

2006 DVO-Guideline for Prevention, Diagnosis, and Therapy of Osteoporosis for Women after Menopause, for Men after Age 60

Executive Summary

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The letters (A-D) show the relevant grade of recommendation with reference to fracture prediction or fracture reduction according to the SIGN criteria (treatment) and Oxford criteria (diagnostic assessment). It is referred to the full-text version for the detailed description of the assessment and the references on which the grades of recommendations are based.

Scope of the Guideline, Addressees

The guideline is the 2006 update of the DVO guideline on prevention, diagnosis and therapy of osteoporosis in women after menopause and for men after age 60. The DVO (*Dachverband Osteologie*) is the joint organization of the scientific societies in Germany, Austria and Switzerland, which are predominantly or with a scientific focus involved in bone research. The guideline is based on a systematic literature search until February 2005 and an interdisciplinary internal and external consensus process. The next update is scheduled for 2009.

The subjects of the guideline are prevention, diagnostic assessment and treatment of osteoporosis in post-menopausal women and in older men. For pre-menopausal women, younger men, children, adolescents and for all other types of osteoporosis in which a secondary cause is the essential attributable cause, this guideline does not apply. For these cases it is referred to the recommendations of the respective expert associations, in the area of which those special forms of osteoporosis belong. For the special case of glucocorticoid-induced osteoporosis it is referred to the DVO-guideline on glucocorticoid-induced osteoporosis (www.lutherhaus.de/dvo-leitlinien).

This guideline is addressed to all physicians in primary care and all other physicians who treat patients with osteoporosis.

Definition of Osteoporosis

Osteoporosis is a systemic skeletal disease characterized by insufficient bone strength, resulting in an increase in fracture risk. Bone strength reflects primarily the interaction

between bone density and bone quality (NIH Consensus Development Panel on Osteoporosis 2001).

In the case of one or several fractures resulting from osteoporosis it is spoken of a manifest osteoporosis.

Prevalence and Incidence of Osteoporosis and its Consequences

Prevalence of osteoporosis based on the WHO-Definition of a reduced bone density measurement (DXA T-score < -2.5) is at approximately 7% for post-menopausal women at age 55 and increases to 19% at age 80 (C). For men in the German-speaking area sufficient information is not available.

The annual incidence of morphometrically defined vertebral fractures is at approximately 1% for women between 50-79 years and at 0.6% for men at the same age. For peripheral fractures, often resulting from a combination of osteoporosis and fall, the annual incidence in this age group is at 1.9% for women and 0.7% for men. The incidence of both established forms of osteoporosis increases exponentially with age (C).

Clinical Symptoms of Osteoporosis

Clinical symptoms of osteoporosis which precede fractures are not known (D).

Fractures associated with osteoporosis result in an evident limitation of quality of life for women and men. This is most distinct in the first year after the fracture occurred (A).

Peripheral fractures and vertebral fractures due to osteoporosis are associated with an increased mortality for women and men. The increase in mortality is highest in the first year after the fracture occurred (A).

I. Nonpharmacological Prevention of Osteoporosis and Fractures

Several nonpharmacological measures may improve bone stability or lead to a reduction of peripheral fractures caused by falls. These include the improvement or preservation of muscle strength and coordination, the avoidance of falls, a sufficient intake of vitamin D and calcium, the avoidance of underweight and smoking, and the critical assessment of fall-increasing and/or bone damaging medication.

I.1 Muscle Strength, Coordination and Falls

For women and men in old age an increase in muscle strength leads to a reduction in hip fractures (C) and might lead to a reduction in vertebral fractures (D).

Low physical activity and/or low muscle strength are risk factors for hip fractures (A for women, B for men) and vertebral fractures (B for women, D for men).

Therefore, regular physical activity aiming at improving muscle strength and coordination is recommendable (B-D). An immobilisation should be avoided (C).

A specific fall assessment and intervention against falls decreases the risk of falls for older persons (A). As a consequence, the incidence of hip fractures and associated disease complications can be reduced (C).

Therefore, an annual fall history is recommended as of age 70 (D). If the risk of falls is high, causes should be explored and treatment of avoidable causes of falls should be initiated. Medication which supports falls as sedatives, orthostasis-inducing drugs, or antidepressants should be regularly reevaluated with regard to dose and necessity. Where appropriate, adapted aids and hip protectors should be used (A-D).

Hip protectors reduce the rate of hip fractures for women and men in old people's and nursing homes if they are part of an extensive training programme for the personnel for avoiding falls (A). A sole prescription of hip protectors without adequate patient compliance does not have any reducing effect on fractures (A). For people not living in old people's homes there is presently no evidence for a reduction in hip fractures (A).

A vitamin D deficit (see I.2) increases the fall incidence (A). The compensation of a distinct vitamin D deficit (25-hydroxy-vitamin D serum concentrations < 20 ng/ml) leads to a decrease in hip fractures, possibly in part by a decrease in fall rate (B for women, C for men, D for other fractures). A decrease in the fall rate was also seen for certain subgroups of older women and men for the active vitamin D metabolite alfacalcidol (B).

I.2 Nutrition and Lifestyle

Underweight (body mass index < 20) is a strong risk factor for osteoporotic fractures (A). A decrease in weight is associated with an increase in the risk of hip fractures (A). An increase in weight is associated with a reduction of this risk (D).

