SPECIAL POSITION PAPER

Implications of absolute fracture risk assessment for osteoporosis practice guidelines in the USA

**B. Dawson-Hughes · A. N. A. Tosteson ·
L. J. Melton III · S. Baim · M. J. Favus · S. Khosla ·
R. L. Lindsay**

Abstract

Summary Application of the WHO fracture prediction algorithm in conjunction with an updated US economic analysis indicates that osteoporosis treatment is cost-effective in patients with fragility fractures or osteoporosis, in older individuals at average risk and in younger persons with additional clinical risk factors for fracture, supporting existing practice recommendations.

Introduction The new WHO fracture prediction algorithm was combined with an updated economic analysis to evaluate existing NOF guidance for osteoporosis prevention and treatment.

Methods The WHO fracture prediction algorithm was calibrated to the US population using national age-, sex- and race-specific death rates and age- and sex-specific hip fracture incidence rates from the largely white population of Olmsted County, MN. Fracture incidence for other races was estimated by ratios to white women and men. The WHO algorithm estimated the probability (%) of a hip fracture (or a major osteoporotic fracture) over 10 years, given specific age, gender, race and clinical profiles. The updated economic model suggested that osteoporosis treatment was cost-effective when the 10-year probability of hip fracture reached 3%.

Results It is cost-effective to treat patients with a fragility fracture and those with osteoporosis by WHO criteria, as well as older individuals at average risk and osteopenic patients with additional risk factors. However, the estimated 10-year fracture probability was lower in men and nonwhite women compared to postmenopausal white women.

Conclusions This analysis generally endorsed existing clinical practice recommendations, but specific treatment decisions must be individualized. An estimate of the patient's 10-year fracture risk should facilitate shared decision-making.

The authors comprise the National Osteoporosis Foundation Guide Committee.

B. Dawson-Hughes (✉)
Bone Metabolism Laboratory, Jean Mayer USDA Human
Nutrition Research Center on Aging, Tufts University,
711 Washington Street,
Boston, MA 02111, USA
e-mail: bess.dawson-hughes@tufts.edu

A. N. A. Tosteson
Multidisciplinary Clinical Research Center in Musculoskeletal
Diseases and The Dartmouth Institute for Health Policy and
Clinical Practice, Dartmouth Medical School,
Lebanon, NH, USA

L. J. Melton III
Division of Epidemiology, College of Medicine, Mayo Clinic,
Rochester, MN, USA

S. Baim
The Medical College of Wisconsin,
Milwaukee, WI, USA

M. J. Favus
Department of Medicine, University of Chicago,
Chicago, IL, USA

S. Khosla
Division of Endocrinology, College of Medicine, Mayo Clinic,
Rochester, MN, USA

R. L. Lindsay
Helen Hayes Hospital, Regional Bone Center,
West Haverstraw, NY, USA

A. N. A. Tosteson
HB7505 Clinical Research, Dartmouth Medical School,
One Medical Center Drive,
Lebanon, NH 03756, USA
e-mail: anna.tosteson@dartmouth.edu

Introduction

The current practice guide from the National Osteoporosis Foundation (NOF) makes recommendations for the management of patients with specific clinical presentations [1]. For example, treatment with a pharmacologic agent (along with calcium and vitamin D) is recommended for postmenopausal women who have osteoporosis by World Health Organization (WHO) criteria, i.e., femoral neck bone mineral density (BMD) 2.5 SD or more below the young normal mean [2]. Treatment is advised as well for patients who present with fractures and are thereby at greatly increased risk of additional osteoporotic fractures in the future [3]. The NOF guide also suggests an osteoporosis evaluation for women aged 65 years or over, a recommendation endorsed by the US Preventive Services Task Force [4], and for younger postmenopausal women who have specific clinical risk factors for fracture [1]. These clinical practice recommendations were developed in conjunction with a detailed cost-effectiveness analysis that estimated the likelihood of hip, spine, wrist and other fractures in different risk groups and took into account the complications of these fractures, as well as the expense of managing them, including nursing home care [5]. Potential savings in quality-adjusted life-years (QALY) from fracture prevention were then evaluated in the context of treatment costs, and clinical scenarios were identified where therapy could be expected to deliver a benefit better than $30,000 per QALY saved, a standard threshold at the time for assessing the cost-effectiveness of treatment.

