

Validated Prediction of Imminent Risk of Fracture for Older Adults

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Up to 25% of men and 50% of women will experience a fracture in their remaining lifetime after age 50 years.¹ Osteoporosis-related fractures confer significant direct medical costs, quality-of-life decrements and functional disability, and indirect costs (lost productivity and caregiver burden).²⁻⁷ By 2025, fracture-related direct treatment costs are expected to reach \$25.3 billion in the United States.^{2,6} The impact of fractures to individuals may be long-lasting and result in increased use of healthcare services, a greater likelihood of hospitalization and skilled nursing care, reduced economic circumstances, and increased mortality risk for up to 10 years post fracture.^{3,4,7,8}

Various antiresorptive and bone-forming therapies have received FDA approval based on their ability to reduce the risk of fracture in men and women with osteoporosis.⁹ Fracture risk-assessment tools help clinicians estimate the risk of osteoporosis-related fracture in their patients, and these estimates inform treatment recommendations. The most commonly used tools, such as FRAX,¹⁰ focus exclusively on long-term fracture risk (ie, 10-year time horizon). The literature suggests that the imminent risk (ie, in next 1-2 years) of fracture also has important implications for treatment decisions.¹⁰⁻¹⁵ Imminent risk is responsive to changes in bone mineral density (BMD), fracture, and fall history, as well as factors that influence physical or cognitive functioning in ways that are not captured in existing tools.^{10,13-17} Furthermore, patients with osteoporosis may not perceive fracture risk accurately, and long-term risk assessments, in conjunction with patients' potentially incomplete understanding of the relationship between osteoporosis and fracture risk, may not provide sufficient motivation for treatment initiation.¹⁸⁻²⁰

Elevated imminent risk may require a different treatment approach from fracture risk that accumulates or extends over a longer time frame.^{10,14} The objective of this study was to develop and validate predictive models for imminent risk of fracture in a population of older adults enrolled in Humana's Medicare Advantage and Prescription Drug (MAPD) plans. This paper describes the primary full model, which includes an extensive set of predictors for the outcome of any fracture within a 12-month follow-up, and

ABSTRACT

OBJECTIVES: To develop and validate predictive models for imminent fracture risk in a Medicare population.

STUDY DESIGN: This retrospective administrative claims (Humana Research Database) study assessed imminent risk in Humana's Medicare Advantage and Prescription Drug plan members.

METHODS: Individuals (aged 67-87 years on January 1, 2015 [index]) with 1 year or more of history were followed for 3 months to up to 2 years, with censoring at death/disenrollment. The cohort was split into training and validation samples (1:1). Cox regression models assessed demographics, fracture history, medically significant falls, osteoporosis-related factors, frailty markers, and selected medications and comorbidities for independent predictors ($P < .001$) of incident nontraumatic clinical fractures in 12 and 24 months. A 6-variable model of 12-month risk used a published method for the risk-scoring point system.

RESULTS: Of 1,287,354 individuals (mean age, 74.3 years; 56% female; 84% white), 3.8% had at least 1 fragility fracture at 12-month follow-up; 6.6% experienced fracture at 24 months (women vs men: 12 months, 4.8% vs 2.5%; 24 months, 8.3% vs 4.4%; both $P < .01$). At 12 months, recent fracture conferred approximately 3-fold-higher fracture risk (vs no recent fracture). Older age, white race, female sex, osteoporosis-related screening/diagnosis/medication, antidepressant/antipsychotic/sedative hypnotic/muscle relaxant medications, history of falls, fracture history, and respiratory conditions also increased risk (all $P < .0001$). The simplified model (recent fracture, age, sex, race, falls, antidepressant/antipsychotic/sedative hypnotic/muscle relaxant medications) performed well (C statistic = 0.71).

CONCLUSIONS: Recent fracture, older age, female sex, white race, falls, and antidepressant/antipsychotic/sedative hypnotic/muscle relaxant medications predict imminent fracture risk in an older-adult Medicare Advantage population. Imminent fracture risk can be assessed using 6 easily quantified factors.

