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# Timing of Repeat BMD Measurements: Development of an Absolute Risk-Based Prognostic Model

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**ABSTRACT:** This study attempted to address the following questions: for an individual who is at present nonosteoporotic, given their current age and BMD level, what is the individual's risk of fracture and when is the ideal time to repeat a BMD measurement? Nonosteoporotic women ($n = 1008$) and men ($n = 750$) over the age of 60 in 1989 from the Dubbo Osteoporosis Epidemiology Study were monitored until one of the following outcomes occurred: (1) BMD reached ''osteoporosis'' level (i.e., T-scores $\leq -2.5$) or (2) an incident fragility fracture. During the follow-up period (average, 7 yr), 346 women (34%) and 160 men (21%) developed osteoporosis or sustained a low-trauma fracture. The risk of osteoporosis or fracture increased with advancing age (women: RR/10 yr, 1.3; 95% CI, 1.1–1.6; men: RR/10 yr, 2.3; 95% CI, 1.7–2.9) and lower BMD levels (women: RR per $-0.12$ g/cm$^2$, 3.2; 95% CI, 2.6–4.1; RR per $-0.12$ g/cm$^2$, 2.6; 95% CI, 2.0–3.3). Using the predicted risk (of osteoporosis or fracture) of 10% as a cut-off level for repeating BMD measurement, the estimated time to reach the cut-off level varied from 1.5 (for an 80-yr-old woman with a T-score of $-2.2$) to 10.6 yr (for a 60-yr-old man with a T-score of 0). These results suggest that, based on an individual's current age and BMD T-score, it is possible to estimate the optimal time to repeat BMD testing for the individual. The prognostic model and approach presented in this study may help improve the individualization and management of osteoporosis.
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**Key words: BMD, repeat measurements, T-score**

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## INTRODUCTION

BMD is the most robust and consistent predictor of osteoporotic fracture.[1–3] The magnitude of association between BMD and fracture risk is equivalent to, or stronger than, the relationship between blood pressure and stroke or cholesterol and cardiovascular disease.[4] Currently, measurement of BMD is used to make a diagnosis of osteoporosis (i.e., a woman with a BMD measurement 2.5 SD or lower than the peak BMD level [taken as the average among women between 20 and 30 yr of age]).[5] A similar system of classification for men has been proposed.[6] Individuals with osteoporosis and/or with a low-trauma fracture are currently considered appropriate individuals for pharmacologic intervention.

BMD is a dynamic measurement, in the sense that it changes with time. In the elderly, BMD declines with advancing age, and the rate of decline varies significantly among individuals.[7–9] Therefore, in the absence of intervention, bone loss contributes to the ''natural'' development of osteoporosis in an individual as well as in a population. Indeed, several recent studies have shown that the rate of BMD loss is a risk factor for fracture in elderly men and women.[10,11] Although there was an association between bone loss per se and fracture risk, the benefit of repeated BMD measurement has been questioned.[11] However, given that some individuals in the general population experience excessive bone loss, repeating BMD measurement in these individuals could provide additional preventive information.

Recently, the American College of Physicians have published a guideline for osteoporosis screening in men, in which it recommends individualized assessment of osteoporosis by BMD measurement.[12] The assessment of osteoporosis, at present, does not take into account the rate of bone loss. Importantly, there is no guide to the optimal timing of repeat BMD measurements, except that repeat measurements under 12 mo are unlikely to be informative, and longer intervals are suggested in some jurisdictions.[13]

Therefore, the question of interest is as follows: for an individual (man or woman) without osteoporosis, given their present BMD level, what is the risk of developing osteoporosis and/or fracture, and when is the optimal time to repeat their BMD measurement? This study was designed to address that specific question by developing a prognostic model for

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estimating the short-term and long-term risk of developing osteoporosis or sustaining a fracture in an individual.

## MATERIALS AND METHODS

### *Subjects and setting*

This study is part of the ongoing longitudinal Dubbo Osteoporosis Epidemiology study, whose design and protocol have been described previously.[3] Briefly, in 1989, all men and women ≥60 yr of age living in Dubbo, a city of ~32,000 people, 400 km northwest of Sydney, Australia, were invited to participate in the study. The target population compromised 1581 men and 2095 women ≥60 yr of age; 98.6% were white and 1.4% were indigenous Aboriginal. Dubbo was selected for the study site because the age and sex distribution of the population resembles that of the Australian population, increasing the external validity of the study. This study was approved by the St. Vincent's Campus Research Ethics committee, and informed written consent was obtained from each participant.

Ultimately, the study has recruited 1358 women and 850 men since 1989, all of whom agreed to undergo a BMD assessment and interview. The individuals visit the study coordinating center every 2 yr to have BMD remeasured and other clinical assessments performed.

