| **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, 2012123  Unclear | Men and women age 50 and older from Manitoba, Canada  N=36,730 (92.7%) women  N=2,873(7.3%) men  Mean age: 65.7 (SD 9.8) women  68.2 (SD 10.1) men | BMD NR  History of fracture NR | FRAX (10 year prediction), with and without BMD | Hip and MOF based on hospital discharge abstracts and physician billing claims  Number 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 ( 0.564-0.654  With 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 132  Unclear | Men 65 or older from Japan  N=2012 eligible and 1805 for analysis  Mean 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, 2014124  Unclear | Post-menopausal women ages 50-80 years from 12 practices in southeastern Netherlands  N=506  Mean age: 68 | Mean(SD) femoral neck BMD T-score  Fracture 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 fractures  Self-report with medical record confirmation.  Number of fractures:  All: 48  MOF: 33 | 5 years | *AUC for Fracture Prediction*  FRAX OF fracture risk without BMD: 0.653  FRAX OF fracture risk with BMD: 0.693  FRAX hip fracture risk with BMD: 0.698  Garvan OF fracture risk without BMD: 0.646  Garvan OF fracture risk with BMD: 0.689  Garvan hip fracture risk with BMD: 0.695 |
| Rubin, 2013128  Unclear | Women ages 40 to 90 living in southern Denmark diagnosed and treated for osteoporosis.  N=3614  Mean age: 64 (SD 13) | BMD NR  History of OF: 337 (9%)  Secondary osteoporosis: 655 (18%) | FRAX 3.0 without BMD(10 year prediction), OST, ORAI, OSIRIS, SCORE, Age alone  with followup BMD testing for fx risk >= 9.3% )- 10 yr horizon | FRAX defined MOF, Any OF from registry.  Number of fractures:  OF: 225  MOF: 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& 2012125  Unclear | 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=770  Mean age: 56.8 (SD8.0) | BMD NR  History 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 excluded  Self-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, 2012127  Unclear | Women and men age 50 years and older from Manitoba, Canada  N=20,477  Mean 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 claims  Number 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: reference  Without 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, 2014129  Unclear AUCs, High for NRIs | Men and women age 60 years and older from the Norwegian Tromso Cohort  N = 2992  55% women | Femoral Neck BMD T-Score  Mean:  -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): 0.61  5 yr risk without BMD, nonvertebral fracture (women): 0.57  5 yr risk with BMD, hip fracture (women): 0.78  5 yr risk without BMD, hip fracture (women): 0.70  5 yr risk with BMD, nonvertebral fracture (men): 0.67  5 yr risk without BMD, nonvertebral fracture (men): 0.56  5 yr risk with BMD, hip fracture (men): 0.79  5 yr risk without BMD, hip fracture (men): 0.69  10 yr risk with BMD, nonvertebral fracture (women): 0.62  10 yr risk without BMD, nonvertebral fracture (women): 0.58  10 yr risk with BMD, hip fracture (women): 0.73  10 yr risk without BMD, hip fracture (women): 0.68  10 yr risk with BMD, nonvertebral fracture: (men) 0.61  10 yr risk without BMD, nonvertebral fracture: (men) 0.57  10 yr risk with BMD, hip fracture (men): 0.74  10 yr risk without, hip fracture (men): 0.65 |
| Hippisley-Cox, 2012130  Unclear | 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=1,583,373  Mean age: 50  50.8% 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: 28,685  Number of hip fractures: 9,610  Fractures 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, 2010131  Unclear | Men and women age 50 and older from Manitoba, Canada  N=36,730 (92.7%) women  N=2,873(7.3%) men  Mean age: 65.7 (SD 9.8) women  68.2 (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 claims  Number 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): 341/12,878  Moderate (10-20% 10 yr risk): 748/13,813  High (>20% 10 yr risk): 1291/10,039  p<0.001  With minimum site BMD  Low (<10% 10 yr risk): 231/9866  Moderate (10-20% 10 yr risk): 599/12,960  High (>20% 10 yr risk): 1550/13,904  p <0.001  *Men*  With BMD FN  Low (<10% 10 yr risk): 42/1255  Moderate (10-20% 10 yr risk): 71/1187  High (>20% 10 yr risk): 50/431  p <0.001  With minimum site BMD  Low (<10% 10 yr risk): 33/1120  Moderate (10-20% 10 yr risk): 70/1199  High (>20% 10 yr risk): 60/554  p <0.001 |
| Morin, 2009102  Unclear | Women age 40–59 years who had baseline BMD testing in Manitoba, Canada  N=8,254  Mean 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, 201458  Unclear | 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% );  SCORE  OST | 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.