Hips at Risk
Osteoporosis and Prevention
of Hip Fractures

BY

ANNA EKMAN
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Abstract

Hip fractures are the most serious consequence of osteoporosis, and are one important cause of morbidity and mortality among the elderly. Prophylactic treatment for hip fractures are now available. Early detection of individuals with increased risk for hip fractures is therefor of great interest. A subset of non-institutionalised patients with a first hip fracture (cases; n=118) and controls (n=263), aged 65-85 years, underwent dual X-ray absorptiometry (DXA) of the femoral neck, quantitative ultrasound (QUS) of the heel and phalanges and radiographic absorptiometry (RA) of the phalanges. The entire cohort was followed for approximately four years or to death. In women, DXA of the proximal femur and QUS of the heel showed a high predictive value for an incident first hip fracture, adjusted odds ratio (OR) 3.6 (95% confidence interval (CI) 2.4-5.5) and 3.4 (95% CI 2.2-5.0) respectively. The association was even stronger in men, but only for DXA of the proximal femur with an adjusted OR of 4.8 (95% CI 2.3-9.9). Bone densitometry at non-weight-bearing sites, QUS and RA of the phalanges did not discriminate female cases from controls, but proved capable of separating male cases from controls. The risk of death was higher in cases than in controls, with a multivariate rate ratio (RR) of 3.4 (95% CI 1.7-7.0). There was no significant association between bone density and mortality.

Nursing home residents underwent QUS of the heel and phalanges. Almost all of the female residents and 51% of the male residents were, if the WHO-criterion for osteoporosis was applied, osteoporotic as assessed by heel and finger QUS. The QUS values were approximately 1.5 SD lower than expected for age and gender.

In this randomised controlled intervention study we evaluated the effect of external hip protectors in nursing home residents; 302 residents were allocated to wear such protectors and 442 were controls. External hip protectors were found to be effective in preventing hip fractures in nursing home residents, with an adjusted relative risk for hip fracture of 0.33 (CI 0.11-1.00).

Key words: Bone densitometry, external hip protectors, hip fracture, mortality risk, nursing home residents, osteoporosis.

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<td>BMD</td>
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<td>BMC</td>
<td>Bone mineral content</td>
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<td>BMI</td>
<td>Body mass index</td>
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<td>CI</td>
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<td>SD</td>
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<td>WHO</td>
<td>World health organisation</td>
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<td>SXA</td>
<td>Single X-ray absorptiometry</td>
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<td>DXA</td>
<td>Dual X-ray absorptiometry</td>
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<td>RA</td>
<td>Radiographic absorptiometry</td>
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<td>QCT</td>
<td>Quantitative computerised tomography</td>
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<td>QUS</td>
<td>Quantitative ultrasound</td>
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<td>AU</td>
<td>Aluminium equivalent units</td>
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<td>DPA</td>
<td>Dual photon absorptiometry</td>
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<td>SPA</td>
<td>Single photon absorptiometry</td>
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<tr>
<td>SOS</td>
<td>Speed of sound</td>
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<td>BUA</td>
<td>Broadband ultrasound attenuation</td>
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INTRODUCTION

Hip fractures are the most serious consequence of osteoporosis, and are one important cause of morbidity and mortality among the elderly [1-6]. Approximately half of previously independent elderly hip fracture patients will become partly dependent as a result of the hip fracture and at least one-third eventually totally dependent [1]. Among patients with hip fractures there is an overall 12-20% reduction in expected survival, with most excess mortality occurring within the first year after the fracture [5, 7, 8]. Costs related to hip fractures are high, on account of the need for urgent hospital treatment and subsequent rehabilitation [1, 9, 10].

The incidence of hip fracture is increasing rapidly throughout the world and is expected to exceed 6 million per year globally by the year 2050, as compared to 1.7 million in 1990 [1]. This rise will be due largely to the increase in the elderly population of the world [1, 11]. There is a considerable variation in hip fracture incidence between different ethnic populations, but in every population this incidence of hip fracture increases exponentially with age.

The lifetime risks of hip fracture in Swedish women and men at the age of 45 years are 23.3% and 11.2% respectively [12]. Sweden, with an annual absolute number of hip fractures of 18,000, holds together with Norway, the top position of incidence rates of hip fracture in the world [13-15].

Several reports have shown an increase in the age-adjusted hip fracture incidence during the 50s, 60s, 70s, and 80s [13, 16-23]. In the last decades, however, this has not been a uniform finding, especially in women [24-26]. In Scandinavian women, the age-adjusted incidence of fractures of the femoral neck has been reported to be declining [25, 27, 28]. In contrast, the incidence of both femoral neck and trochanteric fractures seems to be increasing in men [28-30]. In Sweden the mean ages of female and male hip fracture patients are 81 and 78 years respectively [30], which coincide with the mean life expectancies [31]. All over the world the age-specific hip fracture incidences are about twice as high in women as in men [1, 21, 22]. The overrepresentation of women has been explained by the lower bone mineral density (BMD), accelerated bone loss and higher frequency of falling among women [1, 21, 32]. Nevertheless, the risk of hip fracture increases exponentially with age in both men and women and age-related bone loss occurs in both sexes [33].
In fragility fractures such as hip fractures, the single most important factor is a low bone mineral density [34-36]. The association between BMD and bone strength is well documented [37-40]. Compared to younger people, the elderly have, on average, a low BMD with a consequent deterioration in biomechanical properties. A decline in BMD increases the risk of future hip fractures exponentially, with risk estimates of between 2 and 3 per SD reduction in BMD, measured at the hip [41-43].

The hip fracture

Hip fractures are suspected on the basis of clinical findings and confirmed by standard radiographs.

There are two major types of hip fracture; fractures of the femoral neck (intracapsular) and trochanteric (extracapsular) femoral fractures. The vast majority of hip fracture patients are treated surgically, preferably as soon as possible, generally within 24 hours. The aim of the surgical treatment, through internal fixation or hip replacement, is to create a stable situation that is suitable for prompt weight-bearing after surgery.

In most studies the two main types of hip fractures are considered as a single entity, without regard to a possibly different aetiology. There are reports, however, of differences between these two types of fracture. Some studies indicate that patients with trochanteric fractures are more osteoporotic [44-50], older, thinner and shorter [45, 50-56], and have a higher prevalence of previous osteoporotic fractures [50, 57-59] and higher post-fracture mortality [3] than those with fractures of the femoral neck. In a recent Swedish report [51], trochanteric fractures were found to be influenced by hormonal and environmental factors such as duration of menstrual cycling, exogenous oestrogens and smoking, whereas femoral neck fractures were more related to increasing height [51]. This is consistent with the association between increasing stature and hip axis length/ femoral neck length and femoral neck fracture [60-64]. In people under 60 years of age the incidence of trochanteric fractures is lower than that of femoral neck fractures. After 60, the imbalance diminishes progressively, to reach equal ratio in subjects over 85 [65]. In recent decades, however, there has been an increase in the incidence of trochanteric fractures in both men and women, of all age groups [22].

Mortality following hip fracture

On average, patients with hip fracture have increased co-morbidity and disability, more loss of independence, a decreased quality of life, and also an increased risk of death after
the fracture event compared to the general population [1-6, 66]. The reported mortality risk after a hip fracture has been found to vary, but with most excess deaths occurring within the first 6 months after the fracture [2, 67-69]. Survival after hip fracture seems to be worse in men than in women [66-75] and also among subjects suffering from trochanteric compared to femoral neck fracture [3, 75]. Bone mineral density has been found to be associated with non-trauma mortality [76, 77].

Nursing home residents have higher mortality rates following hip fractures than community-living elderly [78]. About 4% of falls in nursing homes (range 1-10%) result in fractures, whereas other serious injuries, such as head injury, soft-tissue injuries and severe lacerations occur in about 12% (range 1-36%) of falls [79]. Although most falls do not lead to physical injury, they might still be harmful if resulting in fear [80] and "post-fall anxiety syndrome".

**Classification of osteoporosis**

Osteoporosis is defined as a systemic skeletal disorder characterised by compromised bone strength predisposing to an increased risk of fracture [81, 82]. Bone strength reflects the integration of two main features: bone density/quantity and bone quality. Bone density is expressed as grams of mineral per area or volume. Bone density is dependent on peak bone mass and amount of bone loss. Bone quality refers to architecture, turnover, damage accumulation (e.g. microfractures) and mineralisation. A fracture occurs when a failure-inducing force, e.g. trauma, is applied and exceeds the resistance of the skeleton. Thus, osteoporosis is a significant risk factor for fracture.

The diagnostic criteria suggested by the World Health Organisation [83] only pay consideration to bone quantity and only in post-menopausal women. The rationale for the WHO criteria is that BMD provides the best means of assessing the risk of fracture. WHO has chosen to express BMD as standard deviation (SD) scores called T-scores, i.e. the difference in SD between the measured individual’s BMD and the mean BMD of healthy young women (20-40 years of age). T-scores indicate therefor the difference between the BMD of the examined woman and the ideal peak bone mass in young women. In clinical practice the use of T-scores has also been adopted for men, although no health authorities have approved any definition of osteoporosis in men. The Z-score is the difference in SD between a measured BMD and the mean value expected for a healthy normal subject matched for sex as well as age and often with adjustment for weight.
WHO operationally defines osteoporosis as a bone density 2.5 SD below the mean for young white adult women (T-score <-2.5 SD), osteopenia as a T-score between -2.5 and -1, and normal conditions as a T-score >-1. Osteoporosis can further be characterised as either primary or secondary. Primary osteoporosis can occur in both genders at all ages, but often follows the menopause in women and occurs later in life in men [84]. In contrast, secondary osteoporosis is a result of a pronounced bone loss secondary to other diseases or medications [84].

The prevalence of osteoporosis in Swedish women above 60 years of age is 37.9% [85]. In its publication, the WHO study group [83], has stated:

“All cut-off values are somewhat arbitrary, but a measured value of bone mineral more than 2.5 standard deviations below the mean for young healthy adult women at any site (spine, hip or mid-radius) identifies 30% of all post-menopausal women as having osteoporosis, more than half of whom will have sustained a prior fracture of the proximal femur, spine, distal forearm, proximal humerus or pelvis.”

Some problems with the T-score introduced by WHO arise. In the absence of any other criterion, the cut-off criterion of -2.5 is used in clinical practice as well as in studies, for many different BMD techniques and different sites, despite the fact that it was based primarily on an epidemiological relationship between forearm measurements with single photon absorptiometry (SPA) and prevalent hip fracture in postmenopausal Caucasian females. It is therefore reasonable to expect that a T-score threshold of -2.5 may be inappropriate for different skeletal sites and methods of densitometry, other than the established single X-ray absorptiometry (SXA) and dual X-ray absorptiometry (DXA) techniques. This could explain the disparity in bone density and the large variation in prevalence of osteoporosis observed when different skeletal sites are measured, with different techniques [86-90].

In 1998 Miller and colleagues [91] concluded that discordance in bone mass is present at different skeletal sites in an individual for at least four reasons, namely

1. a difference in peak adult bone mass among sites,
2. different rates of bone loss among sites after menopause,
3. apparent discordance from the effects of degenerative changes or dystrophic calcification on the measured BMD,
4. accuracy errors using different techniques at different sites.

At present, there is no generally accepted definition of osteoporosis in men. Both the absolute risk and the relative risk (RR) of hip fracture, based on bone densitometry, have been found to be similar in men and women [33, 92, 93]. The risk of hip fracture has
been reported to increase exponentially with age in both sexes, and men have been found about to have the same risk five years later than women; the difference in age-specific incidence is explained by the difference in bone density between men and women [33, 92]. According to these recent data a 1 SD lower BMD confers a similar increase in the relative risk of hip fractures in men and women and the absolute risk conferred by a given hip BMD is also similar in men and women.

**Bone densitometry**

Low BMD is the most important risk factor for fracture later in life. Bone mineral assessment is at least as effective in predicting hip fracture as blood pressure measurements are for predicting stroke, and far better than cholesterol measurements for predicting myocardial infarction in men [35, 83]. In men as in women, BMD measurement has proven to be highly sensitive method for identifying subjects with an increased fracture risk, as documented in prospective studies [92, 94-97]. However, at present the accuracy of BMD is considered to be insufficient for use of this method as a screening tool.

Bone densitometry is mandatory in diagnosing osteoporosis and is essential for decision-making regarding prevention and treatment [35, 83]. At present the clinical assessment of osteoporosis and fracture risk prediction rely mainly on non-invasive measurements of BMD and the bone mineral content (BMC) [98-101]. Several techniques for bone measurements are available, most of them using ionising radiation, such as SXA, DXA, radiographic absorptiometry (RA) and quantitative computerised tomography (QCT). As a non-ionising technique, quantitative ultrasound (QUS) has gained increasing interest. It is relatively inexpensive and user-friendly.

