Journal of Clinical Densitometry: Assessment & Management of Musculoskeletal Health, vol. 26, no. 3, 101378, 2023

1094-6950/26:101378/$36.00
https://doi.org/10.1016/j.jocd.2023.101378

Original Article

FRAX Adjustment by Trabecular Bone Score with or Without Bone Mineral Density: The Manitoba BMD Registry

William D. Leslie,[1] Neil Binkley,[2] Eugene V. McCloskey,[3,4] Helena Johansson,[3,5] Nicholas C. Harvey,[6,7] Mattias Lorentzon,[5,8,9] John A. Kanis,[3,4] and Didier Hans[10]*

[1] Department of Internal Medicine, University of Manitoba, Winnipeg, Manitoba, Canada; [2] University of Wisconsin School of Medicine and Public Health, Madison, WI, USA; [3] Centre for Metabolic Bone Diseases, University of Sheffield Medical School, UK; [4] MRC Versus Arthritis Centre for Integrated Research in Musculoskeletal Ageing, Department of Oncology & Metabolism, University of Sheffield, UK; [5] Mary McKillop Institute for Health Research, Australian Catholic University, Melbourne; [6] MRC Lifecourse Epidemiology Centre, University of Southampton, Southampton, UK; [7] NIHR Southampton Biomedical Research Centre, University of Southampton and University Hospital Southampton NHS Foundation Trust, Southampton, UK; [8] Sahlgrenska Osteoporosis Centre, University of Gothenburg, Gothenburg, Sweden; [9] Region Västra Götaland, Sahlgrenska University Hospital, Mölndal, Sweden; and [10] Bone and Joint Department, Lausanne University Hospital, Lausanne, Switzerland

Abstract

Trabecular bone score (TBS), a texture measure derived from spine dual-energy x-ray absorptiometry (DXA) images, is a FRAX®-independent risk factor for fracture. The TBS adjustment to FRAX assumes the presence of femoral neck BMD in the calculation. However, there are many individuals in whom hip DXA cannot be acquired. Whether the TBS-adjustment would apply to FRAX probabilities calculated without BMD has not been studied. The current analysis was performed to evaluate major osteoporotic fracture (MOF) and hip fracture risk adjusted for FRAX with and without femoral neck BMD. The study cohort consisted of 71,209 individuals (89.8% female, mean age 64.0 years). During mean follow-up 8.7 years, 6743 (9.5%) individuals sustained one or more incident MOF, of which 2037 (2.9%) sustained a hip fracture. Lower TBS was significantly associated with increased fracture risk when adjusted for FRAX probabilities, with a slightly larger effect when BMD was not included. Inclusion of TBS in the risk calculation gave a small but significant increase in stratification for fracture probabilities estimated with and without BMD. Calibration plots showed very minor deviations from the line of identity, indicating overall good calibration. In conclusion, the existing equations for incorporating TBS in FRAX estimates of fracture probability work similarly when femoral neck BMD is not used in the calculation. This potentially extends the range of situations where TBS can be used clinically to those individuals in whom lumbar spine TBS is available but femoral neck BMD is not available.

Keywords: Osteoporosis; Fracture risk assessment; Dual-energy x-ray absorptiometry; Trabecular bone score; Bone mineral density.

Introduction

Dual-energy x-ray absorptiometry (DXA) is widely used in clinical practice for measurement of bone mineral density (BMD) in order to diagnose osteoporosis, determine need for treatment and monitor for change over

Received 02/14/23; Revised 04/16/23; Accepted 04/24/23.
*Corresponding author at: Department of Medicine (C5121) 409 Tache Avenue, Winnipeg, Manitoba R2H 2A6, Canada. E-mail: bleslie@sbgh.mb.ca

time (1,2). The femoral neck is the reference site for osteoporosis diagnosis and for estimating 10-year probability of major osteoporotic fracture (MOF; composite of hip, clinical spine, distal forearm, proximal humerus) and 10-year probability of hip fracture with the FRAX® tool (3), (4). The FRAX tool considers multiple clinical risk factors and optionally BMD at the femoral neck, and is widely used in clinical practice (5-9).

