osteoporosis, a generalized skeletal disease, is one of the most common illnesses of old age. More than 200 million persons suffer from it worldwide. Health-care statistics reveal that patients with this disease in Germany are often undertreated or incorrectly treated (1). The Association of German-Language Scientific Osteological Societies (Dachverband der deutschsprachigen wissenschaftlichen osteologischen Gesellschaften, DVO) has issued S3 guidelines on the prevention, diagnostic evaluation, and treatment of osteoporosis in postmenopausal women and in men aged 60 and over (2). These guidelines form the basis of this article. S3 guidelines are the highest class of German guidelines. They are based on a systematic analysis of the available scientific evidence and produced by a representative panel of experts and are issued after a structured process of consensus building.

The learning objectives of this article are as follows: after reading it, the reader should be able to

- recognize the clinical abnormalities and risk factors that suggest the possible development of osteoporosis,
- apply the correct indications for the diagnostic evaluation of osteoporosis according to the DVO guidelines,
- know the basic practical steps involved in fracture prevention and in the specific pharmacotherapy of osteoporosis.

The literature consulted for this article included not just the publications found in a systematic search of the literature up to January 2005 that was performed for the 2006 DVO guidelines, but also further publications revealed by a PubMed search on 25 November
2007 on the items "osteoporosis," "fracture," and "treatment." The latter search was restricted to randomized controlled trials, meta-analyses, and guidelines. The authors also performed a manual search of relevant German-language primary care journals. In this article, individual publications are cited only if they were not mentioned in the DVO guidelines. The reader is also referred to the DVO guidelines for further information on levels of evidence and strengths of recommendations; the executive summary and the pocket version of the guidelines are particularly useful for this purpose (see www.lutherhaus.de/dvo-leitlinien).

**Definition and epidemiology**

Several definitions of osteoporosis have been proposed. The most commonly accepted at present is the one proposed in 2001 by the National Institutes of Health Consensus Development Panel on Osteoporosis, in which the risk of fracture plays a central role. According to this definition, osteoporosis is a systemic skeletal disease characterized by low bone mass and impaired microarchitecture of bony tissue, as a result of which the bones are more fragile than normal.

Among women aged 50 to 79, the annual incidence of morphometrically demonstrable vertebral body fractures is 1%, and that of peripheral fractures is 1.9%. The corresponding figures in men are 0.6% and 0.7%. The fracture rate rises exponentially with age (figure 1). While the overwhelming majority of vertebral body fractures are due to osteoporosis, peripheral fractures are due to a variable combination of endogenous and exogenous factors depending on their location and on the mechanism of the precipitating injury. In each individual case, the physician must determine whether the fracture should be considered osteoporotic or traumatic. An osteoporotic fracture should be suspected when a fracture has resulted from a fall from the standing position or from a low height. It is also true, however, that patients sustaining peripheral fractures as a result of traumatic forces that ordinarily suffice to cause such fractures tend to have lower than normal bone density (3). Thus, even in cases of this kind, the physician must decide whether to perform a further diagnostic evaluation for osteoporosis.

**Clinical features**

Osteoporosis without fractures is an asymptomatic condition. Osteoporosis that becomes symptomatic by causing one or more fractures is called manifest osteoporosis. Osteoporosis is a systemic disease of the skeleton characterized by low bone mass and an impairment of the microarchitecture of bone.

**Definition**

Marked loss of height, progressively severe kyphosis of the thoracic spine, and a protruding abdomen typify the body habitus of patients with advanced osteoporosis.

**Clinical manifestations of osteoporosis**

Marked loss of height, progressively severe kyphosis of the thoracic spine, and a protruding abdomen typify the body habitus of patients with advanced osteoporosis.
osteoporosis. X-rays then reveal typical vertebral body deformities, such as wedge vertebrae or biconcave ("fish") vertebrae. Osteoporotic fractures and deformities can cause severe acute and chronic pain. Vertebral body fracture is the most common type of osteoporotic fracture, while proximal femoral fracture is the type with the most serious sequelae (4).

