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FEATURE ARTICLE

Philippine Clinical Practice Guidelines on Screening, Diagnosis, Management and Prevention of Primary Osteoporosis and Fragility Fractures Among Postmenopausal Women and Older Men

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Abstract

Background. This first clinical practice guideline (CPG) on osteoporosis prevention and management in the Philippines is the output of a shared undertaking by a multidisciplinary CPG development team spearheaded by the Osteoporosis Society of the Philippines Foundation, Inc. and joined by the Philippine Academy of Family Physicians; the Philippine College of Endocrinology, Diabetes, and Metabolism; the Philippine Orthopedic Association; the Philippine Obstetrics and Gynecological Society and the Philippine Rheumatology Association. This guideline seeks to augment and update the "Consensus statements on osteoporosis diagnosis, prevention and management in the Philippines," initially published in 2011, incorporating evidence-based practices developed in the last decade.

Methodology. The steering committee formulated and prioritized clinical questions based on meetings and stakeholder consultations. A PICO (population, intervention, comparator, outcome) format was used to develop clinical questions and guide the systematic search for evidence. The development of guidelines followed the ADAPTE process. Once completed, panel discussions were done using the Evidence to Decision Framework. After the panel discussions, the final recommendations were revised.

Results. Thirty-four recommendations were formulated to address 27 clinical questions related to screening, prevention, diagnosis, pharmacologic and nonpharmacologic treatment, surgical management, follow-up, and continuity of care. With these recommendations, the developers aim to establish a standard of care in the prevention, diagnosis and management of osteoporosis and fragility fractures in both in-patient and out-patient cases that are appropriate to the Philippine context. Specifically, the CPG development group aims to use these recommendations to define the standard of care for osteoporosis as part of universal healthcare services once the program is implemented nationally. Relevant stakeholders may also use the recommendations to inform public and private payor policies for patients with fragility fractures, as well as by local government units or private companies looking to establish orthogeriatric centers with fracture liaison services.

Conclusion. This guideline is helpful for physicians and other allied health personnel in screening, diagnosis, management and prevention of primary osteoporosis and fragility fractures among postmenopausal women and older men.

Key words: Philippines, guidelines, osteoporosis, older men, postmenopausal women

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INTRODUCTION

Osteoporosis is a chronic bone disease that affects millions of individuals and constitutes a significant public health problem. As the global population continues to age, the burden of osteoporosis is projected to increase in the coming years due to increasing life expectancy, population aging, and the growing prevalence of noncommunicable diseases that impact negatively on osteoporosis risk factors.

METHODOLOGY

This clinical practice guideline is a systematic synthesis of scientific evidence related to primary, secondary and tertiary prevention strategies for osteoporosis in postmenopausal women. Guideline development followed the ADAPTE process, a validated and systematic approach to adapting existing guidelines for use in a specific organizational context or setting with limited time and resource commitments.[1] Developers also planned for a *de novo* systematic review and meta-analysis using the widely accepted grading of recommendations, assessment, development and evaluation (GRADE) approach for clinical questions that were unsuitable for adaptation.[2] Finally, the Evidence to Decision (EtD) Framework was used to guide panel discussions and inform decision-making when the final recommendations were formulated. For ease of interpretation and comparison across source CPGs, all recommendation statements and evidence ratings of the source CPGs (Table 3) were appraised and re-classified by the evidence review expert (ERE) using the GRADE approach, the rating system used for the present CPG (Tables 1 and 2).

RESULTS

After rigorous evidence reviews and panel discussions, the following clinical questions (Q) and recommendations (R) were formulated:

Q1: Among the adult population, who should be screened for osteoporosis?

R1: It is recommended that the following individuals be screened for osteoporosis: all postmenopausal women (PMW), men aged ≥50 years with clinical risk factors, and other adults with clinical risk factors **(Strong recommendation, moderate to high quality of evidence).**[3,4]

Q2: Among the adult population, what factors increase the risk of osteoporosis?

R2: *Screening for the following risk factors is recommended:* advanced age (>70 years), previous fragility fracture, menopause or untreated early menopause, parental history of osteoporosis and/or fractures, excessive alcohol consumption (>3.5 units per day), smoking, frailty or low level of physical activity, coexisting illnesses, and certain medications. *Comorbidities:* diabetes, hyperparathyroidism or other endocrine diseases, rheumatoid arthritis, systemic lupus erythematosus, inflammatory bowel disease, malabsorption, institutionalized patients with epilepsy, chronic liver disease, neurological disease (Alzheimer's, Parkinson's, multiple sclerosis, stroke), moderate to severe chronic kidney disease (CKD), bronchial asthma, human immunodeficiency virus *Medications:* glucocorticoids, antidepressants, anti-epileptic agents (i.e., enzyme-inducing drugs), aromatase inhibitors, gonadotrophin releasing hormone agonists for prostate cancer, proton pump inhibitors, thiazolidinediones, anticoagulants, methotrexate, thyroid hormones **(Strong recommendation, high quality of evidence).**[3,4]

Q3: What tool should be used for osteoporosis screening?

