ORIGINAL ARTICLE

# Hip fracture risk in older US adults by treatment eligibility status based on new National Osteoporosis Foundation guidance

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**Abstract**

*Summary* This analysis of National Health and Nutrition Examination Survey III data found a significant risk of incident hip fracture in adults aged 65 years and older who are candidates for treatment to lower fracture risk, according to the new National Osteoporosis Foundation Clinician's Guide.

*Introduction* The relationship between treatment eligibility by the new National Osteoporosis Foundation (NOF) Guide to the Prevention and Treatment of Osteoporosis and the risk of subsequent hip fracture is unknown.

*Methods* The study sample consisted of 3,208 men and women ages 65 years and older who were examined in the third National Health and Nutrition Examination Survey (NHANES III, 1988–1994), a nationally representative survey. Risk factors used to define treatment eligibility at baseline were measured in NHANES III or were simulated using World Health Organization study cohorts. Incident hip fractures were ascertained using linked mortality and Medicare records that were obtained for NHANES III participants through December 31, 2000. Cox proportional hazards models were used to estimate the relative risk (RR) of hip fracture by treatment eligibility status.

*Results* The RR for subsequent hip fracture was 4.9 (95% CI 3.30, 7.94) in treatment-eligible vs treatment-ineligible persons. The increased risk for treatment-eligible persons remained statistically significant when examined by sex or age: $RR_{men}=5.5$ (2.6, 11.4) and $RR_{women}=4.3$ (2.2, 8.4); $RR_{65-79\ y}=4.8$ (2.6, 8.7) and $RR_{80+\ y}=4.6$ (2.1, 10.1).

*Conclusions* Treatment-eligible persons were about five times more likely to experience a subsequent hip fracture than the non-eligible persons. The new NOF guidelines appear to predict future hip fracture risk equally in men as in women, and fracture risk prediction did not appear to diminish with age.

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## Introduction

The National Osteoporosis Foundation (NOF) recently released guidance to help identify persons who would

likely benefit from pharmacologic treatment to reduce their future fracture risk [1]. The new guide applies to men and to nonwhites in addition to postmenopausal white women, who were the subject of previous guidance from the NOF [2]. The new guide is partly based on the World Health Organization (WHO) FRAX® algorithm, which estimates the 10-year probability of a hip fracture as well as the 10-year probability of any major osteoporotic fracture [3]. It is also based on an economic analysis to determine the levels of fracture risk at which it is cost-effective to consider osteoporosis treatment [4]. We recently examined the potential impact of the new guidelines on treatment recommendations in the USA using data from the third National Health and Nutrition Examination Survey (NHANES III, 1988–1994) [5]. In this study, we extend that evaluation by examining the risk of incident hip fracture in older US adults by treatment eligibility status as defined by the new guide. Data from NHANES III were used to determine treatment eligibility status at baseline, and incident hip fractures were assessed using linked mortality and Medicare records for NHANES III participants who were aged 65 years and older at baseline.

## Methods

### Sample

The baseline data for this study came from NHANES III, which was conducted by the National Center for Health Statistics (NCHS), Centers for Disease Control and Prevention, to assess the health and nutritional status of a large representative sample of the non-institutionalized, civilian population of the USA. NHANES III data were collected via household interviews and standardized physical examinations conducted in specially equipped mobile examination centers [6]. Our study was given a longitudinal component by utilizing linked data from Medicare enrollment and claims records [7] and from the NHANES III Linked Mortality File [8]. The NCHS Institutional Review Board approved all procedures in the survey, and all subjects provided written informed consent.

