CONTENTS:

24. Slovak Republic Ministry of Health Guidelines for the Diagnosis and Treatment of Osteoporosis
Slovak Republic Ministry of Health
Guidelines for the Diagnosis and Treatment of Osteoporosis

The Slovak Republic Ministry of Health, pursuant to § 45, Paragraph 1, Subparagraph b) of Act No. 576/2004 on healthcare and related services, and upon the amendment and completion of certain acts, as amended, issues this guideline:

Article I
Definition of Osteoporosis

(1) Osteoporosis is a systemic skeletal disease characterized by low bone mass and micro-architectural deterioration of bone tissue, with resulting increase in bone fragility and susceptibility to fractures (WHO definition).

(2) The most common sites of osteoporotic fractures are the distal forearm, vertebrae, and proximal femur. The estimated prevalence rate of osteoporosis in our population is 6 percent. The likelihood of an osteoporotic fracture at any of these locations in postmenopausal women is approximately 40 percent. The mortality rate in patients with vertebral and proximal femoral fractures is approximately 6- to 8-fold higher when compared to the healthy population.

(3) The diagnosis and management of osteoporosis should involve a multidisciplinary team. Complex medical care – prevention, diagnosis, and osteoporosis treatment, including active early detection and treatment of individuals requiring ongoing medical or preventive care, is provided by clinicians dedicated to osteology (osteologists) specialised in orthopaedic surgery, rheumatology, endocrinology, as well as osteologists specialised in internal medicine and gynaecology practicing in an osteology clinic/office for at least 3 years. Other medical specialists provide consultative services to establish the diagnosis, differential diagnosis, and treatment.

Article II
Methods of Investigation

(1) Methods of investigation:
   a) Routine
   b) Specialised
   c) Bone mineral density measurement

(2) Routine methods of investigation:
   a) History and physical examination
   b) Blood tests, sedimentation rate
   c) Serum calcium, albumin, alkaline phosphatase
   d) Transaminases, creatinine, serum protein electrophoresis
   e) Urine chemistry analysis
   f) 24-hour urine calcium and phosphate output measurement (or fractional excretion of calcium and phosphate)
Specialised investigations:

a) X-ray evaluation (spine, pelvis, skull, upper extremities, lower extremities)
b) CT and MRI
c) Serum and urine biochemical markers of bone remodelling (Appendix 3)
d) Investigations to evaluate secondary aetiologies of osteoporosis: serum PTH, 25-OHD, TSH, fT4, STH, IGF1, gonadotropins (LH, FSH), prolactin, free urine cortisol, serum ACTH, sex hormones (estradiol, testosterone), bone biopsy, small bowel biopsy, and antigliadin antibodies, oncomarkers

The aim of the biochemical investigations is to differentiate osteoporosis from other osteopathies, to assess phosphate and calcium metabolism, and to evaluate bone metabolism activity (to differentiate high turnover osteoporosis from low turnover osteoporosis).

Bone mineral density measurement, densitometry techniques:

a) Peripheral bone densitometry:
   - Single-energy X-ray absorptiometry (SXA) - measures trabecular and cortical volumetric bone density of the forearm
   - Dual-energy X-ray absorptiometry (DXA) - measures trabecular and cortical volumetric bone density of the forearm
   - Quantitative ultrasound densitometry (UZD) - measures trabecular and cortical volumetric bone density of the heel

b) Central bone densitometry (DXA):
   - Standard measurements:
     • proximal femur and spine
   - Additional measurements:
     • whole body (including body composition)
     • morphometric measurements of the spine in the lateral projection
     • densitometry in patients with total joint replacement

c) Quantitative computed tomography (qCT) - measures trabecular and cortical volumetric bone density of the spine

