Round Table Discussion

Reducing osteoporosis: prevention during childhood and adolescence

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Osteoporosis will become a large-scale global health issue as the world's population continues to age. In their article, Delmas and Fraser present a compelling argument describing the potential health crisis the world will face if osteoporosis is not made a high priority by the world health community. They estimate that the worldwide lifetime risk for osteoporotic fractures is as high as 40% in women and 13% in men and describe several health-related consequences of this disease, especially in terms of increases in human pain and suffering and the continual increase in global health care costs (*1*).

Osteoporosis greatly affects the health of ageing women and is recognized as a major area of focus in women's health. In comparison to men, women are at higher risk from osteoporosis and have a lifetime risk of an osteoporotic fracture as high as one in three (*2*). Osteoporotic fractures, commonly of the hip and spine, often result in secondary complications, such as functional impairment, increased hospital stays that may result in further health problems, increased medical costs, and increased dependence on others for living assistance (*2*). The loss of bone strength and the potential for the onset of osteoporosis do not reflect normal ageing (*1*).

These fractures can be prevented and bone loss reduced by the introduction and continuation of certain behaviours throughout life. While commonly associated with older women, the origins of osteoporosis are linked to strong bones being built during childhood and adolescence and being maintained throughout adult life. While the clinical manifestations of osteoporosis usually appear later in life, there is an opportunity for prevention during childhood and adolescence. Delmas and Fraser call for a decrease in the extent of osteoporosis through prevention, early and accurate diagnosis, and increased research and availability of information (*1*). Currently, there is no medical intervention to reverse completely the effects of osteoporosis and the most powerful tool to reduce the incidence of osteoporosis is prevention through health education (*2*).

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In the USA, 28 million people are estimated as being at risk of developing osteoporosis and one in three women over the age of 50 will suffer an osteoporotic fracture in her lifetime (*3*). In addition to a decreased quality of life for individuals affected by osteoporosis, the United States faces increasing health care costs due to the extent of the problem. Estimated by the actual cost of health care and lost productivity, the United States spent US$ 13.8 billion in 1996 on osteoporosis and its related health problems (*2*). The costs in human pain and in health care will only increase as the number of older people in the United States doubles by the year 2030 (*2*). As women continue to outnumber men in older age groups, osteoporosis is a growing women's public health issue (*3*).

The millions of women affected by osteoporosis and the increasing health care costs to treat the disease and its complications accurately depict the extent and severity of this health issue. However, left out of this picture is the decrease in the quality of life of women affected by osteoporosis. Osteoporotic fractures, such as hip fractures, may render an individual unable to walk independently following the fracture (*2*). The negative health consequences following osteoporotic fractures often result in a decrease of individual independence, compromising not only the physical health but the general quality of life of women affected by this disease.

Osteoporosis is a disease that may be prevented throughout life, but it is particularly important to begin primary prevention during childhood and adolescence (*2*). Current evidence indicates that young women can increase their peak bone mass, promote long-term bone health and reduce the risk of disease later in life by following effective dietary, exercise and lifestyle practices (*2*). Additionally, adherence to healthy behaviours helps ensure a healthier ageing experience later in life. Nevertheless, studies reveal that adolescent girls are not taking the necessary steps to promote bone health (*4*). Currently, 85% of girls aged 12–19 do not meet the recommended daily allowance of calcium, which is necessary for developing the structure of strong bones (*4*). Furthermore, calcium consumption declines in girls during adolescence (*5, 6*). In addition to adequate calcium consumption, participation in physical activity is important, and it has been demonstrated that girls consistently participate less frequently in vigorous and strengthening exercises (*7*). Clearly there is a gap in health knowledge and practices among young girls, which may be rectified through education and the introduction of healthy behaviours.

In September 1996, the United States Public Health Service's Office on Women's Health (PHS OWH) convened a task force to design a

blueprint for a national osteoporosis education campaign. The task force recommended providing osteoporosis prevention messages to girls aged 9–18 years when they begin to make their own decisions about diet and exercise. These years of physical and psychological development are critical because 90% of total bone mass will be established by the end of the adolescent period (*4*). Childhood and adolescence represent important times in which to initiate and strengthen patterns of healthy habits, such as increased calcium intake, increased physical exercise, and avoidance of health-compromising behaviours, like smoking and alcohol consumption, which will hopefully be continued throughout adulthood.

The PHS OWH, in collaboration with the Centers for Disease Control and Prevention and the National Osteoporosis Foundation, has begun to design the National Bone Health Campaign to promote bone health awareness. This campaign will first target 9–12-year-old girls who are approaching their peak bone-building years and will later target girls aged 13–18. As the campaign develops, it will also target the parents of adolescent girls as they may serve as critical role models of healthy behaviours. The PHS OWH, Centers for Disease Control and Prevention, and the National Osteoporosis Foundation hope to make significant strides to reverse current trends in adolescent health behaviours and ultimately increase physical activity, consumption of calcium and adoption of other healthy lifestyle behaviours associated with better bone and total health.

Delmas and Fraser described the importance of a major educational effort focused on the importance of preventing osteoporosis to improve the health of the globally ageing population (*1*). In the United States, the National Bone Health Campaign will not only increase the awareness of the public and of health professionals about osteoporosis, but will also provide viable methods for adolescent females to increase their bone health to retain greater bone strength later in life. Ideally, the National Bone Health Campaign will prevent the onset of osteoporosis in women by increasing healthy behaviours during adolescence. The prevention of osteoporosis will ultimately improve the quality of life for ageing women in the United States.

Improved bone health is a necessity for the overall health of women of all ages. A decrease in the incidence of osteoporosis will lead to a decrease in other conditions associated with osteoporosis and financial savings worldwide. The money currently spent to treat osteoporosis and its related problems may eventually be redirected to other areas of women's health. By pioneering education on bone health for adolescents and their parents, gathering data from the intervention, and assessing its impact on osteoporosis and on women's health, the National Bone Health Campaign will contribute to the global improvement of women's health.