Much has changed in the succeeding decade. Questions have been raised about the utility of estrogen therapy [6, 7], the mainstay of earlier treatment recommendations for postmenopausal women [5], and new drugs have been introduced [8]. More is known about fracture risk in men and non-white women [9, 10], who were excluded from the previous analysis for lack of data. Thresholds for evaluating the cost-effectiveness of treatment have been revised [11], and of course, costs have also increased [10]. More importantly, the WHO has introduced a new fracture prediction algorithm (FRAX™) to determine a patient's absolute (%), as opposed to relative, fracture risk [12], and the NOF has completed an updated economic analysis, which suggests that osteoporosis treatment would generally be cost-effective in patients with a 10-year hip fracture probability of around 3% [13]. Compared to BMD T-scores, the use of absolute fracture risk estimates may provide a better basis for shared decision making between patient and physician

[14] but may also dictate changes in current management recommendations [15]. The purpose of this report is to evaluate the effect of this new approach to risk assessment in the context of a revision of the NOF practice guidelines.

Methods

WHO algorithm

The WHO fracture risk algorithm is presented in detail elsewhere [16], and its derivation, results and application are summarized in the companion paper by Kanis and colleagues in this issue [12]. Briefly, robust clinical risk factors were identified, and their interactions quantified, along with femoral neck BMD, in an analysis of nine large prospective population-based study cohorts from around the world. The combined cohort comprised over 60,000 subjects, who were followed for a quarter of a million person-years; 5,563 fractures were observed during follow-up, including 978 hip fractures [3]. Using these interrelationships, researchers have estimated that the probability of a hip fracture (or a major osteoporotic fracture encompassing hip fractures, clinically evident vertebral fractures, proximal humerus and distal forearm fractures) for various combinations of risk factors in a Poisson regression model with death taken into account as a competing risk [17]. As described elsewhere [12], the risk factors include age, femoral neck BMD (T-score or Z-score compared to norms from the National Health and Nutrition Examination Survey [18]) and body mass index (BMI) as continuous variables, along with a personal history of prior fragility fracture, rheumatoid arthritis, other putative causes of secondary osteoporosis (e.g., inflammatory bowel disease), a parental history of hip fracture, long-term (e.g., 3 months or more) exposure to systemic corticosteroids, high alcohol intake (3 or more units, or about 3 ounces of alcohol, daily) and cigarette smoking as dichotomous (yes/no) variables. Separate models can be run for women and men. The model output is the estimated 10-year probability of a hip fracture alone, or the 10-year risk of the major osteoporotic fractures combined (hip, spine, shoulder or wrist fracture). The model has been validated in 11 additional study cohorts that were not used in building the fracture prediction algorithm [19].

Application to the USA

The WHO fracture prediction algorithm is applied by assuming that the interrelations among the clinical risk factors and hip BMD with respect to fracture risk are constant across populations. The model then is calibrated to the population of interest on the basis of available data about hip fracture incidence and death rates in that specific population. In this

Table 1 Risk of death (per 10,000) among United States residents in 2001, by race, gender and age

Age	White	Black	Asian	Hispanic
Men				
50–54	60	120	30	53
55–59	90	172	50	75
60–64	143	242	78	116
65–69	224	350	122	182
70–74	351	505	200	279
75–79	554	726	339	446
80–84	877	1,026	553	678
≥ 85	1,694	1,644	1,131	1,289
Women				
50–54	35	70	20	28
55–59	56	101	30	43
60–64	90	147	48	70
65–69	143	218	85	108
70–74	226	314	132	180
75–79	367	471	216	292
80–84	617	689	391	471
≥ 85	1,460	1,385	871	1,130

Modified from [20]

instance, age-, sex- and race-specific death rates (Table 1) were obtained from US national death data [20]. Although incidence rates for hip fractures recently became available from the Nationwide Inpatient Sample, a large US hospital discharge database [10], the model had already been calibrated to population-based data from the largely white community of Olmsted County, MN [21]. However, as illustrated in Fig. 1, these incidence rates are similar: Comparably adjusted to the 2000 US white population age 50 years and older, the age-and sex-adjusted hip fracture incidence rate for Olmsted County was 38.6 (95% CI, 34.0–43.1) compared to 39.1 per 10,000 for all US whites. The discrepancy is partly due to the fact that subtrochanteric fractures, which account for approximately 5% of all prox-

imal femur fractures [22], are excluded from the Olmsted County data. The model was calibrated to other races by assuming a ratio to the sex-specific hip fracture incidence rates for white women and men based on data then available: For the black population, 0.43 for women and 0.53 for men [23–29]; for Hispanics, 0.53 for women and 0.58 for men [23, 24, 29, 30]; and for those of Asian ancestry, 0.50 for women and 0.64 for men [24, 29, 31]. These respective ratios fall within the bounds of previous reports [32].

