EDITORIAL ARTICLE

OSTEOPOROSIS IN THE OLDEST OLD: TIME TO STAND UP AND TO ACT

Turkish Journal of Geriatrics
2025; 28(1):1–7

DOI: 10.29400/tjgeri.2025.416

René RIZZOLI[1]
Thierry CHEVALLEY[1]

[1] Geneva University Hospitals, Service of Bone Diseases, Geneva, Switzerland

By the age of 50 years, the lifetime risk of sustaining a fracture is approximately 50% for women and 20% for men (1). For hip fracture, this risk is 23 and 7 % in women and men, respectively. These data are coming from a region with a particularly high longevity, indicating that such elevated lifetime fracture risk is a threat for many countries where life expectancy is growing and population aging. Since the median age for a hip fracture is above 80 years, 50 % of these fractures are occurring in the oldest olds (2). The term 'the oldest old' refers to the oldest subset of older adults and comprises a group of patients which may have substantial differences in pharmacokinetics and higher levels of co-morbidities and are often not included in pivotal randomised controlled trials. Chronological age cut-off values for this group vary, as the European Medicines Agency considers ≥85 years as 'oldest old', while the American Geriatrics Society and World Health Organisation set a chronological threshold at ≥80 years (3).

Fracture incidence varies according to type of fracture (4). There is an exponential increase in the incidence of fractures of the femoral neck and trochanter with increasing age (4). The incidence is much lower in men. In addition, there is variation in the distribution of incidence by age. With trochanteric fractures there is a fairly rapid increase from the age of 75 years, and, for fractures of the femoral neck, a more constant, almost linear increase in incidence from the age of 65 years (5). The exponential increase in trochanteric fractures continues in the 10th decade of life (those aged between 90-100 years). Fracture risk considerably varies according to the region (6). In addition, it also changes over time (7), with a decrease of secular trend for hip fracture in several places (8). Although Turkey was among the countries with low hip fracture rates in Europe, the incidence has increased markedly between 1989 and 2009 (9).

Correspondence

René RIZZOLI
Phone : +41223729950
e-mail : rene.rizzoli@unige.ch

Received : Jan 06, 2025
Accepted: Jan 06, 2025

Cite this article as:
Rizzoli R, Chevalley T. Osteoporosis in The Oldest Old: Time to Stand Up and to Act. Turkish Journal of Geriatrics 2025; 28(1):1–7. doi: 10.29400/tjgeri.2025.416

Fragility fracture is the clinical expression of the disease osteoporosis (2). Among the complications of osteoporosis, hip fracture represents the most dramatic event, in terms of morbidity, mortality and medical costs. Increased mortality has been consistently demonstrated after hip or vertebral fracture. For instance, hip fracture is associated with a 20% excess mortality within the first year after surgery (2, 10,11). Reduced survival cannot be attributed directly to the fracture, but to underlying cardiovascular or pulmonary diseases, which might become decompensated because of the fracture event. By the prolonged handicaps they cause, fractures are a major threat for the quality of life of the elderly and represent a significant cause of health expenses. By one year after hip fracture, close to 20% of the patients still require rehabilitation in hospital.

Osteoporosis is defined as a systemic skeletal disease characterized by low bone mass and micro-architectural deterioration of bone tissue, with a consequent increase in bone fragility and in susceptibility to fracture risk (12). The diagnosis of the disease relies on the quantitative assessment of areal bone mineral density (aBMD) at hip or spine, using dual energy x-ray absorptiometry (DXA), which represents an important determinant of bone strength and thereby of fracture risk. Depending on the experimental model, aBMD accounts for about two thirds of the variance of bone strength as determined *in vitro* on isolated bones (13), as aBMD integrates the size of the bone and its thickness, as well as the true volumetric density, all being determinants of bone strength.