### *BMD measurement*

Lumbar spine and femoral neck BMD was measured at baseline and follow-up (average interval, 2.2 yr) by DXA using a LUNAR DPX densitometer (GE-LUNAR, Madison, WI, USA). All BMD measurements were performed by a qualified technologist using a standard protocol. The coefficient of reliability at our institution in normal subjects at the femoral neck is 0.98.[14] This study focused on femoral neck BMD, because it is minimally affected by degenerative change that may artificially elevate lumbar spine BMD. The femoral neck was also chosen as the site for observing bone loss because of its strong relationship to fracture risk.[2] During the study period, the densitometer underwent daily quality control, which included phantom scans and monitoring of changes in precision over time (using a running scattergram). Whenever significant drift was observed, the machine would receive servicing by the manufacturer. The metal spinal scanning phantom (submerged in water) supplied by the manufacturer was used during quality control of the LUNAR DPX.

Classification of osteopenia and osteoporosis was based on T-scores derived from the sex-specific Australian Reference Database.[15] To assess the longitudinal change in BMD, this study was restricted to participants with at least one follow-up visit after baseline measurement of BMD. Because osteoporosis at the femoral neck is one of the outcomes, this study was limited to women and men with osteopenia or normal BMD (T-score > −2.5). The ultimate sample size for analysis was 1008 women and 750 men ≥60 yr of age in 1989.

### *Fracture ascertainment*

One of the primary outcomes of the study was the incidence of low-trauma fractures: low-trauma fractures occurring during the study period were identified for residents of the Dubbo local government area through radiologist's reports from the only two, at times three, centers providing X-ray services as previously described.[16,17] Fractures were only included if the report of fracture was definite and, on interview, had occurred with minimal or no trauma, including a fall from standing height or less. Fractures clearly caused by major trauma, such as motor vehicle accident, or associated with malignancy were excluded from the analysis. Morphometric vertebral fractures were not considered in this study.

### *Development of prognostic model*

The primary endpoint of this study was the time to reach osteoporosis or fracture in the presence of the competing risk of death. Because an individual could have experienced multiple events (e.g., osteoporosis and then fracture), we considered three scenarios of interest: osteoporosis, fracture, and osteoporosis and fracture. The basic statistical model was the modified Cox's proportional hazards regression,[18] which included a stratifying factor (e.g., osteoporosis, fracture, or death) to take into account the competing risk of death. For each individual, we estimated the absolute risk of developing osteoporosis or sustaining a fracture for a given time $T$. Let the mean predicted risk for an individual be $m$, and the lower 90% CI of the individual's predicted risk be $L$. We set the value of $L$ at 10% and 20% as the cut-off values for working backward to estimate the time $T$ to reach $L > 10\%$ or $L > 20\%$. We used the bootstrap method to estimate the 90% CI of time to reach the risk of osteoporosis or fracture.[19]

The prognostic performance of the model was assessed by the area under the receiver operator characteristics curve (AUC).[19] Internal validation was undertaken with the bootstrap method.[20] Verification of the proportional hazards assumption of Cox models was based on a visual inspection of smoothed Schoenfeld residual plots.[21] The analysis was performed with a competing risk R package developed by Fine and Gray.[22]

## RESULTS

At baseline, 1008 women and 750 men had femoral neck BMD T-scores greater than −2.5 (nonosteoporosis). During the follow-up period (median, 7.1 yr), in women, 13.8% ($n$ = 139) had sustained a fracture without developing osteoporosis, 11.9% ($n$ = 120) had developed osteoporosis without a fracture, and 8.6% ($n$ = 87) had a fracture and developed osteoporosis (Fig. 1). The corresponding proportions for men were 12.0% ($n$ = 90), 7.2% ($n$ = 54), and 2.1% ($n$ = 16). Overall, 34% of women and 21% of men experienced at least one event. Women and men with at least one event were, as a group, older, lighter in weight, and had lower BMD compared with those without any event (Table 1).

In women, the risk of fracture and/or osteoporosis was increased by 3.2-fold (95% CI: 2.6–4.1) for each SD lower BMD and 1.3-fold (95% CI: 1.1–1.6) for each 10-yr increase in age. In men, advancing age (RR, 2.3; 95% CI: 1.7–2.9) and lower BMD (RR, 2.6; 95% CI: 2.0–3.3) were

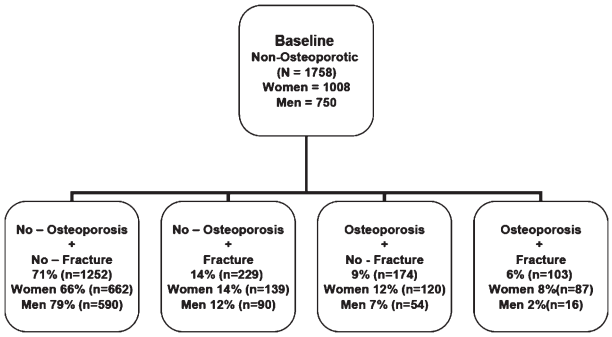


**FIG. 1.** Schematic summary of study outcomes.

also independent predictors of the risk of fracture and/or osteoporosis. The AUC was 0.74 for men and 0.76 for women (Table 2). Based on the estimated parameters, we developed a model (Appendix 1) for estimating 5- and 10-yr probabilities of developing osteoporosis, sustaining a fracture, and the composite event (e.g., osteoporosis or fracture), and typical estimates from this model are shown in Table 3. For example, a 70-yr-old woman with a BMD T-score of −2.0 was predicted to have a 27% probability of developing osteoporosis or sustaining a fracture within the next 5 yr, whereas for a man of the same age and the same BMD T-score, the 5-yr risk was 13%.

