REVIEW



Executive summary of the European guidance for the diagnosis and management of osteoporosis in postmenopausal women

J. A. Kanis^{1,2} · C. Cooper^{3,4} · R. Rizzoli⁵ · J.-Y. Reginster^{6,7} on behalf of the Scientific Advisory Board of the European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis (ESCEO) and the Committees of Scientific Advisors and National Societies of the International Osteoporosis Foundation (IOF)

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Abstract

A guidance on the assessment and treatment of postmenopausal women at risk from fractures due to osteoporosis was recently published in Osteoporosis International as a joint effort of the International Osteoporosis Foundation and European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis (Kanis et al. in Osteoporos Int https://doi.org/10.1007/s00198-018-4704-5, 2018). This manuscript updates the previous guidelines document, published in 2013 (Kanis et al. in Osteoporos Int 24:23–57, 2013) and is written in a European perspective. The present article reports and summarizes the main recommendations included in this 2018 guidance document.

Keywords Bone mineral density \cdot Diagnosis of osteoporosis \cdot Fracture risk assessment \cdot FRAX \cdot Health economics \cdot Treatment of osteoporosis

Summary of Main Recommendations [1, 2]

Diagnosis of Osteoporosis (Fig. 1)

 The operational definition of osteoporosis is based on the T-score for BMD assessed by DXA at the femoral

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- ☒ R. RizzoliRene.Rizzoli@unige.ch
- Centre for Metabolic Bone Diseases, University of Sheffield, University of Sheffield Medical School, Sheffield, UK
- Mary McKillop Health Institute, Australian Catholic University, Melbourne, Australia
- MRC Lifecourse Epidemiology Unit, University of Southampton, Southampton, UK

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- neck or spine and is defined as a value for BMD 2.5 SD or more below the young female adult mean.
- 2. For clinical purposes, other sites and techniques can be used for diagnosis.
- 3. Low bone mass (osteopenia) should not be considered a disease category but is intended solely for purpose of epidemiological description.

Risk Factors for Fragility Fractures

- Several factors contribute significantly to fracture risk over and above that provided by bone mineral density measurements. These include age, sex, low body mass index, previous fragility fracture, parental history of hip fracture, glucocorticoid treatment, current smoking,
- NIHR Musculoskeletal Biomedical Research Unit, University of Oxford, Oxford, UK
- Service of Bone Diseases, Faculty of Medicine of Geneva, Geneva University Hospitals, 1211 Geneva 14, Switzerland
- Prince Mutaib Chair for Biomarkers, College of Science, King Saud University, Riyadh, Saudi Arabia
- Department of Public Health, Epidemiology and Health Economics, University of Liège, Liège, Belgium



Fig. 1 Algorithm for the diagnosis and management of osteoporosis in postmenopausal women

Osteoporosis Diagnosis and Management

Diagnosis

- DXA-based BMD at spine or hip
- ▶ T-score s -2.5

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Fracture risk assessment

- Country (region)-specific FRAX[™] fracture probability, modulated by BMD, TBS, glucocorticoid therapy, fall history, type 2 diabetes, hip axis length
- Vertebral fracture (VFA or X-ray if height loss, hyperkyphosis)

Major Risk Factors for Fragility Fractures

- ▶ Age
- ▶ Sex
- ▶ Low BMI
- Prior fragility fracture
- ▶ Parental hip fracture history
- ▶ Height loss (> 4cm)
- Secondary osteoporosis
- ▶ Glucocorticoid therapy
- Excessive alcohol and/or smoking

fic FRAX™ Additional information

- ▶ Bone turnover markers
- Renal function and blood cell count
- Secondary osteoporosis (rheumatoid arthritis, hyperthyroidism, primary hyperparathyroidism, hypogonadism, diabetes, inflammatory bowel diseases, aromatase inhibitora, anoresia nervosa, organ tranplantation, prolonged immobility, COPO, HIV)

Lifestyle

- Nutrition: calcium 800-1000 mg/day, protein ≥ 1g/kg BW/ day
- ▶ Vitamin D: 800 IU/day
- Daily weight-bearing physical activity
- Fall prevention measures

Pharmacological treatment

a. Intervention threshold

- ▶ FRAX* Score for major osteoporotic fractures (or hip fracture) ≥ risk equivalent to that associated with a prevalent fragility fracture
- Fragility spine or hip fracture (role of Fracture Liaison Service)
- Intervention type (selection based on osteoporosis severity, patient preference and regional drug reimbursement policy)
- ▶ Oral bisphosphonates (gastro-resistant formulation may increase adherence)
- Intravenous bisphosphonates
- ▶ Denosumab
- Menopausal Hormone Therapy, raloxifene, bazedoxifene
- Teriparatide (if high fracture risk or imminent risk)
- Local osteo-enhancement procedure (if increased hip fracture risk)

