



# Diagnosis and management of osteoporosis in postmenopausal women in Gulf Cooperation Council (GCC) countries: consensus statement of the GCC countries' osteoporosis societies under the auspices of the European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis (ESCEO)

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## Abstract

**Summary** A consensus platform is provided by the experts of the Gulf Cooperation Council (GCC) countries' respective osteoporosis societies, on which specific guidelines can be developed further for regional use on the assessment and treatment of postmenopausal women at risk from fractures due to osteoporosis.

**Introduction** Guidance is provided in a Gulf Cooperation Council (GCC) country setting on the assessment and treatment of postmenopausal women at risk from fractures due to osteoporosis, which is an adaptation of the European guidance by Kanis et al., jointly published by the International Osteoporosis Foundation and the European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis (ESCEO). The respective osteoporosis societies of the Gulf Cooperation Council (GCC) countries assembled for a unifying consensus on the diagnosis and management of osteoporosis in postmenopausal women for the region.

**Methods** The Chair for Biomarkers of Chronic Diseases (CBCD) in King Saud University (KSU), Riyadh, Kingdom of Saudi Arabia (KSA), in cooperation with the Saudi Osteoporosis Society (SOS), hosted regional experts and respective leaders from different GCC osteoporosis societies, together with an adviser from the ESCEO. An assembly of experts representing the different osteoporosis societies from Saudi Arabia, the UAE, Bahrain, Oman, and Kuwait gathered on February 15–16, 2019 in Riyadh, KSA for the formulation of a general osteoporosis consensus for the region.

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**Results** The following areas were covered: diagnosis of osteoporosis and assessment of fracture risk; general and pharmacological management of osteoporosis; and hip fractures, vitamin D, recommendation on which FRAX tool to follow, and the importance of country-specific FRAX® and fracture liaison services for secondary fracture prevention.

**Conclusions** A platform is provided on which specific guidelines can be developed for regional use in GCC.

**Keywords** Osteoporosis · Consensus · Gulf Cooperation Council · Management

## Introduction

Osteoporosis is a skeletal disorder described as a decline in bone density or quality leading to reduced mechanical strength and increased propensity to fracture [1]. It is more common in the elderly, with postmenopausal osteoporosis and age-related osteoporosis considered the most common forms seen in clinical practice [1]. As a major global threat to healthy aging, countries with large populations of senior citizens are theoretically anticipated to carry the biggest burden of osteoporosis, but this may not be entirely true since worldwide variations have been reported, owing to issues in definition and diagnosis secondary to the systemic nature of osteoporosis [2]. A more accurate way to gauge prevalence differences amongst nations is the incidence of osteoporotic fracture rates. Currently, North America, Europe, and Oceania have the highest rates of hip fracture globally, but shifting demographics over the next decades indicate a major surge and eventual dominance of Africa, Asia, and Latin America, in the prevalence of age-related fracture and high fracture risk probability [3, 4]. Hence, it makes sense that major guidelines and guidance for the prevention and management of osteoporosis for global adoption are framed by western experts [5–7], since the bulk of the osteoporosis burden are currently on their side. Nevertheless, in preparation for the already ongoing and projected significant impact of osteoporosis amongst developing regions, these adopted guidelines should be tailored accordingly to suit the regional needs, among which is the Middle Eastern region.

In 2017, major osteoporosis and rheumatology societies representing several countries from the Middle East and North African (MENA) region, collectively known as the Pan Arab Osteoporosis Society (PAOS), published the most recent guidelines for osteoporosis management [8]. The PAOS guideline was a unified recommendation for healthcare providers in their approach to screening, diagnosis, and treatment of osteoporosis within the MENA region [8]. Prior to this guideline, regional and country-specific guidelines are already in place within MENA [9], including guidelines from select Gulf Cooperation Council (GCC) countries, the Saudi Osteoporosis Guidelines published in 2015 [10], an economic and political union of Saudi Arabia, Kuwait, the UAE, Qatar, Bahrain, and Oman. While differences in management are mostly due to customized approach per country, the approach to osteoporosis management

also does not have a consistent pattern due to differences in resources, access to diagnostics and medications, and physicians' perceptions and practices [11, 12]. The scope of the present position paper is to update knowledge regarding the assessment of osteoporosis and available therapeutic interventions, specifically within GCC, for implementation by the GCC osteoporosis societies and its allied healthcare professionals. The paper also identifies several issues that were not given due highlight from past regional guidelines. The recommendations in this position statement were endorsed by the Scientific Advisory Board of the European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis (ESCEO) and the Committee of Scientific Advisors and the Committee of National Societies of the International Osteoporosis Foundation (IOF).