To address the study's primary question (e.g., when to repeat the BMD measurement), we used the risk of developing or sustaining a fracture as a metric of outcome. However, an estimate of risk of developing or sustaining a fracture is subject to sampling variation; therefore, to ensure a high sensitivity of optimal time estimates to repeat BMD, we chose the lower 90% CI as the benchmark values. Estimates of the mean time (yr) to reach the benchmarks and 90% CIs for men and women are presented in Table 4.

### *Clinical application of the model*

Figures 2 and 3 present estimates in time (yr) to reach 10% or 20% risk of osteoporosis or fracture based on age and femoral neck BMD T-score. We present the following hypothetical, but typical, examples to illustrate the clinical application of the model to nonosteoporotic women or men to obtain an optimal time to repeat BMD measurement.

### *Clinical case 1*

A 75-yr-old man had a BMD T-score of −1.5. Using Table 3 (or method shown in the Appendix), the 5-yr risk of osteoporosis or fracture is ~0.18. Table 4 suggests that the time to reach 10% risk of osteoporosis or fracture is 2.7 yr (90% CI: 2.4–3.1 yr). Therefore, the suggested time for repeating BMD measurement is ~2.5 yr (Fig. 2A).

### *Clinical case 2*

An 80-yr-old women had a BMD T-score of −2. Table 3 suggests that the 5-yr risk of fracture or osteoporosis of the woman is 0.45. Moreover, Table 4 suggests that the time to reach 10% risk of fracture or osteoporosis for the woman is 2 yr (90% CI: 1.5–2.1 yr). Thus, the woman would be advised to return for bone densitometry in 1.5 yr (Fig. 3A).

## DISCUSSION

One of the current problems in osteoporosis management is that ~75% of men and 55% of women ≥60 yr of age with fracture do not have osteoporosis,[23] and yet most current guidelines recommend to treat those with osteoporosis. As a result, a large number of nonosteoporotic individuals with a significant risk of fracture are not treated. In this study, we developed models for estimating 5- and 10-yr risk of fracture and/or osteoporosis for men and women. As the field of osteoporosis is moving toward an absolute risk assessment,[12] the prognostic model can help select appropriate individuals for intervention.

Furthermore, in nonosteoporotic men and women, there is no explicit guideline to repeat BMD measurement for an individual where the risk of osteoporosis or fracture is marginal. This study, to our knowledge, is the first to address this issue by using the risk of osteoporosis or fracture as the benchmark for the decision. We developed a simple model to estimate the risk of osteoporosis and/or fracture, and from which the time to repeat BMD measurement can be derived.

A BMD T-score of −2.5 or low-trauma fracture has been considered a treatment threshold in many instances. Age and BMD are considered among the most robust predictors of future osteoporotic fracture. We estimated the average time to reach an absolute 10% and 20% risk of osteoporotic BMD or fracture for an individual based on their current age and femoral neck BMD T-score. Using these results, clinicians will be able to decide the future optimal timing of bone densitometry and/or treatment based on an individual's future risk.

Importantly, this study has quantified the future risk of fracture and/or osteoporosis for a nonosteoporosis and nonfracture individual. Using the model developed here, clinicians and patients could make decisions on the immediate need for treatment, or the timing of the next DXA measurement to assess progression of bone loss, simply based on the individual's age, sex, and BMD, could be made. Also, these results enable the estimate of future risk of reaching osteoporosis or fracture, thus allowing informed decisions related to immediate treatment or a ''watch and wait'' approach to bone health.

Given the fact that longitudinal change in BMD is a risk factor for fracture[10] and mortality,[24,25] it seems logical that repeating BMD measurements can provide additional risk information over and above that of an initial BMD measurement. However, a recent study has questioned the utility of repeated BMD measurement.[11] In the presence of divergent views and data, our prognostic model offers a solution. Indeed, it is clear that repeating BMD measurement, and for that matter, the timing of repeated BMD, can not be recommended for all individuals without some selected criteria. For example, using the lower CI cut-off of 10% as a benchmark, a 60-yr-old woman with a T-score of −1.0 does not need to have BMD repeated for 4.5 yr; however, it would be justifiable for an 80-yr-old woman with the same T-score to have a second BMD measurement in 2 yr.

