

10-Year Probability of Recurrent Fractures Following Wrist and Other Osteoporotic Fractures in a Large Clinical Cohort

An Analysis From the Manitoba Bone Density Program

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Background: Wrist fractures are the most prevalent type of fracture occurring in postmenopausal women. We sought to contrast the probability of recurrent osteoporotic fractures after a primary wrist fracture with other important primary fracture sites.

Methods: A historical cohort study comprising 21 432 women 45 years or older referred for bone mineral density (BMD) testing. Longitudinal health service records were assessed for the presence of fracture codes before and after BMD testing (359 737 person-years of observation).

Results: A total of 2652 women (12.4%) experienced a primary fracture (wrist, vertebra, humerus, hip) prior to BMD testing, of which wrist fractures were the largest single group (1225 [46.2%]). The adjusted hazard ratio (HR) for recurrent osteoporotic fracture following a primary wrist fracture (HR, 1.58; 95% confidence interval [CI], 1.29-1.93) was lower than for other primary fractures (HR, 2.66; 95% CI, 2.30-3.08). Primary wrist fractures were not significantly associated with subsequent hip fractures (adjusted HR, 1.29; 95% CI, 0.88-1.89), whereas other primary fracture sites were individually

and collectively significant predictors of future hip fractures (HR, 1.72; 95% CI, 1.31-2.26). The 10-year probability of any recurrent fracture after a primary wrist fracture was 14.2% (95% CI, 11.9%-16.5%), which was significantly less than for other primary fractures (spine, 25.7%; hip, 24.9%; humerus, 23.7%; $P < .001$ for all comparisons vs wrist) but greater than in those without prior fractures (10.8%; $P < .001$). The relationship between BMD and fracture risk was much stronger after a primary wrist fracture (HR, 2.20 per standard deviation; 95% CI, 1.70-2.80) than after other primary osteoporotic fractures (HR, 1.21; 95% CI, 1.05-1.40), reflecting the dominance of the other fracture information over BMD.

Conclusions: Wrist fractures are the most common of the clinical osteoporotic fractures in patients referred for BMD testing. However, the risk of recurrent fractures in the 10 years following a wrist fracture is substantially lower than that following other osteoporotic fractures, although it remains significantly higher than for those who have yet to experience a fracture.

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PATIENTS WHO ARE SEEN FOR emergency treatment of long bone fractures are infrequently assessed for the presence of underlying osteoporosis.¹⁻³ Wrist fractures incurred as a result of a fall from a standing height or less are designated as “fragility” fractures and traditionally associated with osteoporosis. Efforts to raise awareness of the possibility of an underlying diagnosis of osteoporosis in older fracture patients have been shown to lead to further consideration of this diagnosis.^{1,2}

In 2007, Osteoporosis Canada⁴ published revised bone mineral density (BMD) guidelines in which age, sex, and BMD were used to provide 10-year probabilities for osteoporotic fractures. Zones of 10-year fracture probability were defined as low (<10%), moderate (10%-20%), and

high (>20%), similar to the risk zones defined for cardiovascular disease.^{5,6} A prevalent fragility fracture was taken as an independent indicator of increased fracture risk over and above that defined by age, sex, and BMD alone.⁴ This position was based on evidence that prevalent fragility fractures greatly increased the risk of subsequent fractures⁷ and therefore constituted a more compelling reason to initiate therapy than reduced BMD alone. However, these recommendations make the assumption that all osteoporotic fractures confer equally increased risks for future fractures. This question is especially valid when considering that wrist fractures comprise 26% to 46% of all observed skeletal fractures⁸⁻¹³ and are the single most common fragility fracture seen in a fracture clinic in this age group.

This study was undertaken to provide insight into the risk of recurrent fracture after a wrist or other osteoporotic fracture. The clinical database of the Manitoba Bone Density Program was linked to other provincial health databases to directly estimate 5- and 10-year probabilities of a further fragility fracture after a woman presents with a wrist fracture as her first fracture. These estimates were contrasted with other “typical” osteoporotic fractures, such as spine, humeral, or hip fractures.

METHODS

STUDY DESIGN

In this retrospective cohort study, we identified women 45 years or older at the time of baseline BMD testing who had experienced a nontraumatic “osteoporotic” fracture of the wrist (including forearm), humerus, hip, or vertebra between 1987 and the date of BMD testing. We defined the first fracture event as the “primary” fracture site, and subsequent fractures in that individual as “recurrent” events.

The administrative databases of Manitoba Health contain detailed health records on virtually the entire population of Manitoba, Canada (approximately 1.1 million according to a 2001 census).¹⁴ These data include diagnostic codes (*International Statistical Classification of Diseases, 10th Revision, Clinical Modification (ICD-9-CM)*) and procedures from hospital discharges and physician billings for all inpatient, outpatient, and office-based contacts. Data on pharmacy dispensations are also available. These population-based databases were linked to the clinical database of the Manitoba Bone Density Program through an anonymous identifier that preserves patient confidentiality.

