Taiwanese Guidelines for the Prevention and Treatment of Osteoporosis
The Taiwanese Osteoporosis Association

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Taiwanese Guidelines for the Prevention and Treatment of Osteoporosis

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The Radiological Society of the Republic of China
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The Chinese Society of Immunology
Joint Reconstruction Society, R.O.C.
Society of Nuclear Medicine, Taiwan (R.O.C.)
Taiwan Academy of Physical Medicine and Rehabilitation
Taiwan Association of Obstetrics and Gynecology
Taiwan Association of Family Medicine
The Taiwanese Menopause Society
Taiwan Association of Gerontology and Geriatrics
Taiwan Spine Society
Taiwan Orthopaedic Research Society
Taiwan College of Family Physicians.
Taiwanese Guidelines for the Prevention and Treatment of Osteoporosis

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I. Introduction:

The purpose of this set of guidelines is to serve as a reference for healthcare providers to improve assessment of osteoporosis and to assist in the development of best osteoporosis management strategy for each individual patient. This work is based on relevant new regional and international guidelines including the International Osteoporosis Foundation (IOF) guidelines, the U.S. National Osteoporosis Foundation (NOF) guidelines, the United Kingdom National guidelines (the National Health service, NHS, and National Institute for Clinical Excellence, NICE), the Asia-Pacific consensus, the Singapore guidelines, the Japan guidelines, and the prior Taiwanese Osteoporosis Association (TOA) guidelines [Chinese Edition] (2007), and incorporates the latest advances in the diagnosis, prevention, and treatment of osteoporosis.

In order to review and update osteoporosis management, these guidelines now will include Taiwan-specific osteoporosis epidemiological data, medication adherences, the FRAX® 10-year fracture risk rate of assessment and application, also addresses the needs of men and postmenopausal women. The guidelines are based on evidence-based medicine and public health considerations, hoping to minimize the medical, social, and financial burdens imposed on the public health system by this disease. Recommendations are not limited to the reimbursement policy and scope of the National Health Insurance of Taiwan (Appendix I, and II). These guidelines will be revised every two years to meet the latest international consensus standards.

These guidelines have been endorsed by Taiwan Orthopaedic Association, The Endocrine Society of the Republic of China (Taiwan), The Radiological Society of the Republic of China, The Rheumatology Association of the Republic of China, The Chinese Society of Immunology, Joint Reconstruction Society, R.O.C, Society of Nuclear Medicine, Taiwan (R.O.C.), Taiwan Academy of Physical Medicine and Rehabilitation, Taiwan Association of Obstetrics and Gynecology, Taiwan Association of Family Medicine, The Taiwanese Menopause Society, Taiwan Association of Gerontology and Geriatrics, Taiwan Spine Society, Taiwan Orthopaedic Research Society and Taiwan College of Family Physicians.

II. The definition of osteoporosis:

Osteoporosis is defined as a disease characterized by low bone mass and structural deterioration of bone tissue, leading to bone fragility and an increased
susceptibility to fractures by WHO (1994), and according to the National Institutes of Health (NIH) new perspectives, osteoporosis is defined as a skeletal disorder characterized by compromised bone strength predisposing to an increased risk of fracture. Bone strength reflects the integration of two main features: bone density and bone quality. Bone quality refers to architecture, turnover, damage accumulation and mineralization (2000).

III. The principles of the diagnosis of osteoporosis:

A clinical diagnosis can be made in individuals who sustain a low-trauma fracture, or when the diagnosis of osteoporosis is established by the measurement of spine and hip BMD as less than or equal to 2.5 standard deviations below the young normal mean. The most widely validated technique to measure BMD is central dual energy X-ray absorptiometry (DXA), and BMD measured by DXA at the one-third (33 percent) radius site can be used to assist in making the diagnosis of osteoporosis when the spine and hip cannot be measured (2010 the ISCD of the Asia-Pacific consensus). Central DXA measurements at the spine and hip are preferred when making therapeutic decisions. The Caucasian female normative database is used as a reference for T-scores which should be applicable to Taiwanese postmenopausal women, and may also be applied to Taiwanese men. Based on the World Health Organization (WHO) diagnostic classification, subjects are categorized as normal bone: T-score better than –1; osteopenia (low bone mass): T-score between -1 and -2.5; osteoporosis: T-score less than -2.5; established (severe) osteoporosis: T-score less than -2.5 and the presence of a non-traumatic or low-traumatic fracture. In addition, any vertebral body deformation of more than 20%, also can be diagnosed as osteoporosis.

