Population screening for osteoporosis to prevent fractures

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Fracture of the hip, wrist, and spinal vertebrae is common in elderly subjects, especially among women. The incidence of fractures increases with age,\(^1\)\(^2\) and the mean age of fracture is around 75 years. The increasing incidence of hip and spine fractures,\(^3\) combined with the increase in the numbers of elderly people, constitutes a major public health problem which results in a large amount of illness, associated death, and human suffering. It also represents a major claim on health service resources.

Many of these fractures are the result of loss of bone mass (osteoporosis) which results in the development of weaker bones which are more likely to fracture, an effect which is particularly pronounced in women after the menopause and is associated with declining levels of oestrogen.

There is considerable pressure to set up population bone screening programmes in order to reduce the number of fractures in elderly women as part of public health policy. It is important to have evidence that screening can prevent fractures in a significant proportion of those screened before it becomes routinely available.\(^4\) To invite women to attend for screening without such evidence of benefit raises ethical issues. Experience shows that once a health programme becomes widely used it is difficult to withdraw if it is subsequently shown to be ineffective.

The effectiveness of bone screening in preventing fractures in elderly women is evaluated using a widely accepted guide (box),\(^5\) the elements of which will be considered in turn.

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### Guidelines for evaluating a screening programme

1. Has the programme's effectiveness been shown in a randomised controlled trial?
   - If a trial has not been carried out all of the following points must be satisfied:
2. Does the current burden of suffering warrant screening?
3. Are there efficacious treatments or preventive measures available?
4. Is there a good screening test?
5. Will people at risk of the disease attend for screening and will people with a positive test result comply with subsequent advice and interventions?

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**Has the programme's effectiveness in preventing fractures been shown in a randomised controlled trial?**

The only sure way to determine the likely outcome of a screening programme is by means of a properly designed and executed randomised controlled trial.\(^6\) There have been no randomised controlled trials assessing the effectiveness of bone screening programmes for preventing fractures in later life. We therefore have to rely on answering the points 2-5 (see box) to reach some conclusions on the expected effectiveness of such a programme.

**Does the current burden of suffering warrant screening?**

Fractures in postmenopausal women are an important cause of illness, death, and private and social costs.\(^7\) During any five year period 10% of a population of women aged 70 and over will sustain a hip fracture, of whom 10-20% will die. Patients with hip fracture account for over 20% of all orthopaedic beds, and the average cost per admission is around £2500.\(^8\) After six months only about one third of survivors are fully mobile.\(^9\)

**Is there an efficacious treatment for preventing fractures?**

Established osteoporosis is more difficult to treat, and so it is advisable to start therapy at the time of the menopause, before rapid bone loss occurs. Hormone replacement therapy (HRT) based on oestrogen alone or combined with progesterone has been shown to retard, stop, or even temporarily reverse the process of bone loss which immediately follows the menopause.\(^10\)\(^-\)\(^15\)

HRT is recommended conventionally for a maximum of only 10 years, and so there will be a gap of about 15 years between stopping HRT and the time when women commonly sustain fractures. Studies comparing those women who have and have not received HRT show a reduction in the incidence of fracture of about 50%.\(^16\)\(^-\)\(^22\) However, most of these studies examined a group of only fairly young postmenopausal women and just for a few years after starting HRT. As such, they are likely to overestimate the overall protective effect of HRT in preventing fractures in elderly women. Furthermore, what is not clear.
is how much of the protective effect of HRT persists after the termination of treatment (fig 1).

If the protective effect lasts for the remainder of a woman’s life then a significant delay in fractures will occur compared with that in an untreated woman (see fig 1). There is evidence, however, that the protective effect diminishes after treatment is stopped because the rate of bone loss after withdrawal of treatment may be as rapid or possibly even steeper than in untreated women at the time of the menopause (fig 1, line 3). Within a few years the protective effect may have worn off, though this is debated.

Prospective studies have not followed up women for long enough to provide reliable estimates of the long term efficacy of HRT in preventing fractures in elderly women. Until good evidence is obtained for the long term efficacy of HRT in reducing fractures several years after stopping therapy it is impossible to estimate the net impact of a screening and treatment programme. There is also uncertainty whether the effectiveness of HRT is the same for women with different bone densities.

**IS BONE DENSITY MEASUREMENT A GOOD SCREENING TEST?**

There are various non-invasive techniques for measuring bone density. The DEXA method is the most precise and is most commonly used, and ultrasound is becoming popular. A good screening test should be able accurately to distinguish between those subjects who will not go on to have a fracture in later life (specificity) and those who will if not treated (sensitivity). If specificity and sensitivity are present then the test will have a high predictive accuracy in common conditions like fracture.

