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Review article

Current issues in evaluation and management of osteoporosis in Thailand

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ABSTRACT

Osteoporosis is a major public health issue in Thailand, which increased morbidity, mortality, and healthcare utilization. The objective of this review is to provide current perspectives on epidemiology, evaluation and management of osteoporosis in Thailand. According to epidemiologic data, the prevalence of osteoporosis and the incidence of hip fracture were comparable to the rest of the world. However, among Thai postmenopausal women, the prevalence of asymptomatic vertebral fracture was disproportionately high. In addition to established risk factors, conditions that may affect the risk of osteoporosis in the Thai population include certain genetic variants, thalassemia, vitamin D deficiency, and low dietary calcium intake, which requires further investigations to draw conclusions. In 2021, the Thai Osteoporosis Foundation released a new Clinical Practice Guideline that provides up-to-date evidence-based recommendations for evaluation and management of osteoporosis. Nonetheless, more research is required to provide local evidence in a variety of areas to guide management of osteoporosis in Thailand. These include epidemiology of distal radial fracture, the optimal intervention threshold of the Thai-specific Fracture Risk Assessment Tool model, screening for asymptomatic vertebral fracture, and the economic evaluation of osteoporosis management options, including fracture liaison service.

1. Introduction

Osteoporosis is the most common metabolic bone disorder, characterized by low bone mass and loss of bone connectivity and structural integrity, which increases the risk of fragility fracture [1]. It is estimated that more than 200 million people are affected by osteoporosis, and that 1 in every 3 women over the age of 50 years and 1 in every 5 men will suffer from fragility fractures during their lifetime [2]. Given that the epidemiology, burden, and resources for osteoporosis management differ across different countries, it is critical to investigate these factors in a context and population-specific manner.

Thailand is an upper middle-income Southeast Asian country with a gross national product (GDP) of approximately 500 billion USD in 2020 and a population of approximately 69 million people [3]. Since 2002, Thailand's major health scheme has been universal health coverage with referral up system, which provides all Thai citizens with access to essential preventive and curative health services [4]. As Thailand becomes an aging society, with a median age of the total population ranging from 45 to 54 years in 2020 [5], osteoporosis has emerged as a major public health concern, as its prevalence and disease burden increase exponentially with age [6–8]. The goal of this review is to provide current perspectives on epidemiology, evaluation and management of osteoporosis in Thailand.

2. Trend in prevalence and consequences of osteoporosis in Thailand

The prevalence of osteoporosis in the Thai population is comparable to the global prevalence, at around 20% in women and 10% in men [9], and has been relatively unchanged over the last 2 decades. According to a nationwide study conducted between 2000 and 2001, the age-adjusted prevalence of osteoporosis of the lumbar spine and femoral neck in Thai women over the age of 40 years was 19.8% and 13.6%, respectively [10]. In 2006, the age-

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adjusted prevalence of osteoporosis among Thai men was 12.6% and 4.6% at the femoral neck and lumbar spine, respectively [8]. In a more recent 2019 study, the prevalence of osteoporosis among early postmenopausal women visiting a tertiary care hospital's menopausal clinic was 21.3% [7].

There is an increasing trend of incidence of hip fracture. Based on the data from the Thai Osteoporosis Foundation study in 2006 compared with the Chiang Mai hip fracture study in 1997, the age-adjusted incidence of hip fracture increased by 2% per year 192.9 (males: 110.8; females: 272.1) to 253.3 (males: 135.9; females: 367.9) per 100,000 person-year [11,12]. Hip fracture risk was found to increase exponentially with age, from 19.5 per 100,000 person-year among those under the age of 55–1238.9 per 100,000 person-year among those 85 and older. Given the temporal increase in incidence, it is estimated that the number of hip fracture cases in Thailand will reach 34,246 cases in 2025 and 56,443 cases in 2050 [11].

Hip fracture is well-documented to be associated with an extremely high mortality rate, which is confirmed by a series of studies in the north of Thailand showing 1-year mortality rates of approximately 20% [13–17]. During 1997–1998, 1998–2003, 2006–2007 and 2014–2018, the 1-year mortality rate among patients sustaining hip fractures over the aged of 50 in Chiang Mai was 17%, 18% and 21%, respectively [13–15]. The 5-year and 10-year mortality rates among the 1998–2003 cohort were found to be 45% and 68%, respectively, which is approximately 8 times higher than the age-adjusted general population [13]. In a more recent prospective cohort study of 1004 patients with hip fracture aged over 50 years admitted at the same institution between 2014 and 2018, the cohort's mortality rate was approximately 14% (median follow-up duration 914 days), while another study of 1412 hip fracture patients aged over 50 years in Nan between 2014 and 2018 showed that the 1-year mortality rate was 19% [16,17]. Unsurprisingly, these studies revealed that factors influencing hip fracture mortality risk include increasing age, medical comorbidities and decreased mobility both before and after the fracture [13–17].

