

# Risk of Subsequent Fracture After Low-Trauma Fracture in Men and Women

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**D**ESPITE SUBSTANTIAL EVIDENCE that a prior fracture results in an increased risk of subsequent fracture, less than 30% of postmenopausal women and less than 10% of men with prior fracture are treated.<sup>1-6</sup> Although some of this deficiency in clinical care is due to the overall lack of awareness of osteoporosis by the public and primary caregivers, the relative importance of prior fracture in relation to subsequent fracture risk does not appear to be fully appreciated, particularly in men.

Most of the studies to date on subsequent fracture (refracture) risk after an initial fracture have concentrated on women rather than men and examined a single fracture outcome type (mainly forearm, vertebral, or hip). Thus, although 2 recent meta-analyses<sup>7,8</sup> concluded that a previous fracture resulted in an approximately 2-fold increased relative risk (RR) for subsequent fracture and 4-fold for prior vertebral and subsequent vertebral fracture, these ratios are less clear for men.<sup>9-11</sup> The subsequent fracture risk appears to be greatest soon after a fracture, particularly in the first year, albeit in short-term studies.<sup>12-14</sup>

Relative risk, which is dependent on background risk, has limited meaning for an individual.<sup>15</sup> Absolute risk, such as is used for cardiovascular disease, is more relevant to an individual's understanding of his/her risk. However, its

**Context** There are few published long-term data on absolute risk of subsequent fracture (refracture) following initial low-trauma fracture in women and fewer in men.

**Objective** To examine long-term risk of subsequent fracture following initial osteoporotic fracture in men and women.

**Design, Setting, and Participants** Prospective cohort study (Dubbo Osteoporosis Epidemiology Study) in Australia of 2245 community-dwelling women and 1760 men aged 60 years or older followed up for 16 years from July 1989 through April 2005.

**Main Outcome Measure** Incidence of first (initial) fracture and incidence of subsequent fracture according to sex, age group, and time since first fracture. Relative risk was determined by comparing risk of subsequent fracture with risk of initial fracture.

**Results** There were 905 women and 337 men with an initial fracture, of whom 253 women and 71 men experienced a subsequent fracture. Relative risk (RR) of subsequent fracture in women was 1.95 (95% confidence interval [CI], 1.70-2.25) and in men was 3.47 (95% CI, 2.68-4.48). As a result, absolute risk of subsequent fracture was similar in women and men and at least as great as the initial fracture risk for a woman 10 years older. Thus, women and men aged 60 to 69 years had absolute refracture rates of 36/1000 person-years (95% CI, 26-48/1000) and 37/1000 person-years (95% CI, 23-59/1000), respectively. The increase in absolute fracture risk remained for up to 10 years, by which time 40% to 60% of surviving women and men experienced a subsequent fracture. All fracture locations apart from rib (men) and ankle (women) resulted in increased subsequent fracture risk, with highest RRs following hip (RR, 9.97; 95% CI, 1.38-71.98) and clinical vertebral (RR, 15.12; 95% CI, 6.06-37.69) fractures in younger men. In multivariate analyses, femoral neck bone mineral density, age, and smoking were predictors of subsequent fracture in women and femoral neck bone mineral density, physical activity, and calcium intake were predictors in men.

**Conclusion** After an initial low-trauma fracture, absolute risk of subsequent fracture was similar for men and women. This increased risk occurred for virtually all clinical fractures and persisted for up to 10 years.

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assessment requires larger sample sizes followed up over extended periods. In addition, to compare absolute risks between the sexes, concurrent data on women and men are required but are rarely available.

Therefore, the aim of this study was to examine absolute as well as relative refracture risks for a variety of fracture types in a concurrent cohort of community-dwelling men and women for more than 15 years.

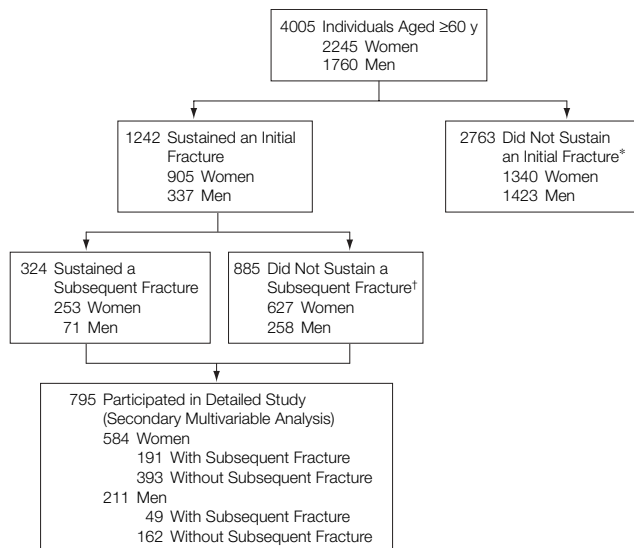
## METHODS

### Study Population

This study was carried out as part of the Dubbo Osteoporosis Epidemiology Study as previously described.<sup>16,17</sup> In

