



Complete Summary

GUIDELINE TITLE

Osteoporosis: prevention and treatment.

BIBLIOGRAPHIC SOURCE(S)

University of Michigan Health System. Osteoporosis: prevention and treatment. Ann Arbor (MI): University of Michigan Health System; 2002 Mar. 12 p. [3 references]

COMPLETE SUMMARY CONTENT

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SCOPE

DISEASE/CONDITION(S)

Osteoporosis in postmenopausal women and secondary osteoporosis related to long-term glucocorticoid use, organ transplant, or other medical conditions

GUIDELINE CATEGORY

Diagnosis
Evaluation
Management
Prevention
Risk Assessment
Treatment

CLINICAL SPECIALTY

Endocrinology
Family Practice

Internal Medicine
Obstetrics and Gynecology

INTENDED USERS

Physicians

GUIDELINE OBJECTIVE(S)

To decrease osteoporotic fractures and their associated morbidity and mortality

TARGET POPULATION

Postmenopausal women and persons at risk for secondary osteoporosis related to long-term glucocorticoid use, organ transplant, or other medical conditions

INTERVENTIONS AND PRACTICES CONSIDERED

Prevention

1. Weight bearing exercise
2. Adequate dietary calcium and vitamin D
3. Preventive use of bisphosphonates or calcitonin during glucocorticoid therapy

Risk Assessment and Diagnosis

1. Assessment of risk factors, e.g., age, smoking status, body weight, frailty, history of fracture, chronic glucocorticoid use, organ transplant status, chronic medical conditions, other medical conditions
2. Dual emission X-ray absorptiometry (DEXA) measurement of bone mineral density (BMD)
3. Measurement of biochemical markers of bone resorption (considered but not recommended)
4. Evaluation for secondary causes of osteoporosis
5. Referral to specialists

Treatment/Management

1. Pharmacologic therapies
 - Calcium with vitamin D
 - Bisphosphonates such as alendronate (Fosamax®) or risedronate (Actonel™)
 - Selective estrogen receptor modulators (SERMs), e.g., raloxifene (Evista®)
 - Estrogen or hormone replacement therapy (HRT), i.e., estrogens (estradiol [Estrace®], esterified estrogens [Estratab®], estropipate [Ogen®], conjugated estrogens [Premarin®], transdermal estradiol; progestins (medroxyprogesterone [Provera®], micronized progesterone [Prometrium®]; combined estrogen with progestin [Prempro™])
 - Calcitonin nasal spray (Miacalcin®)

Considered but not necessarily recommended at this time:

- Combined estrogen and bisphosphonate
 - Testosterone replacement or supplement in men
 - Calcitriol
 - Tamoxifen
 - Thiazide diuretics (e.g., hydrochlorothiazide)
 - HMG-coA-reductase inhibitors (statins)
 - Phytoestrogens
2. Non-pharmacologic therapies
- Weight bearing or balance exercises
 - Fall prevention measures
 - Anatomically designed hip protectors

Follow-up

Repeat DEXA measurement

MAJOR OUTCOMES CONSIDERED

- Risk for osteoporosis or osteoporotic fractures
- Incidence of osteoporosis or osteoporotic fractures
- Bone mineral density, bone turnover and loss
- Predictive value of diagnostic tests
- Mortality related to osteoporotic hip fractures
- Morbidity (chronic pain, disability, deformity, depression) related to osteoporotic fractures
- Pain relief
- Medication side effects