The radiographic techniques are based on the absorption of the x-ray beam in bone tissue, which is converted by an algorithm to so-called bone mineral density or equivalents. However, since only QCT measures true density, all other techniques, including SXA and DXA, provide a two-dimensional image of the bone and present the result as BMD in g/cm², more accurately termed areal BMD, although this is most often referred to as just BMD. DXA has become the reference method, which is typically used at the posterior-anterior spine and proximal femur.

Standard hand films have been used for quantitative bone measurements in the past and are still used in some clinics today. **Radiographic absorptiometry** is a technique by which the levels of a conventional x-ray are calibrated to a standard, often an aluminium
step wedge, placed on the film. Two films are obtained at different X-ray settings, and are sent to the laboratory for analysis. The results are presented as aluminium equivalent units, AU. The primary advantage of RA is equipment cost and accessibility, as all medical institutions have standard X-ray units. Disadvantages are the costs associated with RA incurred by the centralised analysis and the cost of shipping and the delayed report. The precision error for repeated measurements of BMD by RA has been reported to be 0.6% [102].

The physical principle of SPA/SXA is that a fixed amount of energy is emitted through an object, e.g. the forearm, and the resulting energy is detected on the other side. The difference is called the attenuation. SPA/SXA is limited to measuring peripheral bone, as the measurement site should preferably be covered by a minimum of overlying soft tissue. The accuracy is approximately 9% and the precision 1-2% [103, 104].

The problem of the influence of different thicknesses of overlying soft tissues was overcome when the use of dual-energy radiation was introduced. With this method, two different energies are used to separate the contributions from bone and soft tissue. The physical principle of a DPA/DXA system is the same as that of SPA/SXA. With DXA measurements can be made at central sites such as the lumbar spine and the hip, as well as at peripheral sites. The accuracy is approximately 10% and the precision 1-1.5%. [105-108].

Quantitative computed tomography is the only truly three-dimensional bone mass measurement technique available. The QCT result is a volumetric density (g/cm³), as opposed to the area density (g/cm²) obtained with other techniques. QCT is used clinically to measure the bone density of the spine, although commercial systems for use at other anatomical sites such as the distal forearm and the hip are available. The projectional limitations of DXA are overcome by using QCT, which also allows a selective measurement of the trabecular bone. QCT can be performed on most commercial CT systems. Scan analysis is carried out either with software added to the scanner or at off-line workstations. Peripheral QCT (pQCT) using specialised scanners is mostly performed at the ultradistal forearm. The cost of pQCT is much lower than that of standard QCT, although currently, pQCT costs as much as DXA devices, which are capable of density measurements at multiple skeletal sites. Disadvantages of QCT are related to its high cost, considerably higher radiation dose than DXA and at least in Sweden its limited accessibility. Its accuracy is approximately 10-20% and precision 2-4% [100, 109, 110].
Quantitative ultrasound is a measure of a mechanical wave that can be influenced by the microstructure as well as the density of bone [111, 112]. QUS seems therefore to offer an alternative to conventional absorptiometry, in providing structural information in addition to information on density [113]. In ultrasonic propagation through bone, both the velocity of transmission (speed of sound, SOS, in m/s) and the amplitude (broadband ultrasound attenuation, BUA, in dB/MHz) are affected by the medium [111]. The results are expressed as the speed of sound (SOS, m/s), broad band ultrasound attenuation (BUA, dB/MHz). With some equipments the stiffness index (%) – expressed by an algorithm of the combination of SOS and BUA is also used to express the results. The heel (calcaneus) is the most common site of QUS measurement. Recently QUS of the fingers has been developed for fast, accessible and less expensive use, as well as QUS of the tibia, patella and multiple other sites.

The accuracy is approximately 20% and the precision 0.2% [114-116]. However, the use of QUS is restricted for several reasons. It has been reported that the WHO definition of osteoporosis may not be appropriate at other skeletal sites than the spine, hip or forearm, or for different technologies such as QUS [117-120]. These studies have shown that few patients have a QUS T-score value below –2.5 and suggest that it may be necessary to provide a T-score criterion specific to the measurement technology employed. In addition many different QUS devices are available worldwide, all using manufacturer-supplied reference databases, which will further increase the heterogeneity between devices. Moreover, to date there are no standardised methods or phantoms for calibration between the different manufacturers’ QUS equipments. Altogether this makes it difficult to compare studies performed with different QUS machines.

Other risk factors for hip fracture

The aetiology of hip fractures is multifactorial, but the three principal factors can be summarised as: a fall, loss of protective mechanism and low bone strength [121, 122]. Numerous risk factors have been established in addition to low BMD, such as prior fracture, use of corticosteroids, hypogonadism, female gender, white race, decreased weight and high age [33, 122, 123].

In addition to bone strength and lifestyle factors of the individual, the falling mechanism and the impact energy created by the fall, as well as the energy absorption by the soft tissues, determine whether a hip fracture will occur as a result of a fall [121, 124-130].
Over 90% of hip fractures are the result of a fall [121, 124, 125, 127, 131], but only 1-2% of all falls in the elderly lead to a hip fracture [80, 132].

In communities with a high risk of hip fracture in women, the risk is also high in men [14, 133, 134]. As the majority of hip fractures occur in women, most attention has been focused on bone loss and other risk factors, and their association with hip fracture risk in women. However, data from several studies indicate that risk factors for hip fracture in men are much the same as in women, including hypogonadism [94, 96, 123, 135-140]. However, as in women, clinical risk factors, except for prior fractures and age, are rather poor as predictors of hip fractures in men.

Nursing home residents are a frail population in several aspects. The prevalence of osteoporosis in nursing home residents has been reported to be high. From measurements with composite forearm BMD, Zimmerman et al [141] reported an osteoporosis prevalence of 63.5% among women aged 65-74 years and of 85.8% among women over the age of 85. In a population of elderly nursing home residents there are several risk factors for osteoporosis, such as a high proportion of women, high age, low physical activity, vitamin D deficiency and a low calcium intake, hyperparathyroidism, low body weight, and chronic diseases [142, 143]. The mean incidence of falls in nursing homes is about three times the rate among community-living elderly, where the mean is 1.5 falls per bed per year [79], and thus in nursing home residents there is a higher risk of hip fracture [92, 144-147].

However, living in a nursing home is not in itself an independent risk factor for hip fracture [145].

There are some known fall-related factors associated with a hip fracture risk, all of which are common in institutionalised people, e.g., decreased visual acuity, impaired neuromuscular function and cognitive impairment [36, 124, 142, 148-151]. Moreover, some medications have been found to increase the risk of falling, for example psychotropic drugs and antidepressants [152]. Falling is also related to the degree of mobility [153, 154]. In a recent prospective study of falls, BMD and function in institutionalised elderly persons [155], Greenspan et al found impairment of mobility, a fall to the side and a low hip bone density to be independent risk factors for hip fracture.

**Prevention of hip fractures**

It has been said that it is never too early to reduce the risk of osteoporosis and never too late to prevent hip fractures [156]. At the population level, strategies must be oriented
towards prevention of osteoporosis and reduction of the number and severity of falls in the elderly. Concerning the prevention of osteoporosis, physical activity (through improvement of peak bone mass and reduction of bone loss) has been suggested as beneficial for the skeleton [157-159]. Physical activity is also associated with improvement of muscle strength, stability, the reaction time, balance and co-ordination, which is probably associated with a decreased number and severity of falls. As physical activity is important through multiple mechanisms, it is also of great importance to minimise immobilisation, since immobilisation is associated with rapid bone loss which is partly irreversible [157, 160-163]. A woman who stops smoking before the menopause will reduce the fracture risk by about one-fourth [157]. Excessive alcohol intake should be avoided, since this has been found to decrease the bone density and increase the risk of falls [164-167]. Also, optimising treatment of and eliminating secondary causes of osteoporosis, such as corticosteroid use, hypogonadism and primary hyperparathyroidism are important steps in prevention.

Hip fractures very rarely occur without a preceding fall (in about 2%), and prevention of the number and severity of falls in elderly people is therefore likely to be effective in prevention of hip fractures [168].

Currently used pharmaceutical agents for prevention or treatment of osteoporosis have an antiresorptive action. From epidemiological studies the preventive effect of oestrogens on the risk of hip fracture is well documented [169-172]. In randomised placebo-controlled trials antiresorptive drugs such as Alendronate and Risendronate, as well as a combination of calcium and vitamin D, have proven effective in increasing BMD and preventing future hip fractures [173-176].

Altogether, it is probable that the most successful prevention of hip fractures is achieved through a multidimensional approach. At the population level, preventive measures must be cheap, readily available and acceptable, such as exercise, cessation of smoking and reduction of alcohol abuse. Among individuals at high risk, the prevention can be targeted.

**Prevention of hip fractures with external hip protectors**

In the pathogenesis of hip fractures, the falling mechanism, impact energy, energy absorption capacity of the trochanteric soft tissue, and bone strength have been reported as main determinants of hip fracture [121, 124, 125, 127, 131, 149, 177-180]. In a recent study by Parkkari et al, 81% of the hip fracture patients stated that the main impact
during the fall was directed towards the greater trochanter, and in 56% of the patients a fresh haematoma was observed over the greater trochanter. It was also found that most elderly fallers did not manage to break the fall, for example with an outstretched arm [131]. Most hip fractures are caused by a sideways fall with a direct impact on the greater trochanter [121, 122, 124, 127, 131, 155, 177-179, 181]. In 25% the result of such a sideways fall is a hip fracture, whereas less than 2% of all falls result in a hip fracture [80, 121, 132, 144].

The thickness of the soft tissue covering the trochanter is linearly correlated to the body mass index (BMI) [182]. Experimental studies [177, 183] have shown that this soft tissue improves energy absorption during a fall, and thereby allows less energy to be transmitted to the proximal femur. These findings might partly explain the reduced risk of hip fracture in elderly women who are overweight [124, 125, 127, 177, 184]. The higher bone density found in overweight women may also of course be relevant [185, 186].

Moreover, one must also bear in mind that there may be great variation in the thickness and energy absorptive capacity of the soft tissue covering the hip [182]. The majority of hip fractures occur in elderly individuals whose BMD is already below the theoretical fracture threshold [127, 155], and interventions directed at factors unrelated to bone mass, such as falls, may be an effective alternative or complement to pharmacological treatment. One example is the use of external hip protectors.

An external hip protector can attenuate the impact force delivered to the proximal femur in a fall either by absorbing the impact energy or by shunting the impact energy away from the greater trochanter to surrounding tissues anterior-posterior and superior to the proximal femur, or by both these mechanisms. The greatest reduction in peak femoral impact force has been found to be produced by an energy shunting pad (65% reduction); this is better than the force reduction provided by the best energy absorbing pad (approximately 33% reduction) [183]. Parkkari et al found that with use of various hip-padding materials of reasonable thickness, it was impossible to lower the femoral impact force to below the theoretical fracture threshold [187]. The energy shunting mechanism of the hip protector is thus more effective than the absorptive mechanism in attenuating impact energy, as has been established in vitro in studies with simulated falling conditions in the elderly [188].
Only modest rates of compliance to hip protectors (27-68%) have been reported [144, 189-191], which is a problem, since the effect of the external hip protector is highly dependent on compliance.
AIMS OF THE STUDY

This thesis focuses on bone densitometry as a method for hip fracture assessment and mortality risk assessment and for evaluation of the prevalence of osteoporosis. Three different densitometric techniques at four different anatomical sites were utilised and compared. The studies were conducted in two different kinds of elderly populations: one relatively healthy population, possibly suitable for early detection of the risk of hip fracture, and the other a nursing home population with considerably high morbidity and high risk of hip fracture. In addition, the effects of intervention with an external hip protector to prevent hip fractures were evaluated in a nursing home population.

The specific aims of the different studies were as follows:
- To investigate and compare the capability of three different bone densitometry techniques in a relatively healthy population of independently living elderly persons who would be likely to benefit most from treatment and would possibly be suitable for screening. Subjects with a first hip fracture were compared with age- and gender-matched, randomly selected controls without previous hip fractures (papers I and II).
- To investigate the use of the three different bone densitometry techniques and the role of hip fracture in mortality risk assessment (paper III).
- To study and evaluate ultrasound measurements of the fingers and the heel bone in an elderly, mostly non-ambulant population of nursing home residents with an expected high risk of fractures, and to estimate the prevalence of osteoporosis as measured by these techniques in this population. A further aim was to evaluate the association between heel and finger QUS results and clinical risk factors for osteoporosis (paper IV).
- To study the preventive effect of the use of external hip protectors on the risk of hip fracture in nursing home residents (paper V).