The operational definition of osteoporosis is based on aBMD lower than the lower limit of normal range of young healthy women, as defined in a World Health Organisation (WHO) document (12). The operational definition of osteoporosis (endorsed by the WHO) is aBMD T-score (T-Score = [measured BMD – Young Adult Women aBMD] / Young Adult Women SD) of -2.5 or lower (i.e. at least 2.5 standard deviations below average bone mineral density of healthy young women), where aBMD is assessed by dual X-ray absorptiometry (DXA) at spine or hip (12). A women database is also applicable to men. Between -1.0 and -2.5 standard deviations corresponds to low bone mineral mass or osteopenia. An osteodensitometry-based diagnosis of osteoporosis together with a prevalent fragility fracture defines severe osteoporosis. Indications to treatment depend on the evaluation of fracture risk, which also integrates other clinical risk factors than osteoporosis densitometric diagnosis (12). Above the age of 65, osteoarthritis makes the measurement of lumbar spine BMD is less reliable for diagnosis purpose. Femoral neck BMD appears to be a good predictor of fracture of the proximal femur (14), though up to 50% of hip fracture could occur in patients with aBMD above -2.5 T-score (15), emphasizing the need to take into consideration prevalent fracture (16, 17), as well as clinical risk factors in fracture risk assessment. Recently, it was also reported that after adjusting for age, sex, and site of initial fracture, an increasing number of frailty deficit items was associated with increased risk of subsequent fracture (18).

Moderate or severe vertebral fractures, even when asymptomatic, are strong risk factors for subsequent fracture (16). Vertebral fracture assessment should therefore be considered in high-risk individuals, using either lateral lumbar and thoracic spine radiographs or lateral spine DXA imaging. Vertebral fracture assessment should be considered in postmenopausal women if there is a history of ≥4cm height loss, kyphosis, recent or current long-term oral glucocorticoid therapy, as well as in individuals with a history of non-vertebral fracture (12).

Of the various risk assessment tools developed in osteoporosis, the FRAX® model is the most widely used (12). FRAX® is a computer based algorithm (http://www.shef.ac.uk/FRAX) that integrates age, sex, clinical risk factors such as prevalent

fracture, parental hip fracture, current smoking, ≥3 alcoholic drinks/day, rheumatoid arthritis, current corticosteroid use, body mass index (BMI) <20 kg/m^2, or secondary osteoporosis, and calculates the 10-year probability of a major osteoporotic fracture (hip, clinical spine, humerus or wrist fracture) and the 10-year probability of hip fracture, but is also capable of predicting asymptomatic vertebral fractures. It is calibrated for local fracture incidence and mortality. Assessment of fall risk predictors should be one of the major pillars in the physical evaluation of osteoporotic patients as recently reported in a Fracture Liaison Service of Turkey (19).

In addition to the risk factors included in the FRAX tool, malnutrition and particularly protein-energy malnutrition is a risk factor for osteoporosis, sarcopenia and frailty (20). In addition, malnutrition impairs the rehabilitation after fracture, leading to higher risk of medical complications and prolonged hospital stays (2). Protein-energy malnutrition is as high as 4-10% in oldest olds living at home, 15-38% in those in institutional care, and 30-70% in hospitalized older patients (21). Patients who have recovered from a major fracture are significantly more likely to fall. Intrinsic risk factors for falls include gait deficits, dizziness and orthostasis, visual impairment, depression, functional and cognitive impairment, low body mass index, urinary incontinence, chronic musculoskeletal pain, some drugs and age 80 years and older.

A diagnosis threshold as determined by aBMD, should not be automatically translated into a therapeutic threshold. Other factors such as those included in the FRAX tool, bone turnover level or treatment cost/benefits, should be considered in the treatment decision (12). Thus, the risk of fracture for an individual is related to BMD and to a series a number of factors independent from BMD. For instance, the same T-Score has a different significance at different ages. For any BMD, fracture risk is much higher in the oldest olds than in the young (12). The objective of the risk estimation is to identify the individuals at higher fracture risk, and to provide treatment accordingly, to reduce the risk of fracture. However, given the above epidemiology which emphasises the predilection for fractures in the oldest old, there is recognised undertreatment for those requiring anti-osteoporosis medication in this population (22). Many people at high risk of fracture receive no treatment or highly inadequate treatment (12). There is now sufficient evidence of the short-term benefits of treatment and of the long-term safety profile of anti-osteoporosis treatments particularly in the oldest old population (20). Many older people are under-nourished and vitamin D deficient. These are situations that should be easily improved. In order to promote awareness and encourage proactive treatment in high-risk patients, the *Capture the Fracture Campaign* of the International Osteoporosis Foundation and a wide implementation of fracture liaison services (23) to strengthen secondary fracture prevention should be strongly advocated (24). Since its launch in 2013 and as of November 15th, 2024, the Capture the Fracture® program (https://www.capturethefracture.org) has welcomed 1'043 FLS, spread across 60 countries and 6 continents, which constitutes a very important network across the world. The inclusion of patients with a recent fracture in such as pathway is associated with a decreased fracture risk and a lower mortality (25, 26), this with a favorable cost-effectiveness ratio (27-29).

