*Regular Review*

# Strategies for prevention of osteoporosis and hip fracture

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In England in 1985, 37 600 people aged 65 years and over fractured a hip.[1] On average 3170 acute hospital beds a day were committed to people over 65 with hip fracture—nearly a quarter of all orthopaedic beds. Table I shows the age and sex distribution of patients with hip fracture. In all, 82% of those aged 65 and over were women, of whom 83% were aged 75 and over. On the basis of the present incidence (table II) almost one women in four living to the age of 90 in England can expect to have a hip fracture. Age specific rates doubled over the 25 years to about 1980,[2,3] and while rates seem not to have further increased over the past decade,[3] the absolute number of fractures occurring each year is still expected to increase for the next few decades as the proportion of elderly people in the population rises. With serious complications such as failure to regain mobility, pressure sores, pneumonia, and the precipitation of confusional states and dementia, hip fracture is a major cause of morbidity and institutional care in elderly people. In this review we assess quantitatively the relative merits of different strategies for preventing the loss of bone mineral density (osteoporosis) that is the pathological basis for hip fracture.

TABLE I—*Number of hospital discharges and deaths (rate per 10 000 population) for fractured neck of femur, by age and sex in England, 1985 (from Hospital Inpatient Enquiry data[1])*

| Age (years) | No (rate/10 000) in men | No (rate/10 000) in women |
|---|---|---|
| 0-44 | 1330 (0·9) | 650 (0·5) |
| 45-64 | 1370 (2·7) | 2240 (4·3) |
| 65-74 | 1890 (10·4) | 5330 (23·0) |
| 75-84 | 3010 (34·1) | 14 310 (90·1) |
| ≥85 | 1840 (136·2) | 11 260 (252·5) |
| Total No ≥65 | 6740 | 30 900 |

TABLE II—*Cumulative probability of person aged 45 sustaining hip fracture by age (calculated on life table basis from data in table I)*

| Age (years) | Probability in men (%) | Probability in women (%) |
|---|---|---|
| 65 | 0·5 | 1 |
| 75 | 2 | 3 |
| 85 | 5 | 11 |
| 90 | 11 | 22 |

## Bone mineral density and fracture

The mineral density of bone is essentially the mass of calcium salts per unit volume. It is calculated directly from the ash weight of bone after incineration, but can be accurately estimated by techniques such as photon or *x* ray absorptiometry.[4] A direct linear association between bone mineral density and the minimum force needed to fracture the neck of the femur has been shown by experiments in which incremental mechanical forces were applied to the necks of human femurs mounted in blocks.[4-6] For a given bone density, however, there was about a twofold range of values among femurs for the minimum force needed for fracture, suggesting that the overall mineral density may be a relatively crude measure of the resistance to fracture of an individual neck of a femur.

Several longitudinal and cross sectional studies have examined changes in bone mineral density with age.[7-17] Bone density approaches its peak value by early adulthood, and remains stable for some years. In women, premenopausal bone loss from the femur and other long bones is normally slight, but rapid bone loss begins at the menopause. Thereafter bone loss continues throughout life, although the rate slows after several years. Peak bone density and subsequent rate of bone loss may not be closely associated; both are important determinants of individual bone density in old age. At any age bone density is on average lower in women than in men, but there is a wide range among individuals. Women on average lose between a third and a half of their peak bone mass over their lifetime, while men lose less. Differences in bone density are likely, at least in part, to account for the sex difference in incidence of hip fracture in elderly people and for the increasing incidence in both sexes with advancing age. Bone loss in older people is largely irreplaceable, though it may not be completely so. Strategies aimed at preventing low bone density in old age should be directed particularly at women and should begin at the time of the menopause because of the rapid and largely irreversible bone loss thereafter.

## Preventive strategies

When the risk of a disease varies according to the magnitude of a continuously distributed variable (in this case bone density) two different preventive strategies can be adopted—screening, in which intervention is restricted to people with results beyond a specified cut off level, and the population approach, in which the aim is to shift the entire distribution of the variable in a favourable direction by intervention in everyone, without necessarily measuring the variable.

Screening is unlikely to be worth while if there is little difference between the average bone density of those who do and those who do not suffer fractures. The potential value of measurement of bone density in menopausal women as a screening test for future hip fracture is best assessed by estimating the separation between the distribution of bone density in elderly women who fracture their hip and that in elderly women who do not fracture their hip. This can be done either retrospectively, by measuring bone density in patients with hip fractures and in control subjects, or prospectively, by measuring bone density in a large population and recording hip fractures as they occur.