The use of visionary and long-term prevention strategies will be critical to improving women's health. Only by preparing young girls for a lifetime of healthy behaviours will this goal be achieved. With sustained and directed national and international efforts towards the prevention of osteoporosis, women's health may be improved worldwide. ■

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Osteoporosis: a global perspective

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The article by Delmas and Fraser draws attention to osteoporosis as an increasingly large global health problem, while not ignoring the protracted pain and disability often experienced by individual sufferers. The case is made persuasively that more needs to be done in developed countries, but a desperate lack of information about even the basic epidemiology of osteoporosis in many parts of the developing world also is evident. The situation in India, which is currently the world's second most populous nation, is illustrative. The report from which the descriptive data on hip fractures in India were derived was published in 1966 *(1)* and refers to a hospital case series. While it is commendable for the year in which it was produced, much more data are now needed and are not available in the literature.

Increased longevity alone is predicted to increase dramatically the number of hip fractures worldwide to 6.3 million per year by the year 2050. More than half of the total number of fractures will occur in Asia and Latin America. The people who will suffer these fractures are currently young adults,

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many being women in their reproductive years. Apart from a few notable exceptions, relatively little is being done to characterize determinants of bone mass and to improve understanding of risk factors for osteoporosis and fractures in these populations. In most countries, women interact with health care providers for child-bearing and during child-rearing, as well as for assistance with contraception. These interactions should provide a precious opportunity for much-needed research from which evidence-based programmes for bone health can arise.

The magnitude of the problem of osteoporosis in the developing world may be even greater than predicted above. Much valuable research on osteoporosis and hip fractures has been conducted in Hong Kong. Rates of age-specific hip fracture more than doubled in this country between 1966 and 1991 *(2)*. A clear need exists to continue this research and to conduct similar studies in other centres in the developing world.

Delmas and Fraser rightly draw attention to the importance of prevention and early detection of osteoporosis. Access to reliable bone density testing is essential for the implementation of effective programmes to detect and manage pre-fracture osteoporosis. However, major barriers for access to such testing exist, which include poor instrument availability, high cost to patients and restrictive indications for testing in many parts of the world.

Other useful predictors, particularly of hip fracture risk, should not be ignored. Some of the potentially useful predictors include the following: maternal history of hip fractures, a history of falls, use of psychotropic medication, detection of low body weight, muscle weakness and increased body sway *(3,4)*. A number of risk factors for fracture, including low bone mineral density, have additive effects and should be useful in identifying individuals at risk of hip fracture. The role of these and other indices of risk fracture (for example, a history of low-trauma fractures) must be validated for case management. One appealing approach is to validate a strategy of case-finding linked to the systematic mitigation of remediable risk factors.

Impressive advances in our understanding of risk factors for low-trauma fractures have occurred during the last decade. Linked with these advances has been considerable progress in understanding the pathogenesis of osteoporotic fractures, but much remains to be learned. A specific example is the doubling of hip fracture risk associated with a maternal history of hip fracture *(4)*. The high degree of heritability of bone mass is an obvious mechanism for this association. However, genetic-epidemiological modelling suggests that the heritability of bone mass might explain only about 20% of this familial aggregation of hip fractures *(5)*. Understanding why osteoporotic fractures cluster in families may have major implications for fracture prevention.

Several classes of drugs have been identified for which there are sound data on the prevention of fractures. However, the appropriate target populations for these interventions are uncertain. Phase IV studies of these agents must be significantly expanded to establish their true risk-benefit and cost-effectiveness profiles for various potential target populations. Funding and implementation of such research are essential.

Cost and scepticism are not the only barriers to intervention to prevent osteoporotic fractures and the associated impoverishment of quality of life. Currently, even the adoption of cheap, simple, safe and effective interventions remains at a low level. One study reports that 30–50% of the elderly in residential care in Australia are deficient in vitamin D using conventional criteria *(6)*. However, few experts doubt that vitamin D deficiency leads to fractures, morbidity and mortality and that simple intervention with vitamin D and calcium supplementation is appropriate in this high-risk population *(7)*. Practical solutions must be found and education at multiple levels must occur to overcome this inertia. Policy-makers, industry, health authorities, primary care physicians, care-givers and patients all need to contribute for even simple strategies to work.

Long-term strategies for the primary prevention of osteoporosis are an exciting, if challenging, prospect. The objective is to find broadly applicable interventions to augment and maintain the peak level of bone mass normally achieved by early adult life. At least two such interventions are already under investigation: dietary calcium supplementation and physical activity. To date, intervention studies with calcium for up to three years during childhood and adolescence have shown only modest bone gain in Caucasian populations and evidence is lacking that any benefit is maintained to increase peak bone mass *(8)*. A study in China suggests that children on an habitually low dietary calcium intake may respond more sensitively to calcium supplementation *(9)*. More work and, in particular, long-term follow-up studies are needed to determine the role of augmented calcium intake in increasing peak bone mass. Such research should be conducted in a range of different populations living under various environmental conditions.

Many retrospective, cross-sectional and longitudinal observational studies have established a clear association between weight-bearing physical activity and increased bone mass. Some research has supported the proposition that early adolescence represents a "window of opportunity" when the sensitivity of the skeleton to beneficial anabolic effects by mechanical loading is optimal *(10)*. Short-term controlled intervention studies have also supported this proposition *(11)*. These findings are encouraging, but much more needs to be done. This should include definition of the nature and amount of exercise that is beneficial, confirmation that benefits to bone health are maintained in the long term, the introduction of effective physical-activity regimens that will encourage retention through adolescence and into adult life, and the rigorous assessment of

potential adverse effects so that risk-benefit comparisons can be made.