While the incidence of hip fracture in Thailand is comparable to that of other countries around the world [18], vertebral fracture is found to be disproportionately more common in the Thai population. The incidence of vertebral fracture in the Thai population was reported to be 3210 per 100,000 person-year in Thai women and 5450 per 100,000 person-year in Thai men between 1997 and 2002 [19]. These figures are significantly higher than the incidence rate reported in other countries, which range from 73 to 1393 per 100,000 person-year in women and 41 to 447 per 100,000 person-year in men [20]. Furthermore, a recent multi-center observational study in 1062 Thai postmenopausal women found that nearly one-third (29%) of the participants had undiagnosed vertebral fracture regardless of bone mineral density (BMD) status [21]. Another single-center study of 490 otherwise healthy postmenopausal women with low bone mass (defined by T-score −1 to −2.5 at the lumbar spine and/or femoral neck) found the same rate of morphometric vertebral fracture (29%), with advancing age and high Fracture Risk Assessment Tool (FRAX) score being the predictors of the outcome [22]. It is worth noting that there is a scarcity of data on the epidemiology of distal radial and other major osteoporotic fractures (ie, humoral and femoral fractures). To better characterize the burden of osteoporosis in Thailand, studies are needed to investigate the incidence and risk factors associated with this condition. Main findings of epidemiological studies on osteoporosis and fracture in Thailand are summarized in Table 1.

3. Potential specific risk factors of osteoporosis in the Thai population

Age, female sex, family history, premature menopause, lack of physical activity, low body mass index, smoking, calcium and vitamin D deficiency and the presence of systemic inflammatory diseases are all traditional risk factors for osteoporosis [23]. In this section, we looked at the specific factors that are believed to have a significant impact on the prevalence and risk of osteoporosis in the Thai population, which requires further investigations.

Table 1
Summary of epidemiological studies of osteoporosis and fracture in Thailand.

Studies	Population of study	Summary of main findings
Limpaphayom et al., 2001	1935 women aged 40–80 years randomly selected strata using multistage sampling and stratifying from six representative provinces of the country	The age-adjusted prevalence of osteoporosis of the lumbar spine and femoral neck was 19.8% and 13.6%, respectively
Pongchaiyakul et al., 2006	412 men aged 20–87 years recruited from Khon Kaen (Northeast-rural) and Bangkok (Central-urban).	The age-adjusted prevalence of osteoporosis among Thai men was 12.6% and 4.6% at the femoral neck and lumbar spine, respectively
Boonyachan et al., 2019	150 middle-aged postmenopausal women visited menopause clinic of Phramongkutklao Hospita	The prevalence of osteoporosis middle-aged postmenopausal women was 21.3%.
Wongtriratanachai et al., 2013	Hip fracture patients aged over 50 years recruited from hospitals in Chiang Mai, Thailand from in 2006–2007. Data were compared with hip fracture patients from the 1997 Chiang Mai hip fracture.	The age-adjusted incidence of hip fracture increased by 2% per year from 192.9 (males: 110.8; females: 272.1) to 253.3 (males: 135.9; females: 367.9) per 100,000 person-year
Chariyalertsak et al., 2001	330 patients with hip fracture admitted to Chiang Mai University Hospital from 1997 to 1998.	The 1-year mortality rate of sustaining hip fractures over the aged of 50 was 17%.
Vaseenon et al., 2010	632 patients with hip fracture admitted to Chiang Mai University Hospital from 1998 to 2003	The 1-year, 5-year and 10-year mortality rates of sustaining hip fractures over the aged of 50 were 18%, 45% and 68%, respectively.
Chaysri et al., 2015	275 patients with hip fracture admitted to Chiang Mai University Hospital from 2006 to 2007	1-year mortality rate sustaining hip fractures over the aged of 50 was 21%.
Atthakomol et al., 2020	775 patients with hip fracture admitted to Chiang Mai University Hospital from 2014 to 2018	The mortality rate of sustaining hip fractures over the aged of 50 was 14% (median follow-up duration 914 days)
Daraphongsataporn et al., 2020	1412 patients with hip fracture in Nan province between 2014 and 2018.	1-year mortality rate sustaining hip fractures over the aged of 50 was 19%.
Jirapunkul et al., 2008	332 elderly men and women with lateral thoracic and lumbar spine radiographs obtained between 1997 and 2002	The incidence of vertebral fracture in the Thai population was 3210 per 100,000 person-year in women and 5450 per 100,000 person-year in men between 1997 and 2002
Pongchaiyakul et al., 2020	1062 postmenopausal women recruited from five university hospital in a multi-center study	29% of the participants had undiagnosed vertebral fracture.
Wattanachanya et al., 2020	490 postmenopausal women with low bone mass (defined by T-score −1 to −2.5 at the lumbar spine and/or femoral neck) recruited in a single-center study	29% of the participants had morphometric vertebral fracture.

