

The perspective of the International Osteoporosis Foundation on the official positions of the International Society for Clinical Densitometry

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Introduction

The International Society for Clinical Densitometry (ISCD) has published position statements on topics relating to the use and interpretation of measurements of bone mineral density (BMD). The most recent appeared in the *Journal of Clinical Densitometry* [1] and was republished in the *Journal of Endocrinology and Metabolism* and in *Osteoporosis International* [2, 3]. The topics included the indications for testing with BMD, the use of central dual energy X-ray absorptiometry (DXA) for the diagnosis of osteoporosis, the use of the Z-score and some recommendations for the spelling of the T-score and Z-score. Although these topics were chosen in an attempt to produce international consistency and consensus, most of the position statements lack a scientific basis.

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Indications for bone density testing

The ISCD recommends that BMD testing be undertaken in all women aged 65 years or more and in all men aged 70 years or more. In adult men and postmenopausal women below this threshold age, indications for BMD testing rely on the presence of risk factors for osteoporosis as recommended by the National Osteoporosis Foundation and ISCD elsewhere [4, 5]. Justification for this view comes from the report of the US Preventive Services Task Force that promotes screening with BMD in women aged 65 years or more [6]. Many healthcare agencies, however, do not support population-based screening with BMD [7, 8, 9, 10, 11].

Despite the intuitive appeal of screening populations for disease, the use of BMD as a screening tool is not universally accepted because the potential impact of screening on the burden of fractures is limited. Most fractures in the community occur in the low to moderate risk categories of fracture risk [8, 12, 13, 14, 15]. The same holds true for screening with serum cholesterol or blood pressure to manage stroke or myocardial infarction. Most clinical events arise in those with a negative test who would be measured and discharged from a screening program—a phenomenon termed the screening paradox [16], that relates to the sensitivity of the test.

Over most reasonable assumptions, the screening tool (BMD) has a detection rate (i.e., sensitivity) that is too low to convince many health care agencies of the merit of population screening. The gradient of fracture risk prediction is approximately 1.5 per SD [12]. In other words, fracture risk increases 1.5-fold or by 50% for each standard deviation decrease in BMD. If it were desired to select at the age of 65 years the 10% of the female population with the lowest BMD, then the sensitivity (detection rate) would be 18% over a 10-year interval. In other words, 82% of all fractures would occur in that segment of the population designated to be at low risk. The positive predictive value (the proportion of patients with a positive test to sustain a fracture over

a 10-year interval) is approximately 15% [17]. Thus, neither a positive nor a negative test is especially helpful, and in particular, false reassurance is given to those with a negative test. Under this scenario, if drugs were 50% effective in decreasing fracture risk, 1,000 women would be screened to detect 100 females, and 12 fractures would be prevented.

The conflicting position also arises in part because of differing clinical practices, the availability of DXA machines and willingness to pay for healthcare. In the USA, the gross domestic product (GDP) per capita is \$37,600 and that of the UK is lower at \$25,300. The proportion of GDP spent on healthcare is 13.9% in the USA and 7.6% in the UK [18]. Thus, healthcare positions need to take account of the local healthcare priorities, which will differ in different regions of the world, not only for reasons of affordability [19], but also because of the large regional differences in the risk of fracture [20, 21, 22, 23, 23].

For these reasons, the IOF is concerned that, as an international society, the ISCD has issued position statements more aligned to the policies of the USA than elsewhere.

Diagnostic criteria for osteoporosis

The ISCD endorses the view that measurement of DXA provides the reference standard for the diagnosis of osteoporosis, as outlined by the WHO [8]. The IOF and the NOF further recommend that the reference standard should be DXA at the hip [24, 25]. There is some ambiguity over the region to be used (femoral neck or total hip). The femoral neck may be preferred since most data are available for this site and meta-analyses have characterized carefully the gradient of fracture risk provided at this site [12, 26]. Thus, osteoporosis is defined as bone mineral density that lies 2.5 or more standard deviations below that of young healthy women (aged 20–29 years) using the NHANES reference base [27, 28]. By contrast, the recent position of the ISCD undermines the concept of a reference standard.