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**Figure 1.** Flowchart of Dubbo Fracture Population Aged at Least 60 Years in 1989 and Detailed Follow-up Study Group

\*Includes 18 individuals with possible pathologic fracture (9 women and 9 men).

†Includes those lost to follow-up (approximately 5.3% of those who sustained an initial fracture).

summary, it is a longitudinal study of community-dwelling men and women aged 60 years and older living in the city of Dubbo, Australia. The study started in April 1989 and is ongoing. The study was approved by the St Vincent's Hospital Ethics Committee. Dubbo is a semi-urban city, approximately 400 km northwest of Sydney with a population of 32 000 in 1989, of whom 98.6% were white. Race was determined by self-report. Dubbo was chosen as an ideal site because the population is relatively stable, its structure closely matches the general Australian population,<sup>18</sup> and health care is centralized with 1 hospital servicing the area. In 1989 there were 2245 women and 1760 men aged at least 60 years residing in the Dubbo area.

The major component and basis of this study involved assessment of all fractures occurring in the population aged at least 60 years (FIGURE 1). Study investigators had access to all radiological services, thus enabling virtually complete ascertainment of all clinical fractures. Given the stability of the population, loss to follow-up is minimal and only includes those who moved

and sustained an out-of-area fracture. Any out-of-area death would have most likely been reported or obtained locally and the data collected. It is estimated that 5.3% of the population were lost to follow-up. This analysis involves 905 women and 337 men, representing all individuals aged at least 60 years who sustained an initial low-trauma fracture over a median of 16 years from the beginning of 1989 through April 2005. The population initial fracture risk was calculated from those fractures that were recorded between April 1989 and December 2004, which was the period for which population census and mortality data for the Dubbo population were available from the Australian Bureau of Statistics.

Of the group that experienced a fracture, 65% of the women (n=584) and 63% of the men (n=211) participated in a detailed, ongoing assessment by responding to an invitation sent in 1989 to the Dubbo population aged at least 60 years and gave written consent. The assessment included smoking, alcohol and dietary calcium intake, number of falls in the last year, comorbid

conditions and medications, anthropometric measurements, bone mineral density (BMD) of the lumbar spine and femoral neck, quadriceps strength, and body sway. The interview and measurements were carried out every other year by a nurse coordinator at the study center.

### Assessment of Fractures

Fractures were recorded by review of all radiography reports from all radiological services within the Dubbo area. The circumstances surrounding each fracture event were determined by personal interview by a study coordinator following each fracture. Only low-trauma fractures caused by a fall from a standing height or less were included in this analysis. Individuals with skull fractures or with an underlying condition that could predispose to pathological fracture, such as cancer or Paget disease, were excluded.

Fractures were classified according to site such as upper and lower limb and also by type according to the following criteria: hip, major, and minor. These major and minor fracture groupings were specifically chosen because they had been previously shown to relate to mortality outcomes.<sup>19</sup> Major fractures included vertebra, pelvis, distal femur, proximal tibia, multiple rib, and proximal humerus. Minor fractures included all remaining osteoporotic fractures but excluded fingers and toes. Vertebral fractures were those coming to clinical attention without systematic screening for vertebral deformities. Clinical vertebral fractures were those for which radiography was performed consistent with a recent fracture such as for back pain and there had not been a radiograph demonstrating such a fracture in the past. Prevalent vertebral fractures were those for which radiography was performed for a different reason, such as a chest x-ray prior to surgery.

Mortality information on study participants was obtained by regular review of local death and funeral listings. Population and mortality data for the Dubbo community were obtained

for each year of the study from the Australian Bureau of Statistics.

### Statistical Analysis

Initial fracture rates for the whole Dubbo population aged 60 years or older were calculated as annual incidence based on the population data in 5-year age groups. Once a person had a fracture, he/she was excluded from the population at risk. Only initial fractures occurring at age 60 years or older were considered in this analysis and any high-trauma fractures were ignored.