### 1 Screening by measuring bone mineral density

STUDIES OF BONE MINERAL DENSITY AND HIP FRACTURE

Table III summarises data from studies that have compared bone mineral density in women with hip

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fracture with that in age matched controls representing the normal population. These studies estimated the average difference in bone density at the time of the fracture. Units of measurement vary among the studies, and to permit a valid comparison we have expressed each case-control difference as a proportion of the standard deviation of the bone density of the controls in that study. (This assumes a linear relation between the different units of measurement, which may not be strictly true but is a reasonable approximation.)

Measurement of bone density of the contralateral femoral neck provides the most direct evidence (the left and right sides are normally highly correlated[4]). Immobility after a fracture, however, will cause bone loss from the femur and introduce bias if the measurement is not performed soon after the fracture. The five studies included in table III that measured bone density of the contralateral neck of the femur minimised this bias either by performing the measurement within 10 days of the fracture or by mobilising the patients within a few days of the fracture. Three studies that did not meet these criteria were excluded.[24 25 36]

For the five studies included in table III that measured bone density directly at the neck of the femur the difference in bone density between patients with hip fracture and controls was only about half a standard deviation—too small for an effective screening test. The figure illustrates this by showing the Gaussian distributions of bone density in patients with hip fracture and controls, half a standard deviation apart. The area under the hip fracture curve to the left of a given cut off level, expressed as a proportion of the area under the whole curve, indicates the detection rate—that is, the proportion of women who have hip fracture with a bone mineral density less than or equal to the given cut off value. Similarly, the area under the control curve to the left of the same cut off level indicates the corresponding false positive rate—that is, the proportion of unaffected women with a bone mineral density value less than or equal to the given cut off value. For example, at a cut off of two standard deviations below the mean for the controls the detection rate would be 6% and the false positive rate 2%; at 1·6 standard deviations below the mean the rates would be 13% and 5% respectively. There is too much overlap between the two distributions for measurement of bone density to be a worthwhile screening test. In practice the discrimination would be even worse because with measurement at the menopause, 20-30 years before the fracture, the degree of overlap would be greater than that at the time of the fracture. The expected benefits of screening would be still further reduced because no treatment is likely to prevent all hip fractures.

The studies listed in table III that measured bone density at sites other than the neck of the femur confirm that bone density measurement is a poor screening test. The average difference between cases and controls was 0·3 standard deviations, and the correlation coefficient between bone density at the neck of the femur and at other sites is about 0·6[18 19 25]; the average difference divided by the correlation coefficient estimates the difference in bone density between cases and controls at the neck of the femur; in this case the estimate is half a standard deviation, the same as the direct result.

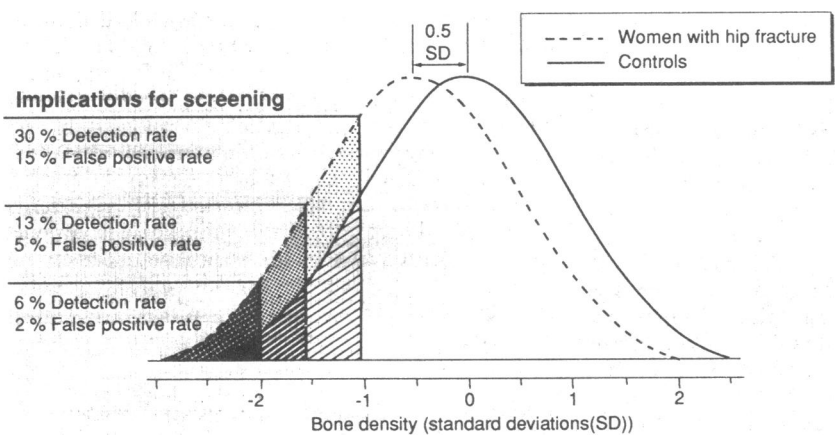
Prospective studies of bone density and hip fracture have not been conducted over a long enough period to determine the value of measurement of bone density at the menopause in predicting hip fractures some 20 or 30 years later. They have, however, shown that the risk of a hip fracture within a few years of measurement of bone density is similar to that estimated from the case-control studies. The variation in risk from the 10th to 90th centile values of bone density was only twofold to fourfold,[37-42] a weak gradient that can be shown to be equivalent to a separation of about half a standard deviation between the bone density distributions of those who will subsequently have a hip fracture and those who will not—the same estimate as was derived from the case-control studies. On the basis of all the epidemiological evidence, retrospective and prospective, there is at present no scientific case for screening.

