# Y Hui 許 書 Osteoporosis: should there be a screening programme in Hong Kong?

## 香港是否應該有骨質疏鬆症的普查計劃?

**Objective.** Osteoporosis is rapidly becoming a major health problem in Hong Kong with the ever-increasing population of elderly people. Its importance lies in the predisposition to fragility fractures of patients with the disease. These fractures incur morbidity and mortality to the elderly. Measures are needed to reduce the prevalence of osteoporosis and the incidence of osteoporotic fractures. A screening programme is potentially the way forward in achieving such a goal. **Study selection and data extraction.** The need for, and the feasibility of, a screening programme for osteoporosis in Hong Kong were evaluated. A comprehensive examination of the relevant issues was carried out within the framework of the World Health Organization criteria on screening of diseases. Major studies from abroad and Hong Kong were discussed and the strength of evidence was assessed.

**Data synthesis.** Osteoporosis satisfies some of the World Health Organization criteria for screening of diseases: it is a significant health problem, the natural history is fairly well understood, and early detection is possible. Nevertheless, there remain unresolved issues related to the screening tests, the treatments currently available, and the selection criteria for treatment. Several therapeutic options have been tested in trials. However, more work is needed to determine whether, in addition to increasing bone mass, they reduce the incidence of fracture. Moreover, the duration of therapy needed to achieve long-term benefit has yet to be established. More studies are also needed to evaluate the cost-effectiveness of such a programme.

**Conclusion.** There undoubtedly needs to be a means of identifying individuals who have osteoporosis and are susceptible to fragility fractures. However, based on the currently available evidence, large-scale screening is not a valid option. Before instituting such a programme in Hong Kong, more studies are needed to determine the most appropriate and cost-effective way forward.

**目的:**隨著老年人口的不斷增長,骨質疏鬆症正迅速成為香港的主要健康問題。它 的重要性在於此病易導致患者骨折。這種骨折可使老年人發病和死亡。要減少骨質 疏鬆症的流行和骨質疏鬆性骨折的可能性,需要採取一定的措施。普查是達到這目 標的可能方式。

**研究選取和數據提取:**本文對在香港進行骨質疏鬆症普查的需要和可行性作了評估,以世界衛生組織疾病普查標準作為框架,對相關問題進行了全面探討,討論了 外國和香港的主要研究,並對其可信程度進行了評估。

**資料綜合**:骨質疏鬆症符合世界衛生組織的疾病普查的部份標準:它是一個重要的 健康問題,其成因已被相當了解,且可於病情早期成功診斷。但還有一些與普查測 試、現有治療、及治療的選擇標準等有關問題尚未解決。雖然已對幾種治療選擇進 行了試驗,然而,需要做更多的工作,以確定這些治療除了增加骨質外,是否能減 少骨折的機會。此外,達致長期效益所需的持續治療時間亦有待確定,而該項普查 計劃的成本效益仍需透過更多研究作出評估。

**結論:**毫無疑問,需要有方法來鑒別患上骨質疏鬆症和易骨折的患者。然而,基於 現有證據,大規模普查方式並非有效的選擇。在香港制定這種計劃之前,需要更多 的研究來找出最適當和最符合成本效益的方式。

Key words: Mass screening; Osteoporosis

#### 關鍵詞:

大眾普查; *骨質疏鬆症* 

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Osteoporosis is "a systemic skeletal disorder characterized by low bone mass and microarchitectural deterioration of bone tissue, with a consequent increase in bone fragility and susceptibility to fracture".<sup>1</sup> Osteoporosis per se is asymptomatic. It is the resultant susceptibility to fracture and the consequent morbidity and mortality that make it an important topic of health care today.

Osteoporosis is a major health problem in America and Europe.<sup>2</sup> In Hong Kong, the health burden caused by osteoporotic fractures is escalating. As new treatment options for osteoporosis become available, two questions remain: who should be investigated and treated; and should some kind of screening strategy be considered? A successful screening programme identifies patients with osteoporosis, thus allowing effective therapy to begin. This reduces the prevalence of osteoporosis and incidence of related complications. As the general public becomes more health conscious, there may be an increasing demand for services such as the diagnosis of and treatment for osteoporosis, in both symptomatic and asymptomatic individuals. An alternative to providing such services in a demand-driven and ad hoc manner is to take the initiative and invite at-risk individuals to participate in a screening programme.

In 1998, a working group formed by several medical societies and academic colleges published clinical management guidelines for osteoporosis in Hong Kong.<sup>3</sup> In 1999 the Royal College of Physicians in the United Kingdom also issued clinical guidelines for prevention and treatment of osteoporosis.<sup>4</sup> These guidelines focus on diagnostic and therapeutic issues. The need for population screening was also discussed briefly. Neither set of guidelines recommended that population screening be carried out. In the United States, however, the National Osteoporosis Foundation (NOF) has recommended screening for osteoporosis in women aged over 65 years.<sup>5</sup>

This review addresses the issue in a systematic manner. The evidence for and against an osteoporosis screening programme for Hong Kong is analysed. Results from local and overseas studies are discussed. The suitability and feasibility of such a screening programme is assessed according to the World Health Organization (WHO) criteria for effective screening strategies (Box 1).<sup>6</sup> A Medline search was carried out to identify relevant publications, while evidence-based reviews were obtained from the Cochrane library.

