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Identification of patient profile for treatment

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The WHO clinical definition of osteoporosis, based on a measurement of bone mineral density (BMD) by Dual Energy X-ray Absorptiometry, has been used globally since the mid-1990s. However, although this definition identifies those at greatest individual risk of fracture, in the population overall a greater total number of fractures occur in individuals with BMD values above the osteoporosis threshold. The inclusion of clinical risk factors, with or without BMD, in fracture prediction algorithms can improve the identification of individuals at high fracture risk; thus a number of web-based tools have been developed, the most commonly used globally being FRAX®. In this review, we will discuss the epidemiology of osteoporosis, clinical risk factors for fragility fracture, and how this knowledge is being used to aid risk stratification. Importantly, research is on-going to demonstrate the clinical efficacy and cost-effectiveness of such case-finding strategies.

Introduction

Osteoporosis is characterised by low bone mass and microarchitectural deterioration of bone tissue. The result is bone fragility, and increased risk of the major clinical consequence, fracture. Since a

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histological definition is of limited utility in such a widespread condition, a clinical definition was devised, in the mid-1990s, by the World Health Organisation. This is based on bone mineral density (BMD) measured at the femoral neck by Dual Energy X-ray Absorptiometry (DXA). Independent of age and sex, individual BMD is related to data from a reference population comprised of healthy young adult females to generate a standard deviate "T-score". A BMD that is 2.5 standard deviations or more below the young adult female mean defines osteoporosis; a T-score between −1 and −2.5 SDS as osteopenia [1]. Although this definition has proved to be valuable for the identification of those individuals at high individual risk of fracture, it is clear that BMD alone does not encompass all factors that are associated with increased fracture risk. Understanding the epidemiology of osteoporosis and osteoporotic fracture is therefore important to identifying patients who are at greatest risk. This has led to the development of fracture probability tools that can be used to guide health care providers in deciding when to implement therapies aimed at primary and secondary fracture prevention. In this review, we will describe the epidemiology of, and risk factors for, osteoporotic fractures, and the tools available with which to undertake risk stratification.

Global burden of osteoporosis

Osteoporosis is common: a recent report estimated that in 2010, 6.6% of men and 22.1% of women aged over 50 years living in the European Union (EU) had osteoporosis, and that there were 3.5 million fragility fractures [2]. The annual direct costs attributable to fracture treatment in the EU equate to approximately €24 billion. However inclusion of the indirect costs of osteoporosis, such as fracture prevention therapies and long-term post-fracture care, which account for 29% and 5% of the total costs, raises this figure to €37 billion per year [2]. Although historically it has been thought that hip fractures contribute the vast majority of this burden, recent data suggest that this is not the case: thus approximately half (54%) of these costs are attributable to hip fractures. Non-hip, non-wrist and non-spine fractures account for 39% of the economic burden, with vertebral and wrist fractures contributing 5% and 2%, respectively [2].

Globally, there is marked heterogeneity in annual age-standardised hip fracture rates: the highest rates are observed in Scandinavia (Denmark 439/100,000 person-years; Norway 420/100,000 person-years; Sweden 401/100,000 person-years) and the lowest in Tunisia (50/100,000 person-years), Ecuador (55/100,000 person-years) and Morocco (69/100,000 person-years) [3,4]. This is illustrated in Fig. 1 [3], which demonstrates that the highest incidence of hip fracture is generally observed in countries furthest from the equator and in countries in which extensive skin covering due to religious or cultural practices is the norm. Although the exact mechanisms underlying this variation remain to be elucidated, the geographic distribution would suggest that vitamin D status might be an important factor. Worldwide, the number of hip fractures is increasing due to improvements in life expectancy and an aging population; in 1990 there were estimated to be 1.7 million hip fractures worldwide, but this is predicted to reach 6.3 million annually by 2050 [5]. These estimates assume a constant age-specific hip fracture incidence, yet varying secular changes in fracture rates across the globe have been observed. Whilst age and sex-specific hip fracture rates increased in Europe and North America until the late twentieth century, with subsequent plateauing or even a decline, there is evidence to suggest that fracture rates are continuing to rise in developing countries (Fig. 2) [6,7]. As such, the economic burden of osteoporotic fracture in developing countries is likely to increase markedly.

Importantly, the burden of fragility fracture extends beyond the economic costs: mortality is elevated for most fracture types, although it is highest for hip fracture [8]. Mortality risk is elevated by 5–8 times in the first three months following a hip fracture [9], and whilst this risk does decrease with time, at 10 years post-fracture it still remains above baseline [9,10]. Although hip fractures are more common in women than men, short-term mortality is greater in men [9,10], which might result from greater prevalence of co-morbidities at fracture in men and more frequent perioperative complications, including infection [11] and cardiovascular events [12]. Poorer quality of life [13] and functional decline are also common following an osteoporotic fracture, particularly after hip, pelvis and vertebral fractures [13]. Fewer than 40% of individuals who sustain a hip fracture will regain their pre-fracture ambulatory status within two years of the fracture, and poorer post-fracture function is more likely in those who have an underlying malignancy or cognitive impairment [14]. Furthermore, rates of