Report on osteoporosis in the European Community

Action for prevention

Health

I've made up my mind never to fall again. (A)

It's essential to take responsibility. (FIN)

I realised that if I didn't want the rest of my life to pass me by, I had to do something. (UK)

When I think that my mother died of a hip fracture I get really worried. (P)

I'm confident that due to the treatment I receive I won't be crippled in the future. (EL)

I'm worried about the future. (NL)

I miss my normal life, very, very much. (S)

The doctors promised a miracle. (L)

Don't worry and take charge of your life. (B)

I wish I had the bone scan earlier. (IRL)

I felt useless and depressed. (F)

Fishing, even though it sometimes hurts, is good therapy. (DK)

Osteoporosis no longer disrupts my daily life. (E)

The local osteoporosis patient support group helped me a lot. (D)

Be careful around Grandma! She can break. (I)

Employment & social affairs

European Commission

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Health

European Commission
Directorate-General for Employment, Industrial Relations
and Social Affairs
Directorate V/F.2

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A great deal of additional information on the European Union is available on the Internet.
It can be accessed through the Europa server (http://europa.eu.int).

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Thank you to the osteoporosis patients and people at high risk of osteoporosis for supplying the photographs for the front cover of this report.

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Preface

The dramatic increase in the incidence of osteoporosis demands a strategy for all interested groups to work together. The *Report on Osteoporosis in the European Community - Action for Prevention*, taking into consideration existing national guidelines and consensus statements (Annexe 1), provides a common basis for action by presenting recommendations and detailed information on all relevant areas: epidemiology and demographics, nutrition, physical exercise, diagnosis, therapy and facilitating communication on osteoporosis. This chapter offers strategies and specific actions on how to make the Report work, on the basis of clear objectives and defined target groups.

Objectives

The overriding objectives, by which all actions and initiatives must be measured, are:

a) to reach a significant reduction in the incidence of osteoporosis and related fractures, and

b) securing an acceptable quality of life for patients with osteoporosis.

Specific operational objectives associated with these aims are to make:

- Politicians and health administrators implement appropriate recommendations to improve resources available for osteoporosis prevention, early detection and treatment.
- Physicians and other health professionals become familiar with the Report and perceive it as a valuable resource in their interaction with patients and colleagues.
- National osteoporosis societies create and develop effective networks involving all target groups.
- The Report facilitate communication between target groups and further heighten recognition of common interests.
- The Report with the related communication materials accessible to all interested parties and the general public (e.g. via the Internet), thus also directly raising the awareness of the population about osteoporosis, risk factors and preventative measures.
- A united approach for an extensive media campaign and thereby significantly heightening the ‘noise-level’ of osteoporosis and related issues.

Target Groups

- To obtain these objectives active co-operation of several target groups is essential:
- Politicians and health administrators at European, national and regional levels.
- General practitioners and physicians in clinics, representatives of medical specialities, e.g. physiotherapists, occupational therapists, pharmacists.
- National osteoporosis societies and regional self-help groups who support osteoporosis sufferers and educate the general public about osteoporosis prevention.
- Print media, radio and television journalists.
- All age-groups of the population.

Specific as well as common interests of the target groups must be recognised. To raise awareness of osteoporosis and generate interest in the Report among as many people as possible, a detailed agenda and course of action directed at each group has to be defined and implemented. Motivation to co-operate within and between target groups should be encouraged wherever possible.

The interest of the popular media and the general public is to receive all information in a clearly structured, easy to understand form, which plainly states the relationship between actions and consequences. Physicians also want practical recommendations, as well as effective tools to facilitate their day-to-day interaction with patients. Scientific and social interests can be assumed for all health professionals, health administrators, and politicians. Those who are actively taking part in a national osteoporosis Organisation or a support group are often motivated either by having osteoporosis themselves, belonging to a high-risk group, or having a relative affected by the disease.

Actions - Making the Report Work

Initial Steps

The value of a scientific report is not only measured by its contents, but also by the way it is presented, how effectively it is disseminated, and the level of acceptance reached among target audiences. Only when the information in the Report on Osteoporosis in the *European Community - Action for Prevention* reaches all relevant groups and the recommendations become implemented, is there a chance to realise the goal of decreasing the incidence of osteoporosis. Therefore initial steps for an effective introduction have been taken at:

- The European Parliament in Brussels in the presence of European and national representatives of the target groups on June 10th, 1998.
- The European Congress on Osteoporosis in Berlin, September 11-15, 1998, which provided an ideal occasion to present and disseminate the Report among professional groups.

Presentation

The *Report on Osteoporosis in the European Community - Action for Prevention* and several linked communication tools are available in the 11 official languages (Danish, Dutch, English, Finish, French, German, Greek, Italian, Portuguese, Spanish and Swedish) of the 15 European Union member states and Arabic. Additionally the press pack materials are available in Chinese and Russian. The communication tools consist of:

- The full scientific report.
- A summary report which provides a quick overview.
- A leaflet for the general public.
- A Powerpoint slide presentation for health care professionals to download from the European Foundation or Osteoporosis's website.
- A comprehensive press pack including a press release jointly issued by the European Commission, the World Health Organization and the European Foundation For Osteoporosis, the summary report, leaflet, a fact sheet, a case history of an osteoporosis sufferer, or person at high risk of osteoporosis, from each of the European Union member states and the contact details of national osteoporosis and related organisations.

Dissemination

The dissemination of the Report is a team effort and includes the European Commission, the European Foundation for Osteoporosis, the German Green Cross, national osteoporosis societies, professional organisations, and osteoporosis support / self-help groups. Major activities in 1998 by national osteoporosis organisations centred around World Osteoporosis Day on June 24, 1998.

Further dissemination is achieved by:

- The World Health Organization's distribution of the press pack to regional and national World Health Organization offices around the world, on the occasion of World Osteoporosis Day, as the Report can be used in other countries to raise awareness about osteoporosis and the need to allocate greater resources to the disease.
- Institutions organising education programmes for general practitioners, hospital physicians and representatives of medical specialities.
- Making all the materials mentioned, in all the languages, accessible via the Internet pages of the European Foundation For Osteoporosis (http://www.effo.org). *[Now the International Osteoporosis Foundation: http://www.osteofound.org/]*

Other Recommended Actions

In order to maximise efficiency, and in view of limited resources, activities should focus on result-oriented, recurring events, on training and empowerment of relevant target group organisations (e.g. self-help groups) and physicians, on facilitating interaction and communication between all groups, and on mobilising the press. The potential „snowball effect" of a particular action should always be considered.

Examples of such actions are:

- Co-ordinated activities organised by the European Foundation For Osteoporosis in collaboration with the World Health Organization and national organisations on the occasion of World Osteoporosis Day each year to educate the general public about osteoporosis prevention.
- Annual one-week or one-month campaigns on osteoporosis initiated and organised by the national osteoporosis societies and related organisations. The main subjects should vary: for example raising awareness (e.g. opportunities to talk to experts), nutrition (e.g. „healthy bone menus" in restaurants and work canteens, distribution of recipes), appropriate physical activities, and consultation (e.g. advisory service for osteoporosis sufferers and interested people).
- The formation of new support groups and the ongoing development of an effective network of support groups by encouraging appropriate partnerships (e.g. between new and established groups).

The Next Step

An appropriate next step is to develop a scientific evaluation process to measure changes in parameters such as knowledge on osteoporosis, relevant attitudes and behaviour. A continuing and critical evaluation must be an integral part of the above described action programme in order to reach the stated objectives of reducing the incidence of osteoporosis and securing an acceptable quality of life for the patients.

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INTRODUCTION

Osteoporosis is defined as a reduction in bone mass and disruption of bone architecture, resulting in reduced bone strength and increased fracture risk. Fragility fractures are the hallmark of osteoporosis and are particularly common in the spine, hip and forearm. They show a steep age-related increase and have a major impact on the health of elderly populations in the Western world, causing significant morbidity and mortality and imposing huge financial burdens on health services throughout the European Union. Demographic changes and increasing life expectancy will lead to a dramatic increase in the number of people suffering from fractures over the next few decades unless more effective action is taken to prevent the disease.

In recent years there has been significant progress in our understanding of the causes, diagnosis and treatment of osteoporosis but these have not always been fully exploited by health care systems and much remains to be learnt. Although awareness of the enormous medical, social and financial impact created by osteoporotic fractures has grown, insufficiently high priority is currently given to the disease by governments and health care providers. This has resulted in inadequate provision of diagnostic facilities in many European Union member states and failure to provide optimal care for individuals suffering from osteoporosis.

In order to address these concerns, a working party of experts from the European Union member states was set up by the European Commission Directorate General V to produce a report on osteoporosis. The Report on Osteoporosis in the European Community - Action for Prevention provides a detailed analysis of the epidemiology, pathogenesis and clinical management of the disease throughout the European Union with particular emphasis on prevention in the future. The report underlines the differences between European Union member states not only in the prevalence and incidence of the disease but also in projected increases in fracture rate in the next half century and the financial resource reallocations which will be required to manage this epidemic. It draws attention to the pathogenesis of osteoporosis and to the importance of nutrition in building and maintaining healthy bones. The assessment of risk in individuals is discussed and the need for better diagnostic resources emphasised. The increasing number of non-pharmacological and pharmacological interventions which may prevent osteoporotic fractures is covered and the importance of other aspects of patient care stressed, particularly rehabilitation and self-help groups.

The report contains a number of specific recommendations which are primarily targeted at improving prevention of osteoporosis in the future. They acknowledge the need to obtain more information on the incidence and prevalence of osteoporotic fractures and to form strategies which deal with the impending increase in these fractures. Coherent nutritional policies are required across the European Union and adequate diagnostic facilities must be provided in all member states. Improvements in patient treatment are needed, with better education both of health care professionals and the public and more active promotion of self-help groups. Finally, funding for key research areas should be given high priority. The active support of the European Union and the governments of its member states is essential if these important goals are to be realised.

1. EPIDEMIOLOGY

1.1 Introduction

Osteoporotic fractures typically occur at the hip, spine and distal forearm but may also affect other sites, including the humerus, tibia, pelvis and ribs. These fractures constitute a major public health problem (Cooper et al, 1992a). The estimated remaining lifetime risk of these fractures in Caucasian women at age 50 years, based on incidence rates in North America is 17.5%, 15.6% and 16% for hip, spine and forearm respectively; the remaining lifetime risk for any fragility fracture approaches 40% in women and 13% in men (Melton et al, 1992). Similar rates have been reported from parts of Europe, although there is a marked variation in the incidence of fractures between countries and regions (Johnell et al, 1992) and even within countries (Elffors et al, 1994). Hip fractures have an overall mortality of 15-30% (Browner et al, 1996; Keene et al, 1993), the majority of excess deaths occurring within the first six months after the fracture. They are associated with considerable morbidity, necessitating hospital admission for an average of 20-30 days (Johnell et al, 1992). Vertebral fractures are also associated with reduced survival (Cooper et al, 1993), probably due to clustering of co-morbidity which predisposes independently to osteoporosis and premature death. Although less than one half of vertebral fractures come to clinical attention and only one-third to one-fifth of these require hospitalisation (Cooper et al, 1992b; Kanis & McCloskey, 1992), the economic burden is considerable; the incidence of vertebral fractures is similar to that of hip fractures and, in those admitted to hospital, the length of stay is between 10 and 30 days (Johnell et al, 1997). The estimated costs arising from hip fractures are shown in Table 1.1 for the EU member states.

Hip fractures typically follow a fall from the standing position and their incidence rises exponentially with age (Elffors et al, 1994). Above the age of 50 years there is a female to male ratio of approximately 2:1. Hip fracture incidence shows a marked seasonality, with substantial increases during the winter months in countries with temperate climates. Nevertheless, the majority of hip fractures follow falls indoors and are not related to slipping on icy pavements.

Age and sex-adjusted hip fracture rates are generally higher in Caucasian than in Asian populations and are lower in countries close to the equator. The latter observation has been attributed to the impact of sun exposure, although this is not universally accepted (Karagas et al, 1996a; Karagas et al, 1996b). Furthermore, the pronounced female preponderance in fracture incidence observed in white populations is not seen in blacks or Asians, in whom age-adjusted female to male ratios approximate unity. These variations in incidence have not been explained but may be related, in part, to genetic differences. Some studies show a trend for age-adjusted incidence rates to increase over time (Melton et al, 1987; WHO Study Group, 1994), although this finding is not universal (Melton et al, 1996). Urbanisation in central parts of Africa has led to a secular increase in hip fracture incidence rates, although even recently derived African rates are considerably lower than those found in North American or European whites.

The incidence of clinically diagnosed vertebral fractures also rises steeply with age and the female to male incidence ratio after age adjustment is around 2:1 (Cooper et al, 1992b). Vertebral fractures may occur in the absence of trauma or after minimal trauma, for example bending, lifting or turning. Variations with ethnicity are not well studied but there is some evidence that vertebral fractures are less common in black than white women and that the prevalence of these fractures in Japanese women is similar to that observed in white

populations. Vertebral fractures may result in pain, kyphosis, loss of height and resulting disability; although their impact on health remains to be accurately quantified, a proportion of patients suffer long-term pain and disability.

Fractures of the distal forearm (Colles' fractures) usually follow a fall forward onto the outstretched hand. In women, there is a linear increase in incidence between the age of around 45 and 60 years, followed by a plateau. No age-related increase in the incidence of these fractures has been documented in men and the age-adjusted female to male ratio is 4:1 (Cooper, 1996). The incidence of distal forearm fractures shows a peak in winter months which is related to the higher risk of falling outdoors in icy weather. The majority of these fractures are treated in hospital out-patient departments, although very elderly women may require in-patient treatment. Algodystrophy occurs after fracture in one-quarter to one-third of patients and there may also be lasting deformity and dysfunction in a minority.

1.2 Incidence/prevalence rates for osteoporotic fractures in Europe

The occurrence of a disease or of an event can be expressed either as the prevalence, i.e. the number of persons suffering from the disease at a given time point, or the incidence, which is the number of new events occurring over a specified period of time. The major osteoporotic complications, hip and vertebral fractures, differ in their mode of presentation. Whereas hip fractures invariably come to clinical attention (Johnell et al, 1992; Bacon et al, 1996), vertebral fractures have a much more variable clinical presentation; the majority are asymptomatic and in the remaining cases there may be variable degrees of pain, deformity and disability (Cooper et al, 1993; Melton et al, 1993; Chrischilles et al, 1994; Johnell et al, 1997). These differing presentations of the two fracture types necessitate different measures of occurrence, namely incidence for hip fractures and prevalence for vertebral fractures.

In this report the incidence of hip fracture and prevalence of vertebral fracture in European Union member states was compiled from published data or information obtained by personal communication. The data have been obtained from two types of source; survey data (direct assessment of fracture rates in defined populations) and official health services administrative data. In some countries, however, no information on incidence/prevalence rates was available and, in these cases, information from other countries was substituted (Table 1.2).

1.2.1 Hip fracture

Incidence data on hip fractures, both cervical and trochanteric, were collected from several sources. For Portugal, Spain, France, Italy and Greece incidence figures were obtained from the MEDOS study (Elffors et al, 1994). In countries with more than one centre, the age-specific incidences were weighted according to the size of the catchment areas.

For Finland, data from a register study were utilised (Bacon et al, 1996) and for Sweden from a Stockholm register study (Hedlund, 1985). Data for Denmark were obtained from a population-based survey performed between 1964 and 1993 and comprising 68,246 and 56,345 person-years in men and women respectively aged 65 years or more (M Schroll, personal communication), For the Netherlands, data were obtained from a report for the Dutch Institute for Medical Technology (IMTA; de Laet et al, 1996); this was a register study, covering all hip fractures in the entire population of 7,535,268 and 7,703,914 men and women respectively. Data for the UK were obtained from a recent study from the South of England (McColl et al, in press).

Incidence was considered to increase exponentially with age. Therefore, all age-specific incidence data were transformed into natural logarithms at the mid-point of the age range, after which the linear regression was computed and incidence figures with a „smoother" distribution could be processed. Incidence was calculated according to the following algorithm:

$In_{incidence} = a*In_{age} + b$

This procedure was performed to adjust for small sample sizes and to make age groups homogeneously distributed. The resulting age-specific incidence data are shown in Table 1.3.

1.2.2 Vertebral fractures

Data on the prevalence of vertebral fractures were collected from the EVOS study (O'Neill et al, 1996), in which fracture prevalence was estimated using two different methods of standardised radiological assessment. The prevalence rates shown in Table 1.4 represent the mean of the results of the two methods for each centre.

Since data reported from the EVOS study provided age-specific data only on an aggregated basis, the distribution over age was considered parallel for all countries but at different levels, depending on the respective age-adjusted total prevalences. Smoothing of the prevalence data was performed using the method described for hip fracture. When more than one centre in a country contributed to the study, a weighted mean value was used based on the number of participants, since the necessary information of the catchment area populations was not available. The revised age-specific prevalence data are shown in Table 1.4.

1.3 Demographic and socio-economic forecasts for Europe

The population of the fifteen EU member states (Austria, Belgium, Denmark, Finland, France, Germany, Greece, Ireland, Italy, Luxembourg, Netherlands, Portugal, Spain, Sweden and the UK) consisted of 373 million inhabitants in 1995. This number will increase during the next two decades, levelling off around 2015, with the peak for women slightly before that for men. From its highest level of just below 390 million people, there will be a rapid decline such that in 2050, the population of the EU member states is estimated at 170 million women and 163 million men, a decrease almost equal to loss of the entire population of Italy. The decline in population number will not, however, be evenly distributed across all ages, since Europe has passed on to the fourth stage of the demographic transition, with low birth and death rates. As a consequence, there will be a disproportionate decrease in the potential labour force.

The potential labour force (men and women aged between 20 and 64 years) will increase from 227 million in 1995 to 234 million in 2010 but will subsequently decrease rapidly to 172 million in 2050. Pensioners (men and women aged 65 years or more), on the other hand, will steadily increase in number from 58 million in 1995 to 108 million in 2040, after which there will be a levelling off.

The most dramatic changes are seen in the oldest age group (80 years and above), in whom the incidence of osteoporotic fracture is greatest. This population will grow from 8.9 million women and 4.5 million men in 1995 to 26.4 million and 17.4 million women and men respectively in 2050. Thus the reduction in potential labour force of 62 million over this period will be accompanied by an increase in the very elderly population of 31 million. These

figures represent a decrease from 60% to 50% of the population composed of the labour force and an increase from 15% to 30% of pensioners. At the present time, 16 people are in the labour force for each one of our eldest citizens; this proportion will fail to 4 persons per eldest citizen by 2050.

1.4 Forecasts for osteoporotic fractures in the future

Because of the increase in incidence rates of osteoporotic fractures with age, the above demographic changes and increasing life expectancy will have a huge impact on the number of fractures which can be expected to occur. Using baseline incidence/prevalence data for hip and vertebral fractures and population projections for five year periods, the expected number of hip and vertebral fractures was estimated over the period 1990 to 2050. An exponential increase with age was assumed for both types of fracture and country-specific data were used where available. No adjustment was made for secular trends, about which current evidence is conflicting; assuming a yearly increase in hip fracture incidence between 0.5% and 3%, as reported in prospective studies (Gullberg et al, 1997), this could underestimate the true increase in number of fractures by between 50% and 300% over a 50 year period. However, in the light of a recent report (Melton et al, 1996) this adjustment may be inappropriate.

The number of hip fractures occurring each year is estimated to rise from 414,000 by the turn of the century to 972,000 fifty years later (Table 1.5), representing an increase of 135%. As reported previously, this increase will be greatest in men and will result in a decreasing female to male ratio. From the year 2035, however, this trend will change; because of the continuous ageing of the European populations and the steeper risk-over-age slope for women, the female dominance in incidence will re-emerge.

In several studies of hip fracture incidence a decline has been observed in the very elderly. This may reflect selection bias, or simply fewer „hips at risk“, since a large proportion of the population has already broken one or more hips. This has not been accounted for in our exponential model, but would not significantly reduce the number of fractures because of the relatively low contribution to the population of this subset.

Projected prevalences of vertebral fractures are shown in Table 1.6. Although the yearly incidence is believed to be similar to that for hip fracture, the increase in number of vertebral fractures is not expected to be of the same magnitude as for hip fractures; thus the estimated increase is from 23.7 million in the year 2000 to 37.3 million in 2050, representing a rise of 57%.

The female to male ratio is expected to decrease during the first 20 years of the next century, after which it will increase. Again, this is an effect of the ageing of the population and a steeper slope of risk increase in women. In addition, mortality has to be taken into account when assessing prevalence; as longevity increases, incidence rises but so does mortality and thus prevalence will not rise as rapidly as incidence.

It should be stressed that these forecasts are estimates of the mean changes. These will be affected not only by the baseline data for fracture occurrence and the projected demographic changes, but also several other variables:
a). If, as discussed above, the age-specific incidence rates of hip fracture continue to increase, this will result in a substantial underestimation of fracture occurrence.

b). Risk factors for osteoporosis and fragility fractures may change over the next fifty years, although it is not possible to predict these changes.

c). Birth-rates may deviate from the estimates used. Since the vast majority of osteoporotic fractures occur late in life, virtually all fractures in the period of the forecast will occur in people who have already been born. However, a change in birth-rate could result in substantial changes in the ratio of providers to pensioners.
d). If major changes are introduced into the welfare systems, for example shifts in the age of retirement, these will affect the ability of society to care for its elderly, diseased and disabled.
e). Another factor which may affect the ability to provide care is the unemployment rate of the potential labour force, a population which is steadily decreasing.

Overall, in view of the above uncertainties, the forecasts for fracture occurrence provided in this report are likely to be optimistic, as are the predictions made about the ability of current resources to meet future demands on the social and health care systems.

1.5 Financial considerations

The dramatic increase in the proportion of elderly to providers resulting from the predicted demographic changes adds strain to health care systems, although the burden on other parts of the social welfare system is likely to grow faster as the population grows older. A four-fold reduction of the ratio between providers and the elderly is not accompanied by a four-fold increase in health care expenditure even though growing demands are made on other facilities such as nursing, caring and housing. Thus, the future demographic changes in Europe may require a reallocation of financial resources within the social welfare system from health care to general support of the elderly.

In the case of diseases showing a marked exponential rise with age and requiring relatively long-term hospitalisation, for example hip fracture, health care costs follow the growing incidence rate. This necessitates changing priorities within the health care system. Conditions such as vertebral fracture, on the other hand, primarily increase the suffering of the population. Whilst incidence is the appropriate measure of occurrence for hip fracture, therefore, prevalence is the most suitable measure for vertebral fracture.

Finally, the decrease in number of employees supporting each pensioner, from 3.8 at the turn of the century to 1.6 fifty years later, will be difficult to compensate for by redistribution and, to maintain quality, economic expansion is imperative.