**TABLE 1.** Characteristics of Participants at Baseline Classified by Subsequent Event

| | *No osteoporosis + no fracture* | *No osteoporosis + fracture* | *Osteoporosis + no fracture* | *Osteoporosis + fracture* |
|---|---|---|---|---|
| Women | *n* = 662 | *n* = 139 | *n* = 120 | *n* = 87 |
| Age (yr) | 68 (6) | 69 (6) | 69 (6) | 70 (6) |
| Baseline femoral neck BMD (g/cm$^2$) | 0.88 (0.10) | 0.85 (0.09) | 0.76 (0.05) | 0.76 (0.06) |
| Weight (kg) | 70 (13) | 71 (12) | 63 (10) | 65 (10) |
| Height (cm) | 161 (6) | 162 (6) | 160 (6) | 161 (6) |
| BMI (kg/m$^2$) | 27 (5) | 27 (5) | 25 (4) | 25 (4) |
| BMI category [*N* (%)]* | | | | |
| Underweight | 24 (4%) | 3 (2%) | 15 (12%) | 8 (9%) |
| Normal | 234 (35%) | 50 (36%) | 47 (39%) | 40 (46%) |
| Overweight | 254 (38%) | 51 (37%) | 52 (43%) | 29 (33%) |
| Obese | 150 (23%) | 34 (25%) | 6 (5%) | 10 (11%) |
| No. of BMD measurements | 4 (2) | 4 (2) | 5 (2) | 5 (2) |
| Duration of follow-up (yr) | 8 (5) | 7 (5) | 6 (4) | 5 (3) |
| Men | *n* = 590 | *n* = 90 | *n* = 54 | *n* = 16 |
| Age (yr) | 69 (6) | 71 (6) | 71 (6) | 71 (6) |
| Baseline femoral neck BMD (g/cm$^2$) | 0.97 (0.13) | 0.91 (0.11) | 0.80 (0.05) | 0.84 (0.08) |
| Weight (kg) | 82 (13) | 78 (11) | 75 (10) | 72 (9) |
| Height (cm) | 175 (23) | 174 (6) | 174 (7) | 173 (6) |
| BMI (kg/m$^2$) | 27 (4) | 26 (3) | 25 (3) | 24 (2) |
| BMI category [*N* (%)]* | | | | |
| Underweight | 9 (2%) | 1 (1%) | 2 (4%) | 0 |
| Normal | 170 (29%) | 40 (45%) | 30 (56%) | 12 (75%) |
| Overweight | 299 (51%) | 42 (37%) | 18 (33%) | 4 (25%) |
| Obese | 111 (19%) | 11 (12%) | 4 (7%) | 0 |
| No. of BMD measurements | 4 (2) | 4 (2) | 5 (2) | 5 (1) |
| Duration of follow-up (yr) | 8 (5) | 7 (5) | 6 (4) | 6 (3) |

All participants did not have osteoporosis at baseline (T score > −2.5). Data are mean (SD), unless otherwise indicated.
* BMI category: obese, ≥30 kg/m$^2$; overweight, 25–30 kg/m$^2$; normal, ≤25 and ≥20 kg/m$^2$; underweight, <20 kg/m$^2$.

**TABLE 2.** Final Model Risk Factors of Osteoporosis or a Low-Trauma Fracture

| | *Hazard ratio (95% CI) of* | | |
|---|---|---|---|
| | *Osteoporosis only* | *Fracture only* | *Osteoporosis and/or fracture* |
| Women | | | |
| Age (+10 yr) | 1.5 (1.1–1.9) | 2.0 (1.6–2.5) | 1.3 (1.1–1.6) |
| Initial FNBMD (−0.12 g/cm$^2$) | 10.9 (6.8–17.4) | 1.5 (1.2–1.9) | 3.2 (2.6–4.1) |
| Men | | | |
| Age (+10 yr) | 2.0 (1.3–3.0) | 3.5 (2.5–4.8) | 2.3 (1.7–2.9) |
| Initial FNBMD (−0.12 g/cm$^2$) | 9.4 (5.2–17.2) | 1.4 (1.1–1.7) | 2.6 (2.0–3.3) |

This is because the latter woman is expected to lose BMD faster and have a higher risk of fracture than the former.

Because the outcome of osteoporosis is fracture, we considered that fracture should be taken into account in the development of any prognostic model for repeating BMD measurement. Ultimately, the timing of repeated BMD measurement is dependent on the absolute risk of fracture or osteoporosis that is considered high enough to justify intervention. Therefore, the time to reach the risk of 20% is longer than the time to reach 10% risk. At present, there is no consensus on the absolute risk level that can be considered ''high.'' However, it is reasonable to regard a 5-yr fracture risk of 10% as a starting point for consideration; we decided to choose the lower 90% CI risk of 10% and 20% as the cut-off values for estimating the time to repeat BMD measurement.

