Title	Utility of osteoporosis self-assessment tool as a screening tool for osteoporosis in Irish men and women: Results of the DXA-HIP project
Author(s)	Erjiang E.; Wang, Tingyan; Yang, Lan; Dempsey, Mary; Brennan, Attracta; Yu, Ming; Chan, Wing P.; Whelan, Bryan; Silke, Carmel; O'Sullivan, Miriam; Rooney, Bridie; McPartland, Aoife; O'Malley, Gráinne; Carey, John J.
Publication Date	2021-03-03
Publication Information	Erjiang, E., Wang, Tingyan, Yang, Lan, Dempsey, Mary, Brennan, Attracta, Yu, Ming, Chan, Wing P., Whelan, Bryan, Silke, Carmel, O'Sullivan, Miriam, Rooney, Bridie, McPartland, Aoife, O'Malley, Gráinne, Carey, John J. (2021). Utility of Osteoporosis Self-Assessment Tool as a Screening Tool for Osteoporosis in Irish Men and Women: Results of the DXA-HIP Project. Journal of Clinical Densitometry. doi:https://doi.org/10.1016/j.jocd.2021.03.003
Publisher	Elsevier
Link to publisher's version	https://doi.org/10.1016/j.jocd.2021.03.003
Item record	http://hdl.handle.net/10379/16809
DOI	http://dx.doi.org/10.1016/j.jocd.2021.03.003

Utility of Osteoporosis Self-Assessment Tool as a Screening Tool for Osteoporosis in Irish Men and Women: Results of the DXA-HIP Project

Authors: Erjiang E[1], Tingyan Wang[1,2], Lan Yang[1,3], Mary Dempsey[3], Attracta Brennan[4], Ming Yu[1], Wing P. Chan[5], Bryan Whelan[6,7], Carmel Silke[6,7], Miriam O'Sullivan[6,7], Bridie Rooney[8], Aoife McPartland[7], Gráinne O'Malley[6,8], John J. Carey[6,9*]

Affiliations:

1. Department of Industrial Engineering, Tsinghua University, Beijing, China
2. Nuffield Department of Medicine, University of Oxford, Oxford, UK
3. School of Engineering, National University of Ireland, Galway, Ireland
4. School of Computer Science, National University of Ireland, Galway, Ireland
5. Department of Radiology, Wan Fang Hospital, Taipei Medical University, Taiwan
6. School of Medicine, National University of Ireland, Galway, Ireland
7. Department of Rheumatology, Our Lady's Hospital, Manorhamilton, Co. Leitrim, Ireland
8. Department of Geriatric Medicine, Sligo University Hospital, Sligo, Ireland
9. Department of Rheumatology, Galway University Hospitals, Galway, Ireland

* Corresponding author: John J. Carey

Email: john.j.carey@nuigalway.ie

Abstract

Many algorithms have been developed and publicised over the past 2 decades for identifying those most likely to have osteoporosis or low BMD, or at increased risk of fragility fracture. The Osteoporosis Self-assessment Tool index (OSTi) is one of the oldest, simplest, and widely used for identifying men and women with low BMD or osteoporosis. OSTi has been validated in many cohorts worldwide but large studies with robust analyses evaluating this or other algorithms in adult populations residing in the Republic of Ireland are lacking, where waiting times for public DXA facilities are long. In this study we evaluated the validity of OSTi in men and women drawn from a sampling frame of more than 36,000 patients scanned at one of 3 centres in the West of Ireland. 18,670 men and women aged 40 years and older had a baseline scan of the lumbar spine femoral neck and total hip available for analysis. 15,964 (86%) were female, 5,343 (29%) had no major clinical risk factors other than age, while 5,093 (27%) had a prior fracture. Approximately 2/3 had a T-score ≤-1.0 at one or more skeletal sites and 1/3 had a T-score ≤-1.0 at all 3 skeletal sites, while 1 in 5 had a DXA T-score ≤-2.5 at one or more skeletal sites and 5% had a T-score ≤-2.5 at all 3 sites. OSTi generally performed well in our population with area under the curve (AUC) values ranging from 0.581 to 0.881 in men and 0.701 to 0.911 in women. The performance of OSTi appeared robust across multiple sub-group analyses. AUC values were greater for women, proximal femur sites, those without prior fractures

and those not taking osteoporosis medication. Optimal OSTi cut-points were '2' for men and '0' for women in our study population. OSTi is a simple and effective tool to aid identification of Irish men and women with low BMD or osteoporosis. Use of OSTi could improve the effectiveness of DXA screening programmes for older adults in Ireland.

Key Words: BMD; DXA; Osteoporosis; Osteoporosis Self-assessment Tool; Ireland.

Introduction

A global pandemic of osteoporosis exists today resulting in millions of fragility fractures each year, with associated morbidity, increased mortality and billions of euros in healthcare costs (1-4). Within France, Germany, Italy, Spain, Sweden, and the UK alone, annual health spending on fragility fracture will increase up to €47 billion (a greater than 20% increase) by 2030 (5). Identifying those at risk before these events occur has received considerable attention (6-9). Low bone mineral density (BMD) has been established as the most important risk factor for men and women for primary prevention (2, 7, 10-12). This knowledge is reflected in professional guidelines when recommending BMD measurement by Dual-energy X-ray Absorptiometry (DXA) to screen for those at increased risk of fracture, or to make a diagnosis of osteoporosis before one occurs (2, 7-15).

BMD can be measured by various techniques at multiple skeletal sites, in particular DXA of the lumbar spine and proximal femur (15). Access to quality DXA

scanning and diagnostics is a desirable requirement among at risk populations (16), but availability is limited in many parts of the world (16-18). Globally, only 25% of those patients who suffer a fragility fracture are scanned and treated (5). Identifying those most likely to have low BMD can improve the effectiveness of scanning and diagnostics services by reducing unnecessary testing (8, 9, 18, 19). Many algorithms have been established over the past 2 decades to help identify those at risk for, or with low BMD, with varying effectiveness within and between populations (7-10, 14, 20). Evidence shows that simpler tools may perform as well as, or even better than, more complex ones (7-10, 13, 21). In particular, the Osteoporosis Self-assessment Tool index (OSTi) has been validated in many different populations around the world and has been shown to help identify those most likely to have low BMD or osteoporosis (8, 10, 18, 19, 21-28).

Ireland has one of the highest incidences of hip fractures worldwide (29). Hip fracture admissions to public hospitals in the Republic of Ireland accounts for almost 1 in 3 fracture admissions in men and women >50 years, but almost 2/3 of bed days (30). Between 2010 and 2014, there was a 40% increase in fragility fracture admissions for men and a 27% increase for women (28). Public hospital bed day use for fragility fractures has also increased by almost 50% over the past decade (30). Projections suggest that by 2046, there will be up to a 300% increase in hospital admissions for hip fractures and a greater than 50% increase in osteoporotic fracture bed days (28). This is a similar trend experienced in other countries (5, 31). An evidence based strategy to reduce this burden is urgently needed. This strategy in

turn requires detailed validated data. One approach is to identify those with a DXA classification of osteoporosis, however robust studies of the epidemiology, classification, risk assessment and burden of illness for Ireland are limited (30, 32). In this study, we evaluate the performance of the OSTi for identifying men and women with osteoporosis by DXA criteria in the Republic of Ireland.