3.1. Genetic variations

Multiple genetic variations have been identified as being associated with BMD and the presence of osteoporosis in the Thai population, as shown in Table 2. These include polymorphisms of genes involved in estrogen signaling pathway (estrogen receptor α, *ERα*), vitamin D metabolism (vitamin D receptor, *VDR*; vitamin D-binding protein, *DBP*), folate metabolism (methylenetetrahydrofolate reductase, *MTHFR*) and osteogenesis (transforming growth factor-beta-1, *TGFβ-1;* inhibitor of DNA binding 4, *ID4*; α_2 Heremans–Schmid glycoprotein, *ASHG*) [24–31]. In studies of Thai postmenopausal women, however, genetic variations known to predispose osteoporosis in other populations (eg, *FDPS*, *LRP5* and *TNFSF11* genes) were not associated with osteoporosis [28,32,33]. Most genetic research in Thailand were undertaken in small groups with few participants, and none were reproduced to corroborate findings. A larger genome-wide association study in the Thai population is needed to establish strong results.

3.2. Vitamin D deficiency and low dietary calcium intake

Vitamin D and calcium deficiency are known to precipitate bone loss through secondary hyperparathyroidism, which causes bone resorption. Despite the fact that Thailand is a tropical country (latitude 5–20°N) with abundant sunlight throughout the year, a high prevalence of vitamin D deficiency and insufficiency (defined by serum 25-hydroxyvitamin D levels of < 20 and 20 – < 30 ng/mL, respectively) remains a major health problem that affects 30–70% of the Thai population in various settings [34,35]. This is thought to be due to use of sunscreen and avoidance of sunlight exposure in order to maintain a fair complexion, as well as the fact that Thai foods contain very few vitamin D-rich diets and that dairy products are not fortified with vitamin D [35]. It should be noted that only 13.6% of elderly males living in rural areas, compared with 48.0% of elderly males in urban areas had serum 25-hydroxyvitamin D level of less than 40 ng/mL, indicating that urban lifestyle is most likely a major cause of vitamin D deficiency in Thais [36,37].

In addition to vitamin D deficiency, low dietary calcium intake is believed to be another common risk factor for osteoporosis in the Thai population. In a survey of 436 healthy adults living in rural areas of Northeastern Thailand, 60% of men and 80% of women had less dietary calcium intake than half of the recommended level (< 400 mg/day), while 6% and 3% had an adequate intake of more than 800 mg/day, respectively [38]. This observation is supported by a more recent study in 213 patients with type 2 diabetes, which found that only 0.5% of patients reported getting at least 1000 mg/day from diets [39]. Another study in 1475 adults showed that only approximately 10% consumed adequate amount of calcium based on food frequency questionnaire [40]. Based on the questionnaires, it was also that although the subjects were aware of dietary sources of calcium and had positive attitudes towards calcium, most of them did not know the Thai daily recommendation intake for calcium [40]. Taken together, inadequate vitamin D and calcium intake is a major risk factor of osteoporosis in the Thai population. As a result, public health interventions are required to address this problem, which may include health education and dietary fortification of vitamin D and calcium.