Intervention thresholds for the USA

An analysis to identify the level of absolute hip fracture risk (%) at which intervention becomes cost effective, given country-specific estimates of fracture incidence, morbidity, mortality and cost from the USA, is described in detail elsewhere [13]. Results showed that the cost-effectiveness of treatment was particularly influenced by the intervention cost. However, under the base case of 35% treatment anti-fracture efficacy, with a 5-year offset of effect upon stopping therapy and drug costs of $600 annually, treatment was generally cost-effective (at a threshold of $60,000 per QALY gained) when the 10-year hip fracture probability was approximately 3%, and this threshold risk was used in the present analysis.

Clinical scenarios

Since the patient population of interest is very diverse, this analysis evaluated the cost-effectiveness of treatment for patients with specific clinical presentations, based on their future fracture risk as estimated by the WHO algorithm. These scenarios addressed a number of common clinical situations, including a patient who presents with a fragility fracture, a patient with osteoporosis by WHO criteria, a patient with a history of long-term systemic corticosteroid exposure, a patient with secondary osteoporosis, an older patient (≥ 65 years) concerned about osteoporotic fractures,

Fig. 1 Annual hip fracture incidence per 10,000 for Olmsted County, MN residents versus the National Inpatient Sample (NIS) for white women and men, by age
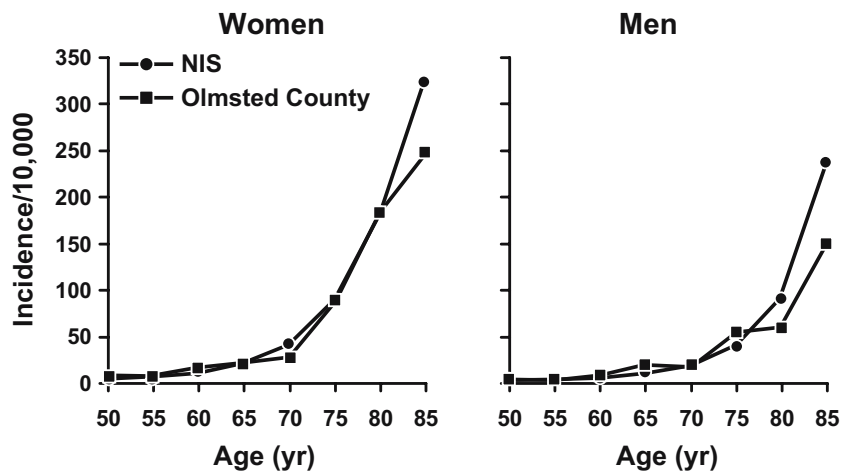
a younger patient with multiple risk factors for fracture and an asymptomatic woman at the menopause (or man age 55 years). The analysis focused on postmenopausal white women but also considered white men, as well as men and women of other races/ethnicities. Since BMI is strongly correlated with femoral neck BMD, and is less useful for fracture risk prediction when hip BMD is available [33], analyses were adjusted to the upper limit of "healthy" weight, a BMI of 24.9 [34]. Given mean heights in 60–74 year-olds of 69 inches for men and 63 inches for women [35], this implies weights of 166 and 140 pounds for men and women, respectively.

Results

With a prior fracture

As might be expected, patients who present with a fracture generally have a future 10-year hip fracture probability high enough to warrant treatment. Detailed data are presented for white women and men in Table 2, which shows that the presence of any of the clinical risk factors included in the WHO fracture prediction algorithm is sufficient to generate a 10-year hip fracture probability of 3% or greater among most white women and men age 65 years or more who have a prior fracture and normal BMI. By contrast, in the absence of clinical risk factors, hip BMD T-scores higher (better) than −2.0 are not associated with substantial 10-year hip fracture

risk in the younger age-groups. When an osteopenic level of BMD (T-score −2.0) is combined with a clinical risk factor; however, the absolute fracture probability estimate meets or exceeds the 3% cost-effectiveness threshold in all instances. Similar relationships among the risk factors are seen when estimating the 10-year probability of any major osteoporotic fracture (Table 3).

