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RESEARCH ARTICLE

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Effect of BMI-Discordant Abdominal Tissue Thickness on Fracture Probability: A Registry-Based Study

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ABSTRACT

FRAX, which is used to assess fracture probability, considers body mass index (BMI), but BMI may not reflect individual variation in body composition and distribution. We examined the effect of BMI-discordant abdominal thickness on FRAX-derived fracture probability for major osteoporotic fracture (MOF) and hip fracture. We studied 73,105 individuals, mean age 64.2 years. During mean 8.7 years, 7048 (9.6%) individuals sustained incident MOF, including 2155 (3.0%) hip fractures. We defined abdominal thickness index (ATI) as the difference between abdominal thickness measured by dual-energy X-ray absorptiometry (DXA) and thickness predicted by BMI using sex-stratified regression. ATI was categorized from lower (<−2 cm, −2 to −1 cm) to higher (1–2 cm, >+2 cm) with referent around zero (−1 to +1 cm). Adjusted for FRAX probability, increasing ATI was associated with incident MOF and hip fracture ($p < 0.001$). For the highest ATI category, MOF risk was increased (hazard ratio [HR] = 1.23, 95% confidence interval [CI] 1.12–1.35) independent of FRAX probability. Similar findings were noted for hip fracture probability (HR = 1.28, 95% CI 1.09–1.51). There was significant age-interaction with much larger effects before age 65 years (HR = 1.44, 95% CI 1.23–1.69 for MOF; 2.29, 95% CI 1.65–3.18 for hip fracture). In contrast, for the subset of individuals with diabetes, there was also increased risk for those in the lowest ATI category (HR = 1.73, 95% CI 1.12–2.65 for MOF; 2.81, 95% CI 1.59–4.97 for hip fracture). Calibration plots across ATI categories demonstrated deviation from the line of identity in women (calibration slope 2.26 for MOF, 2.83 for hip fracture). An effect of ATI was not found in men, but this was inconclusive as the sex-interaction terms did not show significant effect modification. In conclusion, these data support the need to investigate increased abdominal thickness beyond that predicted by BMI and sex as a FRAX-independent risk factor for fracture. © 2023 The Authors. *Journal of Bone and Mineral Research* published by Wiley Periodicals LLC on behalf of American Society for Bone and Mineral Research (ASBMR).

KEY WORDS: DUAL-ENERGY X-RAY ABSORPTIOMETRY; FRACTURE RISK ASSESSMENT; FRAX; OBESITY; OSTEOPOROSIS

Introduction

Bone mineral density (BMD) measured from dual-energy X-ray absorptiometry (DXA) is used to diagnose osteoporosis, initiate antifracture therapy, and monitor response.[1,2] The FRAX tool estimates 10-year probability of major osteoporotic fracture (MOF; composite of hip, clinical spine, distal forearm, proximal humerus) and 10-year probability of hip fracture from femoral neck BMD (an optional input) and multiple clinical risk factors that are at least partially BMD-independent.[3,4]

FRAX considers body mass index (BMI) as a primary input, but BMI may not always reflect individual variation in body composition and distribution.[5,6] Meta-analysis in adults shows that BMI-defined obesity is positively associated with BMD and is

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protective against osteoporosis.[7] BMI has a more complicated relationship with fractures, which is nonlinear and differs according to fracture site and when adjusted for BMD.[8] Obesity increases the risk for some fracture sites (for example, upper arm) and the protection forwarded by higher BMD is less than expected.[8,9] Visceral adiposity, which is associated with greater waist circumference and abdominal tissue thickness, may have an additional negative impact on bone independent of BMI because of associations with diabetes and systemic inflammation.[10-12] However, the effects of abdominal obesity on BMD and fracture risk have been inconsistent.[13-22] Importantly, none of the previous studies specifically examined clinical implications for FRAX or adjusted for competing mortality, which is increased by central obesity in both women and men even after adjusting for BMI.[23]

The current analysis was performed to evaluate the effect of abdominal tissue thickness that deviates from BMI-predicted abdominal tissue thickness on performance of FRAX for MOF and hip fracture prediction. We conducted this "real world" analysis using a large clinical registry that includes all DXA tests for the Province of Manitoba, Canada.

Materials and Methods

Study population

DXA testing in Manitoba has been managed as an integrated program since 1997.[24] The study cohort consisted of all individuals aged 40 years or older registered for health care in Manitoba undergoing baseline spine and hip DXA assessment (designated the index date). The Manitoba BMD Program database contains all DXA results for the population, has >99% completeness and accuracy, and can be linked with other health services databases through an anonymized (scrambled) personal identifier.[25] Study approval was obtained from the Research Ethics Board of the University of Manitoba, and data access was granted through the Health Information Privacy Committee of Manitoba Health.