SUBJECTS, METHODS AND CALCULATIONS

Studies I-II: These were population-based studies with an observational case-control design in which three different techniques of bone densitometry, applied at four anatomical sites were studied in hip fracture cases and controls. All men and women with a first hip fracture who met the inclusion criteria and who agreed to participate
were included. Inclusion criteria were: non-institutionalised subject, 65-85 years of age, of Swedish Caucasian origin, living in the municipality of Uppsala, with no previous or on-going bone-specific therapy, and no previous hip joint replacement or lower limb amputation. Patients with hip fractures due to malignancy or high-energy trauma and those who could not be examined during the first week after the fracture event because of death or serious medical conditions were not considered eligible. Uppsala University Hospital is responsible for all hip fracture surgery not only in residents of the municipality of Uppsala but also in more than 75% of the county population. Potential controls were randomly selected from the population register of the municipality of Uppsala and frequency-matched (two controls/ one case) to the expected age-distribution of cases within each 5-year age group. The inclusion criteria for patients and controls were identical, apart from the presence of an incident first hip fracture among cases. The study was conducted over a period of 28 months, from November 1995 to February 1998. Of 46 eligible male cases with a first hip fracture, 31 (67%) underwent bone densitometry. Of 117 eligible female cases, 87 (74%) were examined. Thus in a total of 45 (30 women and 15 men) out of 163 eligible cases no bone densitometry was performed. 16 because of lack of personnel; the remaining 29 declined to participate. Of the controls selected, 68% of the men and 72% of the women agreed to undergo bone densitometry. Reasons for non-participation were medical reasons, refusal, non-attendance or travel reasons.

The protocol for all patients and controls included DXA of the proximal femur, QUS of the heel and fingers, and RA of the fingers.

**DXA** was performed on the proximal femur using a DPX-L™ apparatus (Lunar Co, Madison, WI, USA). Bone mineral density, expressed in g/cm², was measured in the non-fractured proximal femur in the patients and in the left proximal femur in the controls. The DPX-L equipment provides results for three hip regions of interest: the neck, Ward’s triangle and the trochanter region. The manufacturer’s reference population was used for calculation of an individual T-score for BMD-DXA. The precision error for BMD in g/cm², estimated as the coefficient of variation (CV) as tested on a spine phantom, was less than 1% during the study period.

**Heel QUS** measurements were performed with an Achilles+™ ultrasound apparatus (Lunar Co, Madison, WI, USA) [111, 192, 193], on the non-dominant heel when possible. The results are expressed as the speed of sound (m/s), broad band ultrasound attenuation (dB/MHz), and stiffness index (%). The manufacturer’s reference population
for stiffness index was used to calculate the stiffness index T-score. The precision error for Achilles+™ was tested with five repeated measurements on ten individuals. The CV values for stiffness index, SOS and BUA were 2.5%, 0.2%, and 2.6%, respectively.

For finger QUS, the amplitude-dependent ultrasound velocity, expressed as amplitude-dependent speed of sound (AD-SOS m/s) through the proximal phalanges of the fingers [111, 194] was measured with a DBM Sonic 1200™ (IGEA, Carpi, Italy). This device consists of a central unit and an electronic caliper. Measurements were made on the distal metaphysis of the proximal phalanges of the fingers (not the thumb) of the non-dominant hand. The mean AD-SOS of the fingers (digits 2-5) was calculated. The manufacturer's reference population for calculation of AD-SOS finger T scores was used, but this was only possible for women, since no reference population for men was available. Before commencement of the study, reliability measurements were performed. The CV for AD-SOS was 0.9 % for three repeated daily measurements in ten subjects.

Radiographic absorptiometry (Osteogram™), was performed for subsequent measurements on X-ray films. The non-dominant hand was examined, using films without a screen, by a conventional X-ray unit. Exposures were chosen by CompuMed™ after testfilms were evaluated by CompuMed™. The results were given for the middle phalanges of digits 2-4. A manufacturer-specific aluminium wedge was used as reference phantom. The X-ray film could not be automatically processed in a standard rapid processor, but had to be manually de-wrapped in a dark-room and processed in a slow processor in order to minimise the risk of film artifacts. Developed films were sent to CompuMed™, Manhattan Beach, CA, USA. The films were digitised by the Osteogram Analysis Center (El Segundo, CA, USA) using a Lumisys (Sunnyvale, CA, USA) Model 75 laser film digitizer, and regions of interest were identified, i.e. the middle phalanx of the index, third and fourth fingers. The results are presented as an average for digits 2-4 in aluminium equivalent units, AU [195]. The manufacturer's reference population was used to calculate the T-score for finger RA. The precision error for repeated measurements of BMD-AU by RA has been reported to be 0.6% [102].

Weight was measured on a standard analogue scale and height with a ruler in patients (the patients were often unable to assume a fully upright position) and a stadiometer in
controls. All patients were examined within the first week after the hip fracture event, most often within four days.

Adjusted mean bone density values were computed on the basis of the regression estimates with age and weight held at their mean values, by using the General Linear Models procedure of the statistical package SAS. All p values for differences between cases and controls are two-tailed. A p value of <0.05 was adopted as statistically significant.

We used odds ratios and 95% confidence intervals calculated by unconditional logistic regression as measures of association between bone density values, expressed both in original continuous form divided by the standard deviation among the controls and in categorised form, and hip fracture risk. Both univariate and odd ratios (OR), adjusted for age (65-70, 71-75, 76-80, 81-85 years) and weight according to the quartile distribution of the controls, are presented.

The patients and controls were classified according to the WHO criteria for osteopenia and osteoporosis and the sensitivity and specificity at this cut-off were calculated. In addition, and in the study of women (study I), in analysing the area under receiver-operating curves (ROC; MedCalc version 4.20), we identified each method’s optimal T-score for discriminating cases from controls. On the basis of the cases and controls in whom all four measurements were performed, we analysed the ROC area for each bone density method and estimated the differences between these areas.

**Study III:** All Swedish citizens are uniquely identified by a national ten-digit identification number. The included cases and controls in study I and II (Cohort A) were followed up for the occurrence of death up to December 1st, 2000 by matching to the continuously updated Swedish national registration through their individual identification numbers.

**Cohort B.** All non-responding and non-eligible hip fracture patients, of ages 65-85 years who presented with a hip fracture from November 1995 through February 1998, who were not included in cohort A (n=233), were also followed up to the time of death through November 2000 by use of the national identification number and the Swedish national registration. We excluded from the analyses 18 subjects who had had a pathological fracture, two who were not native born in Sweden, one with a high-energy trauma as the cause of the hip fracture, and one who was living abroad.
One hundred of those included in cohort B were institutionalised, 45 were non-responders to cohort A and the remainder were non-eligible for cohort A by reason of several different exclusion criteria.

As measures of associations, rate ratios (RRs) and 95% confidence intervals were computed by Cox’s proportional hazards model using Proc Phreg in SAS (SAS Release 6.12). The follow-up time was calculated from the day of fracture in cases and from the day of bone density measurement in controls to the day of censoring by death or in the case of survival, until November 30th, 2000. We estimated RRs for mortality of fracture status in an age-adjusted model and in a multivariate model including age in four classes (<71, 71-75, 76-80 and >80 years), body mass index (by quartiles of the controls), sex and bone mineral density of the femoral neck (continuous). Categorisation of age into six classes and bone density in categories revealed similar risk estimates. Additionally, we separately calculated RRs by sex and hip fracture type (trochanteric or femoral neck). To estimate the proportion of mortality due to hip fracture, we determined the attributable risk by: \( p \frac{(RR-1)}{1 + p(RR-1)} \) where \( p \) is the proportion of cases in cohort A and RR is the rate ratio of mortality for fracture patients.

Survival was presented graphically using Kaplan-Meier curves. The differences in survival probabilities between fracture patients and controls (cohort A) and those between institutionalised and non-institutionalised patients (cohort B) were compared by log-rank statistics. Curves to describe the expected survival of the respective cohorts were calculated by using life tables for 1995-1999 published by Statistics Sweden. We assumed that the expected survival in the municipality of Uppsala was similar to that in the Swedish population. The influence of bone density, measured by the different techniques, on the risk of mortality in cases and controls separately, was estimated and expressed in RRs per standard deviation decrease in bone density both by an age-adjusted model and a multivariate model with age, sex and body mass index as covariates.
Study IV: In a cross-sectional study, QUS of the heel (Achilles+™) and fingers (DBM Sonic 1200™) was performed in nursing home residents. The subjects were recruited from and investigated at four nursing homes, to which they had been admitted because of a need for care. Out of 584 residents, 366 were chosen at random, and invited to take part in the investigation. Of these, 45 did not want to participate or were otherwise not co-operative (the majority of these persons were senile or in a terminal stage). Thus 321 residents (237 women and 84 men) gave informed consent and were included in the study. All measurements were performed at the nursing homes, between November 1995 and April 1997. In the absence of any accepted criterion for QUS and for the anatomical sites heel and fingers, the WHO criterion for osteoporosis was applied for stiffness index of the heel and SOS of the fingers in the women, in order to classify them as osteoporotic or not. The same cut-off was used for stiffness index of the heel in the men, but using a male reference population. For each resident the following information was also collected: duration of stay at the nursing home, current weight (based on nurse’s records), medication, walking ability, number of falls registered during the study period, and previous fractures of osteoporotic origin. Information on the occurrence of previous osteoporotic fractures was obtained for the past (30 years). Eighty per cent of the residents were followed up for the entire 18-month period and 20% died before the end of this period. BMI and height were not included in the calculations, because of difficulties in measuring height accurately.

Pearson product-moment correlation coefficients were used to study relationships between stiffness, SOS and BUA of the heel and SOS of the fingers. The associations between QUS measurements and weight (continuous), age (continuous), walking ability (no/yes) and previous osteoporotic fractures (no/yes) were determined by simple and multiple linear regression analyses. In addition, the coefficient of determination ($R^2$), was used to characterise the multivariate models. Odds ratios and 95% confidence intervals were computed by unconditional logistic regression as measures of association between a previous osteoporotic fracture and the explanatory variables. In the multivariate logistic regression model we included walking ability (no/yes), number of falls during the study period, ultrasound measures (either BUA, SOS or stiffness of the heel, or SOS at finger ultrasound), weight and age (all in continuous form) as explanatory variables. No additional information was gained by categorisation of the continuous variables by tertiles. Adjusted mean QUS parameters for men and women were also calculated by the least square means option of General Linear Models by
introducing gender into the model together with the covariates age and weight. The estimated QUS values were calculated with the covariates set to their mean value.

**Study V:** In a randomised controlled intervention study in nursing home residents, the preventive effect of external hip protectors on the hip fracture risk was investigated. One of the homes with 302 residents (197 women and 105 men) during the study period was selected randomly and the residents were offered the opportunity of wearing external hip protectors. The three nursing homes where the controls resided had 442 residents (318 women and 124 men) during the same period. The total numbers of subjects in the study groups were constant since new residents replaced subjects who had died. The four nursing homes were the same four as in study IV.

Prior to the study all caregivers in the four nursing homes were given the same introductory session, where they received information on osteoporosis and hip fractures and on risk factors for osteoporosis and hip fractures and on recording of falls. The age and weight of all residents and the duration of their stay at the nursing home were recorded. Any history of previous fractures (hip, distal radius, proximal humerus, fractures of the ramii and vertebral fractures) and total hip replacements recorded within at least the last 10 years, according to medical records from the Department of Orthopedics or the Department of Radiology at the University Hospital, Uppsala, was documented for all residents. The number of hips at risk, i.e. hips that were not fractured or had undergone hip replacement and therefore were at risk for hip fractures, was calculated. The ability to walk 30 metres, with or without a walking aid, was documented. The use of drugs was recorded, with emphasis on bone-specific treatment, i.e. oestrogen, vitamin D and calcium, calcitonin, bisphosphonates, and use of sedatives (including drugs with sedation or dizziness as side-effects) and hypnotics. A record was made of all falls in the four nursing homes occurring during the period 20-month from 1st May 1996 to 31st January 1998, and of where, when, injury if present, and if possible how they occurred. Recording of falls was initiated 9 months before commencement of the study of external hip protectors. The rationale for this was to train the nursing home staff in fall recording. Recording of accidental falls and compliance in the intervention group was done by nursing home staff and the records were collected every month during the 11-month study period.

The external hip protector (JOFA AB, Malung, Sweden) was placed lateral to the area of the greater trochanter, in a pair of ordinary underwear, without any special fixation. The
mechanism is theoretically energy shunting, diverting the direct impact away from the trochanter area during a fall. The protector is 17 cm long, 12 cm wide and has a maximum depth in the middle of 3.5/4 cm (medium/large). The outer shield is made of 2.5 mm thick polyethylene and the inner energy-absorbing part of 6 mm thick plastatzote (Figure 1).