This poor performance of measurement of bone density as a screening test does not imply that bone density is unimportant in the aetiology of hip fracture, it simply indicates that most elderly women have lost sufficient bone for the hip to fracture with the impact of an unprotected fall. Differences in bone density between individual women are not great enough to discriminate between who will and who will not later suffer a fracture; this will be determined by chance, by conditions that increase the risk of falling or cause loss of the normal protective reflexes, and by illness

TABLE III—*Bone density measurements in women with hip fracture and age matched controls in various studies*

| Study | Site | Measurement technique | No of cases/controls | Difference between cases and controls in bone density* (standard deviations) |
|---|---|---|---|---|
| | | *Neck of femur†* | | |
| Bohr and Schaadt[18] | Contralateral neck of femur | Dual photon absorptiometry | 46/38 | −0·4 |
| Eriksson and Widhe[19] | | | 62/39 | −0·5 |
| Riggs, Melton *et al*[15 16 20] | | | 49/166 | −0·4 |
| Norimatsu *et al*[17] | | | 12/31 | −0·7§ |
| Chevalley *et al*[21] | | | 57/82 | −0·6 |
| Weighted average | | | | −0·5 |
| | | *Other sites†* | | |
| Bohr and Schaadt[18] | Lumbar spine | Dual photon absorptiometry | 46/38 | −0·1 |
| Chevalley *et al*[21] | | | 57/82 | −0·1 |
| Krolner and Pors Nielsen[22] | | | 36/38 | +0·4 |
| Cornell *et al*[23] | | | 54/269 | −0·3 |
| Riggs *et al*[16] | | | 22/95 | +0·2 |
| Meltzer *et al*[24] | | | 16/92 | −0·3 |
| Mazess *et al*[25] | | | 37/278 | −0·7 |
| Härmä *et al*[26] | Lumbar spine | Computed tomography | 30/49 | −0·8 |
| Firooznia *et al*[27] | | | 83/207 | −0·3† |
| Wootton *et al*[28] | Forearm | Single proton absorptiometry | 30/23 | −0·2 |
| Riggs *et al*[16] | | | 26/95 | +0·1 |
| Jensen *et al*[29] | | | 10/160 | −0·8 |
| Meltzer *et al*[24] | | | 16/92 | −0·1 |
| Mazess *et al*[25] | | | 37/278 | −0·5 |
| Elsasser *et al*[30] | Radius | Computed tomography | 32/28 | −0·4 |
| Härmä *et al*[26] | | | 29/49 | −0·6 |
| Lips *et al*[31] | Metacarpals | Radiographic | 67/54 | −0·4 |
| Aitken[32] | | | 195/317 | +0·2† |
| Cook *et al*[33] | | | 314/370 | −0·5† |
| Horsman *et al*[34] | | | 58/58 | −0·4 |
| Horsman *et al*[34] | Femoral shaft | Radiographic | 58/58 | −0·7 |
| Chevalley *et al*[21] | Femoral shaft | Dual photon absorptiometry | 57/82 | −0·2 |
| Bohr and Schaadt[18] | | | 46/38 | −0·6 |
| Hassager and Christiansen[35] | Total body | Dual photon absorptiometry | 27/26 | −0·9 |
| Weighted average | | | | −0·3 |

*A negative value indicates lower bone density in cases. †Difference estimated from data displayed graphically.




*Distribution of bone mineral density in women with hip fracture and age matched controls. Implied vertical axis is proportion of cases and controls within a marginal unit of bone density. Expected screening performance of measurement is shown by three examples*

TABLE IV—*Cumulative percentages of the Singh index grades in case-control studies of patients with hip fracture by age*