#### World Health Organization criterion 1

# Is osteoporosis a significant health problem in Hong Kong?

#### Epidemiology of osteoporosis and fragility fractures

The number of people suffering from osteoporosis in Hong Kong is unknown. However, results from local studies indicate that the prevalence of the disease might be similar

### Box 1. Principles for a disease-screening programme based on World Health Organization criteria

- (1) The disease should be a significant health problem
- (2) The natural history of the disease should be understood
- (3) Suitable screening tests should be available
- (4) The disease should be detectable at an early stage
- (5) Screening tests should be acceptable to the population to be tested
- (6) Accepted treatment should be available for patients with the diagnosed disease
- (7) The criteria for selecting patients for treatment should be well established
- (8) Facilities for diagnosis and treatment should be available(9) Cost of diagnosis and treatment should be economically
- balanced relative to the whole medical expenditure(10) The process of case finding must continue beyond the period of screening

to that of western countries. One cross-sectional study of 769 community-based female subjects in Hong Kong found that the mean bone mass of women over the age of 60 years was 30% lower than that of young healthy women.<sup>7</sup> More than 50% of women over the age of 70 years had the disease. The study concluded that the prevalence of osteoporosis in Hong Kong increased exponentially with age. With the increasing size of our elderly population, the disease is likely to become a major health problem.

Osteoporosis predisposes individuals to fragility fractures. These result in significant morbidity and mortality. The association between osteoporosis and increased fracture risk is based on a large number of prospective and case-control studies that have correlated bone mineral density (BMD) with fracture risk. A meta-analysis of such studies suggested that the predictive value of BMD for fracture is at least as good as that of blood pressure for stroke.<sup>8</sup> It is nevertheless important to emphasise that the use of BMD alone to assess fracture risk has a high specificity but low sensitivity. The low sensitivity (approximately 50%) means that half of all osteoporosis.<sup>4</sup>

#### Burden of osteoporosis on the health care system

The impact of the increasing prevalence of osteoporosis can be judged by the overall fracture rates. The hip fracture rate in Hong Kong has been rising over the years and appears to be catching up with the figures from the West.<sup>9</sup> Table 1 shows the age-specific hip fracture rates in Hong Kong for men and women in 1966, 1985, and 1991. Meanwhile, the prevalence of vertebral fractures among Chinese women aged 70-79 years was 29%. This is similar to that for American Caucasians.<sup>10</sup> Current projections indicate that in the year 2015, 5293 women and 2349 men will have a hip fracture.<sup>9</sup>

#### World Health Organization criterion 2

# What do we know about osteoporosis and osteoporotic fracture?

#### Natural history of osteoporosis

Bone loss in postmenopausal women and older men represents an imbalance between rates of resorption and

		Men			Women		
Age-group (years)	1966	1985	1991	1966	1985	1991	
40-49	6	13	9	7	11	6	
50-59	16	28	27	22	32	26	
60-69	67	54	73	54	135	112	
70-79	224	339	321	173	501	581	
<u>≥</u> 80	321	1156	1191	716	1521	1916	

Table 1. Age-specific hip fracture rates in Hong Kong people (per 100 000 population) for three different decades<sup>9</sup>

formation, or 'uncoupled' bone remodelling.<sup>11</sup> The consequence is a paucity of qualitatively normal bone, reduced mechanical strength of the skeleton, and increased fragility. Reduced peak bone mass is a major factor in the development of osteoporosis. Individuals with higher peak bone mass have more reserve later in life.<sup>12,13</sup> Both genetic and environmental factors influence peak bone mass. Studies on twins and relatives of women with osteoporosis show that 50% to 80% of the variance of spinal and hip BMD is due to genetic factors. Calcium intake and physical activity during growth significantly influence peak bone mass. Individuals with a history of low calcium intake have a higher risk of developing osteoporosis.<sup>12-15</sup>

# Fragility fracture—risk factors other than low bone mass

Osteoporosis is not the sole cause of fractures and not all osteoporotic patients suffer from fractures. In a meta-analysis of studies on how well BMD predicted occurrence of osteoporotic fractures, Marshall et al<sup>8</sup> demonstrated that the population attributable risks (Table 2) for a drop in BMD of 1 standard deviation (SD) below age-adjusted means were between 21% and 36%, depending on the lifetime incidence. In fact, there are multiple risk factors for hip fracture. In one prospective study these were identified as change in eyesight depth perception, change in weight, walking for exercise, anticonvulsant therapy, benzodiazepine use, history of fracture, and so forth.<sup>16</sup> Some of these factors may act by reducing bone mass, while others may act by influencing characteristics of bone other than density or by increasing the risk of falling. The study clearly indicates that even if we do treat osteoporosis successfully, fractures associated with other risk factors may still occur.

#### World Health Organization criteria 3-5

#### Diagnostic tests for osteoporosis

#### Diagnosis using bone mineral density

Quantification of BMD can be achieved by X-ray absorptiometry, photon absorptiometry, and quantitative computed tomography. The most commonly used method for measuring BMD is dual energy X-ray absorptiometry (DEXA). It is fast, precise, and has a relatively low absorptive dose compared with other methods.