The analytic sample in this study was restricted to individuals aged 65 years and older at the time of their NHANES III interview because Medicare provides comprehensive health care for roughly 98% of the US population in this age range [9]. The present study was limited to men and women with available data for femoral neck bone mineral density (BMD), height, and weight because these variables are key factors in calculating FRAX® scores. The sample was also limited to those in whom the lumbar spine T-score could be simulated [5] since this variable is used in the new NOF guidelines to assess treatment eligibility. A total of 6,648 adults aged 65 years and older were eligible to participate in NHANES III, of whom 5,252 (79%) were interviewed and 4,092 (62%) were examined. Of these older 4,092 adults examined in NHANES III, the following were excluded: 221 persons who did not match the Medicare files; 13 who lacked cause of death information on their death certificate; one who was ineligible for mortality follow-up because of insufficient identifying data to create a National Death Index (NDI) submission record; ten who were lost to follow-up; 167 who were enrolled in Medicare-managed care plans at the time of their baseline examination; and 472 persons with missing data for treatment eligibility due to missing height, weight, hip BMD, or spine T-score data. The final analytic sample consisted of 3,208 men and postmenopausal women aged 65 years and older, who represent 48% of the sample in this age range that was selected to participate in NHANES III, 61% of the sample that was interviewed, and 78% of the sample that was examined.

We compared descriptive characteristics and risk factors between the analytic sample and persons who were excluded from the analysis in order to assess the potential for nonresponse bias in our results. The excluded individuals differed significantly from the analytic sample as follows: They were older (75 vs 73 years) and had lower femur neck BMD (0.64 vs 0.69 g/cm$^2$). They were also more likely to be in poor health (37% vs 28%), have had a fracture (22% vs 14%) or chronic condition (46% vs 40%) prior to baseline, and to report being less physically active than others of their same age and sex (26% vs 12%). NHANES III participants self-reported their race and ethnicity using categories based on the 1977 Office of Management and Budget directive [10]. Non-respondents were more likely to classify themselves as black (12% vs 7%) or "other race" (8% vs 3%).

### Ascertainment of outcomes

#### Mortality

Vital status of study participants was determined from the NHANES III Linked Mortality File [8], which is based on a probabilistic match between the eligible NHANES III sample and the NDI. Vital status data available for individuals from the date of their participation in the NHANES III survey through December 31, 2000 were used in the present study. In addition to data on vital status, information on underlying and multiple causes of death were available.

#### Hip fracture

Hip fracture cases were identified using diagnosis and procedure codes from the linked Medicare records or cause

of death information from the NHANES III Linked Mortality File. Medicare enrollment and utilization data were available for NHANES III respondents who agreed to provide personal identification [7]. Of the 6,648 respondents aged 65 years and older at baseline who were eligible to participate in NHANES III, 6,427 (97%) were successfully validated and matched with Medicare administrative records. Medicare claims data were provided from 1991 through 2000 for respondents who participated in fee-for-service care (claims data were not available for those who enrolled in Medicare-managed care plans). The Medicare Denominator files were used to restrict the analytic sample to those who were successfully matched to the Medicare claims data, as well as to obtain information about enrollment in managed care plans.

Hip fracture cases were defined from Medicare records using an approach that was developed by Ray et al. [11] based on a study in which they compared data collected from medical records with Medicare claims data. Following this approach, we used medical records from both hospital (Medicare Provider Analysis and Review (MEDPAR) Inpatient Hospital Stay File) and nonhospital (MEDPAR Skilled Nursing Facility (SNF) File, Carrier Standard Analytic File, and Outpatient Standard Analytic File) sources to identify hip fracture cases. Criteria for defining hip fracture depended on the source of the medical record (generally more stringent for nonhospital files than for hospital files) and type of code (generally more stringent for procedure codes than for diagnosis codes). For example, a person with an inpatient medical record containing any diagnosis of ICD-9-CM code 820 was considered a hip fracture case unless there was a concurrent code indicating care for a previous fracture or other bone disease. However, persons with a hospital medical record containing ICD codes for procedures related to hip fracture but without such a diagnosis code had to have a concurrent carrier, outpatient, or SNF medical record with a diagnosis code of 820. An exception to this requirement was made for persons with a carrier, outpatient, or SNF medical record containing Current Procedural Terminology (CPT) codes for selected surgical procedures related to the hip (CPT codes 27125–27127, 27230, 27232, 27234–27236, 27238, 27240, 27242, 27244, 27246, 27248); the presence of these specific CPT codes was considered sufficient to define a hip fracture case without a concurrent diagnosis code. Details regarding the definition of cases from Medicare records, including specific codes, have been published elsewhere [12]. Persons with an ICD-9 code 820 or ICD-10 code S72.0-S72.2 listed as a cause of death on their death certificate were also considered to be hip fracture cases. We did not exclude cases on the basis of trauma (ICD-9-CM 800–819, 821–829, 860–869, 870–897, 925–929)

[13] because recent data suggest that osteoporosis may contribute to fractures associated with high trauma [14].