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TAKEAWAY POINTS

- ▶ Guideline-recommended tools that estimate long-term (10-year) fracture risk are used for osteoporosis treatment decisions, but these tools do not quantify imminent (in the next 1-2 years) risk.
- ▶ In our validated predictive models for imminent (1-year) fracture risk in the elderly population, age, race, sex, osteoporosis-related screening/diagnosis, medically significant falls, antidepressant/antipsychotic/sedative hypnotic/muscle relaxant medications, history of fracture, respiratory disorders, nervous system disorders, physical factors, and additional comorbidities/medications were significantly associated with greater imminent fracture risk.
- ▶ A simplified model (recent fracture, age, sex, race, falls, and antidepressant/antipsychotic/sedative hypnotic/muscle relaxant medications) supports feasibility for hand-calculating imminent risk during routine visits.

a parsimonious model, which was developed to provide proof of concept for a risk-assessment tool that could easily be used for hand-calculating risk during a routine physician office visit.

METHODS

Data Source and Population

This retrospective database study used a cohort design and multivariate analysis to identify predictors of imminent fracture risk in older adults enrolled in Humana MAPD plans. The Humana Research Database (Humana; Louisville, Kentucky), which contains administrative data for Humana's fully insured commercial and Medicare individuals, was used. Data on MAPD enrollment, medical claims, and outpatient pharmacy claims were linked for each individual. The study period—January 1, 2014, through December 31, 2016—was split into a 1-year baseline period (January 1, 2014, through December 31, 2014) and a 2-year follow-up period (January 1, 2015, through December 31, 2016).

All study individuals were aged 67 to 87 years on the index date (January 1, 2015) and had continuous enrollment in an MAPD plan throughout the baseline period and for at least the first 3 months of the follow-up period. Follow-up was censored at the date of death or plan disenrollment for individuals lost to follow-up before the end of study. Individuals with an *International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM)* or *International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM)* diagnosis of either nonmelanomatous cancer or Paget disease of the bone and individuals enrolled in administrative services-only health plans or in a Humana health plan which is contractually excluded from research studies were excluded.

The sample was split into a randomly generated training (development) sample and a validation sample, with a 1:1 ratio. The primary study outcome was defined as incident fragility fracture. These fractures were identified using a combination of *ICD-9-CM* and *ICD-10-CM* diagnosis codes. Clinical fragility (nontraumatic) fractures with an osteoporosis likelihood score of 8 or greater, as defined by Warriner et al,²¹ were identified during 12- and 24-month follow-up intervals. This published algorithm was developed to enhance the accuracy of identifying osteoporosis-related fractures

in administrative claims data and was used in the current study to reduce the potential for misclassification of the primary study outcome. Fracture codes recorded during the follow-up period but within 60 days of a baseline fracture were considered as a continuation of care for the baseline fracture and, therefore, not considered in the analysis of fracture outcomes during follow-up.

Covariates considered as potential independent variables for the predictive models included patient demographics (age, sex, race, and geographic region), history of fracture,

falls that result in medical encounters or that require treatment (ie, medically significant falls), BMD testing, comorbidities, medication use, and markers of frailty. Comorbidities were quantified by the Deyo-Charlson Comorbidity Index²² score and yes/no indicator variables for selected comorbidities, including those associated with an increased likelihood of fractures/medically significant falls. Osteoporosis treatments, as well as medications associated with an increased likelihood of fractures/medically significant falls (eg, antihypertensives, anticonvulsants, antidepressants, antipsychotics), were assessed. Markers of frailty included data on difficulty walking, use of durable medical equipment or ambulance/life support, paralysis, weakness, and podiatric care.

Statistical Analysis

The training sample was used to construct risk-prediction models for any fragility fracture occurring in the 12- and 24-month follow-up intervals. The primary analysis focused on incident fractures that occurred in the 12-month follow-up, and data from the 24-month follow-up provided a sensitivity analysis. Here we present predictive models for any fragility fracture in these 2 follow-up periods, as well as results from a model specific to hip fracture risk during a 12-month follow-up.

To accommodate variable length of follow-up for individuals in the training and validation samples, Cox regression models²³ were used to estimate adjusted hazard ratios (HRs) for potential predictor variables. Variables significantly associated with fracture risk ($P < .001$), after controlling for all other predictors in the model, were considered to be independent predictors. Using the validation sample, the predictor coefficients from the finalized predictive models of fracture risk for hip fracture were applied to the patient baseline characteristics to obtain the likelihood of fracture risk for each patient. C statistics and other measures (false-positive rate, false-negative rate, sensitivity, specificity, positive predictive value, negative predictive value, and efficiency [ie, percentage of accurately predicted patients in the study sample]) were computed to assess model performance when data from the validation sample were used. Models are typically considered effective when the C statistic is greater than 0.7 and strong when it exceeds 0.8.^{24,25} Therefore, a minimum threshold of 0.7 for the C statistic was considered when

