

Fig. 2 a Nomogram for predicting the 5-year and 10-year probability of any fracture for a woman, based on Model I. Instruction for usage: Mark the age of an individual on the “Age” axis and draw a vertical line to the “Point” axis to determine how many points toward the probability of fracture the individual receives for his/her age value. Repeat the process for each additional risk factor. Sum the points of the risk factors. Locate the final sum on the “Total points” axis. Draw a vertical line down to the 5-year or 10-year risk line to find the individual’s probability of sustaining a fracture within next 5 or 10 years. Example: Mrs. A, 70 years old, has a BMD T-score of -2.5, had a prior fracture and a fall

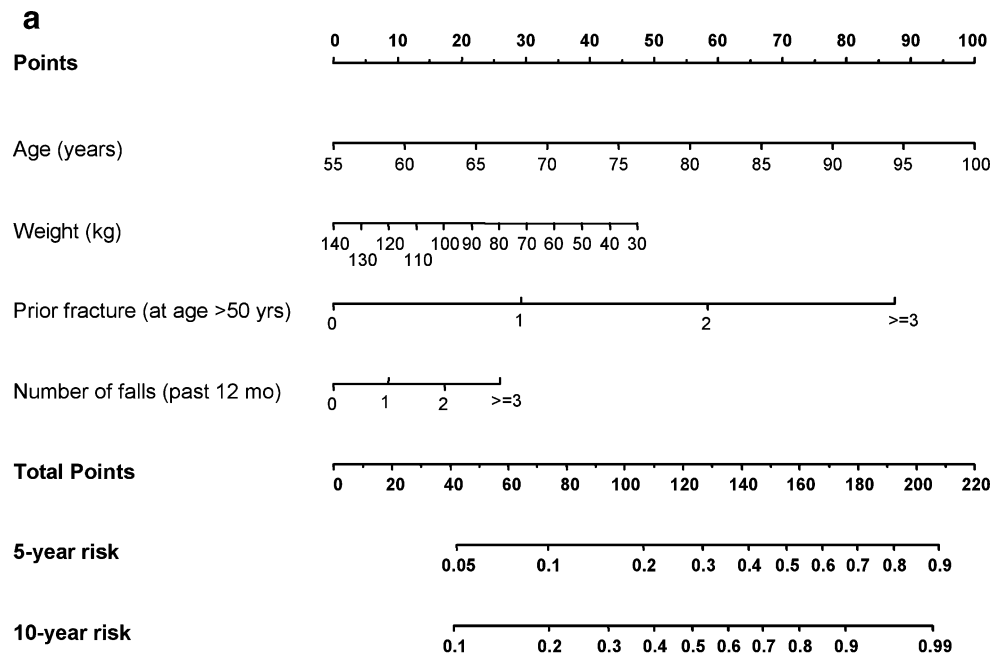
in the past 12 months; her points for age is approximately 12, her BMD points is 65; prior fracture point is 13 and fall point is 4. Her total points are, therefore, 12+65+13+4=94, and her probability of having a hip fracture is around 0.21 in the next 5 years and 0.40 in the next 10 years. In other words, in 100 women like her, one would expect 21 and 40 of them will have a fracture in the next 5 years and next 10 years, respectively. **b:** Calibration of nomogram for any fracture for women (Model I). The diagonal dotted line indicates reference line on which ideal nomogram would lie (perfect prediction). Solid line indicates current nomogram performance

all men aged 70 years and with a prior fracture can also be considered high risk, regardless of their BMD measurement. Among women aged 60 years, their 5-year risk of fracture is greater than 10% only when their T-scores are ≤ -3.0 . None of 60-year-old men have 5-year risk of fracture greater than 10%.