Future fracture risk is lower in non-white than white women and men who present with a prior fracture. However, if they have at least osteopenia (T-score −2.0) and one or more risk factors (e.g., common risk factors like smoking and alcohol use), then their absolute hip fracture probability is elevated beyond the treatment threshold though still less than that of postmenopausal white women (Fig. 2).

With no prior fracture

This analysis also confirms that it is cost-effective to treat subjects without fractures who have osteoporosis by WHO criteria (Table 4). Even in the absence of any clinical risk factors, the 10-year hip fracture probability is generally 3% or more in osteoporotic middle-aged and elderly white women and men but is somewhat lower among those of other races (Fig. 3). Consequently, the analysis focuses on osteopenic levels of BMD (e.g., T-score −2.0) where the economic benefit of treatment for middle-aged women and men is uncertain. In the absence of any clinical risk factors, their 10-year hip fracture probability is only about 1%,

Table 2 Ten-year hip fracture probability among patients with a prior fracture and normal body mass index

Age	White women				White men			
	55	65	75	85	55	65	75	85
Risk factors	No BMD* but risk factor in addition to fracture							
None	1.8	3.0	9.9	13	1.2	1.9	5.6	7.3
Corticosteroids	3.9	6.3	19	21	2.4	3.7	9.9	12
Rheumatoid arthritis	3.2	5.3	17	21	2.0	3.3	9.6	12
Family history	2.4	3.9	30	36	1.5	2.4	18	22
Smoker	2.8	4.5	14	16	1.7	2.7	7.4	9.2
Alcohol	2.8	4.6	15	18	1.8	2.8	8.4	11
Femoral neck T-score	BMD but no risk factors other than fracture							
−1.0	0.8	1.0	2.6	3.2	1.3	1.4	3.0	3.0
−1.5	1.6	1.6	4.0	4.3	2.4	2.2	4.3	3.8
−2.0	2.9	2.7	6.0	5.9	4.3	3.6	6.1	4.9
−2.5	5.4	4.7	9.3	8.0	7.7	5.8	8.7	6.3
Risk factors	Osteopenia (T-score −2.0) and one risk factor plus fracture							
Corticosteroids	5.4	5.0	10	9.5	7.7	6.3	9.8	7.5
Rheumatoid arthritis	4.1	3.9	8.4	8.2	6.0	5.0	8.6	6.9
Family history	3.1	2.9	23	23	4.5	3.8	23	19
Smoker	5.0	4.6	9.6	8.7	7.1	5.8	9.0	6.8
Alcohol	4.4	4.1	9.0	8.8	6.5	5.4	9.2	7.4

*Average BMD for the group is assumed

Table 3 Ten-year probability of a major osteoporotic fracture (hip, clinical vertebral, proximal humerus, distal forearm) among patients with a prior fracture and normal body mass index

Age	White women				White men			
	55	65	75	85	55	65	75	85
Risk factors	No BMD* but one risk factor in addition to fracture							
None	15	26	46	51	11	16	24	26
Corticosteroids	24	39	61	60	17	24	33	32
Rheumatoid arthritis	20	34	57	61	15	21	32	34
Family history	28	45	59	63	21	29	35	37
Smoker	16	27	48	50	12	16	24	25
Alcohol	18	31	53	57	13	19	29	31
Femoral neck T-score	BMD but no risk factors other than fracture							
−1.0	13	21	32	31	12	15	19	17
−1.5	16	22	35	35	14	17	22	19
−2.0	18	26	39	38	17	20	26	22
−2.5	22	31	46	43	21	24	30	25
Risk factors	Osteopenia (T-score −2.0) and one risk factor plus fracture							
Corticosteroids	28	39	53	49	26	30	34	28
Rheumatoid arthritis	23	33	47	46	22	26	32	27
Family history	33	46	52	50	29	36	40	34
Smoker	19	26	39	36	18	21	25	20
Alcohol	22	31	45	44	21	24	31	26

*Average BMD for the group is assumed

although it is greater in the presence of risk factors (Table 4). Again, similar relative results are seen for major osteoporotic fractures combined (Table 5).