For the refracture analyses, time to subsequent fracture was calculated as the time between the first and the next low-trauma fracture. For those who did not sustain a subsequent fracture, follow-up time was calculated as time to either death or the end of the study period (April 30, 2005). Subsequent fracture risk was analyzed according to sex and age at the time of initial fracture and differences between the groups were analyzed using the log-rank test. Risk of subsequent fracture was calculated in intervals of 0 to 2, 0 to 5, 5 to 10, and 10 or more years after the initial fracture. Relative risks and confidence intervals (CIs) were compared with the population rates of initial fracture based on Poisson assumption and were 2-sided. Rate changes over the speci-

fied time intervals were analyzed using PROC GENMOD in SAS.<sup>20</sup>  $P < .05$  was set a priori as the level of significance.

Risks of subsequent fracture were also calculated according to initial fracture site. Subsequent fractures were then classified according to the broader groups of hip, major, and minor fractures.

The survival distribution for initial and subsequent fracture in individuals was plotted using Kaplan-Meier methods with the Lifetest function in SAS. For the Dubbo population, the initial at-risk population figures were based on the 1989 census data from the Australian Bureau of Statistics. Actual deaths per year were obtained and death rates calculated for each year over the 15-year period and applied to the 1989 figures. The population was censored for fracture and death so the Australian Bureau of Statistics death rates were adjusted each year for the known post-fracture deaths to avoid double censoring.

The contribution of baseline characteristics to refracture risk in the detailed follow-up sample was analyzed using Cox proportional hazards models. Multivariate analyses of univariate contributors were performed as well as forward and backward stepwise models.

## RESULTS

### Population Incident Fracture Risk

There were 905 incident fractures in women (mean [SD] age, 78 [8] years) and 337 incident fractures in men (mean [SD] age, 77 [8] years) over 28 661 and 20 561 person-years for women and men, respectively. Fracture risk increased with age and, as expected, was higher in women than in men (TABLE 1).

### Subsequent Fracture Risk

The median follow-up was 16 years in women (interquartile range [IQR], 11-16 years) and 15 years in men (IQR, 9-16 years). Median follow-up from initial fracture to subsequent fracture, death, or end of study was 3.25 years in women (IQR, 1.14-6.97 years) and 2.13 years in men (IQR, 0.64-5.35 years). There were 253 subsequent osteoporotic fractures from 905 initial fractures in 4076 person-years of follow-up for women and 71 subsequent fractures from 337 initial fractures over 1248 person-years for men. There were similar absolute refracture risks for women and men (62/1000 person-years; 95% CI, 55-70/1000 and 57/1000 person-years; 95% CI, 45-72/1000, respectively). Given the lower initial population risk in men, this similar absolute refracture risk meant that the RR was significantly higher in men

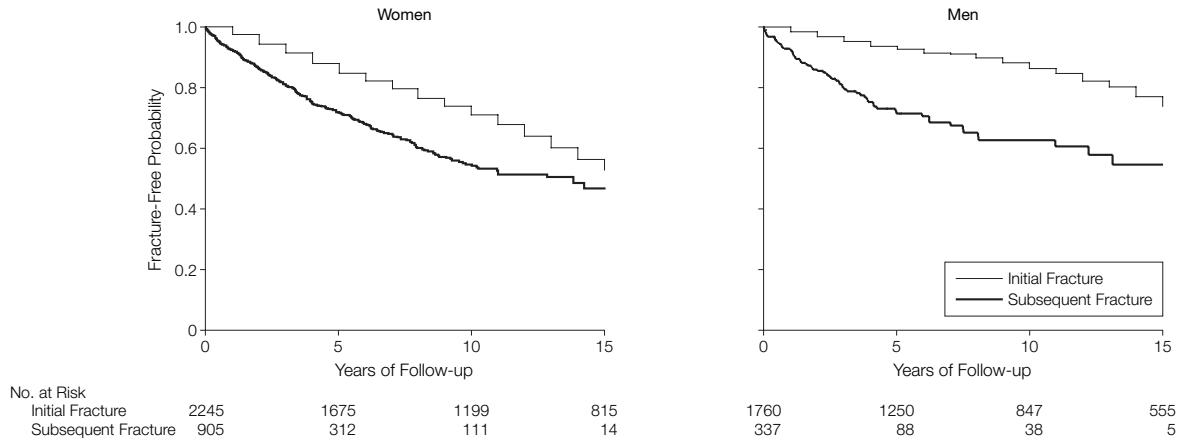
**Table 1.** First and Subsequent Fractures According to Age at First Fracture\*