More recently, lumbar spine trabecular bone score (TBS), a grey-level texture measure derived from spine dual-energy x-ray absorptiometry (DXA) images, has been shown to be a FRAX-independent risk factor for fracture (10). A TBS-adjusted FRAX score, which can be computed through the FRAX website and through software on the DXA instrument, incrementally improves fracture prediction compared with the conventional FRAX score (11,12). The use of TBS-adjusted FRAX for guiding patient management is supported by guidelines from several organizations (13-15). The derived TBS adjustment assumes availability femoral neck BMD in the calculation since spine DXA required for TBS would usually be performed in conjunction with hip DXA. However, there is an increasing number of older individuals in whom hip DXA cannot be acquired due to severe osteoarthritis, bilateral joint replacements, fractures or other conditions. Lumbar spine TBS may still be available in such individuals, as TBS is relatively unaffected by degenerative changes (16,17).

Whether the TBS-adjustment applied to FRAX calculated without BMD would enhance fracture prediction has not been studied. Since TBS and BMD are only modestly correlated (6.7-10.7% explained variance (18)), it was hypothesized that the existing TBS adjustment for FRAX with BMD would likely also apply to FRAX without BMD. The current analysis was performed to evaluate the effect of TBS and performance of the TBS adjustment on MOF and hip fracture risk adjusted for FRAX with and without femoral neck BMD. This was assessed in the routine clinical practice setting using a large clinical registry that includes all DXA tests for the Province of Manitoba, Canada.

Methods

Study population

The study cohort consisted of all individuals age 40 years or older at the time of baseline spine and hip DXA assessment (designated the index date) through the Manitoba BMD Program. We excluded individuals without healthcare coverage in Manitoba for assessment of fracture outcomes, or when body mass index (BMI) was outside of the manufacture recommended range (15-37 kg/m^2). Since FRAX with BMD is the reference standard for fracture probability assessment, we also excluded cases where femoral neck BMD could not be measured (N=1,051). The study was approved by the Research Ethics Board of the University of Manitoba and the Health Information Privacy Committee of Manitoba Health.

Bone densitometry and trabecular bone score

In Canada, health services including DXA testing are provided to nearly all residents through a single public health care system (19). DXA testing through the Manitoba Density Program has been managed as an integrated program (20). The Manitoba Density Program maintains a database of all DXA results that can be linked with other population-based databases through an anonymous personal identifier. The associated database exceeds 99% in terms of completeness and accuracy (21). All DXA scans were performed with a narrow fan-beam DXA configuration (Prodigy before November 2012, iDXA from November 2012 onwards, GE Healthcare, Madison, WI, USA) and analyzed in accordance with manufacturer recommendations. All DXA images were assessed by International Society for Clinical Densitometry (ISCD) certified physicians. Lumbar spine TBS measurements (L1-L4 without vertebral body exclusions) were retrospectively performed in the Bone Disease Unit at the University Hospital of Lausanne, Switzerland (TBS iNsight Software, Version 3.03, Medimaps Group, Geneva, Switzerland), using anonymized spine DXA files to ensure blinding of the Swiss investigators to all clinical parameters and outcomes. No TBS phantom was available for densitometer cross-calibration given the retrospective study design.

Fracture risk estimation

Ten-year probabilities of MOF and hip fracture were calculated using the standalone desktop version of the fracture risk assessment tool with and without femoral neck BMD, Canadian version (FRAX® Desktop Multi-Patient Entry, version 3.7) (22,23). This FRAX tool has been calibrated using nationwide hip fracture and mortality data (23). Predictions agree closely with observed fracture risk in this population (24,25). Briefly, age, BMI, femoral neck BMD and other data required for calculating fracture risk with FRAX were assessed from on-site measurements (including height and weight), and other necessary information collected directly from subjects through the intake questionnaire at the time of each DXA scan (26). Questionnaire information was supplemented with population-based healthcare data (hospital discharge abstracts, medical claims diagnoses, province-wide retail pharmacy database) as recently described, thereby ensuring complete information for all subjects (27). In addition to conventional FRAX probabilities, we also recalculated MOF and hip fracture probabilities after adjusting for TBS, using previously published equations as implemented through the FRAX website (12).