Since the incidence of hip and vertebral fractures is approximately the same (Johnell et al, 1997) and 10% of all patients with vertebral fractures require hospital attention, the need for hospital admission for both fracture types together can be estimated to be 110% of hip fracture incidence. Since the crude incidence rates are likely to rise more steeply for hip than for vertebral fracture, this figure could be reduced to 105% during the period of projection.

In addition, the length of hospital stay for both fracture types is very similar (Johnell et al, 1992; Jaglal et al, 1996; Johnell et al, 1997). Table 1.7 shows the estimated need for hospital beds, based on a mean length of stay in hospital of 20 days. The total number of available hospital beds in the EU member states today is just above 2.8 million; the proportion of hospital beds used for patients with hip or vertebral fracture will thus rise from 0.88% to 1.97%, unless the total financial resources for health care increase significantly in the future.

1.6 Country-specific predictions

Demographic forecasts differ between the EU member states. The best conditions can be expected in countries with a high birth rate and a low proportion of elderly in the population, resulting in a favourable provider to pensioner ratio. Other important factors involved in meeting the health demands of the next century include the financial resources allocated to health care and the number of existing hospital beds. It should be noted that three EU member states, Ireland Sweden, and the UK will experience a decrease in the pensioner to provider ratio in the next decade, providing a unique opportunity to plan the required reallocation of resources.

Some key figures representing the different needs for EU member states are shown in Table 1.8. Broadly, EU member states can be divided into three main groups on the basis of changes in the ratio of pensioners to labour force; those with a rapidly increasing pensioner to provider ratio, those in which the ratio is slowly increasing and an intermediate group. These are considered in more detail below.

1.6.1 Countries with a rapidly increasing pensioner to provider ratio

These five countries, Germany, Ireland, Luxembourg, the Netherlands and Spain, will experience an increase in the pensioner to provider ratio of 157-171%. This change requires an increase in the GNP of more than 2% in order to keep up with the economic demands of the pension systems, leaving little or no margin to increase financial support to the social health and welfare systems. These extended needs must therefore be met by redistribution within and between the systems.

1.6.1.1 Germany

Germany faces the greatest need for reallocation of resources to the welfare system for the elderly, with its more than five-fold increase in the ratio of very old citizens (i.e. those aged 80 years or more) to financial providers. The prevalence of vertebral fractures will also increase relatively fast, resulting in increased infirmity and the need for greater support. The health care sector in Germany is reasonably well financed, however, providing scope for the required redistribution of resources, especially since the availability of hospital beds is good and the demand for more beds for the treatment of osteoporotic fractures will be moderate.

The most dramatic increase in hip fracture incidence and vertebral fracture prevalence is estimated to occur from 2010 onwards for women and between 2010 and 2030 for men. The female population at risk is now approaching the age of retirement, but large cohorts will become menopausal during the next 50 years.

1.6.1.2 Ireland

Ireland has the youngest population of the EU member states because of its high birth-rate. While this is expected to persist over the next 50 years, the need for reallocation of resources to the social sector is less pronounced than for Germany because of the slower increase in the number of elderly in the population. However, health care resource utilisation is relatively low in Ireland at present, precluding significant shifts from health care to social services. Osteoporotic fractures are estimated to consume a rapidly increasing number of hospital beds. Since the availability of hospital beds is low at present, this will necessitate changing

priorities within the health care system. Currently, the largest at risk cohorts in the population are men between 40 and 75 years of age and women aged 35-65 years.

1.6.1.3 Luxembourg

Luxembourg, like Germany, will need to redistribute financial support from the relatively well financed health care sector to the social sector. The large expected rise in hip fracture incidence will increase the demand on hospital beds; however, the availability of beds is good so that the health care needs can be met, even in the event of reduced financial support. The largest at risk cohorts in the population are similar to those in Ireland.

1.6.1.4 Netherlands

The Netherlands faces the greatest increase in number of vertebral fractures of all the EU member states. It spends comparatively large amounts on health care and possesses the largest number of hospital beds per capita; thus the future demands for reallocation of resources and hospital beds can probably be met.

The greatest rate of increase in hip fractures will occur in women between the years 2025 and 2035, although the increase will start around the year 2010. The same pattern will be seen for men.

1.6.1.5 Spain

Spain will experience an increase in both hip and vertebral fractures relative to the working population. This increase will affect lower age groups to a greater extent than in more Northern countries. The need for reallocation of resources will thus be more specifically directed towards people with chronic disabling disorders such as vertebral fractures than towards supporting the elderly. The rapidly increasing need for hospital beds in combination with their present low availability will require large shifts in priorities within the health care system.

An increase in fracture incidence is already occurring but this will decrease for a short period around 2025 in both men and women and will then increase again, maintaining a high level throughout the remainder of the 50 year period.

1.6.2 Countries with a slowly increasing pensioner to provider ratio

The five countries at the other extreme, Belgium, Denmark, France, Sweden and the UK, will elevate the ratio of pensioners to the potential labour force by 85%-121%. This will create the demand for a 1-1.5% increase yearly in the GNP, although some needs can be met by redistribution within the existing systems.

1.6.2.1 Belgium

Belgium has the greatest need for redistribution of financial support between the systems of all five countries in this group. Nevertheless, this need is relatively low as compared to the

first group because of the ratios of very elderly to workers and of people with vertebral fractures to the labour force. The health care sector has a strong economy, well suited to meet the relatively high need for hospital beds.

The most marked increase in osteoporotic fractures will start in men around the year 2010 and will proceed at a lower rate during the last decade of the fifty year period. In women, the pattern is similar but more pronounced and there will be a levelling off in vertebral fracture prevalence from around 2035.

1.6.2.2 Denmark

Denmark will require a comparatively large number of additional hospital beds to adapt to the future situation. In view of the low number of beds currently available and a reluctance to divert resources away from health care, the Danish will need to accept significant changes in priorities within the health care sector, in favour of patients with osteoporotic fractures.

Together with Sweden and the UK, Denmark already has a large number of patients with osteoporotic fractures. Unlike the situation in Belgium, the occurrence of fractures will increase uniformly throughout the period; a levelling off of vertebral fracture prevalence after 2030 will be seen only in men.

1.6.2.3 France

The demands on French resources are similar to those in Denmark. However, in France there is a greater readiness to meet demands, with stronger financial resources and better bed availability.

France has a relatively low incidence of hip fractures and moderate prevalence of vertebral fractures. The most rapid increase in fractures will occur from 2010 onwards in men and, in women, between 2030 and 2040.

1.6.2.4 Sweden

Sweden has both the highest prevalence of osteoporosis and the most favourable demographic forecast of the EU member states. The relatively modest requirements for reallocation within the system should be met by improved productivity, since available resources for redistribution are relatively limited. The need for extra hospital resources for osteoporotic fracture can be achieved with only minor changes in priorities within the health care system, because of the relatively good availability of existing hospital beds.

An increase in the occurrence of hip fractures will occur in women 20 years from now, whilst there will be a rapid increase in vertebral fracture prevalence between 2015 and 2030.

1.6.2.5 UK

The UK has, next to Sweden, the most favourable demographic outlook and also has a high incidence of osteoporotic fractures. However, the availability of hospital beds is much lower than in Sweden and changes in health care priorities therefore more urgent.

The changes over time also resemble those for Sweden, although the more rapid increase in female hip fracture incidence commences slightly later.

1.6.3 Countries with an intermediate increase in the pensioner to provider ratio

In these five countries, Austria, Finland, Greece, Italy and Portugal, the relationship between pensioners and workers will increase by 134-153%, corresponding to a need for an increase in GNP of 1.5%-2%.

1.6.3.1 Austria

Demographic changes in Austria will require a redistribution of resources between health care and social care for the elderly. Because of the relatively strong financial position of Austrian health care, the demands can probably be met. The beds required for osteoporotic fractures should be available since the country has one of the highest number of hospital beds per capita.

Between 2010 and 2040 there will be a rapid increase in fracture occurrence in men and in women, from 2020 onwards.

1.6.3.2 Finland

The Finnish population will require more social support for the elderly and more hospital beds for patients with osteoporotic fractures. It is probable that both these needs can be met, particularly the reallocation of hospital beds for patients with fractures and their subsequent rehabilitation.

Since Finland already carries a relatively high fracture burden, the changing priorities need to be initiated in the immediate future. Fractures in women will increase slowly at first (hip fracture numbers may even decrease slowly around the turn of the century), increase more rapidly from 2010 and eventually level off. In men, fracture numbers will be stable at first, accelerate during the second decade and then level off again after 2035.

1.6.3.3 Greece

Claims on resource redistribution will be moderate but nevertheless hard to meet, since extra resources are not available. Significant shifts in priority will be required to satisfy the relatively modest demand for hospital beds in the future, unless a substantial economic expansion takes place.

A relatively rapid increase in fracture incidence and prevalence is already ongoing, although some reduction can be expected towards the last decade of the projected period for hip and vertebral fractures in women and for vertebral fractures in men.

1.6.3.4 Italy

The situation in Italy is similar to that in Finland in terms of its future need for social support and hospital beds. These, particularly the latter, will require changes in health care priorities.

From 2025 or 2030 the prevalence of vertebral fractures will stabilise in both men and women after an initial increase. For hip fractures, there will be a continuous increase over the entire 50 year period.

1.6.3.5 Portugal

The situation in Portugal is possibly the most problematic. There is a strong need for reallocation of resources but little or no capacity for redistribution within existing services. The increasing need for hospital beds, although moderate, will require significant changes in health care priorities and an expansion of the total economy.

Both hip and vertebral fractures appear to be relatively common in younger Portuguese men. The number of fractures will increase steadily in both sexes with a greater rate of increase in women between 2025 and 2040.

Country	Price Year and cost components	Number of hip fractures (1995)	Cost per hip fracture		Total hospital costs of hip fractures	
			in national currency	in ECUS	in national currency	in ECUS
Austria	1994 Hospital treatment	10 160	170 991	14 402	1 737 268 056	146 324 320
Belgium	1992 Hospital treatment	11 930	338 000	9 542	4 032 340 000	113 836 060
Denmark	1991 Hospital treatment	8 310	50 575	6 228	420 278 250	51 754 680
Finland	1996 Hospital treatment	5 730	22 000	3 959	126 060 000	22 685 070
France	1995 Hospital treatment	46 310	75 578	12 111	3 500 017 180	560 860 410
Germany	1994 Hospital treatment	108 900	24 859	12 874	2 707 145 100	1 401 978 600
Greece	1996 Hospital treatment	9 450	1 058 201	5 060	9 999 999 450	47 817 000
Ireland	1996 Hospital treatment	2 678	896	1 486	2 399 488	3 979 508
Italy	1993 Hospital treatment	38 130	8 244 630	5 374	314 367 741 900	204 910 620
Luxembourg	1993 Hospital treatment	419	424 324	11 979	177 791 756	5 019 201
Netherlands	1993 Hospital treatment	15 110	23 359	11 979	352 954 490	181 002 690
Portugal	1996 Hospital treatment	6 040	1 000 000	4 545	6 040 000 000	27 451 800
Spain	1996 Hospital treatment	30 460	848 569	7 093	25 847 411 740	216 052 780
Sweden	1994 Hospital treatment	18 980	49 493	5 323	939 377 140	101 030 540
United Kingdom	1996 Hospital treatment	69 600	4 808	7 618	334 636 800	530 212 800
					Total hospital costs	3 614 916 079
					Estimated total care cost of hip fracture*	9 037 290 197

All figures relate to direct hospital costs of hip fracture and have been inflated to 1996 using OECD inflation factors for retail price index of individual countries. All national currencies have then been converted to $US using 1996 purchasing power parities (PPPs) and to Ecus according to 1998' rates. Austrian figures are based on German costs and Luxembourg figures are based on Dutch costs. *For Sweden and the UK where there are better data on other hip fracture costs the total figure is 2.5 times greater than the acute hospital costs (both countries supply a surprisingly similar denominator). Data for Sweden are based on a single health district and might therefore be unstable.

Table 1.1: The estimated costs arising from hip fractures for EU Member States

Country	Hip fracture incidence	Vertebral fracture prevalence
Austria	Subst with Switzerland (Bacon et al, 1996)	Original data (O'Neill et al, 1996)
Belgium	Subst with Netherlands (de Laet et al, 1996)	Original data (ref as above)
Denmark	Original data (M.Schroll, personal communication)	Subst with Sweden (ref as above)
Finland	Original data (Bacon et al, 1996)	Subst with Sweden (ref as above)
France	Original data (Elffors et al, 1994)	Original data (ref as above)
Germany	Subst with Switzerland (Bacon et al, 1996)	Original data (ref as above)
Greece	Original data (Elffors et al, 1994)	Original data (ref as above)
Ireland	Subst with UK (McColl et al, in press)	Subst with UK (ref as above)
Italy	Original data (Elffors et al, 1994)	Original data (ref as above)
Luxembourg	Subst with Netherlands (de Laet et al, 1996)	Subst with Belgium (ref as above)
Netherlands	Original data (de Laet et al, 1996)	Original data (ref as above)
Portugal	Original data (Elffors et al 1994)	Original data (ref as above)
Spain	Original data (Elffors et al, 1994)	Original data (ref as above)
Sweden	Original data (Hedlund 1985)	Original data (ref as above)
United Kingdom	Original data (McColl et al, in press)	Original data (ref as above)

Table 1.2: Sources of information on baseline occurrence data

Country	**Age-group**							
Women								
	50-54	55-59	60-64	65-69	70-74	75-79	80-84	85+
Austria	3.360	7.11	14.10	26.50	47.7	82.4	138.0	351
Belgium	2.720	5.86	11.80	22.60	41.1	72.0	122.0	317
Denmark	4.100	8.62	17.00	31.90	57.2	98.4	164.0	416
Finland	2.720	5.93	12.10	23.40	43.1	76.2	130.0	346
France	0.598	1.66	4.21	9.94	22.1	46.5	93.4	262
Germany	3.360	7.11	14.10	26.50	47.7	82.4	138.0	351
Greece	2.530	5.40	10.80	20.40	36.9	64.2	108.0	232
Ireland	1.820	4.27	9.32	19.10	37.3	69.5	125.0	362
Italy	1.600	3.49	7.16	13.90	25.6	45.4	77.6	172
Luxembourg	2.720	5.86	11.80	22.60	41.1	72.0	122.0	317
Netherlands	2.720	5.86	11.80	22.60	41.1	72.0	122.0	317
Portugal	2.630	5.18	9.64	17.10	29.0	47.7	75.8.0	151
Spain	0.613	1.72	4.42	10.50	23.7	50.3	102.0	290
Sweden	4.730	9.81	19.20	35.50	63.0	107.0	177.0	443
UK	1.820	4.27	9.32	19.10	37.3	69.5	125.0	362
Men								
	50-54	55-59	60-64	65-69	70-74	75-79	80-84	85+
Austria	3.220	5.69	9.57	15.50	24.2	36.6	54.0	110.0
Belgium	1.910	3.89	7.47	13.60	23.8	40.1	65.4	160.0
Denmark	2.820	5.59	10.50	18.70	32.0	52.8	84.5	199.0
Finland	2.950	5.71	10.40	18.20	30.5	49.4	77.5	177.0
France	0.477	1.19	2.73	5.90	12.0	23.5	43.8	110.0
Germany	3.220	5.69	9.57	15.50	24.2	36.6	54.0	110.0
Greece	1.400	2.96	5.88	11.10	20.0	34.6	58.0	124.0
Ireland	1.340	2.85	5.70	10.80	19.6	34.0	57.1	147.0
Italy	1.120	2.22	4.15	7.40	12.7	20.9	33.4	67.0
Luxembourg	1.910	3.89	7.47	13.60	23.8	40.1	65.4	160.0
Netherlands	1.910	3.89	7.47	13.60	23.8	40.1	65.4	160.0
Portugal	2.690	4.58	7.46	11.70	17.7	26.2	37.7	64.6
Spain	0.545	1.35	3.12	6.73	13.8	26.8	50.0	126.0
Sweden	4.510	8.76	16.10	28.20	47.4	77.1	122.0	280.0
UK	1.340	2.85	5.70	10.80	19.6	34.0	57.1	147.0

Table 1.3: Age-specific incidence figures for hip fracture in the EU member states (/10.000population).

Country	**Age Group**							
Women	50-54	55-59	60-64	65-69	70-74	75-79	80-84	85+
Austria	858	1 150	1 510	1 930	2 430	3 020	3 690	5 330
Belgium	1 200	1 620	2 120	2 710	3 420	4 230	5 180	7 480
Denmark	1 220	1 630	2 140	2 740	3 450	4 280	5 230	7 560
Finland	1 220	1 630	2 140	2 740	3 450	4 280	5 230	7 560
France	838	1 120	1 470	1 890	2 380	2 950	3 600	5 210
Germany	730	980	1 280	1 640	2 070	2 570	3 140	4 540
Greece	1 010	1 360	1 780	2 280	2 870	3 550	4 350	6 280
Ireland	699	938	1 230	1 570	1 980	2 460	3 000	4 340
Italy	743	996	1 300	1 670	2 110	2 610	3 190	4 610
Luxembourg	1 200	1 620	2 120	2 710	3 420	4 230	5 180	7 480
Netherlands	896	1 200	1 570	2 020	2 540	3 150	3 850	5 570
Portugal	846	1 130	1 490	1 900	2 400	2 970	3 630	5 250
Spain	846	1 130	1 490	1 900	2 400	2 970	3 630	5 250
Sweden	1 220	1 630	2 140	2 740	3 450	4 280	5 230	7 560
United Kingdom	699	938	1 230	1 570	1 980	2 460	3 000	4 340
Men	50-54	55-59	60-64	65-69	70-74	75-79	80-84	85+
Austria	1 580	1 760	1 940	2 120	2 310	2 500	2 690	3 080
Belgium	1 600	1 790	1 970	2 160	2 350	2 540	2 740	3 140
Denmark	1 760	1 960	2 160	2 370	2 580	2 790	3 000	3 440
Finland	1 760	1 960	2 160	2 370	2 580	2 790	3 000	3 440
France	1 450	1 620	1 790	1 960	2 130	2 310	2 480	2 840
Germany	1 130	1 260	1 390	1 520	1 650	1 790	1 920	2 200
Greece	1 340	1 490	1 650	1 810	1 960	2 130	2 290	2 620
Ireland	1 350	1 500	1 660	1 810	1 980	2 140	2 300	2 630
Italy	973	1 080	1 200	1 310	1 420	1 540	1 660	1 900
Luxembourg	1 600	1 790	1 970	2 160	2 350	2 540	2 740	3 140
Netherlands	1 330	1 480	1 630	1 790	1 950	2 110	2 270	2 600
Portugal	2 060	2 300	2 540	2 780	3 020	3 270	3 520	4 030
Spain	1 370	1 520	1 680	1 840	2 000	2 160	2 330	2 670
Sweden	1 760	1 960	2 160	2 370	2 580	2 790	3 000	3 440
United Kingdom	1 350	1 500	1 660	1 810	1 980	2 140	2 300	2 630

Table 1.4: Age-specific prevalence figures for vertebral fractures in the EU member states (/10.000 population).

Country	**Year**						
Women							
	1995	2000	2010	2020	2030	2040	2050
Austria	8.330	8.830	10.100	11.600	14.400	17.200	19.90
Belgium	9.210	9.980	11.700	13.700	16.000	19.400	21.50
Denmark	6.340	6.980	7.980	9.300	11.700	13.600	14.90
Finland	4.340	4.220	4.640	5.870	8.050	10.200	11.00
France	37.400	40.900	51.300	60.600	70.300	87.000	95.20
Germany	89.500	94.000	108.000	129.000	157.000	185.000	212.00
Greece	6.800	7.770	10.200	12.800	14.400	16.400	18.00
Ireland	2.050	2.210	2.550	3.150	4.360	5.830	6.86
Italy	29.900	33.800	41.900	49.200	56.100	63.700	70.20
Luxembourg	0.324	0.381	0.526	0.676	0.816	0.987	1.11
Netherlands	11.600	12.600	15.100	18.700	24.500	30.900	35.00
Portugal	4.370	4.890	6.090	7.320	8.750	10.300	11.50
Spain	23.500	27.500	36.800	44.800	50.900	60.400	71.10
Sweden	13.200	13.700	14.700	16.800	21.000	24.200	26.60
United Kingdom	55.700	58.600	63.700	72.200	89.500	109.000	126.00
Total		326.000	385.000	456.000	547.000	654.000	742.000
Men							
	1995	2000	2010	2020	2030	2040	2050
Austria	1.830	2.000	2.490	3.200	4.050	4.830	5.360
Belgium	2.720	3.020	3.760	4.620	5.720	6.980	7.670
Denmark	1.970	2.110	2.470	3.110	4.040	4.740	5.200
Finland	1.390	1.610	2.140	2.830	3.640	4.270	4.420
France	8.910	10.000	13.300	16.700	20.600	25.400	27.700
Germany	19.400	21.400	27.700	36.500	45.200	53.700	59.100
Greece	2.650	2.970	3.750	4.610	5.340	6.300	6.980
Ireland	0.628	0.661	0.763	0.988	1.350	1.760	2.090
Italy	8.230	9.280	11.500	13.900	16.400	19.000	20.700
Luxembourg	0.095	0.115	0.174	0.250	0.321	0.388	0.423
Netherlands	3.510	3.900	5.070	6.880	9.310	11.600	12.900
Portugal	1.670	1.800	2.080	2.470	3.040	3.640	4.090
Spain	6.960	8.110	10.900	13.400	15.800	19.200	22.700
Sweden	5.780	6.070	6.800	8.120	10.200	11.500	12.600
United Kingdom	13.900	15.000	17.600	21.500	27.500	33.500	38.300
Total		88.100	110.000	139.000	172.000	207.000	230.000
Women + men							
		2000	2010	2020	2030	2040	2050
Total		414.100	495.000	595.000	719.000	861.000	972.000
F/M ratio		3.70:1	3.50:1	3.28:1	3.18:1	3.16:1	3.23:1

Table 1.5: Projected numbers of yearly incident hip fractures in the EU member states, n*1000. The total represents the annual male + female number (*1000) of incident hip fractures for all EU member states

Country	**Year**						
Women							
	1995	2000	2010	2020	2030	2040	2050
Austria	307.0	318.0	351.0	406.0	463.0	507.0	524.0
Belgium	539.0	570.0	641.0	722.0	807.0	874.0	890.0
Denmark	273.0	293.0	330.0	380.0	434.0	461.0	475.0
Finland	255.0	260.0	289.0	339.0	393.0	426.0	432.0
France	2050.0	2210.0	2610.0	2990.0	3360.0	3650.0	3690.0
Germany	2830.0	2930.0	3270.0	3790.0	4240.0	4600.0	4700.0
Greece	449.0	492.0	584.0	673.0	740.0	794.0	809.0
Ireland	76.3	80.3	91.7	110.0	136.0	159.0	174.0
Italy	1930.0	2100.0	2390.0	2690.0	2950.0	3080.0	3070.0
Luxembourg	19.7	22.0	28.2	34.9	40.4	44.6	46.0
Netherlands	519.0	563.0	666.0	810.0	955.0	1050.0	1080.0
Portugal	334.0	362.0	419.0	479.0	553.0	609.0	634.0
Spain	1370.0	1490.0	1740.0	1990.0	2260.0	2460.0	2530.0
Sweden	503.0	521.0	560.0	634.0	722.0	777.0	814.0
United Kingdom	1780.0	1830.0	1970.0	2250.0	2560.0	2790.0	2920.0
Total		14100.0	15900.0	18300.0	20600.0	22300.0	22800.0
Men							
	1995	2000	2010	2020	2030	2040	2050
Austria	216.0	234.0	279.0	345.0	379.0	394.0	386.0
Belgium	300.0	324.0	375.0	431.0	464.0	472.0	465.0
Denmark	172.0	187.0	213.0	248.0	271.0	273.0	275.0
Finland	148.0	172.0	212.0	242.0	254.0	257.0	252.0
France	1450.0	1620.0	1940.0	2230.0	2440.0	2530.0	2490.0
Germany	1750.0	1880.0	2270.0	2790.0	3020.0	3110.0	2970.0
Greece	279.0	300.0	347.0	402.0	443.0	456.0	437.0
Ireland	70.0	73.7	85.0	97.9	119.0	137.0	144.0
Italy	1090.0	1170.0	1310.0	1520.0	1650.0	1620.0	1530.0
Luxembourg	11.3	13.1	17.7	22.4	24.9	25.7	25.3
Netherlands	337.0	384.0	478.0	589.0	646.0	655.0	640.0
Portugal	355.0	373.0	414.0	475.0	560.0	598.0	599.0
Spain	972.0	1040.0	1190.0	1400.0	1610.0	1650.0	1580.0
Sweden	317.0	338.0	374.0	426.0	458.0	474.0	484.0
United Kingdom	1430.0	1520.0	1700.0	1990.0	2160.0	2250.0	2280.0
Total		9630.0	11200.0	13200.0	14400.0	14900.0	14600.0
Women + men							
		2000	2010	2020	2030	2040	2050
Total		23700.0	27200.0	31500.0	35000.0	37200.0	37300.0
F:M ratio		1.46:1	1.42:1	1.39:1	1.43:1	1.49:1	1.56:1

Table 1.6: Projected numbers of prevalent vertebral fractures in the EU member states, n*1000. The total represents the male + female annual number (*1000) of prevalent vertebral fractures in all EU member states.