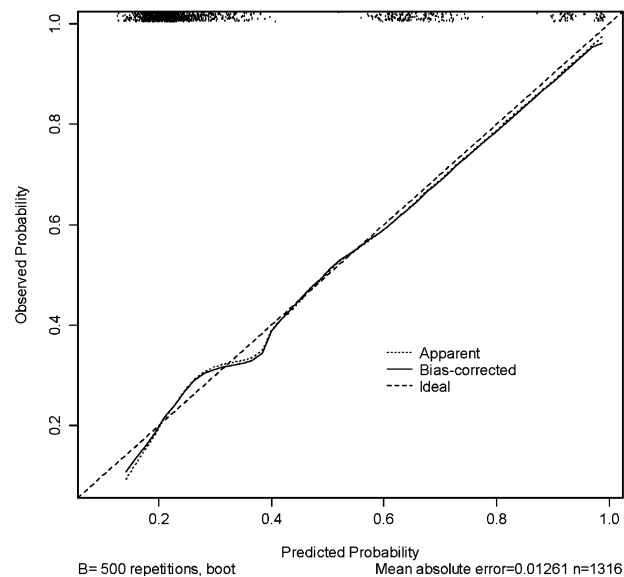
Discussion

Despite the fact that several fracture risk factors have been identified by epidemiologic research, the synthesis of these risk factors into a prognostic model for clinical use has not been realized. Part of the problems is that many risk factors

Fig. 3 a Nomogram for predicting the 5-year and 10-year probability of any fracture for a woman, based on Model II. Instruction for usage is similar to Fig. 2a. **b**: Calibration of nomogram for any fracture for women, model II. The diagonal dotted line indicates reference line on which ideal nomogram would lie (perfect prediction). Solid line indicates current nomogram performance



b

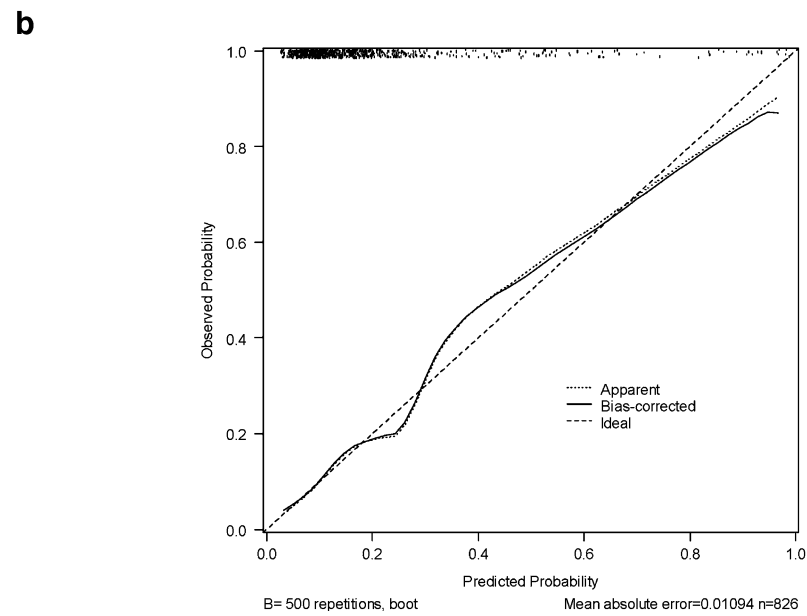
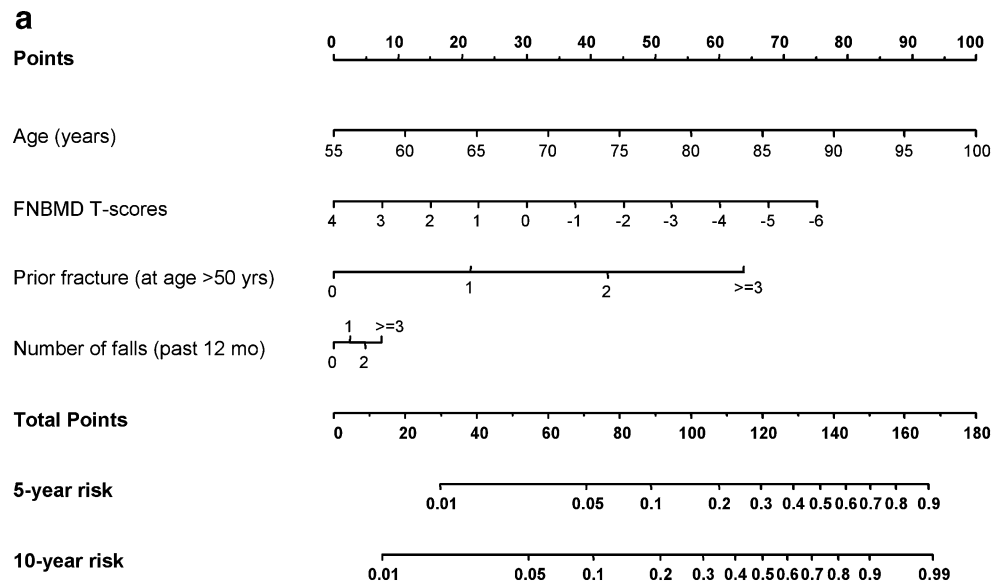