#### World Health Organization definition of osteoporosis the pros and cons

In 1994, a committee of the WHO defined the criteria for the diagnosis of osteopenia and osteoporosis using BMD measurement.<sup>17</sup> They are based on the patient's comparison Table 2. Sensitivity, specificity, positive predictive value, and population attributable risks for a cut-off point in bone mineral density of 1 standard deviation below age-adjusted means associated with three different lifetime incidences of hip fracture<sup>8</sup> Relative risk of hip fracture is assumed to be 2.6 per 1 standard deviation decrease in bone mineral density

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	Lifetime incidence (%)			
	3	15	30	
Sensitivity (%)	47	37	34	
Specificity (%)	83	88	89	
Positive predictive value (%)	9	36	58	
Population attributable risk (%)	36	26	21	

with mean peak adult bone mass (PABM) and use a standardised score (T-score).

> (Patient's BMD) - (Mean BMD of the young normal reference population)

Osteoporosis is diagnosed when a patient's BMD is 2.5 SD below the mean PABM of the young normal reference population. The WHO further created a second category of osteopenia for patients with low bone mass (T-score between -2.5 and -1.0) to include individuals with a smaller reduction in bone mass who may also merit attention.

The cut-off point of 2.5 SD below mean PABM is based on epidemiological data derived from a population of postmenopausal Caucasian women, 50% of whom had already suffered a fragility fracture. The WHO criteria provide a simple objective diagnostic reference for clinicians to use. They also stress the importance of early diagnosis of low bone mass (osteopenia) before first fracture occurs. The disease can be diagnosed at an early stage based on these criteria.

One limitation of the criteria is that they may not be applicable to people of other races. There are limited epidemiological data on the correlation between fracture rates and BMD in Asian populations. However, lower bone mass has been associated with a high fracture rate in women in Hong Kong<sup>18</sup> and among Japanese women in Hawaii.<sup>19,20</sup> Another limitation of the WHO criteria is the need for a local PABM reference database. In Hong Kong, reference databases of BMD for Chinese women of different age-groups have been established in a number of local studies.<sup>7,21,22</sup> Though such databases would certainly be valuable in future screening programmes, it should be noted that differences exist among these databases. This could be due partly to the use of machines from different manufacturers.<sup>22</sup> It may also reflect, however, the difficulty of establishing a common reference database for different institutes. In addition, more than one reference database may be needed due to the heterogeneity of the Hong Kong population. For instance, it is not known whether people of northern Chinese ancestry have a similar bone mass to those of southern Chinese ancestry. More studies are needed to evaluate such issues.

#### Quantitative ultrasound

A new method for measuring quality of bone is quantitative ultrasound (QUS). It has the advantages of being portable and radiation-free. Quantitative ultrasound does not measure BMD directly. It measures broadband ultrasound attenuation (BUA) and speed of ultrasound (SOS) which can be correlated with BMD. The microarchitecture of the bone may also be assessed using QUS.

In one Hong Kong study, Kung et al<sup>23</sup> found that QUS was able to differentiate between osteoporotic and nonosteoporotic Chinese women. In this study, lower BUA and SOS parameters were also associated with increased risk of vertebral fracture even after adjustment for BMD and other confounding factors. When the WHO threshold of T-score <-2.5 was used as a cut-off, QUS was equivalent to BMD in correctly identifying patients with osteoporotic vertebral fractures. This suggests that similar criteria could be used for QUS diagnosis of osteoporosis. However, results from a subsequent study comparing BMD measurement with DEXA and calcaneal QUS parameters using three different ultrasound devices suggest some modification of the criteria may be needed.<sup>24</sup> Improvement is also needed in the ability of QUS to detect bone loss during the perimenopausal period. One study found that although QUS parameters were predictors of osteoporosis diagnosed on DEXA in perimenopausal women, a high false positive rate limits its use as the sole diagnostic technique.<sup>25</sup> Another limitation of QUS is the lack of precision as estimated by intrasubject coefficient of variation (CV).<sup>26</sup> The short-term CV is reported to be 1% to 5% for BUA and less than 1% for SOS. In contrast, the reproducibility of BMD measurement using DEXA is higher, with a CV between 0.9% and 1.4%.<sup>27</sup>

Regardless of the screening method, whether it is acceptable to the population cannot be judged from the artificial settings in previous diagnosis or treatment trials. Though the investigative tools for measuring bone mass are non-invasive, a prospective pilot or feasibility study is needed to determine whether a screening programme will be accepted by mainly asymptomatic individuals.

#### World Health Organization criteria 6-8

#### Prevention and treatment of osteoporosis

A number of drugs are currently thought to be effective for the prevention or treatment of osteoporosis. These include hormone replacement therapy (HRT), bisphosphonates, fluoride, calcium, vitamin D, calcitonin, parathyroid hormone, and selective oestrogen receptor modulator therapy. Though one of the goals of a successful treatment is an increase in BMD, it is the key end-point of fracture rate that is important. The following discussion will concentrate on drugs that have been more extensively tested and studies in which fracture was used as the end-point.

