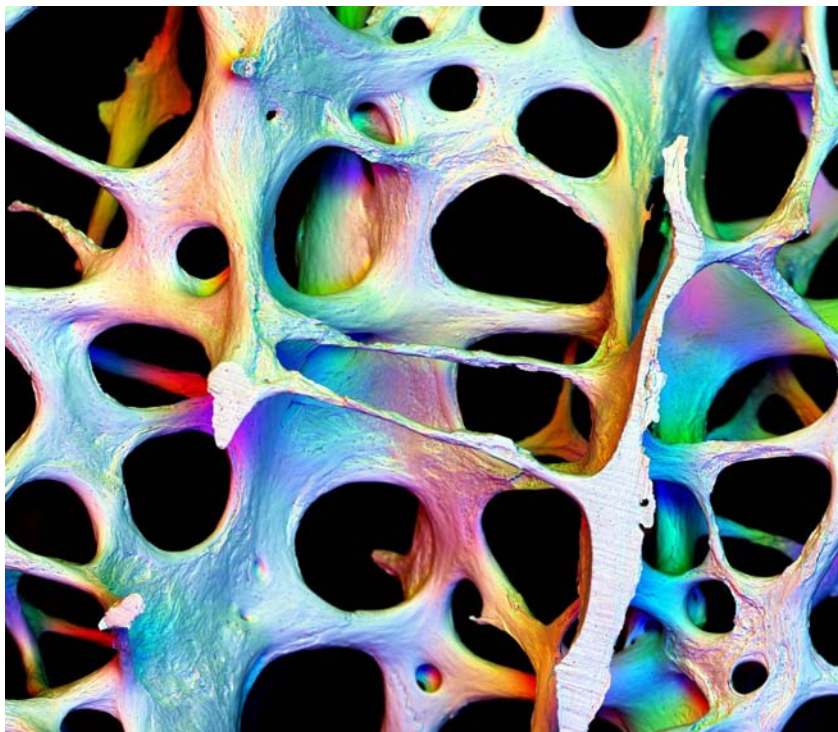


Fast Facts



Fast Facts: Osteoporosis

Juliet E Compston and Clifford J Rosen
Sixth edition





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Declaration of Independence

This book is as balanced and as practical as we can make it.
Ideas for improvement are always welcome: feedback@fastfacts.com



Fast Facts: Osteoporosis

First published 1997; second edition 1999; third edition 2002;
fourth edition 2004; fifth edition 2006
Sixth edition March 2009

Text © 2009 Juliet E Compston, Clifford J Rosen

© 2009 in this edition Health Press Limited

Health Press Limited, Elizabeth House, Queen Street, Abingdon,
Oxford OX14 3LN, UK

Tel: +44 (0)1235 523233

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Book orders can be placed by telephone or via the website.

For regional distributors or to order via the website, please go to:

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For telephone orders, please call +44 (0)1752 202301 (UK and Europe),

1 800 247 6553 (USA, toll free), +1 419 281 1802 (Americas) or

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ISBN 978-1-905832-51-4

The cover image is a composite BSE scanning electron microscopy image of a parasagittal slice of L4 from 89-year-old female. Information from three 'overhead' fast electron detectors was coded as red, green or blue components in order to create the composite image. Color hue shows orientation and color intensity shows the slope of the surface. Field, 4.24 mm wide and high. Sample, 2.8mm thick. Reproduced with the permission of Professor Alan Boyde, Queen Mary, University of London, UK.

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Fast Facts: Osteoporosis/

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Medical illustrations by Dee McLean, London, UK.

Typesetting and page layout by Zed, Oxford, UK.

Printed by Latimer Trend & Company Limited, Plymouth, UK.

Text printed with vegetable inks on biodegradable and recyclable paper manufactured from sustainable forests.



Low
chlorine



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Glossary of abbreviations

Anabolic hormones: synthetic or natural hormones that stimulate bone remodeling, particularly by enhancing bone formation more than bone resorption

Antiresorptive drugs: hormonal or synthetic agents (including estrogens, raloxifene, bisphosphonates and calcitonin) that work by suppressing bone remodeling, particularly bone resorption

Bisphosphonates: drugs that bind to bone mineral with antiresorptive properties

BMD: bone mineral density

BMU: bone multicellular (or remodeling) unit

Calcitonin: a naturally occurring polypeptide that inhibits bone resorption

DXA: dual-energy X-ray absorptiometry

HRT: hormone replacement therapy

Osteoblast: a cell responsible for the formation of bone

Osteoclast: a large multinuclear cell that resorbs bone

Osteogenesis imperfecta: an inherited disorder of collagen characterized by bones that fracture easily