R3: Osteoporosis screening should be performed using the fracture risk assessment (FRAX®) tool[5] (Figure 1) **(Strong recommendation, high quality of evidence)**.[5,6]

Table 1. Rating quality of the evidence using the GRADE approach[7]

Quality of Evidence	Interpretation
High	We are confident that the actual effect is close to the effect estimate. Further research is unlikely to change our confidence in the effect estimate.
Moderate	We are moderately confident in the effect estimate. The actual effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different. Further research is expected to impact our confidence in the estimate of effect and may change the estimate.
Low	Our confidence in the effect estimate is limited. The actual effect may be substantially different from the estimate of the effect. Further research is very likely to impact our confidence in the estimate of effect and is expected to change the estimate.
Very Low	We have very little confidence in the effect estimate. The true effect is likely to be substantially different from the estimate of effect. Any estimate of the effect is very uncertain.

Table 2. Rating strength of recommendation using the GRADE approach[7]

Strength of Recommendation	Interpretation
Strong	The desirable effects of an intervention clearly outweigh the undesirable effects (strong recommendation of an intervention). The undesirable effects of an intervention clearly outweigh the desirable effects (strong recommendation against an intervention).
Weak/Conditional	The trade-offs between desirable and undesirable effects are less certain, either because of low-quality evidence or because evidence suggests that desirable and undesirable effects are closely balanced.

R4: The Osteoporosis Self-assessment Tool for Asians (OSTA) tool[7] may be used as an alternative to FRAX® for osteoporosis screening (Figure 1) **(Strong recommendation, high quality of evidence).**[6]

Q4: Among the adult population, what is the clinical presentation of osteoporosis?

R5: Patients who present with the following history, signs and symptoms should be suspected to have osteoporosis: acute onset back pain, height loss, previous fragility fracture, menopause or untreated early menopause, parental history of osteoporosis, and/or fractures. Physical examination findings include any of the following: low weight or body mass index (BMI) (<18.5 kg/m^2), ≥4 cm height loss, or thoracic kyphosis **(Strong recommendation, high quality of evidence).**[3,4]

Q5: Among at-risk PMW, should bone mineral density measurement using dual- energy x-ray absorptiometry be used to diagnose osteoporosis?

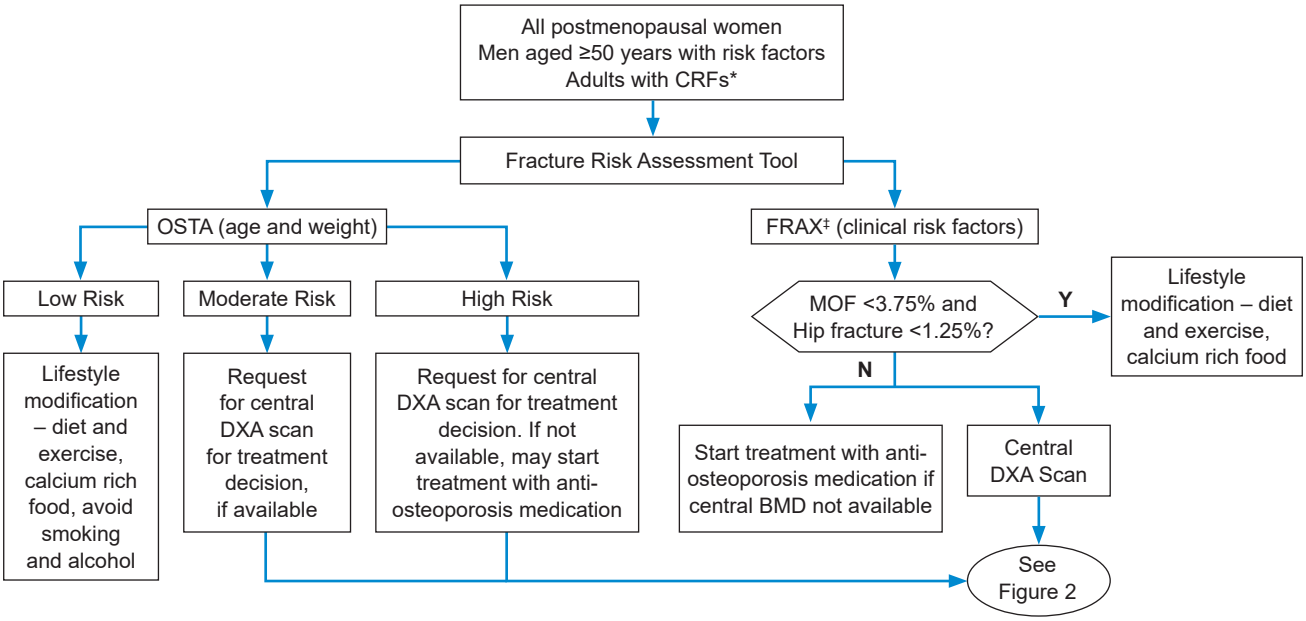
R6: Among at-risk PMW, it is recommended that a bone mineral densitometry (BMD) test using dual-energy x-ray absorptiometry (DXA) and WHO classification criteria be used for the diagnosis of osteoporosis (Figure 2) **(Strong recommendation, high quality of evidence).**[3,8]