Country	Year					
	2000	2010	2020	2030	2040	2050
Hip fractures *1000	414	495	595	719	861	972
Vertebral fracture factor†	1.10	1.09	1.08	1.07	1.06	1.05
Beds required	25000	30000	35000	42000	50000	56000
% of available 1993	0.88	1.06	1.23	1.48	1.76	1.97

Table 1.7: Estimated need for hospital beds to treat patients with hip and vertebral fractures in the EU member states.

† Assuming that vertebral fracture incidence at present is equal to hip fracture incidence, that 10% of vertebral fracture patients need hospital care in the acute phase and that the length of hospital stay is 20 days for both hip and vertebral fractures, the demand for hospital beds for the vertebral fracture population is currently 10% of that for patients with hip fracture. The total demand for hospital beds is therefore 1.10 x the number of hip fractures in the year 2000. Thereafter, it is assumed that the vertebral fracture incidence will increase at half the rate of the increase in hip fracture incidence.

Country	Pens /prov % incr	Index					
		80+ /prov % incr	vert fr. /prov % incr	hip fr. /prov % incr	Health care expenditure, 1993		Hospital beds 1993/1000
					ecu / p	% GNP	
Austria	149	366	125	218	1886	6.0	9.5
Belgium	103	280	96	190	1699	7.3	7.7
Denmark	121	231	98	180	1376	5.5	5.0
Finland	141	366	114	257	1447	7.0	11.0
France	108	257	96	194	1948	7.3	9.4
Germany	157	416	125	232	1926	6.0	10.1
Greece	134	320	118	222	531	4.3	5.0
Ireland	164	264	128	244	980	5.1	5.0
Italy	141	377	123	235	1617	6.2	6.7
Luxembourg	163	390	129	248	2116	6.3	11.3
Netherlands	171	395	141	285	1626	6.8	11.3
Portugal	153	353	128	217	919	4.1	4.4
Spain	162	335	138	286	1032	5.7	4.2
Sweden	85	155	74	128	1344	6.2	7.0
United Kingdom	95	212	84	164	1288	5.9	5.4

Table 1.8: Some key indices regarding consequences over a fifty year period of an ageing population and an increasing number of osteoporotic complications.

Pens = pensioner, aged 65+
Prov = provider, aged 20-64
Vert fr = vertebral fracture
Incr = increase

2. BONE PHYSIOLOGY AND THE PATHOGENESIS OF OSTEOPOROSIS

2.1 Bone structure

Bone consists of an extracellular collagenous matrix, composed predominantly of type I collagen, in which bone mineral is deposited in the form of calcium salts. Cortical or compact bone, which forms approximately 90% of the skeleton, is found mainly in the shafts of long bones and surface of flat bones whereas cancellous or trabecular bone is situated at the ends of long bones and in the inner parts of flat bones.

The skeleton contains 99% of the total body calcium, mainly in the form of the hydroxyapatite salt. Calcium homeostasis and bone metabolism are closely linked. Serum calcium concentration is regulated mainly by parathyroid hormone and calcitriol, the biologically active metabolite of vitamin D. Parathyroid hormone and calcitriol are also important in the regulation of phosphate homeostasis

2.2 Vitamin D

In man, vitamin D is obtained from the diet and through cutaneous synthesis in the presence of ultra-violet irradiation supplied by sunlight. Vitamin D is converted to 25-hydroxyvitamin D [25(OH)D; calcidiol] in the liver; circulating calcidiol levels provide a reasonably accurate assessment of vitamin D status. The biologically active form of vitamin D, 1,25-dihydroxyvitamin D_3 ($1,25(OH)_2D_3$; calcitriol) is formed in the kidney from calcidiol. Calcitriol stimulates bone resorption and intestinal calcium absorption, leading to an increase in serum calcium concentration.

2.3 Parathyroid hormone

Parathyroid hormone is secreted by the parathyroid glands and affects calcium homeostasis via effects on bone, kidney and vitamin D metabolism. Increased parathyroid hormone levels raise serum calcium concentration by increasing bone resorption, renal tubular calcium reabsorption and the synthesis of calcitriol. Conversely, an increase in serum calcium concentration results in decreased production of parathyroid hormone and reduced synthesis of calcitriol leading, in turn, to increased urinary calcium excretion and a reduction in bone resorption and intestinal calcium absorption.

2.4 Bone remodelling

During adult life the mechanical integrity of the skeleton is maintained by the process of bone remodelling, in which old bone is removed by osteoclasts and subsequently replaced by new bone, formed by osteoblasts. This occurs in bone remodelling units (BMUs) and consists of the removal of a quantum of bone followed by the formation, within the cavity so formed, of new bone (Figure 2.1). Under normal circumstances resorption always precedes formation and the amounts of bone resorbed and formed are similar. Bone turnover is determined by the number of remodelling units present on the bone surface at any one time

whereas remodelling balance depends on the amounts of bone resorbed and formed within each remodelling unit. The regulation of bone remodelling is complex and results from the interaction of mechanical forces induced by physical activity, systemic hormones, and locally produced cytokines and growth factors.

2.5 Pathophysiology of osteoporosis

2.5.1 Changes in bone remodelling and structure

During the menopause, there is an increase in bone turnover and a decrease in bone formation within individual remodelling units, leading to rapid bone loss (Compston 1994; Figure 2.2). There is also an increase in the activity of osteoclasts, resulting in deep resorption cavities and disruption of cancellous bone architecture with loss of its connectivity. Increased resorption on the endosteal surface of cortical bone leads to thinning of the cortex and increased porosity also occurs as a result of increased osteoclastic activity in remodelling units within cortical bone.

2.5.2 Determinants of bone strength

The mechanical strength of bone is a major determinant of fracture risk and is itself determined by bone mass, the geometry and architecture of bone, bone matrix and mineral composition and the balance between fatigue damage and repair in bone. Geometric parameters which influence mechanical strength include bone size and, at the hip, femoral neck length; architectural determinants in cortical bone are cortical thickness and porosity and, in cancellous bone, connectivity and trabecular size, shape and anisotropy.

2.6 Age-related changes in bone mass

2.6.1 Peak bone mass

During childhood and adolescence there is rapid linear and appositional skeletal growth, the former reaching a maximum between the ages of 15 and 20 years. Bone mass then continues to increase by appositional growth and the peak bone mass is probably attained during the third decade of life (Figure 2.3). Peak bone mass is greater in men than in women and shows large inter-individual and geographic differences. The risk of osteoporosis depends both on the peak bone mass achieved in young adulthood and the rate of bone loss later in life.

The regulation of peak bone mass is not fully understood but a number of factors have been identified. Of these the most important are genetic influences; other determinants, which are potentially modifiable, include physical activity, nutritional factors and hormonal status.

2.6.1.1 Genetic factors affecting bone mass

Studies in twins indicate that between 60 and 80% of peak bone mass is genetically determined and there is also evidence that some aspects of bone architecture and geometry

relevant to bone strength are inherited. The heritability of peak bone mass is believed to be polygenic and has been demonstrated at multiple skeletal sites, although genetic effects appear to be stronger in the lumbar spine than in the femoral neck or distal forearm. The physiological mechanisms by which genetic factors influence bone mass have not been clarified; effects on body size are likely to be important in this respect and there may also be genetic effects on bone modelling and remodelling.

A number of potential candidate genes have been explored in linkage and association studies. Although earlier reports indicated that vitamin D receptor gene polymorphisms were strongly related to bone mass (Morrison et al, 1994), subsequent studies have not always confirmed these findings and some have reported the inverse relationship between genotype and phenotype to that originally described (Houston et al, 1996). In a recent study, a polymorphism in the promotor region of the COL1A1 gene (the gene encoding synthesis of type 1 collagen) was shown to be significantly related to bone mass in the spine and to the presence or absence of osteoporotic spine fractures (Grant et al, 1996). Other candidate genes which are being investigated include the oestrogen receptor gene and cytokine and growth factor genes.

2.6.1.2 Nutritional factors

A number of aspects of diet and nutrition influence peak bone mass, including calcium, vitamin D, protein, salt and energy intake. These are discussed in detail in Chapter 3.

2.6.1.3 Physical activity

Physical activity has important effects on bone growth and architecture during childhood and adolescence and there is some evidence that higher levels of weight-bearing physical activity in childhood and early adulthood are associated with greater bone mass (Slemenda et al, 1994; Välimäki et al, 1994).

2.6.1.4 Sex hormones

Peak bone mass may also be modified by hormonal factors. Primary hypogonadism in either sex is associated with low bone mass and secondary amenorrhoea in women, due for example to anorexia nervosa, excessive exercise or chronic disease, results in low peak bone mass and increased risk of osteoporosis. There is some evidence that a late menarche is associated with lower peak bone mass. Finally, some studies indicate that oral contraceptive use may be associated with higher bone mass, although this finding has not been universal (Mazess & Barden, 1991; Murphy et al, 1993).

2.7 Age-related bone loss

After peak bone mass has been attained, there is a period of consolidation in which the transverse diameter of the long bones and vertebrae continues to increase by subperiosteal appositional growth. The age at which bone loss commences is uncertain but is believed to be around the age of 40 years, both in men and women. Bone loss then continues throughout life, affecting both cortical and cancellous bone throughout the skeleton. In men, bone loss averages between 0.5 and 1% per year.

In women, there is an acceleration in the rate of bone loss around the time of the menopause to about 2% per year, although reported rates of bone loss vary widely, from less than 1% to 6% per year. In the early postmenopausal years, bone loss from the spine exceeds that at other sites and overall it is estimated that, in women, approximately 35% and 50% of cortical and cancellous bone respectively are lost from the skeleton over the course of a lifetime (Mazess, 1982; Riggs et al, 1981). Lower peak bone mass, accelerated bone loss during the menopause, and greater longevity all contribute to the higher incidence of osteoporotic fractures in women than in men.

The question of whether there is a sub-group of women who lose bone more rapidly than normal during the menopause („fast losers“) is controversial. Although there are large variations in rates of menopausal bone loss among individual women, there is no strong evidence that the distribution of rates of loss is bimodal and bone loss measured over longer periods of time shows less variability (Hui et al, 1989).

2.7.1 Pathogenesis of age-related bone loss

The factors responsible for age-related bone loss are incompletely understood. Oestrogen deficiency is an important determinant of menopausal bone loss and premature menopause is associated with a greatly increased risk of osteoporosis. In men, declining production of sex hormones may also contribute to age-related bone loss, although this is less well documented than in women. Decreasing physical activity with age is another likely contributory factor, both in men and women. Nutritional factors have also been implicated; vitamin D deficiency is common in many elderly populations and results in secondary hyperparathyroidism and increased bone turnover (Parfitt et al, 1982) and in middle-aged women there is evidence that bone mass is positively related to serum 25-hydroxyvitamin D levels and inversely related to serum parathyroid hormone concentrations (Khaw et al, 1992), although this finding has not been universal. Vitamin D deficiency in the elderly is mainly privational, although reduced renal synthesis of 1,25-dihydroxyvitamin D as a result of declining renal function with age and reduced intestinal absorption may also contribute. Finally, calcium deficiency due to reduced intestinal absorption and increased renal excretion may contribute to age-related bone loss.

2.8 Pathogenesis of osteoporosis

Primary osteoporosis has traditionally been classified into Type 1 or postmenopausal osteoporosis and Type II, or senile osteoporosis (Riggs & Melton, 1983). Oestrogen deficiency due to declining ovarian function during the menopause is believed to be the major pathogenetic factor responsible for Type I osteoporosis, which is characterised by predominantly cancellous bone loss resulting in vertebral and distal radius fractures and occurs in the first 15-20 years after the menopause. Type II osteoporosis, which occurs in elderly men and women, results from loss of both cortical and cancellous bone and is associated with fractures of the vertebrae and proximal femur. In this type of osteoporosis it is postulated that vitamin D deficiency and secondary hyperparathyroidism are largely responsible for bone loss. However, it is increasingly recognised that multiple pathogenetic factors operate in many cases of osteoporosis and that peak bone mass and, in women, menopausal bone loss, are major determinants of fracture risk at all ages.

A number of secondary causes of osteoporosis have been identified. These include glucocorticoid therapy, endocrine disorders, malignant disease, immobilisation and a variety of other disorders (Table 2.1).

Table 2.1: Secondary causes of osteoporosis

Endocrine disorders

- Primary and secondary hypogonadism
- Hyperthyroidism
- Hyperparathyroidism
- Cushing's syndrome
- Hyperprolactinaemia

Malignant disease

- Myeloma
- Leukaemia, lymphoma
- Mastocytosis

Drugs

- Glucocorticoids
- Heparin
- Alcohol

Others

- Connective tissue disorders
- Gastrointestinal disease
- Chronic liver disease
- Chronic renal disease
- Post-transplantation
- Immobilisation

Bone Remodelling

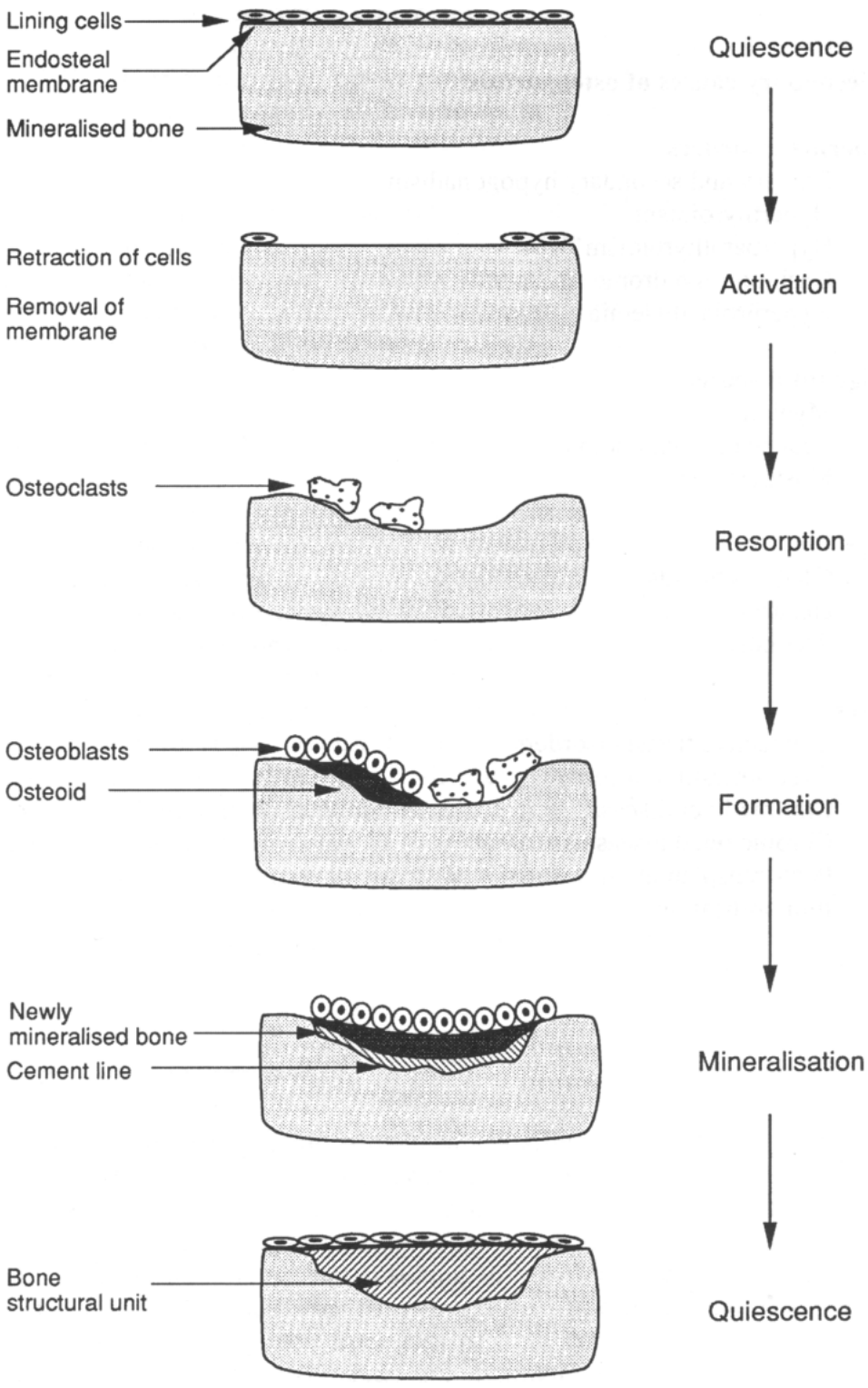


Figure 1: Schematic representation of bone remodelling in cancellous bone.
Reprinted with permission from Compston JE. Bone morphology: quality, quantity and strength. In: Oestrogen deficiency. Causes and consequences. ed. Shaw RW. Advances in Reproductive Endocrinology 1996; 8: 63-84. Parthenon Publishing Group Ltd UK.

Mechanisms of Menopausal Bone Loss

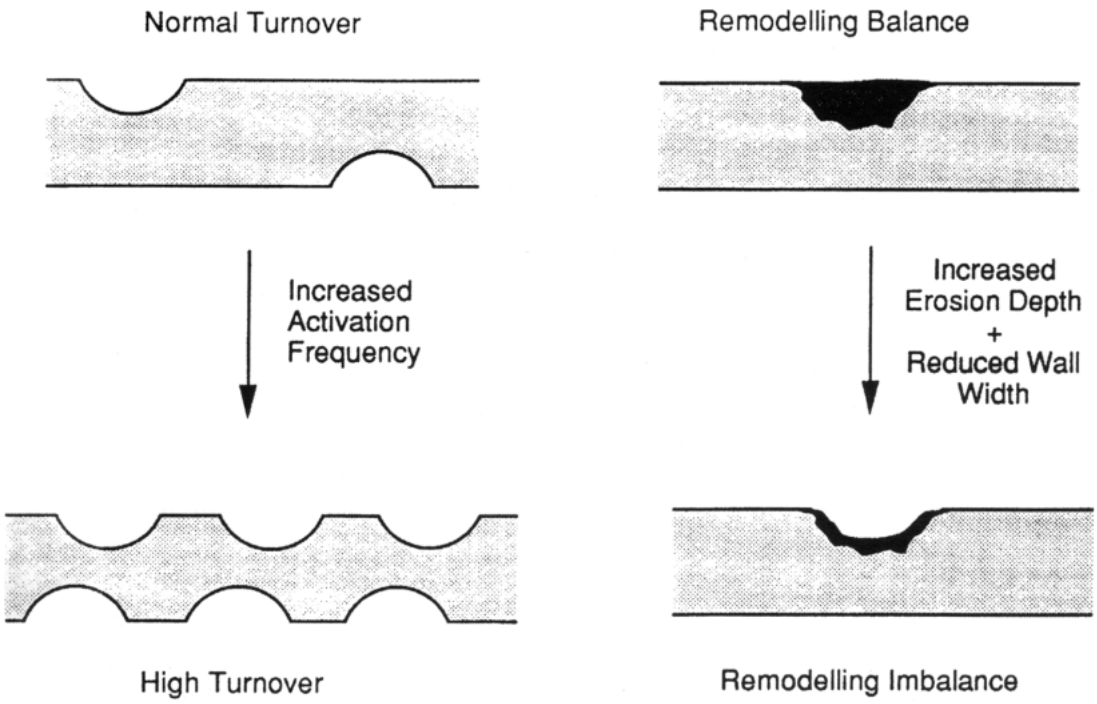


Figure 2: Mechanisms of menopausal bone loss in cancellous bone.