Material and Methods

Data were obtained from a convenience cohort scanned on four DXA machines in three hospitals in the West of Ireland; Manorhamilton Hospital (MH), Merlin Park University Hospital (MPH) and Sligo University Hospital (SH). Subject height and weight were obtained using calibrated scientific scales by trained and experienced DXA personnel. BMD measurements were obtained at the hip and anteroposterior lumbar spine L1-L4 using GE Lunar central DXA (Madison WN, USA). Technologists and clinicians are trained, International Society for Clinical Densitometry (ISCD) certified and experienced. All scans were performed between January 2000 and November 2018.

Each local hospital Research Ethics Committee approved the collection, use and analysis of data, and study protocol. Data were then harvested, cleaned and merged, following which, all identifiers were deleted. A password protected cleaned, completely anonymised and untraceable data set remains for analyses, as previously described, which includes detailed clinical data (33, 34). The majority of patients (>99%) were referred for clinical reasons as part of a dedicated hospital osteoporosis

service, or a clinical service for clinicians in the region. An audit of 7,187 DXA referrals over a 4 year period at one clinical site (MPH) shows that the majority of patients are referred from primary care clinics (69%) and hospital outpatient specialist clinics (27%), whilst <4% are referred from inpatient services. Our analyses of >2,000 of those referrals during this period, have previously been published including details of the indications for DXA on the request (35).

In the process of subject selection, we excluded those under 40 years of age at the time of their first scan (5.3%), non-Caucasians (<1%), and those without complete scans of all 3 central sites (lumbar spine L1-L4, total hip and proximal femur: 43.4%). Our analyses are based on the 18,670 men and women selected from a sampling frame of 36,590 subjects, detailed in Figure 1.

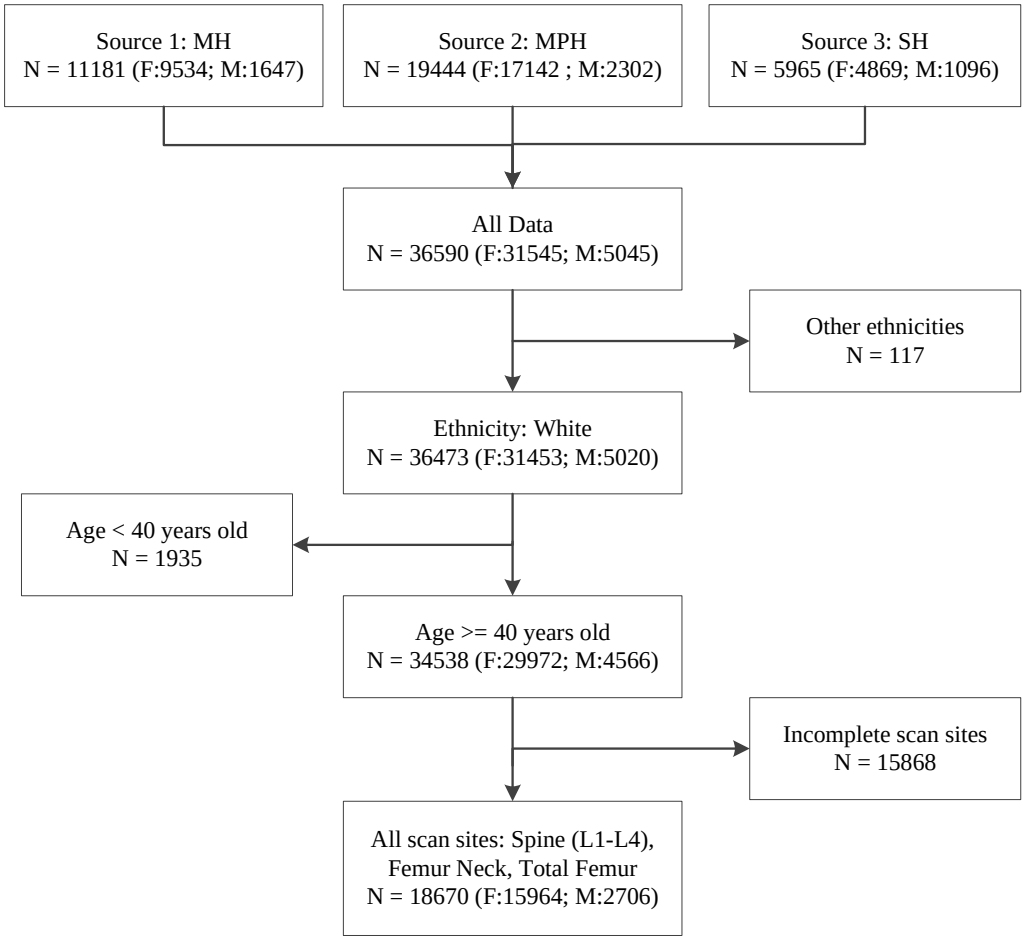

Fig. 1. Flow diagram of the subject selection process.

We examined the performance of the OSTi as previously described to correctly identify men and women classified as osteoporotic using ISCD criteria for postmenopausal women and older men (15). We applied the ISCD criteria on premenopausal women and men aged 40-49 years for the purpose of this study, so that we could perform uniform analyses for each age group, and compare our results to other publications with younger adults. T-scores were calculated using GE

software NHANES III/USA white female reference for both men and women. Those whose T-score was ≤ -2.5 were therefore considered 'osteoporotic'.

Outcomes

We calculated OSTi using the following method (10, 18, 21, 25, 27, 28):

OST index = (body weight in kilograms - age in years) x 0.2, rounded to the nearest integer. The OSTi was calculated for the purposes of this study, not for individuals around the time of their scan.

We compared the AUC values, sensitivity and specificity of OSTi for men and women at each skeletal site (lumbar spine 1-4, femoral neck and total hip), those with a T-score threshold of ≤ -2.5 at a single site and those whose T-score were ≤ -2.5 at all 3 sites. We also evaluated these across a range of OSTi values to obtain the optimum threshold value for deciding who should be tested for osteoporosis by DXA. We evaluated the robustness of OSTi by further sub-dividing the men and women into 4 groups:

i) those without fractures or risk factors other than age or weight;

ii) those with additional clinical risk factors such as having an illness or taking a medication known to increase the risk of osteoporosis or fracture;

iii) those with a prior fragility fracture but without other clinical risk factors; and

iv) those with a prior fragility fracture but having other clinical risk factors.