A strength of this study is that it is based on a long-term population-based osteoporosis epidemiology study, with a significant number of follow-up BMD measurements. Because of Dubbo's relative isolated geographical location, it was possible to completely ascertain all types of fracture. Therefore, the incidence of fractures reported in this paper represents a real-world setting. However, the applicability of a predictive model is based on a number of predefined conditions, namely (1) the characteristics of individuals the model was based on, (2) the reliability of both the outcome predictors included in the model, (3) accuracy of the predictive model, and (4) validation of the model. Concerning the first condition, the model was developed using a well-defined population of women and men ≥60 yr of age at baseline (1989), who have been followed for up to 15 yr, thus enabling identification of the time course of the

**TABLE 3.** Predicted 5- and 10-yr Risks of Sustaining a Fracture and/or Developing Osteoporosis for a Given Age and T-Score

| | | *5-yr risk* | | | | | | *10-yr risk* | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | *Women* | | | *Men* | | | *Women* | | | *Men* | | |
| *Age* | *T-score* | *Ost* | *Fx* | *Ost/Fx* | *Ost* | *Fx* | *Ost/Fx* | *Ost* | *Fx* | *Ost/Fx* | *Ost* | *Fx* | *Ost/Fx* |
| 60 | 0 | 0.025 | 0.035 | 0.058 | 0.018 | 0.016 | 0.031 | 0.046 | 0.077 | 0.108 | 0.038 | 0.046 | 0.074 |
| | −1.0 | 0.048 | 0.041 | 0.093 | 0.022 | 0.017 | 0.039 | 0.088 | 0.090 | 0.170 | 0.047 | 0.050 | 0.093 |
| | −1.5 | 0.066 | 0.044 | 0.117 | 0.025 | 0.018 | 0.044 | 0.120 | 0.096 | 0.212 | 0.052 | 0.052 | 0.104 |
| | −2.0 | 0.091 | 0.047 | 0.147 | 0.027 | 0.019 | 0.049 | 0.164 | 0.104 | 0.262 | 0.058 | 0.054 | 0.116 |
| | −2.2 | 0.103 | 0.049 | 0.161 | 0.029 | 0.019 | 0.052 | 0.186 | 0.107 | 0.285 | 0.060 | 0.055 | 0.121 |
| 65 | 0 | 0.036 | 0.053 | 0.080 | 0.029 | 0.027 | 0.051 | 0.067 | 0.116 | 0.147 | 0.061 | 0.077 | 0.119 |
| | −1.0 | 0.069 | 0.062 | 0.127 | 0.036 | 0.029 | 0.063 | 0.127 | 0.134 | 0.229 | 0.075 | 0.083 | 0.147 |
| | −1.5 | 0.096 | 0.066 | 0.160 | 0.040 | 0.030 | 0.071 | 0.172 | 0.143 | 0.282 | 0.083 | 0.086 | 0.164 |
| | −2.0 | 0.131 | 0.072 | 0.199 | 0.044 | 0.031 | 0.079 | 0.233 | 0.154 | 0.345 | 0.092 | 0.089 | 0.182 |
| | −2.2 | 0.149 | 0.074 | 0.217 | 0.046 | 0.032 | 0.083 | 0.261 | 0.158 | 0.373 | 0.095 | 0.090 | 0.190 |
| 70 | 0 | 0.053 | 0.080 | 0.110 | 0.047 | 0.044 | 0.081 | 0.097 | 0.171 | 0.199 | 0.096 | 0.126 | 0.186 |
| | −1.0 | 0.101 | 0.093 | 0.173 | 0.057 | 0.048 | 0.102 | 0.181 | 0.197 | 0.304 | 0.118 | 0.135 | 0.229 |
| | −1.5 | 0.138 | 0.100 | 0.215 | 0.064 | 0.050 | 0.113 | 0.244 | 0.211 | 0.370 | 0.131 | 0.140 | 0.253 |
| | −2.0 | 0.187 | 0.107 | 0.266 | 0.071 | 0.052 | 0.126 | 0.323 | 0.225 | 0.445 | 0.144 | 0.145 | 0.280 |
| | −2.2 | 0.211 | 0.110 | 0.289 | 0.074 | 0.052 | 0.132 | 0.360 | 0.232 | 0.478 | 0.150 | 0.147 | 0.291 |
| 75 | 0 | 0.077 | 0.120 | 0.150 | 0.074 | 0.073 | 0.130 | 0.140 | 0.249 | 0.266 | 0.151 | 0.202 | 0.286 |
| | −1.0 | 0.145 | 0.138 | 0.232 | 0.091 | 0.079 | 0.161 | 0.255 | 0.284 | 0.396 | 0.184 | 0.216 | 0.346 |
| | −1.5 | 0.197 | 0.148 | 0.286 | 0.101 | 0.082 | 0.179 | 0.337 | 0.303 | 0.474 | 0.203 | 0.224 | 0.380 |
| | −2.0 | 0.264 | 0.159 | 0.350 | 0.112 | 0.085 | 0.198 | 0.438 | 0.323 | 0.560 | 0.223 | 0.231 | 0.415 |
| | −2.2 | 0.295 | 0.164 | 0.378 | 0.116 | 0.086 | 0.207 | 0.482 | 0.331 | 0.595 | 0.232 | 0.234 | 0.430 |
| 80 | 0 | 0.111 | 0.177 | 0.202 | 0.118 | 0.120 | 0.203 | 0.199 | 0.355 | 0.350 | 0.234 | 0.315 | 0.424 |
| | −1.0 | 0.206 | 0.203 | 0.308 | 0.144 | 0.129 | 0.249 | 0.352 | 0.400 | 0.504 | 0.281 | 0.336 | 0.501 |
| | −1.5 | 0.276 | 0.217 | 0.375 | 0.159 | 0.134 | 0.275 | 0.455 | 0.424 | 0.592 | 0.307 | 0.346 | 0.542 |
| | −2.0 | 0.363 | 0.233 | 0.451 | 0.175 | 0.139 | 0.303 | 0.572 | 0.449 | 0.681 | 0.336 | 0.357 | 0.584 |
| | −2.2 | 0.403 | 0.239 | 0.484 | 0.182 | 0.141 | 0.315 | 0.621 | 0.459 | 0.716 | 0.347 | 0.362 | 0.601 |