Fracture outcomes

Manitoba Health records were assessed for the presence of fracture diagnostic codes to March 31, 2018 through a combination of hospital discharge abstracts (diagnoses and procedures coded using the International

Classification of Diseases, Ninth Revision, Clinical Modification [ICD-9-CM] prior to 2004 and International Classification of Diseases, Tenth Revision, Canadian Enhancements [ICD-10-CA] thereafter) and physician billing claims (coded using ICD-9-CM). Analysis was based upon incident hip, clinical vertebral, forearm, and humerus fracture diagnostic codes (collectively designated MOF) that did not appear in association with high trauma codes using previously validated algorithms *(28,29)*. We required that hip and forearm fractures codes be associated with site-specific fracture reduction, fixation or casting codes to enhance specificity for an acute fracture event. To minimize potential overcounting of incident fractures, we conservatively required that there be no hospitalization or physician visit(s) with the same fracture type in the six months preceding an incident fracture diagnosis.

Statistical analyses

Statistical analyses were performed with IBM SPSS for Windows (Version 28). Descriptive statistics for demographic and baseline characteristics are presented as mean ± SD for continuous variables or number (%) for categorical variables. In Cox proportional hazards models we estimated hazard ratios (HR) with 95% confidence intervals (CI) per SD decrease in TBS adjusted for FRAX probabilities with and without BMD (FRAX probabilities log-transformed due to a skewed distribution). The proportional hazards assumption was confirmed. Area underneath the curve (AUC) for incident fracture risk stratification was estimated from the conventional FRAX probabilities without TBS, and then for the TBS-adjusted FRAX probabilities. The incremental change in AUC before versus after applying the TBS adjustment was calculated, and significance was tested using the Hanley-McNeil method given the correlated measures *(30)*. We also derived calibration slopes for FRAX with and without BMD, before and after applying the TBS adjustment, using risk deciles.

Results

Table 1 summarizes the baseline study population characteristics. The study cohort consisted of 71,209 individuals, mean age 64.0 years (SD 10.7), predominantly White females, but with 7292 (10.2%) males, 2506 (3.5%) non-White individuals and 7208 (10.1%) with diabetes. Mean TBS was 1.257 (SD 0.121). During follow-up (mean 8.7 years), 6743 (9.5%) individuals sustained one or more incident MOF, of which 2037 (2.9%) sustained a hip fracture.

Table 1
Study population characteristics (N=71,209).

Characteristic	
Age, years	64 .0 ± 10.7
Sex male	7292 (10.2)
Race/ethnicity non-White	2506 (3.5)
Diabetes	7208 (10.1)
BMI, kg/m^2	26.4 ± 4.4
Trabecular bone score L1-L4, unitless	1.257 ± 0.121
FRAX with BMD, MOF %	10.0 ± 7.0
TBS-adjusted FRAX with BMD, MOF %	10.9 ± 7.3
FRAX without BMD, MOF %	11.0 ± 8.2
TBS-adjusted FRAX without BMD. MOF %	11.7 ± 8.2
FRAX with BMD, HIP %	2.3 ± 3.8
TBS-adjusted FRAX with BMD, HIP %	2.5 ± 3.9
FRAX without BMD, HIP %	3.1 ± 4.9
TBS-adjusted FRAX without BMD. HIP %	3.3 ± 4.7
Observation time, years	8.7 ± 5.2
Incident MOF	6743 (9.5)
Incident hip fracture	2037 (2.9)

Data are Mean ± SD or N (percent). BMI, body mass index. MOF, major osteoporotic fracture.

As seen in Table 2, lower TBS was significantly associated with increased fracture risk when adjusted for FRAX probabilities, with a slightly stronger association when BMD was not included. For incident MOF the HR per SD decrease in TBS was 1.23 (95% CI 1.20-1.26) without BMD and 1.17 (95% CI 1.14-1.20) with BMD. For incident hip fracture the HR per SD decrease in TBS was slightly greater at 1.26 (95% CI 1.21-1.32) without BMD, and only 1.08 (95% CI 1.03-1.13) with BMD.