R7: Among at-risk PMW, it is recommended that the following criteria be used to diagnose osteoporosis: low bone mass (BMD T-score between <-1.0 and >-2.5) with a fragility fracture, or those at high fracture risk according to country-specific FRAX® **(Strong recommendation, high quality of evidence).**[3,8]

R8: Among at-risk PMW of vertebral fracture, it is recommended that vertebral fracture assessment (VFA) using DXA or lateral spine radiograph be done **(Strong recommendation, high quality of evidence).**[3,8]

R9: Among at-risk PMW without fracture, where BMD measurement via DXA is unavailable or not feasible, starting anti-osteoporosis therapy is suggested in the following:

a. A fracture intervention threshold of 3.75% for major osteoporotic fractures and/or 1.25% for hip fractures using FRAX® tool, or
b. Patients who fall under high risk category using Osteoporosis Screening Tool for Asians **(Strong recommendation, high quality of evidence).**[3,8]



**Clinical Risk Factors that increase the risk of osteoporosis include:* advanced age (>70 years), previous fragility fracture, menopause or untreated early menopause, parental history of osteoporosis and/or fractures, excessive alcohol consumption (>3.5 units per day), smoking, frailty or low level of physical activity, coexisting illnesses, and certain medications.

Comorbidities: diabetes, hyperparathyroidism or other endocrine diseases, rheumatoid arthritis, systemic lupus erythematosus, inflammatory bowel disease, malabsorption, institutionalized patients with epilepsy, chronic liver disease, neurological disease (Alzheimer's, Parkinson's, multiple sclerosis, stroke), moderate to severe chronic kidney disease, bronchial asthma, human immunodeficiency virus.

Medications: glucocorticoids, antidepressants, anti-epileptic agents (i.e. enzyme-inducing drugs), aromatase inhibitors, GnRH agonists for prostate cancer, PPIs, thiazolidinediones, anticoagulants, methotrexate, thyroid hormones.

‡*FRAX clinical risk factors:* Age, gender, weight, height, parental history of hip fracture, personal history of fracture, glucocorticoid use, rheumatoid arthritis, secondary cause of bone loss, current smoking, alcohol intake of ≥3 units per day, ± femoral neck BMD using central DXA.

Figure 1. Primary prevention of bone loss.