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

The literature search for this project started with the results of a literature search performed by the National Osteoporosis Foundation (Osteoporosis: review of the evidence for prevention, diagnosis and treatment and cost-effectiveness analysis), published in 1998 and including literature through 1996. We searched subsequent literature. The search was conducted prospectively using the major key words of: osteoporosis (or osteoporosis, postmenopausal); osteopenia; either hip fractures or spinal fractures with either osteoporosis or osteopenia; English language; cost savings, cost and cost analysis; sensitivity and specificity, false negative reactions, false positive reactions, likelihood functions, sensitivity, diagnosis; clinical protocols, physician's practice patterns, algorithms, outcome and process assessment (health care), consensus development conferences, practice

guidelines, guideline; clinical trials, clinical trials phase IV, controlled clinical trials, multicenter studies, randomized controlled trials, cohort studies. Specific searches were performed for (1) postmenopausal osteoporosis (1996-99), for (2) steroids (1994-99), and for organ transplantation, transplantation (1990-99) with each of the following: densitometry x-ray, bone density, absorptiometry photon; calcium, calcium carbonate, calcium citrate; Vitamin D; estrogens, progestational hormones, androgens, estrogen replacement therapy; diphosphonates; tamoxifen; piperidines; calcitonin; exercise; accident prevention. Searches were also performed for men, male; alternative medicine, isoflavones; alkaline phosphatase, hydroxyproline, osteocalcin, bone marker, bone and bones; osteopenia (1990-99).

The search was conducted in components each keyed to a specific causal link in a formal problem structure (available upon request). The search was supplemented with very recent clinical trials known to expert members of the panel. Negative trials were specifically sought. The search was a single cycle.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Levels of Evidence

- A. Randomized controlled trials
- B. Controlled trials, no randomization
- C. Observational trials
- D. Opinion of expert panel

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Not stated

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Not stated

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Note from the National Guideline Clearinghouse (NGC): The following key points summarize the content of the guideline. Refer to the full text for additional information on drug dosing, DEXA-T scoring, patient screening criteria, etc. The levels of evidence (A, B, C, D) are repeated at the end of the Major Recommendations field.

Definitions

- Bone mineral density (BMD) correlates with skeletal strength and fracture risk.
- Dual emission X-ray absorptiometry (DEXA) measures BMD.
- A DEXA T-score is the number of standard deviations from mean BMD in young adult women.
- Osteoporosis is defined as a DEXA T-score ≤ -2.5 , osteopenia as > -2.5 but < -1.0 (refer to Table 1 in the original guideline document for details).

General Clinical Relevance

Fractures related to osteoporosis are common and have high morbidity [C].

Glucocorticoids can cause significant bone loss, particularly during the first 6 to 12 months of use [C].

Prevention

Recommend weight bearing exercise and adequate calcium and vitamin D across the life span (refer to Table 6 in the original guideline document for details) [D].

Risk Assessment and Diagnosis

- Assess all adults for clinical risk factors for osteoporotic fracture (refer to Table 2 in the original guideline document for details) [C]
 - Postmenopausal woman with one or more of the following:

- Age ≥ 65 years
- Current smoking
- Low body weight
- Frailty
- Personal history of fracture without substantial trauma age ≥ 40
- Hip, wrist, or spine fracture without substantial trauma in 1st degree relative ≥ 50
- Chronic glucocorticoid use (prednisone ≥ 7.5 mg daily, or equivalent, for ≥ 6 months)
- Organ transplant or pending transplant
- Other associated medical conditions and medications
- Order DEXA based on clinical risk factors and potential impact of results on management (refer to Table 3 in the original guideline document for details).
- Evaluate appropriately and refer, when indicated, for secondary causes of osteoporosis (refer to Table 4 in the original guideline document for details) [D].

Treatment

- Treat based on DEXA T-score and clinical risk factors for fracture (refer to Table 2 and Table 6 in the original guideline document for details)
 - Prior osteoporosis-related fracture [A].
 - T-score ≤ -1 and (a) glucocorticoid use or (b) pending or post-transplant, especially if on steroids or (c) postmenopausal woman at high risk (i.e., with other risk factors for fracture but not already receiving hormone replacement therapy [HRT] [A]).
 - T-score < -2 and (a) postmenopausal woman [A] or (b) man [A] or (c) person with other risk factors [D].
- When starting glucocorticoids consider therapy for prevention or treatment of osteoporosis [A].
- Base management strategies on benefits and risks (refer to Table 6, Table 7, and Table 8 in the original guideline document for details)
 - In post-menopausal women with osteoporosis:
 - Alendronate and risedronate reduce hip and vertebral fracture risk [A].
 - Raloxifene and calcitonin reduce vertebral fracture risk [A].
 - Hormone replacement therapy reduces vertebral and hip fracture risk [C].
 - In men with osteoporosis alendronate reduces vertebral fracture risk [A].
 - In glucocorticoid use risedronate (and perhaps alendronate) reduces vertebral fracture risk [A].