Osteoporosis may well be one of the great health problems of the 21st century: it is a disorder linked with ageing and affluence, but it need not be so. Already, much can be done to prevent and to mitigate the effects of osteoporosis. We need to find ways to implement the effective interventions that are currently available while maintaining our efforts to find new solutions in prevention and treatment. ■

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The view from Brazil: desirable but not yet feasible

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The article by Delmas and Fraser is both important and timely, as is WHO's concern about osteoporosis. Although their article is about osteoporosis in a global perspective, I believe important aspects of this condition still need elucidation before recommendations on prevention and control turn an individual necessity into an economic burden, especially in the case of less developed countries.

We all agree that osteoporosis is a severe disorder that manifests itself only when bone loss and fragility are far advanced. The authors choose to call it a disease, but I would prefer it to be considered a syndrome, because even the "involutional", postmenopausal and senile forms of it are heterogeneous in both their pathophysiology and clinical presentation. This point of view could also encourage the primary care physician to look for the secondary causes of osteoporosis, and choose the appropriate treatment.

It is true that we have medications that are effective in reducing osteoporotic fracture rates by 30–50%. However these medications do not build strong bones, do not stop this disorder, are very expensive for most people and need to be maintained for a long time, if not for the rest of one's life (*1*).

Most physicians also agree that osteoporosis is a global problem and that governments have either failed to respond or responded inconsistently to this serious threat. WHO has emphasized that developing countries may experience a heavy burden from osteoporosis because their populations are ageing more rapidly than the industrialized ones (*2*). It is also known that the prevalence of osteoporosis varies both from country to country, as in Europe, and within countries, as in the USA (*3*). Differences in race, nutrition, physical activity, lifestyle and living conditions all contribute to it.

This variability makes it very difficult to know who is at risk of osteoporosis. As Delmas and Fraser admit, in many communities there are no solid estimates of the magnitude of this problem. This is true of Brazil, which has a very heterogeneous racial, economic and cultural background. Also, where life expectancy is shorter the prevalence of osteoporosis and its economic impact tend to be smaller.

In many countries, especially developing ones, data on fragility fractures are not available. Fragility fractures are the main manifestation of osteoporosis (*2*). As about 70–80% of the variance of bone strength can be explained by the bone mass, there is a tendency to use bone mass measurements as a substitute for estimates of bone resistance to trauma (*4*). The authors point out that other risk factors and falls can contribute to fragility fractures, but most physicians rely only on bone densitometry for the diagnosis of osteoporosis and for the assessment of patients' fracture risk.

In 1994, a WHO panel of experts recommended a classification for bone mass measurement based on bone densitometry (*2*). Although well intended, writing "osteoporosis" as a test result has caused confusion among non-specialist physicians, and unnecessary fright in patients who read that word in bone densitometry reports. I would like to suggest, as I have in the past, that this degree of low bone mass should be called severe osteopenia.

As nobody can predict who will or will not have strong bones, a cost-effective test is needed for early detection. The main article shows how in almost all countries most of the available equipment consists of central units that are both expensive and impractical for population surveys. Peripheral bone densitometry

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units and ultrasound devices are smaller and more affordable, but their results do not correlate well with the ones obtained from central bone densitometry units for which there are currently no commonly adopted reference values.

In this situation it is hardly surprising, although unjustifiable, that many governments, especially in poorer countries, do not yet have policies for fighting osteoporosis. A programme to detect those at risk of osteoporosis needs clear guidelines, inexpensive devices and standardized results, both for diagnostics and for fracture risk assessment.

Delmas and Fraser suggest that any post-menopausal woman not taking estrogen should be tested. Can this be accepted worldwide? How early should a test be performed? They do not say. Maybe this omission was intentional, because there is much to be learnt about the impact of osteoporosis in many countries. Recently, the American National Osteoporosis Foundation suggested that all women over the age of 65 or all post-menopausal women with an additional risk factor should be tested, but they too failed to specify which of the many tests available should be used (*5*). The age of 65 could be too late for some women, if the intention is to maintain bone strength. I think there is enough evidence to suggest that all perimenopausal women, except black women who are better protected from osteoporosis, should be tested provided an inexpensive and reliable test is available to estimate bone mass or bone strength. This may also be valid for men with clinical risk factors or with a family history of osteoporosis.

An important aspect of osteoporosis that was not stressed in Delmas and Fraser's article is primary prevention, especially by non-pharmacological means. Very little is known about it although many studies mention its importance. It is already known that most of one's bone mass is gained during infancy and adolescence (*6*). One can only expect to build strong bones while the bones are growing. During this period of life many nutritional, physical and other habits are formed and, if they are not appropriate, they may cause failure to attain peak bone mass that may contribute to fractures later in life (*7, 8*). This has not been sufficiently studied, and it is time to look into it more deeply if an effective plan to prevent osteoporosis is sought.

Finally, treatments and tests are still too expensive and, as the authors say, "there is a lamentable lack of accurate data on osteoporosis", along with lack of agreement about when and how to detect osteoporosis, and in whom. One can only assume, therefore, that what is needed, early detection and effective prevention, will remain a luxury, worldwide, at least for the time being. ■

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The view from Tunisia: need for an inclusive approach

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Although the problems of detecting and preventing osteoporosis concern almost everyone in the world on account of the marked improvement in life expectancy, they do not have the same priority in the developing countries as in the industrialized ones. The main reasons for this are demographic, epidemiological and socioeconomic.

Demographic factors

In most developing countries, despite greater life expectancy and more or less effective birth control policy, the majority of the population is young. In 1998, almost 50% of the population of the developing countries was aged under 20, less than 6% was aged over 65 and less than 1% was over 80. According to projections for the year 2010, persons aged over 65 will make up about 6.5% of the population, while the proportion of persons aged over 80 will increase to approximately 1.3%. These figures are very low in comparison to those for Japan, Australia, the United States and the countries of Europe.