TABLE 1. Baseline Characteristics of Study Individuals (Medicare Advantage and Prescription Drug plans)

Demographics	Individuals N = 1,287,354
Age in years, mean (SD)	74.3 (5.5)
Age category in years, n (%)	
67-69	289,984 (22.5)
70-74	448,164 (34.8)
75-79	291,976 (22.7)
80-84	185,706 (14.4)
85-87	71,524 (5.6)
Female sex, n (%)	724,856 (56.3)
White race, n (%)	1,077,997 (83.7)
History, n (%)	
Falls	78,368 (6.1)
Medical claim for recent (2014) fracture	46,626 (3.6)
Recorded history of fracture ^a	12,137 (0.9)
Use of medications, n (%)	
Antihypertensives	819,051 (63.6)
Antipsychotics	269,169 (20.9)
Opioids/opioid analgesics	265,630 (20.6)
Antidepressants	258,310 (20.1)
Glucocorticoids	193,711 (15.0)
Osteoporosis medications ^b	82,455 (6.4)
Comorbidities	
Deyo-Charlson Comorbidity Index score, mean (SD)	1.2 (1.7)
Hypertension, n (%)	927,152 (72.0)
Other cardiovascular disease, n (%)	601,859 (46.8)
Diabetes, n (%)	413,949 (32.2)
Osteoarthritis, n (%)	356,734 (27.7)
Thyroid disease, n (%)	300,317 (23.3)
Osteoporosis, n (%)	242,655 (18.8)
Gastrointestinal disorders and toxicities, n (%)	211,046 (16.4)
Depression, n (%)	188,273 (14.6)
Dementia, n (%)	90,812 (7.1)
Physical function, n (%)	
Weakness	275,335 (21.4)
Use of durable medical equipment	271,298 (21.1)
Physical/occupational therapy	174,311 (13.5)

^aInternational Classification of Diseases, Ninth Revision, Clinical Modification codes for personal history of traumatic fracture (V13.51, V15.51) or stress fracture (V15.52).

^bBisphosphonates, calcitonins, selective estrogen receptor modulators, denosumab, and teriparatide.

comparing the models. Additional performance metrics were assessed at fracture probabilities of 5% or greater, 10% or greater, 15% or greater, 20% or greater, and 25% or greater.

A parsimonious version of the primary predictive model was developed to adapt the results of the analysis for use as an imminent (12-month) fracture risk assessment for an individual patient in the routine care setting. The goal was to create a parsimonious model

TABLE 2. Fracture Incidence Over 1 and 2 Years

Incidence, n (%)	All Patients N = 1,287,354	Women n = 724,856	Men n = 562,498
1-year fracture incidence			
All fractures	48,622 (3.8)	34,637 (4.8)	13,985 (2.5)
Hip fractures	9604 (0.7)	6884 (0.9)	2720 (0.5)
Vertebral fractures	17,910 (1.4)	12,595 (1.7)	5315 (0.9)
Nonhip, nonvertebral fractures	28,587 (2.2)	20,669 (2.9)	7918 (1.4)
2-year fracture incidence			
All fractures	85,046 (6.6)	60,058 (8.3)	24,988 (4.4)
Hip fractures	17,588 (1.4)	12,537 (1.7)	5051 (0.9)
Vertebral fractures	31,079 (2.4)	21,719 (3.0)	9360 (1.7)
Nonhip, nonvertebral fractures	50,948 (4.0)	36,707 (5.1)	14,241 (2.5)

with approximately 5 variables and to incorporate a risk-scoring point system based on the Sullivan methodology²⁶ adapted for use with 1-year incidence estimates. In the parsimonious model, increasing numbers of points were assigned to increasing levels of risk (eg, increasing age was associated with a greater number of points), and the totaled points corresponded to an individual's predicted fracture probability during 12 months of follow-up.