#### Hormone replacement therapy

Results from several randomised controlled trials have demonstrated the beneficial effects of HRT on BMD. One such study is the Postmenopausal Estrogen/Progestin Interventions Trial, which showed a 1.7% loss in hip BMD in the placebo group compared with a 1.7% gain in the treatment group.<sup>28</sup> The effect of HRT on BMD was dosedependent and was more marked on the vertebrae than the hip.<sup>29</sup>

Most of the evidence of the effect of HRT on reducing the likelihood of fracture is, however, derived from observational data. The Study of Osteoporotic Fractures examined a sample of postmenopausal women and found that current users of oestrogen had a 40% reduction in incidence of hip fracture and a 61% reduction in incidence of wrist fracture compared with women who had never used HRT.<sup>30</sup> The beneficial effect was more marked in women who began HRT within 5 years of menopause. Such benefits were not confirmed in The Heart and Estrogen/ Progestin Replacement Study.<sup>31</sup> This study was a secondary prevention trial of HRT on the occurrence of nonfatal myocardial infarction or cardiac death among 2763 postmenopausal women. Only 408 subjects had BMD measured and fewer than 20% were osteoporotic. When the secondary end-point of fractures was assessed, no benefit was seen after 4 years of HRT. The study, however, had limited power to detect reduction in fracture risk.

The effect of hormone replacement on fracture risk has been assessed in only a few randomised controlled studies. Lufkin et al<sup>29</sup> studied a group of postmenopausal women who had already suffered osteoporotic fractures. Patients were treated with transdermal oestradiol or placebo. The treatment group showed a 61% reduction in fracture risk over the following year compared with the placebo group. In another randomised controlled study of postmenopausal women, 464 subjects were randomly assigned to treatment with HRT (sequential combined oestradiol and cyproterone), vitamin D, HRT and vitamin D, or placebo.<sup>32</sup> During the 4-year trial there was significant reduction in non-vertebral fractures in the women treated with HRT alone and those treated with HRT plus vitamin D.

The beneficial effects of HRT attenuate after the treatment is discontinued. It is hence necessary to continue HRT on a long-term basis to maintain protection against osteoporosis. Since the risk of fracture increases with age, the corollary is that patients may well need to continue HRT into their 70s. Yet the question is, how long could one take HRT before the potential risks of breast carcinoma and thromboembolism outweigh the benefit of reduced fracture risk? Furthermore, it is important to note that although HRT has for some years been approved by the Food and Drug Administration (FDA) for both prevention and treatment of osteoporosis, recent FDA-approved labelling changes for HRT have altered the indication to prevention only.

#### **Bisphosphonates**

Intermittent cyclical etidronate was found to increase BMD and decrease vertebral fracture rate in some studies in the early 1990s.<sup>33,34</sup> The studies, however, have been criticised for the relatively small number of patients recruited. Furthermore, both trials used fracture per 1000 patient-years (fracture rate), instead of actual fracture incidence or number of patients with fracture, in data analysis. This is now deemed inappropriate as it is based on the assumption that occurrence of one event does not increase the likelihood of a subsequent event, which is obviously not true for osteoporotic fracture.<sup>35</sup>

Alendronate has also been tested extensively in several clinical trials.<sup>36</sup> Results from one local study (n=70) showed that alendronate treatment for 1 year increased the BMD of spine and hip by 5.8% and 3.4%, respectively, in osteoporotic Chinese women.<sup>37</sup> The drug was well tolerated by the subjects. In the Fracture Intervention Trial conducted in the United States, 4432 postmenopausal women with low BMD (T-score <-1.6) without pre-existing fracture were randomised into alendronate or placebo treatment groups.<sup>38</sup> Both groups were treated with calcium supplementation if daily intake was below 1000 mg. After 4 years of treatment, the risk of clinical fracture (ie fracture that needs medical attention) was reduced by 14% with alendronate therapy. Radiological vertebral fracture was decreased by 44%. More importantly, the trial showed that in women meeting the WHO criteria for osteoporosis, ie T-score <-2.5, the clinical fracture rate was reduced by 36%. This shows that 15 patients need to be treated in order to prevent one fracture. There was no significant reduction in fracture risk in women with higher BMD.

Risedronate is a new bisphosphonate and, at a dose of 5 mg daily, it was shown to be beneficial in two randomised controlled studies of postmenopausal women with established osteoporotic fracture.<sup>39,40</sup> Furthermore, the results of a large study investigating the efficacy of risedronate 2.5 mg or 5 mg daily in primary prevention of hip fracture have recently been published.<sup>41</sup> Results from the latter study demonstrate that risedronate reduces the risk of hip fracture among elderly women with osteoporosis confirmed by BMD measurement.

#### Calcitonin

When administered subcutaneously, intramuscularly, or intranasally, calcitonin has been shown to increase BMD. In one non-blind study, it decreased vertebral fracture rate.<sup>42</sup> A review of data on the effects of calcitonin on

fracture rates was published in 1999.<sup>43</sup> It suggests that the relative risk of any fracture in a calcitonin-treated patient is 0.43 when compared with individuals receiving no treatment. When data from studies identifying patients with fractures, rather than number of fractures, were pooled, the relative risk was reduced to 0.74.