Epidemiological factors

The majority of the developing countries are going through a major epidemiological transition as a result of rapid changes in lifestyle marked by a more sedentary way of life and a nutritional imbalance most notably characterized by the overconsumption of refined carbohydrates and saturated lipids. As a result, these developing countries are feeling the full

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impact of the dramatic increase in chronic noncommunicable diseases: obesity, lipid disorders, arterial hypertension and diabetes, which are major risk factors affecting morbidity and mortality from cardiovascular diseases. The victims of these diseases in the developing countries are increasingly young (in Tunisia, for example, cardiovascular diseases are responsible for one out of every four deaths among adults, but the corresponding numbers of deaths are declining in the industrialized countries). These problems are compounded by the pathologies associated with ageing: neurological, neoplastic and osteoarticular disorders such as arthrosis and osteoporosis.

The detection and prevention of these diseases is thus a matter of the utmost importance and requires the following:

- sound knowledge of local circumstances, with precise epidemiological data on the incidence of these pathologies and the risk factors contributing to their development;
- material and human resources to detect and manage patients at an early stage;
- a strategy of prevention among the population at high risk.

Such facilities are rare even in the wealthiest countries, and virtually non-existent in the majority of the developing ones. This makes it especially difficult for developing countries to develop an effective strategy for dealing with the rapid increase of noncommunicable diseases.

Socioeconomic factors

For disease control, socioeconomic factors are inseparable from factors related to the health systems currently in place. The most important socioeconomic factors may be listed as follows:

- A high rate of illiteracy, which in some countries exceeds 50% of the total population and 75% of women.
- Excessive focus of the health system on curative care and insufficient attention to early detection and prevention of diseases.
- Medical training that is frequently too theoretical and ill-adjusted to the needs of the population; physicians are often ill-equipped to deal with these epidemiological situations and to develop sound preventive strategies.
- Inadequate medical information and health education: the dietary advice given by a physician in his surgery cannot compete with relentless television advertisements for unsuitable products.
- No census of the different diseases and no reliable statistics on the causes of mortality on account of failure to use the standard international death certificate.
- Scant material and human resources to detect and manage diseases at an early stage.
- Inadequate and inefficient health insurance systems that frequently fail to cover screening examinations and preventive treatment.

Regarding osteoporosis in particular, we are convinced that the increase in life expectancy and the ageing of the population make it necessary for health officials and specialists to focus their attention on this disease, on account of its increasing social and economic consequences in both the industrialized and the developing countries. However, the problem of detecting and preventing the disease does not assume the same urgency, because of the prevailing epidemiological situation in the developing countries. There are no precise data on the incidence of osteoporosis and its progression; means of detection are inadequate. For instance, Tunisia has a single biophotonic densitometer for a population of 9.4 million, 5.6% of whom are aged over 65. There is no effective social insurance coverage; post-menopausal replacement therapy is rarely reimbursed. The population is very young and very much under threat from the rapid increase in cardiovascular risk factors. The problem of osteoporosis prevention should be integrated into the broader framework of a strategy to prevent noncommunicable diseases.

To do so, attention must be drawn to the importance of nutrition at the very beginning of life, during gestation, during which deficiencies lead to numerous diseases in adult life. This means that every effort must be made to ensure that mothers are guaranteed early on, from the moment they become pregnant, the best possible nutrition and hygiene to ensure that their children develop normally and have satisfactory bone mass.

Later on, it is necessary to teach a lifelong awareness of health, emphasizing the importance of a balanced diet that naturally ensures a proper intake of vitamins and calcium, and the importance of regular physical exercise to avert demineralization and to consolidate bone mass.

Hormone replacement therapy at the menopause is not yet accepted by all women. An effort should be made to introduce treatment, particularly because of its usefulness in preventing post-menopausal growth problems providing protection against cardiovascular risk factors, whose incidence increases significantly among post-menopausal women, and promoting a better quality of life in the elderly.

Ensuring that people have strong bones throughout their life is no luxury. Indeed, the notion of luxury is not appropriate where health is concerned and it is a question rather of need. This need must be met as early in life as possible through the development of an integrated strategy suited to each country's epidemiological situation. ■

Osteoporosis care in Hungary

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Hungary has a high standard of osteoporosis care although it is less affluent than many of the industrialized countries. This is attributable to the efforts of the Hungarian Osteoporosis and Osteoarthrology Society (HOOS) which started a comprehensive national osteoporosis programme in 1994.

This special programme was launched because a survey showed that the prevalence of osteoporosis in the country was high: 32.3% in women and 23.6% in men according to a stratified random sample of people aged 50 years and over (*1*). Lumbar bone mineral density values in Hungary have been found to be very low compared to those in 15 other countries surveyed in the European Vertebral Osteoporosis Study (EVOS) (*2*). The EVOS study indicated that the prevalence of vertebral fractures was as high in Eastern Europe as in Western Europe.

The prevalence in Hungary was 16.7% for women and 18.7 % for men, which were the highest values outside Scandinavia for both sexes (*3*). Vertebral fractures were almost equally frequent in men and women in other EVOS countries as well. Since this is the most frequent type of osteoporotic fracture, the lifetime risk for osteoporotic fractures in men, currently estimated at 13%, may need to be revised upwards.

In the Hungarian sample, the prevalence of both osteoporosis and vertebral fractures increased with age in women but not in men. Therefore, our data do not confirm that increasing age would correlate strongly with an increased risk of osteoporosis in men as stated by Delmas and Fraser. This may be explained by the strong influence of other risk factors such as heavy smoking and alcohol consumption and by the high prevalence of secondary osteoporosis in Hungarian men. Vitamin D deficiency is frequent (34%) in the elderly population and the frequency of the vitamin D receptor BB genotype is high (24.6%) which might be related to lower bone mass as well (*4*). The effect of age was demonstrated, however, in the age-specific incidence of hip fractures in both sexes. Data from the national health register showed that the incidence of hip fractures was high in Hungary (in 1995 it was 3.2 per 1000 in women and 1.9 per 1000 in men) compared to other European countries.