Definition of treatment eligibility

Eligibility for treatment based on the new NOF guide [1] was defined as meeting any of the following criteria:

1. A self-reported hip or spine fracture after age 20 years
2. A femoral neck or spine BMD T-score≤ −2.5
3. A femoral neck or spine T-score between −1 and −2.5 SD with a 10-year hip fracture probability ≥3% or major fracture probability ≥20%

The reference group for T-score calculation consisted of 409 non-Hispanic white women aged 20–29 years from NHANES III, as recommended for use in the FRAX® model [3].

Risk scores were calculated for hip fracture and for major osteoporotic fractures combined (hip, spine, shoulder, or wrist fracture) using the recently revised (version 3.0) FRAX® algorithm [15] that incorporates updated hip fracture incidence and mortality rates for the US population [16]. The algorithm employs a Poisson regression model to estimate fracture and death hazard functions on the basis of the following risk factors included in the present study: age, femoral neck BMD T-score, body mass index, personal history of prior fragility fracture, rheumatoid arthritis, parental history of hip fracture, long-term use (≥3 months) of systemic corticosteroids, high alcohol intake (≥3 units), and cigarette smoking. The derivation of these risk factors from the baseline NHANES III data, including simulation of risk factors that were not measured directly in NHANES III, is exhaustively described in a separate publication [5]. Death is taken into account as a competing risk in the Poisson model. The 10-year probability of a hip fracture was estimated for non-Hispanic whites and non-Hispanic blacks using the algorithm for "whites" and "blacks," respectively [17]. "Other Hispanics" were combined with Mexican-Americans and analyzed as "Hispanic" in the FRAX® algorithm; the remaining "Other Races" category was analyzed as Asian since internally available NHANES III records on ancestry revealed that 80% were Asian. Asians and Other Hispanics were handled in this manner when calculating FRAX® scores in order to obtain the best estimates of absolute fracture risk for these individuals. When performing all subsequent data analyses, however, Asians and Other Hispanics were combined as "Other Races" in order to be consistent with sampling domains used in the NHANES III survey. In addition, the Asian sample itself was too small to permit statistically reliable estimates.

Statistical analysis

All analyses were performed using SUDAAN software [18] for analysis of data from complex sample surveys. Persons

missing measured femur neck BMD, height, or weight or missing simulated spine T-scores were excluded from the analytic sample, but those with missing data for other risk factors were assumed not to have the risk factor, consistent with the approach used in calculating FRAX® scores. Weighted incidence rates for hip fracture were calculated per 10,000 person-years of follow-up. Descriptive characteristics and risk factors at baseline were compared between fracture cases and non-cases using linear regression models and chi-square analyses.

Cox proportional hazards models were used to account for unequal length of follow-up. The relative risk (RR) of hip fracture was estimated with hazard ratios. For cases, length of follow-up was calculated as the time from date of examination to date of hip fracture diagnosis or procedure for those identified by Medicare records or date of death for those identified by death certificates. For non-cases, follow-up was calculated from baseline exam to date of death for decedents, date of entry into managed care for those who enrolled in a Medicare-managed care program, or end of follow-up on December 31, 2000 for those who did not fall into the first two categories. A test of the proportional hazards assumption did not indicate a significantly increasing or decreasing trend in RR with time ($p=0.18$), suggesting that the assumption was not violated.

Differences in the relationship between hip fracture and treatment eligibility by sex or race/ethnicity were examined by including interaction terms in separate Cox proportional hazards model that included age and sex or race/ethnicity only. Because the interaction terms were not significant, results were combined for both sexes; and all models were adjusted for sex in addition to age. Results are also presented for all races combined in addition to those shown separately for non-Hispanic whites. Results for all races combined are adjusted for race/ethnicity in addition to sex and age. Hip fracture risk by treatment eligibility (yes/no) and number and specific type of eligibility criteria that were met were tested in separate Cox models. Number/type of criteria met were represented by a four-category variable: (1) none; (2) osteopenia at hip and a qualifying FRAX® score; (3) self-reported fracture *or* osteoporosis at hip or spine; 4) two or more of the criteria shown in (2) or (3) above. Although they are separate criteria in the NOF Guide, self-reported fracture and osteoporosis at hip and spine were combined into a single category for this analysis in order to have sufficient hip fracture cases in this category.