IV. The impact of osteoporosis on the health of the people of Taiwan:

As life expectancies increase, osteoporosis remains the most common bone disease among humans, and it represents a major public health problem. Fractures associated with osteoporosis have been proven to cause considerable disability, loss of quality of life and mortality. The most common fractures are those of the vertebrae and hip. In 1993, a Taiwan epidemiological survey, showed that for urban women and
men that were over 65 years old, 19.8% and 12.5%, respectively, had more than one vertebral fracture. This study also estimated that 30% of postmenopausal women had osteoporosis based on BMD. National Health Insurance data, from 1999-2001 in Taiwan showed that the diagnosis of osteoporosis in adults over the age of 50 was underestimated. The 2005-2008 National Nutrition Survey in Taiwan also reported that for men and women over the age of 50, osteoporosis prevalence was 23.9% and 38.3%, respectively. According to the National Health Insurance database from 1996 through 2002, overall incidence of hip fracture in those individuals over 65, had increased from 49 to 64 cases per one million people annually. Since the life expectancy for Taiwanese women in 2006 was 80.8 years and for Taiwanese men was 74.6 years, that could mean that approximately one-third of women and one-fifth of men in their lifetime would have one vertebral, hip or wrist fracture. In Taiwan, based on the national health care records, the mortality rate of hip fractures in the elderly within the first year for women and men is about 15% and 22%, respectively, with the main cause of death being bedridden related infection. In addition the average medical costs of fracture per case are more than NT $100,000 (roughly US$ 3,300) for the acute care and may consume a significant amount of family and social resources.

Furthermore, according to the 2006-2007 Taiwan National Health Insurance hip fracture data, only 27% of hip fracture patients received bone density examinations, and 34% received drug treatment of osteoporosis, showing that many patients were not given the opportunity to have appropriate test to diagnose osteoporosis and, not being treated. The awareness of osteoporosis management among patients and physicians clearly needs to be improved.

V. Osteoporosis screening

The osteoporosis screening should analyze the existence of a variety of clinical risk factors (CRF). The IOF One-Minute Osteoporosis Risk Test, which analyzes personal lifestyle, family history, medical history and drug history, is worth considering. If any obvious CRFs exist, bone mineral density (BMD) should be assessed. Women aged 65 and older have greater fracture risk and should be referred following the female osteoporotic assessment and treatment guidelines for early prevention and detection in Taiwan. Elderly men aged 65 and older have greater fracture risk, and are also advised to confer on the male osteoporosis assessment and treatment guidelines for early screening for osteoporosis in Taiwan.

Clinically, it is possible to screen for osteoporosis by a physical examination. However, X-ray or DXA is needed to be arranged to confirm such a diagnosis.
i. Body height at present and in the youth

If the body height at present is lower than that in the youth by 3 cm or more, osteoporosis should be highly suspected. At the same time, the regular follow-up of height change every six months is also helpful to reveal whether new lumbar osteoporotic fractures have occurred. However, many people may be unable to clearly remember their height in their youth and such data can not explicitly be used.

ii. Body weight

Body weight and bone mineral density are inversely related. Being underweight is also one of the risk factors for osteoporosis. Osteoporosis should be highly suspected especially when the body mass index [weight (kg) / height squared (in meters)] is less than 18.5 kg/m². The Osteoporosis Self-assessment Tool for Asians (OSTA) is a simple self-assessment tool for women. From the two major variables (age and weight), we found that people with either lower weight or older age frequently suffered from osteoporosis (Figure 1). A simple and clear spreadsheet with weight and age classification is provided below, enabling the quick self-assessment of the potential risk.

![Figure 1. Osteoporosis Self-assessment Tool for Asians (OSTA)](image)

iii. Wall-occiput distance (WOD)
This is a quick method of screening for latent thoracic vertebral compression fractures. Ask the patient to stand up and look straight forward and then measure the horizontal distance between his/her occiput and the wall. The normal distance is almost zero or less than 1 cm. If the distance is greater than 3 cm, then abnormality should be highly suspected. If the distance is greater than 6 cm (or a fist distance), it is almost certainly abnormal (Figure 2A).

iv. Rib-pelvis distance (RPD)