Article III

Diagnosis of Osteoporosis

(1) Indications for BMD testing:

a) Oestrogen-deficient females: early menopause (age < 45 years), prolonged secondary amenorrhea (>1 year), primary hypogonadism
b) Measurement of bone density is required before initiating administration of glucocorticoids if estimated treatment duration is more than 3 months and daily prednisone dose is 5 mg or more
c) History of maternal femoral neck fracture
d) Low body mass index (BMI < 19 kg/m²)
e) Diseases causing or contributing to osteoporosis: anorexia nervosa, malabsorption, primary hyperparathyroidism, diffuse connective tissue disease, rheumatoid arthritis, chronic diseases causing intestinal inflammation, post-transplantation syndrome, chronic renal insufficiency, hyperthyroidism, prolonged immobilization, Cushing syndrome, chronic hepatopathy, myeloproliferative disorders, genetic and other metabolic bone disorders

f) Predisposition to osteoporosis on X-ray or presence of vertebral deformity

g) Low-energy fracture of the femur, spine and wrist

h) Significant loss of height or presence of thoracic kyphosis

i) Monitoring the response or effectiveness of an approved osteoporosis drug therapy

j) Chronic exposure to blood thinners, anticonvulsants, thyroid hormones, immunosuppressants, cytostatics

k) females older than age 65 years

l) males older than age 70 years

(2) The decision to perform a bone density assessment is based on indication criteria. Referring physicians are specialists in rheumatology, endocrinology, orthopaedic surgery, and physicians with specialisation in internal medicine as well as gynaecology working in an osteology clinic/office. Other physicians should refer patients to an osteology clinic/office for bone density assessment.

(3) Diagnosis of osteoporosis in postmenopausal females:
The WHO diagnostic T-score criteria should be followed (Appendix 1); lumbar spine T-score should be below $-2.5$ in at least one following: lumbar spine AP view, proximal femur, femoral neck, and trochanter.

(4) Diagnosis of osteoporosis in premenopausal females:
The use of Z-score is appropriate to diagnose osteoporosis. The diagnosis of osteoporosis should be made based on low BMD (Z-score below $-2.5$ SD) in the presence of secondary causes of osteoporosis or fracture risk factors listed in Appendix 2.

In premenopausal females, the diagnosis of osteoporosis should not be made based on densitometry criteria alone. A Z-score below $-2.5$ alone should be defined as a low BMD, not as osteopenia or osteoporosis. The Z-score is the number of standard deviations below the mean for an age and gender-matched population).

(5) Diagnosis of osteoporosis in males:
In males over the age of 65 years, a bone mineral density measurement T-score of $-2.5$ or less indicates osteoporosis.

In males aged 50-64 years, osteoporosis is diagnosed when the T-score less than $-2.5$ in the presence of other fracture risk factors (Appendix 2).

Males under the age of 50 years may be diagnosed clinically with osteoporosis when the Z-score is less than $-2.0$ SD, in the presence of secondary causes of low BMD according to Appendix 2.
Diagnosis of osteoporosis in children and adolescents up to 20 years of age:

Evaluation in children is based on the assessment of Z-score. If the Z-score is less than −2.0, the recommended term to use is "low density due to age". In children, bone mineral density (BMD) measurements of the spine and whole body are preferred. The relationship between BMD and fracture risk is not clearly defined.

The role of peripheral densitometry in the diagnosis of osteoporosis:

Measurement of the forearm can be used to diagnose osteoporosis only in following situations:

In patients with primary hyperparathyroidism, extreme obesity (exceeding densitometry table limits), and in patients where the spine and femur cannot be assessed. Establishing the diagnosis of osteoporosis using forearm measurements requires BMD assessment at the 33% or 1/3 radius of the non-dominant upper extremity. UZD densitometry of the heel is only of predictive value for fracture risk but does not allow one to establish the diagnosis of osteoporosis. Additional DXA testing in the area of the spine and femur is indicated if there exists a high degree of suspicion of osteoporosis (from clinical findings or X-rays) and axial skeleton measured bone density is normal or within the range of osteopenia. If bone density is in the range of osteoporosis using axial skeleton measurements, it is necessary to perform DXA measurements (in areas assigned for diagnosis–femur and L1-L4 spine) and to initiate anti-osteoporosis therapy. For those already treated with calcium and vitamin D, confirmation of the diagnosis of osteoporosis is not necessary.

Quantitative computed tomography (qCT) is important to assess the risk of fracture, morphological changes of the vertebrae, but cannot establish a diagnosis of osteoporosis.

Follow-up (control) densitometry:

Method of measurement:

To assess the dynamics of bone change, measurement of the AP spine or proximal femur, referred to as "total femur", is recommended. Peripheral forearm densitometry (SXA and DXA) and heel densitometry (UZD) are not appropriate for monitoring osteoporosis treatment effectiveness.