Harrell's $R^2$ was calculated to compare the ability of the NOF guidelines to predict incident hip fracture between sexes and age groups [19]. Harrell's $R^2$ is an estimate of the proportion of explained variance and is calculated as: $R_H^2 = (\log L_R - \log L_U)/\log L_R$, where $\log L_R$ is the log-likelihood ratio statistic for the Cox model without covariates, and $\log L_U$ is the log-likelihood ratio statistics for the Cox model with covariates [19].

## Results

In follow-up averaging 6.6 years, a total of 203 hip fracture cases were identified: 18 cases from both Medicare and death records, 183 from Medicare records only, and two from death records only. The vast majority of cases ($n=185$ or 91%) had diagnoses consistent with hip fracture on records from more than one source (e.g., inpatient hospital, SNF, carrier, outpatient, and/or death records). Likewise, 88% of those with a hospital record containing a discharge diagnosis of 820 also had relevant surgical codes for hip fracture. There were 25 hip fracture cases with ICD codes consistent with significant trauma.

Incidence rates for hip fracture by age and sex for the analytic sample are shown in Table 1. Rates were substantially higher in those ages 80 and older compared to the younger age group, and women had a higher hip fracture incidence than men. Mean age at fracture was 82.2 years for men and 82.5 years for women.

Baseline characteristics of the 203 hip fracture cases vs the remaining non-cases are compared in the overall analytic sample (all races combined) in Table 2. Only four variables (smoking, alcohol use, rheumatoid arthritis, and parental history of hip fracture) did not differ between cases and non-cases at baseline. The other risk factors differed between cases and non-cases in the expected ways. Specifically, cases were older, thinner, and had lower BMD and higher FRAX® scores. They were more likely to be female, non-Hispanic white, and to have been previously fractured. They were also significantly more likely to be eligible for treatment based on the new NOF guidelines.

Altogether, 47% of the analytic sample (29% of men, 60% of women) was eligible for treatment according to the

**Table 1** Weighted incidence (per 10,000 person-years) of hip fracture by sex and age group among adults aged 65 years and older

| Age at baseline (years) | $n$ of cases | Incidence (95% CI) |
|---|---|---|
| Men | | |
| 65–79 | 29 | 39.4 (22.8, 56.1) |
| 80+ | 46 | 213.9 (163.2, 264.6) |
| Subtotal | 73 | 60.7 (42.8, 78.7) |
| Women | | |
| 65–79 | 57 | 72.5 (49.7, 95.4) |
| 80+ | 71 | 258.4 (199.1, 317.9) |
| Subtotal | 128 | 104.8 (85.4, 124.2) |
| Both sexes | 203 | 86.4 (70.8, 102.0) |

**Table 2** Selected baseline characteristics of study sample by hip fracture status among adults 65 years of age or older