The previous NOF guide recommended an osteoporosis evaluation for average risk white women age 65 years or older. In this analysis, the 10-year hip fracture probability is estimated at 2% in such patients but exceeds the 3% cost-effectiveness threshold at older ages (Fig. 4). Average risk women of other races did not have 10-year hip fracture probabilities exceeding 3% until they were over 80 years old, and comparable men not until age 75 years. As indicated above, however, treatment would appear cost-effective in high risk subsets of these populations.

Discussion

In this paper, we have examined how the WHO fracture risk algorithm (FRAX™) might influence current guidance for osteoporosis management under an updated US economic analysis [13], which identified cost-effective intervention thresholds on the basis of 10-year absolute hip fracture risk. We provide evidence that existing clinical recommendations will need to change very little. In part, this is due to the fact that the WHO algorithm includes many of the same risk factors used in the original NOF analysis (i.e., age, femoral neck BMD, weight, personal fracture history, family history of fracture and cigarette use)

Fig. 2 Ten-year hip fracture probabilities for patients with prior fracture plus osteopenia (T-score −2.0) who smoke and drink and who are women or men, by age and race
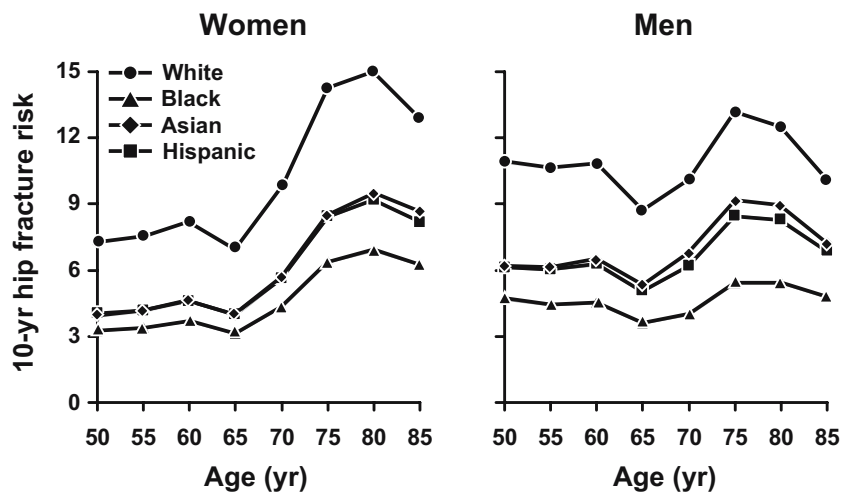
Table 4 Ten-year hip fracture probability among patients with no prior fracture and normal body mass index

Age	White women				White men			
	55	65	75	85	55	65	75	85
Risk factors	No BMD* but one risk factor							
None	0.5	1.2	5.6	8.3	0.3	0.8	3.1	4.8
Corticosteroids	1.2	2.6	11	14	0.7	1.5	5.6	7.9
Rheumatoid arthritis	1.0	2.1	9.6	14	0.6	1.3	5.4	8.2
Family history	0.7	1.6	18	26	0.5	1.0	10	15
Smoker	0.8	1.8	7.9	11	0.5	1.1	4.2	6.1
Alcohol	0.8	1.9	8.4	12	0.5	1.1	4.7	7.2
Femoral neck T-score	BMD but no risk factors							
−1.0	0.4	0.6	1.8	2.4	0.7	0.8	2.1	2.3
−1.5	0.8	1.0	2.8	3.3	1.2	1.3	3.0	2.9
−2.0	1.5	1.6	4.2	4.5	2.2	2.1	4.4	3.8
−2.5	2.8	2.8	6.6	6.1	4.0	3.5	6.2	4.9
Risk factors	Osteopenia (T-score −2.0) and one risk factor							
Corticosteroids	2.8	3.0	7.4	7.4	4.0	3.8	7.0	5.8
Rheumatoid arthritis	2.1	2.3	6.0	6.3	3.1	3.0	6.1	5.3
Family history	1.6	1.7	17	18	2.3	2.3	17	15
Smoker	2.6	2.8	6.8	6.7	3.7	3.5	6.4	5.2
Alcohol	2.3	2.5	6.4	6.8	3.3	3.3	6.5	5.7

*Average BMD for the group is assumed

[5], although some new ones have been added (i.e., race, gender, corticosteroid use, history of secondary osteoporosis, including rheumatoid arthritis, and alcohol use) [12]. Consequently, this analysis supports existing NOF guidance insofar as osteoporosis evaluation and treatment appear to be justified economically, as well as clinically, for patients who present with fractures and those with osteoporosis. This is not controversial since essentially all clinical guidelines, in this country and elsewhere (e.g., [36–38]), recommend osteoporosis evaluation and consideration of treatment for patients who present with frank osteoporosis and/or a personal history of fragility fracture. Cost-effectiveness analyses support that policy [5, 39, 40].