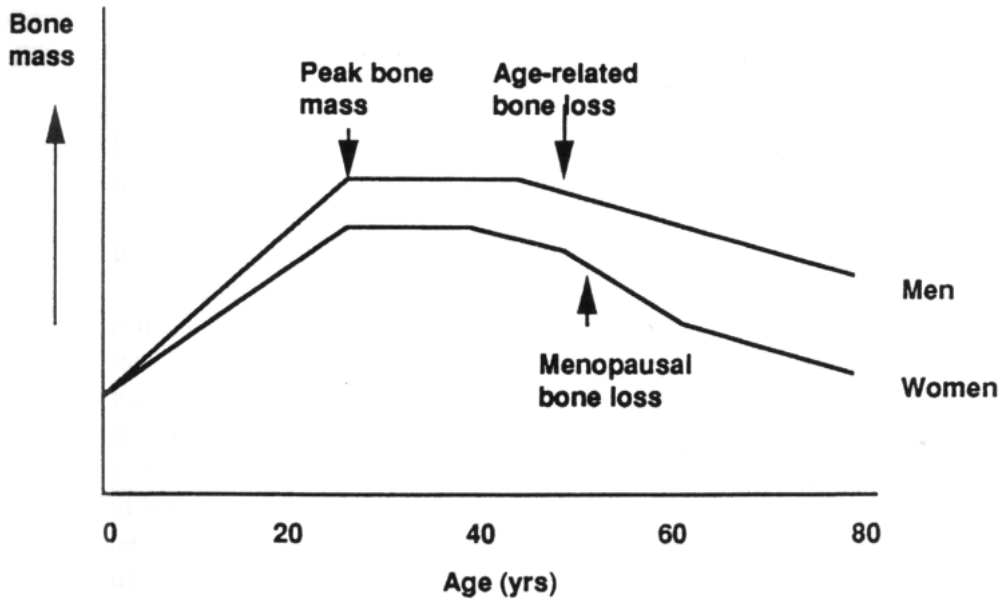


Figure 3: Age-related changes in bone mass in men and women.
Reprinted with permission from Compston JE. Aliment Pharmacol Ther 1995; 9: 237-50. Blackwell Science Ltd.

3. NUTRITIONAL FACTORS RELATED TO BONE HEALTH

3.1 Calcium

In recent years convincing evidence has emerged with respect to effects of calcium on bone health in all age groups. Intervention and cross-sectional studies have reported a positive effect of calcium on bone mass in children and adolescents (Kanders et al, 1988; Johnston et al, 1992; Dawson-Hughes, 1996) and, in a prospective study, Välimäki et al (1994) reported that dietary calcium intake in childhood and adolescence was positively related to bone mineral density in young women. A meta-analysis of 33 studies concluded that there was an overall association between calcium intake and bone mass in premenopausal women (Welten et al, 1995); no conclusions could be drawn about this relationship in men because of insufficient data. In general the most consistent effects of calcium supplementation are observed in the appendicular skeleton and effects on spinal bone appear to be transient (Compston, 1995). Older women seem to be more responsive than younger postmenopausal women (Dawson-Hughes, 1996).

The relationship between calcium intake and fracture rate is less certain. Whilst some studies have reported inverse correlations between dietary calcium intake and fracture (mainly of the hip), others have not demonstrated any significant correlation and some have even shown a positive correlation between calcium intake and hip fracture (Compston, 1995).

The effects of calcium on bone mass may be mediated, at least in part, by changes in parathyroid hormone secretion. Doses of calcium as small as 250 mg result in acute suppression of serum parathyroid hormone concentrations and low habitual calcium intakes are associated with higher serum parathyroid hormone levels than higher intakes (Kärkkäinen et al, 1996; McKane et al, 1996). The beneficial skeletal effects of calcium may therefore be mediated via an anti-resorptive effect.

3.1.1 Calcium requirements and current recommended dietary allowances

Intestinal calcium absorption shows considerable inter-individual variation and is influenced both by vitamin D status and dietary calcium intake. The efficiency of absorption increases with lower calcium intakes and decreases when calcium intake is high; the age-related decline in intestinal calcium absorption is mainly due to reduced production of calcitriol.

There has been considerable dispute over recommendations for dietary calcium intake. The present US recommendations (Institute of Medicine, 1997; Table 3.1) are higher in almost all age-groups than the former ones from 1989 (National Institute of Health, 1989) , in which the recommended intakes in children, adolescents and postmenopausal women had been criticised as being too low (Nordin & Heaney 1990). The optimal calcium intakes recommended by the NIB Consensus Conference (Table 3.1) are even higher than the new ones from the Institute of Medicine (1997). However, the calculations on which the NIH recommendations are based have also been criticised (Kanis, 1994). Current recommendations for the European Community and the Nordic countries are presented in Table 3.1.

3.1.2 Dietary calcium intake

The daily average calcium intake in some age groups in European countries is shown in Table 3.2.

The bioavailability of calcium varies according to the source. Milk and milk products are good sources with both a high calcium content and good bioavailability. Fish is also a good source of calcium, particularly if the bones are eaten as well. Calcium rich mineral waters and some fruit juices are also good sources. Although some vegetable foods have a high calcium content, the bioavailability is often poor (Table 3.3). The bioavailability of calcium may also be adversely affected by other constituents of food, for example dietary fibre, phytates and tannins, although the effects of these are unlikely to be significant in a normal diet.

Policies for the fortification of food with calcium differ between the member states, being very strict in some countries, for example Finland, and more liberal in others such as Belgium. The addition of calcium to foods is not compulsory in any country with the exception of the United Kingdom, where calcium is added to all flours. Other examples of fortification of food with calcium include breakfast drinks (Austria), oatflakes (Denmark), cereals, milk, juices, soy drinks and sweets (Germany), milk (Greece), flour (Iceland and Ireland), milk (The Netherlands) and soy drinks and cereal gruels (Sweden) (Report of SCOOP Task 7.1.1, 1997).

3.2 Vitamin D

Two forms of bone disease may accompany vitamin D deficiency. Severe deficiency results in rickets in children and osteomalacia in adults, these conditions being characterised by defective mineralisation of bone. Lesser degrees of vitamin D deficiency are associated with an increase in parathyroid hormone production, resulting in increased bone turnover and bone loss in the absence of any significant mineralisation defect.

Low serum calcidiol levels, indicating vitamin D deficiency, are common in many elderly populations in western Europe (Wielen et al, 1995) and are believed to contribute to the pathogenesis of fractures, particularly at the hip. A positive association between serum calcidiol concentrations and bone mineral density has been reported in middle-aged and elderly women (Villareal et al, 1991; Khaw et al, 1992), whilst an inverse relationship was observed between serum parathyroid hormone levels and bone mineral density. Vitamin D supplementation prevents the fall in bone mineral density that occurs during the winter months in normal subjects (Dawson-Hughes et al, 1991). Vitamin D deficiency in the elderly is thought to be mainly privational, although reduced intestinal absorption of dietary vitamin D, impaired cutaneous synthesis and reduced conversion of calcidiol to calcitriol may also contribute (Bouillon et al, 1997).

There is also evidence that relatively small amounts of vitamin D reduce non-vertebral fracture rate; this is reviewed in detail in Chapter 5. Further studies are required to establish the optimum dose; there is some evidence that 10 µg (400 IU) daily as an oral dose or single injections of large doses (e.g. 150,000 units or 3,750 µg) may be suboptimal in terms of the serum calcidiol levels achieved and the resulting suppression of parathyroid hormone secretion. However, based on current evidence the vitamin D requirement in the elderly appears to be between 10-20 µg daily (400-800 IU). Maintenance of an adequate vitamin D

status in the elderly may also improve muscle strength and hence reduce both the risk and consequences of falling.

3.2.1 Current recommended dietary allowances for vitamin D

These are presented in Table 3.4.

3.2.2 Dietary vitamin D

Data on dietary vitamin D intake are not available in many European countries. The main sources of vitamin D in Europe are fish, fish products and food to which vitamins have been added (Table 3.5). However, in many countries endogenous synthesis in the skin is the main source of vitamin D. Policies in Europe for the fortification of vitamin D are presented in Table 3.6.

3.3 Other nutritional factors

The prevalence of malnutrition and undernutrition increases with advancing age and is increased in patients with hip fracture (Bonjour et al, 1996). Deficiency both of macronutrients and micronutrients is strongly implicated in the pathogenesis and consequences of hip fracture in the elderly. Undernutrition increases the risk of hip fracture for a number of reasons. It may increase the risk of falling by impairing neuromuscular co-ordination and reducing muscle strength. In addition, a reduction in the protective layer of soft tissue increases the likelihood of hip fracture following a fall.

3.3.1 Protein

In the elderly, an association between low protein intake, low bone mineral density and reduced mobility has been shown. Low protein intake is often associated with overall malnutrition and normalising protein intake is therefore of importance in the elderly. A high protein intake is associated with increased urinary calcium excretion and may thus result in decreased bone mineral density; however, this effect is of minor importance in young people.

3.3.2 Phosphate

A high dietary intake of phosphate in combination with a low intake of calcium increases serum parathyroid hormone concentrations and may thus have adverse effects on bone mineral density. It has also been shown that acutely increasing dietary phosphate intake leads to increased parathyroid hormone secretion and has an inhibitory effect on bone formation (Kärkkäinen & Lamberg-Allardt, 1996). Milk and animal products are the main sources of dietary phosphate, but it should be emphasised that the use of phosphates in food additives is increasing.

3.3.3 Magnesium

Approximately 50% of total body magnesium is found in the skeleton. Magnesium deficiency is rare and usually associated with disease, for example malabsorption or medication. Magnesium and calcium homeostasis are closely related and further studies are required to establish the relationship between dietary magnesium intake and bone health.

3.3.4 Sodium

Renal tubular reabsorption of calcium parallels that of sodium and hence increases in urinary sodium excretion are accompanied by increased urinary calcium excretion. Thus a high sodium intake may have adverse effects on calcium homeostasis and bone mass (Massey & Whiting, 1996). Devine et al (1995) reported a positive association between urinary sodium excretion and bone loss in a 2 year prospective study of postmenopausal women; however, no relationship between sodium excretion and bone mineral density was found in another study of men and women aged over 65 years (Dawson-Hughes et al, 1996). Further work is needed in this area; in general, sodium intake in Europe is higher than currently recommended.

3.3.5 Fluoride

Fluoride is one of the few agents which are known to enhance bone formation. Pharmacological doses of fluoride increase bone mass but may have negative effects on bone strength and fracture risk. Fluoride-rich water could theoretically affect bone mass, although the study of Kröger et al (1994) does not support this view.

3.3.6 Vitamin C

Vitamin C is required for the formation of collagen, the most abundant protein in bone and osteoporosis is common in patients with florid scurvy. However, there are no population-based data on the relationship between vitamin C intake and bone mineral density.

3.3.7 Vitamin K

Vitamin K is required for the synthesis of osteocalcin, which is synthesised by osteoblasts and is the most abundant non-collagenous protein in bone. There is some evidence that vitamin K deficiency is associated with an increased fracture rate in the elderly (Bitensky et al, 1988; Hodges et al, 1993) but further studies are required.

3.4 The effect of alcohol, coffee and smoking on bone mineral density and fracture risk

3.4.1 Alcohol

Fracture risk is increased in male alcoholics, partly because they are more susceptible to falls (Laitinen & Välimäki, 1993). In addition, bone mineral density is reduced in male alcoholics;

this may result from a number of factors including malnutrition, liver dysfunction, and a direct effect of alcohol on osteoblast function.

Moderate alcohol intake may have beneficial effects on bone mass. In one study, bone mineral density in postmenopausal women who drank more than 200 ml per week, equivalent to 2-3 glasses of wine each day, was 7.7% higher than age-matched controls who drank less than 30 ml per week (approximately one glass of wine per week) (Felson et al, 1995). Men with a moderate alcohol intake, as defined above, also had a higher bone mineral density than those with low intake, the mean difference being 4%.

3.4.2 Caffeine

Caffeine increases urinary calcium excretion. Epidemiological data on the relationship between caffeine intake and bone mass are conflicting; however, in two recent studies in postmenopausal and elderly women, it was shown that an optimal calcium intake could protect against the harmful effects of caffeine on bone (Barrett-Connor et al, 1994; Harris & Dawson-Hughes, 1994).

3.4.3 Smoking

There is evidence from epidemiological studies that smokers have lower bone mass than non-smokers (Laitinen & Välimäki, 1993; Hopper & Seeman, 1994). Contributory factors include lower body weight in smokers, a direct inhibitory effect of tobacco on osteoblasts and, in women, an earlier menopause in those who smoke. In a recent meta-analysis, it was concluded that smoking increases the lifetime risk of hip fracture in women by approximately 50% (Law & Hackshaw, 1997).

3.5 Recommendations for dietary nutrient intake and assessment of those at high risk

3.5.1 Calcium intake

The most feasible way to assess the intake of calcium is to use a short food frequency questionnaire (FFQ). This should be designed specifically for each country, taking into account the local sources of calcium.

Gender-specific recommendations for different age-groups are shown in Table 3.7. It should be noted that the requirement for calcium may be influenced by other dietary, lifestyle and environmental factors which are specific to each country. The optimal way to achieve adequate calcium intake is through a balanced diet. However, calcium supplements may be used if dietary sources are scarce or cannot be tolerated. Fortified foods may also improve calcium intake; attention should be paid to the selection of products so that they reach the target groups.

Although dietary calcium intake is below the recommended levels in many individuals, those at particular risk from inadequate calcium intake are the elderly, postmenopausal women, subjects with lactose intolerance and those on special diets or who are anorexic.

3.5.2 Vitamin D intake

Vitamin D deficiency is best assessed on the basis of the serum calcidiol level (taking seasonal variations into account) and the serum parathyroid hormone concentration. In addition, information on dietary intake of vitamin D and exposure to sunlight of uncovered skin may be helpful.

The recommended daily allowances of vitamin D are shown in Table 3.8. In order to improve vitamin D status, individuals should also be encouraged to spend time out-of-doors. Intakes of 250 µg (10,000 IU) daily of vitamin D have been reported to be harmful, resulting in hypercalcaemia and hypercalciuria. Although the maximum safe dose is unknown, intakes of 50 µg (2,000 IU) daily in adults appear safe and, in general, should not be exceeded.

As discussed earlier, there is increasing evidence that vitamin D supplements may be beneficial in high-risk sections of the elderly population. Other at risk groups include strict vegetarians and Asian immigrants. Fortification of foods provides an alternative approach; as with calcium, the products should be selected with a view to reaching high-risk groups.

3.5.3 Other recommendations regarding nutrition

Maintenance of good nutrition is important in the elderly both in the prevention of fractures and recovery in those who have suffered a fracture. In particular, an adequate intake of energy and protein are important in this respect. As regards other nutrients, there is insufficient evidence at present to enable the provision of definite guidelines.

Table 3.1: Recommended dietary allowances for calcium (mg/day)

Institute of Medicine (USA): Adequate Intake for calcium [1]		
	age (yrs)	mg/day
	0-0.5	210
	0.5-1.0	270
	1-3	500
	4-8	800
	9-13	1300
	14-18	1300
	19-30	1000
	31-50	1000
	51-70	1200
	70+	1200
Pregnancy	=18	1300
	19-50	1000
Lactation	=18	1300
	19-50	1000

European Community's Population Reference Intake (PRI) [3]		
	age (yrs)	mg/day
	6-11m	400
	l-3y	400
	4-6	450
	7-10	550
Males	11-17	1000
Females	11-17	800
Adults	PRI	700
	AR	550
	LTI	400
Pregnancy		700
Lactation		1200

National Institute of Health: Optimal Calcium Intake [2]		
	age (yrs)	mg/day
Infants	0-0.5	400
	0.5-1.0	600
Children	1-5	800
	6-10	800-1200
Males	11-24	1200-1500
	25-65	1000
	65+	1500
Females	11-24	1200-1500
	25-50	1000
	50-65	1500
	50-65, using oestrogens	1000
	65+	1500
Pregnancy		1200
Lactation		1200

Nordic Nutrition Recommendations [4]		
	age (yrs)	mg/day
Infants	0-0.5	360
	0.5-1.0	540
Children	1-3	600
	4-6	600
	7-10	700
Males	11-20	900
	20-60	800
	61-75+	800
	75+	800
Females	11-20	900
	20-60	800
	61-75*	800
	75+*	800
Pregnancy		900
Lactation		1200
* Supplementation with 500-1000 mg/day may delay bone loss		

Table 3.1

[1] Institute of Medicine, 1997
Adequate Intake=When sufficient scientific evidence is not available to estimate an average requirement, adequate intakes (Al) have been set. Individuals should use the AI as a goal when no Recommended Dietary Allowances exist. The AI is derived through experimental or observational data that show a mean intake which appears to sustain a desired indicator of health, such as calcium retention in bone, for most members of a population group.

[2] Optimal Calcium Intake. NIH Consensus Development Panel on Optimal Calcium Intake 1994

[3] Commission of the European Communities. Reports of the scientific committee for food (31st series), 1993.
PRI = Population reference intake: The intake is enough for practically all healthy people in a group.
AR = Average requirement
LTI = Lowest threshold limit: The intake below which, on the basis of current knowledge, almost all individuals will be unlikely to maintain metabolic integrity according to the criterion chosen.

[4] Nordic Nutrition Recommendations, 1996.
The values for recommended intake are intended for the planning of diets for groups of subjects. The values include a safety margin which make it likely that a diet containing these amounts will cover the needs of almost the entire population.

Table 3.2: Dietary calcium intake in some European countries

The Seneca-study[1]. The calcium intake in 1993 of elderly participants aged 75-80 years

		Calcium intake mg/day		
	number of participants	P10	P50	P90
Women				
Hamme, Belgium	61	287	676	1 101
Roskilde, Denmark	58	545	983	1 529
Haguenau, France	53	429	635	944
Romans, France	72	445	629	976
Padua, Italy	66	471	740	1 204
Culembourg, Netherlands	69	612	1 110	1 616
Vila Franca de Xira, Portugal	80	254	548	974
Betanzos, Spain	47	412	909	1 570
Yverdon, Switzerland	79	448	773	1 245
Coimbra, Portugal	14	265	554	1 375
Marki, Poland	73	300	676	1 357
Ballymoney-Portsteward-Limavady, Northern Ireland	38	465	773	1 350
Men				
Hamme, Belgium	68	324	748	1 166
Roskilde, Denmark	57	710	1 145	1 895
Haguenau, France	56	402	620	1 010
Romans, France	70	540	823	1 176
Padua, Italy	69	432	718	1 091
Culembourg, Netherlands	52	725	1 036	1 447
Vila Franca de Xira, Portugal	77	441	766	1 251
Betanzos, Spain	35	548	930	1 678
Yverdon, Switzerland	71	568	961	1 482
Coimbra, Portugal	13	272	578	828
Marki, Poland	47	449	732	1 230
Ballymoney-Portsteward-Limavady, Northern Ireland	32	628	1028	1 311

[1] Amorim-Cruz et al, 1996.

Dietary intake data were collected by a validated modified dietary history method. Each country used its own nutrient database. The data were collected in 12 European towns. The data are presented in percentiles.

Table 3.3: Examples of important sources of calcium in the diet (mg/portion)

Source		**Calcium content per portion**
Milk, sour milk		205 mg/glass (170g)
Yoghurts		150-285 mg/carton (150g)
Cheese		
	Fermented cheese i.e. Emmental, Edam, Gouda, Cheddar	120-200 mg/piece (20g)
	Soft cheese i.e. Brie, Roquefort, Camembert	70-100 mg/piece (20g)
Fish		70-150 mg/portion (150g)
Sardines, with bones		300 mg/can (70g)
Vegetables, fruits, berries and seeds		10-1000 mg (bioavailability poor, with a few exceptions)

Holland et al, 1995.

Table 3.4: Recommendations for daily dietary intake of vitamin D (µg/day)

Institute of Medicine (USA): Adequate Intake [1]		
	age (yrs)	µg/day
	0-0.5	5
	0.5-1.0	5
	1-3	5
	4-8	5
	9-13	5
	14-18	5
	19-30	5
	31-50	5
	51-70	10
	70+	15
Pregnancy		5
Lactation		5

Nordic Nutrition Recommendations [3]		
	age (yrs)	µg/day
Infants	0-0.5	10
	0.5-1.0	10
Children	1-3	10
	4-6	5
	7-10	5
Males	11-60	5
	61-75	10
	75+	10
Females	11-60	5
	61-75	10
	75+	10
Pregnancy		10
Lactation		10

1 µg vitamin D = 40 IU

European Community's PopulationReference Intake (PRI)[2]		
	age (yrs)	µg/day
	6-11m	10-25
	l-3y	10
	4-6	0-10
	7-10	0-10
	11-17	0-15
	18-64	0-10
	65+	10
Pregnancy		10
Lactation		10

[1] Institute of Medicine, 1997.

[2] Commission of the European Communities. Reports of the scientific committee for food (31st series), 1993.
A range of values up from zero indicates that all members of the group should be able to produce adequate vitamin D

[3] Nordic Nutrition Recommendations 1996.
The values for recommended intake are intended for the planning of diets for groups of subjects. The values include a safety margin which make it likely that a diet containing these amounts will cover the needs of almost the entire population.

Table 3.5: Examples of important dietary sources of Vitamin D (µg/portion)

Source		**vitamin D content µg/portion**
Fish		The vitamin D content depends on where the fish is caught
	Pike, perch	9-12/portion (150g)
	Salmon	20/portion (150g)
	Sardines, canned	2.2/can (70g fish)
	Tuna, canned	1.2-2.0/can (70g fish)
Wild mushrooms	Wild chantarelles	13/100g
Meat products		The vitamin D content of meat products depends probably on the feed of the animals
	liver	1.8-2.7/l00g
	chicken	1.7/100g
Eggs		1.4/100g
Margarines	vitamin D is added to margarines in most European countries	

1 µg vitamin D = 40 IU

Rastas et al, 1993.
Mattila P. 1995.

Table 3.6: Foods that are fortified with vitamin D in the European countries (situation in 1996)

Country	Foods to which vitamin D is added
Austria	Margarine, oils, breakfast cereals
Belgium	Compulsory to margarines, minarines and cooking fats
Denmark	✂
Finland	Margarine and fat spreads, milk (fat-reduced, restoration)
France	✂
Germany	Permitted only in margarines, mixed fat spreads and energy-reduced milks
Greece	May be added to margarines, milk and instant beverage preparations
Ireland	Margarines, liquid milks, dehydrated milks
Italy	✂
Luxembourg	✂
Netherlands	Compulsory to margarines
Portugal	Breakfast cereals (some brands), milk (some brands)
Spain	✂
Sweden	May or must be added to some oils and margarines, low fat and sour milk, soy drinks, cereal gruels
United Kingdom	Compulsory to margarines, can be added to many food stuffs

Report of SCOOP Task 7.1.1 Working group. Scientific considerations for the development of measures on the addition of vitamins and minerals to foodstuffs, April, 1997.

Table 3.7: Recommended daily dietary allowances for calcium (based on European and Nordic recommendations)

Group	Age (years)	Range (mg)
Newborn	0-0.5	400
	0.5-1.0	360-400
Children	1-3	400-600
	4-6	450-600
	7-10	550-700
Men	11-24	900-1000
	25-65	700-800
	65-	700-800
Women	11-24	900-1000
	25-50	700-800
	50-65	800
	65-	700-800
Pregnant		700-900
Lactating		1200

Table 3.8: Recommended dietary allowances for vitamin D (based on European and Nordic recommendations)

The requirement for dietary vitamin D depends on the amount of sunshine exposure. The higher end of the range is the estimated dietary requirement of an individual with minimal endogenous synthesis, whereas the lower end indicates that all members of a group should be able to produce adequate vitamin D by themselves.