Sufficient levels of vitamin D are a prerequisite for the efficacy of anti-osteoporosis medications as all studies on these agents have been conducted in calcium and vitamin D-supplemented patients. The recommendation of a dose of 800 IU/day (20µg/day) in older adults (>70 years) has been adopted by most European guidelines, as well as the International Osteoporosis Foundation (IOF) and the Institute of Medicine (IOM) and was also advised in ESCEO consensus paper (30). There is no strong necessity to systematically measure circulating levels of 25(OH) D in older patients with suspected high fracture

risk since the cost of testing far exceeds that of supplementation. Vitamin D supplementation should precede any anti-osteoporosis therapy. Overall, it can be concluded that (31) 1-Calcium and vitamin D supplementation may lead to a modest reduction in fracture risk, although population-level intervention has not been shown to be an effective public health strategy; 2-Supplementation with calcium alone does not reduce fracture risk; 3-Side effects of calcium supplementation include renal stones and gastrointestinal symptoms; 4-Vitamin D supplementation, rather than calcium, may reduce falls risk; 5-Increased cardiovascular risk consequent to calcium supplementation is not convincingly supported by current evidence, particularly if calcium is of dietary origin; 6-Calcium and vitamin D supplementation is recommended for patients at high risk of calcium and vitamin D insufficiency, and in those who are receiving treatment for osteoporosis.

Correction of protein insufficiency can lead to a rapid normalisation of IGF-I levels in frail older adults and in patients with a recent hip fracture (20). In view of the impaired protein assimilation of older individuals, the RDA (0.8 g/ kg body weight) should be increased to 1.0 or 1.2 g/kg per day in the older age group without adverse event (32, 33). Dairy products are a source of both protein and calcium, since one litre of milk provides 32 g of protein and 1,200 mg of calcium. Dairy products, some being fortified with calcium or vitamin D, decrease circulating PTH, increase IGF-I, and decrease bone resorption markers (34). Dairy products are associated with higher bone strength (35). Higher dairy products consumption, particularly fermented dairy products is associated with a lower hip fracture risk (34, 36).

Anti-osteoporosis drugs are either anti-resorbers or stimulators of bone formation. The efficacy of the available anti-osteoporosis agents in increasing bone strength and reducing osteoporotic fracture risk is well established thanks to randomized placebo-controlled trials with fracture incidence as primary outcome (2, 12). Reduction of fracture risk in patients with osteoporosis is as high as 50-70% for vertebral fractures (75-96% for multiple vertebral fractures) and 20-35% for non-vertebral fractures, as well as 40-50% for hip fractures with some drugs (37). Moreover, osteoporosis medication does not lose its efficacy among frail adults (38). There is a large variety of regimens with oral, Intravenous or subcutaneous administration, and daily, weekly, monthly, 3-monthly, 6-monthly or yearly schedules.

Agents that have been approved for the treatment of osteoporosis in postmenopausal women include selective estrogen receptor modulators (SERMs), bisphosphonates (alendronate, risedronate, zoledronic acid and ibandronate), denosumab as antiresorbers, and teriparatide, the PTH-related protein analog abaloparatide and the monoclonal antibody against sclerostin romosozumab as bone formation stimulators (2, 39).

Anti-osteoporosis treatments are frequently under-prescribed, even in patients who have sustained an osteoporotic fracture and are at increased risk of a subsequent fracture (22). Clinicians may be reluctant to prescribe treatment because of doubts they might have over the effectiveness of treatment in a short period of time in patients with a limited life expectancy. Clinically significant benefits in terms of fracture reduction have been demonstrated within the first year of treatment (20). Thus, even in an oldest old patient population, treatment with an anti-osteoporosis agent is worth to be introduced, because of an early onset of fracture risk reduction. Over the long-term, anti-osteoporosis treatments seem to maintain effectiveness and remain safe (2). For patients at very high risk of fracture or at imminent risk, a bone formation stimulator followed by an antiresorber is an efficacious option in terms of rapidity of action and magnitude of the fracture risk reduction (39). Various guidelines recommend

treatment re-evaluation every 3 years for parenteral bisphosphonate administration and 5 years for oral formulations (40).