## GCC task force

The Chair for Biomarkers of Chronic Diseases (CBCD) in King Saud University (KSU), Riyadh, Saudi Arabia, in cooperation with the Saudi Osteoporosis Society (SOS), hosted regional experts and respective leaders from different GCC osteoporosis societies, together with an adviser from the ESCEO. The closed-door assembly of experts commenced on February 15–16, 2019 in Riyadh, KSA. Each regional expert was assigned a specific topic relevant to the formulation of consensus statement within the region. Timeframes and draft submissions were also discussed. A survey was also distributed amongst experts and colleagues from their respective societies to determine actual clinical presentations of patients with osteoporosis, real-time approach to management, and available resources at the tertiary and primary care levels.

## Diagnosis and screening of osteoporosis

Bone mineral density (BMD) is universally labeled as a unit of standard deviation (SD), as either *T* or *Z* score. The *T* score is defined as the number of SDs in which the patient's BMD varies from the expected mean value taken among the young and healthy Caucasian women. The *T* score is also the unit of choice for BMD upon which the operational definition of osteoporosis was created and is evaluated at the femoral neck, defined as a value for  $\geq 2.5$  SD lower than the young female

adult mean [5]. The International Society for Clinical Densitometry (ISCD) and the American Association of Clinical Endocrinologists (AACE), in their recently updated official positions, advocate universal bone densitometry screening for all women > 65 years and women younger than 65 only if they have either osteoporosis risk factors, history of fragility fracture, or receiving osteoporosis medications [7, 13]. For men, universal osteoporosis screening has been recommended by ISCD only, and only for those aged 70 years and above and those with history of fragility fracture and/or considering therapy for osteoporosis [13].

Access to densitometry can be considered unrestricted especially in major government-run tertiary hospitals within GCC. The GCC countries are unique since their healthcare systems are universal, financed not by their citizens but by profits of natural resources [14]. In Saudi Arabia, country-specific guidelines recommend universal BMD assessment using dual-energy X-ray absorptiometry (DXA) for all women above 60 years [10]. In Kuwait, DXA screening has been recommended in all men and women above 50 years old only if they have either a history of fragility fracture or whose fracture risk assessment (FRAX) score is between the upper and lower assessment thresholds [11]. There are other alternative imaging techniques available within the region and they include peripheral DXA using quantitative ultrasound (QUS) which can be used as screening modality and quantitative computed tomography (QCT). DXA is still the gold standard for the diagnosis of osteoporosis.

The panel of experts recommend the use of Caucasian reference for osteoporosis diagnosis in the absence of local and regional data. The group also encourages more densitometry certification courses for GCC physicians and technicians, to minimize common errors encountered in their daily practice. Diagnosis of osteoporosis based on *T* score alone with no increased risk of fracture is not justifiable for therapy.

## Epidemiology of osteoporosis in GCC

Globally, projections indicate that the number of hip fractures in the elderly occurring annually will rise from 1.66 million in 1990 to 6.26 million by 2050, with western nations attributed to half of all hip fractures [4]. Assuming no change in the age- and sex-specific incidence, the number of hip fractures is estimated to approximately double to 2.6 million by the year 2025, and 4.5 million by the year 2050 [15].

In Saudi Arabia, the prevalence of osteoporosis among 830 apparently healthy postmenopausal Saudi women aged 50–89 years is 39.5% [16, 17]. In Saudi men older than 50 years, the prevalence of osteoporosis is 24.3% based on hip scan of 115 cases [18]. In 2007, the prevalence of osteoporosis among 429 Saudi men aged 50 and above was 23.5%, using either the lumbar spine or femoral neck for diagnosis [19]. Among 1980

apparently healthy Saudis aged 20–79, reference values using US/Northern European data when compared with Saudi reference data have been observed to underscore osteoporosis in Saudi men aged > 50 years (33.2% versus 37.8%) and overestimate in Saudi women (44.5% versus 28.2%) on the basis of *T* scores at the lumbar spine and femur [20]. Systematic review of 24 studies involving 5160 women aged 50–79 revealed that the prevalence of osteoporosis was 34% while 36.6% had osteopenia. In Saudi men ( $N = 822$ ), osteopenia was higher at 46.3% and osteoporosis at 30.7%. Incidence of osteoporosis-related fractures was between 20 and 24% [21]. As of 2016, the prevalence of osteoporosis in the UAE was 3.1% (2.7% in men, 3.2% in women) among 3985 Emiratis aged 18–85 years old using quantitative ultrasound (QUS) [22]. In Bahrain, the prevalence of osteoporosis in 2009 was 27.1% ( $N = 170$  postmenopausal women) using ultrasound bone density screening tool which is not the gold standard to diagnose osteoporosis as indicated above [23]. In Kuwait ( $N = 903$  postmenopausal women, mean age  $55.0 \pm 0.3$ ), prevalence of osteoporosis based on BMD of the spine was 20.2% and 12.5% in the femur in 2006 and 2012, respectively [24, 25]. Data from a larger Kuwaiti population of postmenopausal women ( $N = 2296$ , mean age  $59.1 \pm 7.9$ ) gathered from 2003 to mid-2010 found that the overall incidence of osteoporosis was 19.3%, jumping to 39.9% among women above 70 years old [26].