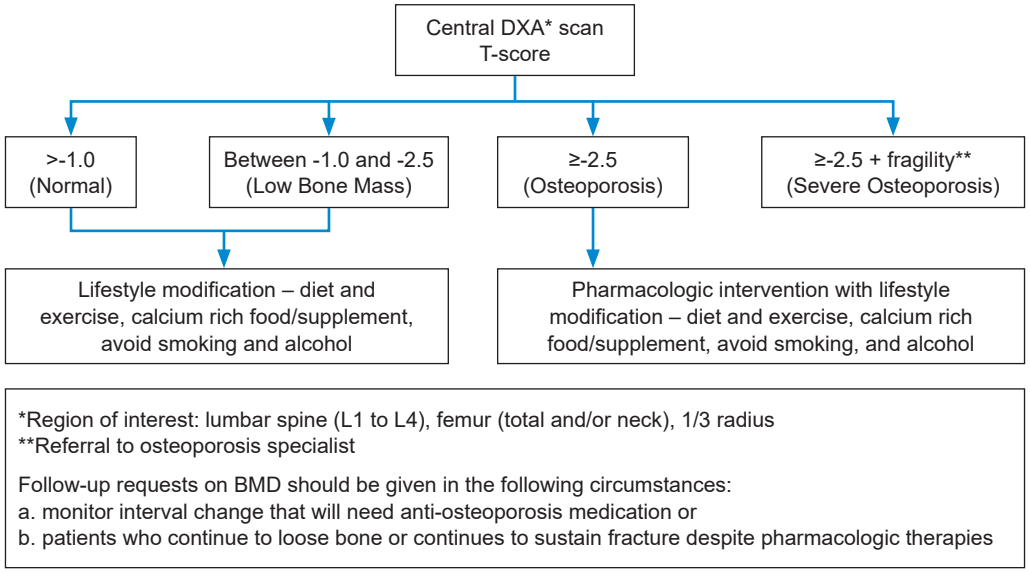


Figure 2. WHO classification criteria for BMD and management approach.

Q6: Among PMW with osteoporosis, are the anti-resorptive agents (e.g., alendronate, ibandronate, zoledronate, denosumab, raloxifene) effective in reducing vertebral, non-vertebral and hip fractures compared to placebo?

R10: Among PMW with osteoporosis, it is recommended that alendronate, denosumab, risedronate, and zoledronate be used as initial therapy to reduce vertebral, non-vertebral and hip fractures **(Strong recommendation, high quality of evidence).**[6]

R11: Ibandronate or raloxifene can be an alternative treatment in reducing vertebral fractures in certain cases **(Strong recommendation, moderate quality of evidence).**[6]

Q7: Among postmenopausal women with severe osteoporosis, are teriparatide, abaloparatide, and romosozumab effective in reducing vertebral, non-vertebral and hip fractures compared to placebo? How long should treatment duration be?

Severe osteoporosis is defined in any of the following situations:

a. **BMD T-score ≤-2.5 plus fragility fractures**
b. **BMD T-score ≤-3.5**
c. **Prior hip fracture**
d. **Recent vertebral fracture (within the last two years)**
e. **Two or more vertebral fractures (at anytime)**

R12: Among PMW with severe osteoporosis, it is recommended that teriparatide, abaloparatide and romosozumab be used. Abaloparatide and romosozumab prevent vertebral, non-vertebral and hip fractures, while teriparatide reduces the risk of further vertebral and nonvertebral fractures. Treatment duration of bone forming agents for maximum treatment benefits is recommended to be referred to specialists. Teriparatide, abaloparatide and romosozumab are highly special drugs which should be dispensed by bone specialists because of local availability and cost concerns **(Strong recommendation, high quality of evidence).**[6,7]

Q8: Among postmenopausal women diagnosed with osteoporosis, should serum calcium and vitamin D levels be normal prior to initiating anti-resorptive therapy?

R13: Among PMW with osteoporosis, it is recommended that calcium insufficiency/deficiency be treated prior to initiation of anti-osteoporosis drugs **(Strong recommendation, moderate quality of evidence).**[3]

R14: It is also recommended that vitamin D insufficiency/deficiency should be addressed alongside the initiation of anti-osteoporosis drugs **(Strong recommendation, high quality of evidence).**[3]

Q9: Among PMW with osteoporosis, should calcium and vitamin D supplementation be given to reduce fragility fracture risk?

R15: Among PMW with osteoporosis, calcium and vitamin D supplementation is recommended along with anti-osteoporosis medication to reduce the risk of fragility fracture. The recommended dose for calcium is 700 to 1200 mg per day, and vitamin D at least 800 IU per day **(Strong recommendation, high quality of evidence).**[8-10]

Q10: Among patients with previous fragility fractures, what is the effect of pharmacologic intervention on the risk of having a subsequent or second fracture?

R16: Among patients with previous or prevalent fragility fractures (regardless if BMD is available or not), pharmacologic therapy, such as bisphosphonates and teriparatide, is recommended to reduce the risk of subsequent fractures **(Moderate quality of evidence, strong recommendation).**[7,11]