Exploration of an inexplicit underweight and sufficient caloric nutrition with the primary aim to maintain or develop muscle mass are, therefore, recommended (A-D).

For persons with a deficit in calcium and vitamin D who live in old people's or nursing homes a daily supplementation of 1200 mg of calcium and 800 units of vitamin D3 lead to a reduction in non-vertebral fractures and particularly in hip fractures (A). For free-living older

women and men and for younger persons the data is inconsistent. The efficacy probably depends on the pre-existing individual degree of the calcium and vitamin D deficit (D).

A daily nutritional intake of 1200-1500 mg of calcium is recommended (D). This is often not the case especially for many persons older than 70 years. If the calcium intake in old age falls short of the recommended dose or in case of predisposing diseases (e.g. malassimilation) a supplementation is, therefore, recommended (A-D).

For a sufficient synthesis of vitamin D, a daily exposure of face and arms to the sun of at least 30 minutes is recommended (D). Again, this is not the case for many persons older than age 70. In case of lower exposure times, a daily supplementation of 400-1200 units of vitamin D3 depending on the assumed degree of the deficit should apply (A-B).

Smoking is an independent risk factor for fractures and should be avoided (A-D).

I.3 Medication Supporting Falls or Osteoporosis

Medication which may support osteoporosis and/or falls, such as antiepileptics (C), antidepressants (C), sedatives (C) medication which causes orthostasis, and oral glucocorticoids (A), should be critically checked with regard to benefit-risk ratio referring to dose and necessity on a regular basis. In case of an L-thyroxine medication the TSH-concentration should be > 0.3 mU/L. Exceptions may be special considerations in the aftercare of some thyroid carcinomas (B-D).

I.4 Commencing of Effects and Duration of Effects of Preventive Measures

All given measures for osteoporosis and fracture prevention show their effects on bone metabolism (A-C) or fall rate (C) within a few months. Therefore, they are also or especially effective in old age. The proof of efficacy of such measures on bone metabolism or fall rate is limited to constant implementation. At present, there is no proof of a persistent long-term effect of these measures for fracture prevention (C). Contrary to other chronic diseases for which early prevention has shown to prevent long-term complications, preventive measures that affect bone metabolism or fall rate have only shown to result in an acute fracture risk reduction (C).

II. Constellations for which a Diagnostic Assessment is recommended by the DVO

II.1 Clinical Risk Profile as Basis for the Recommendation of a Diagnostic Assessment

Diagnostic assessment is recommended for all persons for whom a high fracture rate is to be expected due to their clinical risk profile (D). In this guideline a high fracture risk is defined as a 20% or higher risk to suffer a vertebral and/or hip fracture in the next 10 years based on the currently available epidemiological data.

In the following, those clinical risk factors will be presented and defined individually which contribute to the risk profile as independent or probably independent risk factors. Subsequently, those risk profiles are described for which a 20% or higher fracture risk is to be expected in the next 10 years and a diagnostic assessment is recommended.

II.1.1 Sex

At a comparable age and T-score of bone density, men do have an approximately 50% lower risk of osteoporotic fractures than women (A).

II.1.2 Age

For both genders the fracture risk is decisively determined by age (A). With each decade the fracture risk approximately doubles. Age as fracture risk is independent of bone density and independent of clinical risk factors such as immobilisation or multiple falls which also increase with age (A). Presently, it is not clear which pathogenetic factors are the basis for the risk factor age. It is possible that age is associated with a deterioration of biomechanical factors of bone architecture and bone quality which cannot yet be directly measured at present.

II.1.3 Non-traumatic and Low Trauma Vertebral Fractures

Non-traumatic and low trauma vertebral fractures are other than age the most dominant independent risk factors for future bone fractures (A). This prognostically applies to clinically apparent vertebral fractures (A), as well as to vertebral fractures which are coincidentally detected on radiographs (B).

II.1.4 Peripheral Fractures after Low Impact Trauma

Peripheral fractures after low impact trauma are a moderate independent risk factor for osteoporotic fractures for women and men (A).

Retrospectively, it is difficult to estimate for individual cases the degree of the force which led to the fracture. Therefore, there often remains an uncertainty whether and which part of the fracture was due to an excessively high impact of force and which was due to low bone strength. This is the reason why peripheral fractures as risk factors for future fractures do not have the same impact as vertebral compression fractures which are more clearly associated with reduced bone strength. It can, nevertheless, be assumed that a fracture is partly osteoporotic if it resulted from a fall from a standing height or less.

II.1.5 Paternal or Maternal History of Hip Fractures

Paternal or maternal history of hip fractures is regarded as the most reliable indicator of genetic risk of osteoporotic fractures (B).

II.1.6 Multiple Falls

A history of multiple falls increases the risk of peripheral fractures for post-menopausal women and older men (A). This applies to falls without external impact which occurred more than once in the last 12 months.

II.1.7 Smoking

For women and men smoking is an independent moderate risk factor for vertebral fractures and peripheral fractures (A). The determination of a gradual risk depending on the number of cigarettes is presently still inaccurate. It can, however, be generally said that smokers do have a higher fracture risk than non-smokers.

II.1.8 Immobility

Lack of physical activity is a risk factor for hip fractures (A for women, B for men) and vertebral fractures (B for women, D for men).

Immobility describes for example a person whose mobility is limited to such a degree that she or he cannot leave her or his home or cannot do any housework (A).

