Burden of Osteoporosis and Fractures in Developing Countries

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The burden of osteoporosis in developing countries is increasing dramatically with the aging of the population and demographic trends; however, there is a lack of direct epidemiologic data. There are clear differences at present between and within populations that limits the validity of many estimates and more data is needed. Existing data and estimates are considered in terms of bone mass, bone structure, 10-year and lifetime probability of fracture, numbers sustaining fractures, the outcome of fracture, importance of differences in fracture management, and risk factors for their occurrence and outcome. Future trends are also considered.

Introduction

Osteoporosis is defined as a systemic skeletal disease characterized by a low bone mass and a microarchitectural deterioration of bone tissue, with a consequent increase in bone fragility and susceptibility to fracture [1]. The operational definition is in terms of bone mineral density (BMD) compared with that of young adults [2]. Bone strength and risk for fracture are additionally determined by integration of bone quality, architecture, turnover, damage accumulation, and mineralization [3]. Clinically, osteoporosis is recognized by the occurrence of fracture after minimal trauma. It has been estimated that 1.31 million hip fractures occurred worldwide in 1990 [4••]. These fractures are associated with short and long term disability and also excess mortality.

Loss of bone mass and architectural deterioration occur with advancing age. Falls are more frequent in the elderly and the rates of fracture increase with age as a consequence. The morbidity and mortality associated with fracture also increases with age. The increasing life expectancy in developing countries means that the burden resulting from osteoporosis on individuals, health, and social care is predicted to increase greatly.

For these reasons it is important to understand the burdens of osteoporosis and consequent fracture in developing countries and factors that may influence them. However there are limited data from developing countries and many assumptions need to be made, the validity of which may be questionable in view of different genetic and environmental factors.

In considering the burden of osteoporosis in developing countries we therefore need to take into account possible differences in bone mass, bone structure, 10-year and lifetime probability of fracture, numbers sustaining fractures, the outcome of fracture, importance of differences in fracture management, and risk factors for their occurrence and outcome. None of these can be assumed to be the same as in westernized populations. Are the "at risk" population the same? Is the outcome of fracture the same? Almost certainly not, and data is needed to develop strategies for effective prevention and treatment.

Incidence and Prevalence of Osteoporosis

The incidence of osteoporosis is best measured indirectly as the incidence of fractures resulting from the condition. Prevalence is best measured by the frequency of reduced BMD or based upon rates of those with vertebral deformity [5•]. The lifetime risk or the 10-year probability of fracture can also be considered [6].

Bone Mineral Density

The International Osteoporosis Foundation has recently recommended that, for the purposes of diagnosis as opposed to those of assessment, BMD should be measured at the hip using dual-energy x-ray absorptiometry. Applying these criteria to a European population, the general prevalence of osteoporosis rises from 5% in women at the age of 50 to 50% at the age of 85, and in men the comparable figures are 2.4% and 20% [7]. The proportion increases steeply between the ages of 50 and 80.

Bone density varies between races but the prevalence of osteoporosis in developing countries is not clear as there are few comparable studies. A recent large study of postmenopausal women in the United States has shown a lower bone density in Asians and higher bone density in blacks compared with whites [8]. After adjustment for body weight and other risk factor covariates, black women had the highest

average BMD followed-up by Hispanic women, whereas the bone densities of Asians, Native Americans, and whites were similar. Less is known about the bone density in men but in the National Health and Nutrition Examination Survey database in the United States the prevalence of osteoporosis in men was 7% of whites, 5% blacks, and 3% Hispanic Americans compared with 17%, 8%, and 12% respectively for women [9]. In any population study it needs to be made clear whether comparison is being made with a local reference population or with one acquired in the United States or Europe. Whatever the comparative population, the total number of those with osteoporosis in a developing country is likely to be lower than in the westernized populations because of reduced life expectancy.

The risk for fracture rises with decreasing BMD. For instance, the risk for hip fracture is estimated to increase by a factor of 2.6 for each standard deviation hip BMD is below the mean for young adult females in westernized populations [10]. The relationship between BMD and risk for hip fracture has been shown to be similar in Hong Kong Chinese [11] but it is not known if this population is representative of developing regions.