RESULTS

From Humana's MAPD population, 1,287,354 individuals (mean age, 74.3 years; 56% female; 84% white race) met all criteria for inclusion in this study (eAppendix Figure 1 [eAppendix available at [ajmc.com](#)]; Table 1). Only 6% of these individuals had a history of falls during the baseline period. Approximately 4% of the individuals identified had a claim for a recent fracture (ie, within the baseline year) and fewer than 1% had a historical fracture at any time in recorded medical history. Although 19% of individuals had a diagnosis of osteoporosis, prescription fills for osteoporosis medications during the baseline period were relatively uncommon (6%). By contrast, 72% of individuals had been given a diagnosis of hypertension, and 64% of the total population used antihypertensives. Approximately 15% to 20% of individuals had used other medications of interest.

In the 12-month follow-up period, 3.8% of individuals experienced at least 1 fragility fracture, and the fracture incidence increased to 6.6% over the 24-month follow-up period (Table 2). Fracture incidence was higher among women than men over both follow-up intervals (12 months, 4.8% vs 2.5%; 24 months, 8.3% vs 4.4%; $P < .01$ for both). The incidence of hip fractures in men and women combined was 0.7% in the 12-month follow-up period and 1.4% in the 24-month follow-up period.

In the primary analysis, recent fracture (ie, within the past year prior to the start of the follow-up period) had the strongest association with 1-year fracture risk (Table 3); this factor conferred nearly a 3-fold-higher risk among the affected individuals compared with

METHODS

TABLE 3. Full Model Parameter Estimates for Significant Predictors of 1-Year Fracture Risk

Parameter	All Fractures ^a			Hip Fracture ^b		
	Adjusted Hazard Ratio (95% CI)	P	Points	Adjusted Hazard Ratio (95% CI)	P	Points
Age: 70-74 years	1.11 (1.07-1.16)	<.0001	4	1.27 (1.14-1.42)	<.0001	4
Age: 75-79 years	1.44 (1.38-1.50)	<.0001	14	2.04 (1.83-2.28)	<.0001	12
Age: 80-84 years	1.78 (1.71-1.86)	<.0001	22	3.20 (2.87-3.57)	<.0001	19
Age: 85-87 years	2.21 (2.10-2.33)	<.0001	30	4.55 (4.05-5.12)	<.0001	25
Female sex	1.46 (1.41-1.50)	<.0001	14	1.49 (1.39-1.59)	<.0001	7
Race: Asian	0.86 (0.71-1.04)	.1191	27	1.06 (0.68-1.65)	.8006	8
Race: black	0.59 (0.52-0.66)	<.0001	13	0.75 (0.56-0.99)	.0455	2
Race: Hispanic	0.84 (0.72-0.98)	.0233	26	0.88 (0.61-1.27)	.4972	5
Race: white	1.16 (1.05-1.29)	.0042	39	1.35 (1.04-1.76)	.0241	12
Race: other/unknown	-	-	33	-	-	7
Physical factors	1.25 (1.21-1.28)	<.0001	8	1.38 (1.29-1.47)	<.0001	5
Osteoporosis-related screening and diagnoses	1.19 (1.15-1.23)	<.0001	7	-	-	-
Antidepressant/antipsychotic/sedative hypnotic/ muscle relaxant medications	1.30 (1.27-1.34)	<.0001	10	1.27 (1.19-1.35)	<.0001	4
Arthritis/inflammatory conditions	1.06 (1.03-1.09)	.0001	2	-	-	-
Dementia	1.22 (1.17-1.26)	<.0001	7	1.55 (1.44-1.67)	<.0001	7
Gastrointestinal disorders	1.17 (1.14-1.21)	<.0001	6	1.17 (1.09-1.25)	<.0001	3
Nervous system disorders	1.21 (1.17-1.24)	<.0001	7	-	-	-
Respiratory	1.25 (1.22-1.28)	<.0001	8	1.15 (1.08-1.22)	<.0001	2
Cerebrovascular	1.12 (1.08-1.16)	<.0001	4	1.15 (1.07-1.23)	.0002	2
Osteoporosis medications	1.25 (1.20-1.30)	<.0001	8	1.22 (1.11-1.33)	<.0001	3
Falls	1.24 (1.19-1.29)	<.0001	8	1.57 (1.44-1.70)	<.0001	7
Recent fracture (2014)	2.81 (2.70-2.92)	<.0001	39	2.10 (1.93-2.28)	<.0001	12
History of fracture ^c	1.26 (1.17-1.36)	<.0001	9	-	-	-
Obesity	0.92 (0.88-0.95)	<.0001	3 if no	0.70 (0.63-0.77)	<.0001	6 if no
Vision loss	0.96 (0.93-0.98)	.0007	2 if no	0.86 (0.82-0.92)	<.0001	2 if no
Podiatric care	1.11 (1.07-1.15)	<.0001	4	1.17 (1.08-1.26)	<.0001	3

^aC statistic = 0.73; variables dropped from the model: vision loss, indicator of sicker patient [Deyo-Charlson Comorbidity Index Score >2, liver disease, chronic kidney disease, and complicated hypertension], thyroid disorders, diabetes, hypertension, and cardiovascular disease.