This is also a quick method that can be utilized to screen for latent lumbar vertebral compression fractures. Ask the patient to stand up and lift his/her hands evenly. We then measure the vertical distance between the inferior margin of the ribs and the superior margin of iliac crest. The normal distance is 2 to 3 fingerbreadths or greater than 5 cm. If the distance is less than one fingerbreadth (2 cm), vertebral abnormality is almost certainly confirmed (Figure 2B, adapted from JAMA 2004;292:2890-2900).
VI. Osteoporosis diagnosis

Osteoporosis diagnosis includes low-impact fractures made via clinical history. The most common sites of bone fractures include distal forearm, hip, or vertebrae (compression fracture). Osteoporosis is also diagnosed according to the T-score derived from bone mineral density.

i. Simple X-ray plain film

Traditionally, more than 30% loss of bone mineral density is needed for an X-ray to be diagnosed as osteoporosis. Vertebral fractures are not always obvious and are often clinically overlooked. Many patients have T-scores of bone mineral density that are higher than -2.5, but their lateral view of their thoracolumbar X-ray films (T3 to L4) still show vertebral compression fractures. Therefore X-ray screening of osteoporosis still has its role to play. Vertebral compression fracture interpretation using Genant's semiquantitative technique classification (Figure 3) are shown as below (adapted from the J Bone Miner Res 1993; 8:1137-1148.). In brief, a vertebral height difference greater than 4 mm or deformity by more than 20% is diagnosed as a mild (Grade I) compression fracture when comparing anteroposterior diameter (wedge shape), or anteroposterior and central diameter (biconcave shape) of the same spine. Presence of compression fracture of one vertebra increases the risk of new fracture of adjacent vertebrae and active treatment is therefore warranted. When compression fractures of T7 and above are found, the existence of other diseases should be considered (such as tuberculosis, bone metastases, multiple myeloma, etc).

Figure 3

![Bone mineral density measurement](image)
Bone mineral density (BMD) should be measured at both PA spine and hip regions by the central dual energy X-ray absorptiometry (DXA). Degenerative spondylosis may result in an overestimation of the lumbar BMD measurement. If the PA spine and hip regions can not be measured or interpreted, the 1/3 of the distal forearm BMD is preferred. The vertebral fracture assessment (VFA) has now been discussed extensively. However, VFA can only provide information regarding spinal compression, and can not provide a final diagnosis of osteoporosis. Each DXA machine should have the least significant changes (LSC) derived from its own technician for reference. The details of LSC can be obtained from the 2010 Asia-Pacific consensus of the ISCD official position (www.iscd.org.tw). As there is no significant difference of fracture rate between Caucasians and Taiwanese, the WHO criteria of the osteoporotic diagnosis for Caucasian postmenopausal women can be adapted for postmenopausal women in Taiwan. Considering the guidelines from ISCD and other countries, the criteria can also be applied to elderly males. When the T-score of BMD equals to -1.0 SD or higher (compared to 20-29 y/o young Asian references), a patient will be classified as normal.

Although quantitative ultrasound (QUS) and peripheral DXA (pDXA) have been adapted to the WHO classification of DXA T-score cutoff for clinical diagnosis of postmenopausal osteoporosis, neither evidence-based diagnostic criteria nor consensus of interventional threshold have been well-established for most of the non-central DXA devices. Therefore, these devices should be applied for preliminary screening only, not for diagnosis or monitoring. Whenever an abnormality has been detected by these devices, Central DXA should be arranged for clinical confirmation. If any discordance in the findings between other modalities and central DXA are noted, it is recommended that clinicians rely on the central DXA report.

Who should be suggested as a candidate to receive BMD measurement? According to the 2008 National Osteoporosis Foundation (NOF) and 2010 Asia-Pacific consensus of ISCD official position, the indications in Taiwan are as follows:

1. Women aged 65 and older or men aged 70 and older.
2. Postmenopausal women under age 65 with risk factors for fracture.
3. Women during the menopausal transition with clinical risk factors for fracture, such as low body weight, prior fracture, or high-risk medication use.
4. Men aged between 50 and 70 with clinical risk factors for fracture.
5. Adults with a fragility fracture (low-impact or non-traumatic fracture).
6. Adults with a disease or condition associated with low bone mass or bone loss.
7. Adults taking medications associated with low bone mass or bone loss.
8. Anyone being considered for pharmacologic therapy.
9. Anyone being treated, to monitor treatment effect.
10. Anyone not receiving therapy in whom evidence of bone loss would lead to treatment.