Fracture Probability

The lifetime risk, at the age of 50, for fragility fractures is considerable with more than 50% of women and 20% of men in Westernized countries from age 50 years predicted to experience a fracture [6]. The 10-year probability of fracture increases dramatically with age, being twice as great for women aged 70 years than 50 years. This is relevant when deciding the time that intervention is most cost-effective. Comparable data are needed from developing countries where reduced life-expectancy will result in a lower lifetime fracture probability. However the aging of populations in developing countries means that the lifetime fracture probability will increase considerably (vide infra). The 10-year probability may therefore be more meaningful at present in developing countries.

Fracture

The most common fractures associated with osteoporosis are those of the hip, vertebrae, and forearm. In addition there is an age-related increase and female predominance in other fractures such as proximal humeral, pelvic, rib, and proximal tibial fractures.

Hip fractures

Prevalence and incidence

Worldwide there were estimated to be 1.31 million hip fractures in 1990, approximately 909,000 in women and 405,000 in men [4••].

Available data for the incidence of hip fractures is predominantly from Europe and North America. Case ascertainment is difficult in less developed and developing countries where many fracture cases may not present to hospital care.

In Western populations the incidence of hip fractures increases exponentially with age. Ninety percent of hip fractures occur in people over the age of 50 and the average age of sustaining a hip fracture in developed countries is 80 years. The estimated rates in Western Europe for 1990 were 33 of 100,000 person-years in women aged 50 to 54 rising to 1808 of 100,000 person-years in women 80 years and older; with estimated rates in men of 28 and 880 respectively [12•]. In subjects above 65 years of age there is a female to male incidence ratio of approximately 2:1. Attempts have been made to estimate numbers of hip fracture in different regions of the world and the numbers suffering the consequences of hip fracture [4••,12•].

The highest incidence rates have been reported from northern Europe followed-up by rates in whites living in North America. Data now available from other parts of the world shows that hip fracture occurs less frequently in non-white than in white populations. Incidence rates are extremely low in African countries and intermediate among Asian populations.

Rates vary within regions and in Asia the rates of hip fracture are two-fold higher in Hong Kong than in Hoonan, Korea with intermediate rates reported from Malaysia, Thailand, and mainland China [12•]. Rates are rising in the rapidly developing countries and in a recent study the adjusted rates in the more urbanized countries of Singapore and Hong Kong were similar to those in white Americans, whereas much lower rates were found in Malaysia and Thailand [13].

The female preponderance of hip fractures is not common to all populations, and the incidence of hip fractures in men is equal to or greater than in women in Maoris, New Zealand [14] and Bantus, South Africa [15].

Management

The recommended management of hip fracture is surgery followed-up by rehabilitation [16], however there are enormous differences in access to such appropriate management between and within countries that will affect outcome. For example, traditional bone setting is an ancient trade practiced in Nigeria and most developing countries without regulation and guidance and complications with poor outcomes are common [17].

Outcome

Hip fracture results in pain, loss of mobility, and excess mortality. In Westernized countries, nearly all are hospitalized and most undergo surgical repair of the fracture or replacement of the joint. At 1-year, hip fracture is associated with 20% mortality, 50% loss of function, and only 30% have regained function [18]. Many lose their independence and require long-term care. Co-morbidity is an important contributory factor to the occurrence of hip fractures and a determinant of outcome [19].

There are limited data about the outcome in developing countries. It has been estimated that there were 738,116 deaths in the world in 1990 associated with hip fracture, with half happening outside established market economies [4••]. It was estimated that hip fractures accounted for 1.75 million disability adjusted life-years lost. These estimates were based on Swedish data and assumptions had to be made about mortality and morbidity but there are clearly differences in acute care, rehabilitation, and co-morbidities in less developed countries that will almost certainly result in different mortality and disability in those who survive. This highlights the need for local data.

Vertebral factures

Prevalence and incidence

The prevalence of vertebral deformity identified radiologically increases with age and one in eight men and women over the age of 50 in Europe have vertebral deformity. The rates vary between populations with a demonstrated threefold variation across Europe and up to two-fold variation within European countries [20]. Vertebral deformities in men at the earlier ages may represent developmental changes rather than fractures. The prevalence of vertebral fractures is similar in Asian women and white women [21,22]. They appear to be less common in black [23] and Hispanic populations [24].

The age-adjusted and sex-adjusted incidence rates for vertebral deformity are 1% per year among women and 0.6% per year among men from the European Prospective Osteoporosis Study [25], and similar figures have been found in the United States.