Table 2
FRAX-adjusted hazard ratios (HR, 95% CI) per SD decrease in spine trabecular bone score (TBS) for incident major osteoporotic fracture (MOF) and incident hip fracture (HIP).

Adjusted for:	MOF HR (95% CI) per SD decrease in TBS	HIP HR (95% CI) per SD decrease in TBS
FRAX with BMD	1.17 (1.14-1.20)	1.08 (1.03-1.13)
FRAX without BMD	1.23 (1.20-1.26)	1.26 (1.21-1.32)

Table 3
Incremental change in area under the curve (AUC, 95% CI) for incident major osteoporotic fracture (MOF) and incident hip fracture (HIP) for FRAX before versus after applying the spine trabecular bone score (TBS) adjustment.

	AUC (95% CI) For incident MOF	ΔAUC, FRAX without vs with TBS	p-value, FRAX without vs with TBS
FRAX with BMD, MOF	0.664 (0.658-0.670)	NA	NA
TBS-adjusted FRAX with BMD, MOF	0.673 (0.667-0.679)	0.009	<0.001
FRAX without BMD, MOF	0.639 (0.631-0.647)	NA	NA
TBS-adjusted FRAX without BMD, MOF	0.654 (0.646-0.662)	0.015	<0.001
	AUC (95% CI) For incident HIP	ΔAUC, FRAX without vs with TBS	p-value, FRAX without vs with TBS
FRAX with BMD, HIP	0.792 (0.784-0.800)	NA	NA
TBS-adjusted FRAX with BMD, HIP	0.794 (0.786-0.802)	0.002	0.017
FRAX without BMD, HIP	0.766 (0.756-0.776)	NA	NA
TBS-adjusted FRAX without BMD, HIP	0.774 (0.764-0.784)	0.008	<0.001

AUC for incident fracture risk stratification is summarized in Table 3. AUCs were slightly greater for FRAX with versus without BMD. The inclusion of TBS in the risk calculation gave a small but statistically significant incremental increase in risk stratification for MOF risk estimated with BMD (+0.009), and slightly greater for risk estimated without BMD (+0.015). The incremental improvement in hip fracture risk stratification for FRAX with BMD was small (+0.002) but larger without BMD (+0.008). Incremental change in AUC stratified by sex, age, ethnicity and diabetes status is provided in Supplmenetal Table 1.

Calibration plots in Fig. 1 showed very minor deviations from the line of identity, indicating overall good calibration. For incident MOF, calibration slopes ranged from 0.92 (unadjusted FRAX with BMD) to 0.88 (TBS-adjusted FRAX without BMD). For incident hip fracture, calibration slopes ranged from 1.09 (unadjusted FRAX with BMD) to 1.01 (unadjusted FRAX without and TBS-adjusted FRAX without BMD).

Discussion

We found that lumbar spine TBS improved major osteoporotic fracture and hip fracture prediction when adjusted for FRAX probabilities. Moreover, when the method developed for TBS-adjusting FRAX probabilities with BMD was applied to FRAX probabilities without BMD it gave a slightly greater improvement in fracture risk stratification while maintaining good calibration.

These findings are not unexpected. The inclusion of BMD in FRAX probabilities is known to improve risk prediction compared with scores estimated from clinical risk factors alone *(31)*. Since TBS shows a low degree of correlation with BMD measurements *(10)*, an equation for adjusting FRAX probabilities that includes BMD should be similar to an equation derived without BMD. Of course, it remains possible that such an equation could be further optimized, but that was not the aim of the current analysis.