Statistical Analysis

All statistical analysis was conducted using R Studio for Windows (Version 3.5.1). For continuous variables, mean, standard deviations and range were calculated. For categorical variables, count and percentage were reported. The prevalence of osteoporosis (lowest T-score ≤ -2.5) was calculated in both the female and male cohort, and then further stratified by age. We used scatter plots to present the distribution of T-scores by OSTi in women and men. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated at various cut-offs of OSTi by BMD measurement sites, with reporting of the corresponding AUC values. The optimal cut-off for OSTi was determined using Youden index. Receiver Operating Characteristic (ROC) plots were illustrated for each site and all sites in women and men. To investigate the robustness of OSTi, we also performed sensitivity analysis (subgroup analysis) in the female and male cohorts respectively, stratified by prior fracture, risk factors, and medications. We performed Student's t-test to analyse differences in age, height, weight, BMI (Body Mass Index), and BMD of sites between the subgroups. A p-value of <0.05 was considered statistically significant.

Results

Details of the selection process are shown in Figure 1, and 18,670 (51%) subjects met our inclusion criteria from the total group of 36,590 subjects. 54.2%

were from MPH, 28.5% from MH and 3,327 (17.3%) from SH. This sample is predominantly female (85.5%) and includes 5,343 (28.6%) subjects without a major risk factor for fracture, 5,093 (27.3%) with a prior fracture, 4,064 (21.8%) with a DXA T-score ≤ -2.5 at one or more sites, and 2,003 (10.7%) who were taking osteoporosis medication at the time of their DXA scans, the majority of whom were taking anti-resorptive therapy.

A summary of the characteristics of our study population broken down by gender is shown in Table 1. In general, women were younger, lighter and shorter, and had lower mean BMD than men. However, BMI, fracture prevalence and the proportion of subjects with a DXA classification of osteoporosis were similar between groups (Table 1). 1 in 5 men and women had osteoporosis at 1 or more sites, whilst around 1 in 20 had osteoporosis at all 3 skeletal sites (Table 2). The commonest site of osteoporotic BMD in women was the lumbar spine, whilst in men this was the femoral neck (Table 2). The prevalence of osteoporosis increased steadily with age from 17% and 5% respectively in men and women aged 40 to 49 years to 44% and 61% in men and women aged 80 years and older (Figure 2). Although the prevalence of osteoporosis was highest in those aged 90 years or more, we had far fewer subjects in this age group (65 women and 21 men). Similarly fracture prevalence increased with age with fracture related sites including forearm, vertebrae, hip, humerus and other skeletal sites (data not shown).

Table 1

Main characteristics of the study population broken down by gender

Characteristics	Female (N=15964)	Male (N=2706)
Age (y)	61.39±10.89 (40-100)	64.86±11.69 (40-96)
Weight (kg)	69.52±14.24 (27-156.6)	81.78±15.56 (36.4-147)
Height (cm)	160.43±6.37 (121-188)	172.4±7.12 (135-195.6)
BMI (kg/m^2)	27.01±5.3 (12.16-58.27)	27.46±4.7 (14.45-50.96)
Family History	2505 (15.69)	173 (6.39)
Osteoporotic†	3467 (21.72)	597 (22.06)
Prevalent Fracture	4370 (27.37)	723 (26.27)
Rheumatoid Arthritis	889 (5.57)	320 (11.83)
Glucocorticoid Use	1279 (8.01)	650 (24.02)
Current or Former Smokers	1895 (11.87)	315 (11.64)
No Clinical Risk Factors	4763 (29.84)	580 (21.43)
Osteoporosis Medication Use	1834 (11.49)	169 (6.25)

Mean ± standard deviations (range) or number (percentage) are presented.
† Osteoporotic = lowest DXA T-score ≤ -2.5

Table 2

Prevalence of low BMD and osteoporosis for each skeletal site in men and women

Reference site	Female (N=15964)		Male (N=2706)	
	T-score≤ -2.5	T-score≤ -1	T-score≤ -2.5	T-score≤ -1
Lumbar Spine, N (%)	2696 (16.89)	8247 (51.66)	318 (11.75)	1087 (40.17)
Femur Neck, N (%)	1606 (10.06)	8720 (54.62)	427 (15.78)	1641 (60.64)
Total Femur, N (%)	1514 (9.48)	6963 (43.62)	287 (10.61)	1297 (47.93)
Any site N, (%) †	3467 (21.72)	10683 (66.92)	597 (22.06)	1837 (67.89)

All sites, N (%)‡	772 (4.84)	5347 (33.49)	772 (5.14)	810 (29.93)

†Any site: osteoporosis of at least one skeletal site (lumbar spine, neck of femur, or total femur).
‡ All sites: osteoporosis at all 3 skeletal sites (lumbar spine, neck of femur, or total femur).

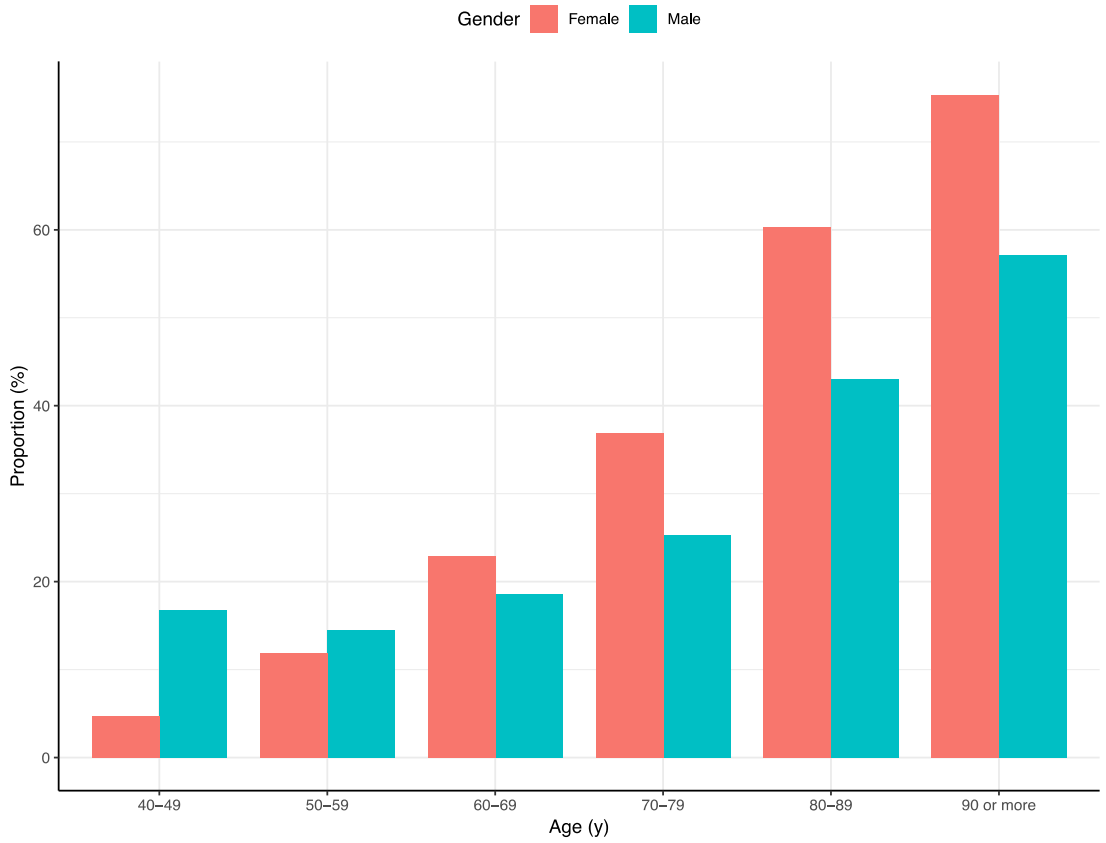

Fig. 2. Prevalence of osteoporosis (lowest T-score ≤ -2.5) in men and women by age group.