Only between 10% and 30% of those who have sustained a vertebral fracture reach primary care in Europe [26] as about a third are asymptomatic. The age-adjusted incidence of clinically diagnosed vertebral fractures has been estimated for white women older than or approximately 50 years of age as 5.3 per thousand person-years, the comparable male rate being around 50% of this.

Management

The acute management is pain control and access to appropriate analgesics is not so much the problem as the lack of recognition of need. In general, pain control is poor in all populations and access to opiate analgesics will affect this. With accumulation of vertebral fractures, there is increasing associated pain and disability and the availability of resources to manage these will affect outcomes.

Outcome

Acute vertebral fracture affects quality of life with limitation of activities and restriction of participation. In Westernized countries up to a fifth of individuals with fracture are hospitalized and some will require subsequent long term care, particularly those of advanced age or with co-morbidity. The outcome may differ in developing countries. Pain and loss of spinal movement cause most limitation. Chronic vertebral osteoporosis is associated with pain and long term impairment of quality of life. Pain and disability worsen with each new vertebral fracture, with an increasing total number of vertebral fractures, and with worsening of spinal deformity. Lumbar fractures have most impact. Vertebral fracture affects all domains of quality of life as measured by generic and osteoporosis-specific quality of life instruments, with pain being affected the most strongly. The effect has been demonstrated several years after the fracture. Physical performance declines even in the absence of significant pain, and undiagnosed vertebral fractures are associated with disability. Co-morbidity is common at this advanced age and contributes to the impact on quality of life and increased mortality. The decline in physical function and changes in appearance contribute to social isolation and loss of self-esteem.

Vertebral fractures are also associated with an increased mortality at 5 years as seen with hip fractures, but onset is gradual over the 5-year period. This has been shown in westernized countries but there are no data from less developed countries.

Distal forearm fractures

Prevalence and incidence

Most distal forearm fractures occur in women (the age-adjusted female to male ratio being 4:1), and around 50% occur in women aged 65 years and older. The most common fracture is the Colles' fracture. A recent multi-center study in the United Kingdom found annual incidences of nine and 37 per 10,000 person-years in men and women respectively, with hospitalization rates of 23% and 19% respectively [27]. A pan-European study of over 13,000 subjects over 50 years of age showed incidence rates of 17 and 73 per 10,000 person years in men and women [28]. The incidence in white women increases linearly with age from 40 to 65 years and some studies have shown a tendency for the incidence rate of distal forearm fracture to continue to increase for women over 70 years of age, perhaps pointing to increasing frailty in the elderly female population of Western countries throughout the last decade of the 20th century and the first decade of the 21st. In men the incidence remains constant between 20 and 80 years.

The geographic variation is not well documented but appears to be similar to that found with hip fractures. They are less frequent in Japanese [29] and black populations compared with whites [30].

Management

The usual management for an uncomplicated fracture of the distal radius is reduction and fixation through a splint. Poor access to care or inappropriate care will result in poor reduction and setting of fractures with worse outcomes.

Outcome
Colles' fracture results in hospitalization rates in the United Kingdom of 23% for men and 19% for women [27]. Only 50% report a good functional outcome at 6 months [31].

Other fractures
The majority of fractures in patients 50 years of age and older are the result of osteoporosis. The incidence rates for proximal humeral, pelvic, and proximal tibial fractures also rise steeply with age and are greater in women than in men. Approximately 80% of proximal humeral fractures occur in individuals 35 years of age and older, three-quarters occurring in women. Similar patterns have been observed for distal femur fracture and fractures of the rib, clavicle, and scapula.

Risk Factors for Osteoporosis and Fracture and Their Epidemiology in Developing Countries

In addition to age and female gender, the major determinants of fracture are falling, low bone mass, maternal history of fracture, glucocorticoid therapy, low body mass index, cigarette smoking, excessive alcohol consumption, previous low trauma fracture, and certain co-morbidities such as rheumatoid arthritis. Skeletal structure such as hip axis length and bone turnover also affect fracture risk. Frailty and co-morbidity are also risk factors for poor outcome after fracture. These risk factors have been predominantly identified in Western populations and there is limited knowledge as to whether they are the same in less developed populations, but it is likely to be so. There are differences in the epidemiology and secular trends of these risk factors in different parts of the globe.