Strengths of this study include a large well-characterized cohort and longitudinal assessment of incident fractures using validated data sources and definitions *(28,29)*. Limitations are also acknowledged. Only a single DXA manufacturer was assessed, although the TBS-adjustment to FRAX has been validated in a meta-analysis that included other manufactures *(11)*. Fracture outcomes were assessed from administrative health care data rather than direct x-ray review, but definitions used have been validated against x-rays *(28)*. Those with bilateral hip replacements will be at low risk for typical hip fractures but remain at risk for periprosthetic femoral fractures *(32)*; it is uncertain how this would impact absolute risk estimation. The current TBS algorithm uses BMI as a proxy for the effect of tissue thickness; the FRAX adjustment may change when an updated algorithm that incorporates tissue thickness directly in the TBS measurement becomes available *(33)*. The additional cost versus incremental benefit of adding TBS needs to be considered in future analyses. Finally, this study was limited to a single FRAX tool for Canada and a population predominantly comprised of White females. This warrants further validation in other populations, ideally with greater non-White and male representation, although to date most data suggest that TBS similarly predicts fractures in non-White populations and males *(11,34)*.

In conclusion, existing equations for incorporating TBS in fracture probability estimates with FRAX works similarly well when femoral neck BMD is not used in the calculation. This potentially extends the range of situations where TBS can be used clinically to individuals in whom lumbar spine TBS is available but femoral neck BMD is not available, and requires only