Patients with osteoporotic fractures have an increased rate of mortality, particularly in the first year after the fracture event, and a high risk of further fractures. The body habitus of patients with osteoporosis is characterized by progressive kyphosis of the thoracic spine ("dowager's hump") and the loss of at least 4 cm of height, sometimes as much as 10 cm or more (figure 2). Shortening of the trunk can bring the lower rib cage into painful contact with the iliac crest; the abdomen protrudes ("osteoporosis belly"), and the limbs seem to be excessively long in relation to the trunk. Typical skin folds appear that run down the back laterally to the flanks. This is commonly referred to as the Tannenbaum-Phänomen ("fir tree phenomenon"), as the folds of skin appear to 'hang' from the spine, thereby resembling the branches and trunk of a fir tree (figure 3). The body's center of gravity is displaced forward. The patient's gait becomes small-stepped and unsteady.

Risk factors
A number of different biological factors that promote fractures need to be taken into consideration: not just bone density, but also the patient's age and sex, any previous fractures typical of osteoporosis, and any other independent risk factors for such fractures (box 1). When all of these things are considered, the individual patient’s risk of fracture can be evaluated much more reliably than with bone densitometry alone, and the expected effects of treatment can be calculated more precisely.

Indications for diagnostic evaluation
The DVO guidelines set the threshold for initiating a diagnostic evaluation for osteoporosis at a 20% 10-year risk of sustaining a fracture that is typical for osteoporosis. This probability is assessed solely on the basis of the patient’s history and physical findings. If the threshold is exceeded, a specific diagnostic evaluation is recommended (table 1).

The specific fracture risk in men is only half of the risk in women of the same age. Consequently, men

**Box 1**

**Risk factors for osteoporotic fractures (according to the osteoporosis guidelines of the DVO)**

- **Sex**: Men have an approximately 50% lower risk of osteoporotic fractures than women of the same age and with comparable T values.
- **Age**: Age is a major determinant of the fracture risk in both women and men. The risk roughly doubles every decade.
- **Vertebral body fractures**: Aside from age, a previous vertebral body fracture in the absence of trauma, or with only minimal trauma, is the most important independent risk factor for future fractures.
- **Peripheral fractures**: Peripheral fractures occurring after only mild trauma are a moderately strong risk factor for osteoporotic fractures.
- **History of a proximal femur fracture in a parent**: The known history of a proximal femur fracture in the patient’s mother or father is considered to be the most reliable prognostic indicator of the genetic risk of osteoporotic fractures.
- **Multiple falls**: Recurrent falls that are not caused by external forces within the preceding 12 months raise the risk of peripheral fractures.
- **Nicotine consumption**: This is a moderately strong risk factor for vertebral body fractures and peripheral fractures.
- **Immobility**
- **Underweight**: A BMI below 20 is associated with a twofold elevation of the relative risk of a proximal femur fracture.

**Risk factor**

A body-mass index below 20 doubles the risk of a proximal femur fracture.

**Fracture rate**

The fracture rate rises exponentially with age. The fracture rate curve for men is shifted rightward by about a decade compared to the fracture rate curve for women.
reach any given level of risk 10 years later than women do.

In addition to age and sex, a previous vertebral body fracture markedly increases the risk of further fractures in the vertebral bodies or elsewhere; peripheral fractures, on the other hand, confer a variably severe risk of further fractures, depending on their localization and the mechanism of injury that produced them. Therefore, when a peripheral fracture occurs, it should be assessed in each individual case whether this particular fracture arouses a high degree of suspicion for osteoporosis. If so, and if the patient is a woman aged 50 or older or a man aged 60 or older, then further diagnostic evaluation is indicated. The treating physician should also initiate a specific diagnostic evaluation for osteoporosis in a woman aged 60 or older, or a man aged 70 or older, if one or more of the risk factors listed in box 1 is present and cannot be eliminated by treatment. Finally, all women aged 70 or older and all men aged 80 or older should undergo a specific diagnostic evaluation for osteoporosis, as long as a positive finding would carry therapeutic implications for the individual patient.