In 2008 among 473 Omani women 50–79 years, prevalence of osteoporosis was 10% using spine and 4% using femur site [27]. Lastly, in Qatar, the prevalence of osteoporosis in postmenopausal women was 12.3% ( $N = 821$ ) [28].

## Hip fractures in GCC, FRAX, and intervention threshold

Data on hip fracture incidence is limited in GCC, with strength of evidence at the fair level and available evidence not considered population-based. Despite ethnic homogeneity in the region, it was reported to vary widely between 250 and 350/year depending on gender and country [29]. The age-adjusted incidence of hip fracture in Oman was 140/100,000 among > 40-year-old citizens based on 2008 single-center data [27]. On the contrary, the incidence in Saudi Arabia was 29/100,000 (582 fractures in 2,071,400) based on a meta-analysis of 5 local studies on osteoporosis-related fractures (ORF) of the vertebra ( $N = 2$ ), proximal femur ( $N = 2$ ), and all sites ( $N = 1$ ) [21]. Low physical activity and  $\geq 60$  years of age were the strongest risk factors associated with fragility fractures based on a study involving 707 postmenopausal Saudi women [30]. Furthermore, incidence rate of hip fracture increased sharply with age, with 60–69-year-old females having an incidence of 134.7/100,000 increasing to 906.1/100,000 among  $\geq 80$ -year-old females [31]. The same study indicated that Saudi patients

with fragility hip fracture therapy have high morbidity and mortality rate at 30% [30]. In Kuwait, the age-standardized incidence rate was 48.4/100,000, with a male:female ratio of 0.9, taken from national data obtained from 2009 to 2012 [32]. In males living in Kuwait, the incidence of hip fracture was 69.5/100,000 among the 60–69-year group and 873.4 in the  $\geq$  80-year-old group [32].

### Who to treat and screen with BMD

Evidence on the use of FRAX® tool is also limited within GCC, with Kuwait and Abu Dhabi (UAE) being the only GCC countries having their own versions of FRAX®. In Kuwait, age-based FRAX intervention thresholds were able to identify women with higher fracture probability versus fixed *T* score thresholds particularly among the elderly [33]. In Saudi Arabia and using the Lebanese version of FRAX®, Amin and colleagues were able to identify around 14.4% and 18.4% of Saudis aged  $\geq$  60 years as eligible for osteoporosis treatment on the basis of 10-year probability of major osteoporotic ( $> 20\%$ ) and hip fracture ( $> 3.0\%$ ), respectively [34]. Given the fact that FRAX algorithms are country-specific, each country within GCC should develop their own model. Nevertheless and with the available but limited data on FRAX in the region, age-dependent FRAX-based intervention thresholds can be used in countries with moderate to high fracture incidence such as Oman and Kuwait in identifying women with higher fracture risk, which is considered more effective than BMD alone [35]. In countries with low incidence such as Saudi Arabia, the hybrid threshold model (use of both fixed and age-dependent thresholds), which was observed to be more effective in neighboring countries such as Lebanon, maybe more suitable as it avoids consideration of drug therapy in large population demographics with low risk for fracture and targets only high-risk elderly patients [36]. The setting of thresholds ideally should remain country-specific [35]. In the meantime, guidance from IOF-ESCEO can be used.

According to the IOF-ESCEO guidance, it is recommended that postmenopausal women with a prior fragility fracture should be treated without further assessment, although BMD measurement and incorporation into the FRAX calculation are sometimes appropriate, particularly in younger postmenopausal women. In women without a previous fragility fracture, the management strategy should be based on assessment of the 10-year probability of a major osteoporotic fracture (clinical spine, hip, forearm, or humerus) [37]. Women with probabilities below the lower assessment threshold can be considered at low risk [37]. Women with probabilities above the upper assessment threshold can be considered for treatment. Women with probabilities between the upper and lower assessment threshold should be referred for BMD measurements

and their fracture probability reassessed [5]. The same thresholds apply to men. Categorization of risk and risk treatment are outlined in Fig. 1.