Odds ratios and 95% confidence intervals calculated by unconditional logistic regression were used as measure of association between use of external hip protector and hip fracture risk, adjusted by sex and age in categories (<60, 61-70, 71-80, >80 years). Adjustments for time spent at the nursing homes, number of hips at risk, walking ability, and frequency of falls or previous fractures did not alter the relative risk substantially when included in the model.
Figure 1. The external hip protector, placed in a pair of ordinary underwear, without any special fixation.
RESULTS

Study I, Women:
Fractures of the femoral neck were slightly more common than trochanteric fractures, occurring 55% as against 45%. Table 1 shows the studied anthropometric characteristics and quantitative bone properties of patients and controls.

The mean bone measurement values obtained at DXA of the proximal femur and QUS of the heel were significantly lower in the cases than in the controls. In contrast, the results of bone densitometry at non-weight-bearing sites, QUS and RA of the phalanges proved incapable of separating fracture from non-fracture subjects.

The cumulative T-scores in cases and controls are presented in Figure 2. On average compared to the controls, the cases had a more than one T-score lower value both at the femoral neck and at the heel, but the differences in finger values were small. T-scores for DXA of the femoral neck were shifted to higher values than with the other three methods of bone measurement. Using the WHO classification of osteoporosis, BMD of the femoral neck identified 62% of the female fracture cases and 19% of the controls as osteoporotic. The corresponding figures for heel ultrasound were 98% and 72%, finger ultrasound 80% and 85%, and RA of the fingers 60% and 51%, respectively.

In the ROC analyses, DXA of the femoral neck, trochanter and ward and heel BUA and stiffness proved more effective in discriminating the hip fracture patients from the controls (Table 2). The diagnostic sensitivities and specificities with the four methods at different cut-off levels are shown in Table 3. None of the methods showed both high sensitivity and high specificity. The sensitivity and specificity at specific T-score levels differed notably between the methods. On the basis of the optimal T-score level, only DXA of the hip was near to the WHO definition of osteoporosis (Table 3).

The linear risk of hip fracture per each SD decrease in bone quantitative properties, both as unadjusted odds ratios and as estimates adjusted for both weight and age (Table 4), was more than tripled for every SD decrease in both femoral neck and heel values. No significant increase in risk was found in relation to finger measurements, either with QUS or RA. Both the stiffness index and BUA, but not SOS, of the heel were associated with a hip fracture risk independently of DXA of femoral neck.

In the non-linear analysis the risk of hip fracture was determined by using the cut-off level for normal BMD, according to the WHO classification, for a categorised analysis of femoral neck DXA-BMD. Compared to individuals classified as normal, those classified as osteopenic (T-scores between -1 and -2.5) had an odds ratio for hip fracture
of 14 (95% CI 2-110), whereas those classified as osteoporotic (T-score of -2.5 or less) had an odds ratio of 63 (95% CI 8-501).
Figure 2. Cumulative T-scores in cases with a first incident hip fracture and controls investigated by DXA of the proximal femur, QUS of the heel and finger phalanges and RA of the finger phalanges.
### Table 1. Descriptive characteristics of female hip fracture cases and controls

<table>
<thead>
<tr>
<th></th>
<th>Cases n=87</th>
<th>Controls n=195</th>
<th>Adjusted mean*</th>
<th>p value*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (years)</strong></td>
<td>76.0 (5.2)</td>
<td>74.5 (4.6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Weight (kg)</strong></td>
<td>61.0 (10.2)</td>
<td>68.1 (12.0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Height (cm)</strong></td>
<td>161.5 (6.3)</td>
<td>160.2 (5.9)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>BMI (kg/m²)</strong></td>
<td>23.3 (3.6)</td>
<td>26.6 (4.8)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DXA neck (g/cm²)</td>
<td>0.64 (0.11)</td>
<td>0.79 (0.12)</td>
<td>0.78</td>
<td>0.0001</td>
</tr>
<tr>
<td>Neck T-score</td>
<td>-2.8 (0.9 )</td>
<td>-1.6 (1.0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neck Z-score</td>
<td>-0.9 (0.8)</td>
<td>0.06 (0.9)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DXA Ward (g/cm²)</td>
<td>0.49 (0.12)</td>
<td>0.65 (0.15)</td>
<td>0.64</td>
<td>0.0001</td>
</tr>
<tr>
<td>Ward T-score</td>
<td>-3.3 (0.9)</td>
<td>-2.0 (1.2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DXA troc (g/cm²)</td>
<td>0.59 (0.11)</td>
<td>0.73 (0.14)</td>
<td>0.72</td>
<td>0.0001</td>
</tr>
<tr>
<td>Troc T-score</td>
<td>-1.8 (1.0)</td>
<td>-0.6 (1.2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stiff. index heel (%)</td>
<td>54.9 (10.9)</td>
<td>67.2 (14.4)</td>
<td>66.9</td>
<td>0.0001</td>
</tr>
<tr>
<td>Stiff. index T-score</td>
<td>-4.1 (1.0)</td>
<td>-3.0 (1.3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stiff. index Z-score</td>
<td>-1.3 (1.0)</td>
<td>-0.3 (1.2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BUA heel (dB/MHz)</td>
<td>93.5 (10.2)</td>
<td>103.8 (10.3)</td>
<td>103.5</td>
<td>0.0001</td>
</tr>
<tr>
<td>SOS heel (m/s)</td>
<td>1473 (21)</td>
<td>1493 (30)</td>
<td>1493</td>
<td>0.0001</td>
</tr>
<tr>
<td>SOS finger (m/s)</td>
<td>1860 (91)</td>
<td>1850 (92)</td>
<td>1852</td>
<td>0.16</td>
</tr>
<tr>
<td>SOS finger T-score</td>
<td>-3.8 (1.3)</td>
<td>-3.9 (1.3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SOS finger Z-score</td>
<td>-0.6 (1.3)</td>
<td>-0.5 (3.8)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>RA (AU)</td>
<td>79.5 (13.9)</td>
<td>82.6 (12.6)</td>
<td>82.2</td>
<td>0.41</td>
</tr>
<tr>
<td>RA T-score</td>
<td>-0.1 (1.1)</td>
<td>0.08 (1.1)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Adjusted for age and weight in continuous form
Table 2. Area under ROC curve for DXA of the hip, QUS of the heel, SOS of the fingers, and RA of the fingers, and area differences between the femoral neck and the other sites

<table>
<thead>
<tr>
<th></th>
<th>ROC area</th>
<th>Area difference from neck</th>
<th>p-value</th>
</tr>
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<tbody>
<tr>
<td>Neck BMD</td>
<td>0.80</td>
<td></td>
<td></td>
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<tr>
<td>Ward’s BMD</td>
<td>0.79</td>
<td>0.01</td>
<td>0.32</td>
</tr>
<tr>
<td>Trochanter BMD</td>
<td>0.79</td>
<td>0.01</td>
<td>0.70</td>
</tr>
<tr>
<td>Stiffness, heel</td>
<td>0.76</td>
<td>0.04</td>
<td>0.12</td>
</tr>
<tr>
<td>BUA, heel</td>
<td>0.76</td>
<td>0.04</td>
<td>0.18</td>
</tr>
<tr>
<td>SOS, heel</td>
<td>0.71</td>
<td>0.09</td>
<td>0.004</td>
</tr>
<tr>
<td>SOS, phalanges</td>
<td>0.52</td>
<td>0.28</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>RA</td>
<td>0.58</td>
<td>0.22</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Table 3. Sensitivity and specificity at various T-score cut-off levels, and optimal cut-off T-score levels for the four different methods of bone measurement

<table>
<thead>
<tr>
<th>T-score</th>
<th>DXA femoral neck</th>
<th>Heel stiffness</th>
<th>SOS phalanges</th>
<th>RA phalanges</th>
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<tr>
<td></td>
<td>Sensitivity</td>
<td>Specificity</td>
<td>Sensitivity</td>
<td>Specificity</td>
</tr>
<tr>
<td>-3.5</td>
<td>25</td>
<td>97</td>
<td>71</td>
<td>66</td>
</tr>
<tr>
<td></td>
<td>42</td>
<td>61</td>
<td>37</td>
<td>78</td>
</tr>
<tr>
<td>-2.5</td>
<td>62</td>
<td>80</td>
<td>98</td>
<td>28</td>
</tr>
<tr>
<td></td>
<td>18</td>
<td>85</td>
<td>61</td>
<td>49</td>
</tr>
<tr>
<td>-2.0</td>
<td>79</td>
<td>68</td>
<td>99</td>
<td>20</td>
</tr>
<tr>
<td></td>
<td>11</td>
<td>92</td>
<td>78</td>
<td>29</td>
</tr>
<tr>
<td>-1.0</td>
<td>99</td>
<td>25</td>
<td>100</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>100</td>
<td>95</td>
<td>9</td>
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</table>

Optimal -2.2 -3.4 -4.0 -3.0

Cut-off

<table>
<thead>
<tr>
<th></th>
<th>Sensitivity</th>
<th>Specificity</th>
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<tbody>
<tr>
<td></td>
<td>76</td>
<td>74</td>
</tr>
<tr>
<td></td>
<td>75</td>
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<td>63</td>
<td>48</td>
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<tr>
<td></td>
<td>58</td>
<td>63</td>
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Table 4. Risk of hip fracture per one SD reduction in bone measurement values

<table>
<thead>
<tr>
<th></th>
<th>Univariate model</th>
<th>Adjusted model*</th>
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<tbody>
<tr>
<td></td>
<td>OR</td>
<td>95% CI</td>
</tr>
<tr>
<td>BMD fem. neck</td>
<td>3.6</td>
<td>2.6-5.2</td>
</tr>
<tr>
<td>BMD Ward’s</td>
<td>3.7</td>
<td>2.6-5.5</td>
</tr>
<tr>
<td>BMD trochanter</td>
<td>3.5</td>
<td>2.4-5.0</td>
</tr>
<tr>
<td>Heel, stiffness</td>
<td>3.2</td>
<td>2.2-4.6</td>
</tr>
<tr>
<td>BUA, heel</td>
<td>3.0</td>
<td>2.2-4.2</td>
</tr>
<tr>
<td>SOS, heel</td>
<td>2.6</td>
<td>1.8-3.7</td>
</tr>
<tr>
<td>SOS, phalanges</td>
<td>0.90</td>
<td>0.7-1.2</td>
</tr>
<tr>
<td>RA, phalanges</td>
<td>1.3</td>
<td>1.0-1.7</td>
</tr>
</tbody>
</table>

*Adjusted for age (<71, 71-75, 76-80, >80 years) and weight (quartiles)
**Study II, Men:**

Fractures of the femoral neck were also somewhat more frequent in the male cases, 18/31 had a femoral neck fracture and 13/31 a trochanteric fracture. Lower mean bone quantitative values were observed in hip fracture cases than in controls for all four techniques (Table 5).

When the WHO criterion for osteoporosis was applied, femoral neck BMD identified 58% of the men with fractures and 15% of the controls as osteoporotic. The corresponding results for heel QUS were 43% and 23%, and for RA of the fingers 50% and 16%, respectively. Since no male reference population was available at the time for the study, this calculation was not possible for the finger QUS measurements.

The ROC areas varied from 0.68 to 0.80; BUA heel having the lowest value and DXA of the femoral neck the highest (Table 6), although the differences between the four methods were not statistically significant.

Evaluation of the risk of hip fracture per each SD decrease in bone density values, expressed both as unadjusted odds ratios and as estimates adjusted for weight and age (Table 7) showed a four-fold increase in this risk for every SD decrease in DXA femoral neck values. Neither heel QUS nor finger densitometry was found to be independently (of femoral neck BMD) capable of predicting hip fractures in the male fracture cases.