The Manitoba Bone Density Program database includes all BMD results obtained by dual-energy x-ray absorptiometry (DEXA) since 1990, and it is more than 99% complete and accurate.¹⁵ All clinical DEXA in the province is performed within a single program structure.¹⁶ The criteria for testing highlight the importance of female sex, age 65 years or older, prior fragility fractures, and other clinical risk factors that increase the risk of fragility fractures. Patients referred for BMD testing can be linked to the presence or absence of fractures in their medical history, both before and after testing. Fractures clearly associated with trauma (eg, motor vehicle accidents) based on *ICD-9-CM* trauma codes were excluded. The procedures for ascertaining the incidence of nontraumatic fractures of the wrist (*ICD-9-CM* 813-814), humerus (*ICD-9-CM* 812), hip (*ICD-9-CM* 820-821), and clinical spine (*ICD-9-CM* 805)—collectively designated as osteoporotic fractures—have been described in detail.¹⁷ To enhance diagnostic specificity for incident fracture events, hip and wrist fractures had to be accompanied by a site-specific fracture reduction, fixation, or casting code. The study was approved by the research ethics board of the University of Manitoba.

PATIENT POPULATION AND MEASUREMENTS

The cohort comprised women 45 years or older who underwent baseline femoral neck BMD testing from January 1990 through October 2002 using one of the program’s primary DEXA instruments (DPX or Prodigy; GE Lunar, Madison, Wisconsin). For women with more than 1 eligible measurement, only the first record was included. All subjects had Manitoba Health coverage during the observation period ending March 31, 2004.

The DEXA scans were performed in accordance with manufacturer recommendations. Femoral neck T scores (number of standard deviations [SDs] above or below the young adult mean

BMD) and z scores (number of SDs above or below age-matched mean BMD) were calculated using reference data for white females from the Third National Health and Nutrition Examination Survey.¹⁸ Instruments showed no clinically significant differences in calibration (in vivo T-score differences, <0.1). Densitometers showed stable long-term performance (phantom coefficient of variation [CV], <0.5%).

Determination of fracture outcomes was performed using 2 different index dates. (1) For women with a primary fracture, we searched for a recurrent osteoporotic fracture occurring after the date of primary fracture. Fracture codes within 90 days of the primary fracture were ignored to minimize the potential for counting health care interactions related to the same injury. (2) For all women, including those without a primary fracture, we also examined for an osteoporotic fracture occurring after the date of BMD testing. Pharmacological covariates were osteoporosis treatment in the year prior to BMD testing (2 or more pharmacy dispensations for a systemic estrogen product, oral bisphosphonate, raloxifene hydrochloride, or salmon calcitonin) and systemic corticosteroid use in the year prior to BMD testing (defined as ≥ 90 days’ possession).

STATISTICAL ANALYSIS

Statistical analyses were performed with Statistica software (version 6.1; StatSoft Inc, Tulsa, Oklahoma). $P < .05$ was taken to indicate a statistically significant effect. Differences in the means between groups were assessed from analysis of variance, with post hoc testing using the Tukey honest significant difference test. Differences in categorical variables were assessed with the χ^2 test.

The 5- and 10-year probabilities of a recurrent fracture, with 95% confidence intervals (CIs), were estimated using the Kaplan-Meier product limit method with time to fracture compared using the log-rank test. Hazard ratios (HRs) for recurrent fractures were derived from the Cox proportional hazards model, based on the site of the primary fracture site, with and without adjustment for age, osteoporosis treatment, corticosteroid use, and femoral neck BMD. Age-adjusted HRs for recurrent fractures, stratified according to primary fracture site, were also calculated for BMD. The HRs to predict future fractures and the Kaplan-Meier curves were essentially identical when previously treated women were excluded from the analysis.

The number of patients needing treatment (NNT) with an oral bisphosphonate to prevent a subsequent fracture following a primary osteoporotic fracture was estimated assuming a relative risk (RR) of 0.75 (treated vs nontreated, for 5 years). This estimate was taken from the meta-analyses by Wells et al¹⁹ in which the pooled RR estimates for nonspine fracture reduction in the randomized clinical trials of both primary and secondary fracture prevention were 0.84 for alendronate (11 trials) and 0.80 for risedronate (7 trials).²⁰ Pooled RR estimates of spine fracture reduction were lower (0.55 for alendronate and 0.63 for risedronate). Assuming a ratio of 25% clinical spine to 75% nonspine fractures, the weighted RR reduction is very close to 0.75. The results reported herein were stratified for primary fracture type, age (cutoff, 65 years), and T score (cutoff, -2.5) but were not adjusted for previous therapy, given the identical future fractures in women (see the previous subsection, “Patient Population and Measurements”).