The risk of osteoporotic fractures is a major healthcare concern. The impact of a major fracture on patients' lives is immense, often leading to frailty and dependence. The costs borne by society are also significant, both in terms of immediate care and rehabilitation, and possible dependence over the longer term. Pharmaceutical anti-osteoporosis treatments are generally cost-effective, and even cost-saving in the oldest old (41). When the costs threshold for one Quality-adjusted Life-Year (QALY) was set at twice the gross domestic product per capita and a first-line treatment with alendronate (original molecule) was evaluated, treatment was cost effective in women having a 10-year risk for a major osteoporotic fracture as low as 13.8% or more, whereas for men the risk estimate should exceed 15% (41).

In summary, osteoporosis increases the risk of fractures, which are associated with increased mortality and altered quality of life. Patients with prevalent fracture are at high risk to sustain another one. Optimal protein and calcium intakes, and vitamin D supplies, together with regular weight bearing physical exercise are the corner stones of fracture prevention. Evidence for anti-fracture efficacy of pharmacological interventions relies on results from randomised controlled trials in postmenopausal women with fractures as the primary outcome. Treatments with bone resorption inhibitors, like bisphosphonates or denosumab, and bone formation stimulator like teriparatide, abaloparatide or romosozumab reduce vertebral and non-vertebral fracture risk. A reduction in vertebral fracture risk can already be detected within a year after starting therapy, justifying to undertake treatments even in the oldest olds.

The International Osteoporosis Foundation has for vision of its action a world without fragility fracture in which healthy mobility is a reality for all.

Take home messages for osteoporosis management in the oldest old

- Correct or prevent vitamin D insufficiency (800-1000 IU/d)
- Ensure dietary calcium intake ≥ 1000 mg /d
- Ensure adequate dietary protein intake ≥ 1.2 g/kg body weight x d
- Promote tailored weight-bearing physical exercise
- Treat any disease that might cause bone loss
- Reduce the risk of falls
- Prescribe pharmaceutical treatment when indicated by risk assessment
- Follow-up patients to ensure compliance and persistence
- Re-evaluate therapeutic options after 3 or 5 years

REFERENCES

1. Lippuner K, Johansson H, Kanis JA, Rizzoli R. Remaining lifetime and absolute 10-year probabilities of osteoporotic fracture in Swiss men and women. Osteoporos Int 2009;20(7):1131-40. doi: 10.1007/s00198-008-0779-8
2. Rizzoli R. Postmenopausal osteoporosis: Assessment and management. Best Pract Res Clin Endocrinol Metab 2018;32(5):739-57. doi: 10.1016/j.beem.2018.09.005
3. Escourrou E, Durrieu F, Chicoulaa B, et al. Cognitive, functional, physical, and nutritional status of the oldest old encountered in primary care: a systematic review. BMC Fam Pract 2020;21(1):58. doi: 10.1186/s12875-020-01128-7
4. Sambrook P, Cooper C. Osteoporosis. Lancet 2006;367(9527):2010-8. doi: 10.1016/s0140-6736(06)68891-0
5. Hagino H, Furukawa K, Fujiwara S, et al. Recent trends in the incidence and lifetime risk of hip fracture in Tottori, Japan. Osteoporos Int 2009;20(4):543-8. doi: 10.1007/s00198-008-0685-0

6. Kanis JA, Odén A, McCloskey EV, Johansson H, Wahl DA, Cooper C. A systematic review of hip fracture incidence and probability of fracture worldwide. Osteoporos Int 2012;23(9):2239-56. doi: 10.1007/s00198-012-1964-3

7. Lippuner K, Kyuchukova M, Schwab P, Rizzoli R. Differences in femoral fracture localizations in men and women in Switzerland between 1998 and 2021-reversal of the secular trend? Osteoporos Int 2024;35(5):893-902. doi: 10.1007/s00198-024-07016-5

8. Chevalley T, Guilley E, Herrmann FR, Hoffmeyer P, Rapin CH, Rizzoli R. Incidence of hip fracture over a 10-year period (1991-2000): reversal of a secular trend. Bone 2007;40(5):1284-9. doi: 10.1016/j.bone.2006.12.063