3.3. Thalassemia and hemoglobinopathies

Thalassemia is well known to be a cause of low BMD and secondary osteoporosis through a variety of mechanisms including bone marrow expansion, dysregulated pro-osteoclastogenic factors, altered Wnt/β-catenin pathway and endocrinopathies secondary hemochromatosis [41]. It is estimated that approximately 1% of the Thai population has thalassemia disease, and more than 12,000 infants are born each year with thalassemia syndromes [42]. According to studies, the risk of fracture and bone loss correlated with the severity of thalassemia disease, and beta thalassemia posed a higher risk of fracture than alpha thalassemia [43–46]. However, there is no evidence on whether bone health is affected in alpha and beta thalassemia traits, as well as hemoglobin E carriers, who account for around 30% of the Thai population [42], which requires further investigations.

3.4. Socioeconomic status

According to research, socioeconomic status is another indicator for the risk of osteoporosis and fragility fractures [47,48]. Currently, socioeconomic inequality is increasing in Thailand and other

Table 2
Characteristics of studies that investigated genetic polymorphisms associated with osteoporosis or bone mineral density in Thailand.

Studies	Subjects	Main findings
Ongphiphadhanakul et al., 2001	228 postmenopausal women recruited by advertising to have BMD screening at Ramathibodi Hospital, Bangkok	*ERα* gene (rs2228480) GG genotype associated with osteoporosis
Songpatanasilp et al., 2011	235 postmenopausal women enrolled from the Phramongkutklao Hospital, Bangkok	*FDPS* gene (rs2297480) polymorphism not associated with osteoporosis
Utennam et al., 2012	228 postmenopausal women recruited by advertising to have BMD screening at Ramathibodi Hospital, Bangkok	*TGFβ-1* gene (rs1800470) CT and CC genotypes associated with decreased serum TGF-β1 levels, osteopenia and osteoporosis
Chupeerach et al., 2012	365 postmenopausal women attending the menopause clinic at Ramathibodi Hospital, Bangkok	*DBP* gene (rs4588) CC genotype associated with higher risk of radial BMD osteoporosis
Tongboonchoo et al., 2013	346 postmenopausal women attending the menopause clinic at Ramathibodi Hospital, Bangkok	*MTHFR* gene (rs1801133) CT genotype associated with osteopenia and osteoporosis
Chupeerach et al., 2014	160 postmenopausal women attending the menopause clinic at Ramathibodi Hospital, Bangkok	*ID4* gene (rs3798339) TT genotype associated with lower BMD
Sritara et al., 2014	1741 healthy workers from the Electricity Generating Authority of Thailand cohort	*ASHG* gene (rs2248690) polymorphism associated with BMD through fetuin-A and body mass index.
Kitjaroentham et al., 2016	277 postmenopausal women attending the menopause clinic at Ramathibodi Hospital, Bangkok	*LRP5* gene polymorphisms not associated with osteoporosis
Techapatiphandee et al., 2018	237 postmenopausal women (105 with osteoporosiss) recruited from Thammasat Hospital, Pathum Thani, and Ramathibodi Hospital, Bangkok	*VDR* gene (rs2228570) TT genotype associated with osteoporosis *TNFSF11* gene polymorphisms not associated with osteoporosis
Wajanavisit et al., 2015	66 postmenopausal women with hip fracture who underwent hip surgery at the Department of Orthopedics, Ramathibodi Hospital, Bangkok	*ERα* gene (rs2228480) GG genotype associated with osteoporosis

ASHG. α_2 Heremans–Schmid glycoprotein; BMD, Bone mineral density; *DBP*: Vitamin D-binding protein; *ERα,* Estrogen receptor α; *FDPS*: Farnesyl pyrophosphate synthase, *ID4*: Inhibitor of DNA binding 4, *LRP5,* Low-density lipoprotein receptor related protein 5; *MTHFR,* Methylenetetrahydrofolate reductase; *TGFβ-1,* transforming growth factor-beta-1; *TNFSF11,* Tumor Necrosis Factor Superfamily Member 11.

Southeast Asian countries [49]. While there is no direct evidence of the impact of socioeconomic status on the risk of osteoporosis, it has been demonstrated that the prevalence of osteoporosis in patients attending a private hospital was 12%, compared to the national prevalence of approximately 20% [7,8,10,50]. This could point to a disparity between patients who went to a private hospital and had private or social security insurance and those who used universal health coverage. Further research is required to investigate and address socioeconomic disparities and geographic differences in the risks of osteoporosis and fracture in the Thai population.