ii. Bone turnover marker

Bone turnover markers cannot be used for clinical diagnosis, but can be used as references to help evaluate the changing speed of bone loss. At 3-6 months after taking anti-osteoporotic medications, blood or urine monitoring of bone turnover markers can be helpful in determining the amelioration of bone loss.

iii. Monitoring with BMD

(1) In untreated patients, monitoring with BMD is not indicated within one year (except for Glucocorticoid induced osteoporosis, GIO) and monitoring after two years is generally recommended.
(2) Nearly all pharmaceutical studies reveal significant fracture risk reduction with more than one year interventions. Taking medication for at least one year (optimal two), is preferred before the monitoring of therapeutic response with DXA.
(3) A significant change was confirmed by therapeutic BMD differences more than LSC. In terms of the available DXA devices, differences more than 3–6% at hip or 2–4% at PA spine by the same device is commonly suggested.

VII. Clinical Application of FRAX®

The FRAX® (fracture risk assessment tool) algorithm (Figure 4) has been promoted by IOF and the WHO. The probability of 10-year major osteoporotic fracture (spine, forearm, hip and shoulder) or hip fracture can be estimated from the medical history obtained from patients. FRAX not only provides information for the prevention and treatment of osteoporosis, but also helps to avoid fracture or sequels that result from severe osteoporosis. The clinical information needed for the FRAX® includes:

1. Country or Race (please choose: Taiwan)
2. Age
3. Sex
4. Body weight (kg)
5. Body height (cm)
6. Previous fracture (non-traumatic, low-impact)
7. Parent fractured hip
8. Current smoking
9. Corticosteroids
10. Rheumatoid arthritis
11. Secondary osteoporosis
12. Alcohol intake
13. Femoral neck BMD

In clinical practice, it is important to select country-specific FRAX® calculator. The reference data from Taiwan is readily available on the web with traditional Chinese format. It is also important to note that the FRAX® algorithm is only applicable for untreated patients between 40 and 90 years of age. If the patient is less than 40 or over 90, the age will be calculated as 40 and 90, respectively. The last item is designed for entering the femoral neck BMD and type of DXA device, with T-score as a second choice. If the BMD is not available, the probability of fracture risk can be calculated without BMD. When the probability of fracture risk is intermediate, the BMD measurement is indicated for the ascertainment of fracture risk.

Patients with high fracture risk should be treated aggressively when there is a 10-year probability of major osteoporosis related fracture (spine, forearm, hip and shoulder) that is ≥20% or a 10-year probability of hip fracture that is ≥3% based on the Taiwan-adapted FRAX® algorithm.

Please refer to website: [http://www.shef.ac.uk/FRAX/tool.jsp?lang=cht](http://www.shef.ac.uk/FRAX/tool.jsp?lang=cht)

**Figure 4. FRAX calculator**
VIII. Drug therapy for osteoporosis and their specific side effects

The ultimate purpose of preventing and treating osteoporosis is to reduce the occurrence of new fractures. Many large-scale clinical trials have proven the efficacy of many osteoporosis drugs. These drugs are generally also useful for secondary osteoporosis such as glucocorticoid induced osteoporosis (GIO), and for male osteoporosis. However, fractures still occur despite these regimes. The reasons for this may be other contributing factors such as trauma or falls. Our guideline emphasizes that fall prevention and nutrition (especially calcium and vitamin D) are also very important.

Before and during the medical treatment, the patients should be informed that it generally takes one year to show significant efficacy, and that if medication adherence is less than 50%, the effect is limited. After discontinuation of medications other than bisphosphonate, bone loss is anticipated. This is especially true for teriparatide because bone turnover is accelerated with teriparatide treatment. Like other chronic diseases, each patient should make a lifelong plan for osteoporosis treatment. Bisphosphonate agents have long lasting effects because they stay in bone tissues years after discontinuation. Current evidence shows that for patients at relatively low risk of fracture, after five years of oral alendronate or three years of intravenous zolendronic acid, the treatment may be discontinued, and restarted only if the patients show significant bone loss, develop new fractures, or show new evidence of fracture risks.
Figure 5. Algorithm for osteoporosis evaluation and treatment for Taiwanese men and women (December 2011)

Enforce dietary calcium and vitamin D intake, avoid tobacco and alcohol, and maintain reasonable weight, exercise, and fall prevention for all.