| Study | Singh grade* | 50-64 years | | 65-74 years | | 75-84 years | | ≥85 years | |
|---|---|---|---|---|---|---|---|---|---|
| | | Cases | Controls | Cases | Controls | Cases | Controls | Cases | Controls |
| Cooper *et al*[43] | | (n=52) | (n=82) | (n=93) | (n=61) | (n=180) | (n=69) | (n=131) | (n=40) |
| | 1-2 | 13% | 1% | 12% | 2% | 24% | 9% | 33% | 15% |
| | 1-3 | 29% | 4% | 43% | 13% | 53% | 23% | 64% | 43% |
| | 1-4 | 73% | 20% | 75% | 39% | 81% | 62% | 94% | 85% |
| Pogrund *et al*[44] | | (n=67) | (n=207) | (n=137) | (n=181) | (n=170) | (n=737) | | |
| | 1-2 | 16% | 0 | 22% | 0 | 25% | 1% | | |
| | 1-3 | 40% | 0 | 39% | 0 | 55% | 5% | | |
| | 1-4 | 60% | 2% | 66% | 1% | 77% | 13% | | |
| Dequeker *et al*[45] | | | | (n=13) | (n=24) | | | | |
| | 1-2 | | | 46% | 0% | | | | |
| | 1-3 | | | 100% | 13% | | | | |
| | 1-4 | | | 100% | 38% | | | | |
| Horsman *et al*[34] | | | | (n=58)† | (n=58) | | | | |
| | 1-2 | | | 26% | 0 | | | | |
| | 1-3 | | | 57% | 7% | | | | |
| | 1-4 | | | 88% | 29% | | | | |
| Lips *et al*[31] | | | | | | (n=118)‡ | (n=74) | | |
| | 1-2 | | | | | 1% | 0 | | |
| | 1-3 | | | | | 18% | 1% | | |
| | 1-4 | | | | | 64% | 20% | | |

*Grade 6=normal trabecular pattern in neck of femur, grade 1=extreme trabecular loss.
†Mean age 70, range 47-92 years.
‡Mean (SD) age 76 (11) years.

TABLE V—*Studies of relative risk of hip fracture in women who had or had not ever received hormone replacement therapy*

| Study centre | Age range (mean) (years) | No of cases who had/had not received hormone replacement therapy | No of controls who had/had not received hormone replacement therapy | Relative risk (95% confidence interval) |
|---|---|---|---|---|
| | | *Case-control studies* | | |
| Seattle[59] | 50-74 | 52/108 | 293/274 | 0·4 (0·3 to 0·6)*† |
| Oregon[60] | 52-80 (70) | 49/119 | 121/215 | 0·7 (0·5 to 1·1) |
| Los Angeles[61] | <80 (72) | 35/46 | 85/80 | 0·7 (0·4 to 1·2)† |
| Connecticut[62] | 45-74 (67) | 14/80 | 213/579 | 0·5 (0·2 to 0·9)* |
| Southampton (UK)[63] | 50-99 (78) | 6/234 | 23/457 | 0·5 (0·2 to 1·3) |
| New Haven[64] | <80 (70) | 3/68 | 12/59 | 0·2 (0·1 to 0·7)† |
| | | *Prospective studies* | | |
| Los Angeles[65] | (76)‡ | 163/166 | | 1·0 (0·8 to 1·3) |
| Framingham[66] | 64-96 (75) | 28/135 | | 0·6 (0·4 to 0·9)* |

*Adjusted for the effect of other risk factors. †Calculated by us from published data. ‡Median age.

and immobility causing bone loss shortly before the fracture.

### SINGH INDEX AND HIP FRACTURE

Table IV lists studies that have measured the Singh index (a radiological estimate of the extent of loss of the bony trabeculae in the femoral neck graded from 1 (gross trabecular loss) to 6 (normal trabecular pattern)) in patients with hip fracture and age matched controls. They suggest that at the time of fracture the Singh index can identify a small proportion of the general population in which most of the hip fractures cluster. For example, many of the cases but few of the controls had Singh grades of 1-3. The separation between cases and controls was weaker over the age of 75, although more data are needed to be certain.

The Singh index correlates poorly with bone mineral density,[5 18] and the reason that it can predict hip fracture risk (at least up to the age of 75) whereas bone mineral density measurements cannot, could be that the contribution of the trabecular elements to the strength of the proximal femur is large (about 70%) compared with their relatively small contribution to overall bone density (cortical and trabecular).[46] Trabecular bone density, measured by quantitative computed tomography, correlated highly with the compressive strength of the proximal femur.[46]

People at high risk of hip fracture may have extensive loss of trabecular bone (and a low Singh index) but not necessarily have low overall bone mineral density in the neck of the femur. Screening by using the Singh index (or quantitative computed tomography) might therefore be feasible in theory, but for several reasons it would not perform well in practice. The Singh index in old age cannot be predicted at the menopause; the reproducibility of Singh index grading between observers is poor[47] (the case-control studies each used only one or two observers); the radiation exposure is significant; and discrimination seems poor over the age of 75, when most people may have lost sufficient trabecular bone for the hip to fracture with the impact of a fall.