require sophisticated measurements that are beyond resources of a typical primary care setting. Thus, a practically useful prognostic model should make use of relevant clinical data that are easily obtained from an individual. The present study, built on previous research of risk factors, analyzed two models of prognosis, which incorporate the established risk factors of age, prior fracture, history of falls, and BMD or body weight. While weight is highly correlated with BMD, it is not surprising to observe that the model with the clinical risk factors and BMD performed better than the model with the clinical risk factors and body weight, because BMD has been shown to be more sensitive and specific in terms of fracture prediction [34, 35].

However, the difference in predictive accuracy between the two models is modest, and given the relatively low incidence of fracture, the difference is of limited practical importance.

The ultimate aim of developing a prognostic model is to provide clinicians and each individual with their risk estimate to guide clinical decisions. At present, individuals with low bone mineral density (i.e., T-scores being less than -2.5) or with a history of prior low trauma fracture are recommended for therapeutic intervention [36, 37]. This recommendation is logical and appropriate, since these individuals—as shown in this study and previous studies [12, 38]—have higher risk of fracture, and treatment can

Fig. 4 a Nomogram for predicting the 5-year and 10-year probability of any fracture for an elderly man, based on Model I. Instruction for usage is similar to Fig. 2a. **b**: Calibration of nomogram for any fracture for men (Model I). The diagonal dotted line indicates reference line on which ideal nomogram would lie (perfect prediction). Solid line indicates current nomogram performance