	Absolute Risk						
	Initial Fracture			Subsequent Fracture			Relative Risk (95% CI) of Fracture (Subsequent/Initial)
	No. of Individuals	Person-Years	Risk per 1000 Person-Years (95% CI)	No. of Individuals	Person-Years	Risk per 1000 Person-Years (95% CI)	
<b>Women</b>							
All ages	905	28 661	32 (30-34)	253	4076	62 (55-70)	1.97 (1.71-2.26)
60-69 y	147	6833	22 (18-25)	43	1209	36 (26-48)	1.65 (1.18-2.32)
70-79 y	378	14 154	27 (24-30)	111	1758	63 (52-76)	2.36 (1.91-2.92)
≥80 y	380	7674	50 (45-55)	99	1109	89 (73-109)	1.80 (1.45-2.25)
<b>Men</b>							
All ages	337	20 561	16 (15-18)	71	1248	57 (45-72)	3.47 (2.69-4.48)
60-69 y	60	6124	10 (8-13)	17	462	37 (23-59)	3.75 (2.19-6.43)
70-79 y	150	10 526	14 (12-17)	36	585	62 (44-85)	4.32 (3.00-6.21)
≥80 y	127	3911	32 (27-39)	18	200	90 (57-143)	2.77 (1.69-4.54)

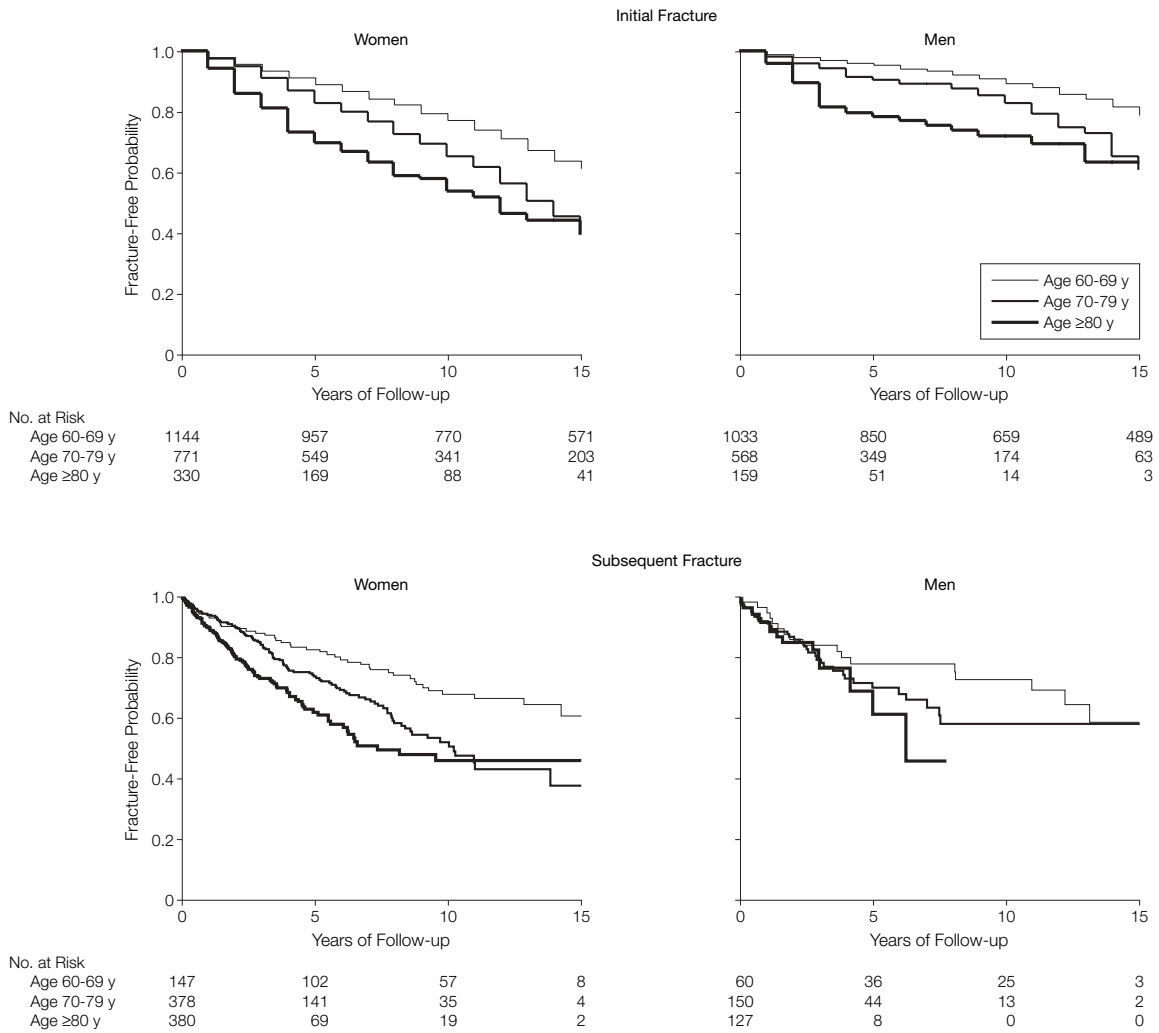
Abbreviation: CI, confidence interval.