Group	Age (years)	Range (µg)
Newborn	0-0.5	10-25
	0.5-1.0	10-25
Children	1-3	10
	4-6	0-10
	7-10	0-10
	11-14	0-15
Men and Women	15-17	0-15
	18-64	0-10
	65+	10
Pregnant		10
Lactating		10

1 µg vitamin D = 40 IU

4. DIAGNOSIS AND ASSESSMENT OF RISK

4.1 Clinical manifestations of osteoporosis

Fragility fractures due to osteoporosis may affect many skeletal sites but most commonly occur at the spine, hip and forearm. Forearm and hip fractures nearly always follow trauma whereas vertebral fractures often occur in the absence of obvious trauma. Forearm and hip fractures are invariably associated with pain at the time of fracture whereas only one-third or less of patients with vertebral fracture present with pain; this may be extremely severe and is localised at the site of fracture in the spine, commonly radiating around the abdomen or thorax to the front of the chest. The natural history of pain after vertebral fracture is extremely variable; in general, there is a slow improvement over time but in some patients, pain or discomfort is a permanent sequel. Long-term effects of vertebral fractures include height loss and spinal deformity (kyphosis), which may result in physical disability, reduced lung function, loss of self-confidence and severe curtailment of normal daily activities. Persistent discomfort also occurs in a minority of forearm fracture sufferers, sometimes with deformity and dysfunction. The long-term morbidity of hip fractures is extremely high, only one-third or less of patients retaining their former level of independence.

4.2 Diagnostic tests

Investigation of the patient with osteoporosis should include exclusion of secondary causes (see chapter 2). Routine haematological and biochemical measurements are usually normal in patients with primary osteoporosis; bone densitometry and radiological assessment provide the main diagnostic tests for osteoporosis and are described in more detail later in this chapter.

4.3 Assessment of risk

Fracture is the only clinical manifestation of osteoporosis and occurs at a relatively late stage of the disease, when bone loss may be advanced. The development of techniques which enable assessment of bone mass has led to significant advances in the diagnosis of osteoporosis, providing the means to detect osteoporosis before fracture has occurred and to target for intervention those at high risk. Non-bone mass related factors are also important in the assessment of risk, particularly those which increase the likelihood of falling or interfere with the protective responses resulting from a fall.

Potential approaches to the assessment of fracture risk in individuals include bone mineral density measurements, ascertainment of clinical risk factors and assessment of biochemical markers of bone turnover. Population-based screening for osteoporosis cannot at present be justified in any age group and in clinical practice a high-risk strategy is thus adopted to select individuals for bone densitometry, based on the presence of strong clinical and historical risk factors. Recognition of these risk factors is important not only to target patients for bone densitometry but also because some are potentially modifiable and may therefore be remediable.

4.3.1 Clinical risk factors

Many risk factors for osteoporosis have been identified (Table 4.1). In general, risk factor scores show relatively poor specificity and sensitivity in predicting either bone mineral density or fracture risk (Compston, 1992; Ribot et al, 1992); this partly reflects the varying strength and prevalence of the risk factors used. Thus, common but relatively weak risk factors such as cigarette smoking and physical inactivity will have a much greater influence on risk factor scores than relatively uncommon but strong risk factors such as glucocorticoid therapy and hypogonadism. Conversely, risk factors for falling such as visual impairment, reduced mobility and treatment with sedatives, are more strongly predictive of hip fracture in the elderly (Cummings et al, 1995).

4.3.1.1 Major risk factors

- Hypogonadism

Hypogonadism is an important risk factor for osteoporosis in both sexes. In premenopausal women hypogonadism may be primary or secondary to conditions such as anorexia nervosa, exercise-induced amenorrhoea, chronic illness, hyperprolactinaemia and gynaecological disorders. Premature menopause, either spontaneous or induced by surgery, chemotherapy or radiotherapy is also associated with increased risk of osteoporosis. In men, hypogonadism may be due to a variety of disorders including Klinefelter's syndrome, hypopituitarism, hyperprolactinaemia and castration, for example after prostatic surgery.

- Glucocorticoid therapy

Glucocorticoids are widely used for the treatment of a number of diseases including rheumatic disorders, asthma and other lung conditions, inflammatory bowel disease, skin disorders and vasculitic syndromes. Bone loss is believed to be most rapid in the first few months of treatment and affects both axial and appendicular skeleton. It has been demonstrated with both parenteral and oral glucocorticoid therapy; bone loss associated with inhaled glucocorticoid therapy is less well documented although there is some evidence that high doses of inhaled glucocorticoids may have adverse skeletal effects. Although the skeletal response to glucocorticoids may vary between individuals high doses are generally associated with greater adverse skeletal effects, whilst daily doses of prednisolone below 7.5 mg are less likely to result in increased rates of bone loss.

- Past history of fracture

A number of studies have demonstrated that a history of fragility fracture is an important independent risk factor for further fracture. Thus the presence of two or more prevalent vertebral fractures was associated with a twelve-fold increase in fracture risk for any given bone mineral density (Ross et al, 1991) and women with a past history of non-vertebral fractures were found to have a three-fold increase in the risk of subsequent spine fractures (Wasnich et al, 1994).

4.3.1.2 Other risk factors

Of the endogenous and exogenous risk factors shown in Table 4.1, smoking, alcohol and nutrition are discussed in Chapter 3. Complete immobilisation leads to rapid bone loss at the

affected sites but evidence that lesser degrees of physical inactivity increase the risk of osteoporosis is less well documented. A low body mass index is an important risk factor for osteoporosis, probably because of its effect on bone size. Finally, a maternal history of hip fracture is an independent risk factor for fracture; for any given bone mineral density, hip fracture risk is increased approximately two-fold.

4.3.2 Bone densitometry

A number of methods are now available for the assessment of bone mass. These include single energy photon and X-ray absorptiometry, dual energy X-ray absorptiometry, quantitative computed tomography and broadband ultrasound velocity and attenuation. These methods are summarised in Table 4.2. Single energy photon and X-ray absorptiometry and broadband ultrasound techniques enable measurements to be made only in the appendicular skeleton, whereas dual energy X-ray absorptiometry and quantitative computed tomography can be applied both to appendicular and axial skeletal sites. In addition, quantitative computed tomography enables differential measurements to be made in cortical or cancellous bone.

Dual energy X-ray absorptiometry is widely used because of its high reproducibility, low radiation dose and ability to measure bone mineral density (BMD) at both appendicular and axial sites in the skeleton. With the exception of quantitative computed tomography, which measures volumetric bone mineral density in g/cm^3, these techniques generate a linear (g/cm) or areal (g/cm^2) bone mineral density value, which reflects bone size as well as true bone density.

Certain limitations of absorptiometric techniques should be recognised. The absolute value for a given bone mineral density varies with different systems and there are also differences in the reference data supplied by different manufacturers (Laskey et al, 1992), although steps have recently been taken to standardise femoral bone mineral density measurements, where these differences are greatest (Hanson, 1997). The accuracy of measurements of spinal bone density is reduced in the presence of osteophytes, extraskeletal calcification, scoliosis and vertebral deformity, all of which become increasingly common in the elderly (Reid et al, 1991). It should also be noted that densitometric techniques do not distinguish between osteoporosis and osteomalacia, in both of which bone mineral density is reduced.

The availability of bone densitometry systems throughout Europe is patchy and many doctors and their patients do not currently have access to bone density measurements. There are marked variations between European Union countries with respect to the resources available, as shown in Figure 4.1

4.3.3 Relationship between bone mass and fracture risk

Bone mass is a major determinant of bone strength and fracture risk. Prospective studies, performed mainly in women in the seventh and eighth decades of life, have shown that there is an increasing gradient of risk of fracture with decreasing bone density, a decrease in the latter of one standard deviation being associated with a 1.5 to 2.5-fold increase in fracture risk (Wasnich et al, 1985; Hui et al, 1988; Gärdsell et al, 1991; Cummings et al, 1993; Kröger et al, 1995; Marshall et al, 1996; Torgerson et al, 1996a). The strength of this relationship is comparable to that between blood pressure and stroke and is equivalent to an eight- to twelve-fold difference in fracture risk across the distribution of bone density in the population. Although measurement of bone density at any of the sites commonly assessed is predictive of fracture, measurement at the potential fracture site may provide the best prediction, particularly for hip fracture (Mazess et al,

1988; Cummings et al, 1993; Melton et al, 1993). Addition of certain risk factors to bone mineral density values may lead to better prediction of fracture; this is the case particularly for past or prevalent fragility fracture and, in the elderly, risk factors for falling. Measurements of hip axis length (an index of the length of the femoral neck) can also be generated by dual energy X-ray absorptiometers and improve prediction of hip fracture, since there is a positive and independent relationship between hip axis length and hip fracture risk (Faulkner et al, 1993; Peacock et al, 1995).

4.3.4 Densitometric criteria for the diagnosis of osteoporosis

The gradient of increasing fracture risk with decreasing bone mineral density is continuous and there is consequently no single cut-off point below which fracture will occur and above which it will not. Any diagnostic threshold of bone density is therefore to some extent arbitrary; nevertheless a bone density level can be selected which will identify most of those women who will sustain a fracture in the future and this forms the basis of the currently used World Health Organization classification (WHO Study Group, 1994), which is based on standard deviation scores expressed in relation to reference data in normal premenopausal women (T scores). The use of standard deviation units avoids problems associated with differences in calibration between instruments; T scores are used in preference to Z scores (age-related SD units) because of the increasing risk of osteoporotic fracture with age, which would not be captured by the use of Z scores.

According to the WHO classification, the following diagnostic categories can be defined:

- Normal — BMD T score greater than -1
- Osteopenia — BMD T score between -1 and -2.5
- Osteoporosis — BMD T score below -2.5
- Established osteoporosis — BMD T score below -2.5 + presence of fragility fracture(s)

These thresholds apply to measurements of bone density in the hip, spine and/or radius although the former two are most commonly used; they are appropriate only for women and corresponding criteria for men, in whom areal bone mineral density values are higher, have not yet been developed. Finally, it should be stressed that these are diagnostic rather than interventional thresholds although they may aid treatment decisions, particularly in the case of patients with osteoporosis or established osteoporosis.

4.3.5 Biochemical markers of bone turnover

Biochemical markers of bone turnover provide information about rates of bone resorption and bone formation (Eastell, 1996). Indices of bone resorption include urinary excretion of hydroxyproline, collagen cross-links (pyridinoline and deoxypyridinoline), hydroxylysine glycosides and N-telopeptides or C-telopeptides of type 1 collagen. The most commonly used markers of bone formation are serum concentrations of bone specific alkaline phosphatase and osteocalcin. Menopausal bone loss is accompanied by an increase both in markers of resorption and formation and similar changes are seen in high turnover osteoporosis, whilst anti-resorptive therapy results in decreased production of these markers (Uebelhart et al, 1991).

When used in combination with bone densitometry, biochemical markers may improve the assessment of fracture risk, particularly hip fracture (Garnero et al, 1996), although on their own they are poorly predictive of bone mineral density. Within individual patients the biological variability of these markers relative to changes in bone turnover induced by disease is

considerable and this makes the sensitivity and specificity of biochemical markers insufficiently high to be useful as a diagnostic tool in clinical practice at the present time. Further research is required to establish the value of biochemical markers in the management of the individual patient, particularly with respect to monitoring the effects of treatment.

4.4 Radiology

Conventional radiological techniques are used to detect the presence of fractures. Radiological osteopenia is an insensitive method of detecting osteoporosis, since reduction in bone mass of as much as 50% may be required before osteopenia can reliably be detected on radiographs.

Lateral radiographs of the thoracic and lumbar spine are used to detect vertebral deformity due to osteoporosis, which may be manifest as biconcavity (loss of middle height), wedging (loss of anterior or posterior height), and compression or crush fractures, in which there is loss of height throughout the vertebral body. Since the dimensions of vertebrae vary between and also within individuals, morphometric approaches have been developed to classify these deformities (Eastell et al, 1991; Black et al, 1995). Semiquantitative or quantitative assessment may be used, based on the ratios of anterior, middle and posterior vertebral heights. The current consensus is that a reduction of three standard deviations or more from the normal mean ratios for that particular vertebral level is a reasonable criterion for prevalent fracture (NOF Working Group on Vertebral Fractures 1995); in order to reduce the number of false positives, it has been suggested that a vertebral deformity should satisfy two or more morphometric criteria before a diagnosis of vertebral fracture is made (McCloskey et al, 1993). The best definition for incident vertebral fractures has not been established, but a 20% or greater reduction in any three of the measured vertebral heights (anterior, middle or posterior) is a relatively specific criterion. In assessing vertebral deformity on radiographs, the procedure used to obtain images is critical and should be carefully standardised.

4.5 Morphometric X-ray analysis (AM)

The latest generation of dual energy X-ray absorptiometers possess the potential to generate good quality lateral images of the thoracic and lumbar spine, upon which morphometric analysis can be performed. This approach has yet to be validated, particularly with respect to its reproducibility; if shown to be comparable to or better than conventional X-ray morphometric methods, MXA is likely to emerge as the technique of choice in view of its significantly lower radiation dose.

4.6 Clinical indications for bone densitometry

In general terms, preventive strategies may be targeted at everyone in the population or confined to high-risk subgroups. The consensus view among experts is that population-based screening of women at the menopause cannot be justified; in the absence of such an approach, selection of patients for bone densitometry on the basis of strong clinical risk factors provides the most rational approach to the prevention and treatment of osteoporosis (Compston et al, 1995). Clinical indications for bone densitometry are shown in Table 4.3. It should be emphasised that bone densitometry is only justified in those individuals in whom the result obtained will influence treatment decisions.

Diagnostic uses of bone densitometry may be divided into two categories, namely to assess fracture risk and to confirm or refute a diagnosis of osteoporosis in individuals with vertebral deformity, previous fragility fracture, radiological osteopenia or height loss. In the former group, if bone density is judged to be insufficiently low to warrant treatment, repeated measurements may be unless the underlying disease has been successfully treated. In patients with multiple vertebral deformities and in elderly patients with hip fracture, bone densitometry is not usually required for diagnostic purposes. In the elderly, the hip is the most useful site for bone mineral density assessment because of the unreliability of spinal measurements in this age group.

Bone density measurements are also used to monitor the effects of treatment on bone mass. The ability of repeated measurements to detect significant changes in individual patients depends on the precision of the measurement technique, the effects of treatment and the expected rate of bone loss in the absence of treatment. Significant treatment effects in the spine can often be detected within two years but three or more years may be required to detect such effects in the proximal femur. In many patients, assessment of bone density is the only means by which the effects of treatment can be judged and repeat measurements are likely to improve compliance. Repeat bone mineral density measurements to monitor treatment are rarely indicated at less than one year intervals.

Assessment of bone density is also useful in aiding decisions about when treatment may be stopped and whether, subsequently, further intervention is required. The same absorptiometry system should be used whenever possible in order to minimise errors due to different machine calibration. It should be noted that the value of broadband ultrasound velocity and attenuation measurements in monitoring the response to treatment has not been validated and that although there is evidence that these measurements can be used to predict fracture risk in elderly women, their predictive value in younger women and their ability to monitor the effects of therapy remain to be established (Glüer, 1997).

Table 4.1: Clinical and historical risk factors for osteoporosis

Endogenous	**Exogenous**
Female gender	Premature menopause
Age	Primary or secondary amenorrhoea
Slight body build	Primary or secondary hypogonadism in man
Asian or Caucasian race	Previous fragility fracture
	Glucocorticoid therapy
	Maternal history of hip fracture
	Low body weight
	Cigarette smoking
	Excessive alcohol consumption
	Prolonged immobilisation
	Low dietary calcium intake
	Vitamin D deficiency

Table 4.2: Methods for the assessment of bone mass

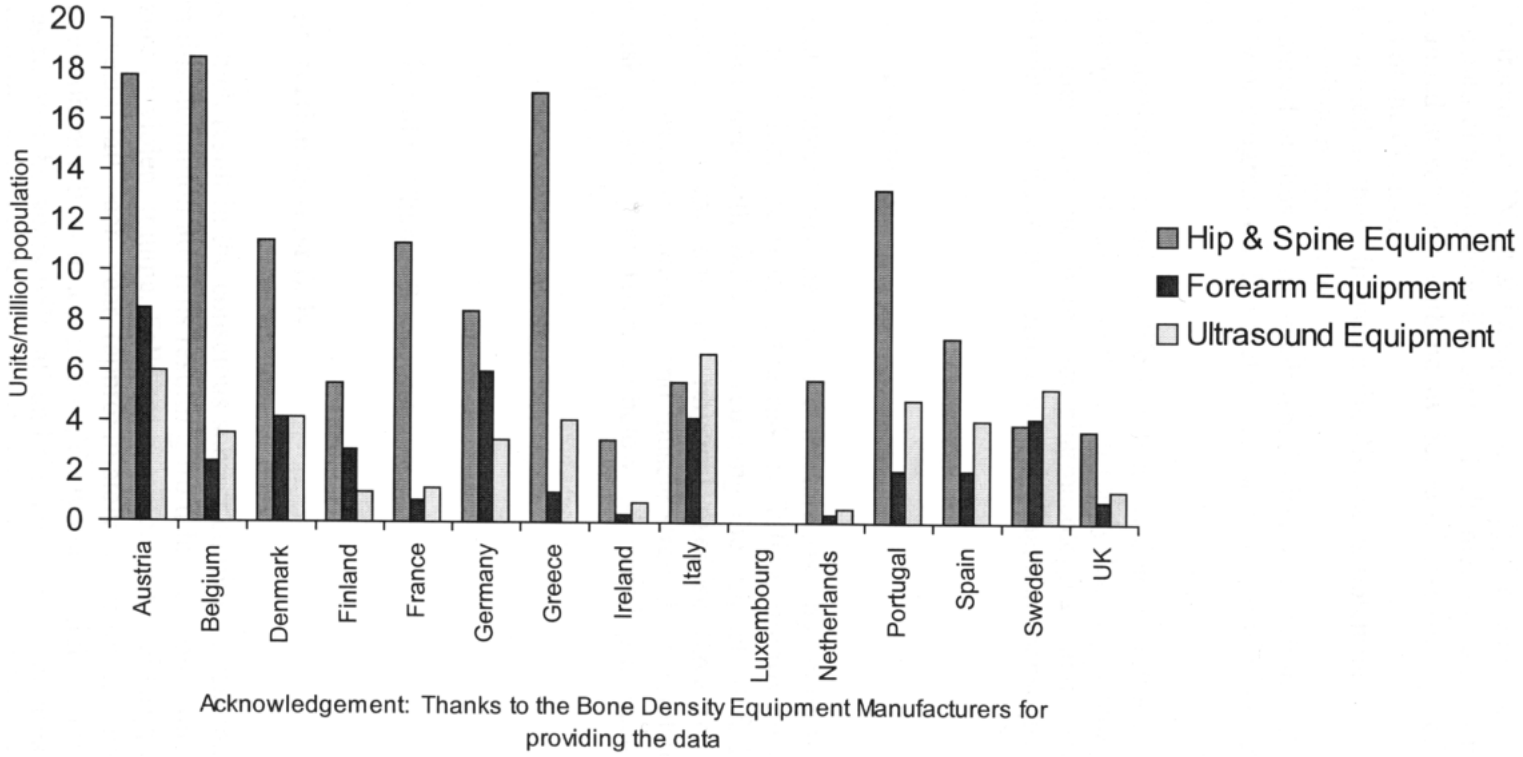
Method	**Skeletal sites**	**Precision (%)**	**EDE (µSv)**
Dual energy X-ray absorptiometry (DXA)	Spine	1	1-3
	Proximal femur	2-3	1
	Total body	1	3
Single energy X-ray absorptiometry (SXA)	Radius	1-2	<1
Single photon absorptiometry (SPA)	Radius	1-2	<1
Quantitative computed tomography (QCT)	Spine: *Single energy*	2-4%	50
	Double energy	4-6%	100
Peripheral QCT (pQCT)	Radius	0.5-1.0	<1
Broadband ultrasound attenuation (BUA)	Os calcis	1-6%	0
	Tibia		
	Patella		

EDE = effective dose equivalent
For comparison: effective dose equivalent of an X-ray of the lumbar spine is 550 µSv and the annual natural background exposure is 2400 µSv

Table 4.3: Clinical indications for bone densitometry

- Presence of strong risk factors
  - Premature menopause (<45 years)
  - Prolonged secondary amenorrhoea
  - Primary hypogonadism
  - Glucocorticoid therapy (>7.5 mg/day oral prednisolone or equivalent for six months or more)
  - Anorexia nervosa
  - Inflammatory bowel disease/malabsorption
  - Primary hyperparathyroidism
  - Organ transplantation
  - Chronic renal failure
  - Chronic liver disease
  - Hyperthyroidism
  - Prolonged immobilization
  - Maternal history of hip fracture
  - Long-term heparin therapy
- Radiological evidence of osteopenia and/or vertebral deformity
- Previous fragility fracture
- Height loss
- Monitoring of therapy

Figure 4.1: An estimate of Bone Densitometry Equipment (units/million population) in the European Union as of mid 1997



Acknowledgement: Thanks to the Bone Density Equipment Manufacturers for providing the data

5. PREVENTION OF OSTEOPOROTIC FRACTURES

The primary aim of any anti-osteoporotic intervention is the prevention of fractures in patients who have not yet fractured or the prevention of progression of the disease in patients who have already sustained a fragility fracture (O'Neill & Papapoulos, 1997). Prevention can be considered according to the stage in the natural history of a disease at which intervention is implemented:

- **Primary** prevention is aimed at subjects with no evidence of disease, by reducing the risk factors for and/or causes of the disease.
- **Secondary** prevention is aimed at those in whom the disease is potentially reversible and in whom intervention may reduce progression.
- **Tertiary** prevention is aimed at those with established disease in whom intervention may limit associated disability or progression. In practice, tertiary prevention is synonymous with treatment of the disease.

Preventive strategies can be applied throughout life but firm evidence supporting anti-fracture efficacy of some of the approaches discussed below is currently lacking. Management of the patient with osteoporosis may include both non-pharmacological and pharmacological interventions; in the following sections the efficacy and financial consequences of such approaches are discussed.

5.1 Non-pharmacological interventions

Several non-pharmacological interventions may reduce fracture risk by increasing peak bone mass, reducing age-related bone loss, decreasing the risk of falling, improving the protective neuromuscular responses associated with falling or reducing the impact of falls. Nutritional factors, particularly vitamin D and calcium, and physical exercise have multiple effects, influencing peak bone mass, age-related bone loss and muscle strength; a number of measures can be taken to reduce the risk of falling, as described below, whereas hip protectors reduce the risk of hip fractures occurring after a fall.