#### Calcium and vitamin D

Studies in Caucasian and Oriental populations have shown that low calcium intake is associated with low bone mass.<sup>13,14</sup> In a separate study of Chinese women in Hong Kong, daily calcium supplementation of 800 mg and a weight-bearing exercise programme resulted in a 5% increase of femoral neck BMD after 1 year.<sup>44</sup>

Reid et al<sup>45</sup> assessed the effects of calcium supplementation of 1.2 g daily in Caucasian women aged over 60 years who normally consumed less than 1 g of calcium a day. This treatment resulted in a 59% reduction in new vertebral fracture in women who had such fracture at baseline. Other studies have demonstrated that vitamin D or its metabolite prevents bone mass loss and reduces fracture rate.<sup>36</sup> These trials were, however, either small, non-blind, or did not have a placebo group. The combination of calcium with vitamin D appears to give more consistent results.<sup>46</sup>

#### Raloxifene

Raloxifene is a selective oestrogen receptor modulator. It has mixed oestrogen-agonist and oestrogen-antagonist activity. Unlike HRT, it does not promote endometrial growth. In a placebo-controlled study of 601 postmenopausal women, raloxifene increased BMD of the hip and lumbar spine by 2% and 3%, respectively, after 2 years.<sup>47</sup> The drug was well tolerated and there was no significant difference in side-effects between the treatment and placebo groups. In the 3-year Multiple Outcomes of Raloxifene Evaluation study, raloxifene reduced the incidence of vertebral fracture by 30% to 50%.<sup>48</sup> The investigators did not observe a significant reduction in hip fractures. The study was designed with the power to detect vertebral fractures but not hip fractures, however. The latter occur at a much lower rate.

# Evidence-based medicine in prevention and treatment trials

It is notable that a review in 1998 of results from trials of osteoporosis prevention and treatment focusing on fracture risk reduction showed that only 2 out of 35 published studies demonstrated benefits.<sup>35</sup> The review used five criteria (Box 2). Only one study of alendronate treatment and

Box 2. Five criteria used by Meunier<sup>35</sup> to assess the validity of results of studies on the effects of drugs on fracture reduction

- (1) Fracture must be the primary end-point of the study
- (2) The study should be double-blind
- (3) Relative risk and statistical significance must be computed using the patients with fracture method as opposed to the fracture rate method
- (4) Consistent results should be reported for the same agent in different trials
- (5) The study should be published in a peer-reviewed journal

another on treatment with vitamin D plus calcium fulfilled all of them.<sup>46,49</sup> Several new treatment trials have since been published but few fulfil the criteria of the review and its conclusion remains valid. It is possible that the criteria used were too stringent. However, these same criteria may be useful for assessing the results from future trials.

#### Are the treatments acceptable to our population?

It is possible that Chinese women would not accept HRT, partly because of cultural reasons but also because of fear of breast cancer and the return of menstruation.<sup>50</sup> A randomised controlled trial was performed recently to investigate the effects of various dosages of oestrogen on the BMD of postmenopausal women in Hong Kong.<sup>51</sup> The study (n=105) reported a withdrawal rate of 12.4%. The reasons cited included side-effects, loss to follow-up, and voluntary withdrawal. Such a withdrawal rate is not high compared with studies elsewhere on the use of bisphosphonate (20% withdrawal rate) and raloxifene (25%).<sup>47,52</sup> Alendronate was well tolerated in one local trial but acceptability of other treatment options has not been assessed in Hong Kong.<sup>37</sup>

#### Patient selection criteria for screening and treatment

In theory, all postmenopausal women and all men over a certain age could be screened. This, however, would impose a heavy workload and financial burden on the health care system. In 1995 the population of postmenopausal women in Hong Kong was estimated to be 700 000.<sup>3</sup> The target population can be made smaller by increasing the age of entry and screening only those with a known risk factor. Appropriate criteria would improve the effectiveness of the screening programme. Furthermore, they would also prevent the misuse of DEXA, excluding inappropriate candidates such as young women without any risk factor for the disease.

The NOF in the United States recommends that women meeting any one of the five categories in Box 3 be tested for BMD.<sup>5</sup> Selection of women aged 65 years or older without additional risk factors is partly a result of cost-benefit analyses, as women at this age are entering the highest period of risk for hip fractures.<sup>53</sup> It should be noted that the NOF guidelines were based largely on data for postmeno-pausal Caucasian women and whether they are equally applicable in Chinese women and men is uncertain.

#### Box 3. The recommendations of the National Osteoporosis Foundation on who should receive bone mineral density testing They apply only to women, and testing is never indicated unless the results could influence a treatment decision

- All postmenopausal women under age 65 who have one or more additional risk factors for osteoporotic fracture (other than menopause)
- (2) All women aged 65 and older regardless of additional risk factors
- (3) Postmenopausal women who present with fractures (to confirm diagnosis and determine disease severity)
- (4) Women who are considering therapy for osteoporosis, if bone mineral density testing would facilitate the decision(5) Women who have been on hormone replacement therapy
- for prolonged periods

There is no consensus on who should be treated after the screening procedure has identified patients with low bone mass. Though the WHO cut-off of T-score <-2.5 can be used, it is important to emphasise that fracture risk is a gradient and T-score <-2.5 should not be taken as a threshold. Individuals with osteopenia (T-score between -2.5 and -1) also benefit from therapy that delays or prevents progression to osteoporosis.