| | Hip fracture | | No fracture | |
|---|---|---|---|---|
| | Mean or % | SE | Mean or % | SE |
| N | 203 | | 3,005 | |
| Sex (% female) | 70.7 | 2.80 | 55.8* | 1.10 |
| Age at baseline (years, mean) | 77.4 | 0.55 | 73.2* | 0.23 |
| Race/ethnicity (%) | | | | |
| Non-Hispanic white | 93.6 | 1.80 | 87.6* | 1.09 |
| Non-Hispanic black | 3.8 | 1.13 | 7.4 | 0.77 |
| Mexican American | 0.8 | 0.24 | 1.8 | 0.15 |
| Other | 1.9 | 1.36 | 3.3 | 0.7 |
| Body mass index (mean) | 24.5 | 0.39 | 26.8* | 0.13 |
| Femur neck BMD t-score (mean) | −2.4 | 0.08 | −1.4* | 0.03 |
| Simulated spine BMD t-score (mean) | −1.0 | 0.10 | −0.4* | 0.04 |
| Eligible for treatment based on new NOF guideline (% yes) | 84.4 | 3.12 | 44.2* | 1.62 |
| Currently smoke (% yes) | 13.8 | 3.55 | 12.0 | 0.79 |
| Drink 3+ units alcohol (% yes) | 4.5 | 1.88 | 6.1 | 0.71 |
| Rheumatoid arthritis (%) | 3.2 | 1.47 | 2.1 | 0.46 |
| Parental history of hip fracture (% yes) | 14.5 | 3.93 | 10.8 | 0.67 |
| Previous fracture after age 20 (% yes) | 49.7 | 3.73 | 36.6* | 1.56 |
| 10-year absolute risk (FRAX[R]) score for hip fracture (mean) | 10.5 | 1.19 | 4.4* | 0.15 |
| Previous hip or spine fracture after age 20 (% yes) | 12.2 | 2.76 | 4.3* | 12.2 |
| Osteopenia at hip or spine and qualifying FRAX™ absolute fracture risk score[a] (% yes) | 52.7 | 4.70 | 33.7* | 1.50 |
| Femur neck osteoporosis (% yes) | 49.3 | 3.90 | 16.8* | 1.06 |
| Spine osteoporosis (% yes) | 15.2 | 3.54 | 5.2* | 0.51 |

*$p<0.05$ comparing hip fracture to no fracture

[a] Ten-year absolute hip fracture risk ≥3% and/or 10-year absolute major fracture risk ≥20%.

current NOF guideline. Thirteen percent of the analytic sample (11% of men, 15% of women) was treatment-eligible by virtue of osteopenia and either a 10-year hip fracture risk ≥3% or a major osteoporotic fracture risk ≥20%, whereas 8% (4% of men, 11% of women) qualified on the basis of osteoporosis or previous hip or spine fracture, and 26% (13% of men, 35% of women) could be considered for treatment on the basis of two or more of the NOF guide criteria.

Table 3 shows the relative risk for subsequent hip fracture by treatment eligibility status at baseline according to the current NOF guide. Overall, treatment-eligible persons were about five times more likely to experience a subsequent hip fracture than the non-eligible persons, but there was a significant trend in risk with increasing severity or number of the guide criteria that were met. Persons with osteopenia and a qualifying FRAX® score at baseline were about three times more likely to have a subsequent hip fracture than persons who were not eligible for treatment. Those who self-reported a hip or spine fracture or who had femur neck or lumbar spine osteoporosis at baseline were roughly five to six times more likely to subsequently fracture their hip than treatment-ineligible persons. Finally, those who met two or more of the NOF guide criteria were six to 6.5 times more likely to have a subsequent hip fracture than non-eligible persons.

In a sub-analysis, hip fracture risk in those with either hip or spine osteopenia *and* a qualifying FRAX® score (but no other qualifying NOF guide criteria) ($n=407$, 42 hip fracture cases) was compared with risk in a reference group defined as those with hip or spine osteopenia without a qualifying FRAX® score or any other NOF guide criteria ($n=808$, 23 hip fracture cases). The analyses were adjusted for age, sex, and race/ethnicity. The RR for osteopenics with a qualifying FRAX® score was 2.55[1] (95% CI 1.18 to 5.52), indicating that their risk of hip fracture was significantly elevated compared to osteopenics without a qualifying FRAX® score.

The relative risk of hip fracture by treatment eligibility after stratifying by sex or age group is shown in Table 4. Both treatment-eligible men and women had a significantly higher risk of hip fracture than non-eligible persons of the same sex. The magnitude of the RR point estimates and Harrell's $R^2$ by sex suggest that the NOF guidelines might be slightly more predictive in men than in women, although the confidence intervals for the RRs overlapped considerably between the sexes. When stratified by age, hip fracture risk remained significantly higher among those who were treatment-eligible. The similarity of RRs and Harrell's $R^2$

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[1] May be unreliable, estimate/standard error >30%