Before age 50
- Avoid risk factors dietary enforcement
  - NO BMD unless with risk factors

50 (menopause) to 65
- No risk (#1)
  - No BMD

Over 65
- 1~2 risk factors
  - BMD
- > 2 risk factors or high risk from FRAX®
  - BMD to ascertain risk

Osteoporotic fracture after age 50 (#2)
- Regular follow-up and re-evaluation
- Low risk
- Mod/high risk (#3)

Fall prevention
Education
Medications (Table 1)
Re-evaluation
Specialist referral (#4, #5)
(#1): Risk factors include: Family history, alcohol, tobacco, glucocorticoid, fracture history, excessive thyroid, parathyroid, adrenal hormones, and propensity to fall.

(#2): Fractures other than at facial, cranium and phalangeal bones.

(#3): High risk from FRAX® usually means hip fracture risk of $\geq 3\%$ or major osteoporotic fracture risk $\geq 20\%$ in the next ten years.

(#4): An osteoporosis specialist in Taiwan refers to a board certified physician that has ISCD certification and has passed the related TOA training courses.

(#5): The following patients are encouraged to visit osteoporosis specialists:
   a. Secondary osteoporosis.
   b. Can not take bisphosphonate or calcium.
   d. Continues to have fracture(s) during treatment.
### Table 1. Medications to treat osteoporosis available in Taiwan

<table>
<thead>
<tr>
<th>Medication</th>
<th>Adm. Frequency</th>
<th>Vert. fracture</th>
<th>Non-vert.</th>
<th>male</th>
<th>GIO</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Bone forming agent:</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Teriparatide</td>
<td>(daily)</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td><strong>Anti resorption agent:</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bisphosphonate:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alendronate</td>
<td>(weekly)</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Zoledronate</td>
<td>(annually)</td>
<td>+</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Ibandronate</td>
<td>(quarterly)</td>
<td>+</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Denosumab</td>
<td>(semiannually)</td>
<td>+</td>
<td>+</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td><strong>Mixed forming and antiresorptive:</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Strontium ranelate</td>
<td>(daily)</td>
<td>+</td>
<td>±</td>
<td>N/A</td>
<td>N/A</td>
</tr>
</tbody>
</table>

+: good evidence
±: equivocal evidence
N/A: no evidence available or not applicable.

mab- monoclonal antibody; RANKL, receptor activator of nuclear factor kappa-B ligand; SERM- Selective estrogen receptor modulators; STEAR-Selective Tissue Estrogenic Activity Regulator The specific side effects of bisphosphonates include, osteonecrosis of the jaw and atypical subtrochanteric fractures.

After receiving bisphosphonate treatment for several years, a small number of patients may be at risk to develop osteomyelitis and osteonecrosis of maxilla or mandible. Most of these complications occur after three years of treatment. The symptoms include pain, swelling, numbness of lips, open wound of gum, discharge, fistula, loss of teeth and so on. The two typical signs are pain and exposure of the jaw bone for more than eight weeks. To prevent this, the patients undergoing bisphosphonate treatment are advised to clearly tell their dentists about the bisphosphonate medications they are receiving and to avoid any unnecessarily invasive dental procedures. If the procedures are unavoidable, bisphosphonates should be discontinued for more than three months before the procedure, and resumed only after the wound heals. Patients should be informed that by doing so, osteonecrosis of the jaw bones may still occur. It is also advised that all the patients should maintain good oral hygiene, and have regular semiannual dental check-ups, before and during bisphosphonate treatment.

A small proportion of patients receiving bisphosphonates may have disturbances in bone remodeling, so that microfractures may accumulate at vulnerable sites. The
results may be a fatigue fracture at the mild-disphyseal or subtrochanteric region of femurs. Before the frank fractures occur, patients may have vague pain at their thighs. An X-ray film may show the typical signs of thickened cortical bones and beak-shaped stress fracture and callus formation.

IX. Glucocorticoid Induced Osteoporosis (GIO)

Although glucocorticoids can effectively be used in the management of several inflammatory diseases, their use is related to subsequent morbidity and mortality. Osteoporosis and associated fragility fracture constitute morbid complications and are associated with significant pain and disability. A rapid decline in BMD begins within the first 3 months of glucocorticoid use and peaks at 6 months, followed by a slower steady loss with continuous use. Even long term use of low dose glucocorticoid (prednisolone or other agents at equivalent dose as low as 2.5-7.5 mg daily) is associated with an increased risk of both vertebral and nonvertebral fractures.