3.5. Geography, physical activity, and body composition

Individuals living in rural area (Khon Kaen province) had higher femoral neck BMD than those living in urban area (Bangkok) [51]. The observed discrepancy could be due to differences in physical activity, as it has been demonstrated in the Thai population that lower energy expenditure of 1682 kcal/day was related with a 1.7-fold greater risk of osteoporosis [52]. This could be further supported by the observation that individuals in the rural area had significantly higher lean mass and lower fat mass compared with those in the urban area [51]. While lean mass has a positive effect on BMD, the impact of fat mass appears to be sex-specific. In women, increased fat mass was positively associated with lumbar spine and femoral neck BMD, whereas in men, increased fat mass had a negative effect on femoral neck BMD [53].

4. Evaluation and management of osteoporosis in Thailand

4.1. The 2021 Thai Osteoporosis Foundation Clinical Practice Guidelines

The Thai Osteoporosis Foundation published the first Clinical Practice Guidelines (CPGs) in 2002 and has since updated the CPGs on a regular basis. The new CPGs was issued in 2021 [54]. This guideline was developed by an expert panel of the 4 Royal Colleges of Thailand (ie, the Orthopaedic Surgeons, Gynecologists and Obstetricians, Physiatrists, Radiologists) and 2 Associations of Endocrinologists and Rheumatologists. It provides a comprehensive positional statement on the diagnosis, prevention, and treatment of osteoporosis in Thailand. In comparison to the preceding 2017 CPGs, the new contents of the 2021 CPGs include suggestions on the following issues [54].

- Fracture risk stratification criteria to distinguish between patients with high and very high risk of fracture.
- Updated recommendations for management of individuals with very high risk of fracture, including the use of sequential treatment of teriparatide or romozosumab followed by antiresorptive therapy.
- Recommendations for osteoporosis management in patients who are unable to go to clinics to acquire their prescriptions due to COVID-19 pandemic-related limitations.
- Recommendations for evaluation and management of atypical femoral fracture and osteonecrosis of the jaw.
- Description and recommendations for multidisciplinary management of osteoporosis and fracture, including the use of Fracture Liaison Service.

4.2. Use of the Fracture Risk Assessment Tool (FRAX) in the Thai population

Established by the World Health Organization (WHO) in 2008, the FRAX is a model designed to evaluate the 10-year risk of hip and major osteoporotic fractures [55]. The FRAX model incorporates multiple risk factors for fragility fractures, including age, sex, prior fractures, and presence of conditions associated with secondary osteoporosis. It is generally recommended that osteoporotic pharmacotherapy be considered in postmenopausal women and men aged $\geq$ 50 years who have diagnosed osteoporosis or low bone mass with a 10-year probability of a major osteoporosis-related fracture of $\geq$ 20% or a hip fracture of $\geq$ 3% based on the FRAX score [56]. Since the Thai-specific FRAX model was available in 2012, and the tool was incorporated in the 2016 National CPG, the FRAX has been increasingly used in Thailand from 2010 to 2018 [57]. Using the Thai-specific FRAX model and the thresholds of $\geq$ 20% and $\geq$ 3%, it is estimated that 37.3% of the Thai postmenopausal women would be eligible for anti-osteoporosis therapy [58].

A few studies have been conducted in order to validate the use of FRAX in the Thai population. A retrospective study conducted between 2008 and 2010 revealed that the original FRAX model with the aforementioned thresholds of $\geq$ 20% and $\geq$ 3% had moderate and low accuracy in predicting 10-year risk of major osteoporotic fracture (73% sensitivity, 63% specificity) and hip fracture (62% sensitivity, 60% specificity), respectively [59,60]. In a more recent study in 2872 postmenopausal Thai women, using the receiver operating characteristic (ROC) curve to determine the optimal intervention threshold of the Thai-specific FRAX model, the optimal FRAX thresholds for hip fracture with and without BMD were 4% (82.2% sensitivity, 78.6% specificity) and 4.9% (71% sensitivity, 83% specificity), while the optimal FRAX thresholds for major osteoporotic fracture (MOF) with and without BMD were 8.9% (87% sensitivity, 71% specificity) and 9.8% (76% sensitivity, 77% specificity) [61]. As a result, these thresholds can be considered as population-specific cutoffs for the initiation of osteoporosis therapy in postmenopausal Thai women. Further studies are needed to confirm this finding and to further define appropriate FRAX thresholds in Thai men.