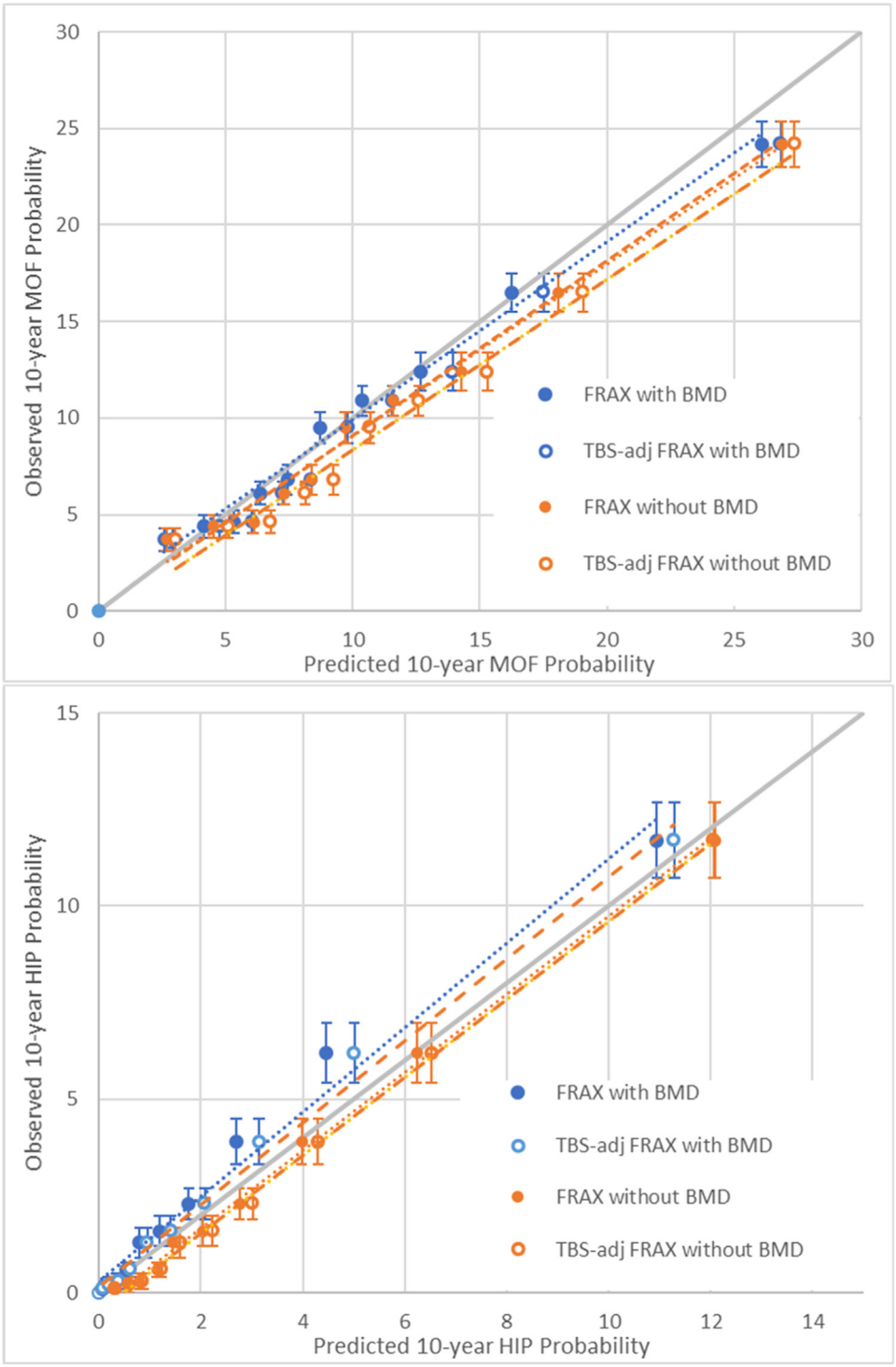

Fig. 1. Calibration plots by decile for predicted (X-axis) versus observed (Y-axis, 95% CI bars) 10-year probability of major osteoporotic fracture (MOF, upper panel) and hip fracture probability (HIP, lower panel). Solid circles are for FRAX before and open circles are for FRAX after applying the trabecular bone score (TBS) adjustment. Line of identity in solid grey.

minor modifications to the FRAX website and/or TBS software.

Funding

This study had no external funding body.

Disclosures

William Leslie, Helena Johansson: No conflicts of interest.

Neil Binkley: Nothing to declare for the context of this paper; research funding from Radius; consultant Amgen.

Eugene McCloskey: Nothing to declare for FRAX and the context of this paper, but numerous ad hoc consultancies/ speaking honoraria and/or research funding from Amgen, Bayer, General Electric, GSK, Hologic, Lilly, Merck Research Labs, Novartis, Novo Nordisk, Nycomed, Ono, Pfizer, ProStrakan, Roche, Sanofi-Aventis, Servier, Tethys, UBS and Warner-Chilcott.

Nicholas Harvey: Nothing to declare for the context of this paper, but has received consultancy/ lecture fees/ honoraria/ grant funding from Alliance for Better Bone Health, Amgen, MSD, Eli Lilly, Servier, Shire, UCB, Kyowa Kirin, Consilient Healthcare and Internis Pharma.

Mattias Lorentzon: Lecture fees from Amgen, Lilly, Meda, Renapharma, UCB Pharma, and consulting fees from Amgen, Radius Health, UCB Pharma, Renapharma, and Consilient Health, all outside the presented work.

John A. Kanis: Architect of FRAX. Nothing to declare for the context of this paper.

Didier Hans: Co-ownership in the TBS patent. Stock options or royalties: Med-Imaps. Research grants: Amgen, Agnovos, GE Healthcare.

Roles

Authors' roles: conception, design, data analysis, drafting the article (WDL), interpretation of data (All Authors); critically revising the article for important intellectual content (All Authors); final approval of the version to be published (All Authors); and agreement to be accountable for all aspects of the work (All Authors). WDL had full access to all the data in the study and takes the responsibility for the integrity of the data and the accuracy of the data analysis.

Data Availability Statement

Data sharing is not permitted under the Researcher Agreement with Manitoba Health and Seniors Care (MHASC). However, researchers may apply for data access through the Health Research Ethics Board for the University of Manitoba and the Health Information and Privacy Committee of MHASC.

Acknowledgments

The authors acknowledge the Manitoba Centre for Health Policy for use of data contained in the Population Health Research Data Repository (HIPC 2016/2017- 29). The results and conclusions are those of the authors and no official endorsement by the Manitoba Centre for Health Policy, Manitoba Health, Healthy Living, and Seniors, or other data providers is intended or should be inferred. This article has been reviewed and approved by the members of the Manitoba Bone Density Program Committee.

Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.jocd.2023.101378.