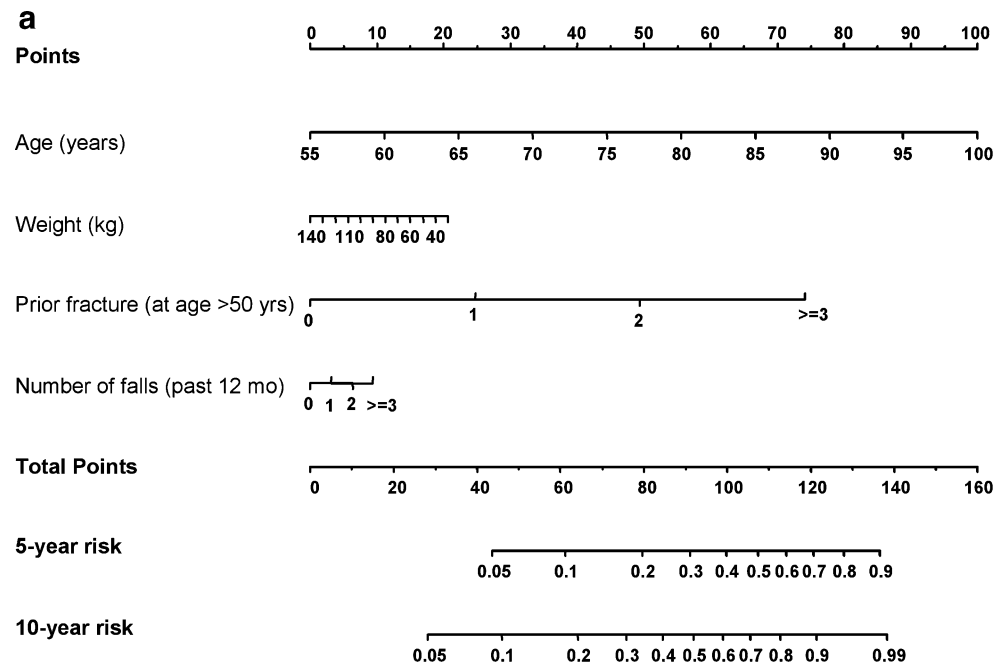


reduce their risk of fracture [39–41]. However, because fracture is a multifactorial event, there is more than one way that an individual can attain the risk conferred by either low BMD or a prior fracture. Indeed, virtually all women aged 70 years with BMD T-scores less than -1.5 and all 80-year-old men with BMD T-scores less than -1.0 can be considered “high risk”. On the other hand, no 60-year-old men or women without a prior fracture and a fall are considered high risk, even when their BMD T-scores were below -2.5. This demonstrates the informativeness of a multivariable prognostic model, and the limitation of a risk stratification-based approach for risk assessment for an individual.

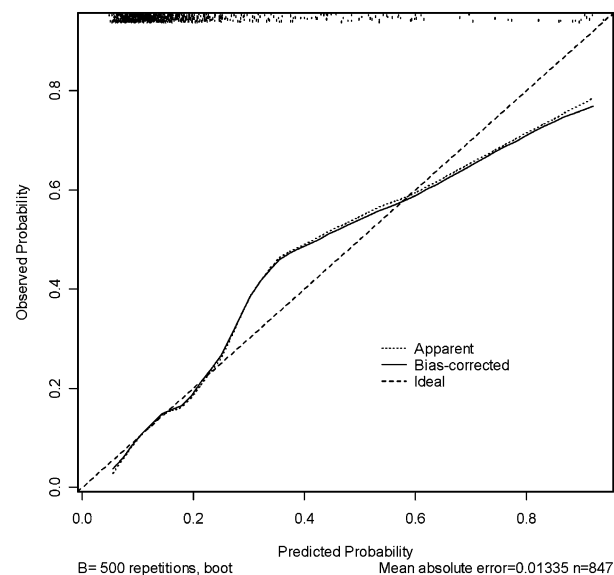
Other clinical factors, such as corticosteroid use, family history of fracture and a condition of underlying rheuma-

toid arthritis, have been shown to be predictors for fracture risk [42–44]. However, in the present study, there were no significant associations between those risk factors and fracture risk in both women and men. Therefore, these factors were not included in the prognostic model, as they did not significantly contribute to the predictiveness of fracture risk. It is likely, nevertheless, that a family history of fracture may in general improve the risk prediction. Vertebral deformity (morphometric fracture) has been shown to be a risk factor for fracture [45]. In the present study, vertebral deformity was not assessed at baseline for all participants; therefore, it was not included in the prognostic models. Nevertheless, there is room for further improvement in the prognosis of fracture by incorporating these clinical risk factors into the prognostic model.

Fig. 5 a Nomogram for predicting the 5-year and 10-year probability of any fracture for a man, based on Model II. Instruction for usage is similar to Fig. 2a. **b**: Calibration of nomogram for any fracture for men, model II. The diagonal dotted line indicates reference line on which ideal nomogram would lie (perfect prediction). Solid line indicates current nomogram performance



b



Each individual is important and unique. Individualization of risk—or the prediction of risk for an individual given a risk profile—is a fundamental aspect of the present models. The present models considered all continuous risk factors (e.g., BMD, body weight and age) in their original units of measurement. This consideration is different from previous models [3, 4], which categorized continuous risk factors into distinct groups based on some thresholds. While the categorization is appealing for its simplicity, it implicitly assumes a discontinuous relationship, which is unlikely to be true for well-known risk factors, such as BMD and body weight. Such a categorization is also known to reduce statistical power [46, 47]. Furthermore, the

risk estimates based on categorization of continuous risk factors can only be applied to a group of individuals, not to an individual. Prognosis is about imparting information of fracture risk to an individual and each individual is a unique case, because there exists no “average individual” in the population. The more risk factors are considered, the greater likelihood of uniqueness of an individual’s profile being defined. Therefore, by modeling risk factors in their continuous scale the present models can be uniquely tailored to an individual.

The idea of using a nomogram to develop a prognosis model for an individual is not new with more than 1,700 nomograms being advocated [48]. Several nomograms