II.1.9 Underweight

In case of underweight the relative risk of a hip fracture is approximately doubled for women and men (A). An increased risk is also probable for other fractures (C). Here, underweight is defined as a body mass index of ≤ 20 .

II.1.10 Remarks on Risk Factors: Reversibility, Impact, Consistency

The risk factors multiple falls, smoking, immobility, and underweight are modifiable risk factors. They are only to be included in the risk profile if an elimination of the risk factor was unsuccessful or if it is foreseeable that an elimination of the risk will not be possible in the next months.

The above mentioned risk factors describe those factors which proved to be consistent in epidemiological studies independent of age, and which in univariate analyses were of sufficient strength (relative risk > 1.5) with regard to fracture prediction. The interactions of those risks are, however, only partly examined. With the exception of a history of vertebral fractures, the presence of one or more risk factors is only to be taken as an indication that the fracture risk is probably increased by factor 1.5 – 2 compared to a situation without those risk factors. Future trials have to even better define the impact of those risk factors with regard to fracture prediction and the interaction of these risk factors and with regard to age and bone density.

Apart from the 9 individual risk factors mentioned, an association of some more clinical risk factors with an increased risk of osteoporotic fractures was described in individual or multiple studies. If and which additional contribution these risk factors have to the total fracture risk independent of the risk factors mentioned above, however, has not yet been clarified.

The evidence for the older man with regard to impact and independence of the risk factors mentioned above is more uncertain than for the post-menopausal woman.

II.2 Recommendations for a Diagnostic Assessment Based on Risk Profile

In the following, clinical risk profiles are defined for women and men of different age groups for which, based on the presently known epidemiological data, an estimated 10 year fracture risk of 20% and higher is assumed. and for which a diagnostic assessment is recommended.

1. Woman Age 50-60; Man Age 60-70:

1.1 A diagnostic assessment is recommended in case of vertebral fractures typical of osteoporosis.

1.2 Due to the different causes of peripheral fractures, a diagnostic assessment in case of peripheral fractures after low impact trauma is not generally recommended. Diagnostic assessment, however, may be pursued on the grounds of an individual decision (D). Decisive here is the clinical overall context.

1.3 In contrast, the probability of a high 10 year fracture risk in this age group without fractures is that low that even in the presence of one or more of the above mentioned risk factors a diagnostic assessment is usually not recommended.

2. Woman Age 60-70; Man Age 70-80:

2.1 A diagnostic assessment is recommended in case of vertebral fractures typical of osteoporosis.

2.2 The fracture risk in combination with one or more of the following risk factors is that high that it is recommended to perform a clinical assessment if at least one of those risk factors is present.

1. peripheral fracture after low impact trauma
2. hip fracture in a parent
3. immobility
4. smoking
5. multiple falls
6. underweight

3. Woman above Age 70 and Man above Age 80:

Age is in this age group such a dominant risk factor that the 10 year probability of a fracture is high even without additional clinical risk factors. Therefore, a diagnostic assessment is generally recommended in this age group if this leads to a therapeutical consequence for the person in question.

The recommendations for a diagnostic assessment are once more summarised in the following table.

Table 1 Recommendations for Diagnostic Assessment

Age (years)		Risk profile for which a diagnostic assessment is recommended if the risk factor(s) cannot be eliminated
Woman	Man	
50-60	60-70	Vertebral fracture (A) Peripheral fracture as individual case decision (C)
60-70	70-80	Vertebral fracture (A) Peripheral fracture (A) Hip fracture in a parent(B) Underweight (A) Smoking (A) Multiple falls (A) Immobility (A-B)
>70	>80	Age sufficient as risk (A)

II.3 Secondary Forms of Osteoporosis

A lot of diseases or conditions are associated with an increased risk of osteoporosis and/or an increased fracture incidence. However, the risk may vary a lot and ranges from a slight increase in risk to a very high risk of fractures. Among the most important forms of secondary

osteoporosis are those due to hypogonadism, hypercortisolism, primary hyperparathyroidism, systemic use of glucocorticoids, severe renal insufficiency, type I diabetes mellitus, malassimilation, use of antiepileptics and anorexia nervosa (A-D).

In case of these diseases the evaluation of the fragility risk, the diagnostic assessment and the therapy offer a lot of particularities. The diagnostic assessment recommended in the DVO-guideline is, therefore, not evaluated for these diseases nor is it suitable in many cases or it is even wrong. The specific recommendations of the relevant expert associations and of bone experts for these secondary bone diseases apply (D).

II.4 Diagnostic Assessment Beyond the Present Recommendations of the DVO

At present, the DVO does not recommend a diagnostic assessment under consideration of benefit, risks and costs beyond the risk profiles listed above apart from few specific exceptions given in the full-text **version** (D). The full-text **version** of the DVO, however, also allows an interpretation of findings from technical measurements beyond the present recommendations of the DVO as the physician is often confronted with these measurements in daily practice. The full-text **version** especially includes interpretations of measurement results of DXA, QCT and quantitative ultrasound for patients without additional risks.

III. Diagnostic Assessment in Case of Increased Fracture Risk

The recommended diagnostic assessment consists of medical history, clinical examination, a DXA bone density measurement and if applicable laboratory tests and radiographs of the thoracic and lumbar spine.