Bone density has the strongest relationship to fracture but tests for bone density are not sensitive as most osteoporotic fractures occur in those with a negative test. The possibility of fracture increases when combining low bone density with the presence of other risk factors for fracture. In particular bone density combined with risk factors that are at least partially independent of bone density [32] can identify those at a greater risk for fracture. The exact interaction of these different risk factors is not established. Efforts are being made to use existing data to describe the absolute risk for the individual patient over a time period that is comprehensible, that is 5 to 10 years [33–35]. This will strengthen the indication for intervention and should improve compliance, however it is currently based on Swedish epidemiologic data and any risk assessment tool will need validating for use in developing countries. Work is in progress to achieve this.

Skeletal structure
Bone geometry can affect fracture risk [36]. Hip axis length varies and a short length gives a stronger structure for any given bone density. Racial differences in hip axis length might explain in part racial differences in rates of hip fracture [37]. Japanese women have a lower incidence of fracture than North American white women despite a lower femoral neck bone mass, which may be explained by shorter femoral necks and perhaps smaller femoral neck angle [38].

Age
The population is aging universally but populations are increasing more quickly in developing regions because of higher birth rates, decreasing mortality, and increased life expectancy.

Approximately 81% of the population currently resides in less developed regions. Those born in developed regions are now expected to live 76 years compared with 65 years in less developed regions. Life expectancy exceeds 61 years in all world regions with the exception of sub-Saharan Africa, where HIV/AIDS lowers the figure to 46 to 52 years. Women, who are at a greater risk for osteoporosis, now live 8 years longer than men in developed regions, and 4 years longer in less developed regions.

Population changes from 2004 to 2050 are predicted to be 55% in less developed areas (69% if China is excluded) compared with 4% in developed regions (Fig. 1). Currently, the elderly constitute a larger (15%) and growing segment of the population in developed regions than in the less developed regions (5%). However, numerically most older people live in developing countries and the predicted inversion of the population pyramid in developing countries will result by 2025 in an estimated 840 million people over the age of 60 living in developing countries representing 70% of all older people worldwide [39]. These demographic changes are predicted to result in an enormous increase in those at risk for osteoporosis and those sustaining fractures in countries with least resources to prevent or manage them.

Physical activity
Lack of physical activity is an important determinant of osteoporosis, risk for falling in later life and risk for sustaining a fracture. Populations are becoming less physically active and fit. These trends are most dramatic in populations that are becoming urbanized such as in developing countries [40••]. The impact of physical inactivity on falls, osteoporosis, and other chronic conditions is estimated to be greatest in the former socialist economies of Europe, accounting for 4.2% and 5.1% of all disability for men and women compared with 3% for the rest of Europe, 2.7% for North America, and 2.4% for the developed countries of the western Pacific region [41]. Physical inactivity accounted for far less disability in the developing regions of the world at present but it is recognized as a rapidly increasing problem in these regions particularly in urbanized poor people [42•].

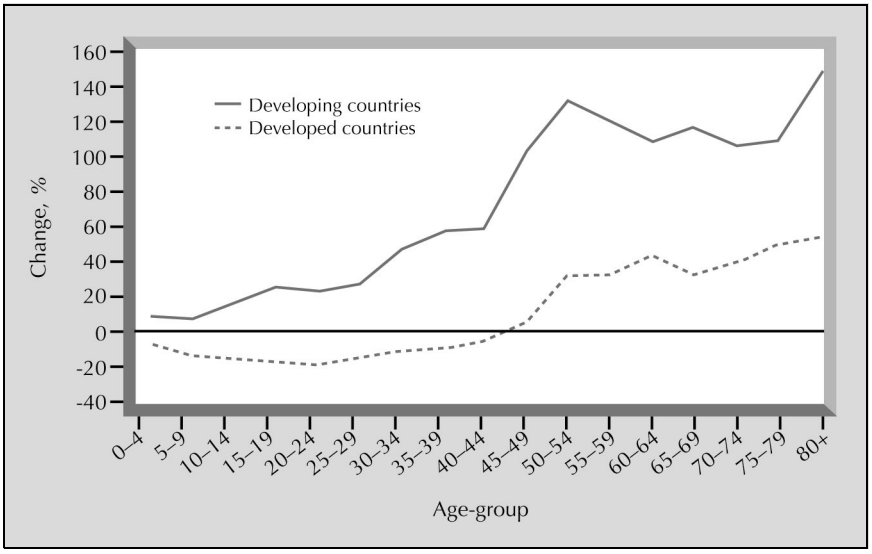

Figure 1. Population growth 1995–2020, by age.