References

1. Cummings SR, Bates D, Black DM. 2002 Clinical use of bone densitometry: scientific review. JAMA 288(15):1889–1897.
2. Lewiecki EM, Gordon CM, Baim S, Leonard MB, Bishop NJ, Bianchi ML, et al. 2008 International Society for Clinical Densitometry 2007 Adult and Pediatric Official Positions. Bone 43(6):1115–1121.
3. Kanis JA, McCloskey EV, Johansson H, Oden A, Melton L. J. 3rd, Khaltaev N. 2008 A reference standard for the description of osteoporosis. Bone 42(3):467–475.
4. Kanis JA. 2007 Assessment of osteoporosis at the primary health-care level. Published by the University of Sheffield.; 2007. Technical Report. Accessible at http://www.shef.ac.uk/FRAX/pdfs/WHO_Technical_Report.pdf.
5. The North American Menopause S. Management of osteoporosis in postmenopausal women: the 2021 position statement of The North American Menopause Society. Menopause 28(9):973–997.
6. Camacho PM, Petak SM, Binkley N, Diab DL, Eldeiry LS, Farooki A, et al. 2020 American Association of Clinical Endocrinologists/American College of Endocrinology Clinical Practice Guidelines for the Diagnosis and Treatment of Postmenopausal Osteoporosis-2020 Update. Endocr Pract 26(Suppl 1):1–46.
7. Compston J, Cooper A, Cooper C, Gittoes N, Gregson C, Harvey N, et al. 2017 UK clinical guideline for the prevention and treatment of osteoporosis. Arch Osteoporos 12 (1):43.
8. Cosman F, de Beur SJ, LeBoff MS, Lewiecki EM, Tanner B, Randall S, et al. 2014 Clinician's Guide to Prevention and Treatment of Osteoporosis. Osteoporos Int 25 (10):2359–2381.
9. Kanis JA, Cooper C, Rizzoli R, Reginster JY. 2019 Scientific Advisory Board of the European Society for Clinical Economic Aspects of Osteoporosis and Osteoarthritis and the Committees of Scientific Advisors and National Societies of the International Osteoporosis Foundation. Executive summary of European guidance for the diagnosis and management of osteoporosis in postmenopausal women. Aging Clin Exp Res.
10. Silva BC, Leslie WD. 2019 Trabecular Bone Score editor. In: Primer on the metabolic bone diseases and disorders of

