| **Study, Year****Risk of Bias**  | **Participant Characteristics,****Sample Size** | **Baseline BMD and Fracture Rate** | **Risk Prediction Instruments Evaluated (Prediction Interval)** | **Fracture Definition Used, Number of Fracture Events** | **Length of Cohort Followup** | **Summary of Results** |
| --- | --- | --- | --- | --- | --- | --- |
| Leslie et al, 2012123Unclear | Men and women age 50 and older from Manitoba, CanadaN=36,730 (92.7%) women N=2,873(7.3%) menMean age:65.7 (SD 9.8) women68.2 (SD 10.1) men | BMD NRHistory of fracture NR | FRAX (10 year prediction), with and without BMD | Hip and MOF based on hospital discharge abstracts and physician billing claimsNumber of fractures: 2,543 | Mean 5.4 years | *AUC (95% CI) for Fracture Prediction*Women (MOF)Femoral neck BMD alone: 0.682 ( 0.670-0.693) Without BMD: 0.666 (0.655-0.678)With BMD: 0.698 ( 0.687-0.708)Men (MOF)Femoral neck BMD alone: 0.645 (0.601-0.689)Without BMD: 0.609 ( 0.564-0.654With BMD: 0.661 (0.619-0.703)Women (Hip)Femoral neck BMD alone: 0.802 ( 0.783-0.820)Without BMD: 0.789 (0.772-0.807)With BMD: 0.822 (0.805-0.838)Men (Hip)Femoral neck BMD alone: 0.798 (0.726-0.870)Without BMD: 0.733 (0.659-0.807)With BMD: 0.789 (0.722-0.855) |
| Iki et al, 2015 132Unclear | Men 65 or older from JapanN=2012 eligible and 1805 for analysisMean age: 73.0 (SD 5.1) | BMD: 0.741 g/cm2 (0.114)History of fracture: 22 | FRAX, version 3.8 for Japan and TBS | MOF (femoral next, spine, distal forearm, proximal humerus) from low-energy trauma | 4.5 years | *AUC*FRAX 10 years (w/BMD) Men MOF : 0.681 (0.586 to 0.776)TBS Men MOF after 4.5 years: 0.669 (0.548 to 0.79) |
| Van Geel, 2014124Unclear | Post-menopausal women ages 50-80 years from 12 practices in southeastern NetherlandsN=506Mean age: 68 | Mean(SD) femoral neck BMD T-scoreFracture group: −1.7(1.0)Non-fracture group: −1.2(1.0)History of fracture NR  | FRAX (10 year prediction), Garvan FRC (5,10 years) | All (included: clinical spine, humerus, forearm, hip, “other”),MOF (all above except other),Hip fracturesSelf-report with medical record confirmation.Number of fractures:All: 48MOF: 33 | 5 years | *AUC for Fracture Prediction*FRAX OF fracture risk without BMD: 0.653FRAX OF fracture risk with BMD: 0.693FRAX hip fracture risk with BMD: 0.698Garvan OF fracture risk without BMD: 0.646Garvan OF fracture risk with BMD: 0.689Garvan hip fracture risk with BMD: 0.695 |
| Rubin, 2013128Unclear | Women ages 40 to 90 living in southern Denmark diagnosed and treated for osteoporosis.N=3614Mean age: 64 (SD 13) | BMD NRHistory of OF: 337 (9%)Secondary osteoporosis: 655 (18%) | FRAX 3.0 without BMD(10 year prediction), OST, ORAI, OSIRIS, SCORE, Age alonewith followup BMD testing for fx risk >= 9.3% )- 10 yr horizon | FRAX defined MOF, Any OF from registry.Number of fractures:OF: 225MOF: 156 | 3 years | *AUC (95% CI) for Fracture Prediction**MOF:*FRAX (no BMD): 0.722 (0.686, 0.758)Age alone: 0.720 (0.685, 0.755)OSIRIS: 0.713 (0.677, 0.749)OST: 0.712 (0.675, 0.750)ORAI 0.704 (0.663, 0.745)SCORE 0.703 (0.664, 0.742)*Any OF:*FRAX (no BMD): 0.701 (0.668, 0.735)Age alone: 0.694 (0.660, 0.727)OSIRIS: 0.690 (0.658, 0.723)OST: 0.691 (0.657, 0.725)ORAI: 0.682 (0.646, 0.717)SCORE: 0.681 (0.646, 0.716) |