### Vitamin D deficiency in GCC

Vitamin D deficiency in the GCC states has been consistently known to be widespread despite year-round sunshine. It has also gained considerable interest within the regional medical and research community. The most recent prevalence shows that vitamin D deficiency prevalence in the general population is 83% in Kuwait, 81% in KSA, 87.5% in Oman, 86.4% in Bahrain, 86% in Qatar, and 82.5% in the UAE [38]. Several GCC nations have already adopted their own guidelines such as Saudi Arabia [39] and the UAE [40]. Most experts agree that serum 25(OH)D levels should be  $> 50$  nmol/l irrespective of the individual's age, particularly in high-risk populations (children, pregnant and lactating women, and elderly). A recent large-scale observational study in Saudi Arabia ( $N = 2131$ , 846 males, 1285 females aged 30–75 years) showed that the recommended cut-off for 25(OH)D targeting bone health (relative to the gold standard PTH cut-off  $> 6.9$  pmol/l) in the Saudi population was 30 nmol/l [41]. Among Arab adolescent females however ( $N = 2000$  aged 12–18 years), suppression of PTH were observed at 25(OH)D 40 nmol/l and above [42]. These findings remain to be replicated before recommending lower target level for vitamin D in GCC countries.

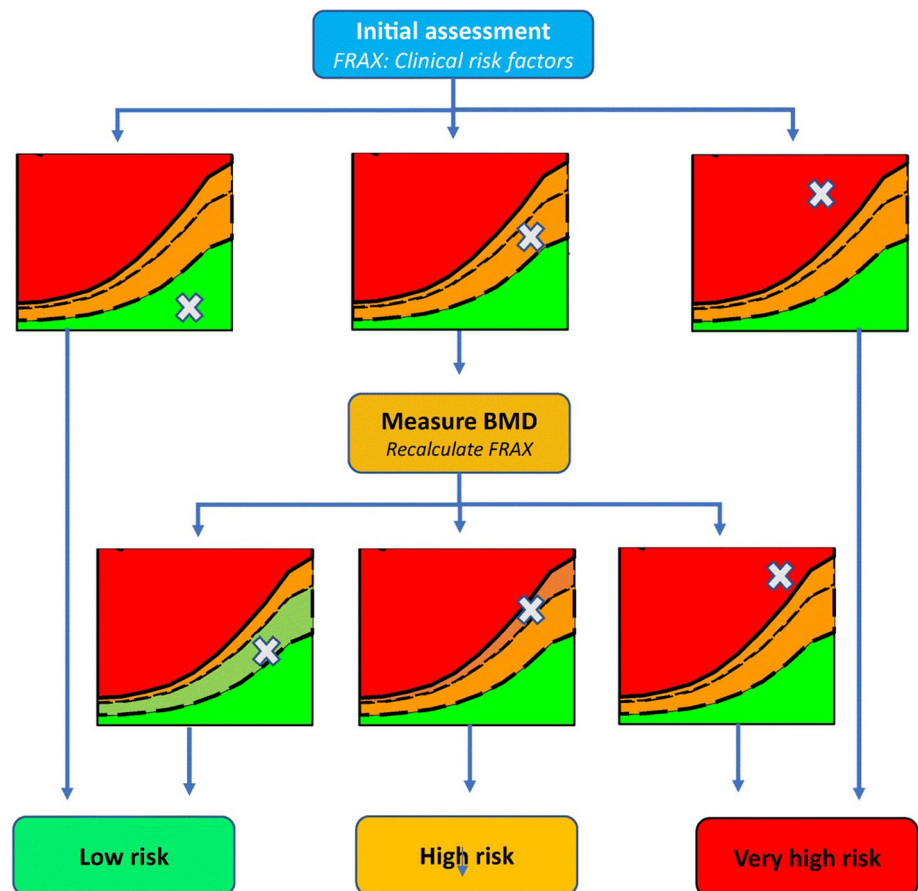
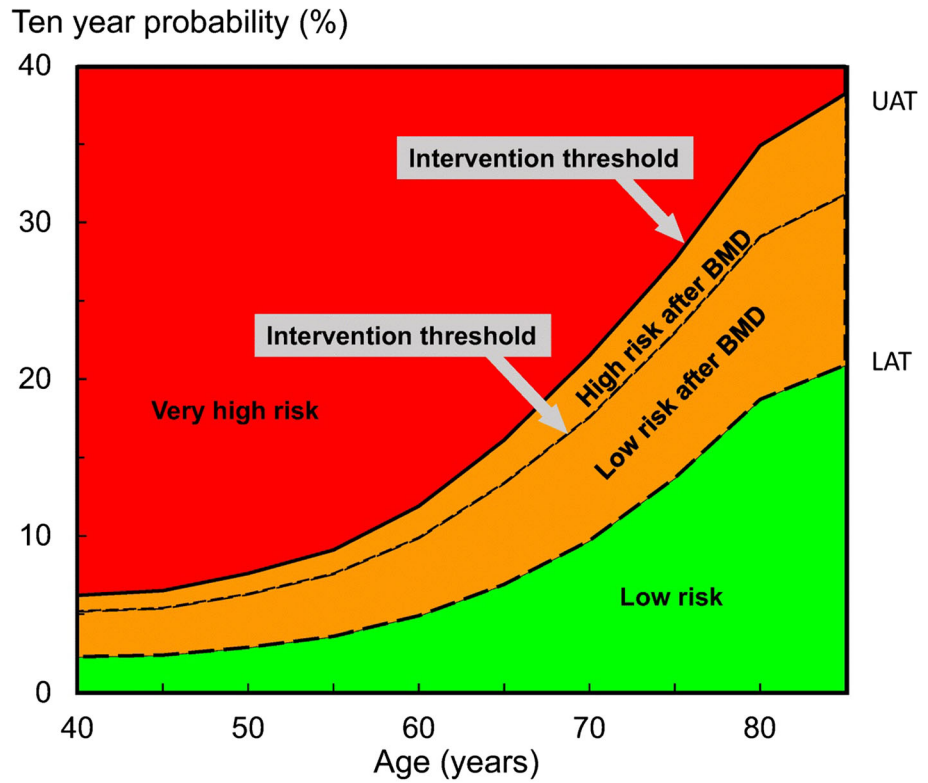
While the entire management for vitamin D deficiency will be dealt as a separate regional guideline, the common practice in the region is provision of 1000–2000 IU/daily cholecalciferol, or higher. This dose was based on the failure of most GCC residents to achieve the optimum level despite high doses of vitamin D. While universal screening for vitamin D deficiency has not gained support from regional policy makers, food fortification is being aggressively campaigned by experts to their respective ministries of health. Among the non-pharmacologic options include increased sunlight exposure and intake of vitamin D-rich foods [43].