The range of OSTi for the total femur varied considerably over several standard deviations for any given BMD T-score in both men and women (Figures 3a and 3b). The sensitivity, specificity, PPV, and NPV of OSTi across a range of values for each skeletal site for men and women is shown in Table 3. As expected, higher values had greater sensitivity but lower specificity. Table 4 and Figure 4 show the AUC and ROC

plots for OSTi for men and women at any and all skeletal sites. OSTi performed considerably better in the female cohort, whilst the total femur and femoral neck yielded greater values than the lumbar spine for both men and women (Table 4). The AUC for all site approached 0.90 for women and 0.80 for men (Table 4). The optimal cut point for OSTi at any site for men was ≤ 2 and women ≤ 0, respectively (Table 3). An OSTi cut-off score of 2 to identify Irish women with osteoporosis at the any site provided a sensitivity of 90% and a specificity of 46%, whilst for men this was 71% and 64% respectively (Table 3). An OSTi cut-off score of 4 yielded a sensitivity of 97% and specificity of 23% for women and a sensitivity of 85% and a specificity of 44% for men respectively. As shown in Figure 3a and 3b, and Table 3, thresholds of -1 and 2 for OSTi at total femur yield lower sensitivity for women (82%, 96%) and men (51%, 82%) but much greater specificity for women (78%, 42%) and men (86%, 61%) respectively.

Table 3

Sensitivity, Specificity, Positive Predictive Value and Negative Predictive Values for OSTi Thresholds in Women and Men at each, any and all Skeletal Sites

OST index (cut-off)	Female (N=15964)				Male (N=2706)			
	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Lumbar Spine								
-2	48.96	86.13	41.77	89.25	32.08	89.70	29.31	90.84
-1	61.42	78.81	37.06	90.95	38.68	84.55	25.00	91.19
0[a]	74.15	68.99	32.70	92.92	46.23	76.97	21.09	91.49

1	83.16	56.96	28.19	94.33	54.09	68.30	18.51	91.78
2[b]	89.47	44.03	24.52	95.36	65.41	58.88	17.48	92.74
3	94.14	32.24	22.01	96.44	73.58	49.12	16.15	93.32
4	97.11	22.10	20.21	97.41	81.76	39.87	15.33	94.26
5	98.18	14.95	19.00	97.59	88.99	31.91	14.82	95.61
Femur Neck								
-2	67.00	85.49	34.05	95.86	41.69	92.54	51.15	89.44
-1[a]	78.21	77.63	28.11	96.96	49.18	87.63	42.68	90.20
0	85.37	66.97	22.42	97.61	59.72	80.61	36.59	91.44
1	91.22	54.82	18.42	98.24	70.02	72.36	32.19	92.80
2[b]	94.40	42.04	15.41	98.53	80.09	62.79	28.74	94.39
3	96.51	30.50	13.44	98.74	85.71	52.48	25.26	95.15
4	98.26	20.77	12.18	99.07	90.63	42.56	22.82	96.04
5	98.88	14.03	11.40	99.11	93.91	33.83	21.01	96.74
Total Femur								
-2	71.47	85.62	34.24	96.63	45.99	91.07	37.93	93.43
-1[a]	81.51	77.62	27.62	97.56	51.22	85.74	29.88	93.68
0	87.85	66.89	21.75	98.13	62.37	78.59	25.68	94.62
1	92.54	54.66	17.62	98.59	71.43	70.07	22.07	95.39
2[b]	95.57	41.93	14.71	98.91	81.88	60.52	19.75	96.57
3	97.29	30.41	12.78	99.08	86.41	50.35	17.12	96.90
4	98.55	20.68	11.52	99.27	89.55	40.51	15.15	97.03
5	99.08	13.97	10.77	99.31	94.43	32.29	14.20	97.99
Any site[†]								
-2	50.97	88.85	55.92	86.72	33.50	92.98	57.47	83.16
-1	63.37	81.83	49.17	88.95	40.37	88.10	48.98	83.92
0[a]	75.25	71.95	42.67	91.29	50.75	81.32	43.47	85.37

1	83.99	59.67	36.62	93.07	60.47	73.07	38.86	86.72
2[b]	89.90	46.22	31.68	94.29	71.19	63.73	35.71	88.65
3	94.17	33.87	28.32	95.45	78.22	53.44	32.23	89.66
4	97.12	23.29	25.99	96.68	85.09	43.67	29.95	91.19
5	98.24	15.77	24.45	97.00	90.79	35.18	28.39	93.10
All sites[‡]								
-2	79.40	83.23	19.40	98.76	51.08	89.21	20.40	97.12
-1[a]	88.08	75.07	15.22	99.20	57.55	83.95	16.26	97.34
0	92.62	64.46	11.69	99.42	66.91	76.47	13.34	97.71
1[b]	95.08	52.49	9.23	99.53	75.54	67.90	11.30	98.09
2	97.28	40.19	7.63	99.66	84.89	58.24	9.92	98.61
3	98.45	29.11	6.59	99.73	88.49	48.34	8.49	98.73
4	99.35	19.78	5.92	99.83	90.65	38.84	7.43	98.71
5	99.61	13.36	5.52	99.85	94.96	30.78	6.91	99.12

[†]Any site: osteoporosis of at least one skeletal site (lumbar spine, neck of femur, or total femur).

[‡] All sites: osteoporosis at all 3 skeletal sites (lumbar spine, neck of femur, or total femur).

a: Optimal cut points for female and, b: male, by Youden method.