The specific diagnostic evaluation for osteoporosis involves the performance of bone densitometry. Dual X-ray absorptiometry (DXA) is the preferred method for this, because all of the large therapeutic studies to date have been based on it. DXA values should be measured in the lumbar spine (vertebrae L1 through L4) and in the proximal femur; the lower of the two values should be used for further calculations. The “T value” is a derived parameter representing the difference between the patient’s bone density and the average value in a population of normal 30-year-old people, expressed in standard deviations from the mean. Thus, a T value of –1, for example, signifies that the patient’s bone density is one standard deviation below the mean. When the T value is less than –2, the patient’s bone density is lower than that of 95% of the normal middle-aged population. Any person with a T value below –1 is said to have osteopenia, while any person with a T value below –2.5 is said to have osteoporosis. The measured T value, however, does not itself constitute an indication for treatment. Statutory health insurance in Germany will reimburse bone densitometry only if there has also been a fracture that is suspect for osteoporosis.

Bone density is relatively stable among persons over age 60 in the absence of other factors such as...
severe vitamin D deficiency, prolonged immobility, and systemic glucocorticoid treatment. Thus, repeated measurements should only be performed for special indications (5). Because bone density, age, sex, and prior osteoporotic fractures are independent risk factors for future fractures, the combination of these data allows a much more accurate estimation of the risk. Prediction becomes even more accurate, though substantially more complicated, when further risk factors are included in the model. Further risk factors do not cumulate without limit, however; they lead, at most, to a doubling of the risk in the model that was used.

Table 2 shows how the threshold for treatment is derived from the T value, age, and sex of the patient. The DVO guidelines recommend specific treatment when the 10-year risk of osteoporotic fractures exceeds 30%.

This level of risk is already reached in persons over age 50 with a vertebral body fracture typical of osteoporosis when the T value is below −2.0.

Further risk factors that can be included in the model are listed in tables 1 and 2. They elevate the risk of fracture by a factor of 1.5 to 2. Thus, for simplicity, if one or more of these factors is present, then the threshold T value for treatment is obtained by considering the patient to be one decade older (i.e., moving two rows down) in table 2. There is no specific therapeutic recommendation if the patient is irreversibly bedridden.

Basic diagnostic evaluation
If the patient has sustained a fracture that arouses the suspicion of osteoporosis, but the bone density is not abnormally low, then the following basic diagnostic evaluation should be performed to detect any of the possible causes of secondary osteoporosis and any modifiable risk factors for further fractures, as well as to provide a baseline for further clinical observation.

- The patient should be asked about any musculoskeletal pain, functional limitations, previous falls, dietary habits, and physical activity, including exposure to sunlight.
- The patient should also be asked about the use of any medications that tend to promote osteoporosis or that increase the likelihood of falling, particularly antiepileptic drugs (e.g., carbamazepine), antidepressants (particularly tricyclic agents), other drugs causing sedation or orthostatic hypertension, and oral glucocorticoids.

### BOX 2

#### The timed up-and-go test
- Equipment: armchair, marking of a 3-meter length on the floor, stopwatch
- The subject sits upright in an armchair and is given the following instructions:
  "Please stand up, walk to the end of the marked line (3 meters away), turn around, and sit down again. I will time how long it takes you to do this."
  (The patient may use whatever walking aids he or she uses in everyday life).
- Evaluation:
  - 10 seconds or less: apparently normal mobility
  - 11 to 29 seconds: this finding can only be interpreted in the light of other clinical parameters
  - 30 seconds or more: impaired mobility and proneness to falls can be assumed