### BONE MINERAL DENSITY AND VERTEBRAL BODY FRACTURES

As for the hip, loss of bone mineral density in the vertebral bodies predisposes to fracture. Particularly low bone density is associated with more extensive fractures,[48] which are more likely to be symptomatic. The difference between cases and controls in bone density for asymptomatic vertebral body crush fractures detected in radiographic surveys was only about half a standard deviation—similar to that for the neck of femur[14 24 39 48-50]—but for hospital outpatients with symptomatic fractures the difference was greater—generally between 1 and 1½ standard deviations.[14 17 22 25-27 35 51-53] There could have been bone loss after the fracture but before the measurement because of immobility in the symptomatic cases, but even with this greater discrimination for the symptomatic cases the effectiveness of screening would be only moderate, with a detection rate of about 25% for a 2% false positive rate, or 35% for a 5% false positive rate. Our knowledge of the incidence and natural course of symptomatic fractures and the effectiveness of preventive measures is limited, and with this uncertainty screening for vertebral body fractures cannot at present be recommended.

### OVERALL INTERPRETATION

Measurement of bone mineral density is not a useful screening test for future hip fracture or for most vertebral fractures because differences in bone density between people who subsequently have a fracture and those who do not are too small to discriminate between them. This does not mean that strategies to increase the average bone mineral density of an entire population will fail to reduce the incidence of hip fracture. On the contrary, as discussed in the next section, such strategies are likely to succeed.

## 2 Directing preventive measures to all women

### HORMONE REPLACEMENT THERAPY

Randomised trials of up to 10 years' duration have shown that oestrogen replacement substantially or totally prevents postmenopausal bone loss.[54-58] Observational studies (up to the age of 80[12]) have shown the same effect; bone loss is prevented for as long as treatment is maintained. Observational studies have also, with one exception, shown that oestrogen protects against hip fracture (table V), with a median reduction in incidence of 50% in women who had at some time received postmenopausal oestrogen therapy. Combined preparations of oestrogen and progestogen have not been used for long enough to provide information on their effect on risk of hip fracture, but a preventive effect is likely because they prevent rapid postmenopausal bone loss in the same way as oestrogen alone.[55-57]

The main limitation of the case-control studies of hormone replacement therapy and hip fracture is that they were generally based on comparatively young women (mostly under 75) who if they took oestrogen, did so for decades. The relative risk estimates therefore tend to reflect current and prolonged use in younger women. Data from four studies (table VI) show that, while current use reduces risk of hip fracture by more than half, this protection is substantially lost within a

TABLE VI—*Age adjusted risk of hip fracture according to time since last taking postmenopausal oestrogen*

| Study centre | Time since last taking oestrogen (years) | Relative risk |
|---|---|---|
| | *Case-control studies* | |
| Seattle[59]* | Current | 0·4 |
| | 1-2 | 0·7 |
| | 3-5 | 1·0 |
| | ⩾6 | 0·8 |
| | Never | 1·0 |
| Los Angeles[61] | Current | 0·4† |
| | 1-2 | 0·7 |
| | 3-5 | 0·8 |
| | 6-9 | 1·5 |
| | ⩾10 | 0·8 |
| | Never | 1·0 |
| | *Prospective studies* | |
| Los Angeles[65] | 0-1 | 0·8 |
| | 2-14 | 0·9 |
| | ⩾15 | 1·2 |
| | Never | 1·0 |
| Framingham[66] | 0-2 | 0·3 |
| | >2 | 0·7 |
| | Never | 1·0 |

*Risk of hip or forearm fracture. †Data provided by author.

few years after stopping hormone replacement therapy. This is consistent with the results of two randomised trials of oestrogen replacement and bone density, which showed that a period of rapid bone loss occurred after stopping oestrogen replacement, similar in magnitude to the rapid postmenopausal bone loss in the controls, who did not take oestrogen.[57 58] Eight years after oophorectomy bone mineral density was only slightly greater in women who took oestrogen for the first four years than in women who had never taken oestrogen.[58]

With protection lost so soon after stopping hormone replacement, taking oestrogen for only a few years after the menopause can have little effect on reducing the risk of hip fracture. Even if oestrogen was taken to the age of 70 there would be little protective effect in women over the age of 75, in whom over 80% of hip fractures occur (including almost all those complicated by loss of mobility and need for institutional care). Hormone replacement therapy is likely to have an appreciable impact on the public health problem of hip fracture only if it is continued indefinitely after the menopause. Such a policy would be a radical departure from current practice in Britain, and assessment of the advantages and disadvantages would be complex. For oestrogen alone the protection against ischaemic heart disease seems substantial while the increase in breast cancer is small.[68] However, if combined (oestrogen plus progestogen) preparations are to be preferred because of their lower risk of endometrial cancer the indefinite prolongation of menstrual bleeding with current preparations could be unacceptable to women, and the effect of progestogen on the risk of cardiovascular diseases has not been established.