These findings on osteoporosis and its consequences convinced us that we should start an extensive project to deal with this disease in Hungary. The HOOS launched its national programme, supported by the Ministry of Health and Welfare, in 1994 (*5*). The first step was to set up a network of well-equipped osteoporosis outpatient centres, consisting of one national coordinating centre, 10 regional centres and 90 local centres, thus covering most of the country. The activity of these units has been based on the collaboration of different specialists, particularly rheumatologists, gynaecologists and interns, supported by exercise therapists, radiologists, laboratory staff and, in some places, orthopaedic surgeons. The teams of specialists have close links with the doctors providing primary care, but diagnosis of the disease, indication and follow-up of the therapy by densitometry are made by the osteoporosis centres. The national centre, all the regional ones and some of the local ones have inpatient facilities for physical therapy and rehabilitation. These centres should guarantee appropriate care for osteoporosis and cases of fracture, and provide postgraduate education. General practitioners are not usually well-informed about osteoporosis in Hungary, since training in osteology is somewhat limited, and most of the information on it is confined to specialized courses and specialized journals. The activities of the HOOS and osteoporosis centres have been supported by the network of patients' clubs, which play a crucial part in raising public awareness of osteoporosis.

All the osteoporosis units are equipped with bone densitometers. The number of machines available increased from 7 in 1994 to 105 in 1998. The proportion of forearm equipment is predominant (80 of the 105), though the more useful machines measure the bone mineral density of the hip and spine. In most cases measurement is free, being reimbursable by the National Health Insurance Service. The use of biochemical markers, approved for monitoring osteoporosis therapy in Hungary, is also largely reimbursable.

All the effective and approved drugs on the market in the European Union are available in Hungary. Drugs prescribed by the specialists of osteoporosis centres are reimbursed at 90% for osteopenia or osteoporosis diagnosed by densitometry, and otherwise at 50%. The proportion of osteoporotic patients receiving drug treatment is only 5–10%. In Hungary, hormone replacement therapy is still used much less than other less effective treatments. Guidelines on diagnostics and management of osteoporosis based on international approaches have been established by the National Osteoporosis Centre at the request of the Ministry of Health and Welfare, but recommendations have sometimes been neglected in clinical practice.

HOOS works closely with the International Osteoporosis Foundation, and in 1998 organized the First Central and Eastern European Meeting on Osteoporosis in Budapest. The purpose was to bring together the efforts of the transitional European countries in this field. The report resulting from this meeting stressed the importance of osteoporosis as a major health care concern and made recommendations for primary prevention, screening of individuals at high risk, appropriate treatment and rehabilitation, and reimbursement.

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In conclusion, Hungary has managed to set up an effective care system for patients suffering from osteoporosis. In doing so, it has shown how personal effort and concerted action are at least as important as high income levels in the strategy against osteoporosis. ■

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Vertebral and hip fractures in Japan

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The article by Delmas and Fraser indicates that the number of hip and vertebral fractures could increase worldwide over the next few decades as the population grows and ages. In Japan, however, recent trends in the number of these fractures seem to differ from those in European and American countries.

Osteoporosis affects both men and women, with an increased risk observed in women after menopause. The average age of menopause in Japanese women is approximately 50 years. Lumbar bone mineral density (BMD) decreases by 2–3% at 50, then declines until 70 years of age and does not substantially decrease thereafter (*1,2*). Total lumbar BMD loss during the first five years after menopause amounts to 10–15%, which is similar to values observed in Caucasians. Thus, the effect of menopause on bone loss in Japanese women seems to be similar to that in Caucasians.

Vertebral fractures in Japanese women have two remarkable features, a high prevalence of multiple (two or more) fractures in the period just after menopause and a different location of fractured vertebrae in the spine. A bimodal distribution of fractures, with the highest number of fractures in the middle thoracic and thoracolumbar regions, has been observed in Caucasian women, but middle thoracic fractures are less frequent in Japanese women (*3*). The prevalence of vertebral fractures in Japanese women starts to increase at the age of 60, and is twice the value observed for Caucasians between 65 and 75 years of age. Above 75 years of age, the prevalence of vertebral fractures in Caucasians rapidly increases, reaching the level observed in Japanese women (*3*). Since the prevalence in second-generation Japanese-Americans in Hawaii was about half that observed in native Japanese, the high prevalence of vertebral fractures in Japan between the ages of 65 and 75 cannot be due to genetic factors. However, a similar distribution of fractures, with the highest number of fractures solely in the thoracolumbar region, was observed in people of Japanese descent living in Hawaii. Thus, the distribution of vertebral fractures could be affected by genetic factors.

Lumbar BMD has been used as a major predictor of prevalent vertebral fracture. However, the number of years between menarche and natural menopause significantly influences the prevalence of vertebral fractures independent of BMD (*4*). Lumbar BMD values in Japanese post-menopausal women are lower than those in Caucasian women. Since the annual rates of bone loss are almost the same in Japanese and Caucasians, the smaller BMD values in Japanese post-menopausal women may be caused by pre-menopausal events. A positive correlation has been established between body weight and lumbar BMD. Thus, the smaller body weights of Japanese women may explain this difference. The difference may also be related to the years between menarche and menopause. Present data on vertebral fractures have been primarily obtained from women born before 1940 (*5*). Menarche in these women was delayed. Japanese women in the latter study had less exposure to estrogen, in terms of number of years, than Caucasian women in the same period (*6*). Therefore, smaller body size and a shorter period of estrogen exposure may cause lower BMD. This may lead to the early occurrence of vertebral fractures in Japan.