### General pharmacological management

The GCC experts endorse the recommendations of the IOF and ESCEO in the pharmacological management of osteoporosis for use in the region [5]. Table 1 shows the different first-line and alternative treatments for the different categories of patients. Table 2 shows the efficacy of pharmacological agents which was adopted from the previous European guidelines published by IOF and ESCEO [44]. A modified algorithm adopted from the same European guidelines [5] has



**Fig. 1** Characterization and treatment pathways of fracture risk by FRAX major osteoporotic fracture probability in postmenopausal women. Initial risk assessment uses FRAX with clinical risk factors alone. Red zone indicates very high risk and that an initial course of anabolic treatment followed by antiresorptive therapy may be appropriate. Green zone suggests low risk, with advice to be given on lifestyle, calcium and vitamin D nutrition, and menopausal hormone treatment considered. Intermediate (orange) zone should be followed by BMD assessment and recalculation of FRAX probability including femoral neck BMD. After recalculation, risk may be in the red zone (very high risk), orange zone (high risk, which suggests initial antiresorptive therapy), or green zone (low risk, either in the original green zone or in the original orange zone but below the intervention threshold). *Note that patients with a prior fragility fracture are at least designated at high risk and possibly at very high risk dependent on the FRAX probability* (with permission from IOF-ESCEO) [37]



**Table 1** Pharmacological management of osteoporosis

Category	First-line therapy	Alternative first-line therapies
Young postmenopausal with only vertebral osteoporosis	Raloxifene	Oral bisphosphonates IV bisphosphonates Denosumab Teriparatide
Older postmenopausal/or younger but with concerns of hip fracture	Oral bisphosphonates	IV Bisphosphonate Denosumab Teriparatide
Osteoporosis in men	Oral bisphosphonates	IV Bisphosphonate Denosumab Teriparatide
Severe osteoporosis	Teriparatide	Oral bisphosphonates
Very low BMD T < - 3.0 + one fracture or < - 2.5 + 2 fractures		IV bisphosphonate Denosumab
Glucocorticoid-induced osteoporosis (GIOP)	Oral bisphosphonates IV bisphosphonate Denosumab Teriparatide	
Patients with imminent fracture risk, in the immediate post fracture period	Teriparatide	
Patients who fracture while on antiresorptive	Teriparatide	

\* Oral bisphosphonate (Only alendronate or risedronate has evidence (Ia) for hip fracture efficacy), IV bisphosphonate (Zoledronic acid)

\*\* Alternative first line is considered if first line were not feasible, contraindicated, or failed. Also can be considered when therapy has to be discontinued but patient still requires treatment

been provided in Fig. 2 and a summary of the recommendations has been provided previously. Below are some of the highlights taken directly from the recent version of the European guidelines [5]:

1. All patients with osteoporosis should receive vitamin D and calcium supplements on top of specific osteoporosis therapy.

