in women aged 70 and 75 years, respectively⁸⁷.

Hormone Replacement Therapy

Hormone replacement therapy must be considered as a first line of treatment of post-menopausal osteoporosis in patients who have indications for its use. These indications include:

- Climacteric syndrome
- Atrophy of the genito-urinary tract
- Early or precocious menopause, spontaneous or surgical
- Gastrointestinal intolerance to bisphosphonates.

The study *Women's Health Initiative* (WHI), prospective, randomized and double-blinded, using conjugated equine estrogens 0.625 mg + medroxyprogesterone 2.5 mg p. o., continuously during 5 years, in a population of women aged 50-79 years, including patients with past history of ACV, hypertension, coronary heart disease, deep vein thrombosis, etc., concluded that this therapy does not prevent cardiovascular disease, and increased the incidence of breast cancer in women aged over 65. The same study found a 34% reduction in the risk of clinical vertebral fractures and hip fractures, and a 23% reduction in the risk of other osteoporotic fractures⁸⁸.

Tibolone can be used in the treatment of the climacteric syndrome; some studies demonstrate increment of BMD, although its antifracture efficacy has not been demonstrated⁸⁹.

Selective Modulators of the Estrogen Receptor (SERMS)

Raloxifene is effective in the prevention of vertebral fractures in postmenopausal women with osteoporosis, and can be considered a first line treatment for that population. Administered at the dose of 60 mg per day during 3 years it reduces the risk of vertebral fractures by 30% in patients with a prevalent vertebral fracture, and by 55% in patients without fractures⁹⁰. The efficacy of raloxifene in the prevention of non-vertebral fractures has been demonstrated, in *post hoc* analysis, for patients with severe prevalent vertebral fractures; RR decreases by 47%⁹¹.

Fluoride

Fluoride (administered as sodium fluoride or sodium monofluorophosphate) amplifies anabolic signals at the osteoblast level, and can increase trabecular bone mass. There is no clear-cut demonstration of its antifracture effect⁹².

Recombinant parathormone

Subcutaneous PTH₁₋₃₄ (teriparatide) at the dose of 20 µg daily reduces the risk of vertebral fractures by 65%, and the risk of non-vertebral fragility fractures by 53% in patients with osteoporosis, after a treatment lasting in average 18 months^{93,94}.

Teriparatide can be considered for treating:

- Men and postmenopausal women with severe osteoporosis
- Women aged over 65 years with T -score < - 2.5 and prevalent vertebral fracture.

Since the cost of this medication is high, its use should be restricted to the treatment of more severely affected patients: more than one fragility fracture and very low BMD (T -score < -3.5). It can also be recommended to patients sustaining new fractures after two or more years of an adequate treatment with a bisphosphonate⁹⁵.

The duration of this treatment should not exceed two years. During the administration of teriparatide calcium intake must be kept around 1.5 g/day, with adequate supplements of vitamin D.

The combined use of teriparatide and bisphosphonates does not have additive or synergistic effects compared to the anabolic action of teriparatide monotherapy, although the indication of bisphosphonates can be considered after completing treatment with this hormone, to avoid a rapid fall in BMD⁹⁶⁻¹⁰⁰.

Strontium ranelate

It is a new anti-osteoporotic agent, orally administered at a dose of 2 g/day. It exerts its effect on bone through two main mechanisms: increasing bone formation and decreasing resorption, although the understanding of its complex effect on bone cells is not complete yet. After one year of treatment it is able to reduce the incidence of vertebral fractures by half compared to placebo; the antifracture effect is maintained along 3 years. Non-vertebral fractures diminish by 16%. In a group of elderly patients (older than 74) with a hip T -score lower than -3.0 there was a decrease in the incidence of hip fracture of 36%¹⁰¹⁻¹⁰³. Among women of 80 years or older the reduction in the incidence of vertebral fractures was 32%, and that of non-vertebral fractures 31%¹⁰⁴.