Recent trends in vertebral fractures in early menarche and late menopause are noteworthy in estimating the future prevalence of vertebral fractures in Japanese women. The average age of menarche in Japanese women born between 1900 and 1904 was approximately 16 years, two years later than the average age in Caucasians born during the same period (*6*). However, recent data show that the age of menarche in Japan is approaching that of Caucasians. At present, menopause tends to occur later in Japanese women. An increase in the duration of estrogen exposure in women could result from the increased consumption of meat, which has replaced vegetables as a primary diet component. Thus, the onset age of vertebral fracture in Japanese women is expected to increase and the prevalence of multiple fractures may decrease in the 21st century. The incidence of thoracic vertebral fractures in young Japanese has decreased progressively in successive generations. Changes to the traditional Japanese

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lifestyle over the last 50 years may have caused alterations in the endogenous levels of female hormones in Japan.

Hip fractures in Japan have clearly increased in the last ten years. A nationwide survey estimated 41 000–48 000 occurrences in 1987 and 77 000–80 000 in 1992. The incidences per 10 000 persons increased in both females and males from the age of 60 onwards. The incidences in females in their 70s and 80s increased from 15 to 45 and from 45 to 140 per 10 000 persons, respectively, from 1987 to 1992. The exact causes of the increases in hip fractures are not known. Since the incidences in females and males increased similarly, increased estrogen exposure does not contribute to reduce the number of hip fractures. Significant risk factors for hip fractures include drinking more than three cups of coffee daily and sleeping in a bed rather than on a mat. In contrast, in addition to a large body mass index, fish consumption appeared to reduce the risk of hip fracture (*7*). The age-adjusted prevalence of falls among native Japanese has also been demonstrated to be about half that observed for Caucasian women (*8*). Thus, changes to the traditional lifestyle of the Japanese elderly may be related to increases in the number of hip fractures.

The prevalence of vertebral fractures has been shown to be high and the incidence of hip fractures low in a Japanese population compared to Caucasians (*3*). However, we have recently observed in Japan that the incidence of vertebral fractures is decreasing while the prevalence of hip fractures is increasing. These changes in the two major fractures associated with osteoporosis appear to be closely related to rapid industrialization and loss of the traditional Japanese lifestyle. There is no denying that there will be a worldwide increase in osteoporosis, but the occurrence of osteoporotic fractures is affected not only by biological factors such as age, bone mass, and estrogen exposure, but is possibly modified by the lifestyle and the degree of industrialization of the community. To prevent osteoporotic fractures in a population in later life, modification of lifestyle to reduce risk factors is an effective means of achieving strong bones. ■

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Strategies for osteoporosis treatment

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The article by Delmas and Fraser has a provocative title, which I suspect was conceived by the editors of the *Bulletin* rather than by the authors. The question posed is difficult to resolve. The authors conclude that the attainment of strong bones is feasible. They emphasize the widespread nature of osteoporosis, the availability of treatments, tools for its diagnosis and the availability, if not the practice, of treatment guidelines. The report focuses on the review of osteoporosis published recently by the European Community (*1*) which is a timely recognition of the importance of osteoporosis to public health. The implication of the review is that we have all the requirements necessary to apply successful treatments to decrease the burden of osteoporosis. My thesis is that, whereas we have effective diagnostic tools and treatments, major problems still remain. Until these are solved, osteoporosis will remain a necessity.

As emphasized by Delmas and Fraser, osteoporosis is now recognized as causing a significant impact on the health of all communities (*2*). Even so, the frequency of osteoporosis for the future is underestimated. Life expectancy is improving in all communities, and the projected burden of osteoporosis has traditionally not taken this into account. For example, the lifetime risk of hip fracture in Sweden for women aged 50 years is given as 14% but is 23% when future estimates of mortality are accounted for (*3*). Additionally, in many communities there are increases in age-specific and sex-specific rates for reasons that are poorly understood (*4*); if these continue, they will have a significant impact on the future. This suggests that the problems of osteoporosis are much greater than currently estimated. With modest assumptions regarding the increase in age-specific and sex-specific incidence, the number of hip fractures worldwide may increase from 1.26 million in 1990 to between 8 and 20 million by 2050 (*4*).

It is important to understand the pathogenesis of osteoporosis because of the ubiquity of postmenopausal osteoporosis. In particular, the reasons

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for the large differences in risk of fracture between communities (*5*) and the increase in age-specific and sex-specific risks of fracture must be established. Reasons that have been offered include decreasing physical activity, and an increase in the impact of falls due to the progressive urbanization of the world.

Consequently, the need to develop preventive strategies is evident. Two distinct but non-mutually exclusive strategies can be envisaged: the first is to identify patients at particular risk and offer intervention (high-risk strategy); the second is population based, where the aim is to modify the risk factors in the general community (global strategy).

Global strategy

Although there are several risk factors that have been identified for osteoporosis or for fracture, they are not necessarily causally related. These uncertainties also exist for smoking and moderate alcohol consumption. A second problem relates to the ability to change lifestyle habits and their impact on risk, and in the context of osteoporosis no studies have addressed these issues. For example, several clinical trials have shown beneficial effects of exercise on bone mass (*6*), but the effects are small, and the impact on the community has not been tested. It is questionable whether a patient of 40 years of age would maintain an exercise programme until 75 years of age when hip fractures arise. A further problem relates to the impact of remedial factors on the frequency of fractures within a community. Uncertainties remain not only with exercise, but also with nutritional risk factors. Despite the high prevalence of many such factors, the increase in relative risk associated with each is small. For all these reasons, population-based strategies of prevention are not presently feasible. Prevention is therefore more appropriately targeted to those segments of the community at high risk.

High-risk strategy

As for population strategy, prevention could be directed to suitable individuals at any age. Since bone mass, at least up to the age of about 75 years, is largely a function of peak bone mass, it could be argued that prevention should be directed towards the optimization of peak bone mass. At present this is not feasible. For this reason, the major thrust of prophylaxis has been directed towards preventing bone loss that occurs in association with the menopause, on the diagnosis of disease, or at the onset of immobilisation. The interventions used are largely pharmacological and there are many effective treatments now available (*7*).