2. Oral bisphosphonates are the primary management option for postmenopausal and male osteoporosis in majority of cases. For women in whom bisphosphonates are either contraindicated, ineffective, or intolerant, intravenous bisphosphonates and denosumab can be considered most appropriate substitutes, with raloxifene, or menopausal hormone therapy as optional alternatives in younger

**Table 2** Anti-fracture efficacy of the most frequently used treatments for postmenopausal osteoporosis when given with calcium and vitamin D, as derived from randomized controlled trials

Treatment	Effect on vertebral fracture risk		Effect on non-vertebral fracture risk	
	Osteoporosis	Established osteoporosis <sup>a</sup>	Osteoporosis	Established osteoporosis <sup>a</sup>
Alendronate	+	+	NA	+(including hip)
Risedronate	+	+	NA	+(including hip)
Ibandronate	NA	+	NA	+ <sup>b</sup>
Zoledronic acid	+	+	NA	+ <sup>c</sup>
HRT	+	+	+	+(including hip)
Raloxifene	+	+	NA	NA
Teriparatide	NA	+	NA	+
Denosumab	+	+ <sup>c</sup>	+(including hip)	+ <sup>c</sup>

NA no evidence available; “+” effective drug

<sup>a</sup> Women with a prior vertebral fracture<sup>b</sup> In subsets of patients only (post hoc analysis)

<sup>c</sup> Mixed group of patients with or without prevalent vertebral fractures [5]

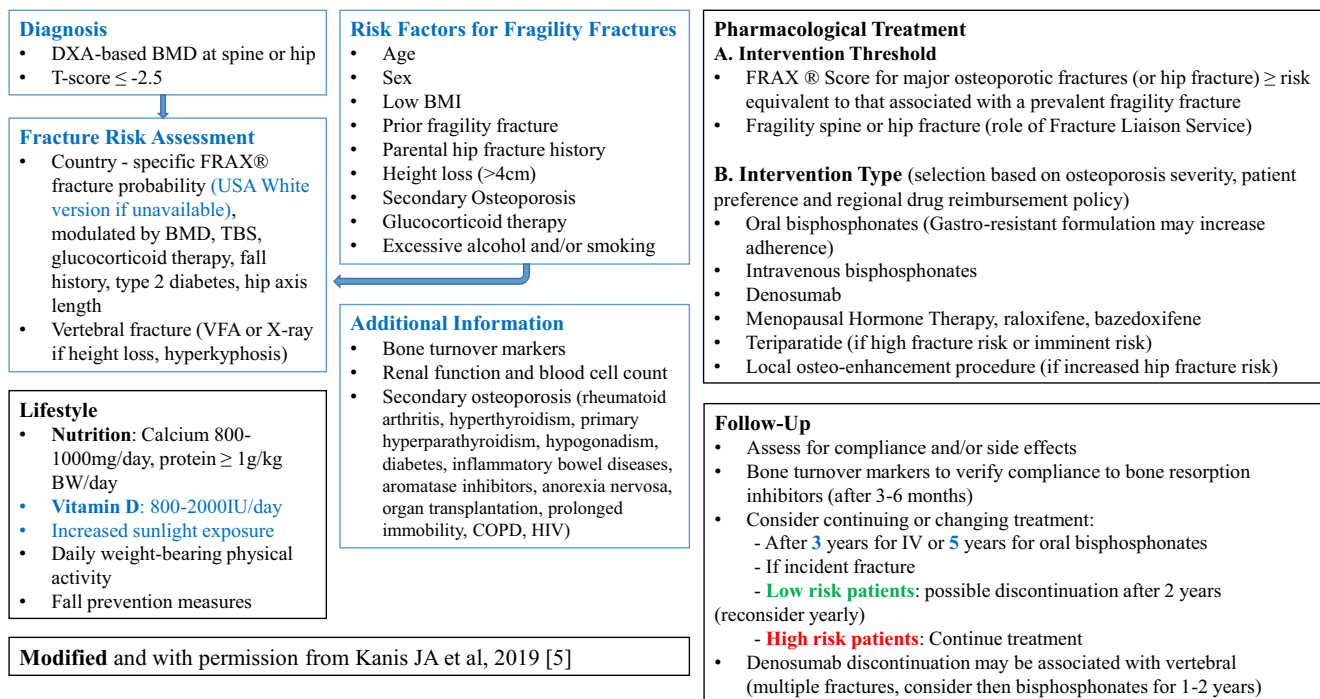


Fig. 2 Diagnosis and management of osteoporosis

patients (with spine osteoporosis for raloxifene). Teriparatide is preferentially recommended for patients at high risk of fracture like those in the immediate post fracture period and those with a fracture and extremely low BMD.