In the non-linear analysis (Table 8) the risk of hip fracture was additionally determined by using the cut-off level for normal BMD of the femoral neck (T-score above –1) as the reference. Those subjects classified as osteopenic (T-scores between -1 to -2.5) had an odds ratio of hip fracture of 3.6 (95% CI 0.7-19.8), whereas those classified as osteoporotic (T-score of -2.5 or less) had an odds ratio of 21.5 (95% CI 3.6-127.9).
### Table 5. Descriptive characteristics of male cases and controls

<table>
<thead>
<tr>
<th></th>
<th>Cases</th>
<th></th>
<th>Controls</th>
<th></th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n mean (SD)</td>
<td>Adjusted mean*</td>
<td>n mean (SD)</td>
<td>Adjusted mean*</td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>31 77.2 (5.6)</td>
<td></td>
<td>68 74.4 (4.9)</td>
<td></td>
<td>0.01</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>31 77.5(10.1)</td>
<td></td>
<td>68 78.7 (11.8)</td>
<td></td>
<td>0.65</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>31 176.9 (6.8)</td>
<td></td>
<td>68 172.6 (6.4)</td>
<td></td>
<td>0.003</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>31 24.7 (2.7)</td>
<td></td>
<td>68 26.4 (3.6)</td>
<td></td>
<td>0.002</td>
</tr>
<tr>
<td>DXA neck</td>
<td>31 0.75 (0.12)</td>
<td>0.76</td>
<td>68 0.90 (0.13)</td>
<td>0.90</td>
<td>0.0001</td>
</tr>
<tr>
<td>Neck T-score</td>
<td>31 -2.6 (0.95)</td>
<td>-2.52</td>
<td>68 -1.4 (1.12)</td>
<td>-1.46</td>
<td>0.0001</td>
</tr>
<tr>
<td>Neck Z-score</td>
<td>31 -1.0(0.9)</td>
<td></td>
<td>68 0.04(1.0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DXA ward</td>
<td>31 0.55 (0.12)</td>
<td>0.56</td>
<td>68 0.73 (0.15)</td>
<td>0.72</td>
<td>0.0001</td>
</tr>
<tr>
<td>Ward’s T-score</td>
<td>31 -3.10(0.94)</td>
<td>-3.01</td>
<td>68 -1.78(1.23)</td>
<td>-1.81</td>
<td>0.0001</td>
</tr>
<tr>
<td>DXA troch</td>
<td>31 0.74 (0.15)</td>
<td>0.75</td>
<td>68 0.88 (0.14)</td>
<td>0.87</td>
<td>0.0001</td>
</tr>
<tr>
<td>Troch T-score</td>
<td>31 -1.64(1.3)</td>
<td>-1.59</td>
<td>68 -0.48(1.3)</td>
<td>-0.50</td>
<td>0.0001</td>
</tr>
<tr>
<td>Stiff. index heel</td>
<td>28 71.6 (14.4)</td>
<td>73.7</td>
<td>65 84.0 (16.1)</td>
<td>83.1</td>
<td>0.011</td>
</tr>
<tr>
<td>Stiff. index T-score</td>
<td>28 -2.6 (1.3)</td>
<td>-2.4</td>
<td>65 -1.5 (1.5)</td>
<td>-1.5</td>
<td>0.012</td>
</tr>
<tr>
<td>Stiff. index Z-score</td>
<td>28 -1.3(1.2)</td>
<td></td>
<td>65 -0.1(1.5)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BUA, heel</td>
<td>28 108.9 (11.4)</td>
<td>109.9</td>
<td>64 116.0 (10.2)</td>
<td>115.6</td>
<td>0.023</td>
</tr>
<tr>
<td>SOS, heel</td>
<td>28 1496.7 (31.7)</td>
<td>1501.8</td>
<td>65 1524.1</td>
<td>1521.9</td>
<td>0.015</td>
</tr>
<tr>
<td>(36.1)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SOS, finger</td>
<td>30 1835.8 (106.7)</td>
<td>1838.9</td>
<td>68 1912.5</td>
<td>1911.1</td>
<td>0.006</td>
</tr>
<tr>
<td>(118.2)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RA</td>
<td>22 82.2 (12.4)</td>
<td>84.1</td>
<td>67 96.3 (16.9)</td>
<td>95.7</td>
<td>0.005</td>
</tr>
<tr>
<td>RA, finger T-score</td>
<td>22 -2.4 (0.9)</td>
<td>-2.3</td>
<td>67 -1.4 (1.2)</td>
<td>-1.4</td>
<td>0.006</td>
</tr>
<tr>
<td>RA, finger Z-score</td>
<td>22 -0.4(1.0)</td>
<td></td>
<td>67 0.6(1.5)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Adjusted for age and weight in continuous form
Table 6. Area under the ROC curve for DXA of the hip, QUS of the heel, SOS of the fingers and RA of the fingers

<table>
<thead>
<tr>
<th></th>
<th>ROC area</th>
<th>95 % CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fem. neck BMD</td>
<td>0.80</td>
<td>0.70-0.87</td>
</tr>
<tr>
<td>Ward’s BMD</td>
<td>0.80</td>
<td>0.70-0.87</td>
</tr>
<tr>
<td>Trochanter BMD</td>
<td>0.73</td>
<td>0.63-0.82</td>
</tr>
<tr>
<td>Stiffness heel</td>
<td>0.69</td>
<td>0.59-0.78</td>
</tr>
<tr>
<td>BUA heel</td>
<td>0.68</td>
<td>0.57-0.77</td>
</tr>
<tr>
<td>SOS heel</td>
<td>0.71</td>
<td>0.61-0.80</td>
</tr>
<tr>
<td>SOS phalanges</td>
<td>0.69</td>
<td>0.64-0.83</td>
</tr>
<tr>
<td>RA</td>
<td>0.75</td>
<td>0.59-0.78</td>
</tr>
</tbody>
</table>

Table 7. Risk of hip fracture per one SD reduction in bone measurement values

<table>
<thead>
<tr>
<th></th>
<th>Univariate model</th>
<th>Adjusted model*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR</td>
<td>95% CI</td>
</tr>
<tr>
<td>Neck BMD</td>
<td>4.0</td>
<td>2.0-7.7</td>
</tr>
<tr>
<td>Ward BMD</td>
<td>4.0</td>
<td>2.1-7.8</td>
</tr>
<tr>
<td>Trochanter BMD</td>
<td>2.6</td>
<td>1.6-4.4</td>
</tr>
<tr>
<td>Stiffness heel</td>
<td>2.2</td>
<td>1.2-3.9</td>
</tr>
<tr>
<td>BUA heel</td>
<td>1.9</td>
<td>1.1-3.1</td>
</tr>
<tr>
<td>SOS heel</td>
<td>1.9</td>
<td>1.2-3.1</td>
</tr>
<tr>
<td>SOS phalanges</td>
<td>2.0</td>
<td>1.2-3.3</td>
</tr>
<tr>
<td>RA</td>
<td>3.1</td>
<td>1.5-6.5</td>
</tr>
</tbody>
</table>

*Adjusted for age (<71, 71-75, 76-80, >80 years) and weight (quartiles)
<table>
<thead>
<tr>
<th>T-score</th>
<th>n cases</th>
<th>n controls</th>
<th>OR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neck BMD</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T-score &gt;-1</td>
<td>2</td>
<td>20</td>
<td>1.0</td>
<td>ref</td>
</tr>
<tr>
<td>-1 _ T score &gt;-2.5</td>
<td>11</td>
<td>38</td>
<td>3.6</td>
<td>0.7-19.8</td>
</tr>
<tr>
<td>T-score &lt;-2.5</td>
<td>18</td>
<td>10</td>
<td>21.5</td>
<td>3.6-127.9</td>
</tr>
</tbody>
</table>

*Adjusted for age (<71, 71-75, 76-80, >80 years) and weight (quartiles)
Study III:

Fracture patients and controls who had died during follow up were on average two years older than the non-deceased participants.

Cohort A. Forty-five individuals died during the follow-up period, with an uneven distribution between cases (n=28; 24%) and controls (n=17; 6%). The mean duration of observation was 3.6 years in cases and 4.0 years in controls, with a total of 413 and 1,036 total person-years of follow-up, respectively. An approximately linear relationship between mortality and time after study entry was found in both cases and controls. The survival curves are displayed in Figure 3. The mortality rate among hip fracture patients was 68/1,000 person-years, compared to 16/1,000 person-years among controls. The overall expected survival was intermediate between the rates observed for cases and controls (Figure 3), but since there was a difference in average age between cases and controls, subdivision of the expected survival curve by case-control status narrowed the respective expected to the observed curves (Figure 4). The overall age-adjusted relative risk of mortality was increased four-fold among hip fracture cases compared to controls (Table 9); a risk estimate which was not substantially influenced by adjustment for sex, body mass index and bone density at the femoral neck. The attributable age-adjusted risk was 0.57 (95% CI 0.52-0.62), i.e. 57% of the mortality observed among hip fracture cases was attributable to the fracture event. Replacement of bone density at the femoral neck in the multivariate model by either of the peripheral site methods gave somewhat stronger RRs (ranging from 4.5 to 5). There was no difference in risk increase between men and women after multivariate adjustments, but the relative risk of death in trochanteric hip fracture patients was twice as high as that in patients with fracture of the femoral neck. The RRs for mortality were similar between cases with low and high bone density and between those with low and high body mass index (stratification by median values of controls).

Bone density values were also analysed as predictors of mortality among both cases and controls (Table 10). No association was found for any of the techniques in cases, but there was a tendency, although not statistically significant, towards increased mortality with lower values for heel ultrasound and radiographic absorptiometry of the fingers.

Cohort B. The mean age of the cohort B members was 79 years, compared to 75 years in cohort A, a difference reflected by the steeper slope of the expected survival curve in Figure 5 compared to that in Figure 3. Twenty-four per cent of the hip fracture patients were admitted from institutions and they were found to have the highest post-fracture
mortality. Half of these cases had died within 2 years after the fracture, a value approximately four times as high as the expected one (Figure 5). Non-responding cases (n=45) had a probability of survival of approximately 60% after four years, which was similar to that of all other non-institutionalised attendees in cohort B, and they thus carried a higher risk of mortality than the responding cases in cohort A.
Figure 3. Survival curves of hip fracture cases (broken line) and controls (unbroken line) and expected survival (dotted line).

Figure 4. Survival curves of hip fracture cases (broken line), expected survival for cases (dotted line), controls (unbroken line) and expected survival for controls (dashed line).
Table 9. Risk of death among cases compared to controls, expressed as rate ratios (RR) with 95% confidence intervals (95% CI), after a first hip fracture

<table>
<thead>
<tr>
<th></th>
<th>Age-adjusted model*</th>
<th></th>
<th>Multivariate model**</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>RR 95% CI</td>
<td>RR 95% CI</td>
<td>RR 95% CI</td>
<td>RR 95% CI</td>
</tr>
<tr>
<td>Overall</td>
<td>4.0 2.2-7.5</td>
<td>3.4 1.7-7.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Women</td>
<td>4.5 2.1-9.6</td>
<td>3.4 1.4-8.2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>2.8 0.9-8.6</td>
<td>3.8 0.9-16.1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cervical type of hip fracture</td>
<td>3.0 1.5-6.3</td>
<td>2.6 1.1-6.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trochanteric type of hip fracture</td>
<td>6.4 3.0-13.7</td>
<td>5.4 2.2-13.0</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* With age categorised into 5-year age groups (<71, 71-75, 76-80, >80 years)
**Including as covariates: age (in 5-year age groups), body mass index (in quartiles of controls), bone mineral density of the femoral neck (in continuous form) and sex.

Table 10. Rate ratios (RR) of death for cases and controls per each SD decrease in bone density values.

<table>
<thead>
<tr>
<th></th>
<th>Cases</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Age-adjusted model*</td>
<td>Multivariate model**</td>
</tr>
<tr>
<td></td>
<td>RR 95% CI</td>
<td>RR 95% CI</td>
</tr>
<tr>
<td>Femoral neck BMD</td>
<td>1.0 0.6-1.6</td>
<td>1.0 0.6-1.6</td>
</tr>
<tr>
<td>Heel ultrasound</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BUA</td>
<td>1.0 0.7-1.5</td>
<td>1.2 0.7-1.7</td>
</tr>
<tr>
<td>SOS</td>
<td>0.7 0.4-1.2</td>
<td>0.7 0.4-1.2</td>
</tr>
<tr>
<td>Stiffness</td>
<td>0.9 0.6-1.4</td>
<td>0.9 0.5-1.5</td>
</tr>
<tr>
<td>RA</td>
<td>1.2 0.8-1.9</td>
<td>1.3 0.8-2.1</td>
</tr>
<tr>
<td>Finger ultrasound</td>
<td>1.0 0.7-1.5</td>
<td>1.1 0.7-1.6</td>
</tr>
</tbody>
</table>

* With age categorised into 5-year age groups (<71, 71-75, 76-80, >80 years)
**Including as covariates: age (in 5-year age groups) body mass index (in quartiles of controls) and bone mineral density of the femoral neck (in continuous form).
Figure 5. Survival curves of institutionalised hip fracture cases (broken line) and other non-included hip fracture cases (unbroken line) and expected survival (dotted line).
**Study IV:**

Altogether 82% (n=263) of the 321 eligible nursing home residents were investigated with QUS of the heel, 65%(n=209) with QUS of the fingers and 41%(n=132) measurements at both sites. Ninety-five per cent of the women who underwent heel QUS were classified as osteoporotic (mean T-score = -4.8) and 92% had Z-scores below zero (mean Z-score = -1.6), whereas the proportion of osteoporotic men was 51% (mean T-score = -2.6) and 77% had Z-scores below zero (mean Z-score = -1.3) (Table 11). Based on finger QUS measurements, 99% of the women were classified as osteoporotic (mean T-score -5.0) and 93% had Z-scores below zero (mean -1.6) (Table 11). The variations in ultrasound values were only moderately explained by age, current weight and walking ability. Bone-specific treatment was prescribed to 2.5% of the residents.