5.1.1 Nutritional factors

These have been described in detail in Chapter 3.

5.1.2 Prevention of and protection against falls

Falls are defined as events which result in the conscious subject coming to rest inadvertently on the ground. Excluded from this definition are falls resulting from loss of consciousness, onset of paralysis, an epileptic seizure or violent trauma. Falls are common in the elderly; about 30% of individuals older than 65 years fall each year (approximately 17 million Europeans). The incidence of falls increases exponentially with age in the elderly and is higher in women than in men. 50% of individuals aged over 80 years will fall and the incidence increases three-fold in residents of long-term care institutions for the elderly (Lauritzen, 1997). The consequences of falls are increased mortality, injuries, fractures, hospitalisation, permanent disability, psychological problems and social isolation, all of which also increase with age, probably as a result of a concurrent increase in disease-related intrinsic risk factors (Tinetti et al, 1986). The

lack of any consistent method of documenting falls which do not result in physical injury makes it impossible to obtain an exact estimate of their burden to society.

Most hip and wrist fractures are due to falls. Although only 6% of falls result in fracture and approximately 1% in a hip fracture, the absolute number of fractures resulting from falls is high. Prevention of falls is therefore an important potential strategy in the reduction of fracture risk, particularly in the hip. Nonetheless, although risk factors for falling have been shown to be important independent risk factors for hip fracture in the elderly (Cummings et al, 1995), at present there is no convincing evidence that interventions aimed at reducing the risk of falls decrease the risk of hip fractures.

5.1.2.1 Risk factors for falls

Several population studies (Prudham and Evans, 1981; Tinetti et al, 1988; Campbell et al, 1990; van Weel et al, 1995) have shown that most falls occur in elderly single women and that the most important predictive factor is previous falls. Contributing factors include increased sway caused by defective proprioception, impaired vision, diminished physical activity and fitness, reduced walking speed, shorter steps and other gait abnormalities, malformed feet, inappropriate footwear, chronic diseases, and use of medications (including alcohol). The greater the number of disabilities the greater the risk of falling. Thus in one study (Graafmans et al, 1996), a risk factor profile was constructed which included immobility, history of stroke, poor mental state, dizziness on standing and orthostatic hypotension; the presence of all these risk factors was associated with an 84% probability of recurrent falls over a 28 week period.

5.1.2.2 Aetiology of falls

- Balance

Falls occur when a person undertakes an activity which requires correction of an unexpected displacement and lacks the capacity to correct the displacement in the available time. Balance, which is critical in avoiding falls, depends on the correct function of several systems which may be influenced by age-related changes or disease. Balance in an upright position is maintained by sensory information about orientation in space, central processing of information from these peripheral structures and performance of the musculoskeletal system (Alexander, 1994).

Adequate vision is particularly important for balance in the elderly. Ageing is often associated with impaired visual acuity, increased susceptibility to dazzling and faulty perception of depth; fall victims tend to make mistakes in establishing true vertical and horizontal positions. Vision may further decline as a result of disease, for example cataract, glaucoma or macular degeneration. Regular visual assessment and, where necessary, correction of visual defects is therefore recommended in the elderly. Defects in vestibular function should also be treated where possible. A walking stick may be helpful in subjects with impaired proprioception and attention should be paid to appropriate footwear. Gait and balance training may also be helpful (Hopkins et al, 1990; Hu & Wollacott, 1994).

A number of disorders are associated with increased risk of falling through their effects on balance. These include cardiac arrhythmias, cerebrovascular disease, dementia, Parkinson's disease and cerebellar disorders. Postural hypotension, resulting either from disease or drugs, also increases the risk of falls. Low muscle mass both increases the risk of falling and reduces the effectiveness of the associated protective response. Improvements in physical fitness, agility and

speed of response through exercise programmes should be encouraged; dance may be particularly useful in this respect (Crilly et al, 1989; Hopkins et al, 1990; Sauvage et al, 1992; McMurdo et al, 1993; Mills 1994; Nelson et al, 1994; McMurdo et al, 1995; Skelton et al, 1995).

- Psychosocial factors

Factors relating psychosocial condition and lifestyle to falls have not been studied in detail. 35% of elderly people with no history of falls and 50% of those who have fallen in the past are afraid of falling. Fear of falling may reduce daily activities and thereby increase the risk of falls and lead to social isolation. Predisposing factors are previous falls, especially when ability to rise unassisted from the floor is compromised. Fear may further decrease the autonomy of the elderly and may lead to institutionalisation (Arfken et al, 1994).

- Drugs and alcohol

Drugs are the most important modifiable risk factor for falls (Ryynänen, 1994). According to some reports any drug treatment may lead to a cumulative increase in the risk of falling; the higher the number of drugs, the greater the risk. These relationships are affected by the diseases for which the drugs are prescribed, which may also be independent risk factors for falling. Many of the drugs commonly used by elderly people have side-effects which predispose to falls. These include drugs prescribed for cardiovascular diseases which may induce muscular weakness and postural hypotension, anti-inflammatory drugs and analgesics with central nervous system side-effects and sedatives. Long-acting sedatives are the only drugs proven to increase the risk of fractures.

Drug consumption increases with age and is greater in women than men. People aged more than 65 years comprise 15% of the population but consume half of prescription medications. Among the elderly, two-thirds take at least one drug every day, the average being two. In nursing homes almost all residents are on medications, on average 4-5 per day, although in some nursing homes a real effort has been made to reduce them (Cummings et al, 1991). Regular adjustment and, where possible, reduction of medications should therefore be strongly recommended.

Alcohol abuse can lead to falls at all ages. In old people, the risk of falling may be increased by interaction of alcohol and other risk factors, especially medications. Although alcohol intake is generally lower in elderly than in younger people, other risk factors present in the elderly may augment the effects of alcohol including interaction with medications. It should be noted that alcohol may be the cause of frequent or otherwise unexplained falls.

5.1.2.3 Environmental factors

The indoor environment is of particular importance for the many elderly confined to their homes. However, no specific risk factors have been identified in the homes of patients who fall as opposed to those of non-fallers. (Clemson et al, 1996). Several campaigns have been designed to inform the public about environmental risk factors, although even if these factors are reduced, falls will still occur because intrinsic risk factors are predominant in old age. The environment in institutions is very dangerous for potential fallers and there is a high fracture incidence; specific risk factors include a long distance from bed or chair to toilets, physical restraints like bed rails and unstable side tables.

Improvement of town planning, traffic conditions and the accessibility of public transport is helpful for everyone with a handicap, including the elderly. For example, older people have difficulty crossing streets as traffic lights do not generally provide sufficient time for slowmoving people to cross and uneven paving stones increase the likelihood of falls. Attention, therefore, should be paid to these and other environmental factors known to increase the risk of falls (Lilley et al, 1995).

5.1.2.4 Management of fallers

- Assessment of individual cases

Medical history and physical examination should focus on specific issues related to falls as discussed above. Balance and ability to function during daily activities should be assessed. Sway testing is important but needs further evaluation in clinical practice. Results from the Nordic Research on Ageing Studies in Jyväskylä, Finland, Göteborg, Sweden and Glostrup, Denmark showed that sway is closely related to vision, vibration and muscle strength and predicts falls (Era et al, 1997). Many authorities recommend the establishment of fall clinics within geriatric departments (Rubenstein et al, 1990; Tinetti et al, 1994).

- Rehabilitation

As a history of falling is the most important single predictor of future falls, comprehensive assessment of underlying causal factors should be undertaken. Falls are multifactorial and some of the medical conditions causing them may be correctable. Balance training has been shown to be effective in the elderly in controlled trials. Special techniques are necessary to improve muscle strength, vestibular function and central adaptation. Apart from these specific measures, fall rehabilitation follows the principles of geriatric rehabilitation and most fallers improve with treatment of medical conditions which cause weakness, pain and anxiety. It is important to promote early restoration of balance and mobility, particularly in older patients who have been confined to a bed or chair. The patient should practice functional exercises such as transferring from chairs and toilets, walking on all types of surfaces and climbing stairs. Ideally, rehabilitation of fall patients should be available in the primary sector (Tinetti et al, 1994; Wagner et al, 1994; Hornbrook et al, 1995; Province et al, 1995; Nyberg et al, 1996).

- Hip protectors

Any bone will break if the force is strong enough, but reducing the impact of the force may prevent fracture. Experiments have shown that energy absorption in soft tissues over the hip may be reduced up to 75% during a fall; this may partially explain the reduced risk of hip fracture in obese subjects. On average, women having a hip fracture weigh 5 kg less and have 30% less fat over the hip than age/height/weight-matched controls. In addition, men in nursing homes have an increased risk of hip fracture (30%) compared to women (25%), because of the greater amount of fat over the hip in women.

Hip protectors have been developed to attenuate the impact force sustained by a fall on the hip; these act by absorbing the impact energy and/or shunting the energy away from the trochanter into the surrounding tissues. In a randomised controlled study of elderly residents of nursing homes, Lauritzen et al (1993) reported a 53% reduction in hip fractures in the group assigned to wear external hip protectors. More recent studies tend to confirm these findings, but compliance is generally poor and requires encouragement (Ekman et al, 1997). The development of new

designs may increase compliance (Lauritzen et al, 1993; Heikinheimo et al, 1996; Lauritzen, 1997).

- Other measures

An alarm carried by an individual cannot prevent a fall, but ensures quick assistance and provides confidence. Some preventive home visits have focused on falls and structured home visits have been evaluated in several clinical trials (Hendriksen et al, 1984; Carpenter & Demopoulos, 1990; Vetter et al, 1992). Outcomes influenced were, among others, hospital admissions, bed days and emergency calls. Interviews help to discover problem areas and to make decisions about actions and follow-up. A few community-based trials have shown an effect on fractures (Ytterstad, 1996).

General recommendations for preventing falls and avoiding environmental hazards are listed in Table 5.1

5.1.3 Exercise

Exercise transmits loads to the skeleton by at least two mechanisms: direct impact from weight-bearing exercise and muscle contraction. Complete immobilisation is associated with loss of up to 40% of total bone mass whereas weight-bearing exercise results in site-specific increases in bone mass. However, in contrast to the magnitude of the skeletal effects of immobilisation, the amount of bone that can be gained by increasing the level of exercise in active individuals is very small. (Snow et al, 1996; Marcus, 1996). High levels of activity before and during puberty have a larger impact on bone mass than when activity starts at adulthood (Kannus et al, 1995) and several studies have demonstrated a positive correlation between weight-bearing physical activity in childhood and adolescence and bone mass; in one of these (Welten et al, 1994), the effect of exercise on peak bone mass was considerably greater than that of calcium intake. There is some evidence that the effects of calcium and exercise on peak bone mass are additive (Kanders et al, 1988). It should also be noted that vigorous exercise programmes in premenopausal women may have adverse effects on bone mass as they may induce gonadal insufficiency.

Cross-sectional studies have demonstrated positive correlations between past and/or present levels of physical activity and bone mineral density in postmenopausal women (Gauthier et al, 1992; Recker et al, 1992; Eickhoff et al, 1993). In two large population-based European surveys (MEDOS and EPOS) of the occurence of osteoporotic fractures, it was reported that regular walking in middle-aged and elderly women was associated with reduced risk of vertebral and hip fractures (Kanis et al, 1992; Silman et al, 1995). However, cross-sectional studies may be biased by a number of confounding factors and prospective data are necessary to demonstrate definitively the effects of physical activity on bone mineral density.

5.1.3.1 Effects of exercise on postmenopausal bone loss

In a recent meta-analysis of 18 prospective intervention studies of the effects of exercise on bone loss in postmenopausal women (Bérard et al, 1997), a significant effect of moderately intense physical activity was detected on lumbar spine bone mineral density, but no consistent effect was seen on femoral neck or forearm bone mass. Exercise programmes in these studies consisted of running, walking, physical conditioning and aerobics. Increases of between 2.5 and 5% in spinal bone mineral density have been reported in sedentary postmenopausal women after 7 to 9 months of an exercise programme involving training at 70-90% of maximum oxygen uptake for 2-3

hours per week (Hatori et al, 1993; Dalsky et al, 1997), although there was no additional benefit up to 22 months and all the gain was lost in those who left the programme. As in young adults, there is some evidence that calcium and exercise have additive effects on bone mass in postmenopausal women (Prince et al, 1995). Overall, the gains from vigorous exercise compared to everyday activities are probably small and must be maintained to preserve any effect.

5.1.3.2 Effects of exercise in the elderly

In the elderly, in whom bone loss is often advanced and different degrees of immobilisation are due to sedentary habits or associated disease, vigorous physical activity is contraindicated. However, exercise programmes based on balance, strength training and low impact aerobics may be beneficial and there is evidence from randomised controlled studies that such regimens reduce the risk of falls (Sowden et al, 1996). Walking and stair-climbing can be beneficial and swimming, daily activities, social dancing and group exercises should be encouraged. The principal benefit from an exercise programme is increased muscle strength and endurance. Motivation for long-term compliance is essential for the success of such programmes. The social aspects of exercising in groups can be an effective way to encourage elderly women to participate. A recent meta-analysis of trials of exercise interventions in community-based subjects suggested that it is possible to increase and maintain levels of activity, particularly if the exercise is of moderate intensity and enjoyable, and to reduce falls by 10% (Province et al, 1995).

5.1.3.3 Conclusions

Weight-bearing physical activity during childhood and adolescence is positively related to peak bone mass. The effects of exercise intervention regimens on bone mass are modest in postmenopausal women and appear to be limited to the spine. Adherence to exercise programmes requires motivation; furthermore, the gains in bone mass are not progressive and are likely to persist only for the duration of the exercise. There is no convincing evidence that exercise can prevent bone loss at the menopause or osteoporotic fractures later in life. On the other hand, exercise may have a significant effect in the prevention of falls which present a major risk factor for fractures. Because of the importance of falls in the pathogenesis of osteoporotic fractures, physical activity in the elderly is likely to have a greater impact on osteoporosis through its effect on falls rather than on bone mineral density. In addition, planned exercise regimens are important for the rehabilitation of individuals with established osteoporosis.

5.2 Pharmacological interventions

5.2.1 Trial design and end-points.

When assessing the efficacy of interventions in the prevention of osteoporotic fractures, certain issues need to be considered. Methodologically, the best approach is the prospective, randomised, controlled trial (RCT). Randomisation ensures that potential confounders are distributed evenly between treatment and control groups and reduces the risk of bias in treatment allocation. Blinding the subject and the investigator to the intervention reduces the chance of bias in the assessment of the outcome. If properly conducted, differences in outcome between groups can be more confidently attributed to the effect of the intervention. Because of its advantage over

other types of study evidence (e.g. cross-sectional, case-cohort studies), the RCT is a prerequisite for the approval of new drugs for the treatment of osteoporosis by regulatory authorities.

Clinical trials should include adequate numbers of patients to allow statistically valid and clinically relevant conclusions and should be planned for periods sufficient to detect differences between the test and the treatment groups. These requirements are particularly relevant if the incidence of fractures is expected to be low (for example, a higher incidence of fractures is anticipated in patients with low bone mass and prevalent fractures than in patients with low bone mass and no prevalent fragility fractures). In addition, the natural history of fractures should be taken into account; vertebral fractures, for example, usually occur in cycles. A study period of three years is generally considered sufficient for the detection of differences in incident fractures and is usually required by regulatory agencies for the approval of anti-osteoporotic drugs. Hip fractures are events which can be easily registered because patients are admitted to hospital. This is not, however, the case with vertebral fractures, about two-thirds of which do not come to clinical attention. Documentation of vertebral fractures in RCT's should therefore be performed blind by an objective and precise method on serial X-rays of the spine. Several objective methods for assessing vertebral morphology are used, but it should be noted that there is currently no gold standard for defining a vertebral fracture and some morphometric methods may overestimate vertebral deformities. Deformities of previously normal vertebrae occurring during the trial rather than progression of pre-existing vertebral deformities should be counted as new events. Finally, the number of patients with new vertebral fractures and not the number of new fractures should be analysed.

5.2.2 Pharmacological agents used in the treatment of osteoporosis.

Current pharmacological interventions for prevention of fractures in patients with osteoporosis aim mainly at reducing bone resorption and bone turnover or stimulating bone formation (Table 5.1). The majority of available data have been obtained with inhibitors of bone turnover. Although beneficial effects of the agents listed in Table 5.2 on bone turnover and/or bone mineral density in postmenopausal women with or without prevalent fractures have been repeatedly shown, there are relatively few randomised controlled studies of their anti-fracture efficacy. In the following paragraphs, clinical trials reporting the effects on fracture incidence of treatment with a pharmacological agent are summarised. It should be emphasised that not all of these trials were adequately powered to detect differences in fracture rates between the control and treatment groups and the strength of evidence for anti-fracture efficacy of the different agents varies markedly. All patients undergoing treatment should be calcium and vitamin D replete, but there is no evidence that combinations of therapies have greater anti-fracture efficacy than single agents. Finally, these studies were performed mainly in women with postmenopausal osteoporosis and their results should not be extrapolated to males or to patients with other forms of osteoporosis.

5.2.2.1 Primary/secondary prevention

- Calcium and vitamin D

Of the various pharmacological interventions the efficacy of calcium, vitamin D and oestrogens in preventing fractures has been examined prospectively under RCT conditions in populations at risk, but not selected by any screening procedure. Chapuy et al (1992,1994) studied over 3,000 institutionalised elderly women (mean age 84 years) during treatment with either vitamin D (cholecalciferol) 800 IU/d (20 µg) and calcium 1.2 gr/d or placebo for three years. Active

treatment significantly reduced the incidence of new hip fractures by 29% and that of all non-vertebral fractures by 24%. In another study with a comparable number of participants, women and men slightly younger (mean age 80 years) but mostly living independently and with a higher calcium intake were given either cholecalciferol 400 IU/d (10 µg) or placebo for a maximum of 3.5 years (Lips et al, 1996). There was no difference in the incidence of hip or other peripheral fractures between the two groups. Apart from the difference in the therapeutic regimens between the two studies, the French cohort had a higher prevalence of vitamin D deficiency/insufficiency and showed a much greater suppression of plasma parathyroid hormone concentrations after treatment than the Dutch cohort. Of particular interest are the results of a recent placebo-controlled trial of the effect of calcium 500 mg/d and cholecalciferol 700 IU/d(17.5 µg) in healthy community-based men and women older than 65 years (Dawson-Hughes et al, 1997), with a mean dietary calcium intake of about 700 mg/d. After 3 years, 26/202 (12.9%) subjects treated with placebo and 11/187 (5.9%) of those treated with vitamin D and calcium had sustained non-vertebral fractures, a statistically significant difference. In a further study, not designed to assess fracture incidence, Reid et al (1993) reported that calcium supplements (1 gr/d) given to healthy postmenopausal women with a mean dietary intake of 700 mg/d, significantly reduced the number of symptomatic osteoporotic fractures compared to placebo after 4 years (2/38 women with fractures in the calcium group compared to 7/40 in the placebo group).

The combined results of these studies underline the need for adequate vitamin D and calcium nutrition in the elderly. They emphasise, in addition, the value of vitamin D and calcium supplements in populations at risk. particularly old frail individuals living indoors in nursing homes who have a high prevalence of vitamin D deficiency or insufficiency. In such cases, the native vitamin rather than its active metabolite or analogue should be administered. Finally, these and other recent studies demonstrate that it is never too late to consider pharmacological intervention in populations with a high fracture risk.

- Oestrogens

The effect of oestrogens (mestranol) or placebo on the prevention of vertebral fractures has been examined in oophorectomized women (Lindsay et al, 1980). After a median period of 9 years, women treated with oestrogens had a significantly better spine score (assessed morphometrically) and fewer crush fractures (l/58 (1.7%) versus 5/42 (11.9%) in women treated with oestrogens or placebo, respectively).

5.2.2.2 Tertiary prevention

Published clinical trials of tertiary prevention of osteoporotic fractures are summarised in Table 5.3.

- Oestrogens

Oestrogens reduce bone turnover and bone loss. Oestrogen receptors have been demonstrated on osteoblasts and on other cells in the bone microenvironment but their precise mechanism of action is not yet known. Numerous large observational studies have provided strong support for the anti-fracture effectiveness of oestrogens (Hutchinson et al, 1979; Weiss et al, 1980; Paganini-Hill et al, 1981; Ettinger et al, 1985; Kiel et al 1987, Grady et al, 1992; Cauley et al, 1995; Henry et al, 1995). However, data from RCT's in women with osteoporosis are scarce. In one such study, a small number of postmenopausal women with prevalent vertebral fractures were treated

with dermal patches of 17ß-oestradiol or placebo for one year (Lufkin et al, 1992). Active treatment significantly reduced the incidence of new vertebral fractures (8 in the oestrogen group vs 20 in the placebo group) but not the number of patients with new fractures, due probably to the small numbers. Despite its limited duration and the small number of patients, this study together with the observational data indicates that oestrogens are effective in the treatment of older women with osteoporosis. There are no RCTs of the effect of oestrogens in the prevention of hip fractures.

The optimal period of oestrogen treatment is not known and 5 to 10 years is usually recommended. Observational data indicate that anti-fracture efficacy is reduced or lost after discontinuation of treatment, suggesting that life-long treatment after the menopause may be required to maintain beneficial effects. Poor compliance with treatment is, however, a long-standing problem of oestrogen use; adverse effects include mastodynia, breakthrough bleeding, deep venous thrombosis, pulmonary embolism and a small increase in the incidence of breast cancer in women on long-term therapy. These should be weighed against its favourable effects on menopausal symptoms, bone loss, ischaemic heart disease and possibly also Alzheimer's disease. The increase in the incidence of endometrial cancer induced by unopposed oestrogen use is minimised with the concurrent use of progestagens; the latter do not affect the beneficial skeletal effects of unopposed oestrogens.

- Bisphosphonates

Bisphosphonates, synthetic stable analogues of natural pyrophosphate, suppress bone resorption and reduce bone turnover by a mechanism which has not yet been elucidated and may differ between bisphosphonates. Various bisphosphonates have been used in the treatment of patients with osteoporosis but RCT's with fracture prevention as end-point have been performed only with etidronate and alendronate. Etidronate is given intermittently (400 mg/d for 2 weeks followed by calcium 500 mg/d for 11 weeks and this regimen is then repeated) while alendronate is given continuously (10 mg/d). Two studies of similar design examined the anti-fracture efficacy of cyclical etidronate in postmenopausal women with prevalent vertebral fractures (Storm et al, 1990; Watts et al, 1990; Harris et al, 1993). Despite methodological problems in fracture assessment and limited statistical power of the trials, the combined results of these studies indicated that this form of treatment is effective in preventing new vertebral fractures in postmenopausal women with low bone mass and multiple prevalent vertebral fractures. There is no RCT evidence of the effect of etidronate given intermittently on hip fractures; a postmarketing survey suggested that it may reduce the incidence of non-vertebral fractures including those of the hip (van Staa et al, 1998). A recent clinical trial reported that cyclical etidronate therapy may reduce the risk of fractures in glucocorticoid-treated postmenopausal women (Adachi et al, 1997).