Follow-up (control) measurement:

Follow-up measurement of bone density to assess treatment effectiveness should not be performed any earlier than 1 year after the baseline measurement. In indicated cases, if it is reasonable to assume that a significant change in bone density (LSC – least significant change) will have occurred earlier than 1 year following baseline measurement (secondary osteoporosis, such as corticoid-induced osteoporosis), it is reasonable to shorten the interval for follow-up measurement to even less than 1 year. In most cases (due to the calculated LSC for the workplace and expected BDM change), follow-up bone density measurement should be done no earlier than 2 years following baseline measurement.

c) Bone densitometry measurement requirements are given in Appendix 5.
d) Requirements for clinical sites performing densitometry:

The quality control (QC) program should be in accordance with the manufacturer’s recommendations for system maintenance. The following QC procedures are recommended by the manufacturer: phantom scanning on a periodic basis (at least once a week) as an independent assessment of systemic calibration, print, and data analysis on calibration and phantom scans; verification of a mean or average BMD after each densitometer servicing operation. Evaluation of the accuracy of measurement pertains to standard clinical practice and every densitometry workstation should establish measurement error and calculate LSC (least significant change). Measurement error provided by the densitometer manufacturer should not be used.

The diagnosis of osteoporosis can be established by X-ray only if vertebral body deformities are already present.

Radiographically, a decrease in vertebral body height of 20% or more (front end, rear edge, or centre semi-quantitative evaluation as per Gennant) or a decrease in vertebral body height in comparison with neighbouring vertebral bodies is considered a fracture. To assess vertebral body deformity, CT, MR or DXA lateral vertebral morphometry can be used. Other causes of vertebral body reduction should be excluded.

Article IV

Osteology Networks

(1) Osteology networks include:
   a) Osteology outpatient clinic/office (dedicated to osteology)
   b) Osteocentre

(2) An osteology clinic/office is a specialised medical practice dedicated to osteoporosis and other metabolic bone diseases. It features comprehensive diagnostics, differential diagnostic procedures, and treatment. The osteology clinic/office provides bone mineral density measurements and examination of bone turnover biomarkers (minimally one for bone resorption and one for bone formation). The osteology clinic/office has an osteologist and a nurse. Physicians’ professional competence is regulated. In cases of dispute, the patient is sent to a competent osteocentre. Establishment of an osteology clinic/office is recommended for an area with 150,000 inhabitants.

(3) An osteocentre is a highly specialised centre with outpatient and hospital healthcare in the field of metabolic bone disease diagnostics and treatment.

(4) Osteocentres provide specialised consultative healthcare for patients referred from other osteology clinics/offices as well as inpatient care for complex cases, focused on comprehensive and differential diagnostics. Osteocentres perform bone mineral densitometry measurement (at minimum, DXA densitometry; peripheral bone densitometry [SXA, DXA, UZD] is optional), evaluation of bone remodelling biochemical markers (measurement of bone formation and bone resorption markers) as well as other specialised diagnostic procedures including bone biopsy, small
bowl biopsy, and other examinations required to establish a differential diagnosis. Targeted rehabilitation is part of osteoporosis therapy. Osteocentres provide education on osteoporosis and conduct osteoporosis clinical research. Osteocentres have physician specialists with modified professional competence as per regulations, physicians-consultants, nurses, physiotherapists, X-ray and laboratory technicians. Establishment of an osteocentre is recommended for areas with 500,000 inhabitants.

Article V

Osteoporosis prevention

(1) Fracture prevention in women older than age 50:
   a) Avoidance of risk factors (alcohol, smoking, drugs)
   b) Maintenance of a physically active lifestyle
   c) Maintenance of a BMI above 19 kg/m²
   d) Adequate exposure to sun, vitamin D supplementation if required (especially in elderly patients)
   e) Adequate dietary calcium intake (1000-15000 mg/day), calcium supplements should be used when an adequate dietary intake cannot be achieved. The recommended daily calcium dose varies based on age, gender, and hormonal status
   f) In postmenopausal women with risk factors for osteoporosis, or reduced bone mineral density verified by densitometry (osteopenia), and climacteric syndrome, hormone replacement therapy should be considered unless there are contraindications

Article VI

Treatment of Osteoporosis

(1) The primary goal of osteoporosis treatment is fracture risk reduction. Prior to initiating treatment, patients should be evaluated for secondary causes of osteoporosis and other low bone density metabolic bone diseases.