Oral contraceptives in current use seem to have little effect on bone density, but previously used preparations with higher oestrogen content may have increased bone density.[8 9 69-71]

## STOPPING SMOKING

Cross sectional studies have shown that among premenopausal women bone density is similar in smokers and non-smokers, but that some years after the menopause a lower bone density becomes apparent in smokers.[70-73] Smoking accelerates the rate of postmenopausal bone loss.[73] Table VII lists risk estimates from 10 observational studies of smoking and hip fracture: Four of the studies recruited only women[59 61 74 78]; the others recruited men and women, and there was no significant sex difference in the effect of smoking on the risk of hip fracture. The risk increases with the amount smoked, but the median relative risk estimate is 1·4. This suggests that a woman who stops smoking before the menopause would, on average, reduce her risk of eventual hip fracture by about a quarter (from 1·4 to 1·0), and that in a community where one third of postmenopausal women smoke about an eighth of all hip fractures are attributable to smoking. For heavier smokers stopping smoking could halve the risk.

As the prevalence of smoking among older women has increased over the past few decades smoking is likely to have been a contributing factor, albeit a minor one, in the doubling of the incidence of hip fracture, at least in women. For vertebral body fractures there is a higher relative risk—about threefold—in smokers.[76]

The lower bone density of older smokers is partly due to their lower body weight,[72] thin people having less dense bones on average. The relative risk estimate for smokers in the Connecticut study, unadjusted for body weight, was 1·5 (table VII), but this reduced to 1·3 if the lower body weight of smokers was allowed for.[74] In the Seattle study the unadjusted relative risk estimate was 1·4 and the adjusted estimate 1·2.[59] People who give up smoking should ideally, on general health grounds, maintain their lower body weight, albeit at the expense of an increased risk of hip fracture. The greater part of the effect of smoking on bone density and the risk of hip fracture is, however, independent of body weight and likely to be mediated through other mechanisms.[72] The suggestion that smoking merely counteracts the protective effect of postmenopausal exogenous oestrogen replacement[78] is inconsistent with the effect of smoking on incidence of hip fracture in the Southampton study (table VII), in which only 3% of the subjects had ever taken postmenopausal oestrogen.

## EXERCISE

Exercise increases peak bone mineral density in youth. Cross sectional studies have shown greater bone mineral density and greater cortical bone mass in sportsmen and sportswomen, athletes, and dancers than in age matched controls.[80-83] Measurements before and after intense physical training have shown increases in bone mineral content and cortical area.[84 85] In six clinical trials in postmenopausal women (mean age between 51 and 63), exercise programmes increased bone density, reversing the normal postmenopausal loss of bone seen in the randomised or matched control women who did not exercise.[86-91] Two trials in elderly people (over 70) showed the same effect.[92 93] Cross sectional studies have shown that women who exercised at least three times a week had

TABLE VII—*Results of studies of effect of cigarette smoking on risk of hip fracture*

| Study centre | Smoking category | Relative risk *v* never smokers (95% confidence interval)* |
|---|---|---|
| | *Case-control studies* | |
| Los Angeles[61] | 1-10 Cigarettes/day after menopause | 1·1† |
| | ⩾11 Cigarettes/day after menopause | 2·0 |
| Connecticut[74] | Ever smokers | 1·5† |
| Seattle[59] | Ever smokers | 1·4 (1·0 to 2·0)†‖ |
| Hong Kong[75] | Ever smokers | 1·3 (1·0 to 1·7)† |
| Oxford[76] | Ever smokers | 1·2 |
| Southampton[93] | 1-9 Pack years | 1·2 (0·8 to 1·9)‡§ |
| | 10-19 Pack years | 2·8 (1·8 to 4·6) |
| | ⩾20 Pack years | 1·6 (1·0 to 2·6) |
| | *Prospective studies* | |
| Los Angeles[65] | 1-10 Cigarettes/day | 1·3 (0·7 to 2·2)†§ |
| | ⩾11 Cigarettes/day | 2·1 (1·5 to 3·0) |
| Britain (DHSS survey)[77] | Smoker at time of interview | 5·6 (1·8 to 17·7) |
| Framingham[78] | Smoker at time of interview | 1·2 (0·8 to 1·6)‡ |
| San Diego[79] | Smoker at time of interview | 1·1‡ |

*Not available for all studies.
†Adjusted for the effect of other risk factors but not body mass index.
‡Adjusted for the effect of other risk factors including body mass index.
§Data supplied by author.
‖Calculated by us from published data.