There is less agreement about what to do for patients with low bone mass, or osteopenia [41, 42]. This is an important issue since postmenopausal women with osteopenia but not osteoporosis accounted for half of the fractures observed in the large National Osteoporosis Risk Assessment (NORA) study [43], and similar results have been reported by others [44, 45]. Sensitivity for identifying fracture risk could be increased by lowering the BMD threshold for clinical concern from the osteoporotic level (T-score of −2.5 SD) to, say, −2.0 SD as done in some clinical trials. Unfortunately, this has the effect of simultaneously reducing specificity; this is also important since lower risk patients might then be subjected unnecessarily to

Fig. 3 Ten-year hip fracture probabilities for patients with osteoporosis (T-score −2.5) but no clinical risk factors who are women or men, by age and race
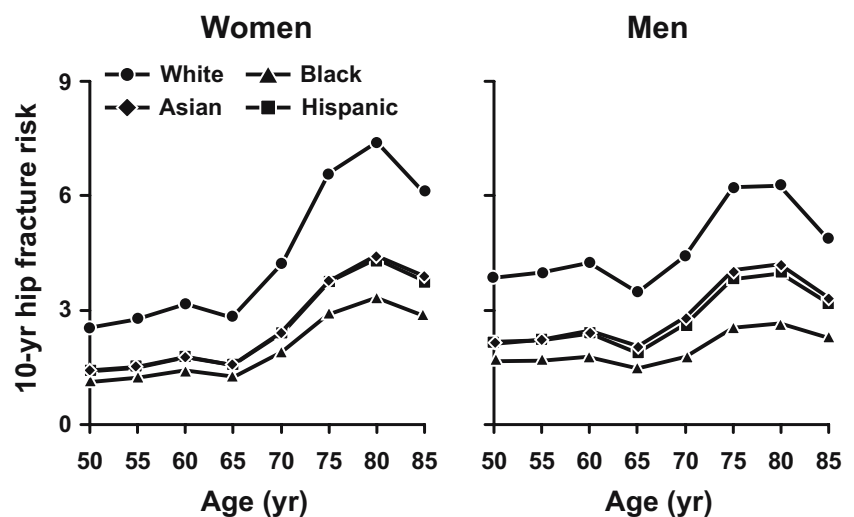
Table 5 Ten-year probability of a major osteoporotic fracture (hip, clinical vertebral, proximal humerus, distal forearm) among patients with no prior fracture and normal body mass index

| Age	White women				White men			
	55	65	75	85	55	65	75	85
Risk factors	No BMD* but one risk factor							
None	7.5	14	29	35	5.4	8.5	14	16
Corticosteroids	12	22	41	44	8.5	13	20	21
Rheumatoid arthritis	10	19	38	44	7.3	11	20	22
Family history	15	26	39	47	11	16	21	25
Smoker	7.9	15	30	34	5.6	8.7	14	16
Alcohol	9.0	17	35	41	6.5	10	18	20
Femoral neck T-score	BMD but no risk factors							
−1.0	7.6	13	22	22	6.6	9.1	13	12
−1.5	8.8	14	24	25	7.8	11	15	13
−2.0	10	16	27	28	9.5	13	18	15
−2.5	13	20	32	32	12	15	21	18
Risk factors	Osteopenia (T-score −2.0) and one risk factor							
Corticosteroids	17	25	39	37	15	19	24	20
Rheumatoid arthritis	13	21	34	34	12	16	22	20
Family history	20	30	39	39	17	23	30	26
Smoker	11	17	27	26	10	13	17	14
Alcohol	13	19	32	33	12	15	21	19

*Average BMD for the group is assumed

the costs and complications of therapy, even presuming that treatment would be efficacious in osteopenic women generally [46]. A more effective alternative is to improve the gradient-of-risk of the screening instrument by combining the BMD test result with clinical risk factors [47]. In the present analysis, for example, the 10-year hip fracture probability in a 55-year-old white woman with osteopenia (T-score −2.0) and no clinical risk factors is only 1%. However, her risk doubled or tripled in the presence of any risk factors. Thus, introduction of the WHO fracture prediction algorithm should not disenfranchise patients for care since treatment can still be justified for those with osteoporosis and/or fractures. Instead, it helps to select for

therapy the subset of higher risk patients from among the large group with osteopenia.