**Table 3** Relative risk (RR) of hip fracture risk by osteoporosis treatment eligibility status as defined by the current NOF guideline among adults aged 65 years or older

| | All races[a] | | | | Non-Hispanic whites[b] | | | |
|---|---|---|---|---|---|---|---|---|
| | n of cases | RR (95% CI) | | | n of cases | RR (95% CI) | | |
| Eligible for treatment according to current NOF guideline | | | | | | | | |
| Both sexes, aged 65+ years | | | | | | | | |
| No | 36 | 1.00 | – | – | 18 | 1.00 | – | – |
| Yes | 167 | 4.90 (3.03, 7.94) | | | 153 | 5.33 (3.13, 9.08) | | |
| Number of eligibility criteria met | | | | | | | | |
| None | 36 | 1.00 | – | – | 18 | 1.00 | – | – |
| 1 criterion | | | | | | | | |
| Osteopenia at hip or spine and qualifying FRAX® absolute fracture risk score[c] | 42 | 3.32 (2.02, 5.44) | | | 39 | 3.45 (2.06, 5.80) | | |
| Self-reported fracture or osteoporosis at hip or spine | 31 | 5.43 (3.16, 9.32) | | | 28 | 6.16 (3.30, 11.50) | | |
| 2 or more of the above single criteria | 94 | 5.75 (3.39, 9.77) | | | 86 | 6.44 (3.62, 11.44) | | |
| p trend | <0.00001 | | | | <0.00001 | | | |

[a] Adjusted for race/ethnicity, age, and sex

[b] Adjusted for age and for sex

[c] Ten-year absolute hip fracture risk ≥3% and/or 10-year absolute major fracture risk ≥20%.

and overlapping confidence intervals for the RRs in the two age categories suggested that the Guide's ability to predict fracture was similar in both age groups.

## Discussion

Previous work to evaluate the new NOF guidelines has focused on cost effectiveness [4] and impact [17], espe-

**Table 4** Relative risk (RR) of hip fracture risk by osteoporosis treatment eligibility status and sex or age among adults aged 65 years or older

| Eligible for treatment under current NOF guidelines | n of cases | RR (95% CI) | Harrell's $R^2$ |
|---|---|---|---|
| By sex | | | |
| Men | | | |
| No | 18 | 1.00 | – |
| Yes | 57 | 5.46 (2.62,11.40) | 0.05 |
| Women | | | |
| No | 18 | 1.00 | – |
| Yes | 110 | 4.29 (2.19,8.43) | 0.02 |
| By age (years) | | | |
| 65–79 | | | |
| No | 26 | 1.00 | – |
| Yes | 60 | 4.78 (2.63, 8.71) | 0.02 |
| 80+ | | | |
| No | 10 | 1.00 | – |
| Yes | 107 | 4.60 (2.10, 10.09) | 0.01 |

cially in terms of the prevalence of middle-aged and older US adults who would be eligible for treatment based on their application [5, 20, 21]. The present study extends this evaluation by examining the risk of subsequent hip fracture in older adults by treatment eligibility status. Our results indicate that the older persons who are defined as eligible for treatment using NOF guidelines are at significantly greater risk of suffering a future hip fracture than those who are not eligible by these criteria.

Finding an elevated risk of future hip fracture in the treatment-eligible group is not unexpected in light of previous data that support the ability of the individual components of the NOF guidelines to predict future fracture [22–31]. However, our results help to quantify the magnitude of risk that results when these risk factors are applied in the combination used by the new guide. We also examined risk by separate components of the NOF guideline and found, as have others, that risk increased with increasing severity [24] or number of contributing factors [23].

Our results indicate that the guide successfully identifies those at significant risk of future hip fracture in some important subgroups. For example, the new guide is the first version designed to be applied to men, and our results indicate that men who are defined as being eligible for treatment have a significantly higher risk of subsequent hip fracture than ineligible men. Whether the guide performs better in one sex vs the other is less clear: The RR point estimate and model comparison statistics suggested a slightly better performance in men, but the confidence interval for the RR in men overlapped the RR in women. At a minimum, however, it appears that the guide works at

least as well in men as in women. The guide also appears to work equally well in those aged 65–79 years and aged 80+ years, based on the similarity of the RR and model comparison statistics.