The ISCD recommends that BMD be measured both at the lumbar spine and at the hip in all patients, and where problems occur at any of these sites, the forearm be measured. The ISCD further recommends that osteoporosis be diagnosed on the basis of the lowest T-score for BMD found at the spine, total proximal femur, femoral neck or trochanter (or distal one-third of the radius). The position is somewhat inconsistent in the sense that the lowest T-score of regions of the proximal femur should be used, but the average value of all regions in the lumbar spine should be used (L1-L4).

The reason for recommending assessment at multiple regions is not clear, but may relate to an assumption that the combined use of two or more sites may improve prognostic ability. The basis for this belief is not, however, evidence based. A meta-analysis undertaken on a

sample of 19,000 men and women from seven population-based cohorts showed that, for the prediction of any osteoporotic fracture, the gradient of risk provided by femoral neck BMD was 1.45/SD. That provided by BMD at the lumbar spine was 1.42/SD. The gradient of risk for the minimum value at either site was 1.45/SD [29]. Thus, as argued on theoretical grounds [30], the choice of the minimum value does not improve the gradient of risk. The same pertains to the prediction of hip fracture [29], indicating that there is no advantage for risk prediction in combining sites in this way. The view is supported by an independent study of the predictive value of hip, spine or the lowest value for vertebral fracture risk in the placebo arm of a large multi-center intervention study [31]. The risk ratio for vertebral fracture was 2.47 (95% confidence interval = 1.79–3.42) using a T-score threshold of -2.5 SD at the femoral neck, 1.84 (1.19–2.85) at the lumbar spine, and 1.75 (1.23–2.49) where the minimum T-score was selected.

The selection of patients on the basis of a minimum value from two or more tests will, however, increase the number of patients selected. For example, the correlation coefficient between BMD at the lumbar spine and femoral neck was 0.64 in the meta-analysis referred to above. From the correlation coefficient, if 10% of individuals in a population were characterized as having osteoporosis on the basis of BMD at the femoral neck alone, the prevalence of osteoporosis would increase to 15.3% with the addition of lumbar spine measurements and taking the minimum value to dichotomize the population. Thus, the effect of this approach is to increase the apparent prevalence of osteoporosis. The effect is compounded when more than two sites are used. The same result can be achieved by a less stringent criterion for the definition of diagnosis, for example, by defining osteoporosis as a T-score of -2.0 SD or less. This conflicts with the ISCD endorsement of the WHO criterion for the diagnosis of osteoporosis.

Diagnostic criteria for men and young women

The ISCD offers differing diagnostic criteria in young men and women. In men from the age of 50–65 years, osteoporosis is defined using WHO criteria, but with the addition of a clinical risk factor. The rationale behind this is not entirely clear, but may relate to the belief that, for any given age and BMD, the risk of fracture is lower in men than in women, a view that runs contrary to the current evidence [25, 26, 32, 33, 34, 35].

The official ISCD position for diagnostic criteria in women from the age of 20 years to menopause is to use the Z-score rather than the T-score. The argument runs that the use of a young healthy reference standard derived from the Caucasian population, as presently recommended, would yield a higher T-score in African-Americans than that derived from an African-American population. This arises because the average BMD is higher in African-Americans than in the

Caucasian population. Since the fracture risk is lower for any given age and BMD in African-Americans, it would seem more appropriate to follow the WHO criteria.

Notwithstanding, the ISCD inadvertently identifies one of the limitations of the use of T-score. The incidence of hip fracture, and probably other fractures, varies by more than 10-fold around the world [20, 21, 22, 23], a variation that cannot be explained solely on the basis of BMD. For this reason, the same T-score in different regions of the world will have a different significance in terms of fracture risk. This means that, for clinical use, the T-score (or Z-score) needs to be interpreted according to the prevailing risk in the community (as does the Z-score!). Even within communities, a given T-score (or Z-score) has quite a different significance depending on age [36]. For example, in Swedish women at the age of 50 years and a T-score of -2.5 SD, the 10-year probability of hip fracture is approximately 2%, whereas with the same T-score in women aged 80 years, the probability is 12% [37]. Thus, the T-score alone does not provide a measurement of risk with the same significance across or within communities.

Comment

For the reasons reviewed above, the IOF considers that the official positions taken by the ISCD on population-based screening are inappropriate for international consumption and that its other positions are not soundly based on scientific evidence. The concern of the IOF is compounded by the endorsement of the ISCD positions by the American Society for Bone and Mineral Research. We urge a further shift of position by the ISCD.