| Azagra, 2011181& 2012125Unclear | Random sample of participations ages 40 to 90 years from the FRIDEX Cohort, comprised of women in Spain referred by general practitioners and specialists for bone density screening.N=770Mean age: 56.8 (SD8.0) | BMD NRHistory of fracture: X (22.8%)Use of medication for osteoporosis: X (27.9%) | FRAX version 3.2 (10 year prediction) calibrated for Spain | Incident fragility fractures of hip or MOF, major trauma associated fractures were excludedSelf-report confirmed by medical records.Number of fractures: 65 | 10 years | *AUC (95% CI) for Fracture Prediction*without BMD, Hip: 0.88 (0.82 to 0.95)without BMD, MOF: 0.69 (0.62 to 0.76)with FN BMD, Hip: 0.85 (0.74 to 0.96)with FN BMD, MOF: 0.72 (0.65 to 0.79)with LS BMD, Hip: 0.77 (0.66 to 0.88)with LS BMD, MOF: 0.71 (0.64 to 0.78)BMD FN only, Hip: 0.78 (0.63 to 0.93)BMD FN only, MOF: 0.66 (0.58 to 0.74)BMD LS only, Hip: 0.63 (CI, 0.49 to 0.77) (p=0.067)BMD LS only, MOF: 0.64 (CI, 0.57 to 0.71)without BMD, vertebral: 0.75 (CI, 0.64 to 0.86)with FN BMD, vertebral: 0.82 (CI, 0.73 to 0.91)with LS BMD, vertebral: 0.71 (CI, 0.58 to 0.84)Age alone, hip: 0.89 (no CI, provided, but comparison with FRAX tool reported as p=0.976)Age alone, MOF: 0.67 (no CI, provided, but comparison with FRAX tool reported as p=0.565 |
| Leslie, 2012127Unclear | Women and men age 50 years and older from Manitoba, CanadaN=20,477Mean age: 65(SD 9)94.1% women  | BMD NR, history of fracture NR | FRAX (10 year prediction) | MOF not associated with major trauma based on hospital discharge abstracts and physician billing claimsNumber of fractures: 1,845 | Mean 8 years | *AUC (95% CI) for Fracture Prediction*With FN BMD: 0.695 (0.683–0.708)Without BMD: 0.668 (0.655–0.681)With LS BMD: 0.685 (0.673–0.698)With minimum BMD: 0.694 (0.681–0.706)With weighted mean BMD: 0.697 (0.685–0.710)With BMD offset: 0.698 (0.685–0.710) *Percent appropriate reclassification:*With FN BMD: referenceWithout BMD: 44.5%With LS BMD: 41.1%With minimum BMD: 10.5%With weighted mean BMD: 50.6%With BMD offset: 52.4% |
| Ahmed, 2014129Unclear AUCs, High for NRIs | Men and women age 60 years and older from the Norwegian Tromso CohortN = 299255% women | Femoral Neck BMD T-ScoreMean: -1.46 (SD 1.19) (Non fracture group)-1.89 (SD 1.10) (Fracture group)History of fracture NR | Garvan Fracture Risk Calculator (FRC) with and without BMD(5 and 10 year prediction) | All fractures except finger, toe, or skull, or vertebral recorded in the fracture registry. Hip fractures were verified through hospital discharge records. | Median 6.9 years | *AUC for Fracture Prediction*5 yr risk with BMD, nonvertebral fracture (women): 0.615 yr risk without BMD, nonvertebral fracture (women): 0.575 yr risk with BMD, hip fracture (women): 0.785 yr risk without BMD, hip fracture (women): 0.705 yr risk with BMD, nonvertebral fracture (men): 0.675 yr risk without BMD, nonvertebral fracture (men): 0.565 yr risk with BMD, hip fracture (men): 0.795 yr risk without BMD, hip fracture (men): 0.6910 yr risk with BMD, nonvertebral fracture (women): 0.6210 yr risk without BMD, nonvertebral fracture (women): 0.5810 yr risk with BMD, hip fracture (women): 0.7310 yr risk without BMD, hip fracture (women): 0.6810 yr risk with BMD, nonvertebral fracture: (men) 0.6110 yr risk without BMD, nonvertebral fracture: (men) 0.5710 yr risk with BMD, hip fracture (men): 0.7410 yr risk without, hip fracture (men): 0.65 |