III.1 Medical History and Clinical Examination

The aims of investigating medical history and clinical findings are:

1. the assessment of the intensity and localization of pain and of the extent of functional limitations in case of manifest osteoporosis as a basis for analgetic treatment and for functional/rehabilitative measures.

In the case of acute, newly developed, severe and/or persistent back pain lasting for days, the possibility of a vertebral fracture should always be considered in the age group to which this guideline applies. Depending on the characteristic and dynamic of the clinical features lateral and anteroposterior radiographs of the thoracic and/or lumbar spine are recommended for confirmation or exclusion of a fracture and in order to differentiate the back pain from other diseases. (D).

Vertebral compression fractures can also cause chronic back pain without a preceding distinct episode of acute fracture pain. Depending on the strength of the clinical symptoms in case of chronic back pain lateral and anteroposterior radiographs of the thoracic and/or lumbar spine are recommended for confirmation or exclusion of a fracture and in order to differentiate back pain from other diseases. (D).

2. Assessment of possible forms of secondary osteoporosis which need further specific diagnostic work up.

3. Assessment of fracture risks and conditions or diseases which negatively affect bone metabolism and/or falls in order to specifically implement nonpharmacological measures and assess the overall fracture risk. This includes among others the determination of body weight and body height.

Easy to perform examinations such as the „timed-up and go“ test or the „chair rising“ test allow a quick assessment of muscle strength and coordination for older persons (A with regard to falls).

Performance of the „timed up & go-test“

Equipment: Chair (with armrest), marked distance (on the floor) 3.0 m, stopwatch

The test person is sitting in an upright position on a chair with armrest. The request is: “Please, get up from this chair, go to the end of the marked distance (3 m), turn around and sit down in the same way! (walking aids normally used in daily life may be used). I will measure the time you need for this task.”

Interpretation:

- Measurement ≤ 10 seconds: Mobility unlikely to be impaired
- Measurement 11 to 29 seconds: Interpretation only possible in combination with other parameters to be looked at
- Measurement ≥ 30 seconds: Impaired mobility and increased fall risk to be assumed

Performance of the “chair-rising-test“

Especially meant to test the strength of the lower extremities

Equipment: Chair (without armrest), stopwatch

The test person is sitting in an upright position on a chair without armrest. The request is: “Please get up 5 times in a row as fast as you can, your legs should be straight! Do not use your arms for help! (if for safety reasons justifiable: Please cross your arms in front of your chest!) I will measure the time you need for this task.”

Interpretation:

- Measurement ≤ 10 seconds: No strength-related walking insecurity to be assumed
- Measurement ≥ 11 seconds: Walking insecurity (mainly due to lacking muscle strength) to be assumed

If necessary an extended geriatric assessment should follow.

III.2 Osteodensitometry

The aims of bone density measurements are:

1. to find out whether bone density is low (T-score < -2.0), as this is the basis for the definition of osteoporosis, as well as the necessary precondition for a proven fracture-reducing effect of antiosteoporotic drugs (A).
2. to determine the precise extent of bone density reduction. This is again important for the assessment of the individual fracture risk and the extent of the recommended therapeutic measures.

The recommended standard procedure for bone density measurement is osteodensitometry by dual X-ray absorptiometry (DXA) of the lumbar spine and the proximal femur.

At the lumbar spine the mean T-score of those vertebrae from L1-L4 is determined for which a measurement with a low probability of an artefact is possible. At the proximal femur, the T-score of the total hip is best suited for risk evaluation (A-D). The evaluation of the 10 year fracture risk in the DVO-guideline is based on the lower of both T-scores of the DXA measurement of the lumbar spine and total hip.

As reference for fracture risk calculation, the T-scores of the NHANES data base were used for the proximal femur. For the lumbar spine the T-scores of the data bases of the manufacturing companies of the DXA equipment were used. A T-score of -2.0 is approximately equivalent to a T-score of -2.5 in older therapy studies. Other methods, standard values, measurement areas or procedures for the determination of bone density are only conditionally applicable for the subsequent risk evaluation.

If radiographs reveal more than one vertebral fracture typical of osteoporosis, bone density measurement may not be necessary before starting a medical therapy if this is appropriate to the clinical overall situation. (B). This recommendation applies for example to multi-morbid older osteoporosis patients with a very high risk of subsequent fractures but difficult access to diagnostic assessment who would not receive proper treatment otherwise. There are also an increasing number of constellations in which cases a meaningful evaluation of bone density is not possible despite fractures typical of osteoporosis. One example is the combination of double-sided hip endoprosthesis and several osteoporotic fractures in the area of the lumbar spine,. In these cases it is generally to be assumed that the bone density measurement would be low and that an efficacy of therapy is ensured (B).

However, for patients with ready access to a bone density measurement, a DXA measurement is recommended even in case of typical vertebral fractures before starting a therapy (D). A normal bone density despite existing fractures should always initiate a diagnostic work up to exclude other potential causes of the fractures. A normal bone density despite typical

vertebral fractures also poses a problem with regard to the usefulness of antiosteoporotic treatment. Such discrepant findings need to be solved on an individual basis. Consultation of a bone expert may be warranted.