RESULTS

Table 1 describes the characteristics of the 21 432 women who underwent baseline BMD measurement at a mean (SD) age of 63.1 (10.3) years. The population was predominantly white with a low prevalence of visible mi-

norities (2.0%). Among these women, 5727 (26.7%) had received some form of antiresorptive therapy in the year prior to BMD measurement (an estrogen product in 4413 [77.1%]), and 1535 (7.2%) were recent corticosteroid users. There were 2652 women (12.4%) with a primary fracture prior to the BMD measurement. Fractures of the wrist represented the largest group of primary fractures (46.2%), followed by clinical spine (20.9%), humerus (20.7%), and hip (12.2%). Of all wrist fractures that were observed in these women, most (92.2%) were primary events (ie, the first fracture in the woman's health record). Lower proportions of clinical spine (81.0%), proximal humerus (80.2%), and hip (67.4%) fractures were primary events. The observation period over which fractures were ascertained prior to BMD testing amounted to 272 398 person-years, with a further 87 339 person-years after the BMD measurement (combined 359 737 patient-years). The period of observation following the primary fracture was 22 851 person-years.

Table 1. Population Characteristics

Characteristic	Value
Cohort size	21 432
Age, mean±SD, y	63.1±10.3
Osteoporosis therapy, No. (%) ^a	5727 (26.7)
Systemic corticosteroid therapy, No. (%) ^b	1535 (7.2)
Primary fracture (before BMD test), No. (%)	2652 (12.4)
Wrist	1225 (5.7)
Spine	554 (2.6)
Hip	323 (1.5)
Humerus	550 (2.6)
None	18 780 (87.6)
Observation period, mean±SD, y (patient-years)	
Prior to BMD testing	12.7±2.4 (272 398)
After BMD testing	4.1±2.3 (87 339)

Abbreviation: BMD, bone mineral density.

^aAll individuals with 2 or more pharmacy dispensations of either an oral bisphosphonate, systemic estrogen, raloxifene hydrochloride, or salmon calcitonin during the year prior to BMD test.

^bAt least 90 days' possession during the year prior to BMD testing.

Table 2 summarizes characteristics according to primary fracture status and site. Within the cohort, 18 780 women were referred for BMD testing without a prior fracture (the nonfracture group), and 853 (4.5%) of these women experienced 1 or more fractures during a mean (SD) follow-up period of 4.1 (2.3) years. Of the 2652 women who had experienced a fracture prior to BMD testing (the primary fracture group), 467 (17.6%) experienced 1 or more recurrent fractures during a mean (SD) follow-up period of 8.6 (10.3) years, of which 367 (13.8%) occurred after the BMD test.

Patients with primary fractures were significantly older than those who had no fractures at the time of BMD testing ($P < .001$). On average, BMD testing was performed 4.7 years after the primary fracture. Those with clinical spine, hip, and humerus fractures were significantly older than those presenting with wrist fractures ($P < .001$).

For the nonfracture group, the mean (SD) z score was 0.0 (1.1), indicating that women referred for BMD testing for reasons other than a prior clinical fracture were similar to the reference population. For women with primary fractures, the mean (SD) z score was -0.5 (1.1), which was significantly lower than for the nonfracture group ($P < .001$). Women with primary hip fractures had lower mean z scores (-0.9 [1.1]) than those with primary fractures at other sites. Mean T scores were also significantly lower in women with a prior fracture than in those without a prior fracture (-2.0 [0.9] vs -1.4 [1.0]; $P < .001$). The hip fracture group (who were considerably older than the other fracture groups) had the lowest mean T scores (-2.5 [0.9]). Only 13.3% of the nonfracture group had a T score in the osteoporotic range. Not surprisingly, a significantly higher proportion of women with primary fractures had osteoporotic T scores ($P < .001$): 33.6% of those with clinical spine fractures, 33.5% with humerus fractures, and 50.8% with hip fractures. However, significantly fewer women with wrist fractures (24.6%) had osteoporosis as defined by BMD testing ($P < .05$).

Table 3 shows the age-adjusted HRs for BMD to predict fractures. For women without a primary fracture, the risk of future fracture increased as BMD fell (HR, 1.80

Table 2. Baseline BMD Measurements, According to Presence or Absence of Primary Osteoporotic Fractures Prior to the Measurement^a

Variable	Nonfracture Group	All Primary Fractures	Wrist	Humerus	Spine (Clinical) ^b	Hip
No., % (N=21 432)	18 780 (87.6)	2652 (12.4)	1225 (5.7)	550 (2.6)	554 (2.6)	323 (1.5)
Age, y						
At BMD test	62.5±10.1	67.9±10.2 ^c	66.6±9.7 ^c	68.1±10.3 ^{c,d}	68.5±10.5 ^{c,d}	71.3±10.2 ^{c,d}
At time of primary fracture	NA	63.2±10.17	61.3±9.9	63.4±10.18 ^d	64.6±11.5 ^d	67.4±10.4 ^d
Femoral neck bone density						
z Score	0.0±1.1	$-0.5±1.1^c$	$-0.4±1.0^c$	$-0.4±1.1^c$	$-0.4±1.2^c$	$-0.9±1.1^c,d$
T score	$-1.4±1.0$	$-2.0±0.9^c$	$-1.9±0.9^c$	$-2.0±0.9^c$	$-2.0±1.0^c$	$-2.5±0.9^c,d$
T score ≤ -2.5 , No. (%)	2503 (13.3)	835 (31.5) ^c	301 (24.6) ^c	184 (33.5) ^{c,d}	186 (33.6) ^{c,d}	164 (50.8) ^{c,d}
Occurrence of osteoporotic fractures, No. (%)						
Any osteoporotic fracture after BMD testing	853 (4.5)	367 (13.8) ^c	108 (8.8) ^c	106 (19.3) ^{c,d}	99 (17.9) ^{c,d}	54 (16.7) ^{c,d}
Recurrent fracture after a primary fracture	NA	467 (17.6) ^c	161 (13.1) ^c	119 (21.6) ^{c,d}	120 (21.7) ^{c,d}	67 (20.7) ^{c,d}