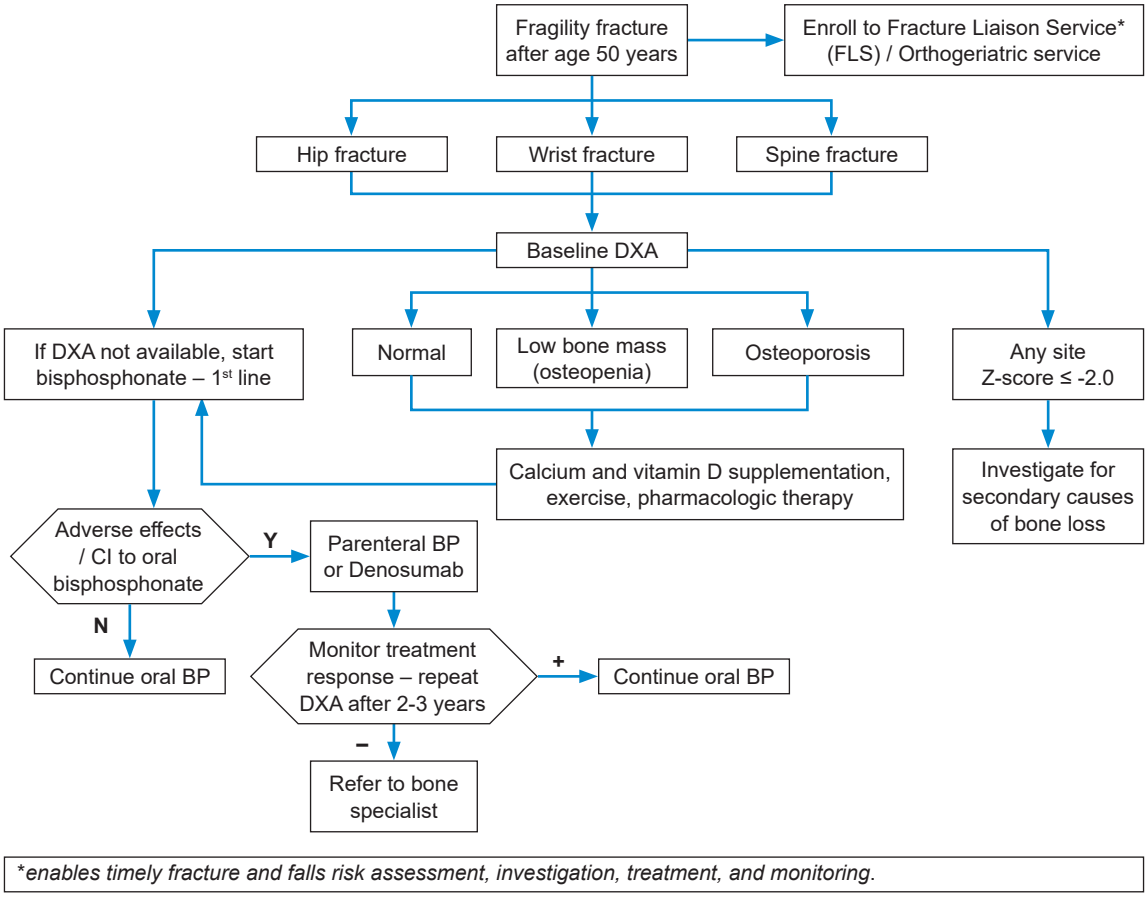


Figure 3. Algorithm on secondary fracture prevention.

Q11: Among patients with acute displaced fragility fractures of the distal radius, is early surgical intervention superior to conservative management for improving functionality? [12]

R17: Among patients 65 years old and older with acute displaced fragility fractures of the distal radius, it is not recommended to proceed with surgery to improve long-term patient functional outcomes (Figure 3) **(Strong recommendation, high quality of evidence).** [9]

Q12: Among patients who have painful osteoporotic compression fractures of the spine, is kyphoplasty superior to nonsurgical management for controlling pain and improving quality of life (QoL)?

R18: Among patients with recent-onset painful osteoporotic compression fractures of the spine refractory to conservative therapy, it is suggested that kyphoplasty be done over non-surgical treatment for acute pain control (six to eight weeks) and improvement of quality of life **(Strong recommendation, moderate quality of evidence).** [7]

Q13: Among patients who sustained fragility fractures of the hip, is early surgical intervention superior to delayed surgical intervention in improving overall survival, morbidity, mortality and functionality of patients?

R19: Among patients who sustained fragility fractures of the hip, it is suggested that early surgical management (within 24 to 48 hours) be done to reduce morbidity and improve survival **(Strong recommendation, moderate quality of evidence).** [13]

Q14: In patients with a previous osteoporotic fragility fracture, will enrollment in a secondary fracture prevention program or fracture liaison service (FLS) improve treatment adherence and prevent re-fractures?