Quantitative Ultrasound Methods (A-D) and bone density measurement procedures apart from DXA standard procedures at the lumbar spine and the proximal femur (A-D) can also give information on the fracture risk. Whereas the measurement of bone density by DXA gives information on the absolute fracture risk and the reduction of fracture risk by a specific antiosteoporotic treatment, the latter has not been examined for ultrasound. Before starting antiosteoporotic treatment therefore presently the measurement of bone density by DXA cannot be replaced with some exceptions of a high total risk of fractures determined by ultrasound and/or additional risk factors. In order to avoid an unnecessary double diagnostics the DVO generally recommends the DXA measurement for diagnostic assessment.

A diagnostic assessment by quantitative ultrasound might be useful under the following exceptional circumstances (D):

1. as part of the risk assessment for high risk patients in regions where no DXA equipment is available as a preliminary test preceding a DXA examination in case of a high total risk.
2. as part of the risk assessments for high risk persons with typical vertebral fractures in regions where no DXA equipment is available with direct therapeutical consequence in case of high total risk with no subsequent DXA examination.

The T-scores of those measurement procedures are not transferable to T-scores of DXA measurements with regard to risk assessment (A). In this case the full-text version gives advice for a risk assessment adequate for those procedures.

III.3 Laboratory Tests

For some percent of the patients at risk, laboratory findings may reveal unsuspected secondary osteoporosis or may influence some aspects of diagnostics and therapy.

The aim of the laboratory tests is, therefore, to exclude to a large extent the most important forms of secondary osteoporosis and other potential bone diseases (B-D). It is especially important to exclude osteomalacia which also comes along with low bone density values.

Laboratory tests should, therefore, follow the medical history, clinical examination and osteodensitometry if:

1. fractures after low traumas were the reason for the diagnostic assessment
2. medical history and/or clinical examination reveal or are compatible with secondary osteoporosis
3. the T-score is < -2.0 measured by DXA

For all other persons, e.g. a woman age 77 without fractures and without clinical or historical findings indicative of a secondary osteoporosis with a T-score of -1.0 at the lowest, no laboratory tests have to be done (D).

Increased biochemical parameters of bone turnover in the blood and/or urine have proved in trials to be an independent risk factor for fractures for women and men (A for women, B for men). The lack of standardisation of these parameters under clinical daily routine conditions and the lack of evaluation in combination with other risk factors does not allow general recommendations for the use in routine diagnostics at present (D). Genetic examinations are not yet sufficiently evaluated as independent risk factor for fractures (D).

The following table shows the recommended laboratory tests and lists some of the most important bone disorders which commonly display distractive abnormalities in these tests:

Table 2. Laboratory Tests

Test parameter	Associated diseases
Serum Calcium (B)	↑ Primary hyperparathyroidism or other causes of hypercalcemia ↓ e.g. secondary hyperparathyroidism, malabsorption
Serum Phosphate (D)	↓ secondary hyperparathyroidism, malabsorption
Alkaline Phosphatase (AP) (Serum) (B)	↑ Osteomalacia
Gamma-GT	helpful in discriminating AP increases of skeletal origin from those of hepatic origin
Serum Creatinine (C)	↑ renal osteodystrophy (depending on muscle mass to be expected if creatinine values are > 2-3 mg/dl)
ESR / C-reactive protein (D)	↑ differential diagnostics of inflammatory causes of spinal deformities
Serum Protein Electrophoresis(C)	multiple myeloma
TSH (B)	< 0.3 mU/L endogenous or caused by L thyroxine medication as risk factor for fractures

In the case of aberrant laboratory test results an expert should be consulted for further diagnostic work up and therapy, if necessary. The following recommendations for therapy do not apply in many cases or have to be modified.

III.4 X-ray of the Spine

The aim of X-ray examinations of the thoracic and lumbar spine is to prove osteoporotic compression fractures and to differentiate fractures from other causes of back pain.

It is recommended to perform lateral and anteroposterior radiographs of the thoracic and lumbar spine in case of:

1. acute, newly developed, severe and/or persistent back pain lasting for days(D)
2. chronic unexplored back pain (D)

In case of more than one clinical risk of vertebral fractures (old age, height reduction of several centimetres since age 25 or of more than 2 cm in the course of follow-up examinations, a hip-pelvic distance of less than 2 centimetres, low bone density and existing peripheral fractures) a radiographic examination should also be considered (B-D).

A vertebral fracture can be assumed if the anterior, middle or posterior vertebral height is reduced by more than 20% or by more than 4 mm compared to normal height if these deformities cannot be explained by other visible causes.

III.5 Other Imaging Procedures, Bone Biopsy

CT-, MRI, and scintigraphic examinations are not part of the routine clinical assessment of osteoporosis (D). These methods are used in order to rule out other causes of vertebral deformities and for certain aspects of treatment.

On top of clinical and laboratory examinations bone biopsy allows the diagnosis of rare secondary forms of osteoporosis (e.g. mastocytosis, non-secretory multiple myeloma). Bone biopsy also allows an exact assessment of mineralisation defects in case of non-decalcified biopsies. Bone biopsies are not part of the routine diagnostic work up, but may be considered in case of non-plausible clinical and/or laboratory findings. (D).

IV. Treatment

IV.1. Implementation of Nonpharmacological Measures, Psychosocial Care

For all persons at risk, an implementation of the nonpharmacological measures of fracture prevention is recommended independent of a specific medical treatment (A-D). Obstacles which make the implementation of these measures more difficult should be found out and, if possible, be eliminated.

By psychosocial care of patients after falls and fractures the fear of further incidents and the vicious circle of a further limitation of mobility should be counteracted. Networking with self-aid groups supported by experts is to be recommended (D).