Abbreviations: BMD, bone mineral density; NA, not applicable.

^aData are given as mean ± SD unless indicated otherwise.

^bThe patient has presented with signs and/or symptoms of vertebral fracture, confirmed by radiography and defined by *International Classification of Diseases, Ninth Revision, Clinical Modification* (see the "Study Design" subsection in the "Results" section).

^c $P < .001$ vs nonfracture group.

^d $P < .05$ compared with primary wrist fracture subgroup.

Table 3. Age-Adjusted HRs for Femoral Neck BMD to Predict Incident Fractures After BMD Testing According to Primary Fracture Status

Site of Primary Fracture	HR (95% CI) per SD	P Value
None	1.80 (1.68-1.93)	<.001
Wrist	2.20 (1.72-2.80)	<.001
Any nonwrist	1.21 (1.05-1.40)	.01
Humerus	1.25 (0.99-1.57)	.06
Spine	1.35 (1.07-1.71)	.01
Hip	1.04 (0.74-1.45)	.83

Abbreviations: BMD, bone mineral density; CI, confidence interval; HR, hazard ratio; SD, standard deviation.

Table 4. Adjusted^a HRs for Incident Fractures After BMD Testing According to Site of Primary Fracture

Site of Primary Fracture	HR (95% CI) for Any Osteoporotic Fracture ^b		HR (95% CI) for Hip Fracture ^b	
	HR (95% CI)	P Value	HR (95% CI)	P Value
Wrist	1.58 (1.29-1.93)	<.001	1.29 (0.88-1.89)	.19
Any nonwrist	2.66 (2.30-3.08)	<.001	1.72 (1.31-2.26)	<.001
Humerus	3.18 (2.56-3.94)	<.001	2.06 (1.35-3.15)	<.001
Spine	2.73 (2.21-3.36)	<.001	1.52 (1.01-2.30)	.046
Hip	2.00 (1.53-2.63)	<.001	1.67 (1.08-2.58)	.02

Abbreviations: BMD, bone mineral density; CI, confidence interval; HR, hazard ratio.

^aAdjusted for age, femoral neck BMD, osteoporosis therapy, and systemic corticosteroid therapy.

^bThe reference group is composed of women without a primary fracture prior to BMD testing.

per SD; 95% CI, 1.68-1.93; $P < .001$), and this risk was not attenuated after a primary wrist fracture (HR, 2.20 per SD; 95% CI, 1.72-2.80; $P < .001$). In contrast, the gradient of risk for BMD was much less after other primary osteoporotic fractures (HR, 1.21; 95% CI, 1.05-1.40; $P = .01$). The BMD was no longer helpful in predicting the risk of future fractures following a primary hip fracture (HR, 1.04; 95% CI, 0.74-1.45; $P = .83$).

Table 4 shows the HRs for any recurrent osteoporotic fracture after BMD testing using women without a primary fracture as the reference group. After adjusting for age, BMD, osteoporosis therapy, and corticosteroid use, the HR for recurrent osteoporotic fracture following a wrist fracture (HR, 1.58; 95% CI, 1.29-1.93; $P < .001$) is lower than for any other nonwrist fracture (HR, 2.66; 95% CI, 2.30-3.08; $P < .001$). In the adjusted model, primary wrist fractures were not significantly associated with incident hip fractures (HR, 1.29; 95% CI, 0.88-1.89; $P = .19$), whereas other primary fracture sites were individually and collectively still significant predictors of future hip fractures (HR, 1.72; 95% CI, 1.31-2.26; $P < .001$).