#### The chair-rising test
- Tests mainly the strength of the lower limbs
- Equipment: chair (without armrests), stopwatch
- The subject sits upright in a chair without armrests and is given the following instructions: "Please stand up and sit down again five times in a row as fast as you can. You should stand up fully each time; in other words, when you are in the standing position, your knees should not be bent at all. Do not use your arms to help you stand up. [The following request can be made if it is safe to do so:] Please keep your arms folded on your chest. I will time how long it takes you to do this."
- Evaluation:
  - 10 seconds or less: no apparent unsteadiness of gait due to impaired strength of the lower limbs
  - 11 seconds or more: apparent unsteadiness of gait (presumably largely due to weakness)

- The risk of falling should be assessed, e.g., with a timed up-and-go test or a chair-rising test, perhaps as part of a more extensive geriatric assessment (box 2).
- The patient’s height and weight should be measured so that the body-mass index (BMI) can be calculated.
- X-rays should be performed to detect vertebral body fractures if there is any suggestive clinical evidence such as a history of sudden, severe back pain or a loss of more than 4 cm of height, and as long as the detection of such fractures would have clinical consequences.
- Basic osteological laboratory parameters should be measured (table 3).

Basic diagnostic evaluation
The detection of causes of secondary osteoporosis and of risk factors for fracture that can be positively influenced is an important aim of the longitudinal observation of the patient.

Testing procedures in the basic diagnostic evaluation
The timed up-and-go test and the chair-rising test are good methods of assessing the risk of falling in osteoporosis patients.
Treatment

The treatment of osteoporosis is divided into basic measures for fracture prevention and the specific pharmacotherapy.

Basic measures for fracture prevention

The first step consists of intensive counseling about living habits that promote bone health. These lifestyle factors should, in principle, be recommended to all patients, even those who have not undergone a specific diagnostic assessment for osteoporosis:

- Avoidance of underweight (the BMI should not fall below 20)
- Smoking cessation
- Adequate calcium intake (1200 to 1500 mg daily)
- Regular physical exercise with adequate weight-bearing to promote strength and coordination, e.g., hiking, dancing, gymnastics, weight training
- An average of 30 minutes of sunlight exposure per day, with uncovered head and hands, to prevent vitamin D deficiency
- Review of the need for, and the doses of, any of the medications mentioned above that promote osteoporosis and increase the likelihood of falling.

Directed exercise programs can, at least, reduce the risk of falling, although the studies performed to date have included too few patients to demonstrate any resulting reduction of the fracture rate (2, 6). Because fractures are relatively rare events, very large studies would be needed to demonstrate this. Thus, the authors can only point to indirect evidence from epidemiological studies showing that more frequent falls (i.e., two or more falls in the past six months) increase the fracture rate. It is reasonable to conclude, therefore, that the fracture rate will be lower if falls are prevented.

It is often difficult to put the recommended basic measures into consistent practice; this is just as true in nursing homes as it is elsewhere (7). Thiazide diuretics promote calcium retention and therefore presumably have a synergistic effect with the basic measures when they are given to treat high blood pressure or for other indications.

Calcium and vitamin D supplementation is a standard recommended element of the specific pharmacotherapy of osteoporosis. The vitamin D dose should be 400 to 1200 IU per day, depending on the presumed severity of the vitamin D deficit. Vitamin D can also be given in higher doses (boluses) at longer intervals.

The daily supplementation of at least 1200 mg of calcium in combination with 800 IU of vitamin D is recommended on the basis of a recent meta-analysis (8).

There are conflicting data on the possible benefit of hip protectors. They are most likely to protect patients in nursing homes if they are worn consistently.

Specific pharmacotherapy

When the 10-year risk of fractures exceeds 30%, specific pharmacotherapy is clearly indicated because the benefit considerably outweighs its risks. The DVO guidelines recommend the following medications (in alphabetical order) for post-menopausal women with a specific indication for treatment: alendronate, ibandronate, raloxifene, risedronate, and strontium ranelate. Estrogens prevent fractures just as effectively, but, because of their risks, they should no longer be used as primary prevention measures.