Osteomalacia: softening of bones caused by a loss of mineral, usually due to a deficiency in vitamin D

PTH: parathyroid hormone

QUS: quantitative ultrasound

SERM: selective estrogen-receptor modulator

T-score: standard deviation score related to mean reference value for peak bone mass

Z-score: standard deviation score related to mean reference value for age-matched bone mineral density

Introduction

The diagnosis and treatment of osteoporosis has been revolutionized in the past decade. The technology for imaging trabecular and cortical bone has improved dramatically through the use of magnetic resonance imaging and quantitative computed tomography (CT). Utilization of bone mineral density (BMD) measurements to assess the risk of fracture has grown exponentially. However, the identification of high-risk individuals for treatment has now been significantly improved by the FRAX™ risk-assessment tool. This online algorithm, supported by the World Health Organization, enables clinicians to estimate the 10-year probability of major osteoporotic fracture using clinical risk factors with or without BMD measurements. Bone quality has taken on a new meaning in light of studies using dual-energy X-ray absorptiometry and CT together. Markers of bone turnover, another indicator of risk, have become more precise and are now easier to use and interpret.

On the treatment side, the results of large randomized trials have broadened our perspective on therapies for preventing and treating this condition. New bisphosphonates with reduced dosing frequency have been approved; the most recent of these, zoledronate, requires only once yearly administration. Parathyroid hormone (PTH) peptides have emerged as exciting new options for building bone mass and preventing devastating fractures in severely osteoporotic individuals. Newer means of administering PTH or altering the frequency of administration may lead to wider utilization of a relatively safe but expensive intervention. Similarly, strontium ranelate has been found to be effective in reducing fractures. New selective estrogen-receptor molecules are being developed and are likely to be approved in the future. Hormone replacement has beneficial effects on the skeleton, but these are outweighed in older postmenopausal women by several adverse outcomes, including a greater risk of stroke and breast cancer. Calcium and vitamin D supplementation is probably useful as an adjunct in patients with established osteoporosis, but its role as global preventive therapy for all postmenopausal women has been questioned by several recent randomized controlled trials.

Thus, this sixth edition of *Fast Facts: Osteoporosis* highlights recent developments in the therapeutic and diagnostic arena, while maintaining the background sections that clarify the pathophysiology of osteoporosis and the homeostatic determinants of peak bone acquisition and maintenance.

As we have maintained from the beginning, family physicians and healthcare professionals play a key role in diagnosing, preventing and treating this disease. In spite of substantial advances in the identification of high-risk individuals and the emergence of new treatments, many patients with fractures still do not receive appropriate management. Successful bridging of this care gap requires keen awareness of risk factors amongst healthcare professionals and the lay public alike, better communication between secondary and primary care, and more widespread use of appropriate therapeutic interventions. Poor adherence to osteoporosis therapy provides a major challenge that may be addressed by better patient education and follow-up in primary care. We believe this book will help all clinicians achieve this goal.

Osteoporosis is a major cause of illness and death in the elderly. The condition is characterized by low bone mass (Figure 1.1), which increases the risk of fracture, particularly of the spine, hip and wrist.

Of people surviving to 80 years of age, 1 in 3 women and 1 in 5 men will suffer a hip fracture. These so-called ‘fragility’ fractures result in annual costs estimated at £2.1 billion in the UK, €25 billion in Europe and US\$19 billion in the USA. In women, the hospital costs for osteoporotic fractures exceed those for stroke and myocardial infarction (Figure 1.2).

Fractures

The total number of fractures attributable to osteoporosis each year is estimated at 250 000 in the UK and 1.5 million in the USA. Worldwide, it is estimated that 200 million women suffer from osteoporosis. By the age of 50, the lifetime risk of a fracture due to osteoporosis in a white woman is nearly 40%, similar to the lifetime risk for coronary heart

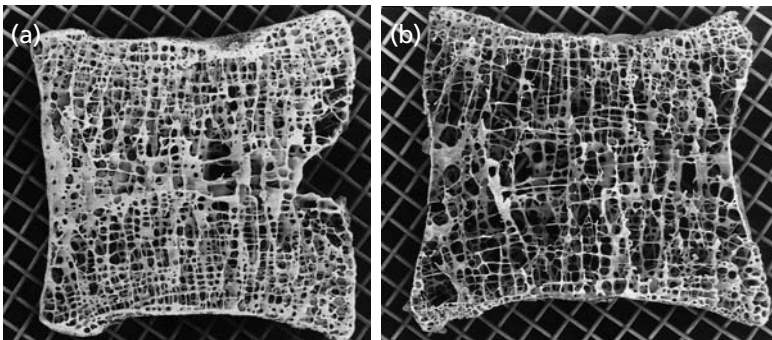


Figure 1.1 Scanning electron micrograph images of 4 mm-thick slices of lumbar vertebrae (vertebral bodies) from (a) a young person and (b) an elderly person, showing the reduction in bone mass and loss of bone structure associated with aging. The samples are resting on a 2.33 periodicity wire mesh grid. Reproduced with the permission of Professor Alan Boyde, Queen Mary, University of London, UK.