Table 4

AUC for OSTi at each, any and all skeletal sites for Classification of Osteoporosis (T-score ≤ -2.5) for men and women

	Lumber spine	Femur neck	Total femur	Any site	All site
Female	0.778	0.847	0.866	0.806	0.888
Male	0.680	0.790	0.788	0.739	0.796

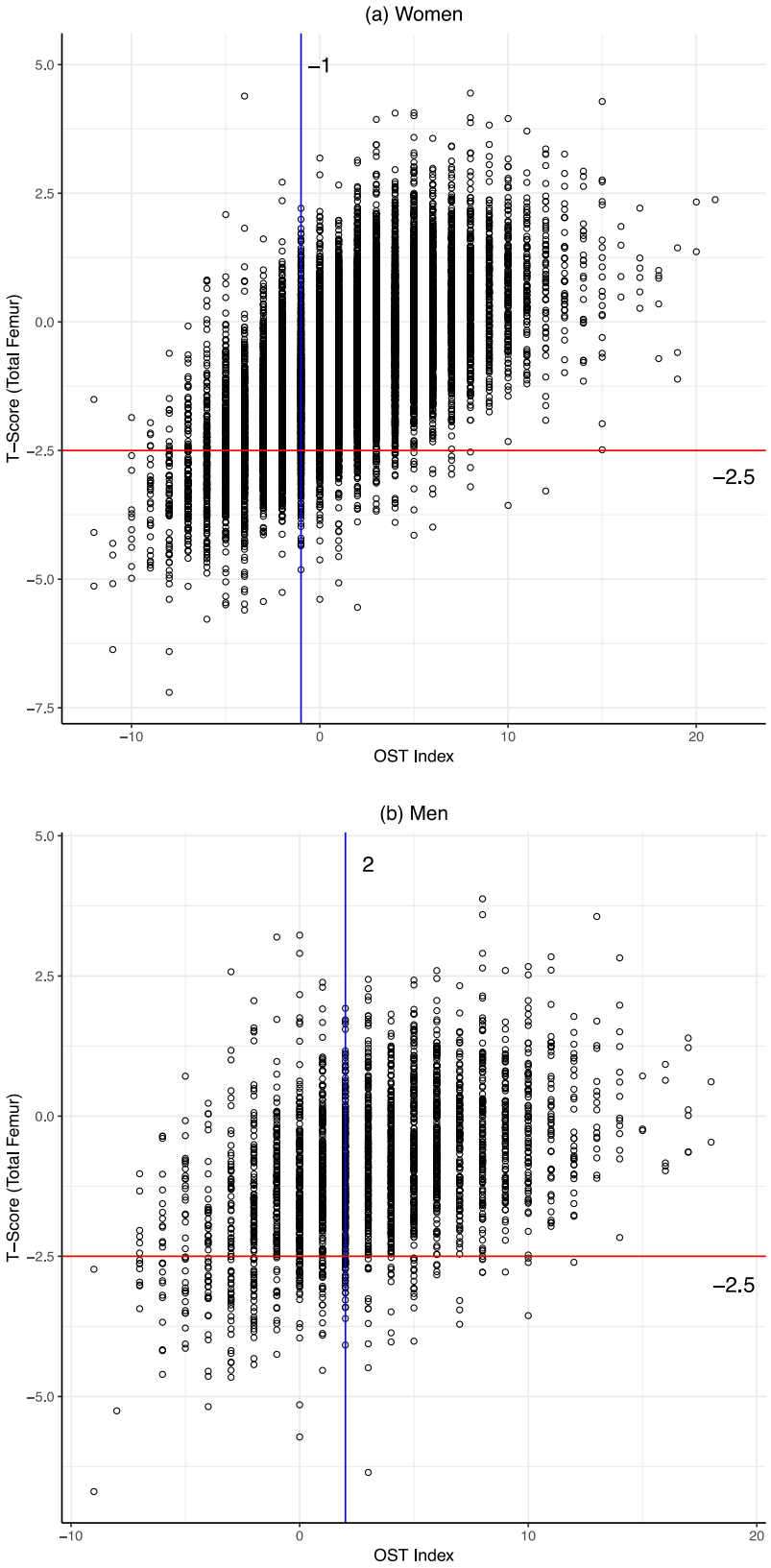

Fig. 3. Distribution of Total Hip T-score in women (a) and men (b) for each level of OSTi.

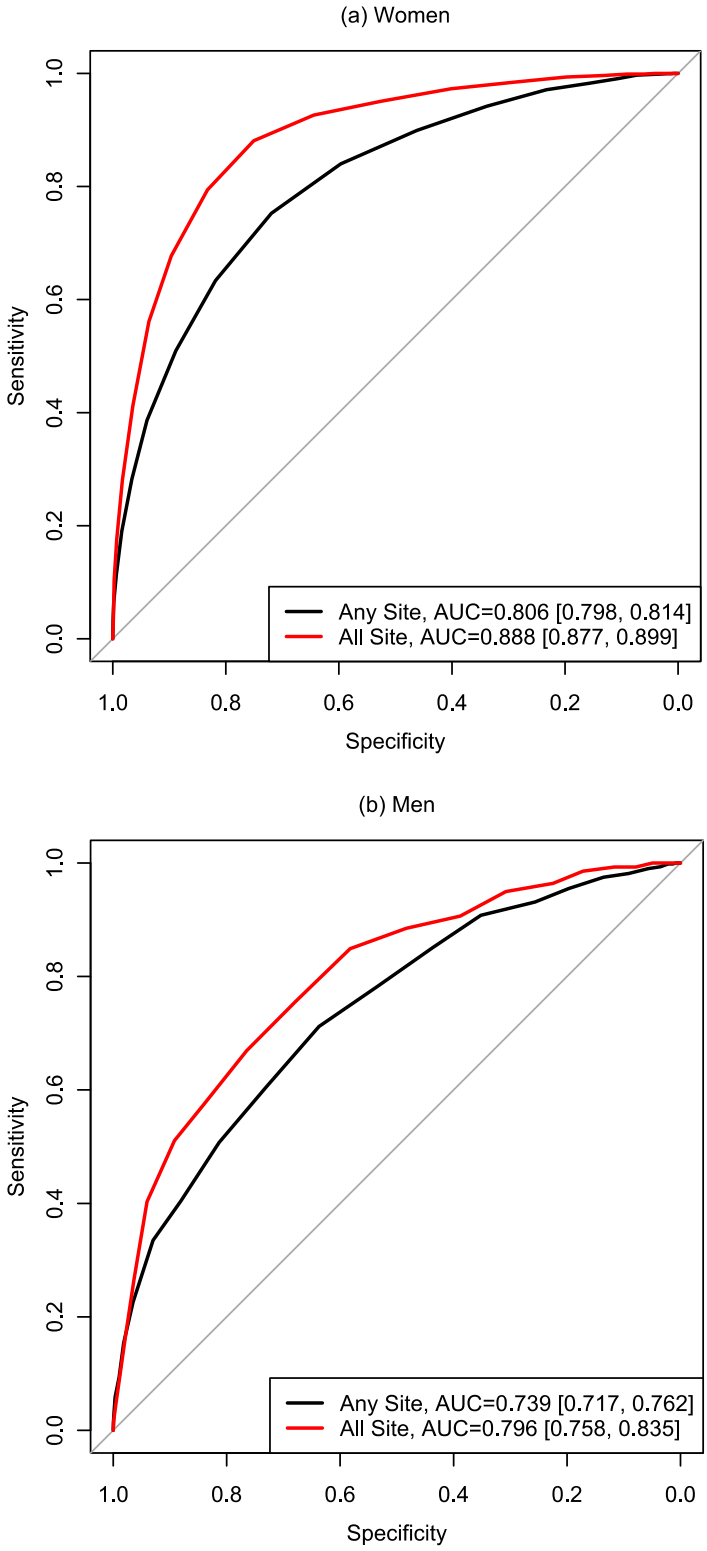

Fig. 4. ROC Curves for OSTi at any and all skeletal sites for women (a) and men (b).