\*Subsequent fractures were identified following 905 initial fractures in women and 337 initial fractures in men occurring between 1989 and 2005, whereas initial fracture risk was determined from 880 fractures in women and 329 in men from the second quarter of 1989 and end of 2004, over which time population census data were available.

**Figure 2.** Overall Initial and Subsequent Fracture Risk by Sex



**Figure 3.** Initial and Subsequent Fracture Risk by Sex and Age at Initial Fracture



(RR, 3.47; 95% CI, 2.68-4.48) than in women (RR, 1.95; 95% CI, 1.70-2.25). The similar absolute refracture risk between men and women persisted across age groups. This is in marked contrast with the risk of initial low-trauma fracture, which was consistently higher in women (Table 1).

For women, the absolute refracture risk was equivalent to or greater than the initial fracture risk of a woman 10 years older. For example a 60- to 69-year-old woman with an initial fracture had an absolute refracture risk comparable to or greater than an initial fracture risk of a 70- to 79-year-old woman. For men, the absolute risk of a subsequent fracture was similar to that of women and equivalent to or greater than an initial fracture risk of a woman 10 years older. For example, a 60- to 69-year-old man's absolute refracture risk was equivalent to or greater than a 70- to 79-year-old woman's initial fracture risk and similar to the initial risk of a man at least 20 years older.

### Change in Excess Fracture Risk Over Time

For both women and men, the absolute refracture risk remained elevated over follow-up. However, with the expected increase in initial fracture risk with age, the excess risk decreased over time from initial fracture ( $P=.003$  and  $P=.001$  for women and men, respectively). Thus, after 10 years of follow-up, the ongoing fracture rate was no longer significantly increased above that of individuals without fracture, with the refracture risk curves approaching the initial fracture curves with increasing time following fracture (FIGURE 2 and FIGURE 3). Notably, though, in the older age groups ( $\geq 80$  years) for women and particularly for men, the proportion of individuals alive beyond 10 years without another fracture was small (Figure 3).

Approximately 41% of refractures in women and 52% of refractures in men occurred in the first 2 years. However, this risk (in women: 74/1000 person-years; 95% CI, 61-90/1000 and in men: 79/1000 person-years; 95% CI, 57-109/1000) was not different from that 0 to

**Table 2.** Absolute and Relative Risks of Subsequent Fractures According to Initial Fracture Type

Initial Fracture Type, by Sex	No.	Person-Years	Absolute Risk per 1000 Person-Years (95% CI)	Relative Risk (95% CI)*
<b>Women</b>				
Hip	44	497	89 (66-119)	2.79 (2.06-3.77)
Vertebral	75	942	80 (64-100)	2.52 (1.99-3.19)
Upper limb	82	1537	53 (43-66)	1.69 (1.35-2.12)
Ribs	15	258	58 (35-96)	1.84 (1.10-3.06)
Lower limb†	37	842	44 (32-61)	1.39 (1.00-1.93)
Ankle	7	263	27 (13-56)	0.84 (0.40-1.78)
<b>Men</b>				
Hip	12	149	81 (46-142)	4.92 (2.77-8.75)
Vertebral	27	267	101 (69-148)	6.18 (4.17-9.14)
Upper limb	11	209	53 (29-95)	3.21 (1.76-5.84)
Ribs	7	327	21 (10-45)	1.31 (0.62-2.76)
Lower limb†	14	297	47 (28-80)	2.87 (1.68-4.90)
Ankle	10	133	75 (40-140)	4.59 (2.45-8.61)

Abbreviation: CI, confidence interval.

\*Relative risk is based on absolute risk (/1000 person-years) divided by initial fracture incidence (32/1000 person-years for women and 16/1000 person-years for men).

†Lower limb fractures include those of the ankle.