However, some important questions regarding the NOF guidelines could not be addressed by our study. For example, demonstrating an elevated RR of hip fracture in the group who are defined as eligible for treatment by the NOF guidelines should not be interpreted to mean that these individuals will benefit from treatment. There are ample data to suggest this is likely to be the case for individuals who meet the NOF guideline criteria of osteoporosis or previous fracture [32]. However, response to treatment in those who meet the NOF guideline criteria of osteopenia combined with an elevated FRAX® score has not yet been tested directly. There is some evidence that FRAX® identifies a population of patients that respond to treatment, which has been recently reviewed [33, 34]. Data from randomized clinical trials of fracture prophylaxis in older women drawn from the general population or in women at high risk of fracture provide some evidence for the utility of 10-year fracture probability scores in identifying women who will benefit from drug treatment [35, 36]. More work is needed, especially to confirm that the NOF guideline criteria that combine osteopenia with an elevated FRAX® score identify persons who will benefit from treatment.

Our study also was not able to examine the ability of the guideline to predict hip fracture in the full spectrum of people to which it applies. Specifically, the eligible age range for the new NOF guide is 50 years and older, and it applies to blacks and Hispanics as well as Caucasians [1]. Unfortunately, the risk of incident hip fracture in the 50–64 year age group cannot be tested in the NHANES III follow-up sample because coverage by Medicare in that age range is incomplete. Similarly, our findings do not pertain to institutionalized elders as NHANES III was a non-institutionalized sample. Moreover, we were not able to provide estimates for separate race/ethnic groups other than whites due to the small number of hip fracture cases in nonwhites. This remains an important issue given projected increases in the hip fracture burden among these other populations [37].

We were also unable to provide observed estimates of 10-year absolute fracture risk due to the relatively short follow-up time available for the study cohort. The mean follow-up time in our sample was only 6.6 years, and 90% of the sample was followed up for <10 years. As a result, we presented relative risk estimates only. These RR compare hip fracture risk in those who were eligible for treatment according to the new NOF guidelines vs those who were not eligible. They are not, however, expressions of absolute risk (AR), which is the actual proportion of each

group that experienced a hip fracture. Both risk estimates are important to consider, since a large RR may be less important in groups with a low AR, and vice versa. Thus, a comparison of observed estimates of absolute fracture risk in those who meet the NOF criteria vs those who do not is needed to further evaluate the utility of the new guideline.

Other study limitations include a relatively small number of hip fracture cases which were identified using Medicare and death records without confirmation by X-ray. Almost all cases had codes consistent with hip fracture on multiple medical records, which suggests that the identified cases likely did suffer a hip fracture. However, some hip fractures may have been mistakenly classified as non-cases, especially since Medicare records prior to 1991 were not available. We previously estimated that 13 undetected hip fracture cases could have occurred in our sample during 1988–1990 [12]. However, this number is small, and misclassification of cases as non-cases would likely tend to attenuate the relative risk estimates observed between hip fracture risk and treatment eligibility. Extending the follow-up to evaluate an additional number of long-term hip fracture outcomes is an important next step.

Our results apply only to that segment of the population ages 65 years and older which was not institutionalized at baseline and participated in Medicare fee-for-service programs because medical records for respondents who received care from managed care programs or in Veterans Administration facilities were not available. Thus, although based on a cohort that was derived from a nationally representative sample of the civilian, non-institutionalized population at baseline, our results cannot be used to generalize to the entire adult population over age 65 years. Furthermore, exclusions for missing data or loss to follow-up were also made. The respondents who were excluded from our sample were more likely to be nonwhite, older, and have lower femur neck BMD, poorer health, more fractures, and chronic conditions at baseline and less activity than respondents who were included. Several of these characteristics (older age, low BMD, poor health, previous fractures, chronic conditions, and less activity) are associated with higher hip fracture risk [24]. Thus, our results may not generalize to this higher-risk segment of the older population.

In summary, our results suggest that the new NOF guide [1] successfully identifies older individuals who are at significant risk of subsequent hip fracture. The new guide appears to predict future hip fracture risk as well in men as in women, and its ability to predict hip fracture did not appear to diminish with age. Our results fill in some of the gaps regarding the evaluation of the new guide. Other aspects, such as the ability to predict hip fracture in those aged 50–65 years and in nonwhites, or overall ease of use in clinical practice [38] still need to be addressed.

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