IV.2 Treatment of Pain and Functional Limitations

The treatment of acute and chronic pain caused by fractures and the avoidance of functional limitations after osteoporotic fractures are important tasks of osteoporosis treatment.

After fractures, mobilisation should be started as soon as possible. Pain reduction can be achieved by analgetic treatment according to the WHO scheme, physio-therapeutic measures, if necessary stabilisation by a supporting spinal orthosis (B), and outpatient or inpatient rehabilitation (A within the scope of a proximal femoral fracture, D within the scope of other acute osteoporotic fractures or chronic pain syndromes).

If pain fails to sufficiently resolve after more than 3 months of conservative, multi-modal analgetic treatment of an acute vertebral fracture, vertebroplasty or kyphoplasty might be considered in the context of an interdisciplinary team decision (D).

This recommendation has arisen from the consideration that on the one hand by those procedures a significant acute pain-relieving effect is described but that on the other hand randomised controlled studies and long-term experiences with regard to risks and benefits of those procedures are missing. Beyond controlled trials those procedures should therefore only be used if under a conservative multi-modal pain management after a duration of approximately 3 months the normally to be expected distinct improvement of the pain is not achieved or if an acceptable pain relief cannot be achieved by conservative means within this period of time.

The present kyphoplasty or vertebroplasty studies do not allow any conclusion with regard to the effect of restoring the height of fractured vertebrae on function and quality of life.

IV.3 Evaluation and Treatment of Secondary Causes

If clinical and/or laboratory findings indicate a secondary cause of a high fracture risk. the underlying disorder or risk should be further examined and treated consulting an expert if necessary. (C with reference to avoiding a TSH-reduction, B with reference to the treatment of a primary hyperparathyroidism, D with reference to most of the other secondary causes).

IV.4 Specific Antiosteoporotic Drug Treatment

IV.4.1 Recommendations for antiosteoporotic treatment in case of manifest osteoporosis with vertebral fractures

A specific antiosteoporotic treatment is recommended due to the high subsequent risk of fractures for all persons after a osteoporotic vertebral fracture if the T-score of the DXA bone density measurement at the lumbar spine or at the proximal total femur is < -2.0 and thus the therapeutic efficacy of the osteoporosis medication is proved.

The future risk of vertebral fractures is especially high in the first months till years after a newly acquired osteoporotic vertebral fracture. This makes it important to start therapy quickly (C).

IV.4.2 Recommendations for antiosteoporotic treatment in case of high fracture risk

A specific antiosteoporotic treatment is also recommended if the estimated 10 year risk of vertebral and proximal femoral fractures based on the available epidemiological data is > 30% and the T-scores of the DXA bone density measurement at the lumbar spine or at the proximal total femur is ≤ -2.0 and thus the therapeutic efficacy of the osteoporosis medication is proved.

Assuming a mean pharmacological fracture reduction of 30-40% for the sum of vertebral fractures and peripheral fractures this corresponds to a number needed to treat of approximately 15-30 for the prevention of vertebral and/or peripheral fractures for the recommended minimum treatment time of 3-5 years.

The following multi-factorial risk assessment gives the physician and the patient a better orientation with regard to the extent of the medium-term fracture risk compared to a risk assessment based on a single risk factor. For practical reasons just the average T-scores which correspond to a 30% fracture risk are shown in Table 3. One should be aware, however, that the actual T-score that constitutes a 30% fracture risk rather corresponds to a value somewhere between the upper and lower 95% confidence intervals of fracture prediction.

Table 3. T-Scores depending on age and sex which are on average associated with a 30% fracture risk of vertebral and proximal femoral fractures within 10 years

Age given in years		T-Score
Woman	Man	(lower value of the two measurements at lumbar spine and proximal total femur)
50-60	60-70	-4.0
60-65	70-75	-3.5
65-70	75-80	-3.0
70-75	80-85	-2.5
>75	>85	-2.0

The assessment of the 10 year fracture risk in Table 3 only includes sex, age and bone density as risk factors. If in addition one of the following risk factors is present, the total fracture risk is approximately 1.5-2 times higher. This means that a 30% fracture probability corresponds to a T-score that is up to one unit higher than suggested in Table 3 (B-D). The

recommendation for an antiosteoporotic drug treatment in case of one or more of those risk factors is accordingly given by a maximum of one T-score higher than without any risk factor. A therapy is for example recommended for a woman age 67 with one of the following risk factors already at T-scores between -3.0 and -2.0 whereas a recommendation without additional risk would only be given at -3.0 or below.

Risks which should be taken into consideration here:

1. hip fracture in a parent
2. peripheral fracture after low trauma
3. continuous smoking
4. multiple falls
5. immobility

For the definition of those risks it is referred to chapter II.1.

Underweight is a clinical risk factor for fractures but does not play a role as an independent risk factor for the assessment of the fracture risk after a DXA measurement. This is because weight is closely associated with bone density measurements and does not constitute an additive risk after inclusion of the bone density measurement (B).

There are various situations, as for example multi-morbidity, short life expectation or the patient's wishes, for which based on the clinical overall context a higher target agreement for the avoidable 10 year fracture risk is acceptable. In line with this a lower treatment limit of up to one T-score can be chosen (D). It would for example be acceptable in such a case to start treatment at a T-score of -3.0 or lower for a 67 year old woman with one additional risk.