Calcium and vitamin D

Low serum levels of 25-hydroxyvitamin D are common in aging populations. The prevalence of low or insufficient levels of vitamin D is relatively high in the Argentinian urban population aged above 60 years¹⁰⁵. For postmenopausal women and men older than 50, a daily intake of at least 1,500 mg calcium and 800 IU (= 20 µg) vitamin D is recommended. Vitamin D₃ (cholecalciferol) should be used preferentially. The determination of serum vitamin D allows, if necessary, to increase the administered dose until an adequate level is reached – above 30 ng/ml¹⁰⁶.

This Consensus strongly recommends the administration of adequate supplements of vitamin D –besides an appropriate calcium intake– as an adjunct of any other anti-osteoporotic treatment.

Patients receiving glucocorticoids

All patients treated with glucocorticoids must receive calcium and vitamin D as primary prevention, after measuring 24-hour urinary calcium excretion. In patients of both sexes older than 65, and in those with prior fractures, it is recommended to start treatment with a bisphosphonate or other anti-osteoporotic drug, independently of the *T*-score value. In patients below age 65 who are going to receive corticosteroids for more than 3 months and present a *T*-score < -1.0 a bisphosphonate must be indicated^{37,39}. The use of bisphosphonates in premenopausal women is a matter of controversy.

ANTIFRACTURE EFFICACY OF AVAILABLE TREATMENTS

In general, the risk of **vertebral fractures** is reduced by 25-50% after 3 years of anti-resorptive treatment, and by 60-70% after 18-36 months of anabolic treatment¹⁰⁷. Protection against **hip fracture** has been demonstrated in primary analysis only for four drugs: alendronate⁷³, risedronate⁷⁵, zoledronate⁸¹, and HRT⁸⁸. Only four drugs were effective to prevent **non-vertebral fractures** in primary analysis: alendronate⁷³, risedronate⁷⁴, strontium ranelate¹⁰², and recombinant human parathyroid hormone –teriparatide⁹³. In these studies the reduction in the risk of **hip fracture** was 40-50%, and the risk of **other non-vertebral fractures** 20-50%. **Table 6** summarizes the effects on BMD and fracture rates of anti-osteoporotic treatments approved in Argentina.

Table 6: Treatment of osteoporosis - Summary of effects on BMD and fracture rate reduction; medications approved in the Argentine Republic.

(Numbers indicate the approximate percentage of fracture reduction)

| Drug: | THR | RLX | CT | ALN | RIS | IBN | ZOL | Sr | PTH₍₁₋₃₄₎ |
|----------------------------|------------|------------|-----------|------------|------------|------------|------------|-----------|-----------------------------|
| Lumbar BMD | + | + | + | + | + | + | + | + | + |
| Femoral BMD | + | + | + | + | + | + | + | + | + |
| Bone markers | - | - | - | - | - | - | - | + - | + |
| Vertebral fractures | 33 | 50 | 36 | 47 | 41 | 50 | 70 | 65 | 65 |
| Femoral fractures | 27 | = | = | 50 | 40-60 | = | 41 | 36* | = |
| Non-vert. fractures | = | 47** | = | 48 | 27 | 69*** | 25 | 16 | 53 |

HRT: hormonal replacement therapy. RLX: raloxifene. CT: calcitonin. ALN: alendronate. RIS: risedronate. IBN: ibandronate. ZOL: zoledronate. PTH₍₁₋₃₄₎: teriparatide. Sr: strontium ranelate.

+ Increase. - Decrease. = Without significant change.

(*) In patients older than 74 years and with femoral neck *T*-score < -3.0; TROPOS study, ref. 102.

(**) In patients with severe prevalent vertebral fractures; MORE study, ref. 91.

(***) In patients with femoral neck *T*-score < -3.0; BONE study, ref. 76.

Evaluation of treatment

The follow-up of an osteoporosis treatment is generally made by changes in axial DXA values. Medications can diminish the risk of fracture even without objective increments in BMD. A 70% reduction in resorption markers is associated with a 40% reduction in the risk of fracture, while a decrease of formation markers is associated to a 44% reduction in the risk of fracture, when using anti-resorptive treatments¹⁰⁸.

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