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**Fig 1. Diagrammatic representation of possible duration of effect of HRT**

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**Fig 2. Bone mass distribution of women who go on to sustain fracture and those who do not, in terms of discrimination by bone density screening:**

A: Poor discrimination

B: Good discrimination

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Although women with lower bone density have weaker bones and thus are at greater risk of fracture, the difference in bone mass between women who go on to sustain a fracture and those who do not is small and there is considerable overlap between them (fig 2A). For the test to be highly sensitive and specific the separation needs to be greater (as in fig 2B).

There is no accepted “cut off” point for bone density below which a women is identified as being at high risk of fracture. With the cut off point taken as the lowest 20% of all bone density measurements, only 28% of those so identified as being at “high risk” would have gone on to sustain a fracture in later life without HRT. More importantly, 63% of all fractures will occur in women with bone densities above this arbitrary cut off point and so will not be identified (table). This limits the potential effectiveness of any bone screening programme.

Alternative methods measuring the rate of loss of bone do not improve the predictive accuracy, and although the predictive value of a bone scan may be improved by additional biochemical estimates of bone loss,

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**Characteristics of screening test for bone mineral content in predicting risk of fracture**

<table>
<thead>
<tr>
<th>Bone mineral content</th>
<th>Lowest 20%</th>
<th>Lowest 40%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity (%)</td>
<td>37</td>
<td>60</td>
</tr>
<tr>
<td>Specificity</td>
<td>83</td>
<td>64</td>
</tr>
</tbody>
</table>

*From Pitt et al.*
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this has not been shown to have significantly greater predictive accuracy over a few decades.42

Because of the fairly short follow up period of prospective studies it is not possible to assess the accuracy of bone density measurements at the menopause in predicting fractures. Only women who will eventually sustain a fracture 25 years subsequently, when fractures are most common. Though long term predictive accuracy is likely to be less than that shown in these studies because factors related to the risk of falling, and other non-bone mass factors are increasingly important in determining the risk of fracture as women get older.34 43 44 So though there is little doubt that bone mass is an important risk factor in fracture, the question of how useful it is for predicting fractures in elderly populations, in which many subjects have a low bone mass, remains unanswered.

There are significant psychological costs (such as increased anxiety) associated with screening people with no symptoms, some of whom are then labelled as at “high risk” for a disease. This is particularly important for those women who are wrongly labelled as being at high risk owing to the poor predictive accuracy of the screening test.

WILL PEOPLE AT RISK ATTEND FOR SCREENING AND WILL WOMEN WITH A POSITIVE TEST RESULT ACCEPT LONG TERM HRT?

The potential effectiveness of any screening programme will also depend on the percentage of women who attend for screening (uptake) and comply with recommended therapy. Results from the national breast cancer screening programme, which targets a similar age group of symptomless women, suggest that there is good reason to assume that uptake rates in routine programmes will not exceed 70%.45

Surveys in Britain46 and elsewhere47 indicate that long term compliance with HRT is less than 30%. Thus calculations of the net impact of the programme reported in the literature which have assumed 100% compliance48 49 50 are likely to be considerable overestimates.26

WHAT IS THE LIKELY OVERALL IMPACT OF BONE SCREENING?

A recent British study50 modelled the impact of such a screening programme using more realistic assumptions (a screening uptake rate of 70%, a sensitivity of 37%, a 10 year duration of HRT, and a compliance of 30%). It is assumed that HRT reduces the risk of fracture by half and that this protective effect lasts the rest of a woman’s life then the model predicts that no more than 4% of expected hip fractures would be prevented in any one year. The costs of the screening and HRT would not be offset by the savings from the reduced incidence of fractures. Alternatively, if it is assumed that the protective effect of HRT will have disappeared by the age of 75 the reduction in incidence of fractures is estimated at only 2.6%.39 This constitutes an approximate reduction of about six out of 219 fractures in postmenopausal women each year in a district of 0.25 million population.

This assessment of the evidence for population bone screening is supported by several other independent reviews.1 16 40 49 In addition, the US Preventive Services Task Force recommended against routine screening for women over 50 years of age, as did the Canadian Task Force on Periodic Health Examinations.51

There have also been calls for a randomised controlled trial to be established to assess the impact of HRT on fractures.32 Other reports, however, have recommended screening around the menopause.53

Conclusion

A population screening programme requires considerable commitment and use of local resources. This would all have to be based on cost effective guidelines that identify an optimal bone mass threshold for instituting HRT. Given current information, it would be inadvisable to establish a routine population based bone screening programme for menopausal women with the aim of preventing fractures. Because of this we have not presented information on the costs of introducing the screening programme. New drugs, such as etidronate, are being considered as potentially more acceptable alternatives to HRT. However, there is even less evidence on their long term effectiveness in reducing the risk of hip fracture.

This paper has reviewed only the evidence for population screening for osteoporosis. However, there is a considerable amount of published material examining the alternative approach to prevention, which concentrates on reducing risk factors of fracture in the whole population. It indicates that it would be worth while for health authorities to investigate the use of population preventive programmes, which could include stopping smoking, exercise, and adequate calcium intake in children’s diets.36

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