Bone densitometry

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). Scans were analyzed in accordance with manufacturer recommendations. All scans were reviewed and reported by International Society for Clinical Densitometry (ISCD)-certified physicians.

Abdominal thickness index

To measure BMD, DXA must correct for soft-tissue attenuation estimated from the non-bone pixels in the region scanned. DXA scans of the lumbar spine therefore provide a direct measure of soft-tissue thickness. We obtained average abdominal tissue thickness from the spine DXA image as automatically measured by the densitometer software (GE enCORE version 14.x) and routinely displayed in the text at the bottom of all DXA reports. DXA-derived tissue thickness shows a high level of agreement with waist circumference (female R^2 0.90, male R^2 0.88),[26] is associated with diabetes risk,[27] and shows high test–retest repeatability with same-day repositioning tissue thickness precision (root mean square) of 0.19 cm and coefficient of variation (CV) 1.0%.[27] After confirming linear correlations between BMI and average tissue thickness, we developed sex-specific prediction equations for average tissue thickness from BMI. We then defined an index of BMI-discordant abdominal thickness, designated abdominal thickness index (ATI), as the difference between measured abdominal thickness from spine DXA and thickness predicted from BMI and sex. This difference was categorized from lower ATI (<−2 cm, −2 to −1 cm) to higher ATI (+1 to +2 cm, >+2 cm) with referent around zero (−1 to +1 cm). This approach is analogous to the use of fat mass index residuals as described by Litwic and colleagues[28] in the Global Longitudinal Study of Osteoporosis in Women (GLOW).

Fracture probability

We used the Canadian version of FRAX to calculate 10-year probability of MOF and hip fracture probability with the inclusion of femoral neck BMD as an input variable (FRAX Desktop Multi-Patient Entry, version 3.7).[29,30] Inputs to the FRAX calculator were assessed from on-site measurements (height, weight, femoral neck BMD) and information collected directly from individuals at the time scanning.[31] Questionnaire-elicited information was supplemented with health care data (hospital discharge abstracts, medical claims diagnoses, retail pharmacy database) as previously described.[32] The Canadian FRAX tool was originally calibrated using nationwide hip fracture and mortality data[30] and shown to provide predictions that agree closely with observed fracture probability.[33,34]

Fracture outcomes

The primary outcome was incident MOF (hip, clinical vertebral, forearm, or humerus fracture) not associated with high-trauma codes using previously validated algorithms.[35,36] We assessed health services records to March 31, 2018, for relevant fracture codes appearing in hospital discharge abstracts (diagnoses and procedures coded using the International Classification of Diseases, Ninth Revision, Clinical Modification [ICD-9-CM] before 2004 and International Classification of Diseases, Tenth Revision, Canadian Enhancements [ICD-10-CA] thereafter) and physician billing claims (coded using ICD-9-CM). To enhance specificity for an acute fracture, hip and forearm fractures had to be accompanied with site-specific fracture reduction, fixation, or casting codes. To minimize double-counting, we required that there be no hospitalization or physician visit(s) with the same fracture type in the 6 months preceding an incident fracture diagnosis.

Statistical analyses

Statistical analyses were performed with IBM SPSS for Windows (version 28; IBM Corp., Armonk, NY, USA). Descriptive statistics for demographic and baseline characteristics are presented as mean ± SD for continuous variables or number (%) for categorical variables. We examined the association of ATI category with baseline characteristics, including diabetes prevalence using a previously validated definition.[37,38] We estimated sex-stratified calibration slopes for observed versus predicted 10-year fracture probability from FRAX according to ATI category. In Cox proportional hazards models, we estimated hazard ratios (HR) with 95% confidence intervals (CI) for incident fracture for ATI category and ATI as a continuous measure adjusted for FRAX probability (log-transformed due to a skewed distribution). The proportional hazards assumption was confirmed. Relevant subgroup analyses were performed, stratified by sex, age (younger than versus older than 65 years), and diabetes status (absent versus present). Two-way interaction terms were included in the models to test for effect modification according to these factors.