5 years after initial fracture for both women (69/1000 person-years; 95% CI, 60-79/1000) and men (71/1000 person-years; 95% CI, 55-92/1000) and 5 to 10 years after initial fracture in women (56/1000 person-years; 95% CI, 43-72/1000). In men, the risk of refracture 5 to 10 years after the initial fracture was lower (27/1000 person-years; 95% CI, 14-54/1000) than that for the 0 to 5 years after initial fracture, but it was still higher than the initial fracture risk of the population without fracture (RR, 2.40; 95% CI, 1.16-4.98).

The fracture-free probability by age and sex shows the marked increased refracture risk, particularly in younger individuals and close to the initial fracture event (Figures 2 and 3). For women, the absolute refracture risk was higher in the older than younger age groups, similar to initial fracture risk ( $P<.001$ ). However, in men absolute refracture risk was similar for the 3 age groups over the first 5 years ( $P=.38$ ), underscoring the greater RR in younger men. Based on life table analyses of those surviving after initial fracture, 39% of women aged 60 to 69 years, 62% aged 70 to 79 years, and 53% aged 80 years or older had experienced a subsequent fracture. These estimates were

similar for men (42%, 41%, and 54%, respectively).

### Influence of Initial Fracture Type on Subsequent Fracture Risk

Absolute risk of subsequent fracture was increased for both women and men across the different age groups for almost all fracture types, including hip, clinical vertebral, upper limb, and lower limb (TABLE 2). Ankle fractures were associated with increased risk in men (RR, 4.58; 95% CI, 2.44-8.60) but not in women (RR, 0.84; 95% CI, 0.40-1.76). Similarly, rib fractures were associated with an overall increase in subsequent fracture risk in women (RR, 1.83; 95% CI, 1.10-3.04) but not in men (RR, 1.30; 95% CI, 0.62-2.76). Notably, hip (RR, 9.97; 95% CI, 1.38-71.94) and clinical vertebral fractures (RR, 15.12; 95% CI, 6.06-37.65) in the younger men were associated with higher RRs.

### Influence of Initial Fracture Type on Subsequent Fracture Type

In women there were 169 hip, 406 major, and 330 minor initial fractures. In men there were 60 hip, 168 major, and 109 minor initial fractures. Subsequent fractures in women were 69 hip, 117 major, and 67 minor fractures and



in men were 15 hip, 28 major, and 28 minor fractures. There was no significant difference in the proportion of subsequent fracture types (hip, major, or minor) following any of these 3 different initial fracture groupings ( $P = .09$  for women and  $P = .27$  for men). Thus, even a minor initial fracture resulted in an increased risk of subsequent major or hip fracture.

### Detailed Study Group

Of the population who sustained a fracture, 65% of women and 63% of men participated in the detailed study (TABLE 3). There was no difference in age between women and men, but as expected men had a higher bone density and were stronger than women. More men were smokers and high alcohol intake was rare in both sexes. A

total of 42% of women and 57% of men had 1 or more comorbidities, the most common being cardiovascular, followed by neurological (stroke or dementia), chronic obstructive pulmonary disease, cancer, and diabetes. Antiresorptive therapy, despite fracture, was uniformly low (14% in women and 4% in men;  $P < .001$ ) as was calcium and/or vitamin D supplementation (23% in women and 3% in men;  $P < .001$ ).

Several baseline factors were associated with subsequent fracture risk in univariate analysis (TABLE 4). The hazard ratios (HRs) for women ranged from 1.5 to 1.2 for femoral neck BMD, age, ever smoking, sway, quadriceps strength, and weight or body mass index. In men, hazard ratios ranged from 2.3 to 1.5 for ever smoking, calcium intake, femoral neck BMD, physical activity, quadriceps strength, sway, and weight (but not body mass index). Age was not associated with refracture risk in men. A multivariate model including all variables is presented alongside the univariate results (Table 4). Collinearity between sway and femoral neck BMD in men largely accounts for the nonsignificance of the latter when both are in the model. However, in simple backward or forward multivariate analyses, the significant independent predictors of refracture risk were femoral neck BMD (HR, 1.31; 95% CI, 1.11-1.55), age (HR, 1.31; 95% CI, 1.10-1.55), and ever smoking (HR, 1.59; 95% CI, 1.02-1.90) in women and femoral neck BMD (HR, 1.60; 95% CI, 1.17-2.19), physical activity (HR, 2.00; 95% CI, 1.36-2.94), and calcium intake (HR, 2.04; 95% CI, 1.31-3.18) in men.