TABLE VIII—*Results of studies of effect of regular exercise on risk of hip fracture*

| Study centre | Extent of habitual exercise | Relative risk (95% confidence interval) |
|---|---|---|
| | *Case-control studies* | |
| Los Angeles[61] | Frequency of active outdoor games: | |
| | Low | 1·0 |
| | Medium | 0·5* |
| | High | 0·3 |
| Hong Kong[75] | Habitual walking uphill: | |
| | <Once/day | 1·0 |
| | ≥Once/day | 0·6 (0·5 to 0·9)* |
| Southampton[63,99] | Physical activity: | |
| | ≤2 Hours/week | 1·0 |
| | 3-4 Hours/week | 0·6 (0·4 to 0·9)*† |
| | ≥5 Hours/week | 0·4 (0·3 to 0·7) |
| | Previous occupation: | |
| | Sedentary | 1·0 |
| | Intermediate | 0·3 (0·2 to 0·6)*† |
| | Weight bearing | 0·3 (0·2 to 0·5) |
| Oxford[100] | Past activity: | |
| | Very inactive | 1·0 |
| | Moderately inactive | 0·7 (0·4 to 1·2)‡ |
| | Active | 0·5 (0·3 to 0·8) |
| | *Prospective studies* | |
| Los Angeles[65] | Active exercise: | |
| | <½ Hour/day | 1·0 |
| | ½-1 Hour/day | 0·7 (0·6 to 0·9)* |
| | ≥ 1 Hour/day | 0·6 (0·5 to 0·7) |
| Britain (DHSS)[77] | Outdoor activity: | |
| | Low | 1·0 |
| | Moderate | 1·1 (0·3 to 4·3)*† |
| | High | 0·3 (0·04 to 1·4) |

*Adjusted for the effect of other risk factors.
†Data supplied by author.
‡Calculated by us from published data.

higher bone density than sedentary women at all ages from 20 to 80[13]; that habitual exercise, physical fitness, and muscle strength were all correlated with bone density in premenopausal and postmenopausal women and in men aged from 31 to 75[94-97]; and that physical fitness and muscle strength were independent determinants of femoral neck bone density.[96] In elderly people exercise is also likely to reduce the risk of falling.[98]

Table VIII lists estimates of the relative risk of hip fracture according to habitual exercise from six observational studies. The effect of regular exercise was substantial, reducing the risk of hip fracture by about half. Five of the studies recruited men and women, and recorded similar estimates for both sexes. The protection is likely to be permanent as the effect of occupation was apparent years after retirement.[99] The effect of exercise on bone density is not localised to the exercised limb,[81,87] and many different types of activity have been shown to increase bone density or reduce risk of hip fracture, although weight bearing exercise is probably preferable.[101] Brisk walking alone did not seem to prevent bone loss,[87,102] although an observational study suggested a modest protective effect against hip fracture.[63]

Reduction in habitual physical activity is likely to be the major reason for the doubling of rates of hip fracture over the past 30 years or so. With increased mechanisation our lives have become less physically demanding. This is shown by the decline in average calorie intake in Britain—from 11·9 MJ (2840 kcal) per person per day in 1965 to 9·8 MJ (2350 kcal) in 1985.[103] Other factors cannot readily account for this decline—there is no indication that people have become thinner, and the effect of the slightly higher mean age of the population in 1985 is trivial—and the 2·1 MJ (490 kcal) fall in energy expenditure over the 20 years reflects a substantial reduction in physical activity. A simple calculation allowing 6·3 MJ (1500 kcal) to sustain resting metabolic rate suggests a fall of about a third in energy expenditure for physical activity (from 5·6 MJ to 3·5 MJ (1340 kcal to 850 kcal) per day).

As exercise is a major protective factor against hip fracture, conversely, immobilisation is an important cause. Immobilisation leads directly to a reduction in bone density, particularly in weight bearing bones such as the femur, and the decline in muscle mass consequent on immobilisation further reduces bone density.[101] A history of immobilisation for more than three weeks in the previous 10 years was associated with a twofold increased incidence of hip fracture in one study,[61] and permanently impaired mobility was associated with a fourfold to fivefold increased incidence.[77,100] The potential for recovery is lost after a few months, and prolonged immobilisation produces irreversible loss of bone.[101] Immobilisation should be avoided if at all possible; exercises may be useful if it is unavoidable.