^bC statistic = 0.77; variables dropped from the model: history of fracture, indicator of sicker patient [Deyo-Charlson Comorbidity Index Score >2, liver disease, chronic kidney disease, and complicated hypertension], thyroid disorders, osteoporosis-related screening/diagnosis, arthritis/inflammatory conditions, diabetes, hypertension, nervous system disorders, and cardiovascular disease.

^cInternational Classification of Diseases, Ninth Revision, Clinical Modification codes for personal history of traumatic fracture (V13.51, V15.51) or stress fracture (V15.52).

the fracture risk in individuals who had no recent fracture. Risk also increased steadily with age and was highest among individuals aged 85 to 87 years. White race and female sex were also strongly associated with increased fracture risk, as were osteoporosis-related screening and diagnosis, the use of osteoporosis-related medications, use of antidepressant/antipsychotic/sedative hypnotic/muscle relaxant medications, falls, history of fracture, and respiratory conditions (all $P < .0001$). The primary model performed well, with a C statistic of 0.73, false-positive rates ranging from 74% to 90%, and false-negative rates ranging from 2% to 4% across fracture probability cut-offs ranging from 5% or greater to 25% or greater (eAppendix Table 1 [A]; eAppendix Figure 2 [A]). Across these same fracture probability categories, the model's specificity was better than its sensitivity. Higher areas under the curve and C statistics were

observed with the 12-month model compared with the 24-month model developed as a sensitivity analysis (eAppendix Table 1 [B]; eAppendix Figure 2 [B]). Risk factors for hip fracture within 12 months exhibited significant overlap with the predictors identified for all fragility fractures during that time interval (Table 3). In particular, older age and recent fracture exerted the greatest influence on risk, with 2- to 3-fold increases in risk associated with these factors. The C statistic for the 12-month hip fracture model was 0.77.

The parsimonious model for any fracture, which included recent fracture, age, sex, race, falls, and antidepressant/antipsychotic/sedative hypnotic/muscle relaxant medications as predictors, exhibited good performance with a C statistic of 0.71 (Table 4). The scored points and corresponding predicted probability of fracture were compared with actual fracture rates in 2015 for individuals

with each point total (Table 5). These rates increased as the number of points increased.

DISCUSSION

This study identified predictors of the imminent risk of fracture (ie, within 12-24 months) among older adults enrolled in Humana’s MAPD plans. Of the 75 patient characteristics initially considered for the predictive models, recent fracture (ie, fracture occurring during the 1-year baseline period), advanced age, and white race were most strongly associated with increased imminent risk of fractures. Other key factors included female sex, indicators of osteoporosis (screening, diagnoses, and medications), any history of fracture, falls, and antidepressant/antipsychotic/sedative hypnotic/muscle relaxant medications.

The risk factors identified in this study are consistent with those identified in prior observational studies that assessed imminent fracture risk in different populations, including individuals with and without osteoporosis. In osteoporosis, generally, white/Caucasian women are at greater risk of fracture than nonwhite women or men of similar age.²⁷ Low BMD, prior fracture, and falls are also well-documented risk factors for fragility fracture.²⁸ The growing body of research on risk factors for imminent fractures indicates that these factors, along with certain comorbidities and medications that affect physical and cognitive functioning, also influence the risk of fracture in the near term.¹⁰⁻¹⁶ The model results for hip fracture illustrate this last point well, with previous research indicating that various mechanisms may influence the association between dementia and hip fractures, including common risk factors for both and the role of dementia and its treatment as an indirect risk factor that increases fracture risk through intermediate risk factors (eg, falls, vitamin D deficiency, treatment adverse effects).²⁹

We found that antidepressant/antipsychotic/sedative hypnotic/muscle relaxant medications had a significant impact on the imminent risk of fracture. It is possible, as recent literature suggests, that these medications increase the risk of falls, thereby indirectly increasing the risk for fragility fractures.³⁰⁻³² Although the 2 variables—antidepressant/antipsychotic/sedative hypnotic/muscle relaxant medications and falls—were not highly correlated (Pearson correlation coefficient = 0.13), this may be because falls are vastly underreported in medical claims data, which would make it difficult to show this association in the available data.