We performed multiple sensitivity analyses to evaluate the robustness of OSTi in our cohort for various subgroups (Table 5). The characteristics of each subgroup are summarised in Supplementary Table S1-S2. Inevitably, the results of OSTi performance differed between subgroups, but importantly these differences were generally negligible (details not shown). The differences in AUC values for all and any sites were smaller in the female cohort across multiple analyses. The AUC range in the female cohort subgroups for all sites was 0.839 to 0.911, whilst the AUC range for the male cohort subgroups was 0.718 to 0.881 (Table 5). Those without fractures or clinical risk factors had the highest AUC value at all 3 skeletal sites for both women and men, whilst they were lowest for those with a combination of other clinical risk factors and fractures. Lumbar spine values were lower in all subgroups for both genders, particularly amongst men taking osteoporosis medication. In this group, the AUC (0.581) for the spine contrasts with the femur sites of 0.782 and 0.769, but as the number of subjects is quite small (N = 169), these results need to be interpreted cautiously.

Table 5

AUC values evaluating the performance of OSTi in various sub-groups to identify men and women as osteoporotic (T-score ≤ -2.5) for any, each and all skeletal sites

	Lumber spine	Femur neck	Total femur	Any site	All site
Female					
All	0.779	0.849	0.867	0.806	0.888
Group A1	0.789	0.887	0.883	0.823	0.911
Group A2	0.780	0.837	0.868	0.798	0.889

Group A3	0.757	0.823	0.847	0.792	0.862
Group A4	0.752	0.817	0.841	0.785	0.859
Group B1	0.771	0.862	0.861	0.805	0.891
Group B2	0.776	0.842	0.864	0.802	0.887
Group B3	0.797	0.863	0.884	0.822	0.891
Group C1	0.787	0.855	0.875	0.814	0.894
Group C2	0.701	0.792	0.810	0.734	0.839
Male					
All	0.682	0.788	0.784	0.739	0.796
Group A1	0.704	0.813	0.807	0.759	0.881
Group A2	0.694	0.795	0.798	0.760	0.758
Group A3	0.663	0.771	0.763	0.716	0.795
Group A4	0.618	0.755	0.745	0.690	0.770
Group B1	0.705	0.800	0.824	0.760	0.835
Group B2	0.657	0.781	0.766	0.729	0.768
Group B3	0.722	0.795	0.776	0.746	0.811
Group C1	0.690	0.788	0.785	0.743	0.803
Group C2	0.581	0.782	0.769	0.693	0.718

A1 = No Fracture, No Risk Factors; A2 = No Fracture; + Risk Factors; A3 = + Fracture, No Risk Factors; A4 = + Fracture, + Risk Factors.
B1 = MH DXA Centre; B2 = MPH DXA Centre; B3 = SH DXA Centre
C1 = Not Taking Osteoporosis Medication; C2 = Taking Osteoporosis Medication.

Discussion

The OSTi is a simple but efficient tool which can be used to help identify men and women who are likely to have osteoporosis by DXA criteria, which has been validated in multiple populations around the world (8, 10, 18, 19, 21-28, 36, 37). In this paper, we have found OSTi produced similar results when applied to a large population referred for DXA scanning at 3 centres in the West of Ireland. The results of our study correlate with other studies where people with a lower OSTi value have a greater likelihood of having a DXA T-score in the osteoporotic range. Our results were robust and verified in multiple subgroup analyses, including those without fractures or risk factors other than age or weight, those with additional clinical risk

factors such as having an illness or taking a medication known to increase the risk of osteoporosis or fracture; those with a prior fragility fracture but without other clinical risk factors; and those with a prior fragility fracture but having other clinical risk factors. These results could help improve the effectiveness of DXA scanning programmes for screening older Irish adults by helping to predict the risk of osteoporosis using a patient's age and weight.

Access to quality DXA scanning and diagnostics is a global prerogative for those at high risk for, or with osteoporosis (16). Unfortunately access is limited in many parts of the world (18, 35-37), and quality receives less attention (16, 17). Although many guidelines recommend DXA testing for patients with diseases or those taking medications which are known to increase the risk of bone loss or fracture, deciding who should be screened for osteoporosis is more contentious (7, 13, 14). A recent update from the United States Preventive Services Task Force concluded that although there was good evidence that BMD is useful for predicting fractures and diagnosing osteoporosis in both men and women, they concluded that there was insufficient evidence to support screening in men (38). This contrasts with the ISCD position which recommends screening in men on the basis of age alone, but at a higher threshold than women (15). Use of OSTi improves the evidence for screening men, by reducing the number needed to screen based on age alone. Other studies have shown that the use of OSTi rather than age alone in older men could result in a 35% reduction in the number needed to be referred for DXA scanning, whilst <1% of

those with osteoporosis would be missed (10). Similarly amongst women, the number needed to be scanned can be greatly reduced (8, 37).

Many algorithms have been evaluated for identifying those with osteoporosis and/or predicting a person's risk of fracture (9, 13). All have strengths and limitations, and more complex methods may not outperform simpler ones (7-9). An important distinction must be made between the identification of those with a low BMD or a DXA classification of osteoporosis and those who fracture, as they are not the same. OSTi was developed to identify those with low BMD, not fractures (18). Fractures are clinical events, which may be partially consequential to having low BMD (2, 12, 35, 39). In addition, measurement of BMD in people who have already had a fracture is generally not considered screening. OSTi has outperformed some algorithms which have also included both BMD and prior fracture (10, 25). Earlier studies have included populations with prevalent fractures ranging from 1% to 17% (18, 21, 23, 25-28, 36). More than a quarter of our cohort had prevalent fractures. Although OSTi performed well in both genders, it was superior in women and in those without prior fracture.

Several studies include men and women taking osteoporosis treatment. The proportion of women taking estrogen therapy ranges from 7% to 49% (18, 21, 25, 27, 28). Since the effect of estrogen on BMD is similar to other anti-resorptive medications it should not be discounted (39, 40). In our cohort 11.5% of women and 6.3% of men were taking osteoporosis medication. OSTi performed slightly better amongst those not on these treatments, particularly at the lumbar spine in men.

Other clinical risk factors may be important, and should not be overlooked (34). Taken together these results suggest that OSTi performs better as a screening tool to aid decisions on who should be considered for a screening DXA scan, such as those without a prior fracture or who are not already on osteoporosis treatment.

The assessment of osteoporosis and appropriate referral for DXA screening can help optimise its use in practice. Although considerable progress has been made, osteoporosis prevalence, acknowledgement and its consequences have been described as a 'crisis' (41, 42). Others opine that osteoporosis care is heading into a 'perfect storm' (43), while more declare there is a 'war' going on against DXA (44). Addressing patient concerns must be part of a strategy to resolve such crises (42). The best use of DXA requires testing the right people, and in equal measure avoiding testing the wrong people where possible (35). This can significantly optimise service use, reduce waiting times and improve the quality of service being delivered (7, 10, 18, 36), particularly in parts of the world where such services are constrained. In one of our centres DXA waiting times increased to more than 10 years as a result of staff shortages and re-allocation, so knowing who to test and who not to test is critical.