mineral metabolism, Bilezikian JP, ed. Ninth edition, John Wiley & Sons, Inc., 277–286.
11. McCloskey EV, Oden A, Harvey NC, Leslie WD, Hans D, Johansson H, et al. 2016 A Meta-Analysis of Trabecular Bone Score in Fracture Risk Prediction and Its Relationship to FRAX. J Bone Miner Res 31(5):940–948.
12. McCloskey EV, Oden A, Harvey NC, Leslie WD, Hans D, Johansson H, et al. 2015 Adjusting fracture probability by trabecular bone score. Calcif Tissue Int 96(6):500–509.
13. Shepherd JA, Schousboe JT, Broy SB, Engelke K, Leslie WD. 2015 Executive Summary of the 2015 ISCD Position Development Conference on Advanced Measures From DXA and QCT: Fracture Prediction Beyond BMD. J Clin Densitom 18(3):274–286.
14. Gregson CL, Armstrong DJ, Bowden J, Cooper C, Edwards J, Gittoes NJL, et al. 2022 UK clinical guideline for the prevention and treatment of osteoporosis. Arch Osteoporos 17 (1):58.
15. LeBoff MS, Greenspan SL, Insogna KL, Lewiecki EM, Saag KG, Singer AJ, et al. 2022 The clinician's guide to prevention and treatment of osteoporosis. Osteoporos Int 33 (10):2049–2102.
16. Kolta S, Briot K, Fechtenbaum J, Paternotte S, Armbrecht G, Felsenberg D, et al. 2014 TBS result is not affected by lumbar spine osteoarthritis. Osteoporos Int 25(6):1759–1764.
17. Anderson KB, Holloway-Kew KL, Mohebbi M, Kotowicz MA, Hans D, Pasco JA. 2018 Is trabecular bone score less affected by degenerative-changes at the spine than lumbar spine BMD? Archives of Osteoporosis 13(1):127.
18. Hans D, Goertzen AL, Krieg MA, Leslie WD. 2011 Bone microarchitecture assessed by TBS predicts osteoporotic fractures independent of bone density: the Manitoba study. J Bone Miner Res 26(11):2762–2769.
19. Roos NP, Shapiro E. 1999 Revisiting the Manitoba Centre for Health Policy and Evaluation and its population-based health information system. Med Care 37(6 Suppl): JS10-JS4.
20. Leslie WD, Metge C. 2003 Establishing a regional bone density program: lessons from the Manitoba experience. J Clin Densitom 6(3):275–282.
21. Leslie WD, Caetano PA, Macwilliam LR, Finlayson GS. 2005 Construction and validation of a population-based bone densitometry database. J Clin Densitom 8(1):25–30.
22. Kanis JA, Oden A, Johansson H, Borgstrom F, Strom O, McCloskey E. 2009 FRAX and its applications to clinical practice. Bone 44(5):734–743.
23. Leslie WD, Lix LM, Langsetmo L, Berger C, Goltzman D, Hanley DA, et al. 2011 Construction of a FRAX(R) model for the assessment of fracture probability in Canada and implications for treatment. Osteoporos Int 22(3):817–827.
24. Leslie WD, Lix LM, Johansson H, Oden A, McCloskey E, Kanis JA, et al. 2010 Independent clinical validation of a Canadian FRAX tool: fracture prediction and model calibration. J Bone Miner Res 25(11):2350–2358.
25. Fraser LA, Langsetmo L, Berger C, Ioannidis G, Goltzman D, Adachi JD, et al. 2011 Fracture prediction and calibration of a Canadian FRAX(R) tool: a population-based report from CaMos. Osteoporos Int 22(3):829–837.
26. Bisson EJ, Finlayson ML, Ekuma O, Marrie RA, Leslie WD. 2019 Accuracy of FRAX(R) in people with multiple sclerosis. J Bone Miner Res.
27. Leslie WD, Morin SN, Lix LM, Niraula S, McCloskey EV, Johansson H, et al. 2019 Performance of FRAX in Women with Breast Cancer Initiating Aromatase Inhibitor Therapy: A Registry-Based Cohort Study. J Bone Miner Res 34 (8):1428–1435.
28. Leslie WD, Epp R, Morin SN, Lix LM. 2021 Assessment of site-specific X-ray procedure codes for fracture ascertainment: a registry-based cohort study. Arch Osteoporos 16 (1):107.
29. Lix LM, Azimaee M, Osman BA, Caetano P, Morin S, Metge C, et al. 2012 Osteoporosis-related fracture case definitions for population-based administrative data. BMC Public Health 12:301.
30. Hanley JA, McNeil BJ. 1983 A method of comparing the areas under receiver operating characteristic curves derived from the same cases. Radiology 148(3):839–843.
31. Kanis JA, Oden A, Johnell O, Johansson H, De Laet C, Brown J, et al. 2007 The use of clinical risk factors enhances the performance of BMD in the prediction of hip and osteoporotic fractures in men and women. Osteoporos Int 18 (8):1033–1046.
32. Abdel MP, Watts CD, Houdek MT, Lewallen DG, Berry DJ. 2016 Epidemiology of periprosthetic fracture of the femur in 32 644 primary total hip arthroplasties: a 40-year experience. The bone & joint journal 98-B(4):461–467.
33. Shevroja E, Aubry-Rozier B, Hans G, Gonzalez- Rodriguez E, Stoll D, Lamy O, et al. 2019 Clinical Performance of the Updated Trabecular Bone Score (TBS) Algorithm, Which Accounts for the Soft Tissue Thickness: The OsteoLaus Study. J Bone Miner Res 34(12):2229–2237.
34. Leslie WD, Binkley N, Hans D. 2023 Ethnicity and Fracture Risk Stratification from Trabecular Bone Score in Canadian Women: The Manitoba BMD Registry. J Clin Densitom 26 (1):83–89.