In 2001, the American College of Rheumatology (ACR) published their first “Recommendations for the Prevention and Treatment of Glucocorticoid-Induced Osteoporosis”. Updated approaches to identify patients at highest risk for fracture have also been developed. BMD alone may not be the only reliable diagnostic approach for some patients receiving glucocorticoids, since fracture in patients receiving glucocorticoids may occur independently of a decline in bone mass. In 2008, the NOF incorporated the 10-year absolute probability of fracture calculated by the FRAX® tool into their guidelines for the treatment and prevention of osteoporosis and included glucocorticoid use as a clinical risk factor. Furthermore, the methodology for guideline development has evolved since 2001, when a more informal consensus approach was used. Collectively, these factors support the need for a reappraisal and update of the 2001 recommendations. A modified version of GIO recommendations was proposed by the ACR in 2010. The figures below illustrate the recommendations by TOA for GIO in 2011 based on the 2010 ACR guideline.
Figure 6. Approach to typical postmenopausal women and men age >50 years with a history of glucocorticoid use at different risk levels predicted by FRAX®

1. Low body mass index, parental history of hip fracture, current smoking, >3 alcoholic drinks per day, higher daily glucocorticoid dose, higher cumulative glucocorticoid dose, intravenous pulse glucocorticoid usage, declining central bone mineral density measurement that exceeds the least significant change

2. The FRAX® tool has been developed by WHO to evaluate fracture risk of patients. Web site: [http://www.shef.ac.uk/FRAX/tool.jsp?lang=cht](http://www.shef.ac.uk/FRAX/tool.jsp?lang=cht)

3. For low- and medium-risk patients, recommendations are for an anticipated or treatment duration of >3 months of glucocorticoids.

4. Ten-year risk of major osteoporotic fracture

Monitoring strategies for patients on glucocorticoid therapy include: fall risk assessment, dual x-ray absorptiometry, weight-bearing activities, smoking cessation, avoidance of excessive alcohol, adequate calcium intake and vitamin D supplementation.
Figure 7. Approach to premenopausal women and men age <50 years initiating or receiving glucocorticoid therapy

Monitoring strategies for patients on glucocorticoid therapy include: fall risk assessment, dual x-ray absorptiometry, weight-bearing activities, smoking cessation, avoidance of excessive alcohol, adequate calcium intake and vitamin D.
X. Nonpharmacological management of osteoporosis

Increasing peak bone mass, decreasing bone loss and preventing falls are important to prevent osteoporosis and related fractures. Nonpharmacological management strategies include living a good lifestyle, adequate intake of calcium and vitamin D, avoiding smoking and alcohol, muscle strengthening and balance exercises, ensuring a safe home and public environment, as well as using protective devices to prevent fracture. Recommendations on calcium and vitamin D intake, and exercise are discussed below.

1. Calcium and vitamin D

Adequate intake of calcium and vitamin D is essential for skeletal health. Intake of low amounts of dietary calcium has been demonstrated to increase the risk of hip fractures, whereas adequate intake of calcium and vitamin D could decrease the risk of hip and nonvertebral fractures in the elderly. A meta-analysis study demonstrated that the intake of calcium and vitamin D decreases the risk of fracture by 12% (RR 0.88, 95% CI 0.83-0.95; p=0.0004) (Tang B, et al. 2007, Kanis JA, et al., 2008). Daily intake of adequate calcium and vitamin D is convenient and economical with regards to the prevention of osteoporosis and decreasing fracture risk.

The National Osteoporosis Foundation (NOF) USA (2008) recommended daily intake of adequate amount of calcium (at least 1,200 mg per day) and vitamin D (800-1,000 IU per day) with supplements when appropriate for postmenopausal women and men aged 50 and older. Other studies recommended the intake of at least 1,000 mg/day calcium in the patients with osteoporosis (Tang B, et al. 2007, Kanis JA, et al., 2008). Dairy products are one of the most convenient sources of calcium, as are beans, cereals, almonds, dark green vegetables (such as broccoli), sesame, dried day lily flower, seaweed, laminaria japonica, mushrooms, dry small fishes, salmon, pilchards, and nostoc commune var. flagelliforme, and so on. Consultation with a dietitian or the use of a simple assessment method can help when calculating the calcium content of an individual’s diet. Calcium supplements can be used if necessary. However, intakes of more than 1,200 to 1,500 mg per day have no additional benefit and may actually increase the risk of renal stones or cardiovascular disease (NOF, 2008).