There is no evidence for the efficacy of antiosteoporotic drug treatment above a DXA T-score of -2.0 (C). There is generally no evidence for the efficacy of drug treatment depending on T-scores of other measuring procedures than the DXA measurement. Therefore those devices, apart from few exceptions described in the full-text version, are not recommended for making a decision on drug treatment (D).

Based on present evidence fracture reduction by antiosteoporotic drug treatment is only proved for the acute situation of a high fracture risk. The is no evidence that drug treatment in persons with a low fracture risk will prevent the increase in fracture risk in later years.

IV.4.4 Drugs

IV.4.4.1 Drugs the fracture reducing effects of which are best proved

The best proved medical therapy options regarding fracture reduction are for post-menopausal women alendronate, oestrogen, ibandronate, raloxifene, risedronate, strontium ranelate, and teriparatide. For all drugs mentioned, a reduction in vertebral fractures is proved to a similar

extent after 3 years (A). For alendronate (A), oestrogen (A), risedronate (A), strontium ranelate (A) and teriparatide (B) a reduction in peripheral fractures is also proved.

For post-menopausal women who are primarily treated with oestrogen due to vasomotoric symptoms generally no additional specific osteoporosis drug treatment is necessary. An exception may be very low dosed oestrogen (D).

Apart from vasomotoric symptoms as a rational for oestrogen treatment, a combination therapy with oestrogens and progesterone for post-menopausal women with high fracture risk can only be recommended as an exception for fracture prevention. This is because of the individually variable, on average, however, unfavourable benefit-risk ratio. The benefit-risk ratio of an oestrogen alone therapy is balanced. Both therapy options are only to be used in case of side effects or contraindications against the other osteoporosis drugs mentioned above. and after carefully taking into consideration together with the patient the individual benefits and risks within the scope of secondary prevention (A). In case of an intact uterus, an additional treatment with progesterone is obligatory.

For men a therapy with alendronate has proved to be reducing vertebral fractures (A). In Switzerland teriparatide is approved for therapy of male osteoporosis.

IV.4.4.2 Individual Choice of Therapy, Combination Therapy

At present there is no proof of a preferential, fracture reducing effect of the substances mentioned above for certain patient groups (e.g. age, degree of bone turnover, degree of the osteoporosis) (B).

The individual drugs show differences with regard to the kind of effect and the pharmacokinetics. Their positive effects also differ with regard to different types of fractures and the long-term fracture reduction in case of continuous or discontinuous intake. Details of those differences can be seen in the full-text version.

A general or for certain patient groups existing superiority of certain drugs with regard to fracture reduction is, however, not proved especially as the study collectives are not fully comparable and head-to-head studies on fracture basis are not available.

For the individual choice of the drugs possible side and additional effects and the intake modalities should be taken into consideration.

The following table gives an overview of dosages and side effects of the drugs mentioned above. Incorporated are only those drugs which were approved and available in Germany, Austria or Switzerland by the end of the literature search period at the beginning of February 2005.

Table 4. Medical Therapy of Osteoporosis

Medicinal product/ trade name/ dosage/ extra-skeletal additional effects	More common side effects (>10% ifap index – German database for drugs) Contraindications
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<p>Alendronate</p> <p>Fosamax® Different generic medicinal products</p> <p>10 mg 1x day p.o. 70 mg 1 x week p.o.</p>	<p>Side Effects</p> <p>Esophagitis, minor hypocalcemia, minor hypophosphatemia</p> <p>Contraindications</p> <ul style="list-style-type: none"> • Diseases of the esophagus and other reasons for a delay of the esophageal emptying as strictures or achalasia. • Inability to stand upright or to sit down for at least 30 minutes • Hypocalcemia • Severe renal insufficiency (GFR < 35 ml/h) • In case of 10 mg dosage: severe gastrointestinal diseases within the last year (e.g. peptic ulceration, active bleeding or surgery at the upper gastrointestinal tract). Here one has to be extremely careful in case of a 70 mg dosage.
<p>Oestrogen</p> <p>Various medicinal products</p> <p>Additional Effects</p> <p>See full-text version</p>	<p>Contraindications</p> <ul style="list-style-type: none"> • Suspicion of or existing uterine carcinoma or breast cancer • Severe liver disease • Jaundice, idiopathic jaundice in medical history • present or in medical history of thrombophlebitis and thromboembolic processes • Unverified vaginal bleedings • Sickle cell anaemia • Otosclerosis • present or recent arterial thromboembolic diseases (particularly angina pectoris, myocardial infarction) • Porphyria <p>Furthermore, oestrogen alone therapy is absolutely contraindicated (without progesterone supplement) for women with intact uterus due to the high risk of an endometrium carcinoma. Personal or family history of breast cancer is not generally regarded as a strict contraindication.</p>
<p>Raloxifene</p> <p>Evista® Optruma®</p> <p>60 mg 1 x day p.o.</p> <p>Additional Effects</p> <p>Level of recommendation B for a reduced incidence of oestrogen receptor-positive breast cancer</p>	<p>Side Effects</p> <ul style="list-style-type: none"> • Vasodilatation (hot flushes) especially in the first 6 months of treatment <p>Contraindications</p> <ul style="list-style-type: none"> • present or history of thromboembolic event, including deep vein thrombosis, pulmonary embolism and thrombosis of the retinal vein • impaired liver function including cholestasis • Severe renal damage • Unverified bleedings of the uterus
<p>Risedronate</p> <p>Actonel® Actonel plus Kalzium®</p> <p>5 mg 1 x day p.o. 35 mg 1 x week p.o. 35 mg 1 x week p.o. + 500 mg calcium/day, day 1-6</p>	<p>Contraindications</p> <ul style="list-style-type: none"> • Hypocalcemia • Severe kidney function disorder with a creatinine clearance of < 30 ml/minute. • In case of 5 mg: in case of esophageal diseases and other factors which delay esophageal emptying as strictures or achalasia or in case of inability to stand upright or to sit down for at least 30 minutes, the medicinal product should be used with extreme care. • Risedronate + calcium in addition: hypocalcemia, hypercalciuria, nephrolithiasis
<p>Strontium Ranelate</p> <p>Protelos®</p> <p>2 grams/day p.o.</p>	<p>Contraindications</p> <ul style="list-style-type: none"> • Severe renal insufficiency (creatinine clearance < 30 ml/min.) • Strontium ranelate should be used with care for female patients with increased risk of or history of venous thromboembolisms.