| Hippisley-Cox, 2012130Unclear | Patients ages 30 to 100 years from a database of 13 million patients in 620 practices nationally representative practices in the United Kingdom using the Egton Medical Information System.N=1,583,373Mean age: 5050.8% women | BMD NR,History of fracture: 1.8% | QFracture (10 yr prediction) | OF defined as a hip, vertebral, proximal humerus, or distal radius fracture during follow-up Number of OF: 28,685Number of hip fractures: 9,610Fractures were recorded either on the general practice record or the linked death record. | Up to 15 years | *AUC (95% CI) for Fracture Prediction*Women OF: 0.790 (0.787 to 0.793)Women Hip Fracture: 0.893 (0.890 to 0.896)Men OF: 0.711 (0.703 to 0.719)Men Hip Fracture: 0.875 (0.868 to 0.883) |
| Leslie, 2010131Unclear | Men and women age 50 and older from Manitoba, CanadaN=36,730 (92.7%) women N=2,873(7.3%) menMean age:65.7 (SD 9.8) women68.2 (SD 10.1) men  | 14.3% of women have a BMD T score of <=-2.5 based on the female reference; 18.9% of men have a lBMD T-score based on the male reference | CAROC, 10-year prediction | MOF not associated with major trauma based on hospital discharge abstracts and physician billing claimsNumber of fractures: 2,543 | Women, mean 5.4 years, men, mean 4.4 years | *Risk categorization, N fracture/N in category**Women*With BMD FN Low (<10% 10yr risk): 341/12,878Moderate (10-20% 10 yr risk): 748/13,813High (>20% 10 yr risk): 1291/10,039p<0.001With minimum site BMD Low (<10% 10 yr risk): 231/9866Moderate (10-20% 10 yr risk): 599/12,960High (>20% 10 yr risk): 1550/13,904p <0.001*Men*With BMD FN Low (<10% 10 yr risk): 42/1255Moderate (10-20% 10 yr risk): 71/1187High (>20% 10 yr risk): 50/431p <0.001With minimum site BMD Low (<10% 10 yr risk): 33/1120Moderate (10-20% 10 yr risk): 70/1199 High (>20% 10 yr risk): 60/554 p <0.001 |
| Morin, 2009102Unclear | Women age 40–59 years who had baseline BMD testing in Manitoba, CanadaN=8,254Mean age: 52.7 | BMD T-Score at any site <=-2.5: 14.9%; history of fracture: 7.1% | Weight, BMI, OST (no prediction time interval specified) | Incident fractures not associated with trauma ascertained by administrative diagnosis codes from longitudinal health record and Number of fractures: 225 | Mean 3.3 years | *AUC (95% CI) for Fracture Prediction*Weight: 0.55 (95% CI, 0.51–0.59)BMI: 0.55 (95% CI, 0.51–0.59)OST: 0.56 (95% CI, 0.52–0.60) |
| Crandall, 201458Unclear | Women ages 50 to 64 years participating in the US Women’s Health Initiative Clinical Trials and Observational Studies. Mean Age 57.9(SD 4.1)N=62,492 | BMD NR, history of fracture NR | USPSTF Strategy (FRAX 3.0 without BMD with followup BMD testing for fx risk >= 9.3% ); SCOREOST | MOF (clinical vertebral, hip, lower arm/wrist, and upper arm fractures)Hip fractures were centrally adjudicated, other fractures were self-report. | 10 years | *AUC (95% CI), Sensitivity (95% CI), Specificity (95% CI) for Fracture Prediction*FRAX without BMD (risk >=9.3%): 0.56 (0.55 to 0.57), 25.8 (24.6 to 27.0), 83.3 (83.0 to 83.6)SCORE: ( >7): 0.53 (0.53 to 0.54), 38.6 (37.3 to 39.9), 65.8 (65.4 to 66.2)OST ( < 2): 0.52 (0.52 to 0.53), 39.8 (38.5 to 41.1), 60.7 (60.3 to 61.1) |

**Abbreviations:** AUC=area under the curve; BMD=bone mineral density; CI=confidence interval; FN=femoral neck; FRAX=fracture risk assessment tool; FRISK=absolute measure of fracture risk; LS=lumbar spine; MOF=major osteoporotic fracture; NR=not reported; OF=osteoporotic fracture; OST=osteoporosis self-assessment tool; SCORE=simple calculated osteoporosis risk estimate; SD=standard deviation; USPSTF=United States Preventive Services Task Force.