The **Figure** shows the incidence of new osteoporotic fractures over 10 years according to the primary fracture site. Relative to women without prior fractures at the time of BMD measurement, primary wrist fractures were associated with a greater risk for a subsequent fracture. Nonetheless, whether the index date was taken as the date of BMD testing or the earlier date of the pri-

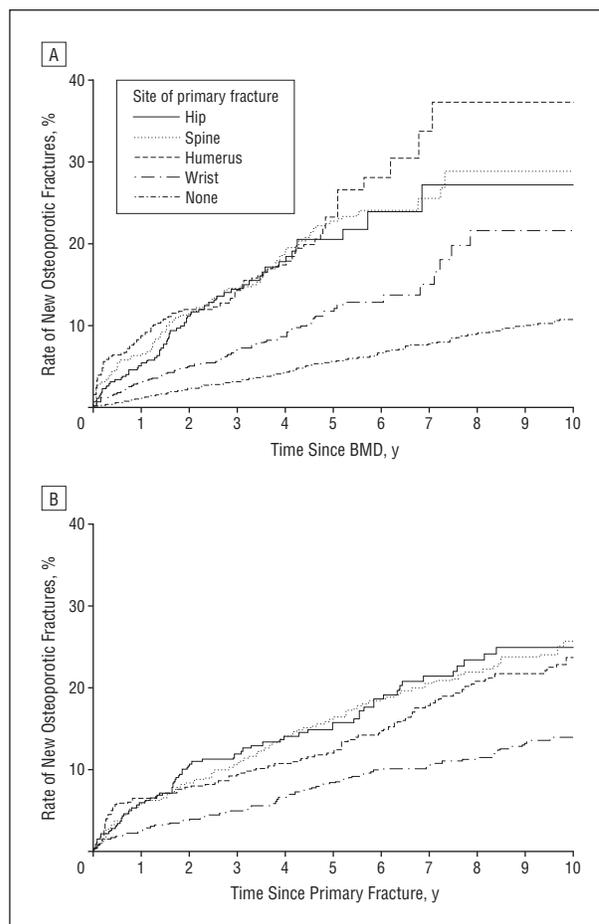


Figure. Kaplan-Meier curves showing incidence of new osteoporotic fractures according to primary fracture site. Incidence rates for (A) 10 years after bone mineral density (BMD) measurement (including women without a primary fracture) and (B) 10 years after primary (earliest) fracture prior to BMD measurement (wrist, clinical spine, hip, or humerus).

mary fracture, recurrent fracture rates were lower after a primary wrist fracture than after any other fracture type.

Table 5 summarizes the cumulative 5- and 10-year risks of new osteoporotic fractures, categorized by primary fracture status. The 10-year risk of a recurrent osteoporotic fracture occurring after a primary wrist fracture was 14.2% (95% CI, 11.9%-16.5%) from the fracture date and 11.7% (95% CI, 9.1%-14.3%) from the date of BMD testing. These values are significantly less than the 10-year probability of further fractures after other primary osteoporotic fractures (spine, 25.7%; hip, 24.9%; humerus, 23.7%; $P < .001$ for all comparisons vs wrist).

Table 6 provides estimates for the NNT for 5 years to prevent a subsequent osteoporotic fracture assuming that therapy reduces the risk of fracture by 25%. Because the 5-year fracture rates after primary humerus, spine, and hip fractures were similar, for simplicity these sites were combined and contrasted with primary wrist fractures. The NNT varied from a maximum of 130 (95% CI, 115-150) in women at lowest risk (age <65 years, nonosteoporotic BMD, no primary fractures) to 12 (95% CI, 11-15) in women at greatest risk (age ≥ 65 years; osteoporotic BMD; primary fracture of the humerus, spine, or hip). In keeping with the dependence of future frac-

Table 5. Cumulative Fracture Risk (CFR) of New Osteoporotic Fractures Categorized by Presence or Absence of Primary Osteoporotic Fracture Prior to BMD Measurement

Site of Primary Fracture	CFR, % (95% CI)						
	From Time of Primary Fracture			From Time of BMD Measurement			
	5 y	10 y	P Value vs Wrist	5 y	10 y	P Value vs None ^a	P Value vs Wrist ^a
None	NA	NA	NA	5.6 (5.2-6.0) ^b	10.8 (9.0-11.4)	NA	NA
Wrist	8.4 (6.8-10.0)	14.2 (11.9-16.5)	NA	11.7 (9.1-14.3)	21.5 (14.1-28.9)	<.001	NA
Humerus	12.0 (9.3-14.8)	23.7 (19.5-27.9)	<.001	24.5 (19.5-29.5)	37.2 (26.4-48.0)	<.001	<.001
Spine	16.3 (13-19.5)	25.7 (21.2-30.1)	<.001	21.6 (17.2-26.0)	27.8 (20.8-34.8)	<.001	<.001
Hip	15.8 (11.6-19.9)	24.9 (19.2-30.6)	<.001	20.3 (14.9-25.7)	27.3 (17.5-37.1)	<.001	<.001

Abbreviations: BMD, bone mineral density; CI, confidence interval; NA, not applicable.

^aLog-rank test for fracture-free survival.

^bEstimate (95% CI).

ture risk on BMD in women with primary wrist fractures, the NNT in those women with T scores higher than -2.5 was significantly greater than that for fractures at other sites ($P < .01$), but was lower than that for women without fractures at the time of BMD testing.