R20: Among patients who have experienced fragility fracture, it is recommended that they be managed within a formal integrated system of care that incorporates a fracture liaison service to prevent re-fractures and improve adherence to osteoporosis treatment (Figure 3) **(Strong recommendation, high quality of evidence).** [3,7]

R21: Among patients who have fragility fracture/s, it is recommended that appropriate interventions, including both pharmacologic and non-pharmacological approaches, be started **(High quality of evidence, strong recommendation).** [3,7]

Q15: Among adults receiving osteoporosis treatment, what is the appropriate interval between central DXA scans in monitoring treatment response?

R22: Among adults receiving osteoporosis treatment, it is recommended that a central DXA test should be done every one to two years, especially in patients at high risk of fracture, then at longer intervals thereafter once a definite satisfactory treatment response is achieved **(Strong recommendation, moderate quality of evidence).**[6,7]

Q16: Among patients with recent fragility fracture/s, should an immediate referral to a bone specialist be done for better evaluation and management?

R23: It is recommended that patients with the following risk factors/conditions be referred to an osteoporosis specialist: patients with fragility fracture and/or subsequent fragility fractures, BMD T-score ≤-3.5, treatment with high-dose glucocorticoids (≥7.5 mg/day of prednisolone or equivalent over three months), patients with comorbidities such as CKD, endocrine and rheumatic diseases **(Strong recommendation, high quality of evidence)**.[6]

Q17: Should at-risk PMW and older men receive calcium supplementation and/or vitamin D supplementation for prevention of osteoporosis and fragility fractures?

R24: Among at-risk adults with normal FRAX® and BMD scores, calcium and vitamin D supplementation is recommended for those who do not meet country-specific reference standards. Potential hazards and adverse effects of calcium and vitamin D supplementation include increased risk for renal insufficiency, myocardial infarction, coronary artery disease and stroke **(Strong recommendation, moderate quality of evidence).**[3,5,12]

Q18: Among PMW and older men, what doses of calcium and Vitamin D are associated with reduced fragility fracture risk?

R25: Among at-risk adults with normal FRAX® and BMD scores who do not meet country-specific reference standards, supplementation with vitamin D at 400 to 600 IU per day and calcium at 700 to 800 mg per day is recommended **(Strong recommendation, moderate quality of evidence).**[3,12]

Q19: Among PMW and older men, what is the benefit of physical activity in the prevention of osteoporosis and fragility fractures?

R26: Among PMW and older men, regular physical activities using a combination of exercise types (such as weight bearing, balance training, flexibility or stretching exercises, endurance and progressive strengthening exercises) are recommended to increase BMD and reduce the risk of fragility fractures. Community-based programs may be sought through the respective Office of the Senior Citizens Affairs in each locality or community **(Strong recommendation, high quality of evidence).**[3,7,15]

Q20: Among PMW and older men, does smoking cessation prevent osteoporosis and fragility fractures?

R27: Among PMW and old men, smoking cessation is recommended to reduce the risk of osteoporotic fractures. Specific guidelines on smoking cessation are outlined in the Philippine Guidelines on Periodic Health Examination – Lifestyle Advice CPG **(Strong recommendation, moderate quality of evidence).**[3,7,12,14,15]

Q21: Among PMW and older men, what diet is effective in the prevention of osteoporosis?

R28: Among PMW and old men, a balanced diet or nutrient-dense diet (fruits, vegetables and whole grains) is recommended to prevent osteoporosis and fragility fractures **(Strong recommendation, moderate level of evidence).**[3,7,12,15]

Q22: Should at-risk postmenopausal women receive menopausal hormone therapy (MHT) for the prevention of fragility fractures? What is the duration of use for MHT?

R29: Among at risk peri- and postmenopausal women with climacteric symptoms but without contraindications to MHT, it is recommended that MHT be given for a minimum duration of two years but not longer than three years to reduce fracture risk **(Strong recommendation, high quality of evidence).**[16]

R30: Among at-risk peri- and post-menopausal women with climacteric symptoms but with contraindications to MHT, MHT is not recommended **(Strong recommendation, high quality of evidence).**[16]

Q23: When should menopausal hormone therapy be initiated to reduce fracture risk?

R31: Among at-risk peri- and postmenopausal women with climacteric symptoms but without contraindications to MHT younger than 60 years of age, initiation of MHT may be of greater benefit in fracture risk reduction **(Strong recommendation, high quality of evidence).**[16]

Q24: Which hormone preparation should be used for fracture risk reduction?

R32: Among hysterectomized PMW, it is recommended to give estrogen-only replacement therapy for fracture risk reduction. Addition of progestins is recommended for women with intact uterus to prevent endometrial pathology **(Strong recommendation, high quality of evidence).**[16]

Q25: What are the safety issues of MHT?