**TABLE 4.** Estimated Time (yr) to Reach 10% and 20% Risk of Osteoporosis or Fracture Based on Age and Femoral Neck BMD T-score

| | | *Time to reach 10% risk of sustaining a fracture or developing osteoporosis [mean (90% CI)]* | | *Time to reach 20% risk of sustaining a fracture or developing osteoporosis [mean (90% CI)]* | |
|---|---|---|---|---|---|
| *Age* | *T-score* | *Women* | *Men* | *Women* | *Men* |
| 60 | 0 | 8.9 (6.7–10.6) | 12.3 (10.6–13.4) | 14.1 (12.7–15.0+) | 15.0$^{+}$ (14.3–15.0+) |
| | −1.0 | 5.1 (4.5–6.1) | 10.6 (8.7–12.2) | 11.3 (10.0–12.3) | 14.8 (13.8–15.0+) |
| | −1.5 | 4.3 (3.4–4.8) | 9.3 (7.9–11.5) | 9.5 (7.5–10.6) | 14.0 (13.4–15.0+) |
| | −2.0 | 3.3 (2.8–4.1) | 8.9 (7.2–10.7) | 7.1 (5.6–8.8) | 13.8 (12.6–14.6) |
| | −2.2 | 3.0 (2.8–3.8) | 8.4 (6.9–10.5) | 6.2 (5.0–7.9) | 13.5 (12.3–14.3) |
| 65 | 0 | 6.0 (4.8–7.7) | 8.6 (7.4–9.8) | 12.3 (10.6–13.4) | 13.6 (12.7–14.2) |
| | −1.0 | 3.8 (3.3–4.6) | 7.4 (6.1–8.1) | 8.3 (7.2–9.8) | 12.6 (11.2–13.4) |
| | −1.5 | 3.0 (2.8–3.5) | 6.8 (5.5–7.6) | 6.5 (5.5–7.3) | 11.7 (9.9–13.1) |
| | −2.0 | 2.7 (2.5–2.9) | 6.1 (4.7–7.2) | 4.9 (4.4–5.9) | 10.8 (9.0–12.7) |
| | −2.2 | 2.6 (2.4–2.6) | 5.7 (4.6–7.0) | 4.6 (3.8–5.4) | 10.6 (8.8–12.3) |
| 70 | 0 | 4.6 (3.5–4.5) | 6.0 (4.7–6.9) | 10.0 (7.7–11.5) | 10.7 (9.0–12.2) |
| | −1.0 | 2.9 (2.7–3.3) | 4.7 (3.8–5.6) | 5.9 (5.0–6.7) | 8.9 (7.8–9.8) |
| | −1.5 | 2.6 (2.4–2.8) | 4.4 (3.1–5.3) | 4.6 (4.2–5.1) | 8.1 (7.2–9.0) |
| | −2.0 | 2.4 (2.2–2.6) | 3.8 (2.9–4.7) | 3.7 (3.1–4.4) | 7.4 (6.5–8.7) |
| | −2.2 | 2.3 (2.1–2.3) | 3.5 (2.8–4.6) | 3.3 (2.9–4.1) | 7.3 (6.1–8.4) |
| 75 | 0 | 3.3 (2.7–4.3) | 3.7 (2.9–4.6) | 7.0 (5.3–9.2) | 7.4 (6.4–8.5) |
| | −1.0 | 2.5 (2.3–2.7) | 2.9 (2.6–3.7) | 4.4 (3.6–4.9) | 6.1 (5.2–7.0) |
| | −1.5 | 2.3 (2.1–2.5) | 2.7 (2.4–3.1) | 3.4 (3.0–4.1) | 5.6 (4.6–6.6) |
| | −2.0 | 2.1 (2.0–2.3) | 2.6 (2.3–3.0) | 2.9 (2.7–3.1) | 5.0 (3.9–6.1) |
| | −2.2 | 2.0 (1.9–2.3) | 2.5 (2.2–2.9) | 2.7 (2.5–3.0) | 4.7 (3.8–6.0) |
| 80 | 0 | 2.7 (2.3–3.1) | 2.6 (2.2–3.0) | 4.8 (3.8–6.5) | 4.7 (3.8–6.1) |
| | −1.0 | 2.3 (2.0–2.4) | 2.4 (2.0–2.6) | 3.1 (2.8–2.8) | 3.8 (3.0–4.7) |
| | −1.5 | 2.1 (1.9–2.3) | 2.2 (1.9–2.6) | 2.7 (2.5–3.0) | 3.2 (2.7–4.5) |
| | −2.0 | 2.0 (1.5–2.1) | 2.1 (1.7–2.4) | 2.5 (2.3–2.7) | 3.0 (2.6–3.9) |
| | −2.2 | 1.9 (1.5–2.0) | 2.0 (1.6–2.4) | 2.4 (2.2–2.6) | 2.9 (2.6–3.8) |