Follow-up

- Follow-up osteoporosis or osteopenia with a repeat DEXA based on a patient's situation (refer to Table 3 and Table 5 in the original guideline document for details).
- For most persons an interval of ≥ 2 years between DEXAs provides the most meaningful information.
- Early in glucocorticoid use and/or after transplantation consider repeating DEXA in 6 to 12 months.

Definitions:

Levels of Evidence

Levels of evidence reflect the best available literature in support of an intervention or test.

- A. Randomized controlled trials
- B. Controlled trials, no randomization
- C. Observational trials
- D. Opinion of expert panel

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for each recommendation (see Major Recommendations).

Conclusions were based on prospective randomized clinical trials if available, to the exclusion of other data; if randomized controlled trials were not available, observational studies were admitted to consideration. If no such data were available for a given link in the problem formulation, expert opinion was used to estimate effect size.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Overall Benefits

- Improved identification of patients at high risk for osteoporosis
- Decreased incidence of osteoporotic fractures and associated morbidity and mortality

Drug Therapies

Alendronate

- Reduces risk for vertebral and hip fracture by 30 to 50% in postmenopausal women with osteoporosis.

Calcitonin

- Stabilizes or even increases spinal bone mineral density (BMD) early and late after menopause
- Reduces vertebral fracture risk and significantly reduces the pain of acute vertebral fractures (in small studies)
- Preserves lumbar bone and prevents vertebral bone loss during glucocorticoid therapy

Calcitriol

- Reduces incidence of vertebral deformity

Estrogen

- Decreases spine and hip fracture
- Provides relief of menopausal symptoms such as hot flashes and genitourinary atrophy, but not urinary incontinence

Estrogen and bisphosphonate, combined

- Produces significant increases in lumbar and hip BMD compared to placebo or either alone

Hydrochlorothiazide

- Provides a modest but significant BMD benefit in doses as low as 12.5 mg per day in normotensive persons

Raloxifene

- Decreased spine fracture in postmenopausal women with osteoporosis

Risedronate

- Reduces risk for vertebral and hip fracture by 30 to 50% in postmenopausal women with osteoporosis

Tamoxifen

- Has a small positive effect on BMD of the hip and spine in postmenopausal women

Testosterone

- Improves BMD in men who are taking glucocorticoids and have low serum testosterone
- Should be strongly considered for any younger man with definite hypogonadism

Non-drug Therapy

Anatomically designed hip protectors:

- Several randomized trials have shown benefit of anatomically designed hip protectors, including a large study of frail elderly at risk for falls, which demonstrated a significant, greater than 40% reduction in hip fractures.

Subgroups Most Likely to Benefit:

Patients with Acute Vertebral Fractures

Calcitriol therapy decreases pain.

Postmenopausal Patients

Drug therapy increased bone mineral density (BMD) when one of the following was used: calcium plus vitamin D, risedronate, raloxifene, estrogen, or calcitonin.

Postmenopausal Patients with Osteoporosis

- Calcium with vitamin D therapy decreased hip fracture (if patient vitamin D deficient).
- Alendronate, risedronate, or estrogen therapy decreased spine and hip fracture.
- Raloxifene therapy decreased spine fracture and showed a trend for decreased non-spine fracture.
- Calcitonin therapy decreased spine fracture.

Men with Osteoporosis

- Calcium with vitamin D therapy increased BMD.
- Alendronate therapy decreased spine fracture.