Calcium and vitamin D

Dietary calcium intake in children is positively correlated with BMD [43,44] although the effects of calcium intake on future fracture risk are less clear. Extremely poor populations that have access to very little variety in nourishment will be more susceptible to deficient calcium intake. This has been demonstrated between urban and rural populations in rural South Africa [45] and between developed and developing countries, with calcium intake being more than double in developed countries compared with developing counties [46]. The aging and urbanization in developing countries is expected to increase nutritional risk for chronic diseases such as osteoporosis [47]. There is however the paradox which needs explaining in that hip fractures are more common in developed countries where the calcium intake is higher than in developing countries where the calcium intake is lower [46].

Severe long-term deficiency of vitamin D results in poor bone mineralization leading to rickets in children and osteomalacia in adults. These conditions are fairly rare, but poor vitamin D status in the elderly is linked to osteoporosis and fracture [40••]. Low levels of vitamin D are more prevalent in populations with inadequate exposure to sunlight, particularly in elderly persons confined indoors, those located at extreme northern latitudes, and those who shield themselves from exposure because of cultural or religious reasons.

Low body weight

Low body mass index (BMI) is correlated with lower peak bone mass and an increase in bone loss [48,49]. Low protein intake is an important determinant of peak bone mass. Conversely, higher BMI provides moderate protection (cushioning) against hip fracture. Risk for hip fracture is elevated in Europeans when the BMI falls below 19 kg/m^2 [50,51]. Under-nutrition may increase the risk for falls and can be associated with a worse outcome for facture [42•]. It is not known if these findings are true in all populations.

Considering men and women separately, of the 25 countries with a mean BMI of 22 or less, for which a sizable percentage of the population will be overly thin, all but three countries fall into the highest infant and adult mortality strata (least developed) [52]. In the developed world, being underweight is more of a cultural issue rather than lack of access to adequate nutrition.

These data suggest lack of adequate nourishment affects persons most in the least developed countries, and has very little effect in the developed world at a population level, but the effects on osteoporosis and fracture are unclear.

Smoking

The smoking of cigarettes reduces BMD due to reduced body weight, early menopause, and enhanced breakdown of exogenous estrogen in women [53]. The World Health Organization Atlas project [54] has collected data on prevalence of tobacco smoking for 133 countries grouped by world region and for the year 2003, male smoking prevalence was highest in the former socialist economies of Europe (54%) and the less developed countries in the western Pacific region (56%). The lowest male prevalence was, generally, the wealthier most developed countries of North America, Europe, and the western Pacific. Prevalence of smoking in females is lower that that for males in all regions and more variable from country to country, ranging from a mean of 5.3% in the more developed Southeast Asian countries to 27% in western Europe. Based on recent trends, predicted levels of smoking for the year 2010 are expected to increase in most developing countries, notably for males in Africa and the Middle East and for females in Africa and the poorer countries in Southeast Asia [54] but decline in countries in North America, western Europe, the developed western Pacific (Japan, New Zealand, Australia), and the more developed countries of southeast Asia.

Excess alcohol

The effects of alcohol on bone strength are not straightforward. High alcohol intake is likely detrimental to bone, but moderate intake could actually have beneficial effects to fracture prevention in postmenopausal women [53,55]. Surveys of alcohol use show percentage of "heavy drinkers" does not follow a geographic or socioeconomic pattern [56]. With the exception of predominantly Muslim countries, where drinking is low, high and low alcohol per capita nations can be found in all world regions [56].