4.3. Evaluation of asymptomatic vertebral fracture

Vertebral fracture is the most common complication of osteoporosis, which can result in a variety of adverse consequences such as chronic pain, loss of height, and impaired daily activities [62]. The majority of patients with vertebral fractures are asymptomatic and diagnosed incidentally on BMD measurement or plain radiography. Individuals who have a single vertebral fracture are approximately 5 times more likely to have subsequent fractures and 2 to 3 times increased risk of hip fractures [63]. Therefore, presence of vertebral fracture in patients with osteoporosis indicates a high or very high risk of subsequent fragility fractures, necessitating antiresorptive or anabolic therapy. It is recommended that not only patients with osteoporosis, but also some individuals at risk whose BMD does not meet the threshold, be evaluated for asymptomatic vertebral fractures using vertebral imaging (ie, lateral spine X-ray or vertebral fracture assessment with DXA) [64,65].

As previous stated, Thailand has a disproportionately high incidence of vertebral fracture when compared to other countries. Although the explanation of the significant disparity in the rate of vertebral fracture is still unknown, it is thought to be due to differences in genetic predisposition, calcium intake, as well as occupation and type of physical activity of the sample cohort. Interestingly, in a multi-country comparative study of community dwelling subjects from Hong Kong, Thailand, Indonesia and Japan, 45% of the Thai participants reported that their longest occupation had been as a farmer, and that this factor was associated with 2.5-fold increased likelihood of vertebral fracture among female participants [66].

It is of particular interest given the findings that asymptomatic vertebral fracture was highly prevalent in Thailand, which rates ranging from 20 to 30% even among postmenopausal women under the age of 70 who did not meet the criteria for vertebral fracture imaging [21,22]. This suggests that screening for vertebral fractures in younger postmenopausal women is warranted. More research in needed to confirm the findings and determine the utility of this intervention.

4.4. Economic perspectives of osteoporosis treatment in Thailand

Osteoporosis and fragility fractures are major health and economic concerns since they represent a significant cost to health care systems. To illustrate, the median total cost per year for management of osteoporosis hip fracture in 2008 was estimated to be US$ 4210.60, with a cost per quality-adjusted life year (QALY) of US$ 6620.52, which is equivalent to approximately 79% of the Thai GDP per capita [67]. Therefore, understanding the economic impact of osteoporosis management in the Thai population is critical in order to wisely allocate the limited resources available to mitigate the problem.

In a cost-effectiveness analysis conducted in 2010, it was demonstrated that, when compared to the standard treatment of calcium plus vitamin D, zoledronic acid, followed by other bisphosphonates, was the most cost-effective treatment option for both primary and secondary fracture prevention in Thai postmenopausal women with osteoporosis [68]. Nevertheless, according to a 2013 study from the Health Intervention and Technology Assessment Program (HITAP), alendronate was the most cost-effective osteoporosis treatment among postmenopausal women over the age of 65 with osteoporosis, followed by zoledronic acid [69].

It should be noted that data appear to be conflicting whether bisphosphonates or denosumab were the most cost-effective treatment option for high-risk Thai postmenopausal women with preexisting fracture. In a cost-effectiveness study conducted in 2020 on high-risk women with osteoporosis (defined by femoral neck T-score of ≤ -2.5 and a history of vertebral fracture), denosumab resulted in the greatest number of life years and QALYs with higher reductions in the incidence of subsequent hip and vertebral fracture compared to patients who received no pharmacologic treatment. Furthermore, the incremental cost-effectiveness ratio (ICER) per QALY gained for denosumab versus no pharmacologic treatment (calcium plus vitamin D) was US$3587 and US$5976 for denosumab versus alendronate [70]. In contrast, another study published in 2021 found that bisphosphonates (alendronate or risedronate) were the most cost-effective treatment for Thai postmenopausal women aged $\geq$ 50 years old with BMD T-score ≤ -2.5 and a history of fractures (not limited to vertebral fracture), with the ICER per QALY gained of US$2997 for bisphosphonates, US$54,848 for denosumab and US$333,699 for teriparatide) [71].

In summary, bisphosphonates are widely recognized as cost-effective treatments for osteoporosis in Thai postmenopausal women. In addition, recent evidence also suggests that denosumab is cost-effective, particularly for high-risk postmenopausal women with a history of vertebral fracture. There is insufficient data to assess the cost-utility of osteoporosis treatment options in men and premenopausal women.