**Table 3.** Characteristics of Individuals With Fracture in the Detailed Study Group

	Women (n = 584)	Men (n = 211)	P Value
Age, mean (SD), y	73 (7)	73 (7)	.20
BMI, mean (SD)	25 (5)	26 (4)	.06
Lumbar spine BMD, mean (SD), g/cm <sup>2</sup>	0.96 (0.18)	1.18 (0.21)	<.001
Femoral neck BMD, mean (SD), g/cm <sup>2</sup>	0.73 (0.13)	0.85 (0.16)	<.001
Quad strength, mean (SD), kg	18 (8)	30 (13)	<.001
Sway, median (quartile 1-3), cm <sup>2</sup>	14 (8-41)	16 (8-44)	.005
Calcium intake, mean (SD), mg/d	660 (392)	615 (376)	.17
Activity, mean (SD), MET/wk	115 (52)	12 (57)	.03
Fall in the last year, No. (%)	252 (43.2)	76 (36.0)	.04
Alcohol intake, No. (%)*	16 (2.7)	9 (4.3)	.27
Smoker, No. (%)	169 (28.9)	130 (61.6)	<.001

Abbreviations: BMD, bone mineral density; BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); MET, metabolic equivalents.

\*Alcohol intake (high vs moderate/none).

**Table 4.** Univariate and Multivariate Analyses of Risk Factors for Subsequent Fracture

Variable	SD Change	Hazard Ratio (95% CI)	
		Univariate	Multivariate
<b>Women</b>			
Age	7.7 y	1.40 (1.21-1.61)	1.33 (1.10-1.61)
Femoral neck BMD	-0.13 g/cm <sup>2</sup>	1.48 (1.26-1.73)	1.31 (1.07-1.60)
Quad strength	-8.2 kg	1.23 (1.06-1.43)	1.02 (0.86-1.22)
Sway	3.82 cm <sup>2</sup>	1.25 (1.08-1.44)	1.00 (0.83-1.21)
BMI	-4.5	1.19 (1.02-1.40)	1.02 (0.84-1.23)
Calcium intake	-392 mg/d	1.09 (0.95-1.24)	1.09 (0.95-1.25)
Physical activity	-52 MET/wk	1.11 (0.96-1.29)	1.01 (0.85-1.19)
Smoking		1.38 (1.03-1.86)	1.43 (1.03-2.00)
Fall in last year		1.00 (0.75-1.32)	0.84 (0.61-1.16)
<b>Men</b>			
Age	7.6 y	1.25 (0.91-1.71)	1.06 (0.65-1.73)
Femoral neck BMD	-0.16 g/cm <sup>2</sup>	1.90 (1.44-2.52)	1.30 (0.90-1.87)
Quad strength	-13.2 kg	1.59 (1.20-2.11)	1.25 (0.82-1.90)
Sway	3.74 cm <sup>2</sup>	1.53 (1.16-2.01)	1.56 (1.01-2.41)
BMI	-3.9	1.35 (0.99-1.84)	1.29 (0.86-1.94)
Calcium intake	-376 mg/d	2.10 (1.34-3.29)	2.22 (1.37-3.58)
Physical activity	-56.7 MET/wk	1.91 (1.44-2.53)	1.81 (1.17-2.82)
Smoking		2.31 (1.20-4.46)	2.43 (0.99-5.94)
Fall in last year		1.00 (0.56-4.46)	0.75 (0.37-1.54)

Abbreviations: BMD, bone mineral density; BMI, body mass index; CI, confidence interval; MET, metabolic equivalents.

### COMMENT

This is the first study, to our knowledge, to comprehensively examine all low-trauma fractures in a concurrent group of men and women aged 60 years and older over a 16-year period. Our findings show a similar absolute risk for sustaining a subsequent fracture in men and women. This similar absolute risk reflected a 2-fold greater increase in refracture risk for men than for women.

Importantly, this was across all age groups and for virtually all fractures, with the increased absolute risk persisting for up to 10 years after the initial fracture event.

For women, the 1.6- to 2.4-fold RR of a subsequent fracture across all ages yielded an absolute refracture risk as high or greater than the initial fracture risk for women in the next 10-year higher age group. For men, an initial fracture conferred a higher relative refracture risk (2.8- to 4.3-fold) that yielded a similar absolute refracture risk to that of women of the same age with an initial fracture. Thus, the reduced risk of initial fracture associated with male sex was lost once a single low-trauma fracture occurred.