#### **World Health Organization criterion 9**

# Do we have the facilities and financial resources for screening for osteoporosis?

Currently, certain public and some private organisations possess DEXA or QUS equipment. Nevertheless, should there be a screening programme, more resources would be needed to cope with the demand. Based on 1995 demographic data, the estimated cost of screening all postmenopausal women with DEXA is HK\$323 million.<sup>3</sup> The additional costs of treating the osteoporotic patients identified were not calculated. In 1995 the total expenditure for acute care of hip and vertebral fractures was HK\$189 million. The economic loss associated with the fractures was not known. On their own, these estimates are not enough to shed light on the cost-effectiveness of a screening programme for osteoporosis in Hong Kong. A detailed study which takes into account the medical, social, and economic aspects of osteoporosis and osteoporotic fracture is needed to fully evaluate this issue.

#### World Health Organization criterion 10

#### The issue of postscreening identification

Osteoporosis identification must continue after the initial screening programme. As the bone mass decreases with advancing age, a single measurement may not be enough to predict an individual's future risk of osteoporosis and fracture. Other common diseases in the elderly population, such as stroke and senile dementia, may emerge and increase the risk of fall and fracture. In addition, the response to treatment for osteoporosis may vary from patient to patient. Regular monitoring is needed to ensure the best possible outcome. Poor compliance may also be a problem. Unless patients are followed up with objective assessment to treatment response, non-compliance may go undetected. Further studies are needed to determine the frequency of repeated BMD measurements in patients treated for osteoporosis.

#### Discussion

There is little doubt that osteoporosis is an increasing problem for our ageing population. The impact of this disease on our health care system should not be underestimated. Would a screening programme for osteoporosis solve the tremendous problem facing us? The reasons for and against implementing such a programme in Hong Kong are summarised below using WHO criteria for a screening programme.

#### Reasons for a screening programme

- (1) The increasing size of the elderly population inevitably means an increasing prevalence of osteoporosis and, in turn, fragility fractures. This is evidenced by the current trend in incidence of hip fractures. The total costs of treating such fractures, and the associated morbidity and mortality, can be enormous.
- (2) Our understanding of the natural history of osteoporosis is increasing. The genetic and environmental factors involved in the development of osteoporosis are being identified and becoming better understood.
- (3) The WHO criteria for diagnosis of osteoporosis are widely accepted. These criteria provide guidance not just within the context of clinical trials but also in day-to-day patient care.
- (4) Equipment is available for measuring BMD. New techniques in QUS may, in future, provide alternative means of diagnosing osteoporosis.
- (5) The efficacy of therapeutic agents for treating osteoporosis has been extensively studied in clinical trials. Results from a number of studies have shown that treatment can increase BMD. Some studies have also demonstrated a reduction in fracture rate after treatment. These drugs appear to be generally well tolerated.

#### Reasons against a screening programme

- (1) Although osteoporosis is undoubtedly associated with increased risk of fracture, it is neither the direct nor the only cause. Other contributing risk factors for falls in the elderly are equally, if not more, important. In addition, BMD has a relatively low sensitivity for predicting fracture. It is therefore possible that screening for osteoporosis by BMD measurement may not necessarily significantly reduce the incidence of fractures.
- (2) A widely accepted database of our normal peak bone mass needs to be established and incorporated into the DEXA equipment for accurate diagnosis based on the WHO criteria. This may not be feasible, especially if different organisations are using machines from different manufacturers.
- (3) The selection criteria for treatment after a diagnosis of low bone mass have not been well defined. Should a patient with osteopenia be treated rather than just those with osteoporosis? The patient may benefit but the total costs may be enormous if everyone with osteopenia is treated.
- (4) The appropriate duration of therapy has not been determined. In addition, more data are needed to establish whether treatment significantly reduces the incidence of fragility fractures as well as increasing BMD.
- (5) Osteoporosis without fracture is asymptomatic and may result in poor patient compliance.
- (6) There is no consensus on the frequency of monitoring BMD after treatment has been initiated.
- (7) The cost-effectiveness of such a programme has not yet been determined. Furthermore, many of the new drugs for treating osteoporosis are expensive and may not be widely available due to budgetary restriction.

#### Conclusion

Available evidence supports treating established osteoporosis in individual cases. Nevertheless, there remain important issues to be resolved when deciding whether population screening should be instituted. Based on the evidence currently available, a screening programme for the population is not a valid option. The need for a cost-benefit analysis can never be overstated. In the current climate of financial constraints, there is a lack of resources for the treatment of established osteoporosis. There are no available funds for testing the BMD of large numbers of postmenopausal women. A properly conducted cost-benefit analysis could provide some guidance to both physicians and administrators on the most appropriate and cost-effective way forward. Meanwhile, other research should focus on the key end-point of fracture or alternatively study the reduction of multiple risk factors of fracture thoroughly. Ultimately, the problem of osteoporosis is just one of the issues in the care of our ageing population, the very nature of which dictates a well-rounded and multidisciplinary approach.