Diagnostic tools are available for osteoporosis. For this reason it has been suggested that screening techniques utilizing bone mass might be used to direct intervention, particularly hormone-replacement treatment at the time of the menopause. There are problems, however, with the use of bone mineral density measurements alone to assess risk in a community setting. The test has high specificity but low sensitivity (*2*). The low sensitivity (approximately 50%) means that half of all osteoporotic fractures will occur in women said not to have osteoporosis. It is possible that the use of other risk factors such as biochemical indices of skeletal turnover may aid in risk assessment in conjunction with bone mineral density measurements. Clinical risk factors such as neuromuscular disorders may also add to the value of bone mineral density measurements. The prevalence of these risk factors is, however, rare at the time of the menopause but increases progressively with age. Thus, the use of risk factors in combination with bone mineral density measurements may provide a strategy for screening elderly individuals rather than women at the time of the menopause (*8*).

In this context, there is a need to develop case-finding strategies so that at least a proportion of individuals at high risk can be assessed for the interventions available. Such strategies have recently been developed by the European Foundation for Osteoporosis and Bone Disease (*9*), and comparable guidelines have been adopted by several European countries and in Singapore. Guidelines in the United States also favour a case-finding strategy (*10*). In this strategy, the presence of risk factors alerts the patient or physician that further investigational treatment is worthwhile. The problems with this approach are that it focuses on the elderly in whom risk factors are widely prevalent and treats rather than prevents osteoporosis. There are therefore large segments of the community that are disadvantaged.

Our current treatment strategies do not provide an adequate means to tackle the increasing problem of osteoporosis. Until such strategies are devised, osteoporosis will remain a necessity in our communities. ■

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A patient's perspective

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It was not until after I had fractured two vertebrae in my lumbar spine that I was diagnosed as having osteoporosis. I was only 19 years old and very frightened. Between the ages of 16 and 18, I had struggled with anorexia nervosa but I was recovering well when I fractured my spine. My regular menstrual cycle had stopped when I was only 16 years old.

I had been experiencing back pain for approximately six months before I fractured my spine. At that time, I was working part time in a residential home, work that involved lifting people unaided. I had put the cause of the back pain down to this. One morning, without any immediate cause, my back suddenly gave way and I collapsed with the most excruciating pain I have ever known.

I was advised to spend two weeks in bed and then to start moving again. The doctor who examined me thought that I had slipped a disc in my spine. I did start to move again, but the pain was still very severe and I was afraid. I knew that something serious had happened. I had lost at least 5 cm in height and my spine was straight. My waist had vanished and I had lost my natural shape. I was sent for an X-ray of my spine; the report stated that I had fractured two lumbar vertebrae and that I had osteoporosis. When I was told this, the doctor informed me that whenever a radiologist did not know what a bone X-ray showed, osteoporosis would always be reported. I was told that at 19 years of age, I could not possibly have osteoporosis, such was the knowledge of osteoporosis ten years ago. My own doctor was more sympathetic and immediately referred me to an endocrinologist at my local hospital, who then referred me for a bone density scan.

None of the local hospitals at that time owned a bone densitometer so I had to pay to have the bone density in my wrist measured at a private hospital. This confirmed the diagnosis of osteoporosis. The consultant told me that I was the first person that he had seen with osteoporosis secondary to anorexia nervosa. Although that was ten years ago, much more education about osteoporosis is needed — it is not just a problem for post-menopausal women.

For treatment, I was started on a low-strength combined oral contraceptive pill for a year and the bone density in my wrist increased by 0.75%. I was then put on a high-strength combined oral contraceptive pill and over the next three years my bone density slowly increased. A local hospital at this time also acquired a bone density scanner, mainly thanks to the dedicated work of local fundraisers. Nearly five years after I fractured my spine, the bone density was measured in my hips and my spine; both results were low.

Slowly, I started to feel stronger and I joined the National Osteoporosis Society. Here, I started to meet other people with osteoporosis and also experts in the field of osteoporosis. I realised how little was known about osteoporosis and its treatment in young women. Previously, I had assumed that the treatment of osteoporosis was standardized for all ages in all places. I started to question my treatment. They say that doctors make the worst patients, but medical students cannot be too far behind.

I stopped taking my prescribed medication and was asked to join a two-year study looking specifically at calcium, vitamin D and bone density in young women. As part of the study, I had three bone density scans over two years. My bone density is now within normal limits (although the scanners are not calibrated for women in their twenties at present). I hope to maintain an optimum bone density as long as possible. My menstrual cycle is regular now, but I do worry that I may be more at risk of osteoporosis when I reach the menopause; and what about pregnancy?

The pain that I experience now is minimal. However, this has only happened over the last few years. At 20, I was unable to walk around shops, because my back would ache if I was standing or walking for a long time. I also had to get up slowly after sitting at my desk and would not be able to stand straight for at least five minutes. Most of all, I feared falling over and dreaded going out on cold frosty mornings in case I slipped.

My life now is very good. I try to walk regularly, as this is exercise that I enjoy. I also try to include foods that are rich in calcium in my diet (although I do not know how much calcium I need; I have seen several different recommendations). One thing that I will never be able to change, however, is my figure. I have lost 5 cm in height and this affects every day of my life in the way that I dress. I still have the legs of a person who is 180-cm tall, but my top half is disproportionately shorter. I prefer to wear clothes that do not accentuate my waist.

I am positive about the future and the research into osteoporosis that is currently being undertaken. More education is still needed, as fracturing bones is a very painful way to discover that one has osteoporosis. Perhaps people with eating disorders should be entitled to a routine bone density scan when osteoporosis may be a risk. However, this would also mean that scanning machines would have to be more widely available and accessible.