The accumulating literature on short-term or imminent risk highlights the fact that fracture risk is not linear but varies over time as a patient’s characteristics and exposures change, and investigators have begun identifying factors that contribute specifically to increased risk within the next 1 to 2 years.^{10,14,33-35} An important aspect of several risk factors identified in our full models of any fracture and in previous studies of imminent risk is that they are dynamic and their influence on fracture risk occurs quickly. Prior fracture illustrates this concept well. There is strong evidence that the risk of fragility fracture is approximately doubled after an

TABLE 4. Parsimonious Model Parameter Estimates for Significant Predictors (all fractures, 1 year)^a

Parameter	Parameter Estimate	Adjusted Hazard Ratio (95% CI)	P	Points
Age: 70-74 years	0.1250	1.13 (1.09-1.18)	<.0001	1
Age: 75-79 years	0.4197	1.52 (1.46-1.59)	<.0001	3
Age: 80-84 years	0.6631	1.94 (1.86-2.03)	<.0001	5
Age: 85-87 years	0.8929	2.44 (2.32-2.57)	<.0001	7
Female sex	0.4543	1.58 (1.53-1.62)	<.0001	4
Race: Asian	-0.1474	0.86 (0.72-1.04)	.1232	5
Race: black	-0.5137	0.60 (0.53-0.67)	<.0001	2
Race: Hispanic	-0.1216	0.89 (0.76-1.03)	.1171	5
Race: white	0.1555	1.17 (1.05-1.30)	.0030	7
Race: other/unknown	-	-	-	6
Falls	0.3709	1.45 (1.39-1.51)	<.0001	3
Antidepressant/antipsychotic/sedative hypnotic/muscle relaxant medications	0.4484	1.57 (1.53-1.61)	<.0001	4
Recent fracture (2014)	1.2719	3.57 (3.44-3.70)	<.0001	10

^aC statistic = 0.71.

TABLE 5. Risk Scoring: Relationship of Points and Predicted Probability of Fracture in Parsimonious Model^a

Points	Predicted Probability	Patients	2015 Fractures	Fracture Incidence
2	0.8%	5790	37	0.6%
3	0.9%	8020	67	0.8%
4-6	1.3%	19,402	200	1.0%
7	1.5%	56,065	697	1.2%
8	1.7%	64,266	1020	1.6%
9	1.9%	12,498	183	1.5%
10	2.2%	49,720	1024	2.1%
11	2.5%	60,744	1329	2.2%
12	2.8%	101,307	2742	2.7%
13	3.2%	7993	254	3.2%
14	3.7%	61,030	2207	3.6%
15	4.1%	31,936	1252	3.9%
16	4.7%	70,299	3469	4.9%
17-18	6.0%	41,459	2658	6.4%
19-20	7.7%	20,741	1745	8.4%
21-22	9.8%	12,016	1414	11.8%
23-24	11.2%	4497	652	14.5%
>24	20.8%	15,894	3361	21.1%

^aThis model included recent fracture, age, sex, race, falls, and antidepressant/antipsychotic/sedative hypnotic/muscle relaxant medications.

METHODS

initial fracture and that the greatest increase in risk occurs within the first year post fracture.^{17,28,36} Our results confirm this pattern of risk by demonstrating that although any history of fracture is a significant predictor of imminent fracture risk (adjusted HR, 1.26; 95% CI, 1.17-1.36), the impact of recent fracture is more than twice as great (adjusted HR, 2.81; 95% CI, 2.70-2.92).

Fracture risk may be particularly variable in older individuals because events that we have identified as predictors of imminent risk, such as the occurrence of a stroke or diagnosis of a neurologic or psychologic disorder (eg, Alzheimer disease, depression, anxiety), generally become more common with age. Similarly, changes in physical or cognitive functioning, which may be related to the onset of new comorbidities or the initiation of new medications, may either increase fracture risk directly or act on fracture risk by increasing a patient's risk of falls as mentioned previously.^{10,14,30-32} This inherent malleability of fracture risk underscores the importance of being able to quantify imminent risk as a patient's medical status changes and to help patients understand the need for timely intervention to reduce the risk of fracture and its related sequelae.