**Women:** In women the association between heel QUS and a prevalent osteoporotic fracture decreased by 43% (95% CI 10-63%) for every SD increase in SOS of the heel (a similar relationship was found for stiffness and BUA, data not shown), but no such relationship was found for finger SOS (Table 12).

The heel QUS values were significantly lower in women with a previous fracture, whereas finger ultrasound could not discriminate these women from those without previous fractures. Age, ability to walk and, to a lesser extent, current weight were also related to the QUS properties of the heel, but not to SOS of the fingers.

**Men:** In the multivariate analysis a statistically significant relationship emerged between finger SOS and previous fracture that was not seen in the women, whereas measurements at the heel showed a less pronounced association with previous fracture among the men. In the men, as in the women, a low body weight was associated with a previous osteoporotic fracture, and in the multivariate analysis it appeared that for every additional 10 kg of weight the association decreased by 52% (95% CI 9-75%). Walking ability was also related to a previous fracture in men, the association being almost four times stronger among those who were able to walk compared to non-walkers, and this again differed from the result in women (Table 13).
### Table 11. Quantitative ultrasound properties in the residents

<table>
<thead>
<tr>
<th></th>
<th>Women</th>
<th></th>
<th>Men</th>
<th></th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>mean</td>
<td>SD</td>
<td>n</td>
<td>mean</td>
</tr>
<tr>
<td>BUA heel</td>
<td>172</td>
<td>82.8</td>
<td>11.8</td>
<td>64</td>
<td>102.0</td>
</tr>
<tr>
<td>SOS heel</td>
<td>172</td>
<td>1473.4</td>
<td>23.9</td>
<td>64</td>
<td>1508.1</td>
</tr>
<tr>
<td>Stiffness heel</td>
<td>171</td>
<td>47.4</td>
<td>12.3</td>
<td>62</td>
<td>70.7</td>
</tr>
<tr>
<td>T-score heel</td>
<td>172</td>
<td>-4.8</td>
<td>1.1</td>
<td>62</td>
<td>-2.6</td>
</tr>
<tr>
<td>Z-score heel</td>
<td>171</td>
<td>-1.6</td>
<td>1.1</td>
<td>62</td>
<td>-1.3</td>
</tr>
<tr>
<td>SOS phalanges</td>
<td>153</td>
<td>1774.9</td>
<td>68.2</td>
<td>57</td>
<td>1799.6</td>
</tr>
<tr>
<td>T-score phalanges</td>
<td>151</td>
<td>-5.0</td>
<td>1.0</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Z-score phalanges</td>
<td>151</td>
<td>-1.6</td>
<td>1.1</td>
<td>NA</td>
<td>NA</td>
</tr>
</tbody>
</table>

*Adjusted for age and weight

### Table 12. Determinants of a previous osteoporotic fracture among women as analysed by logistic regression. All variables are included in the multivariate model

<table>
<thead>
<tr>
<th></th>
<th>Univariate model</th>
<th>Multivariate model</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Odds ratio</td>
<td>95% CI</td>
</tr>
<tr>
<td>Age (per 10 yrs)</td>
<td>0.94</td>
<td>0.69-1.27</td>
</tr>
<tr>
<td>Weight (per 10 kg)</td>
<td>0.79</td>
<td>0.62-1.01</td>
</tr>
<tr>
<td>SOS heel (per SD)</td>
<td>0.57</td>
<td>0.40-0.80</td>
</tr>
<tr>
<td>Able to walk (no/yes)</td>
<td>0.68</td>
<td>0.40-1.17</td>
</tr>
<tr>
<td>Number of falls during the study</td>
<td>1.02</td>
<td>0.95-1.09</td>
</tr>
</tbody>
</table>

### Table 13. Determinants of a previous osteoporotic fracture among men as analysed by logistic regression. All variables are included in the model

<table>
<thead>
<tr>
<th></th>
<th>Univariate model</th>
<th>Multivariate model</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Odds ratio</td>
<td>95% CI</td>
</tr>
<tr>
<td>Age (per 10 yrs)</td>
<td>1.14</td>
<td>0.66-1.96</td>
</tr>
<tr>
<td>Weight (per 10 kg)</td>
<td>0.81</td>
<td>0.51-1.27</td>
</tr>
<tr>
<td>SOS heel (per SD)</td>
<td>0.78</td>
<td>0.46-1.33</td>
</tr>
<tr>
<td>Able to walk (no/yes)</td>
<td>2.57</td>
<td>1.02-6.50</td>
</tr>
<tr>
<td>Number of falls during the study</td>
<td>1.02</td>
<td>0.88-1.20</td>
</tr>
</tbody>
</table>
Study V:
There was no difference in the distribution by gender between the intervention and control group. Among men the number of falls was somewhat higher in the control group than in the intervention group (p=0.048). Descriptive characteristics of the participants are presented in Table 14. In both men and women combined, there was a difference between the intervention and control group regarding falls; among the controls there were more falls (ns) and significantly (p=0.017) more frequent fallers (>5 times), and the duration of stay was longer (p=0.0008). No additional significant differences were observed between the groups.

In the control group 531 falls were recorded during the study period, compared to 294 in the group of residents who were offered hip protectors, including 80 falls with the protector in place. Thirty-three of these falls were verified with the occurrence of direct trauma to the trochanter region.

Twenty-one hip fractures were recorded during the study period, 17 of these among the control residents and four in the group offered hip protectors. No hip fracture occurred in hips protected by hip protectors. The relative risk of hip fracture in residents with hip protectors versus controls was 0.33 (CI 0.11-1.00), adjusted for sex and age in categories (less than 60, 61-70, 71-80, more than 80 years of age), a value similar to the crude estimate. Neither did the relative risk alter substantially when time spent at the nursing homes, number of hips at risk, walking ability, or the frequency of falls among the residents were included in the model (Table 15).

The overall average compliance to our device was 44% (Table 15). Major reasons for not wearing protectors were confinement to bed (50%) and skin irritation (2%).
Table 14. Descriptive characteristics of participants in the study of the effect of external hip protectors

<table>
<thead>
<tr>
<th></th>
<th>Women, controls n= 318</th>
<th>Women, hip protector n=197</th>
<th>Men, controls n= 124</th>
<th>Men, hip protector n= 105</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>85±8</td>
<td>85±9</td>
<td>81±8</td>
<td>81±11</td>
</tr>
<tr>
<td>Hips at risk</td>
<td>1.7</td>
<td>1.6</td>
<td>1.8</td>
<td>1.9</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>57±15</td>
<td>55±12</td>
<td>68±12</td>
<td>69±10</td>
</tr>
<tr>
<td>Prev. fracture</td>
<td>56%</td>
<td>58%</td>
<td>30%</td>
<td>37%</td>
</tr>
<tr>
<td>Prev. hip fracture</td>
<td>32%</td>
<td>39%</td>
<td>13%</td>
<td>14%</td>
</tr>
<tr>
<td>Time of stay (years)</td>
<td>2.8±2.9</td>
<td>2.1±2.6</td>
<td>2.2±2.4</td>
<td>1.2±1.4</td>
</tr>
<tr>
<td>Ambulant</td>
<td>28%</td>
<td>32%</td>
<td>22%</td>
<td>28%</td>
</tr>
<tr>
<td>Fall</td>
<td>36%</td>
<td>29%</td>
<td>31%</td>
<td>25%</td>
</tr>
<tr>
<td>&gt; 5 falls</td>
<td>8%</td>
<td>5%</td>
<td>5%</td>
<td>1%</td>
</tr>
</tbody>
</table>

Table 15. Women and men living at nursing homes. Background data and the effect of a hip protector in preventing hip fracture during an 11-month study period

<table>
<thead>
<tr>
<th></th>
<th>Offered n=302</th>
<th>Not offered n=442</th>
</tr>
</thead>
<tbody>
<tr>
<td>age, yrs</td>
<td>84±10</td>
<td>84±8</td>
</tr>
<tr>
<td>weight, kg</td>
<td>59±13</td>
<td>60±15</td>
</tr>
<tr>
<td>hips at risk</td>
<td>1.7±0.5</td>
<td>1.7±0.5</td>
</tr>
<tr>
<td>walker, yes/no</td>
<td>42%</td>
<td>37%</td>
</tr>
<tr>
<td>faller, yes/no</td>
<td>27%</td>
<td>34%</td>
</tr>
<tr>
<td>prev. fractures, yes/no</td>
<td>49%</td>
<td>47%</td>
</tr>
<tr>
<td>compliance</td>
<td>44%</td>
<td>-</td>
</tr>
<tr>
<td>hip fractures</td>
<td>4</td>
<td>17</td>
</tr>
<tr>
<td>Relative risk</td>
<td>0.33</td>
<td>1.0</td>
</tr>
</tbody>
</table>
DISCUSSION

Study I and II
In these population-based case-control studies among community-dwelling men and women, we compared four bone density techniques regarding their ability to discriminate cases with an incident first hip fracture from randomly selected controls. Both DXA of the proximal femur and QUS of the heel showed a high predictive value for an incident first hip fracture in women, and in men this was even more pronounced but only for DXA of the proximal femur. Bone densitometry at non-weight-bearing sites, i.e. QUS and RA of the phalanges, differed in performance between men and women. In women these methods were incapable of separating cases from controls, whereas in men they proved capable of such discrimination.

DXA of the proximal femur is regarded as the method of choice in bone densitometry for assessment of the hip fracture risk in women, since-site specific measurements have been found to be most effective [35]. Our study confirmed that DXA of the proximal femur is a powerful method for hip fracture risk assessment in men also, with at least of the same degree of ability as in women. A similar result was obtained in a Dutch prospective male cohort study, which showed an odds ratio for hip fracture of 3.0 per one standard deviation reduction in femoral neck BMD [92].

Finger QUS has been reported able to be capable of separating women with fragility fractures from women without fractures [196, 197], although specifically not for hip fractures. In our study of women with hip fractures we did not find this method of value in assessing the hip fracture risk. However, in the study of men, finger QUS yielded values similar to those with heel QUS. This gender discrepancy in performance might be due to difficulties in assessing bone quantitative properties with finger QUS in individuals in the very low bone density range. There might also be differences in phenotype that account for the presumably site-dependent inferior performance of finger densitometry in fracture prediction among Swedish women. Finger QUS and RA have been found capable of detecting age-related bone loss [196, 198-201]. Whether age-related bone loss in the phalanxes is more profound among Swedish women than among other women, rendering this site or these techniques less useful for the evaluation of the hip fracture risk, is not known at present.
In the prospective NHANES cohort study [94, 202], 1,559 women and 1,437 men, relatively young, underwent measurements by RA and were followed up for a maximum of 16 and 22 years, respectively [94]. The adjusted RR for hip fracture was 1.6 (95% CI 1.1-2.3) in women and 1.73 (95%CI 1.1-2.7) in men. The latter figure is considerably lower than our finding of 3.1 but the discrepancy may be attributable to the differences in age at measurement and in the study design.

We found a relatively high risk of hip fracture per reduction of one standard deviation, with an odds ratio in the order of 3.5 for DXA of the proximal femur and heel QUS in women, and an even higher figure for DXA of the proximal femur (adjusted OR 4.8) in men. There are several possible explanations for this finding. The two studies (I and II) were performed in a region with a high incidence of hip fractures, whereas previous studies have been carried out in areas with lower incidence rates. Although population-based, the studies comprised a sub-category of elderly subjects, i.e. non-institutionalised individuals without prior hip surgery or fracture. It is possible that this investigated sub-population might constitute a positive selection regarding bone density as the main causal factor of fracture in comparison with the corresponding age group in the general population.

In our categorised analysis, osteoporotic women showed a more than sixty-fold and osteoporotic men a more than a twenty-fold increase in risk of a first hip fracture as compared to the reference category with normal bone density at the femoral neck. The confidence intervals of the risk estimates in the categorised analysis were generally broad, owing to the limited number of subjects in some categories. Despite this shortcoming, a clear pattern was observed, showing an exponential increase in risk with decreasing bone density. This emphasises that the relative risk, expressed per SD decrease [35] in bone density, is exponential rather than additive. Since a previous osteoporotic fracture only doubles the risk for a subsequent hip fracture [123], our finding further demonstrates the potential of bone densitometry and especially of DXA of the proximal femur for assessment of the hip fracture risk in both men and women.