Our study has important limitations. Firstly, our population may not be reflective of a nationally representative sample, since all patients were referred for a medical reason. However, a significant proportion (29%) had no major risk factors other than age or low body weight, so the results likely have relevance. In addition, we have also compared these results to people taking medications or having a disorder known to cause BMD loss and the results were similar, suggesting they may

be applicable to a much wider population. Men represent a much small proportion of our study population, particularly those taking osteoporosis medication at the time of their first DXA scan. Although not as large as some, we have greater numbers and a greater spectrum of ages than others (10, 19, 22, 23, 26). We used a DXA T-score as the standard for assessing the sensitivity and specificity of the OSTi, but the selection of a T-score threshold has been described as 'too easy' and is not without its flaws (45). Since the majority of fractures occur in people without an osteoporotic T-score, studies of effective methods to identify that group are needed (7, 13, 46, 47). ROC curves have distinct advantages for assessing the accuracy and usefulness of diagnostic tests, although they too have limitations including interpretation of their performance in particular circumstances and when comparing the accuracy of different tests (48). A clear understanding of their properties and how to analyse them, as well as the methods and assumptions used by the software, is required in order to apply the results in practice (49). Notwithstanding, our results are in line with other studies, and using similar analyses helps address some of these concerns. We did not compare OSTi to other instruments in our population, since others have shown comparable or better results with OSTi we see little role for employing more complex ones at present (7, 10, 14, 25, 27). We have not calibrated the difference between machines using the same DXA phantom supplied by the manufacturer due to the distance between centres, and therefore cannot compare values between the different DXA scanners.

Conclusion

In this study, we have shown the value of OSTi for deciding which Irish men and women aged over 40 years should be considered for DXA screening. Presently, younger heavier people are far less likely to have osteoporosis, particularly in the absence of an underlying illness or medication, which can adversely affect the skeleton. Although OSTi performed well across a spectrum of populations, we found quite a wide spectrum of BMD values for any given OSTi threshold. This makes deciding an optimum threshold more difficult, but for the first time a large study has been performed on men and women in Ireland which has carefully examined one of the most efficient and widely studied algorithms world-wide. These results can help address national concerns about DXA use in public clinics where waiting times far exceed their private counterparts.

Conflict of Interest Disclosures

The authors declare that there is no conflict of interests regarding the publication of this paper.

References

1. Borgstrom F, Karlsson L, Ortsater G, Norton N, Halbout P, Cooper C, et al. Fragility fractures in Europe: burden, management and opportunities. Arch Osteoporos. 2020;15(1):59.
2. Compston JE, McClung MR, Leslie WD. Osteoporosis. Lancet. 2019;393(10169):364-76.
3. Tarrant SM, Balogh ZJ. The Global Burden of Surgical Management of Osteoporotic Fractures. World J Surg. 2020;44(4):1009-19.

4. Pisani P, Renna MD, Conversano F, Casciaro E, Di Paola M, Quarta E, et al. Major osteoporotic fragility fractures: Risk factor updates and societal impact. World journal of orthopedics. 2016;7(3):171.
5. International Osteoporosis Foundation. Broken bones, broken lives: a roadmap to solve the fragility fracture crisis in Europe: International Osteoporosis Foundation; 2018 [Available from: http://share.iofbonehealth.org/EU-6-Material/Reports/IOF%20Report_EU.pdf.
6. Curtis EM, Woolford S, Holmes C, Cooper C, Harvey NC. General and Specific Considerations as to why Osteoporosis-Related Care Is Often Suboptimal. Curr Osteoporos Rep. 2020;18(1):38-46.
7. Crandall CJ, Ensrud KE. Osteoporosis Screening in Younger Postmenopausal Women. JAMA. 2020;323(4):367-8.
8. Nayak S, Edwards DL, Saleh AA, Greenspan SL. Systematic review and meta-analysis of the performance of clinical risk assessment instruments for screening for osteoporosis or low bone density. Osteoporos Int. 2015;26(5):1543-54.
9. Rubin KH, Friis‐Holmberg T, Hermann AP, Abrahamsen B, Brixen K. Risk assessment tools to identify women with increased risk of osteoporotic fracture: complexity or simplicity? A systematic review. Journal of Bone and Mineral Research. 2013;28(8):1701-17.
10. Diem SJ, Peters KW, Gourlay ML, Schousboe JT, Taylor BC, Orwoll ES, et al. Screening for Osteoporosis in Older Men: Operating Characteristics of Proposed Strategies for Selecting Men for BMD Testing. J Gen Intern Med. 2017;32(11):1235-41.
11. Kanis JA, Cooper C, Rizzoli R, Abrahamsen B, Al-Daghri NM, Brandi ML, et al. Identification and management of patients at increased risk of osteoporotic fracture: outcomes of an ESCEO expert consensus meeting. Osteoporosis International. 2017;28(7):2023-34.
12. Kanis J, Odén A, Johnell O, Johansson H, De Laet C, Brown J, et al. The use of clinical risk factors enhances the performance of BMD in the prediction of hip and osteoporotic fractures in men and women. Osteoporosis International. 2007;18(8):1033-46.
13. Leslie WD, Crandall CJ. Population-Based Osteoporosis Primary Prevention and Screening for Quality of Care in Osteoporosis, Current Osteoporosis Reports. Curr Osteoporos Rep. 2019;17(6):483-90.
14. Crandall CJ, Larson J, Manson JE, Cauley JA, LaCroix AZ, Wactawski-Wende J, et al. A Comparison of US and Canadian Osteoporosis Screening and Treatment Strategies in Postmenopausal Women. J Bone Miner Res. 2019;34(4):607-15.
15. Densitometry ISfC. ISCD Official Positions On Line: ISCD; 2019 [updated 28th May 2019; cited 2019. Available from: https://iscd.org/learn/official-positions/.
16. Lewiecki EM, Binkley N, Morgan SL, Shuhart CR, Camargos BM, Carey JJ, et al. Best Practices for Dual-Energy X-ray Absorptiometry Measurement and Reporting: International Society for Clinical Densitometry Guidance. J Clin Densitom. 2016;19(2):127-40.
17. Clynes MA, Westbury LD, Dennison EM, Kanis JA, Javaid MK, Harvey NC, et al. Bone densitometry worldwide: a global survey by the ISCD and IOF. Osteoporos Int. 2020;31(9):1779-86.
18. Koh LK, Sedrine WB, Torralba TP, Kung A, Fujiwara S, Chan SP, et al. A simple tool to identify asian women at increased risk of osteoporosis. Osteoporos Int. 2001;12(8):699-705.