Alendronate is the most extensively studied pharmacological agent for the treatment of osteoporosis under RCT conditions. When given in different doses to osteoporotic women, 20% of whom had prevalent vertebral deformities, it reduced significantly the incidence of new vertebral deformities after 3 years (Liberman et al, 1995). Pooling of data for all doses used, which was pre-planned, was required to demonstrate this effect. The overall anti-fracture effectiveness of alendronate was supported by a meta-analysis of five RCT's (Karpf et al, 1997). Its efficacy, however, was demonstrated in a study designed specifically to address this issue [Fracture Intervention Trial (Black et al, 1996)]. In this study women (mean age 71 years) with at least one vertebral fracture and femoral neck BMD of less than 2 SD of peak bone mass were randomised to receive alendronate 5 mg/d or placebo. The dose of alendronate was increased to 10 mg/d after the second year, as in parallel trials this dose was shown to induce optimal effects on bone mass. New vertebral fractures occurred in 145/965 (15%) women in the placebo group

and in 78/981 (8%) in the alendronate group. Active treatment also significantly reduced the risk of multiple vertebral fractures, clinical vertebral fractures and wrist fractures. Moreover, this was the first study to demonstrate a significant reduction in the incidence of new hip fractures (by 50%) in calcium and vitamin D-replete osteoporotic women under RCT conditions.

Bisphosphonates are poorly absorbed by the intestine and their absorption is further reduced by food, especially if it contains calcium. They should, therefore, be administered in the fasting state half to one hour before a meal, only with water. High doses of etidronate can induce osteomalacia. With the regimen used in osteoporosis no clinically significant osteomalacia was reported in two studies (Ott et al, 1994; Storm et al, 1993), although there are anecdotal reports of histologically confirmed osteomalacia with cyclic intermittent etidronate therapy (Thomas et al, 1995; Wimalawansa, 1995). Alendronate can cause irritation of the oesophageal and gastric mucosa, resulting in dyspepsia, heartburn, nausea or vomiting. Although in clinical trials no differences in adverse effects between placebo and alendronate treated patients were observed, a few cases of severe oesophagitis have been reported (De Groen et al, 1996). Its administration in patients with oesophageal pathology (e.g. achalasia) is contraindicated. Instructions for its use should be carefully followed.

- Calcium

Calcium decreases bone turnover by suppressing parathyroid hormone secretion and reducing the rate of bone loss in osteoporotic patients. In epidemiological studies calcium treatment has been reported to reduce the risk of hip fractures (Kanis et al, 1992). In a recently reported RCT, women with a mean age of 73.6 years and a low dietary calcium intake (mean 431 mg/d) were randomly treated with calcium (600 mg twice daily) or placebo (Recker et al, 1996). After 4.3 years 28.4% of the women in the calcium group and 32.3% of those in the placebo group had new vertebral deformities (non-significant difference). When, however, the women were divided according to the presence or absence of prevalent fractures at the beginning of the study, of those with prevalent fractures 15/53 (28.3%) in the calcium group compared to 21/41 (51.2%) in the placebo group developed new fractures ($p=0.023$). Despite a number of methodological problems, this study indicates that relatively high doses of calcium supplements given to calcium-deficient, elderly women with vertebral fractures may reduce the incidence of new fractures. These data complement the results of the previously mentioned studies of calcium and vitamin D administration for the secondary prevention of osteoporosis.
Calcium is a very safe treatment with very few side effects. Some patients may experience gastrointestinal discomfort or constipation. Its use in patients with concurrent disorders of calcium metabolism should be carefully considered.

- Calcitonin

Calcitonin, a polypeptide hormone produced by the C-cells of the thyroid gland, reduces bone resorption by inhibiting the activity of osteoclasts, which contain receptors for the hormone. Calcitonin, given either parenterally or by nasal spray, has been used extensively in different parts of the world for the treatment of osteoporosis. Epidemiological data suggest that it may reduce the risk of hip fractures (Kanis et al, 1992). The anti-fracture efficacy of the intranasal preparation, which is generally the most convenient for the patient, has been examined in one RCT (Overgaard et al, 1992). In this study postmenopausal women (mean age 70 years) with BMC of the forearm less than 2 SD of the mean of healthy premenopausal women, were treated with placebo or three different doses of intranasal salmon calcitonin (50, 100 or 200 IU/d) for two years. The number of prevalent vertebral deformities was low. Of the patients who completed the study, 7 of the 40 in the placebo group (17.5%) vs 5 of the 124 treated with calcitonin (4%) developed new vertebral deformities after 2 years ($p=0.006$). Because of the

small number of patients and the low incidence of fractures, results for all active treatment groups had to be pooled. There is no information from RCTs about the efficacy of calcitonin in the prevention of hip fractures and no recommendations can be made about the optimal dose of intranasal calcitonin in the treatment of postmenopausal osteoporosis. Recently, however, a report published in abstract form (Stock et al, 1997) suggested that intranasal calcitonin 200 IU/d, but not 100 IU/d or 400 IU/d, given with calcium 1000 mg/d and vitamin D 400 IU/d (10 µg) can decrease the incidence of new vertebral fractures in postmenopausal women with prevalent vertebral fractures (19.8% of patients in the placebo group versus 12.2% of patients in the calcitonin group with new vertebral fractures).

Parenteral calcitonin may induce flushing, nausea, vomiting and diarrhoea. Intranasal calcitonin has fewer side-effects. Resistance to the effect of calcitonin may develop in some patients treated with injectable or intranasal preparations. Calcitonin has also been reported to have an analgesic effect in patients with a recent vertebral fracture. During treatment with calcitonin, calcium supplements are recommended to prevent development of secondary hyperparathyroidism.

- Vitamin D metabolites.

Calcitriol is the active metabolite of vitamin D while alfacalcidol is a calcitriol analogue which requires 25-hydroxylation in the body to be activated. These metabolites increase intestinal calcium absorption and promote mineralisation of bone. Their action in osteoporosis is uncertain but probably involves an anti-resorptive element due to the suppression of parathyroid hormone secretion. Reports of the anti-fracture efficacy of these metabolites have been conflicting and mainly confined to small studies (Ott and Chesnut, 1989; Gallagher et al, 1990). Alfacalcidol appears to be effective in Japanese patients, in whom calcium deficiency is prevalent. In a large, randomised, but not placebo-controlled study, postmenopausal women (mean age 63.7 years) with at least one vertebral fracture were given calcitriol 0.5 µg/d or calcium 1 gr/d for 3 years (Tilyard et al, 1992). In the calcitriol group 40/262 (15%) of patients had new vertebral fractures compared to 91/253 (36%) in the calcium group. The difference between the two groups was significant at the end of the second and third years of treatment. Treatment was mainly effective in patients with milder osteoporosis. The intriguing finding in this study was that significance was attained not by a reduction in the rate of new fractures in calcitriol-treated patients but rather by a progressive increase in the incidence of new fractures in calcium-treated patients. Taken together, these data do not allow any firm conclusions to be drawn about the anti-fracture efficacy of synthetic metabolites or analogues of vitamin D.

Active vitamin D metabolites can induce hypercalciuria and in a few cases also hypercalcaemia, especially when given together with calcium supplements. Careful follow-up is mandatory.

- Fluoride

Fluoride is the only marketed agent which stimulates bone formation; it acts by enhancing the recruitment and differentiation of osteoblasts by an as yet unidentified mechanism. Its anti-fracture efficacy has been debated for many years. Two placebo-controlled trials with sodium fluoride failed to detect any difference in the incidence of new fractures in osteoporotic women with prevalent vertebral fractures after 4 years (Riggs et al, 1990; Kleerekoper et al, 1991). In the first study there was even a significant increase in non-vertebral fractures, including incomplete fractures, in the group which received active treatment. This has been attributed to the high dose of sodium fluoride used which may adversely affect bone quality. In a recent European study in which a lower dose of sodium fluoride was given as monofluorophosphate, no difference was shown in the incidence of new vertebral fractures between placebo and fluoride treated groups after 2 years (Meunier, 1996). Only one published study, in which a slow-release preparation of

sodium fluoride was given for 12 months every 14 months, reported a significant reduction in new vertebral fractures in fluoride treated patients (7/48 patients or 14.6% with fractures in the fluoride group vs 22/51 or 43.1% in the placebo group) (Pak et al, 1995).

Overall therefore, the evidence currently available from RCT's does not suggest significant benefits of fluoride salts on vertebral fracture rate in osteoporotic women. The findings of the trial with the slow-release sodium fluoride are interesting but require confirmation. Until then, fluoride salts should only be used under controlled conditions by physicians with expertise in the treatment of osteoporosis.

Sodium fluoride can cause gastric irritation, in a few cases associated with bleeding. Fluoride treatment may cause stress fractures of the lower extremities (lower extremity pain syndrome). About 20% of patients do not respond to treatment, for unknown reasons. Fluoride salts should always be administered with calcium and vitamin D.

5.3 The economics of osteoporosis prevention

As well as being a major source of morbidity fractures due to osteoporosis, particularly hip fractures, are costly in financial terms to society (Cooper, 1993; Barlow, 1994). The problem of osteoporosis is particularly acute for Northern European countries (Johnell et al, 1997). Until recently it was generally assumed that the only method of preventing osteoporotic fracture was through the use of hormone replacement therapy (HRT) at or soon after the menopause (Torgerson et al, 1997). Indeed, most economic evaluations of osteoporosis prevention concentrate on postmenopausal HRT use (Torgerson and Reid, 1997). However, recent evidence suggests that for HRT to be effective it must probably be taken life-long after the menopause, which is not only relatively expensive but also unacceptable for many women and inappropriate for men. Furthermore, such a strategy, no matter how successful, will not prevent significant numbers of fractures until 25-30 years after the start of therapy. This is a particular problem, economically, as the net benefits of any preventive strategy are discounted over a long period of time so that their present value, relative to costs, is small (Torgerson & Raftery, 1997).

An increasing number of non-HRT alternatives are now available for fracture prevention. In order to maximise health gain for any given level of resources, it is important to consider all the costs and benefits of these different interventions and develop cost effective treatment strategies. However, the cost effectiveness of different treatment strategies is likely to vary between different countries. This is due to a number of reasons. While the acquisition costs of the interventions will certainly vary between very similar European countries (for example, costs of bone drugs in Sweden are about 50% lower compared with Denmark) this is not as important as the relative differences between acquisition costs and other treatment costs. For example, let us assume a drug costs 10 ECU in countries A and B; however, in country A hip fracture treatment costs 10,000 ECU whilst in country B it is only 5,000 ECU. Hence, all other things being equal, it will be more cost effective to prevent fractures in country A relative to country B. The cost effectiveness of prevention will also be crucially affected by the differing incidence of the disease across Europe; thus it is likely to be more cost effective to prevent the disease in countries with the highest incidence compared with those with a lower incidence. Variations in medical practice between and within individual countries will also affect the cost effectiveness of prevention, for example the use of bone densitometry to monitor treatment.

5.3.1 Costs of osteoporosis

A key variable in preventing osteoporosis is averted costs. Quantifying averted costs can fulfil two functions. First, the total cost of a disease is the financial equivalent of quantifying the burden of disease in terms of mortality and morbidity. However, many health economists have questioned the value of cost of illness studies. Secondly, and probably more useful, is measuring the avoided cost of an individual fracture. Hence, in the first approach the total cost of osteoporotic fracture is the cost savings which would occur in the highly unlikely event that all osteoporotic fractures could be averted. In contrast, the avoided cost per individual fracture is more helpful in economic appraisal of different alternatives of fracture prevention.

5.3.2 Costs of prevention

There is a large cost variation with respect to the different methods of preventing hip fractures. Table 5.4 shows the approximate cost per patient of different interventions for the United Kingdom. Although the absolute acquisition costs of the different treatments will vary across European countries the relative costs of the treatment are probably similar in all countries. As the table shows the least expensive treatment is a single dose of vitamin D; however, this method of preventing fractures remains unproven (Gillespie et al, 1996). All the other methods of preventing fractures tend to be either relatively expensive, or, in the case of HRT and hip protector pads, will probably result in poor compliance if used in a relatively low risk population. Furthermore, the direct acquisition costs may not reflect the total costs of treatment as some interventions may require further follow-up. These follow-up costs could vary considerably between countries as variations among medical practitioners in terms of follow-up may be greater than differences in drug acquisition costs. In addition, the relative efficacies of different interventions need to be taken into account.

5.3.3 Relationship between prevention costs and risk

One of the main determinants of the cost effectiveness of preventing fracture is the untreated risk of fracture among patients who are offered therapy. In general, offering treatment to older people with a higher risk of fracture is likely to be more cost effective than offering treatment to younger patients. Similarly, offering treatment to people with strong risk factors for fracture is usually more cost effective than offering treatment to those at lower risk (Ankjaer-Jensen and Johnell, 1996; Torgerson et al, 1996b; Torgerson et al, 1997; Tosteson et al, 1990), unless treatment is very inexpensive with few or no undesirable side-effects. For instance, if vitamin D therapy were proven to reduce fractures, it would be worthwhile to offer it to all people at risk because it is so inexpensive. Table 5.5 shows a hypothetical scenario of two treatments for osteoporosis prevention: treatment cheap and treatment expensive. The calculations assume that for 1000 women 20 hip fractures would occur in the absence of treatment and both treatments reduce fractures by 30%. Furthermore, it is assumed that 50% of all hip fractures would occur among women in the highest 20% of risk. As the table shows, for the cheap treatment it is hardly worthwhile targeting treatment as even treating low risk women generates a modest cost per averted hip fracture. Furthermore, the calculations do not allow for any additional costs of targeting such as bone mineral density measurement which could easily mean that targeting becomes more expensive than treating all women (Kanis et al, 1997). However, for the more expensive treatment the incremental costs of treating lower risk women are substantial and may be considered too high for the benefit they produce.

5.3.4 Quality of life

Although cost effectiveness analysis can help to inform treatment priorities, particularly within a disease specialty, as an economic technique it is not particularly helpful in deciding spending priorities across different medical specialities or within the economy at large. A method of translating the health gain of avoiding fractures into a measure which can be used across different health care areas is to use cost utility analysis (CUA) (Drummond et al, 1997). In a CUA the myriad of health effects of preventing osteoporosis, which include the health gain by not having a fracture and the health loss of treatment side-effects, are converted into measures of utility. However, at present there are no suitable published quality of life weights which can be used in a CUA. Good economic evaluations of osteoporosis prevention are therefore required to establish suitable quality of life data on the effects of fracture and treatment effects.

5.3.5 Economic evaluations

Although a number of randomised trials have now been published of interventions for the prevention of osteoporotic fracture, none have included a contemporaneous economic evaluation; current economic data on osteoporosis prevention have come from modelling exercises which utilise estimates of resource use. Whilst economic modelling can usefully inform health policy and help to plan intervention studies (Torgerson et al, 1996c) it is preferable to use cost data generated in the context of randomised trials. Some items of resource use data will be subject to the same range of bias as effectiveness data, which only randomised trial methodology can adequately address.

At least 24 economic evaluations of strategies to prevent osteoporosis have been published, all of which are modelling studies. Twenty-one of these evaluations were reviewed recently (Torgerson and Reid, 1997) and another three have been published since this review (Ankjaer-Jensen and Johnell, 1996; Norlund, 1996; Visentin et al, 1997). Broadly, the conclusions of these studies are that the cost effectiveness of intervention with HRT at or around the menopause is highly dependent on putative cardiovascular benefits and effects on breast cancer risk. Modest changes in the assumptions of each of these parameters can dramatically alter the results. Given high cardiovascular benefits and modest effects on breast cancer risk then, despite osteoporosis screening reducing the cost effectiveness ratios, it is probably worthwhile to offer HRT to all perimenopausal women. However, more significant effects on breast cancer risk and smaller cardiovascular benefits would argue for the use of bone mineral density measurements to target perimenopausal women for treatment, particularly since the risk of breast cancer varies inversely with bone mineral density (Cauley et al, 1996; Zhang et al, 1997). For non HRT therapies the consensus among the published economic evaluations is that intervention should take place sometime after the menopause, say in the seventh or eighth decade of life. This allows the benefits of prevention (i.e. averted fractures) to be closer in time to the costs of prevention. Thus, the benefits are not as heavily discounted as those incurred by interventions at or around the menopause (Torgerson et al, 1997).

5.3.6 Cost effectiveness of fracture prevention in established osteoporosis

Because of the higher risk of fracture in patients with established osteoporosis as compared to those without previous fracture and the likelihood of greater compliance in patients who have already sustained a fracture, cost effectiveness of fracture prevention in these patients is likely to

be greater than in those at lower risk. Using a combination of acquisition costs and effectiveness to assess the cost effectiveness of prevention in patients with established osteoporosis, Francis et al (1995) estimated that treatments with the lowest acquisition cost were most cost effective; however, it is possible that more expensive therapies may be more cost effective if the side-effect profile and/or follow-on costs are favourable. Nevertheless, an example of an intervention which is likely to be highly cost-effective in patients with established osteoporosis (i.e. those who have sustained a hip fracture) is the use of hip protectors. For a 78 year old woman with a history of hip fracture, the relative risk of a second hip fracture is increased six-fold (Schroder et al, 1993), equivalent to an absolute risk of fracture in the next year of around 7%. Assuming that hip protectors cost £75 (UK sterling) per woman and prevent 50% of hip fractures (Lauritzen et al, 1993; Ekman et al, 1997) this will cost only £2143 per hip fracture averted, which is much less than the acute hospital cost of treating a second fracture (French et al, 1995). Given that second hip fractures account for about 10% of hip fracture admissions, the use of hip protectors would reduce the overall number of hip fractures by 5%, (assuming 50% efficacy as above).

5.3.7 Conclusions.

Effective pharmacological interventions are available for the treatment of women with postmenopausal osteoporosis. Increases in bone mineral are not necessarily associated with increased resistance of the skeleton to fractures and documentation of lack of adverse effects of any new agent on bone quality in animal models is therefore mandatory before proceeding with clinical studies. In addition, recent preliminary analyses of large trials have revealed that the reduction in fracture frequency by inhibitors of bone turnover is much greater than would be expected from the observed changes in bone mass. Clinicians confronted with the individual patient are now in a much better position than only a few years ago, when therapeutic decisions were based exclusively on experience, intuition and extrapolation of data. Adequate knowledge, however, of the advantages and disadvantages of pharmacological interventions is essential and should be applied together with other measures which can improve bone health, reduce patients's complaints and risks and improve their quality of life.

Evaluation of the economic costs of osteoporosis prevention have so far been based on modelling studies related to the use of HRT. Further research is required to establish the quality of life effects of different treatments of osteoporosis and to generate cost data from randomised trials. In addition, relatively inexpensive preventive strategies such as hip protectors, vitamin D and HRT warrant further economic evaluation, using simple economic modelling (Torgerson et al, 1996c).

Table 5.1: Some suggestions for preventing falls and avoiding environmental hazards

I. Individual factors

Plenty of liquids and good diet
Adjustment of prescription drugs
Physical exercise to increase strength and balance training from daily walking; learn to rise from a lying position and to dress and undress while sitting
Avoid long bathrobes and wide sleeves
Use good, comfortable footwear
Use correct glasses and a cane
Arrange contents of cupboards so that heavy objects are not too low and those commonly used are at a comfortable height

II. Environmental factors

Indoors
Loud doorbells; extra phone on side table
Light switches at all doors and use of high power bulbs (e.g. for people over 75 years old use 75W bulbs)
Avoid elevated beds, slippery floors, loose carpets and wires, too much furniture, low chairs, dark entrances and corners
Handrails are important and doorsteps should be avoided
Change bathtub to shower with a chair

Outdoors
Good street lighting
Avoid uneven paving stones and steps
Clearly marked kerbs
Allow adequate time for traffic lights

III. Hip protectors

Currently for residents in institutions

Table 5.2: Prevention of osteoporosis: current and potential pharmacological interventions

I. Inhibitors of bone turnover

Bisphosphonates
Calcitonin
Calcium
Oestrogens (including oestrogen derivatives and selective oestrogen receptor modulators)

II. Stimulators of bone formation

Fluoride salts
Parathyroid hormone

III. Uncertain mode of action

Anabolic steroids
Ipriflavone
Strontium ranelate
Thiazide diuretics
Vitamin D and metabolites

Table 5.3: Randomised controlled trials in women with established postmenopausal osteoporosis in which assessment of fracture incidence has been performed

Treatment	*Number*	*Duration (yrs)*	*Patients (No.)*
Oestrogens[1]	1	1	78
Calcitonin[2]	1	2	208
Calcitriol*[3]	1	3	622
Calcium[4]	1	4.3	251
Bisphosphonates			
Cyclical etidronate[5,6]	2	3	489
Alendronate[7,8]	2	3	3,021
Fluoride			
MFP**[9]	1	2	354
NaF[10,11]	2	4	286
NaF-SR[12]	1	3	110

* not placebo-controlled; ** includes NaF arm. MFP=monofluorophosphate, NaF=sodium fluoride, NaF-SR=sodium fluoride slow release.

1. Lufkin et al, 1992.
2. Overgaard et al, 1992.
3. Tilyard et al, 1992.
4. Recker et al, 1996.
5. Storm et al, 1990.
6. Watts et al, 1990.
7. Liberman et al, 1995.
8. Black et al, 1996.
9. Meunier 1996.
10. Riggs et al, 1990.
11. Kleerekoper et al, 1991.
12. Pak et al, 1995.

Table 5.4: Approximate annual cost of different preventive strategies

Intervention	Approximate annual cost	
	£ UK	**ECUS**
Vitamin D injection	5	7.5
HRT	30-150	45-227
Hip protector	75 (1 pair pants = 25)	113
Calcium + vitamin D	80-130	121-196
Etidronate	170	257
Alendronate	350	529
Calcitonin injection	2,000	3021

Calcitonin nasal spray is available in several European Community countries at an approximate annual cost of 1.254 ECUS per patient.

£1 = 0.661944 ECU
Approximate annual cost is shown per patient.