COMMENT

In this large cohort of postmenopausal women, wrist fractures were more than twice as common as clinical spine and humeral fractures, and more than 3 times as common as hip fractures, accounting for 46.2% of the observed primary fracture burden. Women with wrist fractures were significantly younger than those with other fractures ($P < .05$) and were significantly less likely to be categorized as having osteoporosis by BMD testing ($P < .001$). Moreover, the observed 10-year risk of recurrent fracture following the primary wrist fracture event (14.2%) was significantly less than that observed for the other osteoporotic primary fractures, which exceeded 20% ($P < .05$). By comparison, the women referred for BMD testing in the nonfracture group were younger than women in the primary fracture groups and had significantly higher BMD measurements ($P < .001$) and lower fracture risk following BMD testing ($P < .001$).

Wrist fractures have been reported to comprise 26% to 46% of the fracture burden within several cohorts,⁸⁻¹³ consistent with the experience reported herein. It is therefore important to define the consequences of wrist fractures in relation to other osteoporotic fractures. For women who had no fractures at the time of BMD testing, the age-adjusted HR per SD decrease in BMD for any incident fracture after the BMD test was 1.80 (95% CI, 1.68-1.93). Those with a primary wrist fracture prior to the BMD test had a similar HR, compatible with a similar dependence of fracture risk on BMD. However, the HRs for recurrent fractures after BMD testing were significantly lower for those women with a primary humeral, clinical spine, or hip fracture ($P < .05$) and were no longer significant following a hip fracture ($P < .83$). This degradation in the usefulness of BMD for fracture prediction after nonwrist primary fractures reflects the dominance of the prior fracture information. The HRs (per SD decrease in femoral neck BMD) for wrist frac-

Table 6. Estimated NNT for 5 Years to Prevent a New Osteoporotic Fracture, Based on a 5-Year Probability of New Fracture and Stratified by Age and BMD

Site of Primary Fracture	Age, y ^a	
	<65	≥65
Femoral neck nonosteoporotic (T score > -2.5)		
None ^b	130 (115-150)	58 (51-68)
Wrist ^c	50 (35-89)	38 (27-66)
Other sites (humerus, spine, or hip) ^c	23 (18-32)	21 (17-27)
Femoral neck osteoporotic (T score ≤ -2.5)		
None ^b	53 (41-75)	24 (21-28)
Wrist ^c	23 (14-58)	20 (15-29)
Other sites (humerus, spine, or hip) ^c	29 (18-70)	12 (11-15)

Abbreviations: BMD, bone mineral density; NNT, number needed to treat.

^aData are given as number (95% confidence intervals).

^bBased on the 5-year fracture rate after BMD testing.

^cBased on fracture rate after primary fracture. Assumes 0.75 relative risk for fracture during therapy with oral alendronate sodium or risedronate sodium, compared with no treatment (adapted from Wells et al^{19,20}).

tures and hip fractures have been reported from cohort studies in North America,¹¹ Europe,¹² and Australia.²¹ For wrist fractures, the HR is approximately 1.5, and for hip fractures the HR exceeds 2.0. Less than a quarter of the women with a primary wrist fracture had an osteoporotic T score at the time of BMD testing. This finding has also been described by the Study of Osteoporotic Fractures,¹¹ in which only 16% of women with wrist fractures had femoral neck T scores of -2.5 or less.

It is clear that prevalent nonspine fractures are a risk factor for recurrent osteoporotic fractures. In a meta-analysis of published reports from 11 cohorts, Kanis et al²² reported a moderately increased risk (RR, 1.86; 95% CI, 1.75-1.98) compared with individuals with no prior fracture. In other meta-analyses in which wrist fractures could be addressed separately, their occurrence was associated with increased risk for both nonspine fractures and hip fractures.^{23,24} The current report also finds a similar and significantly increased risk of recurrent osteoporotic fractures following either a primary wrist fracture or a primary nonwrist fracture. However, only primary nonwrist fractures were significantly predictive of

hip fractures in the adjusted model presented herein ($P < .001$).

The importance of analyzing a cohort of this magnitude lies in the ability to quantify the risk of recurrent fracture over many years according to the primary fracture site. In this context, a primary wrist fracture clearly signals an increased 10-year risk for recurrent fractures that is higher than that in women without fracture at the time of testing but substantially lower than that for the other primary fractures captured in this analysis (humeral, clinical spine, and hip). Kanis et al²⁵ first proposed that the 10-year probability of a fracture based on age and current T score might give more precise information on fracture risk than the T score alone based on clinical fracture records from Malmö, Sweden. There have been few other reports of observed 10-year fracture probabilities, and these have been limited to postmenopausal women without prior fractures.^{26,27} Although several meta-analyses²²⁻²⁴ clearly demonstrate that the occurrence of 1 osteoporotic fracture predicts an increased RR for recurrent fractures, the absolute risk is not well described or analyzed to determine whether there is a differential in risk according to the primary fracture site. Van Staa et al²⁸ performed an analysis of the General Practitioners' Research Database in the United Kingdom that was similar to the approach reported herein but did not have BMD data available. Although Van Staa et al²⁸ concluded that the standardized incidence ratios for subsequent fractures following a primary wrist, humerus, hip, or clinical spine fracture was very similar, they did not present 10-year site-specific probabilities. In our analysis, the 10-year probability of recurrent fracture following a primary wrist fracture was intermediate between the risk in women without a history of fracture at the time of BMD testing and that following other primary fractures. The reasons behind the more benign prognosis of a wrist fracture cannot be addressed herein; however, baseline differences in age and BMD do not seem to be sufficient because adjustment for these factors did not change the finding of a lower risk after primary wrist fractures than after other primary osteoporotic fractures.