Falls

The majority of fractures in older people are caused by falls. Worldwide it is estimated that 283,000 people died from falls in 2000, three-quarters occurring in low and middle income countries [57]. Over 40% of the global mortality resulting from falls occurs among persons aged 70 years and older, fracture after falling being a major part of that. Almost 20 million disability adjusted life-years were lost in 2000 because of falls. Many factors influence the frequency for falling including hazardous environments, chronic and neurologic diseases, medication use, and other conditions associated with the elderly (weakness, decreased reflexes, and so on). Mortality from falling depends on the energy of the fall (distance, weight), tissue padding, surface hardness, and bone density. Overall mortality rates from falling are lowest in Africa, South America, the Middle East, and parts of Southeast Asia; rates are highest for western and northern Europe. However, when rates are age and gender adjusted the pattern changes. Mortality increases dramatically with age; fatal falls occur at about 1.2 per 100,000 in young adults rising to over 100 per 100,000 in those 80 years and older. Fatality is higher for males than females in all world regions. Rates among those 80 years of age and older are highest in the Americas and Europe but for those 70 to 79 years of age, the rates are highest in Africa and the Eastern Mediterranean. These data suggest the elderly in all world regions are at risk from fatal falls.

Genetics

Candidate genes are being sought for osteoporosis and fracture risk as well as for disability. It is quite likely that such genes will have different distributions in various populations and may account for differences in bone density and fracture risk. Twin and family studies suggest that genetic factors may account for more than 50% of the variance in BMD [58,59].

Economic Impact

There are little data on economic impact of osteoporosis and fracture in developing countries. The economic impact associated with osteoporosis is a result of the costs of acute care of fractures, subsequent rehabilitation, and of social support. These costs will not be apparent if there is a lack of such services or if mortality is high but will become so as the provision of health care within developing counties improves and if the costs of social support fall upon society or economically active members of the family. Therefore, not only will numbers of fractures increase with development, but the costs associated with them will also increase dramatically.

Time Trends in Fracture Rates

The number of hip fractures is increasing throughout the world. It has been estimated that from a total number of hip fractures in men and women in 1990 of 338,000 and 917,000 respectively, the numbers will increase by 2025 to 2.6 million and to 4.5 million worldwide by 2050 [12•] resulting from population trends. The greatest increases will be in Asia and Latin America. In 1990, 26% of all hip fractures occurred in Asia but this could rise to 37% in 2025 and to 45% in 2050. In addition there are secular trends. In the 1960s the age-adjusted incidence of hip fracture in Hong Kong Chinese was approximately 13% to 30% of that observed in whites but it has risen considerably since by more than two-fold in the past two decades. In Singapore the incidence of hip fracture has increased from seven per 10,000 women older than 60 years of age in 1957 to 15 per 10,000 in 1985 [60]. Reasons may relate to changes in risk factors such as physical activity as well as genetic or early environmental factors. With modest assumptions concerning secular trends, the number of hip fractures globally could range between 7.3 and 21.3 million by 2050 [12•]. However it may be necessary to factor in population changes as a result of AIDS in many countries.

Conclusions

Osteoporosis with associated fracture is a major public health problem in developed countries and will become one in the developing world with the aging of the population and the increase in those at risk as a result of lifestyle changes. Effective treatments have been developed that reduce the risk for fracture but the costs preclude them for being a strategy for preventing fractures at a population level. Strategies need to be developed that are applicable to and implementable in developing countries and these will need to be targeted at the risk factors associated with osteoporosis and fracture. This will require better epidemiologic data from developing countries about the prevalence and incidence of osteoporosis, the outcome of fracture, and associated risk factors to enable the development of appropriate strategies and the monitoring of their effectiveness.

References and Recommended Reading

Papers of particular interest, published recently, have been highlighted as:

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An attempt is made to quantify the global burden of osteoporosis as measured by hip fracture. Incidences were computed for the different world regions based on the estimates of Gullberg *et al*. [12•] or from more recent studies. Impact was estimated in terms of years of life lost and disability adjusted life-years. This is a good first attempt but highlights the need for better data to measure the burden in all regions of the world. It is difficult to make assumptions about mortality and morbidity with the paucity of present data about differences in management and outcome of hip fracture between countries.

5. • The Burden of Musculoskeletal Diseases at the Start of the New Millenium. Report of a WHO Scientific Group. *WHO Technical Report Series No 919*. Geneva, Switzerland, World Health Organization 2003.

The global burden of musculoskeletal conditions is reviewed including osteoporosis and fracture. The available evidence is identified for incidence, prevalence, and impact has been collated. Recommendations are made about health and economic indicators that need to be collected. How to describe health status and the consequences of a musculoskeletal condition has been considered and recommendations made.

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