Follow-up

- ▶ Assess for compliance and/or side effects
- ▶ Bone turnover markers to verify compliance to bone resorption inhibitors (after 3-6 months)
- > Consider continuing or changing treatment:
 - . After 3 years for iv or 5 years for oral bisphosphonates
 - . If incident fracture
 - . Low risk patients: possible discontinuation for 2 years (reconsider yearly)
 - . High risk patients: continue treatment
- Denosumab discontinuation may be associated with vertebral (multiple) fractures, consider then bisphosphonates for 1-2 years



- alcohol intake of 3 or more units daily, and causes of secondary osteoporosis.
- 2. Additional risk factors that are of use in case finding include height loss (> 4 cm) and thoracic kyphosis.
- Bone markers (serum procollagen type I N propeptide (s-PINP) and serum C-terminal cross-linking telopeptide of type I collagen (s-CTX) as markers of bone formation and bone resorption, respectively) have some prognostic significance for fracture in situations where BMD is unavailable.

Assessment of Fracture Risk

- 1. Country-specific FRAX® should be used to assess fracture probability in postmenopausal women who have risk factors for fracture. In individuals at intermediate risk, bone mineral density (BMD) measurement should be performed using dual energy X-ray absorptiometry and FRAX fracture probability re-estimated.
- 2. Where BMD testing is unavailable, FRAX can be used without the input of BMD
- 3. Trabecular bone score (TBS) may be used as an adjunct to BMD measurements and FRAX.
- Interpretation of FRAX scores may be influenced by exposure to glucocorticoids, information on lumbar spine BMD, trabecular bone score, hip axis length, falls history, immigration status, and type 2 diabetes mellitus.
- Vertebral fracture assessment should be considered if there is a history of ≥4 cm height loss, kyphosis, recent or current long-term oral glucocorticoid therapy, or a BMD T-score ≤ -2.5.

Lifestyle and Dietary Measures

- Recommendations should include a daily calcium intake of between 800 and 1200 mg and sufficient dietary protein, ideally achieved through dairy products.
- 2. A daily dose of 800 IU cholecalciferol should be advised for postmenopausal women at increased risk of fracture.
- Calcium supplementation is appropriate if the dietary intake is below 800 mg/day, and vitamin D supplementation considered in patients at risk of, or showing evidence of, vitamin D insufficiency.
- 4. Regular weight-bearing exercise should be advised, tailored to the needs and abilities of the individual patient.
- A history of falls should be obtained in individuals at increased risk of fracture with further assessment and appropriate measures undertaken in those at increased risk.

Pharmacological Intervention in Postmenopausal Women

- 1. The oral bisphosphonates (alendronate, risedronate and ibandronate) may be used as initial treatments in the majority of cases. In women intolerant to oral bisphosphonates (or in those for whom they are contraindicated), intravenous bisphosphonates or denosumab provide the most appropriate alternatives, with raloxifene, or menopause hormone therapy as additional options. Teriparatide is preferentially recommended for patients at high risk of fracture.
- 2. Treatments should be reviewed after 3–5 years treatment with bisphosphonate. Fracture risk should be reassessed after a new fracture, regardless of when it occurs. The risk of new clinical and vertebral fractures increases in patients who stop treatment.
- Withdrawal of denosumab therapy is associated with a rebound in vertebral fracture rate. Bisphosphonate therapy can be considered after discontinuation of denosumab.
- 4. There is little evidence to guide decision-making beyond 10 years of treatment and management options in such patients should be considered on an individual basis.

Intervention Thresholds for Pharmacological Intervention

- The thresholds recommended for decision-making are based on probabilities of major osteoporotic and hip fracture derived from FRAX. These vary in different healthcare systems with variation in "willingness to pay".
- Women aged over 65 years with a prior fragility fracture can be considered for treatment without the need for further assessment; BMD measurement may be felt more appropriate in younger postmenopausal women.
- Age-dependent intervention thresholds provide clinically appropriate and equitable access to treatment and have been shown to be cost-effective.

Systems of Care

- 1. The utility of age-dependent FRAX thresholds in population screening approach has recently been validated as feasible, effective, and health economically viable.
- Coordinator-based fracture liaison services (FLS) should be used to systematically identify men and women with fragility fracture. Their effectiveness and cost-effectiveness have been established recently.



Compliance with ethical standards

Conflict of interest JAK reports grants from Amgen, Eli Lilly and Radius Health; non-financial support from Medimaps, and Asahi; and other support from AgNovos. JAK is the architect of FRAX® but has no financial interest. CC reports personal fees from Alliance for Better Bone Health,Amgen, Eli Lilly, GSK,Medtronic,Merck, Novartis, Pfizer, Roche, Servier, Takeda and UCB. RR has received consulting fees or advisory board fees from Radius Health, Labatec, Danone, Nestlé, CNIEL and Sandoz. J-YR has received advisory board or consulting fees from IBSA-Genévrier, Pierre Fabre, Radius Health, TEVA and Mylan; and lecture fees from Anovos, IBSA-Genévrier, Mylan, CNIEL, Dairy Research Council (DRC) and Theramex; and institutional grant support from IBSA-Genévrier, Mylan, CNIEL and Radius Health.

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