Studies I and II were cross sectional case control studies. Although prospective studies are preferred, retrospective and prospective study designs seem to yield comparable results [203].

Further potential limitations of studies I and II are related to their observational case-control design with a restricted study base. The response rate was moderate, but similar among cases and controls. The limited number of included subjects rendered imprecise
risk estimates. The exclusion criterion of frail individuals with a supposedly low bone
density and a high risk of fracture was similar in cases and controls. The reasons for
non-participation should not have introduced a systematic difference in bone status, and
should introduce a conservative bias in the OR analysis. Moreover, eligible participants
did not differ from eligible non-participants regarding age or type of hip fracture. The
absolute proportions of intracapsular and extracapsular hip fractures were identical
among non-participants and participants. We used the manufacturer’s reference
population for all measurements, since a Swedish reference population was not
available. However, the values for QUS of the heel and DXA of the proximal femur are
in conformity with earlier Swedish data [204]. The number of cases who underwent RA
of the phalanges was comparatively small, which might have influenced the results.
Selection bias which is serious concern is, however, unlikely, since our odds ratios were
only marginally altered by restricting the analyses to participants who underwent all four
types of bone measurement.
The WHO criterion for osteoporosis is based upon SPA/SXA and DPA/DXA
measurements of central anatomical sites such as the lumbar spine and the proximal
femur and one distal site, the distal forearm. Quantitative ultrasound has many
advantages, however, being relatively inexpensive, non-ionising, transportable and fast.
Altogether this renders QUS attractive for bone measurements. But, currently there is no
general agreement that QUS can be used in diagnosing osteoporosis [205]. The use of
this method is restricted for several reasons. It has been reported that the definition of
osteoporosis may not be appropriate at other skeletal sites than the spine, hip or forearm
or with different technologies such as QUS [117-120]. These latter studies have shown
that with some QUS equipment few individuals, no matter how old, will have T-scores
below –2.5, suggesting that it may be necessary to provide a T-score criterion specific to
the measurement technology employed [119]. In contrast, the QUS-equipment applied
in studies I and II showed an excessive proportion of individuals with T-scores <-2.5,
reported also in other studies with the same QUS-system [206]. Additionally, there are
no commercially available reference phantoms for cross-calibration between different
types of QUS equipment. Altogether this makes it difficult to compare the results from
different studies performed with different QUS machines.
Except for DXA, no specific recommendations have been made concerning cut-off
values or indicative criteria for osteoporosis for the techniques, or the anatomical sites,
used in studies I-IV. Furthermore, the appropriateness of a specific T-score as an
indication of the presence of osteoporosis in men has not been determined. What we
know, though, is that the QUS technique is available and widely spread and that the data
are presented as T-scores. There are differences in age-related bone loss between
different anatomical sites [207] and between genders [208, 209] as well as in relation to
the different technologies [119]. Furthermore, the reference population and the T-scores
derived from this population, provided with the software (by the manufacturers), might
not be representative of all populations. Without any official recommendations as to
how to interpret the QUS data, it is probable that data will be used according to the
WHO criterion.
Regarding BMD assessments in men, there is currently no consensus as to how BMD
data should be used either for diagnostic purposes or for fracture risk assessment. For
most bone densitometry techniques used in clinical practice, population-based male
reference ranges are available, and risk assessments are made as for women, using the
same T-score criteria, but with a male reference population. It has recently been
suggested that for diagnostic purposes it might be appropriate to use the same absolute
BMD level in both genders [33, 92]. Bone mineral density is a determinant of fracture
risk in both men and women [35, 92]. The question is whether there are gender
differences in the BMD-fracture risk relationship that makes the clinical application
different in the two genders. There are differences between men and women in factors
that probably influence the risk of fracture. For example men fall differently from
women [210] and even after adjustment for weight and height, they have a greater bone
size [211]. Furthermore, age-related bone loss is different in men and women, with more
trabecular decline and endocortical wasting in women [209]. These differences may not
be reflected by BMD-values, but are likely to be important for the fracture risk.
Differences in bone size also affect the accuracy of DXA [212]. This size difference
might be expected to alter the relationship between areal BMD and fracture risk and to
be the source of gender differences in diagnostic thresholds for osteoporosis [213].
Given this uncertain impact of bone size on the BMD-fracture risk relationship, it seems
unlikely that BMD levels associated with a given fracture risk in women will have the
same usefulness in men [213]. A problem with a common diagnostic criterion based on
absolute levels of BMD derived from studies in women would also be that an
inappropriately small number of men would be diagnosed as being osteoporotic and at
risk of fracture [214, 215].
In conclusion, the interpretation of BMD assessments in men in terms of diagnosis and fracture risk is still an unsolved issue. However, until additional data are available it seems rational to use gender-specific criteria.

Since valid norms have not yet been developed for the interpretation of data from measurements by the methods used in study II, the application of the WHO criterion for osteoporosis in our study of men should be regarded as tentative.

In studies I and II, in a population with a high incidence of hip fractures, all of the three techniques investigated were able to separate men with a first hip fracture from controls. However, only DXA of the hip and QUS of the heel proved capable of discriminating female hip fracture patients from controls, and measurement at the non-weight-bearing anatomical sites, the fingers, were not sufficiently able to predict the risk of hip fracture among Swedish women. Our data indicate that site-specific measurement with DXA for hip fracture prediction is superior to peripheral techniques, both in women and men.

Study III

The mortality risk was substantially increased and independent of bone density and body weight for our relatively healthy responding cases with a first hip fracture compared to randomly selected controls. The excess risk was most pronounced for trochanteric hip fracture cases. No significant association was revealed between bone density and mortality. Half of all deaths occurring among hip fracture patients was estimated to be attributable to the fracture. The increased risk of mortality persisted several years after fracture, consistent with the findings by others [5, 216, 217]. Twenty-four percent of the hip fracture patients were admitted from nursing homes, and they were found to have a much higher post-fracture mortality than did non-institutionalised subjects, a finding also reported by others [72, 218]. The reported excess mortality after hip fracture varies considerably [2, 3, 5, 66-70, 72, 219-224]. This wide range of excess mortality probably reflects differences in time of follow-up and in characteristics of the subjects [66, 68, 70-72, 75, 218, 221, 225]. There may be two groups of hip fracture patients [216]. First, a group with co-morbid conditions and older age with a rapid increase in mortality after the fracture event, as was the case for institutionalised patients of cohort B. In the second group of healthier subjects, the hip fracture might either signal or actually induce a progressive decline in health, possibly leading to excess mortality that persists several years after fracture [216, 217, 220, 226]. This progressive decline in health could be the result from lack of mobility, loss in strength and lean mass leading to increased
disability and its associated health consequences. The hip fracture event and fracture treatment per se seems very unlikely to have contributed to the increased mortality since there was a non-significant difference in mortality during the first 6-12 months which is in contrast to findings by others [2]. Thus, our observed continuing divergence of the survival curves for cases and controls in cohort A, resembling the survival curves after vertebral fractures [2], could in consequence be explained.

In our study, bone density measured by three techniques at four different sites, was not associated with mortality, neither in cases nor controls and could therefore not reflect a strong surrogate measure of underlying poor health. Thus, although most efficient in predicting hip fractures [35, 43, 206] and separating hip fracture patients from controls [35], DXA of the proximal femur did not prove capable of predicting excess mortality in our study. However, the rate of bone loss measured by DXA of the proximal femur has, in a recent report from the Study of Osteoporotic Fractures, been found associated with mortality [227]. In this cohort with a similar age-span as the one under study by us, baseline BMD of the femoral neck could not predict mortality [227]. The two previous studies that reported low BMD as predictor of mortality, used peripheral techniques and found both independently of fracture [76, 77], a relative risk for death of 1.2 per each standard deviation decrease in BMD. QUS of the heel and RA in our controls had non-statistically significant risk estimates of similar magnitude.

Potential limitations of the study are related to the restricted study base. The response rate was moderate but similar among cases and controls. The limited number of subjects deceased in cohort A do make the risk for type II error apparent in the analysis of bone density as a predictor of mortality when detecting small risks as indicated by the earlier investigations [76, 77]. Information on health status, apart from bone density, age and body composition, all considered as surrogate measures for general health was not collected and therefore we could not study whether concomitant disorders other than osteoporosis contributed to the mortality, and neither was the cause of death studied.

Sweden’s unique official statistics improved the feasibility of the study [228]. The individual registration number for each citizen together with the Swedish national registration enabled us to identify all subjects deceased at follow up. Furthermore, using officially published life-tables, with sex-specific one-year mortality risks; we could calculate the number of expected deaths during the follow-up period for both cohorts under study with a high degree of precision. We had the possibility to consecutively
identify all hip fracture patients of this setting and compare the risks of mortality among subgroups of hip fracture patients.

The rationale for the study design with the restricted study base of cohort A was to investigate if relatively healthy hip fracture cases, independent of their bone density, have an increased risk of mortality. Only 20% of all hip fracture cases met the inclusion criteria, and the restrictions made could therefore also be considered strength of the study, in that the healthiest elderly were studied. They might have had well controlled hypertension or asthma, but no severe ongoing cardiopulmonary, kidney-or malignant diseases. Responding controls had a higher than expected survival and the cases an expected survival compared to the general population of Sweden which could conceivably reflect selection inadequacies. It is, however, estimated that 10-15% of the Swedish population of both genders, aged 65-85 years, is suffering from severe chronic diseases (Statistics Sweden). Furthermore, according to a publication from the Swedish National Board of Health and Welfare [229] the following proportions of elderly are institutionalised: 14/1000 at age 65-74, 48/1000 at age 75-79, 115/1000 at age 80-84 and 240/1000 at age 85-89. Both these factors are likely to affect mortality risk. Therefore our relatively healthy participants in cohort A are also expected to have, as observed, a lower mortality risk than the general population. The assumption that the studied hip fracture population was relatively healthy is also corroborated by the fact that the mortality was lower at 3 months, 6 months, 1, 2, 3 and 4 years, than most of previous reports [2, 66, 72, 74, 75, 216, 217, 230, 231].

We conclude that also relatively healthy non-institutionalised elderly have a substantially increased risk of mortality after a hip fracture compared to controls. This increase in risk is not associated with differences in bone density or body composition.

**Study IV**

Not only were almost all of the female nursing home residents osteoporotic, and 51% of the men, but these residents also showed QUS values that were approximately 1.5 SD lower than expected for age and gender. In fact, they had lower QUS values than the hip fracture patients of studies I and II, although the nursing home residents were older (Table 16 and 17).

In addition to heel ultrasound, we evaluated a finger QUS device, which has not previously been tested systematically in an elderly population. Although it has certain advantages such as being portable, light, relatively rapid to use and comparatively
inexpensive, the compliance was rather low, 65%. Finger QUS proved able to separate men with previous fractures from men without, but failed to separate women with previous fractures from those without. This is analogous to the incapability of finger QUS of separating women with and without fractures in study I, and the ability of finger QUS to separate men with and without fractures in study II. Densitometry of the fingers has been reported to be of value in detecting early bone loss [200], although its utility in fracture risk assessment is less well documented in the elderly. It is possible that bone loss in these elderly women has proceeded so far that the study population in this respect is too homogeneous.

Our findings support results from both prospective and cross-sectional studies with hip fracture risk assessment and fracture data collection that heel QUS values are considerably lower in elderly persons, predominantly women, in residential care [232-234].

Of 232 women in our study, 95% were classified as osteoporotic from heel QUS and 99% from finger QUS. The corresponding figure for men based on heel QUS was 51%. The prevalence of osteoporosis among female nursing home residents has been reported to be 64-86% when obtained on the grounds of WHO-criterion based techniques such as DXA of the hip and forearm [141, 155]. However, the DXA-hip results for the female cases in study I showed a comparable prevalence of osteoporosis (62%), and with heel QUS (but not finger QUS) the osteoporosis prevalence was 98%. This indicates a similar proportion of individuals with osteoporosis in our female nursing home population as reported by Greenspan [155].

Although only QUS of the heel proved to be sensitive in discriminating women with previous fractures from those without, and furthermore capable of separating ambulant women from non-ambulant, the two QUS techniques used provided almost identical mean values for T- and Z-scores in women.