19. Lynn HS, Woo J, Leung PC, Barrett-Connor EL, Nevitt MC, Cauley JA, et al. An evaluation of osteoporosis screening tools for the osteoporotic fractures in men (MrOS) study. Osteoporos Int. 2008;19(7):1087-92.
20. Beaudoin C, Moore L, Gagne M, Bessette L, Ste-Marie LG, Brown JP, et al. Performance of predictive tools to identify individuals at risk of non-traumatic fracture: a systematic review, meta-analysis, and meta-regression. Osteoporos Int. 2019;30(4):721-40.
21. Richy F, Gourlay M, Ross P, Sen S, Radican L, De Ceulaer F, et al. Validation and comparative evaluation of the osteoporosis self-assessment tool (OST) in a Caucasian population from Belgium. QJM: An International Journal of Medicine. 2004;97(1):39-46.
22. Adler RA, Tran MT, Petkov VI. Performance of the Osteoporosis Self-assessment Screening Tool for osteoporosis in American men. Mayo Clin Proc. 2003;78(6):723-7.
23. Bhat KA, Kakaji M, Awasthi A, Kumar K, Mishra K, Shukla M, et al. Utility of Osteoporosis Self-Assessment Tool as a Screening Tool for Predicting Osteoporosis in Indian Men. J Clin Densitom. 2017;20(2):160-3.
24. Chandran M, Chin YA, Choo KS, Ang WC, Huang XF, Liu XM, et al. Comparison of the Osteoporosis Self-Assessment Tool for Asians and the fracture risk assessment tool - FRAX to identify densitometric defined osteoporosis: A discriminatory value analysis in a multi-ethnic female population in Southeast Asia. Osteoporos Sarcopenia. 2020;6(2):53-8.
25. Crandall CJ, Larson J, Gourlay ML, Donaldson MG, LaCroix A, Cauley JA, et al. Osteoporosis screening in postmenopausal women 50 to 64 years old: comparison of US Preventive Services Task Force strategy and two traditional strategies in the Women's Health Initiative. J Bone Miner Res. 2014;29(7):1661-6.
26. Ghazi M, Mounach A, Nouijai A, Ghozlani I, Bennani L, Achemlal L, et al. Performance of the osteoporosis risk assessment tool in Moroccan men. Clin Rheumatol. 2007;26(12):2037-41.
27. Pecina JL, Romanovsky L, Merry SP, Kennel KA, Thacher TD. Comparison of Clinical Risk Tools for Predicting Osteoporosis in Women Ages 50-64. J Am Board Fam Med. 2016;29(2):233-9.
28. Geusens P, Hochberg MC, van der Voort DJ, Pols H, van der Klift M, Siris E, et al. Performance of risk indices for identifying low bone density in postmenopausal women. Mayo Clin Proc. 2002;77(7):629-37.
29. Kanis JA, Oden A, McCloskey EV, Johansson H, Wahl DA, Cooper C, et al. A systematic review of hip fracture incidence and probability of fracture worldwide. Osteoporos Int. 2012;23(9):2239-56.
30. Kelly MA, McGowan B, McKenna MJ, Bennett K, Carey JJ, Whelan B, et al. Emerging trends in hospitalisation for fragility fractures in Ireland. Ir J Med Sci. 2018;187(3):601-8.
31. Lippuner K, Popp AW, Schwab P, Gitlin M, Schaufler T, Senn C, et al. Fracture hospitalizations between years 2000 and 2007 in Switzerland: a trend analysis. Osteoporosis International. 2011;22(9):2487-97.
32. McCabe E, Ibrahim A, Singh R, Kelly M, Armstrong C, Heaney F, et al. A systematic review of the Irish osteoporotic vertebral fracture literature. Arch Osteoporos. 2020;15(1):34.

33. E E, Wang T, Yang L, Dempsey M, Brennan A, Yu M, et al. The Irish dual-energy X-ray absorptiometry (DXA) Health Informatics Prediction (HIP) for Osteoporosis Project. BMJ Open. 2020(e040488).
34. E E, Wang T, Yang L, Dempsey M, Brennan A, Yu M, et al. Machine Learning Can Improve Clinical Detection of Low BMD: The DXA-HIP Study. J Clin Densitom. 2020.
35. Mohammad A, Aamir MU, Mooney S, Coughlan RJ, Carey JJ. Appropriateness of referrals to a tertiary referral centre for bone mineral density testing. Ir J Med Sci. 2014;183(4):533-7.
36. Saravi FD. Osteoporosis self-assessment tool performance in a large sample of postmenopausal women of mendoza, Argentina. J Osteoporos. 2013;2013:150154.
37. Subramaniam S, Ima-Nirwana S, Chin KY. Performance of Osteoporosis Self-Assessment Tool (OST) in Predicting Osteoporosis-A Review. Int J Environ Res Public Health. 2018;15(7).
38. Force USPST, Curry SJ, Krist AH, Owens DK, Barry MJ, Caughey AB, et al. Screening for Osteoporosis to Prevent Fractures: US Preventive Services Task Force Recommendation Statement. JAMA. 2018;319(24):2521-31.
39. Kendler DL, Compston J, Carey JJ, Wu CH, Ibrahim A, Lewiecki EM. Repeating Measurement of Bone Mineral Density when Monitoring with Dual-energy X-ray Absorptiometry: 2019 ISCD Official Position. J Clin Densitom. 2019;22(4):489-500.
40. Carey JJ, Delaney MF. Utility of DXA for monitoring, technical aspects of DXA BMD measurement and precision testing. Bone. 2017;104:44-53.
41. Roux C, Briot K. Osteoporosis in 2017: Addressing the crisis in the treatment of osteoporosis. Nat Rev Rheumatol. 2018;14(2):67-8.
42. Abbasi J. Amid Osteoporosis Treatment Crisis, Experts Suggest Addressing Patients' Bisphosphonate Concerns. JAMA. 2018;319(24):2464-6.
43. Hamdy RC. Osteoporosis: Heading Towards the Perfect Storm. J Clin Densitom. 2018;21(1):1-2.
44. Lewiecki EM, Binkley N, Bilezikian JP. Stop the war on DXA! Ann N Y Acad Sci. 2018;1433(1):12-7.
45. Mandell BF. Surrogate markers are not 'one-size-fits-all'. Cleve Clin J Med. 2006;73(5):416.
46. Wainwright SA, Marshall LM, Ensrud KE, Cauley JA, Black DM, Hillier TA, et al. Hip fracture in women without osteoporosis. J Clin Endocrinol Metab. 2005;90(5):2787-93.
47. Siris ES, Chen YT, Abbott TA, Barrett-Connor E, Miller PD, Wehren LE, et al. Bone mineral density thresholds for pharmacological intervention to prevent fractures. Arch Intern Med. 2004;164(10):1108-12.
48. Obuchowski NA. Receiver operating characteristic curves and their use in radiology. Radiology. 2003;229(1):3-8.
49. Obuchowski NA. ROC analysis. AJR Am J Roentgenol. 2005;184(2):364-72.