This problem becomes less acute among older individuals since the age-related rise in osteoporotic fracture incidence itself assures a greater potential for reduction in fractures; therefore, savings of the associated costs, with any given treatment efficacy. Our earlier analysis indicated, for example, that it was cost-effective to treat the average-risk white woman age 65 years or over [5]. This conclusion is supported by another recent cost-effectiveness analysis using US data [48] and has been endorsed by the US Preventive Services Task Force [4]. The present analysis suggests that this threshold is not reached until age 68

Fig. 4 Average ten-year hip fracture probabilities for women and men, by age and race
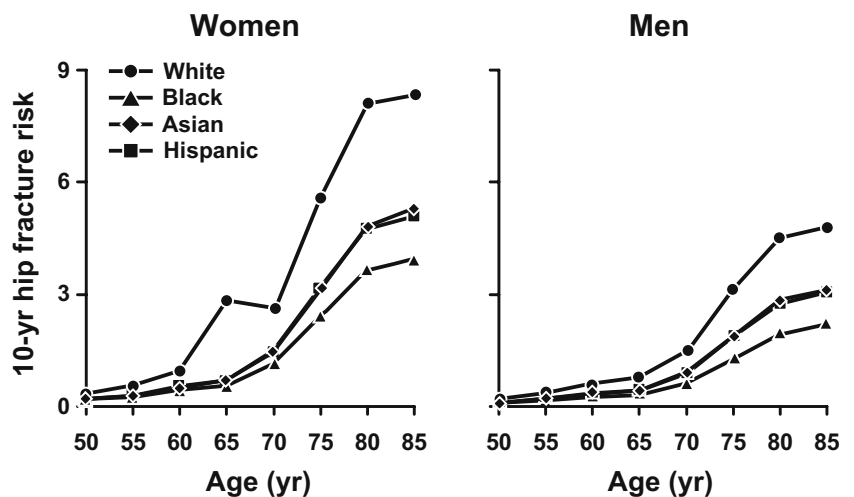
years, but this finding is quite sensitive to different assumptions about drug costs, a major determinant of treatment cost-effectiveness [13]. The earlier analysis focused on estrogen therapy and assumed a treatment cost of $430 annually [5], but estrogen use is now discouraged among older postmenopausal women [6, 7]. The updated NOF economic analysis estimated drug costs at $600 per year in anticipation of generic bisphosphonate [13]; however, if the drug cost were further reduced from $600 to $300, then the level of 10-year hip fracture risk that is cost-effective to treat falls to 1.4% [13]. The average risk 65-year-old white woman clearly meets that threshold (2.2%), as do many of the other patient groups whose low BMD is combined with clinical risk factors for fracture.

Some clinical risk factors have long been considered indications for treatment in and of themselves. In particular, use of systemic corticosteroids is associated with excessive bone loss and fracture risk [49], and the American College of Rheumatology has recommended that patients beginning treatment with ≥ 5 mg/d of prednisone equivalent glucocorticoids for 3 months or more, along with patients already on such doses, implement prophylactic measures including bisphosphonate therapy if their BMD T-score is below −1.0 [50]. The fact that some of these patients, especially younger ones just starting therapy, have an estimated 10-year hip fracture probability less than 3% should not be interpreted as a barrier to the use of good clinical judgment in instituting treatment in specific clinical situations such as this. In addition, a host of other medications, toxic agents, diseases and surgical procedures has also been linked to accelerated bone loss and/or enhanced fracture risk [51]. Since diverse pathophysiologic mechanisms are involved, it is unlikely that each of these bears the same relation to BMD and the other clinical risk factors, but available data are insufficient to quantify any differences. The best data document an adverse impact of rheumatoid arthritis on fracture risk, independent of corticosteroid use [16]. Other conditions also appear to be important, however, and the WHO fracture prediction algorithm accommodates them with a generic "secondary osteoporosis" category.