Because the maximum duration of follow-up was 15 yr, the maximum time to reach 10% of 20% risk of osteoporosis or fracture was 15+ yr.

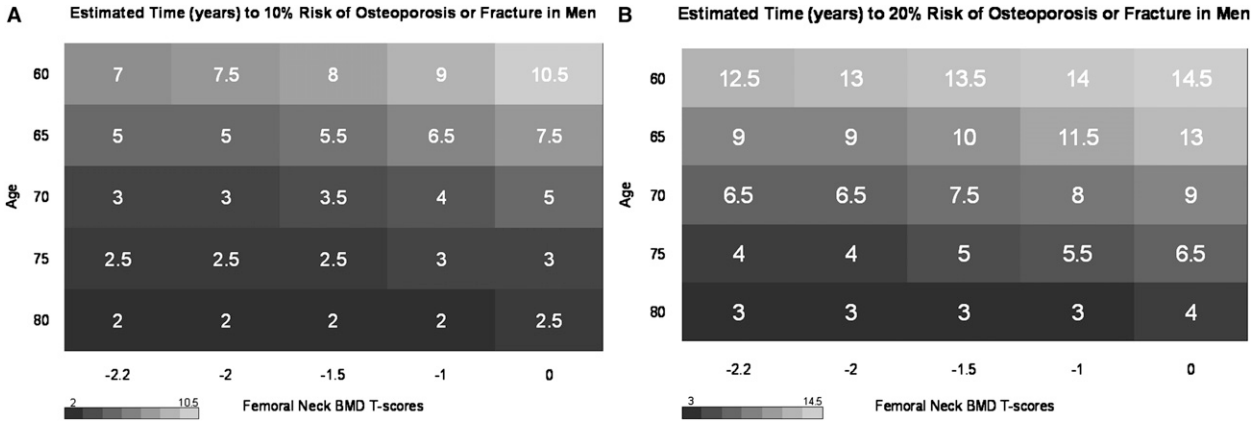


**FIG. 2.** Estimates for determining the optimal time (in 0.5-yr increments) to reach the lower limit of the 90% CI of (A) 10% and (B) 20% risk of osteoporosis or fracture in men.

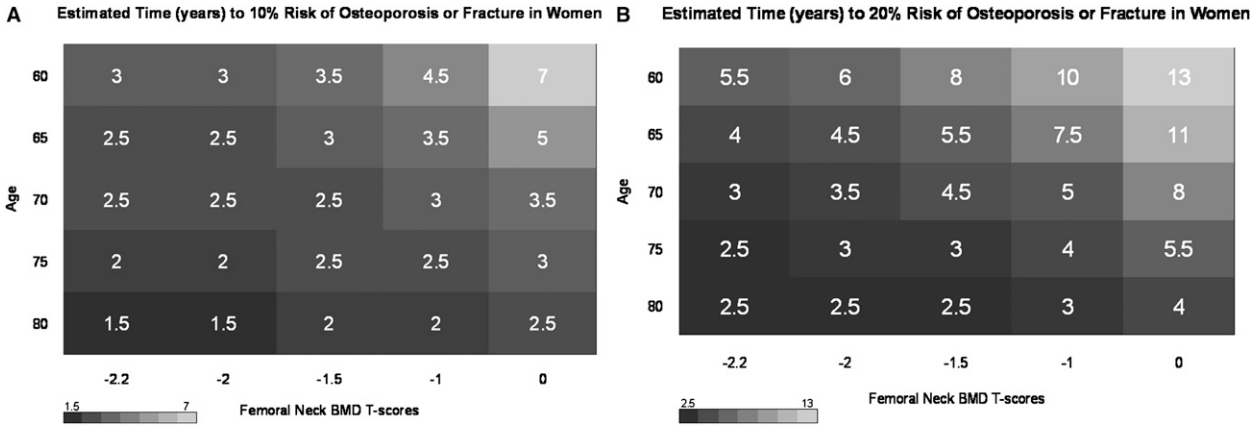


**FIG. 3.** Estimates for determining the optimal time (in 0.5-yr increments) to reach the lower limit of the 90% CI of (A) 10% and (B) 20% risk of osteoporosis or fracture in women.

natural progression to osteoporosis in this age group. The measurement of BMD is considered to be highly reliable; therefore, the second condition was also met. We tested the accuracy and internally validated the prognostic model and found that its performance was good, such that it can be used in clinical practice.