Table 5.5: Illustration of cost effectiveness of targeting treatment

Therapy	Cheap		Expensive	
	£5	**7.5 ECU**	**£100**	**151 ECU**
Treatment cost of treating 1000 women (cost effectiveness ratio)	£5000 (5,000/6=£833)	7554 (7554/6=1259)	£100,000 (100,000/6=£16,666)	151071 (151071/6=25178)
Cost of treating 20% highest risk women (cost effectiveness ratio)	£1000 (1,000/3=£333)	1511 (1511/3=504)	£20,000 (20,000/3=£6,666)	30214 (30214/3=10071)
Extra cost of treating all women (extra fractures averted)	£5,000-£1,000 =£4,000 (6-3=3)	7554-511 =6043 (6-3=3)	£100,000-£20,000 =£80,000 (6-3=3)	151070-30214 =120856 (6-3=3)
Marginal cost per averted hip fracture by treating all women	£4,000/3=£1,330	6043/3=2014	£80,000/3=£26,666	120856/3=40285

The table shows a hypothetical scenario of two treatments for osteoporosis prevention, treatment cheap and treatment expensive. The calculations assume that for 1000 women, 20 hip fractures would occur in the absence of treatment and that both treatments reduce fractures by 30%. The assumption is also made that 50% of all hip fractures would occur in the women in the highest 20% of risk.

£l=0.661944 ECU

6. MANAGEMENT OF THE PATIENT WITH OSTEOPOROSIS: REHABILITATION AND SELF-HELP GROUPS

6.1 General measures

Early mobilisation after a fracture is essential because immobilisation aggravates bone loss. Acute pain due to a recent vertebral fracture responds to bed rest, analgesics, heat or transcutaneous electrical nerve stimulation (TENS) of paravertebral muscles to alleviate the spasm. Total bed rest should not exceed a few days and progressive mobilisation should be recommended. Physiotherapy and an exercise programme to maintain flexibility of the spine and to strengthen muscles are helpful. Lifting of heavy objects should be avoided. The use of a walker provides stability and confidence for the patient, especially following a hip fracture and psychological support is essential. Advice about adequate calcium and vitamin D nutrition and also about protein intake following a hip fracture should be given. Concomitant diseases which affect bone metabolism should be treated and all medications taken by the patient should be reviewed. Those which predispose to falls or adversely affect bone mass and bone turnover should be discontinued or reduced to the lowest possible effective dose.

6.2 Rehabilitation

Established osteoporosis is accompanied by deformities of the spine and fractures of the appendicular skeleton and their consequences: chronic pain, muscle fatigue, limited mobility, height loss, thoracic kyphosis and loss of independence. These symptoms are often aggravated by pre-existing muscle weakness (Silverman, 1992) and the psychological status of the osteoporotic patient (Zimmerman et al, 1995). Fractures of the peripheral skeleton, especially hip fractures, may cause a dramatic impairment of the quality of life (Jensen and Baggar, 1982). Rehabilitation can improve the quality of life by improving muscle strength and mobility and by reducing pain and postural abnormalities.

6.2.1 Physical exercise

Advice about physical activity in osteoporotic patients depends upon the severity of the disease. In patients with asymptomatic osteoporosis a modest programme of exercises including walking, stretching exercises and simple lifting of weights is recommended (Sazy and Hortsman, 1991). Exercises after an osteoporotic fracture should be tailored according to individual needs, taking into account factors such as muscle strength, abnormalities of gait or posture, the range of motion of the joints, cardiovascular fitness and the level of previous physical activity. A graded exercise test should be advised for those with or at high risk from cardiovascular disease. A supervised aerobic exercise programme is initially recommended to increase the general level of physical functioning and restore the sense of well-being (Sinaki, 1982). Under supervision, the osteoporotic patient can use free weights, multistation-type commercial or home gyms, steppers, elasticised exercise stands, therapeutic walking and upper limb/wrist weight bearing exercise. Stretching and flexibility exercises are also valuable. Heat treatment, massage, TENS, hydrotherapy, ultrasound and acupuncture may all be useful in reducing pain during rehabilitation. For those with chronic pain, a multidisciplinary pain treatment team can be of considerable help.

6.2.2 Postural abnormalities

The management of patients with kyphosis includes attention to posture while standing, sitting and lying. Sitting with a cushion behind the neck may be helpful in the presence of kyphosis. Complications other than pain need to be given consideration, such as easy fatiguability. These symptoms may be related to the kyphotic posture and/or a reduction in vital capacity of the lungs as a result of thoracic cage deformity. Attempts should be made to relax involved muscles, increase mobility of stiffened joints and improve chest expansion. Stretching exercises of pectoral muscles such as the intercostals may be helpful.

6.2.3 Hip fracture patients

Rehabilitation after hip fracture is often difficult because of the advanced age and extreme frailty of many of these patients. Complications related to fracture healing occur in one-third of cases five years after a cervical fracture, and arthroplasties are performed in two-thirds of the complicated cases after 10 years (Jonsson et al, 1993). Despite improvements in patient care, including advances in operative technique and implant technology, the outcome of treatment of hip fractures often falls short of expectations and although the operation may be successful in terms of healing of the fracture, patients are often unable to regain their pre-injury level of function and independence (Nilsson et al, 1988). It has been shown that 45% of the community-dwelling persons who fracture a hip are discharged to institutions after hospitalisation, and 15% to 25% remain institutionalised for 1 year or more (Broos et al, 1989). Poorly controlled systemic illnesses have been shown to increase the mortality rate after fracture of the hip (Koval and Zuckerman, 1994). Reported rates of recovery of the ability to walk after fracture of the hip have ranged from 41 to 97% (Jette et al, 1987). Factors associated with recovery of walking ability are younger age, male sex, the absence of pre-existing dementia and lack of the need to use a cane or walker before the fracture. Early identification of patients who are unlikely to return home may be useful for the planning of discharge. The factors that have been identified as important to this include age, post-operative walking ability and the presence of someone else at home.

6.2.4 Psychosocial aspects

Psychological problems in elderly patients with fractures include cognitive disorders and depression, decline in emotional well-being and reduced motivation. Support provided by family and friends is essential for those affected; conversely, restricted social activity, immobility, and fear of injury may isolate a woman and place her at risk of losing contact with her informal support network.

6.2.5 Daily activities

To achieve functional independence, the ability to perform certain daily activities is essential. The functions necessary for community dwelling have been identified and divided into two categories: basic activities of daily living (feeding, bathing, dressing and toiletting) and instrumental activities of daily living (shopping, food preparation, banking, laundry, housework and use of public transportation). Patients suffering from established osteoporosis, especially after hip fracture, can benefit from supplementary aids to activities of daily living. Such aids include a transfer tub bench, long-handled tools such as long-handled bath sponges, extended handled shoe horns, reachers and long-handled cleaning tools.

6.3 Self-help groups

Osteoporosis has a devastating effect on a patient's health, physically and psychologically. Life becomes increasingly difficult with loss of mobility, growing dependency and chronic pain. Opportunities for discussion are limited and many osteoporosis sufferers remain ill-informed about their disease and isolated from the community. It is therefore vital that newly diagnosed patients are given relevant counselling on how to prevent fractures and that patients recovering from fractures are effectively supported in the community on an ongoing basis. Although advice regarding therapeutic interventions is readily available from doctors, further information on osteoporosis management is often lacking. According to a recent 17 country study, although just over 50% of osteoporosis patients were given advice on how to manage their disease at the point of diagnosis, the remaining patients felt that they should have been given advice about diet and nutrition, exercise and medication options.

6.3.1 Functions of self-help groups

Self-help groups can maintain quality of life for osteoporosis patients by improving their understanding of osteoporosis and providing them with information about the prevention and treatment of fractures. They are designed to provide an atmosphere in which the challenges that accompany the disease can be discussed amongst people who are often undergoing similar experiences. These groups may be led by a professional, such as a physician or social worker, or by other patients. Self-help groups can vary in approach, size and in how often they meet. It is important that individuals find a group that meets their particular needs; consultation with such self-help groups can be encouraging and supportive, enabling patients to live more independent lives and avoid institutional care.

Detailed information on how changes in lifestyle, combined with medical therapies, can help to reduce the risk of subsequent fractures and slow down the rate of bone loss is easily imparted in a self-help group situation. Practical recommendations such as taking measures to make falls less likely, i.e. removing hazards such as poor lighting, loose carpeting and dangerous stairs can also be made. Discussions about the pros and cons of new medications, recent innovations, e.g. hip protectors, and relevant clinical study information can increase the well-being of patients and, when appropriate, advice can be given to contact a doctor.

Self-help groups are also an ideal venue for managing psychological issues unique to osteoporosis patients. Height loss and spinal curvature often cause clothes to fit poorly, leading to depression and loss of self-esteem. Self-help groups can offer both sympathetic support and practical clothing advice. The management of chronic pain and emotional stress, pain-related anxiety and depression are topics frequently dealt with in self-help group sessions. Fear of routine activities and of fracture are other issues that are tackled by self-help groups to improve the quality of life for patients.

6.3.2 Self-help groups in the European Union

The European Foundation For Osteoporosis (EFFO), on behalf of the European Commission Working Group on Osteoporosis, recently conducted a survey which questioned national osteoporosis societies throughout the European Union about self-help groups for osteoporosis sufferers. Osteoporosis self-help groups appear to be particularly well formed in Germany with 425 active groups. Many of these groups are part of the service offered by the Bundesselbsthilfeverband für Osteoporose and others are organised by a variety of volunteer

associations. The UK is also comparatively well served with 82 self-help groups organised by the National Osteoporosis Society. There are two particularly active self-help groups functioning in Austria. In other countries, self-help groups are limited or absent.

In some countries with no official self-help groups, national societies take over some of the traditional functions of a self-help support group. For example, Riksföreningen Osteoporotiker in Sweden helped to pioneer „Osteoporosis Classes“ for newly diagnosed osteoporosis patients which are now held in 4 hospitals. In Finland, osteoporosis sufferers rely on the Finnish Rheumatism Association or the Finnish Back Society for patient support. The Dutch Osteoporosis Societies, ‘Osteoporose Stichting’ and ‘Osteoporose Vereninging’, work with 60 volunteers who act as „sufferer supporters“ attached to individuals rather than groups. The Spanish Osteoporosis Foundation (FHOEMO) helps patients with osteoporosis by distributing information, organising exercise classes and offering nutritional advice.

Productive communication with relevant organisations is consistently seen in countries where self-help groups are well established. In Germany the wide variety of self-help groups have worked with regional insurance companies in order to obtain reimbursement for gymnastic classes and with health authorities regarding education. The two Austrian self-help groups are in contact with their appropriate government minister, Kuratorium für Verkehrssicherheit, insurance companies, and hospital associations. In the UK some groups have formed liaisons with their local NHS hospitals, clinics and doctors.

6.3.3 Future strategies for self-help groups in the European Union

An overall need was expressed in the EFFO survey for a larger number of groups per country, since regional location is essential for optimum use. The UK National Osteoporosis Society is planning to increase its number from 82 to 150 groups, resulting in one group per 370,000 people. With approximately 450,000 Austrian women at risk of osteoporosis, Selbsthilfgruppe Osteoporose would like to increase their total to 9 and ideally have a minimum of one group per town or city.

In those countries in which there are currently very few or no self-help osteoporosis groups, namely Belgium, Denmark, Finland, France, Greece, Ireland, Italy, Luxembourg, Portugal and Sweden, a variable number of groups have been proposed by the respective national osteoporosis societies. The general consensus is that each region within a country requires a minimum of one self-help group.

National osteoporosis society feedback suggested that in Belgium, the minimum would be two, one for each language, but the ideal number would be nine, one per province. In Portugal the minimum would be two in the Lisbon area and four in Oporto, but the ideal would be 20, covering all the main cities, districts and the islands. In Ireland, it is proposed that eight groups are set up to co-ordinate with the eight health boards. In Sweden five groups would be considered initially. The geographical configuration of Italy dictates that two groups would be required for each region, North, Central and South. The two outlying islands would also each need to be served by one group. The Italian National Societies would also consider increasing the number of self-help groups in each region if they were shown to be effective. In Germany, already comparatively well-served by self-help groups, the optimum number would be one group per community of 10,000 inhabitants.

6.3.4 Conclusions

The term self-help group implies that patients must help themselves to manage their illness. Asthma and diabetes, diseases that are largely patient managed and controlled, have well developed self-help groups to educate and support sufferers. There are currently 150 self-help groups for asthmatics and 450 for diabetics in the UK alone. An on-line self-help directory is available for diabetes support groups throughout Europe. Cancer patients are also well supported in almost all European countries. A world-wide 'self-help directory' booklet which lists cancer self-help groups all over the world is available from most national cancer societies.

Teaching osteoporosis patients and their families how to cope psychologically and take charge of their lives is as important as any medication or other therapy. Self-help groups are an ideal venue for the discussion of disease management and encouragement of such groups is vital to help the ever increasing number of osteoporosis patients throughout Europe. The harmonisation of osteoporosis self-help groups throughout Europe with respect for cultural differences should ensure that all patients receive appropriate support.

By offering such support, self-help groups can help patients to avoid hospitalisation and institutional care, thereby reducing the considerable burden of osteoporosis on the current health care system. A recent German study examined anxiety levels and bone mineral density in 132 female patients with primary osteoporosis who were receiving identical therapy. The 66 patients who were members of an osteoporosis self-help group were shown to have a reduction in anxiety level and a significant rise in bone density. In non-members this effect was not observed (Seelbach et al, 1995).

The establishment of self-help groups requires financial resources, dedication and commitment from national osteoporosis societies and volunteers. Financial assistance is needed from governments and other responsible institutions to create and encourage self-help groups. A working collaboration between local governments, regional health care authorities, insurance companies and self-help groups is beneficial to both the osteoporosis sufferer and the health care community. The creation of an environment in which osteoporosis self-help groups can flourish and offer the maximum benefit to the ever increasing number of osteoporosis patients throughout Europe can only be achieved with financial support from governments and encouragement from health care authorities.

7. ACTION FOR PREVENTION: RECOMMENDATIONS

The recommendations in this report address both the fuller utilisation of presently available diagnostic techniques and therapies and the need for further research. They also emphasise the inequality of resources throughout EU countries and the urgent need for greater dissemination of information amongst both the public and health professionals.

1. The Report on Osteoporosis in the European Community expert committee provides compelling evidence in their report that fractures caused by osteoporosis pose a major and growing threat to the health of elderly populations in Europe. It is recommended that osteoporosis is explicitly adopted as a **major health care target** by the European Union and the governments of the fifteen member states. Prevention of osteoporosis should be a major priority in health promotion, education and training both for the general public and health professionals.

2. **More information** is required about the incidence and prevalence of osteoporotic fractures, particularly in those countries in which very little information is currently available. Differences between countries may provide important clues about causes of osteoporosis and potential preventive strategies and further research is required to explain these geographical variations. It is recommended that a co-ordinated system for the monitoring of fracture rates, with particular reference to secular trends, is set up at a national and European level. This would facilitate more accurate documentation of osteoporotic fractures in EU member states and enable better estimation of the costs involved in its prevention and treatment.

3. The number of osteoporotic fractures occurring over the next few decades in EU member states will rise dramatically. It is recommended that national systems are co-ordinated throughout the European Union in order to plan effectively for the resulting increase in demands on health care and to institute **appropriate resource reallocations**. These should take account of country-specific demographic forecasts, financial resources and health care systems.

4. **Nutritional factors**, particularly calcium and vitamin D, play an important role in skeletal health. Nonetheless, dietary calcium intakes are below recommended levels in many EU member states and vitamin D deficiency is common, particularly in the elderly. It is recommended that policies are developed and implemented to advise the general public and health professionals about calcium and vitamin D nutrition, based on agreed recommended intakes, at all stages of life. In some countries, fortification of certain foods should be considered.

5. Better provision of **bone densitometry systems** throughout Europe is a major priority. Bone density measurements currently provide the best diagnostic approach for osteoporosis, but resources in Europe are patchy and often inadequate and many doctors and their patients do not have access to bone densitometry systems. In addition, reimbursement for bone density measurements is absent or incomplete in some countries, thus limiting the use of this facility even where resources are available. It is recommended that access to bone density measurements should be universal for subjects with accepted clinical indications and that reimbursement should be available for such individuals. Dual energy X-ray absorptiometry is currently the method of choice, although other approaches such as broadband ultrasound attenuation are being evaluated and may become an acceptable alternative.

6. The number of agents available for the **prevention and treatment of osteoporosis** has increased in recent years and others are currently being developed. There are wide variations in the use of these drugs in individual EU member states; this is partly, but not wholly, a result of the lack of standardisation of criteria for registration. It is recommended that a unified policy is developed to

ensure optimal treatment strategies throughout the European Union, in which all member states use an evidence-based approach to determine which treatments should be advised. Reimbursement, both for pharmacological and non-pharmacological interventions, should be available for all patients receiving treatment according to accepted indications.

7. The **role of national patient and scientific societies** in providing support and information for sufferers, their families and the public is increasingly recognised. However, in some parts of Europe ignorance about osteoporosis is still common, both amongst health professionals and the public, so that sufferers remain isolated by their disease and are unaware of measures which can be taken to help them. It is recommended that governments actively promote these societies, providing financial support and helping to publicise their cause throughout the European Union; appropriate training of health care professionals involved in the management of osteoporosis should also be an important priority.

8. There are a number of areas where **further research is urgently required.** For many of these, long-term prospective studies involving collaboration between European Union member states are particularly appropriate. It is recommended that funding for such studies is given the highest priority in order to enable preventive strategies to be devised and implemented.
a). More information is required about modifiable determinants of peak bone mass, particularly exercise and calcium, and how these might be used to achieve higher peak bone mass in the population.
b). More research is required into the identification of risk factors for falling and the effects of fall prevention strategies on fracture
c). Further evaluation is needed, in different age-groups, of approaches to identify individuals at risk from fracture, for example the use of broadband ultrasound attenuation, biochemical markers of bone turnover and risk factors, either singly or in combination.
d). Although population-based screening in perimenopausal women is not recommended, studies are required to assess the cost/utility ratio of this approach in older women
e).The causes and treatment of osteoporosis in men are important areas for future research.

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Annexe: National osteoporosis guidelines & consensus statements

Country	Guidelines	Consensus Statement	Further Information
Europe	'Guidelines for diagnosis and management of osteoporosis', European Foundation For Osteoporosis (EFFO). Osteoporosis International, 1997; 7: 388-404	Consensus Development Statement. Who Are Candidates for Prevention and Treatment for Osteoporosis? Osteoporosis International, 1997; 7:1-6	EFFO Secretariat, 71, Cours Albert Thomas, F-69003 Lyon Tel. +33 4 72 91 41 77 Fax. +33 4 72 36 90 52 E-mail: effolyon@net.asi.fr
Austria		'Osteoporose Prävention & Therapie Konsensus Statement' Konsensus Meeting November 23, 1995, Wien. Internationale Zeitschrift für ärztliche Fortbildung, 1995; 31: 2-8 Currently under revision.	
Belgium		'Diagnostic de l' ostéoporose', Belgian Bone Club, Medi-Practice, 1997; 21:43-48. 'Prevention & treatment of postmenopausal osteoporosis. National consensus of the Belgian Bone Club', November 1996. Clinical Rheumatology, 1997, 16: 343-345.	Professor Jean-Yves Reginster, Unité d'exploration du métabolisme de l'os et du cartilage, CHU Centre-Ville, 45 Quai Godefroid Kurth, B-4020 Liège Tel. +32 4 3418757 Fax. +32 4 3418753
Denmark	Being produced.		
Finland	Guidelines for Prevention, Diagnosis and Treatment of Osteoporosis. Duodecim 1996; 112: 2065-2176. Guidelines for Prevention of Osteoporosis. Book. National Osteoporosis Society, National Association of Sport for All, UKK-Institute: Helsinki 1997.	1992 Consensus Statement on Prevention and Treatment of Osteoporosis. Consensus Conference 30.3-1.4.1992. Book. Finnish Academy, Duodecim and Finnish Health Ministry: Helsinki 1992.	Dr. O. Simonen, Government Counsellor, Ministry of Social Affairs and Health, PO Box 197, FIN-00531 Helsinki, Tel. +358 9 1604376 Fax. +358 9 1604144 E-mail: olli.simonen@stm.vn.fi

Country	Guidelines	Consensus Statement	Further Information
France	'Ostéoporose: Stratégies de prévention et de traitement', Expertise Collective, INSERM 1996, ISBN 2 85598-676-1.		INSERM, 101 rue de Tolbiac, 75013 Paris or Ministère de l'Emploi et de la Solidarité. Direction Générale de la Santé, Bureau SP2 - Dr. Danièle Mischlich 8 avenue de Ségur, F-75350 Paris 07 SP Tel. +33 1 40565206 Fax. +33 1 40564055
Germany	'Osteoporose – Leitlinien Medizin', Deutsche Arbeitsgemeinschaft Osteoporose (DAGO), second revised edition 1997. DM 19,80 plus postage. ISBN 3-932091-12-4 'Leitlinie zur Diagnostik der Osteoporose', Deutsche Gesellschaft für Osteologie, Zeitschrift für Osteologie 1996; 5 (3): 162-173 AWMF online: awmf@uni-duesseldorf.de		Order from book shops or contact Deutsches Grünes Kreuz, im Kilian, Schuhmarkt 4, D-35037 Marburg. Tel. +49 6421 293128 Fax. +49 6421 163894 E-mail: dgk@kilian.de
Greece	'Guidelines on the Diagnosis and Treatment of Osteoporosis', Ostoun Dec. 1996, 7: 216-328	'Bone Densitometry, Indications and Quality Control', Ostoun 1994, 4: 262-278	
Ireland		Consensus Development Statement. Who Are Candidates for Prevention and Treatment for Osteoporosis? Osteoporosis International, 1997; 7:1-6	Irish Osteoporosis Society Batterstown, Dunboyne, Co. Meath, Ireland. Tel/ Fax +353 1 8258159 E-mail: crowleym@indigo.ie
Italy	Being produced.		
Luxembourg	No	No	
Netherlands	Existing document being revised.		

Country	Guidelines	Consensus Statement	Further Information
Portugal		Consensus Conference held in January 1998	Dr. Jaime C. Branco Portuguese Society of Metabolic Bone Disease (SPODOM) Hospital Egas Moniz Unidade de Reumatologia Rua da Junqueira 126 P-1300 Lisbon Tel. +351 1 365 00 00 Fax. +351 1 295 70 04
Spain		Conferencia Consenso/documento canario Organizado por el Cabildo Canario SEIOMM and FHOEMO, 1998	Fundacion Hispana de Osteoporosis y Enferme-dades Metabolicas Oseas Gil de Santibanes 6-2°D Apartado Postal 60163 E-28001 Madrid Tel. +34 1 5783510
Sweden	'Behandling av osteoporos' (Treatment of osteoporosis) No. 1/97, issued by Swedish Government Medical Products Agency in co-operation with their Norwegian counterpart.		Medical Products Agency PO Box 26 S-751 03 Uppsala. Tel. +46 18 17 46 00
UK	Advisory Group on Osteoporosis Report. Department of Health, November 1994.		Central Print Unit, Department of Health, Room 285D, Skipton house, London Road, UK-London SE1 6LW. Tel. +44 171 9721670

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