The physiological functions of vitamin D are involved in the intestinal absorption of calcium, bone metabolism, muscle function, balance and decreasing falls. Both children and adults require adequate vitamin D supplement to maintain skeletal health. Studies have demonstrated that inadequate intake of vitamin D is associated with increased bone loss, low BMD, and increased fall risks.
Vitamin D can be synthesized after sunlight exposure, or can come from either dietary sources or supplements. The biosynthesis of vitamin D is initiated when the skin is exposed to UVB in the sunshine. The synthesis of vitamin D in the skin is not easy to measure in clinical practice. The amount of biosynthesis is dependent on the exposure timing, season, skin color, and so on. For example, the synthesis of vitamin D decreases in the summer season, influenced by the use of sun-shielding windows or sunscreen lotion, people with deep skin color, residing in the high altitude or in regions with heavy air pollution, and so on. The main dietary sources that include vitamin D are products such as fortified milk and cereals, egg yolks, oily fish and seafood such as tuna, salmon, shrimp, as well as fish liver oils. Some calcium supplements and vitamins supplements also contain vitamin D, but the specific amounts should be checked before use.

Vitamin D deficiency and protein deficiency are common in the elderly, especially in those with malabsorption, chronic renal dysfunction, restricted sun exposure, and chronic illness. Daily doses of vitamin D greater than 700 IU can reduce the risk of falling and fractures (Bischoff-Ferrari HA, et al., 1999, Kanis JA, et al., 2008). NOF recommends daily intake of 400 to 800 international units (IU) vitamin D3 for people younger than 50 years, whereas those aged 50 and older need daily supplements of 800 to 1,000 IU vitamin D3 to maintain serum level of 25(OH)D above 30 ng/ml (75 nmol/L). Other studies also recommend a daily intake of at least 800 IU vitamin D3 in the management of patients with osteoporosis (Tang B, et al. 2007, Kanis JA, et al., 2008). The safe upper limit for vitamin D intake for general adults has been set at 2,000 IU per day (NOF, 2008). A regular monitoring of serum 25(OH)D level is needed for those patients who need to take large amounts to maintain optimal 25(OH)D levels in the serum.

2. Exercise

Exercise can increase BMD, muscle strength, improve balance function and decrease the risk of falls and fractures whereas too much exercise may sometimes be detrimental to the skeletal health (Sinaki M, 2007; National Institutes of Health, 2000). To date there has been no large scale randomized clinical trial assessing the effects of exercise on fractures due to limitations related to ethical considerations and the difficulties of study design.

The types of exercise that are suitable include weight bearing exercise, resistance exercise, weight training, posturing exercise, flexibility exercise, and balance exercise, and so on. Both bone and muscle have adequate impact during weight bearing exercises using legs to support the body. Examples of weight bearing exercises include walking, jogging, Tai Chi Chuan, stair climbing, dancing and tennis. Muscle
strengthening exercise programs include weight training and resistance exercises. In general, weight training, weight bearing aerobic exercise, high impact exercise and resistance exercise are more suitable for premenopausal women, whereas regular aerobic exercise, resistance exercise, and balance training is more suitable for postmenopausal women. Exercise activities such as jogging, Tai Chi Chuan, racquet sports, and swimming are more suitable for older adults. (Sinaki M, 2007; National Institutes of Health, 2000)

There are a number of evidence-based studies that show:

(1) Exercising during childhood and adolescent periods can maximize peak bone mass, decrease the risk of osteoporosis, postpone the age of fracture, as well as decrease the incidence of fracture later in life. Therefore regular weight bearing and muscle strengthening exercise programs are recommended daily.

(2) Weight bearing aerobic exercise, hip loading exercise, and impact exercise during the premenopausal period can obviously improve the lumbar spine BMD. And resistance exercise can increase femur BMD, strengthen muscles, improve balance and decrease the likelihood of falls.

(3) Aerobic exercise, resistance exercise, or combined aerobic and resistance exercise programs during postmenopausal period can obviously decrease bone loss, improve physical function, and maintain independence. Postmenopausal women have to adjust the amount of exercise they perform according to their levels of fitness. Women that have high levels of fitness can do more types of exercises, such as aerobic exercise, various lifting exercises, and gymnastics. However, exercise intensity should be modified for those with medical illness and low level of fitness.