<p>Teriparatide</p> <p>Forsteo®</p> <p>20 µg/day s.c.</p> <p>Maximum duration of therapy is 18 months</p>	<p>Contraindications</p> <ul style="list-style-type: none"> • hypocalcemia • Severe renal insufficiency • Metabolic bone diseases (e.g. hyperparathyroidism or Paget's disease) excluding primary osteoporosis • Unverified increase of alkaline phosphatase • Preceding radiotherapy of the skeleton • Careful use in case of present or recent urolithiasis • Careful use in case of moderately severe renal insufficiency
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IV.4.4.3. Further Antiosteoporotic Drugs

Apart from the drugs mentioned in IV.4.2.2 there are several additional antiosteoporotic drugs which are approved for therapy of post-menopausal osteoporosis the effect of which on the reduction of vertebral fractures is, however, only proved with a lower evidence level (B-D) than it is the case for the drugs mentioned above.

These drugs include: alfacalcidol (B), calcitonin (B), etidronate (B), fluorides (B) and nandrolone decanoate (D).

With the exception of alfacalcidol (here: recommendation level B) a peripheral fracture reduction is not proved for those drugs. Indications for the prescription are incompatibility against drugs with recommendation level A or patient preference (D).

For detailed information on those drugs it is referred to the full-text version.

IV.4.4.4. Combination Treatment

Several studies exist which report about a higher increase in bone density of post-menopausal women by the combination of two antiresorptive substances. For men no data are available. Due to lack of data and the poor association of fracture reduction and bone density changes no conclusions on the efficacy of these combinations can be drawn at present. Thus a recommendation for a combination treatment cannot be given at present. An exception might be a low dose hormone therapy for post-menopausal symptoms with a presumed lack of full effect on bone metabolism. In this case a combination with a specific antiosteoporotic drug is acceptable (D).

IV.4.4.5 Duration of Treatment

Osteoporosis is a chronic disease apart from the few reversible forms of secondary osteoporosis. The duration of the therapy should therefore be at least 3-5 years. This is the shortest period of time in which statements about fracture reducing effects of the drugs can safely be given (A). After this, the patient should be newly evaluated. The present treatment concepts range from a temporary suspension of therapy up to a constant therapy in case of a continuing increased fracture risk (D).

V. Monitoring

V.1 Follow-up for Patients without Antiosteoporotic Drug Treatment

Patients who have an increased risk in the initial examination should be re-evaluated with regard to the implementation of nonpharmacological measures, the risk factors and the future development of the fracture risk in intervals adequate to the risk in question. It is rare that there is a decrease in bone density below the measurement error before a time of 2 years. Follow-up examinations of bone density are in general therefore not recommended in intervals of less than 2 years (B).

A documented decrease in height of more than 2 cm since the last examination or acute back pain may be symptoms of a new fracture. In these cases a radiological examination is recommended (D).

In case of abnormalities in the laboratory tests that are due to potentially treatable conditions or are suggestive of other contributing diseases, laboratory follow-up should be pursued (D).

V.2 Follow-up for Patients Undergoing Antiosteoporotic Drug Treatment

After initiating a specific medical therapy clinical examinations are recommended in the beginning after 3-6 months and later after 6-12 months. The aim is to document pain, functionality, risk factors, implementation of nonpharmacological measures, weight, and height (D).

For the documentation of a successful drug treatment bone density measurements are only partly suitable (B). A non-increase in bone density when taking antiresorptive drugs is not an indication of a decreased fracture reducing effect (B).

At present, there are no evaluated criteria for a medical therapy failure. A therapy failure, however, can be assumed if:

1. there is a decrease in bone density during follow-up beyond the population-based measuring error limit (D)
2. a fracture rate which in relation to the absolute fracture rate is clearly above the expected relative rate of fracture reduction (D)

Under study conditions biochemical parameters of bone turnover give prognostic indications of the extent of the fracture reducing effect of antiresorptive drugs (B). For the use in daily routine those parameters have not yet been sufficiently standardised and evaluated.

VI. Further Information

Details and references of the recommendations of the executive summary as well as further information on risks, measuring procedures and therapy options can be seen in the full-text version of the guideline (<http://www.lutherhaus.de/dvo-leitlinien>).