9. Tuzun S, Eskiyurt N, Akarirmak U, et al. The impact of a FRAX-based intervention threshold in Turkey: the FRAX-TURK study. Arch Osteoporos 2012;7:229-35. doi: 10.1007/s11657-012-0101-4

10. Schurch MA, Rizzoli R, Mermillod B, Vasey H, Michel JP, Bonjour JP. A prospective study on socioeconomic aspects of fracture of the proximal femur. J Bone Miner Res 1996;11(12):1935-42. doi: 10.1002/jbmr.5650111215

11. Schurch MA, Rizzoli R, Mermillod B, Vasey H, Michel JP, Bonjour JP. A prospective study on socioeconomic aspects of fracture of the proximal femur. J Bone Miner Res 1996;11(12):1935-42

12. Kanis JA, Cooper C, Rizzoli R, Reginster JY. European guidance for the diagnosis and management of osteoporosis in postmenopausal women. Osteoporos Int 2019;30(1):3-44. doi: 10.1007/s00198-018-4704-5

13. Ammann P, Rizzoli R. Bone strength and its determinants. Osteoporos Int 2003;14 Suppl 3:S13-8. doi: 10.1007/s00198-002-1345-4

14. Johnell O, Kanis JA, Oden A, et al. Predictive value of BMD for hip and other fractures. J Bone Miner Res 2005;20(7):1185-94. doi: 10.1359/jbmr.050304

15. Wainwright SA, Marshall LM, Ensrud KE, et al. Hip fracture in women without osteoporosis. J Clin Endocrinol Metab 2005;90(5):2787-93. doi: 10.1210/jc.2004-1568

16. Klotzbuecher CM, Ross PD, Landsman PB, Abbott TA, 3rd, Berger M. Patients with prior fractures have an increased risk of future fractures: a summary of the literature and statistical synthesis. J Bone Miner Res 2000;15(4):721-39. doi: 10.1359/jbmr.2000.15.4.721

17. Kanis JA, Johnell O, De Laet C, et al. A meta-analysis of previous fracture and subsequent fracture risk. Bone 2004;35(2):375-82. doi: 10.1016/j.bone.2004.03.024

18. Mai H, Mc Evoy L, Wilson C, et al. Frailty and risk of subsequent fracture among older adults presenting to hospital with a minimal trauma fracture. Osteoporos Int 2023;34(2):399-404. doi: 10.1007/s00198-022-06630-5

19. Tuzun S, Akarirmak U, Kulaksiz B, et al. The association of FRAX with predictors of falls in the assessment of postmenopausal osteoporosis in Turkey: the fracture study of Turkey (FRACT study). Arch Osteoporos 2024;19(1):29. doi: 10.1007/s11657-024-01387-2

20. Rizzoli R, Branco J, Brandi ML, et al. Management of osteoporosis of the oldest old. Osteoporos Int 2014;25(11):2507-29. doi: 10.1007/s00198-014-2755-9

21. Trombetti A, Cheseaux J, Herrmann FR, Rizzoli R. A critical pathway for the management of elderly inpatients with malnutrition: effects on serum insulin-like growth factor-I. Eur J Clin Nutr 2013;67(11):1175-81. doi: 10.1038/ejcn.2013.166

22. Li Q, Yang J, Tang Q, et al. Age-dependent gender differences in the diagnosis and treatment of osteoporosis during hospitalization in patients with fragility fractures. BMC Geriatr 2023;23(1):728. doi: 10.1186/s12877-023-04430-y

23. Chevalley T, Hoffmeyer P, Bonjour JP, Rizzoli R. An osteoporosis clinical pathway for the medical management of patients with low-trauma fracture. Osteoporos Int 2002;13(6):450-5. doi: 10.1007/s001980200053

24. Akesson K, Marsh D, Mitchell PJ, et al. Capture the Fracture: a Best Practice Framework and global campaign to break the fragility fracture cycle. Osteoporos Int 2013;24(8):2135-52. doi: 10.1007/s00198-013-2348-z

25. Wu CH, Tu ST, Chang YF, et al. Fracture liaison services improve outcomes of patients with osteoporosis-related fractures: A systematic literature review and meta-analysis. Bone 2018;111:92-100. doi: 10.1016/j.bone.2018.03.018

26. Li N, Hiligsmann M, Boonen A, et al. The impact of fracture liaison services on subsequent fractures and mortality: a systematic literature review and meta-analysis. Osteoporos Int 2021;32(8):1517-1530. doi: 10.1007/s00198-021-05911-9