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Table 1. Study Population Characteristics

Characteristic	Overall $N = 73,105$	Women $n = 65,440$	Men $n = 7665$	p Value
Age (years)	64.2 ± 10.8	64.1 ± 10.6	65.5 ± 12.0	<0.001
BMI (kg/m^2)	26.4 ± 4.4	26.4 ± 4.5	27.0 ± 4.1	<0.001
Abdominal tissue thickness (cm)	18.4 ± 2.8	18.1 ± 2.7	20.5 ± 2.8	<0.001
Diabetes	7494 (10.3)	6094 (9.3)	1400 (18.3)	<0.001
FRAX with BMD (MOF %)	10.1 ± 7.1	10.3 ± 7.2	8.0 ± 5.1	0.922
FRAX with BMD (hip %)	2.3 ± 3.9	2.3 ± 3.9	2.3 ± 3.3	<0.001
Observation time (years)	8.7 ± 5.2	8.9 ± 5.2	6.6 ± 4.8	<0.001
Incident MOF	7048 (9.6)	6483 (9.9)	565 (7.4)	<0.001
Incident hip fracture	2155 (2.9)	1983 (3.0)	172 (2.2)	<0.001

Note: Data are mean ± SD or *n* (%).
Abbreviations: BMD = bone mineral density; BMI = body mass index; MOF = major osteoporotic fracture.

Results

Table 1 summarizes the baseline study population characteristics. The study cohort consisted of 73,105 individuals, mean age 64.2 years (SD 10.5), predominantly women but with 7665 (10.5%) men. Men had significantly greater mean BMI and average abdominal tissue thickness measured by DXA. There was a strong positive linear association between BMI and average abdominal tissue thickness in women ($r^2 = 0.80$) and men ($r^2 = 0.79$) (Supplemental Fig. S1).

During mean follow-up of 8.7 years, 7048 (9.6%) individuals sustained one or more incident MOF, of which 2155 (3.0%) sustained a hip fracture. As shown in Table 2, most individuals (61%) had ATI between −1 and +1 cm; 38.4% had ATI falling outside this range, and 8.9% had ATI falling within one of the two most extreme categories (<−2 or >+2 cm). Increasing ATI category was strongly associated with increasing average abdominal tissue thickness from DXA, average spine fat percent from DXA and diabetes prevalence, with a much smaller effect of age, height, weight, and BMI.

Increasing ATI category, adjusted for FRAX probability, was significantly associated with incident MOF ($p < 0.001$) and incident hip fracture ($p < 0.001$) (Table 3). For the highest versus middle ATI category, MOF risk was increased (HR = 1.23, 95% CI 1.12–1.35) independent of FRAX probability. Similar findings were noted for hip fracture risk (HR = 1.28, 95% CI 1.09–1.51). There was a trend toward lower fracture risk in individuals with a reduced ATI category, but this was inconsistent. Results were similar in women who represented the majority of the study population; no significant effect of ATI category was found in men, but the sex-interaction term was also nonsignificant, suggesting that this analysis may have been underpowered. There was a significant age-interaction, with larger effect found in individuals younger than 65 years. For younger individuals with ATI category greater than +2 cm, the adjusted HR for MOF was 1.44 (95% CI 1.23–1.69) and for hip fracture was 2.29 (95% CI 1.65–3.18). For individuals aged 65 years or older, the corresponding HRs were 1.15 (95% CI 1.02–1.29) and 1.10 (95% CI 0.90–1.33), respectively. A significant diabetes-interaction was also identified. Among the 7494 individuals with diabetes, there was evidence of a bimodal effect with increased risk in those with the lowest ATI category, less than −2 cm (HR = 1.73, 95% CI 1.12–2.65 for MOF; 2.81, 95% CI 1.59–4.97 for hip fracture) and for those with the highest ATI category, greater than +2 cm (HR = 1.28, 95% CI 1.04–1.57 for MOF; 1.28, 95% CI 0.90–1.81 for hip fracture). In a sensitivity analysis of MOF where hip fractures were excluded (Supplemental Table S1), results were similar except among individuals with diabetes in the lowest ATI category, where risk was no longer significantly increased (HR = 1.18, 95% CI 0.65–2.16).

When ATI was studied as a continuous measure with HR expressed per centimeter increase (Table 4), significant increased risk was found in the overall population for MOF (FRAX-adjusted HR = 1.07, 95% CI 1.05–1.09) and for hip fracture (HR = 1.09, 95% CI 1.05–1.13). As in the categorical analysis, no significant effect was found in men, although the sex-interaction term was nonsignificant. Larger effects were found in those younger than 65 years compared with those age 65 years and older (age-interaction p value ≤0.001). Results were similar in a sensitivity analysis of MOF where hip fractures were excluded (Supplemental Table S2).