(4) There is no conclusive statement on the effect of exercise on BMD in the elderly. In practical terms we need to take into account relatively compromised cardiopulmonary function, muscle weakness, poor balance and coordination. The elderly should avoid fast exercises or high-impact exercises in order to prevent falls and fractures, especially those with comorbidities. Walk-jogging, Tai Chi Chuan, and gymnastics are clearly more suitable for the elderly. Furthermore, if the elderly begin such exercise programs when they are young, such as tennis or hiking, they can continue such exercises but need careful monitoring with regards to related safety issues.

Regular weight bearing exercise and muscle strengthening exercise will improve protection response ability, muscle strength, and posture and balance function that will help to decrease the risk of falls and fractures. However, these aforementioned benefits can not be easily maintained after stopping the exercise program. NOF recommends a lifelong exercise program to maintain full health and to prevent the development of osteoporosis. Patients with osteoporosis should consult their clinical
doctors for a proper assessment before starting any new or strenuous exercise program. Any patient who sustains a fracture should receive proper medical and surgical therapy with use of orthosis when necessary, increase sitting and ambulation time as needed, and participate in an appropriate exercise program to enhance recovery to normal daily life.

References

3. Prevention of osteoporosis and osteoporotic fractures in Asia: recommendation statements from the Strong Bone Asia conference.

Appendix I. Reimbursement regulations for DXA from the National Taiwan Health Insurance Bureau (in effective since April, 1st, 2006)

1. Endocrinological disorders that may accelerate bone loss: (limited to hyperparathyroidism requiring treatment, hyperadrenalism, pituitary disorders that affect calcium metabolism, hyperthyroidism, iatrogenic Cushing syndrome)
2. Non-traumatic fracture
3. Postmenopausal women or women older than 50 year of age who are treated with anti-ostoporotic drugs, to monitor treatment effect
4. Prostate cancer patients before and after receiving anti-androgen therapy (if indicated)

If the beneficiary plans to receive repeated DXA, the minimal allowed interval is at least 1 year apart. Also, the total allowed reimbursements for DXA are 3 times.

Screening DXA is not reimbursed.

Appendix II. Reimbursement regulations for anti-osteoporotic drugs from the National Health Insurance Bureau, Taiwan (in effect since January 1st, 2011).

3.2.2. Active vitamin D3 preparations (alfacalcidol; calcitriol) are reimbursed for the following diseases:
(1). Vitamin D dependent rickets or hypophosphatemic osteomalacia (a diagnostic statement by a medical center should be attached).
(2). Hypoparathyroidism. (a medical record should be attached)
(3). Hypocalcemia associated with renal insufficiency of chronic renal diseases.
(4). Postmenopausal osteoporosis with vertebral or hip fracture(s).

5.6. Drugs for osteoporosis

5.6.1. Antiresorptive agents
(1). Calcitonin preparations: salmon calcitonin nasal spray injection.
(2). Bisphophonate: alendronate (such as Fosamax®), zolendronic acid 5mg (such as Aclasta® 5mg/100ml solution for infusion), risedronate (such as Actonel®), ibandronate 3mg/3ml (such as Bonviva® 3mg/ml for injection).
(3). Selective estrogen receptor modulators (SERMs), Raloxifene (such as Evista® 60mg tablets).
(4). Human monoclonal antibody for RANKL: denosumab 60mg/ml (such as Prolia® 60ml/1ml for injection).

5.6.2. Regulations of reimbursement for antiresorptive drugs.
(1). Postmenopausal women with a DXA BMD T-score ≤ -2.5, and at least one spine or hip fracture; or a DXA BMD T-score between -1 and -2.5, and at least two fractures at either spine or hip. Alendronate and zolendronic acid are also reimbursed for men with same conditions.
(2). Combination of other antiresorptive agents at the same period of time is not reimbursed.

(3). Serum creatinine level should be checked and below the advised level recommended from the package inserts of the bisphosphonate medication.

5.6.3. Parathyroid hormones and analogues: teriparatide (such as Forteo®). This drug is only reimbursed for patients with all of the following conditions.

(1). A postmenopausal woman older than 55 years or men with osteoporosis due to hypogonadism or idiopathic causes.

(2). Had two prevalent fractures, and had been treated with antiresorptive drugs for at least 12 months continuously.

(3). After the 12 months of continuous treatment, the patient still developed a new fracture, or the patient was judged by the physician to be intolerant to the side effects of the antiresorptives used.

(4). A DXA BMD T-score ≤-3.

The total allowed dosages are 18 sets to be used within 2 years. Concomitant usage of other osteoporotic drugs is not reimbursed.