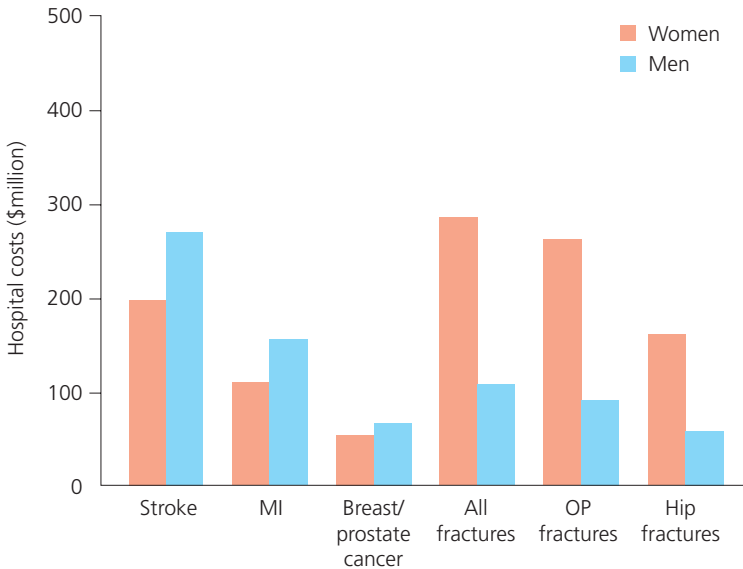


Figure 1.2 Hospital costs attributable to different diseases in Sweden. In women, the costs for treating osteoporotic (OP) fractures are greater than those for treating stroke, myocardial infarction (MI) or breast cancer. The number of bed days occupied by women with OP fractures also exceeds the number attributable to stroke and heart disease (data not shown). Adapted from Johnell et al. 2005.

disease; in men, the corresponding figure is 13% (see Osteoporosis in men, page 87) (Figure 1.3).

In the UK, there are an estimated 60 000 hip fractures, 50 000 fractures of the radius and 40 000 clinically diagnosed vertebral fractures each year; in the USA, the corresponding figures are 300 000, 500 000 and 200 000.

In Europe, approximately 179 000 men and 611 000 women suffer a hip fracture each year, while 11.5% and 35% of women aged 50–54 years and 75–79 years, respectively, have at least one vertebral fracture. Other fragility fractures, particularly those of the pelvis and humerus, are also a significant cause of morbidity in the elderly.

The incidence of osteoporotic fractures increases markedly with age (Figure 1.4). In women, this increase is seen after the age of 45 years and

Bone mineral density and clinical risk factors: the WHO paradigm

In clinical practice, bone mineral density (BMD) values are used to predict fracture risk, in much the same way that blood pressure is used to predict stroke. Prospective studies in postmenopausal women have shown that for each decrease of 1 standard deviation in BMD, there is a two- to three-fold increase in fracture risk (Figure 5.1). The strength of this association is comparable with that between blood pressure and stroke, or serum lipid profile and coronary heart disease. Measurements at the potential fracture site are the most predictive, although bone density at the wrist, spine, calcaneus or hip is related to fracture risk at any skeletal site.