We should all be entitled to strong bones throughout life. This should not be a privilege only for those people who can afford it or have knowledge about it. Loss of height can never be replaced and the pain of osteoporosis and fractures should never be underestimated. With more education, research and standardized treatment, strong bones in early and late life should be possible for everybody, not a luxury for a select few. ■

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The problem of reimbursement

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The article by Delmas and Fraser draws attention to a medical problem that has been under discussion for many years. In collaboration with WHO, several working groups have devoted their efforts towards the global health problem of osteoporosis. A WHO study group prepared a report on the assessment of fracture risk and its application to screening for post-menopausal osteoporosis in 1994 (*1*). In 1998, WHO also published guidelines for preclinical evaluation and clinical trials in osteoporosis after consultation with scientists from academia, the pharmaceutical industry and regulatory agencies (*2*).

Osteoporosis has been defined as a status of "low bone mass and microarchitectural deterioration of bone tissue, leading to enhanced bone fragility and consequent increase in fracture risk" (*3*) and there is no doubt that it affects many people, in particular the elderly. The number affected is expected to rise as the proportion of elderly people in the population increases. Osteoporosis has been defined as a disease by the Consensus Development Conference (*3*) and is an accepted risk factor for fractures, in particular fractures of the hip and spine which are associated with mortality, morbidity and economic burden. Hence, early detection of this risk factor and its prevention to reduce associated fractures have been highlighted as being essential by experts within the European Community and worldwide.

For many years, screening programmes have been recommended and used to detect risk factors. Blood pressure and cholesterol measurements are examples of this approach. Only recently has the use of screening results to develop effective disease prevention strategies been considered. WHO has published criteria for the assessment of screening procedures. The characteristics of osteoporosis and its consequences fulfil the criteria that have been developed (serious condition, high prevalence of the asymptomatic disease stage, known natural course, long latency period between first signs and overt disease). However, it is not established whether the diagnostic techniques fulfil the requirements in terms of sensitivity, specificity and positive predictive value and, in addition, whether the effectiveness of intervention is well documented.

Bone densitometry techniques are available and are accepted methods to measure bone density. Before recommending these techniques for screening purposes, it is necessary to determine whether studies exist that demonstrate the effectiveness of screening followed by intervention in terms of showing that fractures are prevented. Currently, there are no published studies to support the screening of post-menopausal women. Hence, this procedure may not be recommended with confidence as a cost-effective way to deal with the problem.

Current diagnostic techniques have to be judged as unsuitable because of their low sensitivity and inability to distinguish between individuals with high and low fracture risks (*4–9*). Estimates on the prevention of hip fractures by a general screening programme in the post-menopausal population range from less than 1% up to nearly 20% (*4*).

Several groups have tried to define sub-populations at risk of osteoporosis because the benefits of screening would be more pronounced in these populations. Whereas many risk factors of osteoporosis have been identified, it is however difficult to identify accurate and sensitive predictors of fracture (*10–12*). Some authors, including Delmas and Fraser in their article, claim that all post-menopausal women not taking hormone replacement are at risk, but they make this claim without demonstrating that screening followed by intervention in this group would reduce the incidence of fractures as compared to an untreated control group. In addition, Cummings et al. (*13*) showed that the rate of hip fracture is not correlated to one single risk factor, but is increased only when more than four risk factors are present. It should be noted that Cummings et al. restricted their study to hip fractures in the subgroup of female subjects older than 65 years (*13*). As pointed out by Green (*14*), more research is needed to develop rules for making decisions on screening programmes with better predictive power. Hence, current data are not sufficient to give governments advice on reimbursement for costs for screening by bone mineral densitometry measurements in post-menopausal women and the subpopulation of post-menopausal women not taking hormone-replacement therapy.

As far as intervention is concerned, the endpoint under consideration should be clearly stated. Concerning fractures, which are a common endpoint for health agencies, a distinction has to be made between treatment of new fractures in a population having already suffered from fractures and measures to prevent fractures. Whereas several treatment options are available for patients with fractures and their effectiveness has been demonstrated, their cost-effectiveness has not been evaluated and compared in randomized clinical trials that would be a prerequisite to make clear recommendations for reimbursement.

Measures to prevent fractures, so-called primary prevention, depend on the age of the population. Non-pharmacological intervention applies for all age groups, but differs in its targets. In the young population, high peak bone mass is a target that does not need pharmacological intervention. In the adult population, the same non-pharmacological interventions are recommended as for the young with the aim of preventing loss of bone mass.

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The effectiveness of non-pharmacological intervention of this kind has not been well demonstrated and studies to support the concepts for non-pharmacological intervention would be welcome. From a survey of the literature, a modification of risk factors for falling would have a beneficial influence for the elderly (*15*). Recently, Close et al. demonstrated in a high-risk population that preventive measures reduced in a statistically significant way the number of falls and the number of admissions to hospitals (*16*).

Several agents have been tested, in particular in the post-menopausal population, with fracture rates as clinical endpoints. The outcome of pharmacological intervention has been demonstrated by data from different types of studies. Considering randomized controlled trials as an acceptable source of information, it can be stated that significant preventive reduction of fracture rates for vertebral fractures has been demonstrated for hormone replacement, etidronate, alendronate, calcium, and calcitonin treatments. For hip fractures, vitamin D and alendronate reduced the fracture rate in a preventive pharmacological intervention. Observational studies have shown that hip fracture is prevented by intervention with hormone replacement, calcium, calcitonin, and vitamin D treatments (*17*). The cost-effectiveness of these different agents has not been evaluated and compared in randomized clinical trials which would be a prerequisite to make recommendations for reimbursement.

In conclusion, a general recommendation to reimburse the costs for all the pharmacotherapeutic and interventional options cannot be made, because of lack of data. Hence, the generation of comparative cost-effectiveness data is a crucial basis for decision-making. Different countries may draw different conclusions from the same data because allocation of restricted financial resources always includes prioritization which has to take into consideration all health problems in a country. ■

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