Fracture prevention and lifestyle

- Smoking cessation
- Calcium intake: 1200–1500 mg/day
- Regular physical exercise
- Average daily sunlight exposure: 30 minutes
- Optimized medications

When the 10-year risk of fractures exceeds 30%, specific pharmacotherapy is clearly indicated as the benefit considerably outweighs its risks.
Compliance can be improved by intensive education of osteoporosis patients as soon as the diagnosis is made. Among a group of patients who went through the "Nümbrecht osteoporosis school," a standardized and evaluated multimodal osteoporosis education program consisting of nine modules, 72% were still taking their osteoporosis medications six months later, and 62% were still taking them at 1 year. There was, however, no control group of patients that did not undergo patient education (15, 16).

**Duration of pharmacotherapy for osteoporosis**

Bone densitometry should generally be repeated no sooner than two years after the initiation of treatment. It should be performed, in particular, when there is reasonable doubt as to the indication for, or particular choice of, treatment, or when the discontinuation or restarting of pharmacotherapy is being considered.

Medications for osteoporosis should be given for three to five years at first. The patient should then be re-evaluated.

When bisphosphonates are discontinued, their osteoprotective effect declines very slowly, because they remain bound in bone.

In a five-year follow-up study, a group of patients in whom bisphosphonate therapy was continued did better than a control group only with respect to densitometric values and clinically manifest vertebral body fractures. The overall fracture rates were the same.

Thus, the continuation of specific pharmacotherapy is justified in patients who have a relatively long residual life expectancy and whose fracture risk is still high. In other patients, the medications can be discontinued and the further course can be observed (17).

**Summary**

The indications for the diagnostic evaluation of osteoporosis and for its treatment are based on the risk of fracture. Unlike arteriosclerosis, which is a progressive process, bone is continuously being laid down and resorbed throughout the life of the patient. It is, therefore, not an effective means of fracture prevention to initiate maximal treatment in a 50-year-old patient, in order to reduce a risk that will become manifest more than 20 years later. The medical treatment of osteoporosis exerts its effects relatively rapidly: numerous studies have demonstrated significant changes after as little as six to twelve months. If a fracture has already

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**Compliance**

Intensive patient education markedly improves the compliance of osteoporosis patients with their physicians' instructions.

**The duration of pharmacotherapy**

Pharmacotherapy for osteoporosis is generally given for three to five years, after which the patient is re-evaluated.
occurred, however, it is important to intervene rapidly to prevent further fractures and the resulting severe functional limitations. Too little is being done in this area in Germany at present.

A variety of interventions involving changes in physicians’ and patients’ behavior, new computer systems, and improved access to DXA measurements can bring about improvements in the specific diagnostic evaluation of osteoporosis and thereby partly lower fracture rates (18–23). All physicians caring for elderly patients with fractures bear the responsibility of diagnosing and treating osteoporosis adequately. Both screening (i.e., the examination of all probands in a particular age group) and case-finding (i.e., the directed diagnostic evaluation of patients at elevated individual risk) for osteoporosis are cost-effective even in the absence of a previous fracture typical of the disorder and can reduce the frequency of severe functional impairment (25). Unfortunately, however, screening and case-finding are not yet covered by statutory health insurance in Germany. The affected patients should be informed of this if they would be motivated to undergo treatment in the event of a positive diagnosis.

Conflict of interest statement
Professor Peters has received financial reimbursement for lecturing activities from the Procter & Gamble, Novartis, Lilly Deutschland, and Servier Deutschland companies. Professor Baum declares that she has no activities from the Procter & Gamble, Novartis, Lilly Deutschland, and Professor Peters has received financial reimbursement for lecturing activities from the Procter & Gamble, Novartis, Lilly Deutschland, and Servier Deutschland companies. Professor Baum declares that she has no conflict of interest as defined by the International Committee of Medical Journal Editors.

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REFERENCES


Prevention

Changes in physicians’ and patients’ behavior, new computer systems, and improved access to DXA measurements can improve the diagnostic evaluation of osteoporosis and thereby lower fracture rates.


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A case report is available at: www.aerzteblatt-international.de/1008

Further Information

This article has been certified by the North Rhine Academy for Postgraduate and Continuing Medical Education.