However, the study's results should also be interpreted within the context of some potential limitations. Women and men who participated in this study were essentially volunteers and were generally healthier than those who did not participate. Therefore, the rate of bone loss and risk of fracture could have been underestimated. Our models did not include comorbidities such as chronic obstructive pulmonary disease, rheumatoid arthritis, asthma, renal diseases, and high doses of corticosteroids, which have been suggested to be associated with increased bone loss, because they did not increase the discriminatory ability of our models to predict fracture or osteoporosis. However, in practice, the presence of these comorbidities may be an additional indication to shorten the time for repeating BMD measurement.

There is a large variation in background risk of fracture among populations,[26] and this could have an effect on the estimate of time to repeat BMD. A simple comparison of 10-yr probability of fracture estimated by FRAX-UK, FRAX-US (white),[26] and this model shows that among individuals <70 yr of age, risk estimates from our model are either comparable to or slightly higher than estimates from the FRAX-US model. However, the difference is more pronounced in older individuals (e.g., >80 yr old). If the 10-yr risk that is worthwhile to repeat BMD measurement is 20%, an 80-yr-old woman (of average weight and height) with a T-score of −2.2 would not have a repeated BMD measurement in the next 10 yr by the FRAX-UK model. However, this model suggests that the woman should have a repeat BMD measurement in ~2.5 yr, which seems to be consistent with clinical reality.

The accuracy of a predictive model is usually quantified by its discriminatory ability to separate individuals who will from those who will not experience the outcome of interest (e.g., reaching osteoporosis at the femoral neck or fracture). The AUC value for our model was 0.74–0.76, which

indicates a reasonable discrimination and can therefore be used for estimating the optimal time to repeat BMD measurement. The ultimate test of the usefulness of a predictive model is the external validation of the model using an independent population; this is yet to be performed for this model. However, internal validation of the model was undertaken using bootstrap methods, resulting in a high concordance between the cumulative incidence from a competing risk model and that predicted by the modified Cox model including age and BMD T-score at the femoral neck.[20,27] The estimated bias of the model when applied to an external similar population was estimated by bootstrap methods to be <1%, which indicated good discrimination.

In summary, the timing of repeated BMD measurements can not be recommended without some selected criteria. We showed that, based on an individual's current age and BMD T-score at the femoral neck, it is possible to estimate the optimal time to repeat BMD testing for the individual and developed an absolute-risk prognostic model for the estimation. Identification of high-risk individuals for repeating BMD testing is an important issue in osteoporosis management, and it is hoped that the model and approach presented in this study contribute toward the improvement of patient management.

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## APPENDIX: METHOD FOR ESTIMATING THE RISK OF OSTEOPOROSIS AND/OR FRACTURE

The risk of developing osteoporosis and/or sustaining a fracture for any give year $t$ can be estimated by using the parameters from the Cox's proportional hazards model according to the following formula:

$$\text{for women}: risk(women) = 1 - S_0(t)^{\exp(0.0662 \times age - 0.4877 \times Tscore)}$$

$$\text{and for men}: risk(men) = 1 - S_0(t)^{\exp(0.0983 \times age - 0.2318 \times Tscore)}$$

where $S_0$ $(t)$ is the cumulative event-free at year $t$ in the entire population. The values of $S_0$ $(t)$ are dependent on the time $t$, and are tabulated in the following table:

For example, a 70-yr-old woman with a femoral neck BMD T-score of −2.0 is predicted to have a 27% probability of sustaining a fracture or developing osteoporosis in the next 5 yr: $risk = 1 - 0.99887^{\exp(0.0662 \times 70 - 0.4877 \times (-2))} = 0.27$.

| *Time (yr)* | *Women* | *Men* |
|---|---|---|
| 1 | 0.99993 | 0.99999 |
| 2 | 0.99977 | 0.99998 |
| 3 | 0.99935 | 0.99995 |
| 4 | 0.99916 | 0.99993 |
| 5 | 0.99887 | 0.99991 |
| 6 | 0.99864 | 0.99989 |
| 7 | 0.99847 | 0.99987 |
| 8 | 0.99823 | 0.99984 |
| 9 | 0.99812 | 0.99981 |
| 10 | 0.99785 | 0.99979 |
| 11 | 0.99757 | 0.99976 |
| 12 | 0.99711 | 0.99974 |
| 13 | 0.99661 | 0.99969 |
| 14 | 0.99605 | 0.99957 |
| 15 | 0.99531 | 0.99947 |