The inclusion of men and different ethnicities in this analysis is an important advance because osteoporotic fractures are increasing in these groups [10], yet osteoporosis screening and intervention have been largely neglected [52, 53]. This is partly due to the fact that average hip fracture risk in these groups is substantially less than that in white women [32]. However, the present analysis shows that high risk subgroups can be identified. That said, data on the determinants of fracture risk in men and non-white women remain limited, and it is not certain whether their lower fracture incidence rates are an inherent characteristic of ethnicity or are due instead to a different distribution of known risk factors such as bone size or likelihood of falling compared to the white population [54]. In the NORA study, osteoporotic fracture rates in postmenopausal Hispanic, African-American and Asian women were only 91%, 54% and 41%, respectively, of those in white women even after adjusting for age, peripheral BMD and some of the risk factors included in the WHO algorithm [55]. Others have made similar findings [56]. By contrast, race was not an independent predictor of falling when other factors were accounted for in a separate study [57].

Hip fracture incidence rates are used to calibrate the WHO fracture prediction algorithm to each population of interest. In this instance, the calibration employed hip fracture incidence data from Olmsted County [21]; comparably age- and sex-adjusted, this set of rates was similar to data on hip fracture incidence in the white population nationally [10]. The model was further calibrated to different ethnic populations by assuming a ratio of incidence rates for each group relative to hip fracture incidence among white women and men, but the optimal ratios are uncertain since hip fracture incidence can vary even among subpopulations of a given race [31] or ethnicity [30]. Since treatment is cost-effective at similar levels of absolute fracture risk, regardless of race or gender [13], it will be important to refine estimated 10-year hip fracture probabilities in these other groups. In particular, to the extent that fracture risk is similar among members of different racial and ethnic groups who have the same clinical risk profile, this analysis could be too conservative.

Since the model is calibrated to hip fracture incidence, the metric emphasized in this analysis is the 10-year absolute (%) likelihood of a hip fracture. While the metric is quantified in terms of hip fractures, it is necessary to point out that the economic analysis which underpins the conclusions incorporated the health impact of distal forearm, clinical vertebral, proximal humerus, tibia/fibula, rib and pelvis fractures into the results [13]. This is obviously important among younger individuals who are at relatively greater risk of forearm and spine fractures than hip fractures [58]. Alternatively, the WHO algorithm also estimates the absolute risk for a major osteoporotic fracture (hip, clinical vertebral, proximal humerus and distal forearm fractures combined). This, of course, excludes additional osteoporotic fractures, which may be associated with considerable adverse impact [10]. In this regard, the risk estimates again are conservative.

There has been an enormous increase in clinical interest in osteoporosis management since the original WHO definition was introduced over a decade ago [2]. Indeed, data from a representative sample of office-based physicians in the USA revealed a 10-fold increase between 1994 and 2003 in the number of osteoporosis patients identified and treated [59]. However, it is not entirely clear whether this treatment has been directed at the patients most likely

to benefit. Thus, the 10-year fracture probability in an average-risk 50-year-old white woman is quite low [60], suggesting that treatment of such patients will not be cost-effective [13, 61]. Conversely, only a minority of the high risk patients who present with a fracture are treated to reduce the risk of additional fractures in the future [62]. The WHO fracture prediction algorithm could help with these problems by distinguishing the situation where a 35% reduction in 10-year hip fracture risk might be from 1% to 0.7% (e.g., an asymptomatic osteopenic woman age 55 years) from one where the same reduction is from 19% to 12% (e.g., a 75-year-old woman on corticosteroid therapy who presents with a fracture). Although the estimated fracture probabilities themselves are not necessarily precise [63], this is certainly a better way to communicate fracture risk than trying to explain the fracture implications of the BMD T-score, and it should facilitate better decision-making [64].

However, it must be emphasized that a patient's estimated fracture probability cannot be the sole basis for treatment decisions. In particular, it is not clinically sensible to say that it is appropriate to treat a 55-year-old white woman on corticosteroids whose T-score is −2.0 but not a similar woman who happens to be only 50 years old. Moreover, it is not ethically acceptable to refuse treatment to nonwhite women or to men with a given clinical profile, despite the fact that their fracture risk is somewhat lower than rates among postmenopausal white women with the same profile. Consequently, general clinical guidance can be based on broad clinical scenarios like the ones described here, but specific treatment recommendations should be personalized through shared decision-making between patient and physician. When fractures are absent and bone density is in an equivocal range (i.e., osteopenia), the explicit consideration of clinical risk factors using the WHO fracture prediction algorithm should help inform that decision.

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