3. Management should be reviewed 3–5 years post-bisphosphonate treatment. Fracture risk should be reassessed after a new fracture, regardless of when it occurs. There is elevated risk of new clinical and vertebral fractures in patients who stopped treatment.
4. Discontinuation of denosumab therapy is linked to rebound increased vertebral fractures. Bisphosphonate therapy is strongly advisable after denosumab withdrawal.

## Intervention thresholds for pharmacological intervention

1. Recommended thresholds should be based on probabilities of major osteoporotic and hip fracture derived from FRAX.
2. Women > 65 years with a prior fragility fracture can be treated without the need for further assessment; BMD measurement may apply more to the younger postmenopausal women.
3. Intervention thresholds according to age offer clinically suitable and reasonable access to treatment.

In conclusion, the present position paper summarized the recommendations of GCC experts from different osteoporosis societies within the gulf. Clearly, there are still many issues that need to be properly addressed (e.g., bone markers, trabecular bone scores, falls, vertebral fracture assessment) for a more appropriate guideline in the region. For these issues, the regional experts agreed to adapt the European guidance, until new evidence has been gathered. While the GCC citizens use the same medications for osteoporosis as the rest of the world, the widespread vitamin D deficiency is what sets this region apart. As such, we emphasized on ruling out osteomalacia before designating the diagnosis of osteoporosis to suspected patients as well as the adequate treatment of vitamin D deficiency. The guidelines presented should be carefully considered in the management of osteoporosis in the region, taking into account individual cases and clinical judgment.

## Summary of main recommendations

### Diagnosis

1. Diagnosis is made on the basis of *T* score of bone mineral density assessed through dual-energy X-ray absorptiometry (DXA) of femoral neck, spine, or distal radius. A patient with a value of  $\leq -2.5$  SD is considered to have osteoporosis.
2. A patient is diagnosed and is indicated for therapy if she has risk of major osteoporotic fracture (MOF) above the upper intervention threshold using a country-specific

FRAX® model or surrogate model if there is no country-specific model or if the patient has readings above an intervention threshold with known value of measured bone mineral density (BMD).

3. Other diagnostic modalities like heel ultrasound can be used for screening or diagnosis depending on accessibility. However, they lack standardization and confirmatory DXA for abnormal findings is needed.
4. The presence of fragility fracture (especially hip or spine).

### Risk factors for osteoporosis-related fractures

1. Other factors that influence BMD and subsequent fracture risk include age, sex, low body mass index (BMI), history of fragility fracture, family history of hip fracture, history of chronic glucocorticoid use, rheumatoid arthritis, premature menopause (< 45 years), diabetes, current smoking, alcohol abuse, and incidental findings of height loss > 4 cm and thoracic kyphosis.
2. Bone markers of formation (serum procollagen type I N propeptide (s-PINP)) and resorption (serum C-terminal cross-linking telopeptide of type I collagen (s-CTX)) have value in predicting fracture risk and follow-up of treatment response.

### Fracture risk assessment

1. For fracture probability, country-specific FRAX® should be used. If unavailable, use that of a surrogate country. Currently there are FRAX models for 5 countries in the Middle East. The use of Kuwait or Abu Dhabi versions is recommended for GCC countries that do not have FRAX model. Kuwaiti data looks robust with 4 years of data collection.
2. FRAX can be calculated without DXA at baseline, and low-risk patients should be followed, while high-risk patients should be treated. For patients at intermediate risk, BMD should be measured using DXA. Treat those with high FRAX score based on individual country intervention threshold.
3. Trabecular bone score (TBS) may serve as an addition to BMD measurements and FRAX. FRAX score reading should take into consideration exposure to glucocorticoids, data on lumbar spine BMD, trabecular bone score, hip axis length, falls history, immigration status, and diabetes status.
4. Vertebral fracture assessment (VFA) should be done for all patients whenever possible since it will guide patient classification and decision for therapy in case morphometric (asymptomatic) vertebral fractures were found.

History of  $\geq 4$  cm height loss, kyphosis, recent or current long-term oral glucocorticoid therapy, or a BMD  $T$  score  $\leq -2.5$  are additional indications to do VFA.