(2) In accordance with evidence-based medicine, the following medications are registered in Slovakia as effective in reducing osteoporotic fractures: calcium and vitamin D3 (in elderly postmenopausal females with reduced sun exposure, reduced dietary calcium intake, and reduced physical activity), alendronate, risedronate, raloxifene, calcitonin, strontium ranelate, teriparatide, ibandronate

   a) Hormone replacement therapy:

   The beneficial effect of hormone replacement therapy on bone has been established. However, due to the risk/benefit ratio, this treatment is not currently indicated for the prevention and treatment of osteoporosis. Climacteric syndrome is an indication for initiation of osteoporosis treatment. Osteoporosis prevention has an additive effect during the treatment of menopausal syndrome. Along with the listed antiresorptive therapeutic interventions, is compliance with prevention.
(3) Patients with densitometry-verified osteoporosis or osteoporotic fractures can be treated with the medications listed (alendronate, risedronate, raloxifene, calcitonin, strontium ranelate, teriparatide, ibandronate). Treatment with teriparatide must meet specific indication criteria. Calcium and vitamin D are indicated for the prevention and treatment of osteoporosis. Vitamin D supplementation is long-term. Treatment should be continued for at least 3 years, however the upper limit of treatment duration has not yet been defined.

(4) The prescribing of such products is governed by a list of drugs fully reimbursed or partially covered by public health insurance.

(5) Timely information about treatment effectiveness can be provided by examination of bone turnover dynamics prior to and after 3 to 6 months of treatment. Bone marker testing is recommended in patients before treatment initiation and after 3 to 6 months of treatment. Testing must be based on significant change in bone resorption and bone formation markers, using standardized examination procedures. Biochemical markers of bone turnover are listed in Appendix 3.

Article VII
Final Provisions

This guideline for osteoporosis come into effect on March 3, 2006

Rudolf Zajac
Minister of Health
Appendix 1
Slovak Republic Ministry of Health Guidelines for the Diagnosis and Treatment of Osteoporosis

Diagnostic criteria for postmenopausal females (WHO):

- Normal bone: T-score better than -1
- Osteopenia: T-score between -1 and -2.5
- Osteoporosis: T-score less than -2.5
- Established (severe) osteoporosis: T-score less than -2.5 and at least 1 fracture

*T- score is the number of standard deviations above or below the mean value for healthy young adult reference data*

Appendix 2
Slovak Republic Ministry of Health Guidelines for the Diagnosis and Treatment of Osteoporosis

Fracture risk factors and conditions resulting in low BMD:

Hypogonadism, primary hyperparathyroidism, hypercortisolism, thyrotoxicosis, osteomalacia, malabsorption syndrome, diffuse connective tissue diseases, kidney diseases, osteogenesis imperfecta, hypercalciuria, hypophosphatasia, growth hormone deficiency, mastocystosis, myeloproliferative disorders, osteoporosis-inducing drugs.
Appendix 3
Slovak Republic Ministry of Health Guidelines for the Diagnosis and Treatment of Osteoporosis

Biochemical markers of bone remodelling:

**BONE RESORPTION MARKERS:**
- Urinary total deoxypyridinoline (dPyr)
- Urinary C-terminal collagen type I cross-linked C-telopeptide (CTx)
- Urinary N-terminal telopeptide collagen type I cross-linked N-telopeptide (NTx)
- Serum carboxy-terminal telopeptide of type I collagen (ITCP)

**BONE FORMATION MARKERS:**
- Serum bone specific alkaline phosphatase (bALP)
- Serum osteocalcin (OC)
- C-terminal propeptide of type I procollagen (PICP)
- N-terminal propeptide of type I procollagen (PINP)

Appendix 4
Slovak Republic Ministry of Health Guidelines for the Diagnosis and Treatment of Osteoporosis