27. Wu CH, Kao IJ, Hung WC, et al. Economic impact and cost-effectiveness of fracture liaison services: a systematic review of the literature. Osteoporos Int 2018;29(6):1227-42. doi: 10.1007/s00198-018-4411-2

28. Li N, van den Bergh JP, Boonen A, Wyers CE, Bours SPG, Hiligsmann M. Cost-effectiveness analysis of fracture liaison services: a Markov model using Dutch real-world data. Osteoporos Int 2024;35(2):293-307. doi: 10.1007/s00198-023-06924-2

29. Xu L, Zhao T, Perry L, et al. Return on investment of fracture liaison services: a systematic review and analysis. Osteoporos Int 2024;35(6):951-69. doi: 10.1007/s00198-024-07027-2

30. Chevalley T, Brandi ML, Cashman KD, et al. Role of vitamin D supplementation in the management of musculoskeletal diseases: update from an European Society of Clinical and Economical Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Diseases (ESCEO) working group. Aging Clin Exp Res 2022;34(11):2603-23. doi: 10.1007/s40520-022-02279-6

31. Harvey NC, Biver E, Kaufman JM, et al. The role of calcium supplementation in healthy musculoskeletal ageing : An expert consensus meeting of the European Society for Clinical and Economic Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Diseases (ESCEO) and the International Foundation for Osteoporosis (IOF). Osteoporos Int 2017;28(2):447-462. doi: 10.1007/s00198-016-3773-6

32. Rizzoli R, Stevenson JC, Bauer JM, et al. The role of dietary protein and vitamin D in maintaining musculoskeletal health in postmenopausal women: a consensus statement from the European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis (ESCEO). Maturitas 2014;79(1):122-32. doi: 10.1016/j.maturitas.2014.07.005

33. Rizzoli R, Biver E, Bonjour JP, et al. Benefits and safety of dietary protein for bone health-an expert consensus paper endorsed by the European Society for Clinical and Economical Aspects of Osteopororosis, Osteoarthritis, and Musculoskeletal Diseases and by the International Osteoporosis Foundation. Osteoporos Int 2018;29(9):1933-48. doi: 10.1007/s00198-018-4534-5

34. Rizzoli R. Dairy products and bone health. Aging Clin Exp Res 2022;34(1):9-24. doi: 10.1007/s40520-021-01970-4

35. Durosier-Izart C, Biver E, Merminod F, et al. Peripheral skeleton bone strength is positively correlated with total and dairy protein intakes in healthy postmenopausal women. Am J Clin Nutr 2017;105(2):513-525. doi: 10.3945/ajcn.116.134676

36. Rizzoli R, Biver E. Effects of Fermented Milk Products on Bone. Calcif Tissue Int 2018;102(4):489-500. doi: 10.1007/s00223-017-0317-9

37. Saito T, Sterbenz JM, Malay S, Zhong L, MacEachern MP, Chung KC. Effectiveness of anti-osteoporotic drugs to prevent secondary fragility fractures: systematic review and meta-analysis. Osteoporos Int 2017;28(12):3289-300. doi: 10.1007/s00198-017-4175-0

38. Chattaris T, Oh G, Gouskova NA, Kim DH, Kiel DP, Berry SD. Osteoporosis Medications Prevent Subsequent Fracture in Frail Older Adults. J Bone Miner Res 2022;37(11):2103-11. doi: 10.1002/jbmr.4693

39. Veronese N, Briot K, Guañabens N, et al. Recommendations for the optimal use of bone forming agents in osteoporosis. Aging Clin Exp Res 2024;36(1):167. doi: 10.1007/s40520-024-02826-3

40. Adler RA, El-Hajj Fuleihan G, Bauer DC, et al. Managing Osteoporosis in Patients on Long-Term Bisphosphonate Treatment: Report of a Task Force of the American Society for Bone and Mineral Research. J Bone Miner Res 2016;31(10):1910. doi: 10.1002/jbmr.2918

41. Lippuner K, Johansson H, Borgström F, Kanis JA, Rizzoli R. Cost-effective intervention thresholds against osteoporotic fractures based on FRAX® in Switzerland. Osteoporos Int 2012;23(11):2579-89. doi: 10.1007/s00198-011-1869-6)