5. Peripheral scanning using ultrasound machines may help in the initial screening of patients. They should not be used for diagnosing osteoporosis. Persons with abnormal values can be sent for DXA scanning.

### Lifestyle and dietary measures

1. Daily calcium intake of 800–1200 mg and sufficient dietary protein, ideally achieved through dairy products, are recommended.
2. A daily dose of 800–1500 IU cholecalciferol should be advised for postmenopausal women. Initial higher doses are needed in cases of vitamin D deficiency or insufficiency which are prevalent in GCC countries.
3. Calcium supplementation is appropriate if the dietary intake is below 800 mg/day. A dose of 1500 mg per day is recommended for postmenopausal women.
4. Weight-bearing exercises performed on a regular basis are recommended and customized to the individual needs and capacity of the patient.
5. History of falls should be noted among individuals at high risk of fracture with additional clinical assessment undertaken when appropriate.

### Pharmacological intervention in postmenopausal women

1. There is no single treatment modality that fits all patients with osteoporosis. Treatment should be tailored to patient status. Certain medications are contraindicated in particular patients.
2. The oral bisphosphonates (alendronate, risedronate, and ibandronate) are first-line therapies for the majority of patients with osteoporosis. Their use should be limited to maximum of 5 years after which fracture risk should be assessed. Intravenous bisphosphonates, teriparatide, or denosumab are other alternative first-line therapies depending on individual patient condition.
3. Teriparatide is recommended for those at high risk of fracture. Those are patients in the immediate post fracture period where most recurrent fractures occur. Teriparatide is a first-line agent in patients with markedly low BMD readings and fracture.
4. Denosumab is the only first-line treatment approved for the management of osteoporosis in advanced renal impairment and hemodialysis.



5. Initial combination therapy of bone formation and antiresorptive agent is not recommended.
6. Sequential therapy is advisable for many patients. Bone formation agent should be used first for 1½–2 years followed by an antiresorptive agent if needed. Several sequential regimens are available but fracture data are lacking.
7. 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 stopped treatment.
8. Duration of denosumab therapy is not clear. However, denosumab should not be stopped without clear justification as data showed quick loss of bone density gained while on therapy and increased risk of vertebral fractures. A bisphosphonate should be considered after discontinuation of denosumab.

### Intervention thresholds for pharmacological intervention

1. Intervention thresholds are based on probabilities of major osteoporotic and hip fracture from FRAX. These vary in different healthcare systems with discrepancy in health system policies and/or “readiness to pay”. For GCC countries without FRAX model, the use of Kuwait or Abu Dhabi intervention threshold is recommended.
2. Women above 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. Many experts recommend baseline BMD for all patients to follow progress of therapy.
3. 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.
2. Coordinator-based fracture liaison services (FLS) should be developed in the region.

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**Author Contributions** The views expressed in this article represent the outcomes of a working group jointly organized by the Chair for Biomarkers of Chronic Diseases (NMA) and Saudi Osteoporosis Society (YS, RS) in King Saud University, Riyadh, Saudi Arabia, on February 15–16, 2019. The working group are representatives of their respective osteoporosis societies within the GCC, together with the president of ESCEO (JYR) who served as adviser, and were invited for their expertise in osteoporosis. Members of the working group (YS, NMA, TA, AA, MA, JM, SAQ, JYR, AS, and RS) were assigned topics of importance relevant to the region in advance of the meeting for discussion. Following the meeting, a first draft was made (SS) and was circulated to all including those who were not able to attend (FA, SAE) for their review and input. Following 3 rounds of review from all members, the final draft was formatted and submitted by YS. All authors met the ICMJE criteria for authorship and gave final approval of the version to be published.

### Compliance with ethical standards

**Conflicts of interest** YS received speaker honoraria from Eli Lilly and Amgen. TA received speaker honoraria from Amgen and Novartis. JYR received consulting fees and/or paid advisory boards for IBSA-Genevriev, MYLAN, Radius Health, and Pierre Fabre; lecture fees when speaking at the invitation of IBSA-Genevriev, MYLAN, CNIEL, and Diary Research Council (DRC); and grant support from IBSA-Genevriev, MYLAN, CNIEL, and Radius Health. NMA, SS, TA, AA, MA, JM, SAQ, AS, and RS have no conflicts to declare.

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### Endorsements

This consensus report is endorsed by the following societies:

Saudi Osteoporosis Society  
Kuwait Osteoporosis Society  
American Association of Clinical Endocrinologists, Gulf Chapter  
Emirates Osteoporosis Society  
Emirates Diabetes Society  
Oman Medical Association  
Bahrain Osteoporosis Society  
Qatar Osteoporosis Society

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