Knowledge of the probability of recurrent fractures following a wrist fracture allows for extrapolation of the NNT to prevent a subsequent fracture. We have assumed a conservative efficacy for bisphosphonates to reduce the pooled risk for nonspine and symptomatic spine fractures by 25%, after Wells et al.^{19,20} The NNT estimates would be comparable for all patients older than 65 years with T scores lower than -2.5 , whether or not there were prior fractures at the time of BMD (range, 12-24). The NNT would be similar for younger women with better preserved T scores presenting with humeral, hip, or clinical spine fractures (NNT = 23), but significantly higher (NNT = 50) if such women presented only with a primary wrist fracture ($P < .002$).

There are several limitations to this study. Patients referred for BMD testing may not be representative of the general population. Published studies¹⁻³ suggest that over half the patients who experience an appendicular fracture after a fall from standing height are not evaluated for underlying osteoporosis. However, women referred for BMD testing should be representative of patients considered to be at risk for osteoporosis by their physi-

cians. The observed probabilities of fractures do not take into account other potential osteoporotic fractures, particularly those of the pelvis, lower limbs, and ribs, but these sites were not included in the 10-year fracture risk analysis by Kanis et al.²⁹ The efficacy of bisphosphonates to reduce the RR of recurrent spine fractures may be closer to 0.6, as reported in the meta-analysis by Cranney et al,³⁰ but because clinical vertebral fractures comprise only one-quarter of incident fractures (24.8% in our cohort) the RR for all osteoporotic fractures is largely determined by nonvertebral fractures. Using a lower RR would reduce the NNT in all scenarios but would not affect the relative ranking according to prior fracture site. It is important to note that 26.7% of women in our study were receiving antiresorptive therapy at the time of BMD testing (mainly estrogen), a potential confounder that we needed to control for in the analysis. However, exclusion of treated women from the analysis did not materially change the results (data not shown).

In conclusion, wrist fractures are the most common of the fractures typically associated with osteoporosis, but the observed 10-year probability of recurrent fractures after such an event is less than after primary fractures of the humerus, hip, or vertebrae. Selection of women for treatment to prevent recurrent fractures after a wrist fracture may be most efficient if they are older than 65 years or have T scores of less than -2.5 after BMD testing. Women younger than 65 years should be assessed for additional risk factors such as a low BMD or radiographic evidence of concurrent spine compression fractures, for which the evidence of benefit following bisphosphonate therapy is strongest.