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Maurer M, Gabbe J: Urticaria: Its History-Based Diagnosis and Etiologically Oriented Treatment: 1a, 2d, 3d, 4a, 5c, 6b, 7d, 8b, 9a, 10a
Please answer the following questions to participate in our certified Continuing Medical Education program. Only one answer is possible per question. Please select the answer that is most appropriate.

Question 1
A specific diagnostic evaluation for osteoporosis is generally recommended when the 10-year risk of fracture reaches what level?
(a) 15%
(b) 20%
(c) 25%
(d) 30%
(e) 50%

Question 2
For which of the following groups of patients do the DVO guidelines recommend a specific diagnostic evaluation for osteoporosis even if no further risk factors are present?
(a) Women over age 50
(b) Men over age 60
(c) Women over age 60
(d) Men over age 70
(e) Women over age 70

Question 3
How high is a man’s risk of developing an osteoporotic fracture compared to the risk in a woman of the same age and with a comparable T value?
(a) 50% lower
(b) 50% higher
(c) 25% lower
(d) 25% higher
(e) 75% lower

Question 4
Which of the following laboratory tests is recommended so that secondary osteoporosis can be ruled out?
(a) Reticulocyte count
(b) Serum potassium
(c) Protein electrophoresis
(d) Ferritin
(e) Ureic acid

Question 5
Which of the following should always be included in the basic clinical evaluation for osteoporosis?
(a) Height and weight
(b) Skin type
(c) Mobility of the hip joints
(d) Ankle-to-arm index
(e) Asymmetry of the waist triangle

Question 6
Which of the following is a major risk factor for osteoporotic fractures?
(a) Age below 60 years
(b) DXA T value below –2.5
(c) Male sex
(d) Ankle fracture after a fall off a high ladder
(e) Overweight

Question 7
Which of the following drugs or drug families promotes the development of osteoporosis?
(a) Amitriptyline
(b) Insulin
(c) Estrogens
(d) Oral glucocorticoids
(e) Thiazides

Question 8
Which of the following behavioral changes has a preventive effect on the development of osteoporosis?
(a) Smoking cessation
(b) Weight loss
(c) High-protein, low-calcium diet
(d) Avoidance of physical exercise
(e) Avoidance of UV radiation

Question 9
Which of the following medications is approved in Germany for the treatment of osteoporosis in men?
(a) Alendronate
(b) Clodronate
(c) Ibandronate
(d) Raloxifene
(e) Strontium ranelate

Question 10
A 78-year-old woman of normal weight sustains a fall at home and is hospitalized with a femoral neck fracture. What further measure should be undertaken after the injury is taken care of?
(a) Hormone replacement therapy
(b) Pharmacological sedation
(c) Weight reduction
(d) Prolonged immobilization
(e) Diagnostic evaluation for osteoporosis
A 68-year-old woman tripped, fell, and sustained a sub-capital fracture of the humerus. She was under treatment for hypertension with an ACE inhibitor and her blood pressure was usually around 150/85 mmHg. She weighed 60 kg and was 1.52 m (5 feet) tall. Her passport, however, gave her height as 1.58 m (5’ 2”). The remainder of the history and physical examination were unremarkable. The preoperative chest X-ray revealed an old wedge fracture of one of the thoracic vertebral bodies.

**Further course**
After the acute fracture had been dealt with and analgesia had been given as needed, the patient underwent a basic diagnostic evaluation to rule out secondary osteoporosis and then underwent DXA measurement (for which health insurance coverage is obligatory in Germany). The latter yielded a T value of −3.2 for the femur as a whole. The basic osteological laboratory parameters were within normal limits, as was the geriatric assessment, including a timed up-and-go test.

These findings suggested specific pharmacotherapy, e.g., with a bisphosphonate and calcium/vitamin D as a first line treatment. It would also be reasonable to change the antihypertensive medication to a combination of an ACE inhibitor with a thiazide in order to control the patient’s blood pressure better while also possibly exerting an osteoprotective effect.