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Response to “The perspective of the International Osteoporosis Foundation on the official positions of the International Society for Clinical Densitometry” by John A. Kanis et al.

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We greatly appreciate the thoughtful perspective by Kanis and colleagues regarding the Official Positions of the International Society for Clinical Densitometry (ISCD), published in their entirety in the *Journal of Clinical Densitometry* [1] and summarized in the *Journal of Clinical Endocrinology and Metabolism* [2] and *Osteoporosis International* [3]. A robust scientific debate on the clinical applications of bone density testing is desirable and necessary. It is only through open discussion of diverse viewpoints that we will coherently define the clinical utility of bone densitometry. The development of practical standards by which healthcare practitioners can be guided is a major step toward improving patient care worldwide.

It is widely recognized, as Kanis et al. surely would agree, that there are currently many inconsistencies and uncertainties in the acquisition, analysis and interpretation of bone density tests in clinical practice. Understandably, these problems are the root of controversies in the field. The ISCD is a not-for-profit professional society with over 6,000 members worldwide, dedicated to the achievement of excellence in the assessment of skeletal health. Periodically, the ISCD convenes a position development conference (PDC) to address timely controversial issues that are clinically relevant for bone densitometrists and healthcare practitioners. The intention of the PDC is to review thoroughly the available

data and to offer reasonable standards of care. Topics are selected by the PDC Steering Committee and assigned to subcommittees of the ISCD Scientific Advisory Committee. Following a thorough review of the scientific literature, reports with recommendations for clinical practice are presented to an international panel of experts and to the public at a 3-day conference. Official positions of the ISCD are established by a two-thirds majority vote of the expert panel and approval of the ISCD Board of Directors. When the data are incomplete or the available evidence is controversial, the positions are based upon the most reasonable conclusions at the time. In the United States and elsewhere, many professional organizations have a similar system by which they offer guidelines to care that cover a remarkably broad spectrum of medical disorders.

Kanis et al. state that “most of the position statements lack a scientific basis.” While this is undoubtedly true, it is the very essence of an incomplete knowledge base that requires experts to offer opinions. If the data were incontrovertibly clear, there would be no need for any experts to offer any opinions or for there to be such conferences. The lack of overwhelming scientific evidence, coupled with the need for guidelines in clinical practice, was precisely the reason the topics of the PDC were selected in the first place.

Kanis et al. do not agree with the recommendations for bone density testing because “many healthcare agencies do not support population based screening with BMD,” and because they may not be cost effective. However, it is our strong view that we scientists and healthcare practitioners should be the ones who advise the regulatory agencies on healthcare. Rather than referring to the health care agencies as the “gold standard,” we experts should be the ones who direct to them the arguments for and against population-based screening, based upon what is best for the health of the population. We acknowledge that these opinions will be tempered by realities that may restrict the application of such recommendations because of the available

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resources and allocation priorities. We concur with Prof. Kanis et al. that international considerations were not fully addressed in the ISCD recommendations – an issue we intend to address at the next PDC.

Kanis et al. criticize the ISCD recommendations for selection of skeletal sites and regions of interest for application of the WHO criteria for BMD classification. They are also critical of the ISCD's recommendations for diagnostic criteria for osteoporosis among men and premenopausal women. Clearly, the opinions expressed by the ISCD PDC on these matters are controversial, but again, because they are controversial, it is important to express a view. We feel that the recommendations should be practical in the short run and stimulate ongoing debate over time. We fully expect that some of these positions will be modified when newer data are available for review.

The development of generally accepted guidelines and standards in the field of bone densitometry will continue to be a work in progress. The next PDC will be held in July 2005 in Vancouver, BC, Canada. Some of the positions considered at the time of the last PDC will be reconsidered, and new ones will be addressed. Recognizing the importance of collaboration with other authoritative groups, representatives from the ASBMR (an organization that endorsed the current guidelines), the International Osteoporosis Foundation (IOF) and other organizations have been invited to participate. We

are delighted that Professor Kanis will be joining us. We intend not only to review and to define the level of available evidence on the topics for discussion, but also to consider international issues that may mitigate or modify recommendations. The ISCD looks forward to working with all who are interested in BMD testing, diagnostic classification and clinical applications. In turn, we look forward to working with and supporting Prof. Kanis and the World Health Organization in the development of a methodology for reporting fracture risk probability and establishing intervention thresholds [4].

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