This dynamic nature of fracture risk suggests a need for tools that can be used to regularly assess the changing risk of imminent fracture in older adults. In this population, such risk assessments should be done regularly, and more frequent use of a tool such as the one developed in this study might be useful for patients whose health status is in transition or particularly modifiable. Quantifying imminent risk in an ongoing, real-time fashion requires a simple risk-assessment tool. With this in mind, we developed a parsimonious model based on our full model and adapted this model into a prototype for a points-based risk-assessment tool. This model uses only 6 variables (recent fracture, age, sex, race, falls, and antidepressant/antipsychotic/sedative hypnotic/muscle relaxant medications) and was adapted to a point-based system, with total points (risk score) easily computed during a routine physician office visit. Given the importance of falls as a predictor of long-term fracture risk and their association with imminent risk of fracture, additional parsimonious models were tested to assess a composite physical factors variable as a potential predictor of imminent risk. Because physical factors may influence fall risk, in one model, the physical factor variable was simply substituted for falls in the existing parsimonious model, whereas in a second model, falls and physical factors were combined and tested with age, sex, race, and recent fracture. The model performance was similar in both of these versions and resulted in the same number of points being attributed to this fifth variable.

This work supports the feasibility of a formal risk assessment that can quickly and easily be used during physician office visits to identify patients who are at high risk for an imminent fracture. To guide the use of this tool, input could be obtained from physician focus groups to help determine clinically meaningful point score thresholds for fracture prevention initiatives. Such initiatives would aid in the identification of patients in the greatest need of timely osteoporosis management ranging from BMD screening to

interventions including prescription medications and initiatives to reduce the risk of falls.

Limitations

This study is subject to limitations common to administrative claims data research. Identifying fragility fractures and distinguishing incident fractures from prevalent fractures can be challenging with the information available in claims. To address this issue, we excluded all fractures that were recorded as trauma related and examined the timing of fracture-related care to identify and exclude claims most likely to represent care for prevalent fractures that occurred in the baseline period. We also limited the analysis to closed fractures with the highest likelihood of being classified as fragility fractures based on a previously published methodology designed for use with administrative claims data.²¹ Specifically, we included only fractures with an osteoporosis likelihood score of 8 or greater to reduce bias related to potential misclassification of fracture outcomes. There was also potential for selection bias, given the requirement for at least 12 months of continuous insurance coverage in the baseline period. Although the multivariate regression modeling used in this study would have reduced the potential for bias among measured covariates, bias associated with unmeasured covariates would have remained. We also note that results may not generalize to the full US population, as the geographic mix in the sample was not balanced across all regions.

CONCLUSIONS

In summary, recent fracture, older age, female sex, white race, falls, and use of antidepressant/antipsychotic/sedative hypnotic/muscle relaxant medications were strong predictors of the imminent risk of fracture in Medicare-enrolled older adults. A patient's level of imminent risk may change over time, and this work provides proof of concept that the imminent risk of fracture can be assessed by evaluating a small number of factors. Administering such a risk-assessment tool regularly may improve physicians' opportunities to identify elderly patients at high risk of imminent fractures and enhance their ability to provide timely interventions (screening, medications, and fall-prevention strategies). Additional research is needed to set clinically meaningful risk-score thresholds for intervention, determine the applicability and accuracy of this risk-score model to specific patient subgroups, and evaluate the best assessment schedule and optimal ways to implement this tool within the existing physician workflow. ■

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eAppendix Table. Model Performance**A. Full 12-Month Model***

Fracture probability	False positive	False negative	Sensitivity	Specificity	PPV	NPV	Efficiency
≥ 5%	90.4%	2.4%	49.3%	81.9%	9.6%	97.6%	80.6%
≥ 10%	82.3%	3.1%	22.2%	95.9%	17.7%	96.9%	93.2%
≥ 15%	77.8%	3.3%	14.0%	98.1%	22.2%	96.7%	94.9%
≥ 20%	75.5%	3.5%	9.5%	98.9%	24.5%	96.5%	95.5%
≥ 25%	73.9%	3.6%	5.8%	99.3%	26.1%	96.4%	95.8%