**Osteology Workstations:**

Osteocentre Directory

<table>
<thead>
<tr>
<th>REGION</th>
<th>OSTEOCENTRE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bratislava</td>
<td>Osteocentre FNsP Ružinov</td>
</tr>
<tr>
<td></td>
<td>Osteocentre SZU Kramáre</td>
</tr>
<tr>
<td>Trnava</td>
<td>Osteocentre NÚRCH Piešťany</td>
</tr>
<tr>
<td>Žilina</td>
<td>Osteocentre NEDU Lubochňa</td>
</tr>
<tr>
<td>Košice</td>
<td>Osteocentre Hospital Košice-Šaca</td>
</tr>
<tr>
<td>Nitra</td>
<td>Osteocentre ŠN sv. Svorada, Zobor</td>
</tr>
<tr>
<td>Banská Bystrica</td>
<td>Osteocentre NsP F.D.Roosevelta</td>
</tr>
<tr>
<td></td>
<td>Osteocentre NOVAMED</td>
</tr>
<tr>
<td>Prešov</td>
<td>Osteocentre s.r.o. Prešov</td>
</tr>
</tbody>
</table>
Appendix 5
Slovak Republic Ministry of Health Guidelines for the Diagnosis
and Treatment of Osteoporosis

Minimum requirements for DXA reporting:

1. Patient demographic data, manufacturer and model of instrument used
2. The examiner and the indication for BMD measurement
3. Physician who provided the evaluation and indications for the investigation
4. BMD in gm/cm² for each site, T-score and/or Z-score where appropriate
5. WHO classification for diagnosis in postmenopausal females, and in males age 65
   years and older, or males age 50 to 64 years with other risk factors
6. Statement regarding technical quality and measurement restrictions (why specific
   body area is not measured or analysed)

Recommended requirements for osteology reporting:

1. Risk factor identification including information on previous non-traumatic fractures
   and identification of fracture risk not dependent on BMD
2. Fracture risk assessment (may comment on, if all parameters needed to assess fracture
   risk are available - in indicated cases laboratory test results should also be used as
   well as other results that are required for a differential diagnosis)
3. Statement on secondary causes of low BMD
4. Recommendation for further non-BMD testing such as X-ray, magnetic resonance
   imaging, computed tomography, etc.
5. Recommendations for both pharmacologic and non-pharmacologic intervention
6. Recommendations on the need for and schedule of next BMD study

Minimum requirements for follow-up DXA reporting

1. A note about which previous BMD measurements was used as a comparative
2. Indication of the LSC in the centre and the significance of changes
3. Information on possible significant change from the previous measurement, expressed
   in gm/cm² and as a percentage,
4. Statement on other possible measurements (other centres, other machines, other
   models) and suitability for comparison
5. Recommendation regarding the need for and timing of the next BMD examination
Appendix 6
Slovak Republic Ministry of Health Guidelines for the Diagnosis and Treatment of Osteoporosis

Personnel and material – technical provision for osteology clinics/offices and osteocentres

1. Osteology clinic/office:

Osteology clinic/office personnel:

<table>
<thead>
<tr>
<th>Personnel</th>
<th>Number</th>
<th>Employer-defined Number of Hours</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physician</td>
<td>1</td>
<td>0.4</td>
</tr>
<tr>
<td>Nurse</td>
<td>1</td>
<td>0.4</td>
</tr>
<tr>
<td>Radiology Assistant</td>
<td>1</td>
<td>0.4</td>
</tr>
</tbody>
</table>

Minimal technical provisions: Peripheral or Ultrasound Bone Densitometer
Recommended: Whole-Body X-ray Densitometer (anticipated)
Number of rooms: 1; 2 if a Whole-Body Densitometer is in place

2. Osteocentre:

Osteocentre personnel:

<table>
<thead>
<tr>
<th>Personnel</th>
<th>Number</th>
<th>Employer-defined Number of Hours</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physician*</td>
<td>3</td>
<td>2.0</td>
</tr>
<tr>
<td>Nurse</td>
<td>2</td>
<td>1.0</td>
</tr>
<tr>
<td>Radiology Assistant</td>
<td>2</td>
<td>1.0</td>
</tr>
</tbody>
</table>

* Physician labor: 1 physician full-time; 2 physicians at 0.5 employer-defined hours

Minimal technical provisions: Whole-body X-ray Densitometer
Recommended: Ultrasound Bone Densitometer
Number of rooms: 2
Availability of: Quantitative CT (qCT); MRI (anticipated)