R33: The safety issues of MHT include an increased risk for coronary events, stroke, venous thromboembolism (VTE), breast cancer and gallbladder disease. Among at-risk peri- and postmenopausal women with climacteric symptoms but without contraindications to MHT, transdermal estrogen (gel/patch) is recommended over oral estrogen to decrease the risk of VTE **(Strong recommendation, high quality of evidence).**[16]

Q26: Among at-risk postmenopausal women, should selective estrogen receptor modulators (SERMs) be considered an alternative to MHT for prevention of osteoporosis?

R34: Among women at-risk of breast cancer, raloxifene is recommended as an alternative to MHT to reduce the risk of vertebral fractures **(Strong recommendation, high quality of evidence).**[16]

Q27: How are adverse events monitored in women receiving MHT for osteoporosis prevention?

R35: Among women on MHT who are at risk of breast cancer, it is recommended for them to undergo annual mammograms. Among women with postmenopausal bleeding on MHT, it is recommended for them to undergo transvaginal ultrasound every six months for the first year and annually thereafter. Among women on MHT, it is recommended that they be monitored for signs and symptoms of venous thromboembolism, and cardiovascular and cerebrovascular diseases. **(Strong recommendation, high quality of evidence).**[16]

DISCUSSION

The burden of disease is expected to be more pronounced soon as the old population is expected to triple in size. Increasing education and dissemination of osteoporosis prevention, improving resource allocation, and paying more attention to screening and treatment of osteoporosis could help reduce the global burden of disease attributable to low bone mineral density and fracture, especially in low-middle and middle sociodemographic index countries and territories. The lack of high-quality, population-specific local data led to the adaptation of CPGs from Asian and international sources. It is the best option at the time being to address the burden of osteoporosis in the Philippines. The authors of this CPG will spearhead local epidemiologic and cost-analysis studies that will help address the said knowledge gap. Future revisions of this CPG will focus on the said gaps to avoid the possibility of over-screening and over-treatment.

CONCLUSION

This guideline is helpful for physicians and other allied health personnel in the screening, diagnosis, management and prevention of primary osteoporosis and fragility fractures among postmenopausal women and older men. The guideline was submitted and accepted by the Department of Health in early 2024. The full text of the manuscript and supplementary appendix and references can be accessed via https://doh.gov.ph/dpcb/doh-approved-cpg/. Similarly, this guideline has been presented in conferences and annual conventions of various medical societies. This CPG will be updated after three years or earlier to present more recent evidence. Surveys and focused group discussions with end-users of this guideline will be also done to accurately capture their preferences and other views. Cost-evaluation, feasibility and health economic outcome studies will also be done in order to evaluate the impact of this guideline from a budget and financial standpoint. Lastly, to monitor and evaluate adherence of healthcare providers to evidence-based standards on the various domains of osteoporosis, possible key performance indicators include:

1. Screening and risk assessment: Percentage of eligible patients screened for osteoporosis using the validated fracture risk assessment tools (e.g., FRAX®, OSTA);
2. Diagnosis: Percentage of patients with fragility fractures assessed for osteoporosis, and time to diagnosis after incident fracture;
3. Prevention: Percentage of patients who engage in community exercise programs and on calcium and vitamin D supplementation;
4. Treatment initiation: Percentage of high-risk patients on anti-osteoporosis treatment; and
5. Fracture Liaison Service: Percentage of patients who are adherent to medications for 12 months or more, incidence of new fragility fractures in patients ongoing therapy, and time from fracture to osteoporosis care coordination.

Table 3. Summary of guideline content

A check (✓) indicates discussion of the clinical question in the source guideline