B. Full 24-Month Model†

Fracture probability	False positive	False negative	Sensitivity	Specificity	PPV	NPV	Efficiency
≥ 5%	89.8%	3.1%	76.4%	52.5%	10.2%	96.9%	54.1%
≥ 10%	82.8%	4.8%	37.5%	87.2%	17.2%	95.2%	84.0%
≥ 15%	76.9%	5.5%	20.9%	95.1%	23.1%	94.5%	90.2%
≥ 20%	72.2%	5.9%	13.7%	97.5%	27.8%	94.1%	92.0%
≥ 25%	69.1%	6.1%	9.3%	98.5%	30.9%	93.9%	92.6%

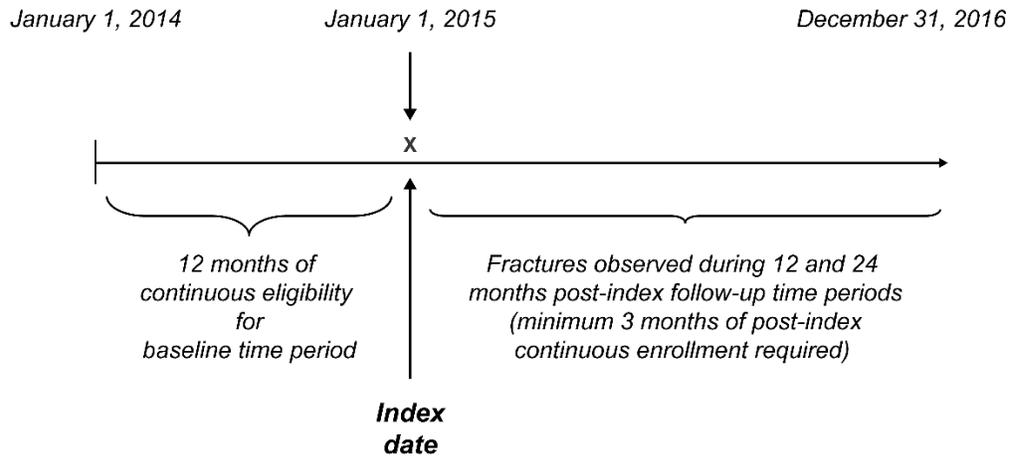
PPV, positive predictive value; NPV, negative predictive value.

*C-statistic = 0.73.

†C-statistic = 0.71.

eAppendix Figure 1. Study Schema

Study period: January 1, 2014, to December 31, 2016



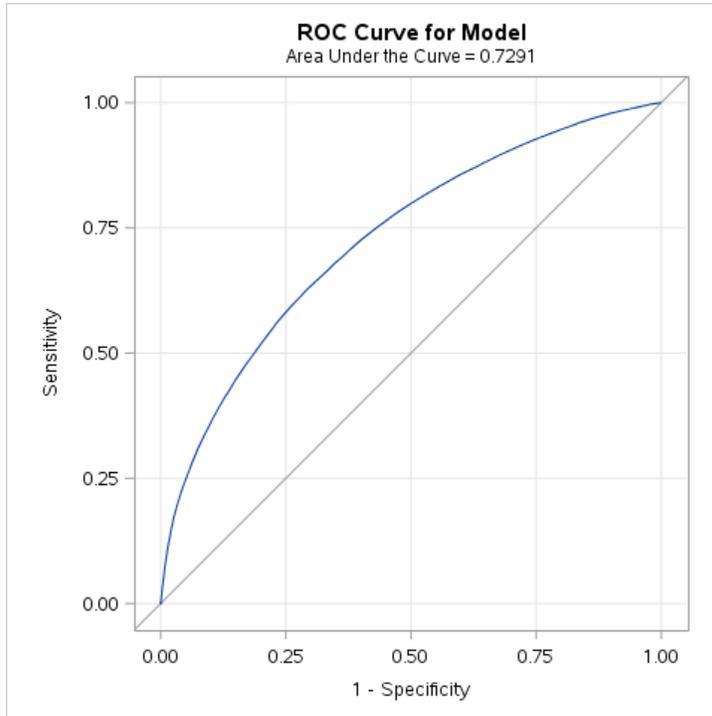
Eligible study sample was split (1:1 ratio) into a randomly generated:

A. Training (development) sample

B. Validation (holdout) sample

eAppendix Figure 2. Receiver Operating Characteristics (ROC) Curve: (A) Full 12-Month Model and (B) Full 24-Month Model

A. Full 12-Month Model



B. Full 24-Month Model