4.5. Studies on trabecular bone score (TBS)

Trabecular bone score (TBS) assessment is a novel technique to evaluate bone microarchitecture using DXA images of the lumbar spine. It involves using variograms to measure the differences in texture among the pixels [72]. A number of studies in Thailand have conducted to assess the reference values and fracture prediction of TBS. In a study of 1372 healthy participants who underwent BMD testing in Khon Kaen, peak TBS was obtained among females aged 30–49 years (mean ± SD: 1.42 ± 0.08) and males aged 30–59 years (mean ± SD: 1.42 ± 0.09) [73]. From 20 to 90 years of age, the rate of L1-L4 TBS decrease is 13.4% (0.27%/year) for females and 5.6% (0.11%/year) for males. Based on the normative value of TBS derived from this study, partially degraded and degraded microarchitecture were defined as L1-L4 TBS of 1.23–<1.34 for male and 1.20–<1.33 for female (T-score of -1 -< -2.5) and L1-L4 TBS of <1.23 for male and <1.20 for female (T-score of < -2.5), respectively [73]. Another study conducted in 848 healthy adults from the Electricity Generating Authority of Thailand (EGAT) cohorts revealed that TBS decreased between the ages of 30–80 years by 19.8% (0.40%/year) in females and 10.1 (0.20%/year) in males, respectively [74]. In addition, women with type 2 diabetes (T2D) had lower TBS than those without T2D (1.29 vs. 1.38, $P < 0.01$); however, the association between TBS and T2D was not shown after adjusting for age and body mass index [75].

According to EGAT cohort data, one standard deviation (SD) decrease in TBS was associated with approximately 1.3-fold greater risk of vertebral fracture in male. Similarly, in another study of 407 postmenopausal women from Police General Hospital in Bangkok, the odds ratio of fracture was 1.35 for a one SD decrease in TBS [76]. Additionally, combined low TBS and BMD was found to be associated with a 4-fold increased risk vertebral fracture among 86 patients with thalassemia [77].

4.6. Fracture liaison service (FLS) in Thailand

FLS is a multidisciplinary approach endorsed by the International Osteoporosis Foundation to reduce the risk of subsequent fracture in patients who have recently suffered a fragility fracture [78]. This service is implemented by identifying patients who are being treated for fractures in the hospital and providing them with access to osteoporosis care. FLS is currently being used in 17 medical centers in Thailand (9 in Bangkok, according to https://www.capturethefracture.org/), and has been shown in numerous studies, including 1 in Thailand, to improve the outcomes of osteoporosis-related fractures [79,80]. A comparison study of 100 hip fracture patients who participated in the FLS at the Police General Hospital in Bangkok from 2014 to 2015 versus 120 patients with hip fracture who did not attend the program at the same hospital in 2013 revealed that the FLS resulted in a significant decrease in the rate of secondary fracture from 30% to 0%, an increase in the rate of post-injury BMD follow up from 28% to 48%, and an increase in post-injury osteoporotic medication administration rate from 41% to 80%. However, no FLS-related mortality benefits was observed after 1 year [80]. In a more recent study of 489 hip fracture patients undergoing FLS at Siriaj hospital, the 1-year and 3-year mortality rates were 13.9% and 20.4% which were relatively lower than other published studies [81].

Despite limited data on the utility of FLS in Thailand, the 2021 Thai Osteoporosis Foundation CPG recommends that FLS be implemented to reduce the risk of subsequent fracture in patients with osteoporosis and osteoporotic fracture. In addition, patients with hip fractures should receive continuous care for at least 1 month after being discharged from the hospital in order to improve mobility and activities of daily living [51]. Further investigations are needed to determine the economic impact of FLS in Thai population.

5. Conclusions

Osteoporosis remains a major health issue in Thailand, with increased morbidity, mortality, and health-care utilization. Based on the available evidence, it is possible to conclude that additional efforts should be made to generate local evidence in a variety of areas to guide osteoporosis management in Thailand. These include, but are not limited to, 1) investigating the epidemiology of distal radial and other major osteoporotic fractures, 2) investigating secondary osteoporosis and population-specific risk factors for osteoporosis, 3) determining the optimal intervention threshold of the Thai-specific FRAX model, 4) determining the appropriate indications for screening for the highly prevalent asymptomatic vertebral fracture, and 5) assessing the cost-effectiveness of osteoporosis management options, including the FLS.

Conflicts of interest

The authors declare no competing interests.

Acknowledgments

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