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#### References

- 1. Consensus development conference: diagnosis, prophylaxis, and treatment of osteoporosis. Am J Med 1993;94:646-50.
- Repa-Eschen L. The necessity of a managed care approach for osteoporosis. In: Avioli LV, editor. The osteoporotic syndrome. San Diego, California: Academic Press; 2000:1-23.
- The working group for formulating clinical management guidelines for osteoporosis in Hong Kong. Clinical management guidelines for osteoporosis in Hong Kong. Hong Kong Med J 1998;4:423-31.
- 4. Royal College of Physicians. Osteoporosis: clinical guidelines for prevention and treatment. London: RCP; 1999.
- 5. Physician's guide to prevention and treatment of osteoporosis. Washington, DC: National Osteoporosis Foundation; 1998.
- Wilson JH, Junguer G. The principle and practice of screening for disease. Public health papers 34. Geneva: World Health Organization; 1968.
- Ho SC, Lau EM, Woo J, et al. The prevalence of osteoporosis in the Hong Kong Chinese female population. Maturitas 1999;32:171-8.
- Marshall D, Johnell O, Wedel H. Meta-analysis of how well measures of bone mineral density predict occurrence of osteoporotic fractures. BMJ 1996;312:1254-9.
- Lau EM. Hip fracture in Asia—trends, risk factors and prevention. In: Christiansen C, Riis B, editors. Proceedings of the Fourth International Symposium on Osteoporosis. Aalborg: Aalborg APS; 1993: 56-81.
- Lau EM, Chan HH, Woo J, et al. Normal ranges for vertebral height ratios and prevalence of vertebral fracture in Hong Kong Chinese: a comparison with American Caucasians. J Bone Miner Res 1996;11: 1364-8.
- Prestwood KM, Raisz LG. Consequences of alterations in bone remodeling. In: Henderson JE, Goltzman D, editors. The osteoporosis primer. Cambridge, UK: Cambridge University Press; 2000:199-210.

- Matkovic V, Kostial K, Simonovic I, Buzina R, Brodarec A, Nordin BE. Bone status and fracture rates in two regions of Yugoslavia. Am J Clin Nutr 1979;32:540-9.
- Matkovic V, Ciganovic M, Tominac C, Kostial K. Osteoporosis and epidemiology of fractures in Croatia. An international comparison. Henry Ford Hosp Med J 1980;28:116-26.
- Hu JF, Zhao XH, Jia JB, Parpia B, Campbell TC. Dietary calcium and bone density among middle-aged and elderly women in China. Am J Clin Nutr 1993;58:219-27.
- McKay HA, Khan KM. Bone mineral acquisition during childhood and adolescence: physical exercise as a preventive measure. In: Henderson JE, Goltzman D, editors. The osteoporosis primer. Cambridge, UK: Cambridge University Press; 2000:170-85.
- Cummings SR, Nevitt MC, Browner WS, et al. Risk factors for hip fracture in white women. Study of Osteoporotic Fractures Research Group. N Engl J Med 1995;332:767-73.
- The WHO Study Group. Assessment of fracture risk and its application to screening for postmenopausal osteoporosis. Geneva: World Health Organization; 1994.
- Lau EM, Cooper C. Epidemiology and prevention of osteoporosis in urbanized Asian populations. Osteoporos Int 1993;3(Suppl 1): 23S-6S.
- Huang C, Ross PD, Wasnich RD. Short-term and long-term fracture prediction by bone mass measurements: a prospective study. J Bone Miner Res 1998;13:107-13.
- 20. Lau EM, Cooper C. The epidemiology of osteoporosis. The oriental perspective in a world context. Clin Orthop 1996;323:65-74.
- Pun KK, Wong FH, Loh T. Rapid postmenopausal loss of total body and regional bone mass in normal southern Chinese females in Hong Kong. Osteoporos Int 1991;1:87-94.
- Kung AW, Tang GW, Luk KD, Chu LW. Evaluation of a new calcaneal quantitative ultrasound system and determination of normative ultrasound values in southern Chinese women. Osteoporos Int 1999; 9:312-7.
- Kung AW, Luk KD, Chu LW, Tang GW. Quantitative ultrasound and symptomatic vertebral fracture risk in Chinese women. Osteoporos Int 1999;10:456-61.
- Frost ML, Blake DM, Fogelman I. Can the WHO criteria for diagnosing osteoporosis be applied to calcaneal quantitative ultrasound? Osteoporos Int 2000;11:321-30.
- Nairus J, Ahmadi S, Baker S, Baran D. Quantitative ultrasound: an indicator of osteoporosis in perimenopausal women. J Clin Densitom 2000;3:141-7.
- Roux C, Dougados M. Quantitative ultrasound in postmenopausal osteoporosis. Curr Opin Rheumatol 2000;12:336-45.
- Pouilles JM, Tremollieres F, Todorovsky N, Ribot C. Precision and sensitivity of dual-energy x-ray absorptiometry in spinal osteoporosis. J Bone Miner Res 1991;6:997-1002.
- The Writing Group for the PEPI. Effects of hormone therapy on bone mineral density: results from the postmenopausal estrogen/progestin interventions (PEPI) trial. JAMA 1996;276:1389-96.
- Lufkin EG, Wahner HW, O'Fallon WM, et al. Treatment of postmenopausal osteoporosis with transdermal estrogen. Ann Intern Med 1992; 117:1-9.
- Cauley JA, Seeley DG, Ensrud K, Ettinger B, Black D, Cummings SR. Estrogen replacement therapy and fractures in older women. Study of Osteoporotic Fractures Research Group. Ann Intern Med 1995;122:9-16.
- Cauley JA, Black DM, Barrett-Connor E, et al. Effects of hormone replacement therapy on clinical fractures and height loss: The Heart and Estrogen/Progestin Replacement Study (HERS). Am J Med 2001; 110:442-50.
- 32. Komulainen MH, Kroger H, Tuppurainen MT, et al. HRT and Vit D in prevention of non-vertebral fractures in postmenopausal women; a 5 year randomized trial. Maturitas 1998;31:45-54.
- Watts NB, Harris ST, Genant HK, et al. Intermittent cyclical etidronate treatment of postmenopausal osteoporosis. N Engl J Med 1990;323: 73-9.
- 34. Storm T, Thamsborg G, Steiniche T, Genant HK, Sorensen OH.