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REFERENCES

1. Majumdar SR, Rowe BH, Folk D, et al. A controlled trial to increase detection and treatment of osteoporosis in older patients with a wrist fracture. *Ann Intern Med.* 2004;141(5):366-373.
2. Ashe M, Khan K, Guy P, et al. Wristwatch-distal radial fracture as a marker for osteoporosis investigation: a controlled trial of patient investigation and a physician alerting system. *J Hand Ther.* 2004;17(3):324-328.
3. Khan SA, de Geus C, Holroyd BH, Russel AS. Osteoporosis follow-up after wrist fractures following minor trauma. *Arch Intern Med.* 2001;161(10):1309-1312.
4. Siminoski KG, Leslie WD, Frame H, et al. Recommendations for bone mineral density reporting in Canada. *Can Assoc Radiol J.* 2007;56(3):178-188.
5. Genest J, Frohlich J, McPherson R; Working Group on Hypercholesterolemia and Other Dyslipidemias. Recommendations for the management of dyslipidemia and the prevention of cardiovascular disease: summary of the 2003 update. *CMAJ.* 2003;169(9):921-924.
6. Grundy SM, Pasternak R, Greenland P, Smith S, Fuster V. Assessment of cardiovascular risk by use of multiple risk factor assessment equations: a statement for Healthcare Professionals from the American Heart Association and the American College of Cardiology. *Circulation.* 1999;100(13):1481-1492.
7. Brown JP, Josse RG. 2002 clinical practice guidelines for the diagnosis and management of osteoporosis in Canada. *CMAJ.* 2001;167(10 suppl):S1-S34.
8. Huopio J, Kroger H, Honkanen R, Saarikoski S, Alhava E. Risk factors for perimenopausal fractures: a prospective study. *Osteoporos Int.* 2000;11(3):219-227.
9. Bach-Mortensen P, Hyldstrup L, Appleyard M, Hindso K, Gebuhr P, Sonne-Holm S. Digital X-ray radiogrammetry identifies women at risk for osteoporotic fracture: results from a prospective study. *Calcif Tissue Int.* 2006;79(1):1-6.
10. Miller PD, Siris ES, Barrett-Connor E, et al. Prediction of fracture risk in postmenopausal white women with peripheral bone densitometry: evidence from the National Osteoporosis Risk Assessment. *J Bone Miner Res.* 2002;17(12):2222-2230.
11. Stone KL, Seeley DG, Lui L-Y, et al. BMD at multiple sites and risk of fracture of multiple types: long-term results from the Study of Osteoporotic Fractures. *J Bone Miner Res.* 2003;18(11):1947-1954.
12. Schuit SCE, van der Klift M, Weel AEAM, et al. Fracture incidence and association with bone mineral density in elderly men and women: the Rotterdam study. *Bone.* 2004;34(1):195-202.
13. Honkanen R, Tuppurainen M, Kroger H, Alhava E, Saarikoski S. Relationships between risk factors and fractures differ by type of fracture: a population-based study of 12192 perimenopausal women. *Osteoporos Int.* 1998;8(1):25-31.
14. Roos NP, Shapiro E. Revisiting the Manitoba Centre for Health Policy and Evaluation and its population-based health information system. *Med Care.* 1999;37(6)(suppl):JS10-JS14.
15. Leslie WD, Caetano PA, MacWilliam LR, Finlayson GS. Construction and validation of a population-based bone densitometry database. *J Clin Densitom.* 2005;8(1):25-30.
16. Leslie WD, Metge C. Establishing a regional bone density program: lessons from the Manitoba experience. *J Clin Densitom.* 2003;6(3):275-282.
17. Cranney A, Jamal SA, Tsang JF, Josse RG, Leslie WD. Low bone mineral density and fracture burden in postmenopausal women. *CMAJ.* 2007;177(6):575-580.
18. Looker AC, Wahner HW, Dunn WL, et al. Updated data on proximal femur bone mineral levels of US adults. *Osteoporos Int.* 1998;8(5):468-89.
19. Wells GA, Cranney A, Peterson J, et al. Alendronate for the primary and secondary prevention of osteoporotic fractures in postmenopausal women. *Cochrane Database Syst Rev.* 2008;(1):CD001155. doi:10.1002/14651858.CD001155.pub2.
20. Wells G, Cranney A, Peterson J, et al. Risedronate for the primary and secondary prevention of osteoporotic fractures in postmenopausal women. *Cochrane Database Syst Rev.* 2008;(1):CD004523. doi:10.1002/14651858.CD004523.pub3.
21. Nguyen TV, Center JR, Sambrook PM, Eisman J. Risk factors for proximal humerus, forearm, and wrist fractures in elderly men and women: the Dubbo Epidemiology Study. *Am J Epidemiol.* 2001;153(6):587-595.
22. Kanis JA, Johnell O, De Laet C, et al. A meta-analysis of previous fracture and subsequent fracture risk. *Bone.* 2004;35(2):375-382.
23. Klotzbuecher CM, Ross PD, Landsman PB, Abbott TA III, Berger M. Patients with prior fractures have an increased risk of future fractures: a summary of the literature and statistical synthesis. *J Bone Miner Res.* 2000;15(4):721-739.
24. Haentjens P, Autier P, Collins J, Velkeniers B, Vanderschueren D, Boonen S. Colles fracture, spine fracture, and subsequent risk of fracture in men and women. *J Bone Joint Surg Am.* 2003;85(10):1936-1943.
25. Kanis JA, Johnell O, Oden A, et al. Long-term risk of osteoporotic fracture in Malmo. *Osteoporos Int.* 2000;11(8):669-674.
26. Abrahamsen B, Vestergaard P, Rud B, et al. Ten-year absolute risk of osteoporotic fractures according to BMD T-score at menopause: the Danish Osteoporosis Prevention Study. *J Bone Miner Res.* 2006;21(5):796-800.
27. Kung AWC, Lee K-K, Ho AYY, Tang G, Luk KDK. Ten-year risk of osteoporotic fractures in postmenopausal Chinese women according to clinical risk factors and BMD T-scores: a prospective study. *J Bone Miner Res.* 2007;22(7):1080-1087.
28. van Staa TP, Leufkens HG, Cooper C. Does a fracture at one site predict later fractures at other sites? a British cohort study. *Osteoporos Int.* 2002;13(8):624-629.
29. Kanis JA, Johnell O, Oden O, Dawson A, De Laet C, Jonsson B. Ten year probabilities of osteoporotic fractures according to BMD and diagnostic thresholds. *Osteoporos Int.* 2001;12(12):989-995.
30. Cranney A, Guyatt G, Griffith L, Wells G, Tugwell P, Rosen C. Meta-analysis of therapies for postmenopausal osteoporosis, IX: summary of meta-analyses of therapies for postmenopausal osteoporosis. *Endocr Rev.* 2002;23(4):517-523.