## ALCOHOL

Alcoholics have low bone density[104,105] and a considerably increased risk of hip fracture—fourfold and eightfold increases in two case-control studies.[63,64] Cross sectional studies of healthy postmenopausal women, however, have shown no deleterious effect of moderate alcohol consumption on bone density.[8,9,70,106] There is an increased risk of hip fracture of about 30% associated with moderate alcohol consumption[61,63,65,79,107] but this need not imply an effect on bone density; alcohol taken before the fracture could have predisposed to the fall.

## CALCIUM SUPPLEMENTATION

The value of calcium supplementation of the diet has recently been discussed at length, but with no consensus.[108-110] Interpretation of the evidence is complex. Peak bone density seems to be associated with dietary calcium intake in childhood.[110,111] Thereafter, in both premenopausal and postmenopausal women some observational studies have shown an association of dietary calcium with bone density or rates of bone loss,[111] while others failed to do so.[70,71,106,111] However, six randomised trials of the effect of pharmaceutical preparations of calcium on bone density in postmenopausal or elderly women have all shown a reduction in the rate of bone loss in the femur[112,113] or forearm[54,93,113-115] (although the reduction was less certain in the spine[113,115]). The effect in the trials was definite but modest—less than half that produced by oestrogen replacement[54,115] and less pronounced in women with higher dietary calcium content.[113] The failure of some of the observational studies to show the weak association may be attributable to the imprecision inherent in estimating calcium intake from food frequency questionnaires[110] and to the variable absorption of dietary calcium.[116] The randomised trials must be given greater evidential weight, and on the basis of these there is evidence that calcium supplementation has a small beneficial effect on bone density.

Observational studies on dietary calcium and hip fracture are also inconclusive, perhaps for the same reasons. A study from Hong Kong showed a significant inverse association, but the average calcium intake was only about a quarter of that typical of Western countries.[75] Of five American and British studies, only one showed a significant association[79] and four suggested very little or no association.[28,63,65,77] Despite these inconclusive results calcium supplementation must offer some protection against hip fracture because it reduces postmenopausal bone loss; but the degree of protection is likely to be small as the effect on bone density is only modest and a large protective effect against hip fracture would have been detected by the observational studies taken collectively. Also, as with oestrogen replacement, the protection against hip fracture would probably be lost rapidly after calcium supplementation had stopped, so that to maintain prophylaxis supplementation would have to be continued indefinitely.

Costs are an important consideration. The trials of calcium supplementation and bone density used an average dose of over 1g a day, much more than could be provided by simple dietary supplementation. Pharmaceutical preparations of calcium are expensive (because simple preparations are poorly absorbed and chewable or effervescent preparations are needed[116]); they cost more than the cheaper forms of hormone replacement. To treat all women aged over 50 in Britain the annual cost would be over £500 million—about 15% of the total NHS drug expenditure. Unlike the other interventions, calcium supplementation lacks other proved health benefits (though it may lower blood pressure). The likely effect on risk of hip fracture is too small to justify recommending that postmenopausal and elderly women should take calcium supplementation.

## Conclusions

Hip fracture is an important cause of morbidity and contributes considerably to the cost of health care in the Western World. Several strategies could help reduce the loss of bone density that underlies hip fracture. Among these, a substantial body of evidence indicates that physical activity is the most important, and it is a method of prevention that can be enjoyable and sociable. Regular exercise would reduce the risk of hip fracture by at least half, thereby preventing some 20 000 cases of hip fracture each year in Britain. Stopping smoking is also important, and a woman who stops smoking before the menopause will reduce her risk by about a quarter. Both these policies can be adopted by both sexes and continued into old age. Postmenopausal oestrogen replacement more than halves the risk of hip fracture, but the loss of this protection within a few years of stopping treatment limits its utility. Oestrogen replacement would need to be continued almost indefinitely if it were to do more than reduce the incidence of hip fracture in younger age groups, in whom hip fracture is uncommon and recovery generally uncomplicated. General calcium supplementation is not justified as the likely benefit is too small.

These preventive measures need to be directed towards the entire population. Their selective use, together with drugs, in a minority of the population identified by measurement of bone mineral density as a screening test is likely to have little impact on the incidence of hip fracture—the detection rate of such a test is too low and the false positive rate too high. Even if a more effective screening test were available, the preventive measures have the additional advantage of being of general health benefit, protecting against ischaemic heart disease in particular, and there is no good reason to confine them to women judged as being at high risk of hip fracture.

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