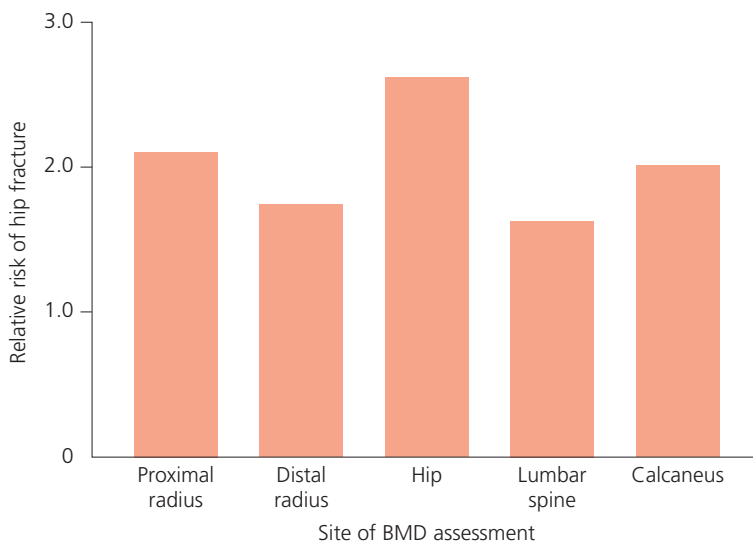


Figure 5.1 Relative risk of hip fracture for every 1 standard deviation (SD) reduction in bone mineral density (BMD) below the age-adjusted mean. Adapted from data in Marshall D et al. *BMJ* 1996;312:1254–9.

BMD measurements have a high specificity but low sensitivity in the prediction of fracture risk, and recent studies have demonstrated that the majority of fractures occur in individuals with osteopenia rather than osteoporosis. This is partly due to the contribution of clinical risk factors that affect fracture risk independently of BMD, and these can be used to improve prediction of fracture risk. They include:

- age
- body mass index $\leq 19 \text{ kg/m}^2$
- glucocorticoid therapy
- previous history of fracture
- family history of hip fracture
- current smoking
- alcohol ≥ 3 units/day
- rheumatoid arthritis.

A World Health Organization-supported algorithm that combines these risk factors with or without BMD measurements to estimate fracture probability has been developed recently, and is available online at www.shef.ac.uk/FRAX (Figure 5.2). This simple and rapid-to-use tool produces estimates of the 10-year probability of major osteoporotic fracture (hip, spine, humerus and radius) and hip fracture alone.

These figures can then be used as a basis for treatment decisions, taking into account cost-effectiveness and clinical effectiveness (Figure 5.3).

Guidelines using this approach have been developed in Europe and the USA.

The FRAX[®] estimation of fracture probability takes no account of previous bone-protective treatment or of dose responses for several risk factors. For example, multiple fractures carry a much higher risk than a single fracture, and the increase in risk of fracture with glucocorticoid therapy is related to both dose and duration of therapy. These limitations emphasize the need for clinical judgment when using FRAX[®] as a basis for treatment decisions.

Country : **UK** Name / ID : [About the risk factors](#)

Questionnaire:

1 Age (between 40-90 years) or Date of birth
Age: Date of birth: Y: M: D:

2 Sex Male Female

3 Weight (kg) 62

4 Height (cm) 168

5 Previous fracture No Yes

6 Parent fractured hip No Yes

7 Current smoking No Yes

8 Glucocorticoids No Yes

9 Rheumatoid arthritis No Yes

10 Secondary osteoporosis No Yes

11 Alcohol 3 more units per day No Yes

12 Femoral neck BMD

BMD: 21.9
The 10 year probability of fracture (%)

without BMD

Major osteoporotic	14
Hip fracture	4.4

Figure 5.2 The FRAX[®] tool: 10-year fracture probability is estimated from the data input, with or without bone mineral density measurement. Note that both the 10-year probability of major osteoporotic fracture (spine, hip, wrist, humerus), at 14%, and hip fracture, at 4.4%, are estimated. Reproduced with permission of the World Health Organization Collaborating Centre for Metabolic Bone Diseases, University of Sheffield Medical School, UK. www.shef.ac.uk/FRAX.

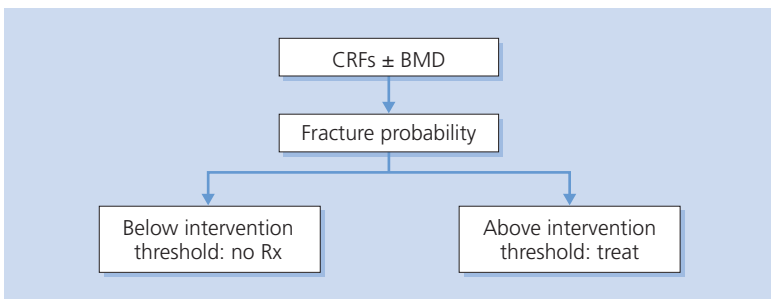


Figure 5.3 Paradigm for risk assessment and treatment decisions. On the basis of clinical risk factors (CRF), with or without bone mineral density (BMD) measurement, the 10-year fracture probability is estimated and used as a basis for management decisions. Intervention thresholds are defined on the basis of both cost-effectiveness and clinical suitability.