Effect of intermittent cyclical etidronate therapy on bone mass and fracture rate in women with postmenopausal osteoporosis. N Engl J Med 1990;322:1265-71.

- Meunier PJ. Evidence-based medicine and osteoporosis: a comparison of fracture risk reduction data from osteoporosis randomised clinical trials. Int J Clin Pract 1999;53:122-9.
- Eastell R. Treatment of postmenopausal osteoporosis. N Engl J Med 1998;338:736-46.
- Kung AW, Yeung SS, Chu LW. The efficacy and tolerability of alendronate in postmenopausal osteoporotic Chinese women: a randomized placebo-controlled study. Calcif Tissue Int 2000;67: 286-90.
- Cummings SR, Black DM, Thompson DE, et al. Effect of alendronate on risk of fracture in women with low bone density but without vertebral fractures: results from the Fracture Intervention Trial. JAMA 1998;280:2077-82.
- Harris ST, Watts NB, Genant HK, et al. Effects of risedronate treatment on vertebral and nonvertebral fractures in women with postmenopausal osteoporosis: a randomized controlled trial. Vertebral Efficacy With Risedronate Therapy (VERT) Study Group. JAMA 1999; 282:1344-52.
- 40. Reginster J, Minne HW, Sorensen OH, et al. Randomized trial of the effects of risedronate on vertebral fractures in women with established postmenopausal osteoporosis. Vertebral Efficacy with Risedronate Therapy (VERT) Study Group. Osteoporos Int 2000;11:83-91.
- McClung MR, Geusens P, Miller PD, et al. Effect of risedronate on the risk of hip fracture in elderly women. Hip Intervention Program Study Group. N Engl J Med 2001;344:333-40.
- 42. Rico H, Revilla M, Hernandez ER, Villa LF, Alvarez de Buergo M. Total and regional bone mineral content and fracture rate in postmenopausal osteoporosis treated with salmon calcitonin: a prospective study. Calcif Tissue Int 1995;56:181-5.
- Kanis JA, McCloskey EV. Effect of calcitonin on vertebral and other fractures. QJM 1999;92:143-9.
- Lau EM, Woo J, Leung PC, Swaminathan R, Leung D. The effects of calcium supplementation and exercise on bone density in elderly Chinese women. Osteoporos Int 1992;2:168-73.
- 45. Reid IR, Ames RW, Evans MC, Gamble GD, Sharpe SJ. Long-term effects of calcium supplementation on bone loss and fractures in postmenopausal women: a randomized controlled trial. Am J Med 1995; 98:331-5.
- Chapuy MC, Arlot ME, Delmas PD, Meunier PJ. Effect of calcium and cholecalciferol treatment for three years on hip fractures in elderly women. BMJ 1994;308:1081-2.
- Delmas PD, Bjarnason NH, Mitlak BH, et al. Effects of raloxifene on bone mineral density, serum cholesterol concentrations, and uterine endometrium in postmenopausal women. N Engl J Med 1997;337: 1641-7.
- 48. Ettinger B, Black DM, Mitlak BH, et al. Reduction of vertebral fracture risk in postmenopausal women with osteoporosis treated with raloxifene: results from a 3-year randomized clinical trial. Multiple Outcomes of Raloxifene Evaluation (MORE) Investigators. JAMA 1999;282:637-45.
- 49. Black DM, Cummings SR, Karpf DB, et al. Randomised trial of effect of alendronate on risk of fracture in women with existing vertebral fractures. Fracture Intervention Trial Research Group. Lancet 1996;348:1535-41.
- Lau EM, Woo J. Osteoporosis–is it really preventable? Hong Kong Med J 1998;4:395-9.
- Leung KY, Lee TK, Lee CN, Sum TK, Chan MY, Tong CM. The effects of different dosages of oestrogen on the bone mineral density of postmenopausal Hong Kong Chinese women: randomised controlled trial. Hong Kong Med J 1999;5:9-14.
- Hosking D, Chilvers CE, Christiansen C, et al. Prevention of bone loss with alendronate in postmenopausal women under 60 years of age. Early Postmenopausal Intervention Cohort Study Group. N Engl J Med 1998;338:485-92.
- Black DM. Screening and treatment in the elderly to reduce osteoporotic fracture risk. Br J Obstet Gynaecol 1996;103(Suppl 13):2S-8S.