Our study has certain limitations. We used the manufacturer's reference values, supported by the report that they are in agreement with recent Swedish heel QUS data [204]. The cut-off level for osteoporosis is still to be defined for QUS techniques, peripheral sites, and men. In this study we used <-2.5 SD, which is the WHO criterion of osteoporosis for DXA of the proximal femur, spine and forearm measurements. Since there is no definition of osteoporosis for men or for QUS, we adopted the calculation method elaborated for women, but using a male reference population. We had a comparatively small male sample size, which might have contributed to the lack of
significance for certain risk estimates. However, the beta estimates for heel QUS values showed congruency of the heel ultrasound results with those of the larger sample of women, and the results are in line with knowledge from the general population and the current understanding of osteoporosis. No actual weight measurements were recorded, but this probably random misclassification should not lead to overestimation of the importance of weight for QUS values or fracture risk. In those residents in whom only one method of measurement was used, we found no major selection bias regarding sex, age, weight or duration of stay in the nursing home, and the female to male ratio was 4 to 1 in each subgroup. Residents not included in the study were frail individuals and it is probable that their QUS values were at least not higher, on average, than those of the subjects included. We therefore do not believe that we overestimated the proportion of individuals with low Z- and T-scores by generalising the results to all subjects in the nursing homes studied.

Osteoporosis and fragility fractures are a common feature among institutionalised elderly persons and an important issue. DXA equipment for central measurements is stationary, and the fragile population of elderly men and women are not readily transported to facilities with such equipment. In this respect peripheral bone densitometry could provide an alternative.

The results from our study in nursing home residents indicate that measurements in such residents with portable/transportable QUS techniques, using the threshold of –2.5 SD, might not add extra information over and above that extractable from clinical risk factors. With a different cut-off, QUS might be of greater value in risk assessment and diagnosis.

Our study confirms the ability of heel ultrasound to separate women with previous fractures from those without. Ultrasound of the phalanges failed to identify women with previous fractures, but proved valuable in identifying such men. Virtually all women were classified as osteoporotic according to the results of the QUS measurements at the heel and fingers. In addition, the nursing home residents had very low values for their age. Our results support the assumption that female nursing home residents are osteoporotic, and thus prophylactic measures against osteoporotic fractures could be generally applied rather than being based on diagnosis of osteoporosis.
Table 16. Comparisons between female hip fracture patients, controls and nursing home residents

<table>
<thead>
<tr>
<th></th>
<th>Cases N=87</th>
<th>Controls N=195</th>
<th>Female nursing home residents N=172</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yrs</td>
<td>76.0(5)</td>
<td>74.5 (5)</td>
<td>84.4±8.7</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>61.0(10)</td>
<td>68.1(12)</td>
<td>56.2±12.0</td>
</tr>
<tr>
<td>Height, cm</td>
<td>161.5(6)</td>
<td>160.2(6)</td>
<td>159.7±8.5</td>
</tr>
<tr>
<td>BUA heel, dB/MHz</td>
<td>93.5(10)</td>
<td>103.8 (10)</td>
<td>82.8(11.8)</td>
</tr>
<tr>
<td>SOS heel, m/s</td>
<td>1473 (21)</td>
<td>1493.0 (30)</td>
<td>1473.4(23.9)</td>
</tr>
<tr>
<td>Stiffness</td>
<td>54.9(11)</td>
<td>67.2(14)</td>
<td>47.7(12.3)</td>
</tr>
<tr>
<td>T-score heel</td>
<td>-4.1(1)</td>
<td>-3.0 (1)</td>
<td>-4.8(1.1)</td>
</tr>
<tr>
<td>Z-score heel</td>
<td>-1.3(1)</td>
<td>-0.3(1)</td>
<td>-1.6(1.1)</td>
</tr>
<tr>
<td>SOS phal, m/s</td>
<td>1860(91)</td>
<td>1850(92)</td>
<td>1774.9(68.2)</td>
</tr>
<tr>
<td>Z-score phal.</td>
<td>0.6 (1.3)</td>
<td>-0.5(3.8)</td>
<td>-1.6(1.1)</td>
</tr>
</tbody>
</table>

Table 17. Comparisons between male hip fracture patients, controls and male nursing home residents

<table>
<thead>
<tr>
<th></th>
<th>Cases N=31</th>
<th>Controls N=68</th>
<th>Male nursing home residents N=64</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yrs</td>
<td>77.2(5.6)</td>
<td>74.4 (4.9)</td>
<td>81.5±8.4</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>77.5(10.1)</td>
<td>78.7(11.8)</td>
<td>67.6±11.2</td>
</tr>
<tr>
<td>Height, cm</td>
<td>176.9(6.8)</td>
<td>172.6(6.4)</td>
<td>172.5±8.0</td>
</tr>
<tr>
<td>BUA heel, dB/MHz</td>
<td>108.9(11.4)</td>
<td>116.0(10.2)</td>
<td>102.0(15.3)</td>
</tr>
<tr>
<td>SOS heel, m/s</td>
<td>1496.7(31.7)</td>
<td>1524.1(36.1)</td>
<td>1508.1(38.9)</td>
</tr>
<tr>
<td>Stiffness</td>
<td>71.6(14.4)</td>
<td>84.0(16.1)</td>
<td>70.7(20.2)</td>
</tr>
<tr>
<td>T-score heel</td>
<td>-2.6(1.3)</td>
<td>-1.5 (1.5)</td>
<td>-2.6(1.9)</td>
</tr>
<tr>
<td>Z-score heel</td>
<td>-1.3(1)</td>
<td>-0.2(1)</td>
<td>-1.3(1.8)</td>
</tr>
<tr>
<td>SOS phal, m/s</td>
<td>1835.8(106.7)</td>
<td>1912.5(118.2)</td>
<td>1799.6(101.7)</td>
</tr>
</tbody>
</table>
Study V

In this randomised, controlled intervention study we evaluated the effect of external hip protectors in a population with a high risk of hip fractures, namely nursing home residents.

A very positive risk reduction of the risk of hip fractures was the main finding of this study, with a relative risk of 0.33 in the hip protector group of men and women combined. This result is consistent with data from randomised controlled intervention trials using hip protectors previously reported by Lauritzen el and recently also by Kannus et al [144, 190]. The effect is clearly more prominent than hip fracture reduction from pharmaceutical prevention [173-176]. Considering also the information that very few hip fractures occurred while hip protectors were used in either of the published studies, there should be very little doubt of the effectiveness of such a preventive regime. The remaining issue is therefore how to identify individuals who will benefit most from prevention and how to improve compliance. Almost all studies on the effect of hip protectors (Table 18) have been performed in nursing home settings, which are documented as high risk environment [92, 144-147].

The compliance to the use of hip protector has varied between 24 and 86% (Table 18). We found a moderate compliance rate of 44% during the 11-month study period, with no hip fractures when the protectors were in use. A large number of nursing home residents randomised to hip protectors were bedridden (24%), and the compliance in this group was very low, almost zero, which affected the compliance in the entire group. The compliance among those suitable for hip protectors, i.e. ambulatory residents and residents mainly in a wheel chair, was better (52%). The other main reasons for poor compliance were related to the caregivers and to skin problems for residents.

Biomechanical properties of different hip protectors have been tested in vitro and in vivo. All tested protectors showed sufficient resistance to low-energy trauma, and two protectors were also resistant to moderate and high energy force [187] [188] [235]. Although not included in those specific tests, the hip protectors used in our study show greatest resemblance both in design and material to the protectors with the highest resistance, which mainly act by energy-shunting.
<table>
<thead>
<tr>
<th>Study</th>
<th>Material And Methods</th>
<th>Intervention</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cameron 2000</td>
<td>131 women living at home</td>
<td>Hip protector; SafeHip, Denmark, fixed in special underwear</td>
<td>Four months. Hip protectors improved falls self-efficacy</td>
</tr>
<tr>
<td>Ekman 1997</td>
<td>Nursing home residents. 302 hip protector 442 controls mean age 84 years</td>
<td>Hip protector; JOFA AB, Malung; Sweden. No special fixation</td>
<td>Follow-up 11 months. 4 hip fx in intervention group, 17 in control group. RR 0.33. Compliance 44%</td>
</tr>
<tr>
<td>Harada 1998</td>
<td>Female nursing home residents. 35 hip protector 24 controls mean age ?</td>
<td>Hip protector; SafeHip, Denmark, fixed in special underwear</td>
<td>Follow-up 19 months. 0 hip fx in intervention group, 4 in control group. Compliance 86%</td>
</tr>
<tr>
<td>Heikinheimo 1996</td>
<td>Nursing home residents. 36 hip protector 36 controls mean age 85.5/84 years</td>
<td>Hip protectors designed by Heikinheimo, fixed in special underwear</td>
<td>Follow-up 12 months 1 hip fx in intervention group (while wearing hip protectors) 5 in control group. Compliance 68%</td>
</tr>
<tr>
<td>Kannus 2000</td>
<td>Geriatric long-stay facilities or outpatient care units for supported living at home 653 hip protector 1,148 controls mean age 82 years</td>
<td>KPH hip protector, fixed in special underwear</td>
<td>Follow-up 24 months 13 hip fx in intervention group (four while wearing hip protectors) 67 in control group RR 0.40. Compliance 48%</td>
</tr>
<tr>
<td>Lauritzen 1993</td>
<td>Nursing home residents. 247 hip protector 418 controls &gt;69 years</td>
<td>Hip protector; SafeHip, Denmark, fixed in special underwear</td>
<td>Follow-up 11 months 8 hip fx in intervention group, 31 in control group. Compliance 24%</td>
</tr>
<tr>
<td>Parkkari 1998</td>
<td>Nursing home residents 19</td>
<td>KPH hip protector, fixed in special underwear</td>
<td>Follow-up 6 months. Compliance 63%, more than 90% of their active day</td>
</tr>
<tr>
<td>Villar 1998</td>
<td>Residents in resident care. 101 hip protector 40 controls 64-98 years. All female</td>
<td>Hip protector; SafeHip, Denmark, fixed in special underwear</td>
<td>Follow-up12 weeks 0 hip fx Compliance 27%</td>
</tr>
</tbody>
</table>

*Table 18. Studies of the effectiveness and acceptability of external hip protectors [236] [237] [238] [189] [190] [144] [239] [191]*
Apart from preventing hip fractures, it has also been reported that the use of external hip protectors improve the self-confidence. As users of hip protectors feel more confident that they can complete tasks safely, they might become more physically active and require less assistance with activities of daily living [236].

We chose to randomise by nursing home and not by participants or by wards. The reason for this was that randomisation by participant would be almost impossible in our population of elderly and often cognitively impaired subjects, because of the risk of confusion and of problems for the caregivers. Randomisation by ward would have been possible, but since the staff of some wards expressed a strong wish for their ward to be allocated for hip protectors, this would have been a bias. We found that the most unbiased and stringent way would be to randomise by nursing home. There were no major differences between the populations in the four nursing homes as expressed in clinical risk factors or QUS values, a situation which might have been difficult to achieve on randomising by ward since some wards (at each nursing home) have only senile residents and other wards residents who are cognitively fairly unimpaired.

Osteoporosis does not give rise to any symptoms before a fracture occurs, and external hip protectors are highly obvious. A positive attitude of the elderly individual and, where appropriate, the caregivers, to the use of a hip protector is therefore of great importance. Such an attitude is in turn based on awareness of the prevalence, causes and consequences of a hip fracture. One must also bear in mind that in contrast to pharmacological treatment, where a forgotten pill on rare occasions is forgivable, external hip protectors only work while in place, but on the other hand the preventive effect is immediate.

The present study was the first to confirm the ability of external hip protectors to prevent hip fractures [144]. Furthermore, the external hip protectors proved effective in an unselected population of nursing home residents. This is likely since the majority of nursing home residents were osteoporotic at least when measured by heel and finger QUS (study III), given the limitation of using the WHO definition. External hip protectors are inexpensive, they have no serious side-effects and have proven effective in hip fracture prevention in three prospective studies. Thus it would seem appropriate to offer hip protectors to nursing home residents, except for bedridden patients, in order to decrease the incidence of hip fractures in nursing homes.
CONCLUSIONS

- We conclude that site-specific measurement with DXA of the proximal femur and QUS of the heel are highly predictive of an incident first hip fracture and superior to peripheral techniques of the non weight bearing phalanges in non-institutionalised elderly women.

- We conclude that site-specific measurement with DXA of the proximal femur is superior to peripheral techniques in predicting an incident first hip fracture in non-institutionalised men, and even more pronounced than in women.

- The relative risk of hip fracture predicted from bone quantitative measurements, is exponential rather than additive.

- A first hip fracture has a strong impact of on excess mortality in non-institutionalised elderly.

- QUS measurements at the heel and fingers, showed that virtually all institutionalised women could be classified as osteoporotic In addition, the nursing home residents had very low values for their age.

- External hip protectors were found to be effective in preventing hip fractures.
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