	1 AACE[8]	2 AAOS[13]	3 AAOS[14]	4 African[10]	5 ASBMR	6 BBC[12]	7 LatAm	8 NAMS[8]	9 RAGCP[15]	10 SIGN[9]	11 UK NOGG[3]	12 USPSTF[6]
Screening												
Among the adult population, who should be screened for osteoporosis?											✓	
Among the adult population, what factors increase the risk for osteoporosis?											✓	
Among the adult population, what tool should be used for osteoporosis screening?												✓
Among the adult population, what is the clinical presentation of osteoporosis?											✓	
Diagnosis												
Among at-risk PMW, should bone mineral density measurement using dual energy x-ray absorptiometry be used to diagnose osteoporosis?	✓					✓				✓		✓
Management: Pharmacologic												
Among PMW with osteoporosis, are alendronate, ibandronate, zoledronate, denosumab, raloxifene effective in reducing vertebral, non-vertebral, hip fractures compared to placebo?	✓											
Among PMW with severe osteoporosis, are teriparatide, abaloparatide, and romosozumab effective in reducing vertebral, non-vertebral and hip fractures compared to placebo? How long should treatment duration be?	✓						✓			✓	✓	
Management: Non-Pharmacologic												
Among PMW women with osteoporosis, should calcium and vitamin D supplement be given to reduce the risk of fragility fractures?				✓	✓	✓					✓	
Among PMW with osteoporosis, should serum calcium and vitamin D levels be normal before initiation of anti-osteoporosis medication?	✓									✓	✓	
Surgical Management												
Among patients with previous fragility fractures, what is the effect of pharmacologic intervention on the risk of having a subsequent or second fracture?										✓		
Among patients with acute displaced fragility fractures of the distal radius, is early surgical intervention superior to conservative management to improve functionality?		✓										
Among patients who have painful osteoporotic compression fractures of the spine, is kyphoplasty superior to nonsurgical management for controlling pain and improvement of quality of life (QOL)?										✓		
Among patients who sustained fragility fractures of the hip, is early surgical intervention superior to delayed surgical intervention in improving overall survival, morbidity, mortality and functionality of patients?			✓									
Among patients with previous osteoporotic fragility fracture, will enrollment in a secondary fracture prevention program or fracture liaison service (FLS) improve treatment adherence and prevent re-fractures?										✓	✓	
Follow-up Care												
Among PMW receiving osteoporosis treatment, what is the appropriate interval between central DXA scans in monitoring treatment response?	✓									✓		
Among patients with recent fragility fracture, should an immediate referral to an osteoporosis specialist be done for better evaluation and management?	✓										✓	
Prevention												
Among at-risk PMW and old men, should calcium and/or Vitamin D supplementation be recommended for prevention of osteoporosis and fragility fractures?									✓		✓	
Among PMW and old men, what doses of calcium and Vitamin D are associated with reduced fragility fracture risk?											✓	✓
Among PMW and old men, what is the benefit of physical activity in the prevention of osteoporosis and fragility fractures?									✓		✓	
Among PMW and old men, does smoking cessation prevent osteoporosis and fragility fractures?									✓	✓	✓	
Among PMW and old men, what diet is effective in the prevention of osteoporosis?									✓	✓	✓	
Prevention – MHT												
Among at-risk postmenopausal women, should menopausal hormone therapy (MHT) be recommended to prevent fragility fractures? For how long will the duration of use be?								✓				
Among at-risk postmenopausal women, when should MHT be initiated to reduce fracture risk?								✓				
Among at-risk postmenopausal women, what hormone preparation should be used for fracture risk reduction?								✓				
Among peri- and postmenopausal women, what are the safety issues of MHT?								✓				
Among at-risk PMW, should SERMS be given as an alternative to MHT for the prevention of osteoporosis?								✓				
Among at-risk PMW on MHT for osteoporosis prevention, what adverse events should be monitored?								✓				

Statement of Authorship
All authors certified fulfillment of ICMJE authorship criteria.

CRediT Author Statement
JTLY: Conceptualization, Methodology, Investigation, Resources, Writing – review and editing, Visualization, Supervision, Project administration, Funding acquisition; **ASA:** Conceptualization, Methodology, Investigation, Resources; **IAT:** Conceptualization, Methodology, Investigation, Resources; **JB:** Investigation, Resources, Writing – review and editing; **EVMC:** Investigation, Resources, Writing – review and editing; **SSE:** Investigation, Resources, Writing – review and editing; **MEF:** Investigation, Resources, Writing – review and editing; **JGT:** Investigation, Resources, Writing – review and editing; **TGB:** Investigation, Resources, Writing – review and editing; **LLL:** Investigation, Resources, Writing – review and editing; **EIYM:** Investigation, Resources, Writing – review and editing; **EM:** Investigation, Resources, Writing – review and editing; **DM:** Investigation, Resources, Writing – review and editing; **QNS:** Investigation, Resources, Writing – review and editing; **NSOJ:** Investigation, Resources, Writing – review and editing; **MRAP:** Investigation, Resources, Writing – review and editing; **JP:** Investigation, Resources, Writing – review and editing; **JR:** Investigation, Resources, Writing – review and editing; **MCARP:** Investigation, Resources, Writing – review and editing; **HUC:** Investigation, Resources, Writing – review and editing; **AWW:** Writing – review and editing; **IGP:** Writing – review and editing.

Data Availability Statement
No datasets were generated or analyzed for this study.

Author Disclosure
The authors declared no conflict of interest.

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