Patients using Glucocorticoids

- Calcium with vitamin D therapy or estrogen therapy increased BMD.
- Alendronate or calcitonin therapy increased BMD and showed a trend for decreased spine fracture.
- Risedronate therapy decreased spine fracture.

POTENTIAL HARMS

Adverse Effects of Drug Therapies

Calcium

- Constipation is common.

Bisphosphonates

- Mild gastrointestinal effects and rare severe gastrointestinal effects

Raloxifene

- Risk of deep venous thrombosis and pulmonary embolism approximately the same as hormone replacement therapy
- Hot flashes

Calcitriol and Other Forms of Vitamin D

- Side effects of calcitriol or high doses of other forms of vitamin D include hypercalcemia, hypercalciuria, and nephrolithiasis, and therefore serum and urinary calcium levels must be monitored by a subspecialist or others familiar with their use.

Estrogens

- Estrogen in a woman with an intact uterus raises her risk of endometrial cancer, although adding a progestin reduces the risk to baseline.
- The potential increase in breast cancer risk remains controversial. Long-term use of estrogen (>8 years) may increase breast cancer relative risk to 1.25.
- Associated with an increased risk of venous thromboembolic disease and cholecystitis.

Calcitonin

- Rhinitis has been observed in 5% excess compared with placebo.

Tamoxifen

- May cause a significant decrease in BMD in premenopausal women (due to interference with estrogen).

Non-drug Therapies

Anatomically designed hip protectors:

- Patient discomfort and concern about appearance limit compliance.

Subgroups Most Likely to be Harmed:

Bisphosphonates

- Should be avoided if creatinine clearance is <30-35.
- Safety is not known for women during childbearing years

Calcitonin Nasal Spray

- Caution is urged in renal failure.

Premenopausal Women Using Tamoxifen

- May cause a significant decrease in BMD.

Women Patients with Intact Uterus Using Hormone Replacement Therapy (HRT)

- Raises her risk of endometrial cancer, although adding a progestin reduces the risk to baseline.

CONTRAINDICATIONS

CONTRAINDICATIONS

Bisphosphonates

Reflux without esophagitis is a relative but not an absolute contraindication.

QUALIFYING STATEMENTS

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These guidelines should not be construed as including all proper methods of care or excluding other acceptable methods of care reasonably directed to obtaining the same results. The ultimate judgment regarding any specific clinical procedure or treatment must be made by the physician in light of the circumstances presented by the patient.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Staying Healthy

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

University of Michigan Health System. Osteoporosis: prevention and treatment. Ann Arbor (MI): University of Michigan Health System; 2002 Mar. 12 p. [3 references]

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2002 Mar

GUIDELINE DEVELOPER(S)

University of Michigan Health System - Academic Institution

SOURCE(S) OF FUNDING

University of Michigan Health System

GUIDELINE COMMITTEE

Osteoporosis Guideline Team

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

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Guidelines Oversight Team: Connie Standiford, MD; Lee Green, MD, MPH; Van Harrison, PhD

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

The University of Michigan Health System endorses the Guidelines of the Association of American Medical Colleges and the Standards of the Accreditation Council for Continuing Medical Education that the individuals who present educational activities disclose significant relationships with commercial companies whose products or services are discussed. Disclosure of a relationship is not intended to suggest bias in the information presented, but is made to provide readers with information that might be of potential importance to their evaluation of the information.

Team Member	Company	Relationship
Van Harrison, PhD	(None)	

Robert Lash, MD	Merck, Aventis, Procter & Gamble, Lilly	Consultant
Jane McCort, MD	(None)	
Yolanda Smith, MD	Pfizer, Eli Lilly	Research Grant
Lourdes Velez, MD	(None)	

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from the [University of Michigan Health System Web site](#).

AVAILABILITY OF COMPANION DOCUMENTS

None available

PATIENT RESOURCES

None available

NGC STATUS

This NGC summary was completed by ECRI on March 19, 2003. The information was verified by the guideline developer on April 23, 2003.

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