The higher RR of subsequent fractures, especially in the first few years,<sup>12,13</sup> observed in men compared with women is consistent with some,<sup>10-12,21</sup> but not all,<sup>22</sup> studies. However, participants in these earlier studies were generally followed up for shorter time intervals and even 5-year risk could therefore only be estimated from life tables.<sup>10,22</sup>

In our study, for both sexes there was a gradual return of the initial high excess fracture rate toward the baseline population rate, which was increasing over time (as expected with the increasing population age). The majority of the fractures occurred in the first 5 years after the initial fracture and by about 10 years, if individuals were still alive and had not experienced a subsequent fracture, their fracture rate was not different from the population's initial fracture rate, possibly reflecting a healthier subset. By the end of 10 years about half of both women and men had experienced a subsequent fracture.

Importantly, the increased subsequent fracture risk was observed for virtually all types of low-trauma fractures, with the exception of rib fractures in men and ankle fractures in women. The discrepancy between the sexes of rib fracture on subsequent fracture risk is consistent with a recent European study of recalled rib fractures.<sup>23</sup> Ankle fractures, not generally thought to be osteoporotic fractures,<sup>24,25</sup> were previously shown

in the Dubbo Osteoporosis Epidemiology Study to be associated with increased refracture risk in men but not in women.<sup>26</sup> Of major clinical importance, even if the initial fracture was a minor one, the subsequent fracture was not limited to other minor ones but could be a hip or other major fracture.

In the subset in whom detailed follow-up was available, factors that have been reported as risk factors for initial fracture<sup>27-30</sup> were also risk factors for refracture.

This study has a number of major advantages. It is a large population-based prospective study of a concurrent group of men and women followed up for more than 15 years. Thus, it is possible to make valid comparisons between the sexes. The stable population base and access to all radiological services allowed virtually 100% ascertainment of fractures. In addition, the circumstances surrounding the fracture were obtained by personal interview, allowing the nature and type of fracture to be verified accurately. The large sample size and length of the study yielded enough fractures to be classified by site and analyzed by major groupings with respect to subsequent risk. The long follow-up also enabled direct examination of fractures over time within specific age groups, which, to our knowledge, has not been previously reported.

There are, however, also some limitations. The population is almost 99% white and the findings may not be the same in other racial/ethnic groups. Vertebral fractures were those coming to clinical attention, arguably the more serious vertebral fractures, and the results may not be the same for morphometric vertebral fractures. It was not possible to examine all the individual fracture types for each age group, and peripheral fractures were analyzed together in upper limb or lower limb or major and minor groupings. Thus, individual fracture types may signal greater or lesser refracture risk. There were few individuals alive without refracture available for follow-up of more than 10 years after the initial fracture.

Thus, the extent of the decline in subsequent fracture rate would require larger, longer-term studies. Although the percentage of individuals receiving antiresorptive treatment after fracture was small, there were more women treated than men. However, if all those treated (including with hormone therapy) were adherent with medication for 5 years and the clinical fracture reduction was 30%, fractures prevented would not have substantially changed the 5-year refracture risk.

In conclusion, we have demonstrated a similar increased absolute risk of subsequent fracture in both women and men following virtually all low-trauma fractures except ankle fractures in women and rib fractures in men. For both sexes, absolute subsequent fracture risk was equal to or greater than the risk of an initial fracture for a woman in a 10-year-older age bracket or for a man 20 years older. The increased risk persisted for up to 10 years depending on age and sex, with about 50% of surviving men and women having another fracture. The critical clinical relevance of these findings is that incident low-trauma fracture is a signal for increased risk of all types of subsequent osteoporotic fracture, particularly in the next 5 to 10 years. Thus, virtually all low-trauma fractures indicate the clinical need for fracture preventive therapy, and given the early peak of refracture, such preventive treatment should not be delayed. The lack of consideration of osteoporosis and treatment initiatives by the medical profession and the public, particularly in relation to men, should be the focus of education initiatives.

**Author Contributions:** Drs Center and Bliuc had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

**Study concept and design:** Center, Bliuc, Nguyen, Eisman.

**Acquisition of data:** Center, Eisman.

**Analysis and interpretation of data:** Center, Bliuc.

**Drafting of the manuscript:** Center, Eisman.

**Critical revision of the manuscript for important intellectual content:** Center, Bliuc, Nguyen, Eisman.

**Statistical analysis:** Center, Bliuc.

**Obtained funding:** Center, Nguyen, Eisman.

**Administrative, technical, or material support:** Eisman.

**Study supervision:** Center, Eisman.

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