Calibration plots in Figure 1 across ATI categories showed deviation from the line of identity with FRAX probability in women with calibration slope 2.26 for MOF and 2.83 for hip fracture. Deviation from the line of identity was most extreme for

Table 2. Associations of Abdominal Thickness Index (ATI) Category With Baseline Characteristics

ATI category	n	Age (years)	Men (%)	BMI (kg/m^2)	Diabetes (%)	Femoral neck BMD (g/cm^2)	Femoral neck T-score	FRAX with BMD (MOF %)	FRAX with BMD (hip %)
<−2 cm (lowest)	2784	62.1	12.8	28.8	5.2	0.863	−1.3	8.9	1.9
−2 to −1 cm	11414	62.5	10.6	26.7	5.6	0.854	−1.3	9.1	1.9
−1 to 0 cm	23569	63.6	10.0	25.9	6.9	0.844	−1.4	9.7	2.2
0 to +1 cm	21473	65.0	10.3	26.1	10.9	0.839	−1.4	10.4	2.5
+1 to +2 cm	10137	66.0	11.3	27.0	17.5	0.841	−1.4	11.0	2.7
>+2 cm (highest)	3728	65.9	11.1	27.6	26.5	0.839	−1.4	11.5	2.8
Overall	73105	64.2	10.5	26.4	10.3	0.844	−1.4	10.1	2.3

Note: Data are mean except for men and diabetes, which are percent.
Abbreviations: BMD = bone mineral density; BMI = body mass index; MOF = major osteoporotic fracture.

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Table 3. Hazard Ratios (HR, 95% CI) for Incident Major Osteoporotic Fracture (MOF) and Incident Hip Fracture (HIP) According to Abdominal Thickness Index (ATI) Category, Adjusted for FRAX Probability

	Total population $N = 73{,}105$	Women $n = 65{,}444$	Men $n = 7661$	Age <65 years $n = 37{,}168$	Age ≥65 years $n = 35{,}937$	Diabetes absent $n = 65{,}611$	Diabetes present $n = 7494$
ATI category	Incident MOF HR (95% CI)	Incident MOF HR (95% CI)	Incident MOF HR (95% CI)	Incident MOF HR (95% CI)	Incident MOF HR (95% CI)	Incident MOF HR (95% CI)	Incident MOF HR (95% CI)
<−2 cm	0.95 (0.83–1.09)	0.93 (0.81–1.08)	1.10 (0.72–1.66)	0.82 (0.66–1.02)	1.05 (0.89–1.24)	0.91 (0.79–1.05)	**1.73 (1.12–2.65)**
−2 to −1 cm	**0.90 (0.84–0.97)**	**0.90 (0.84–0.97)**	0.94 (0.73–1.21)	0.92 (0.83–1.03)	**0.89 (0.81–0.98)**	**0.92 (0.86–0.99)**	**0.68 (0.49–0.96)**
−1 to +1 cm	Referent	Referent	Referent	Referent	Referent	Referent	Referent
+1 to +2 cm	**1.13 (1.06–1.20)**	**1.13 (1.05–1.21)**	1.11 (0.88–1.38)	**1.28 (1.15–1.43)**	1.06 (0.98–1.15)	**1.12 (1.05–1.20)**	1.10 (0.92–1.32)
>+2 cm	**1.23 (1.12–1.35)**	**1.25 (1.13–1.38)**	1.01 (0.73–1.42)	**1.44 (1.23–1.69)**	**1.15 (1.02–1.29)**	**1.19 (1.06–1.32)**	**1.28 (1.04–1.57)**
p value, between categories	**<0.001**	**<0.001**	0.853	**<0.001**	**0.004**	**<0.001**	**0.001**
p value, interaction			0.053		**0.017**		**0.019**
ATI category	Incident hip HR (95% CI)	Incident hip HR (95% CI)	Incident hip HR (95% CI)	Incident hip HR (95% CI)	Incident hip HR (95% CI)	Incident hip HR (95% CI)	Incident hip HR (95% CI)
<−2 cm	1.02 (0.79–1.31)	0.99 (0.76–1.29)	1.34 (0.65–2.75)	1.04 (0.60–1.83)	1.03 (0.78–1.36)	0.89 (0.67–1.17)	**2.81 (1.59–4.97)**
−2 to −1 cm	0.89 (0.78–1.02)	0.91 (0.79–1.04)	0.74 (0.43–1.25)	0.82 (0.59–1.14)	0.92 (0.79–1.06)	0.92 (0.80–1.06)	0.68 (0.39–1.20)
−1 to +1 cm	Referent	Referent	Referent	Referent	Referent	Referent	Referent
+1 to +2 cm	**1.32 (1.18–1.48)**	**1.34 (1.19–1.51)**	1.15 (0.77–1.70)	**2.15 (1.67–2.76)**	**1.17 (1.04–1.33)**	**1.34 (1.19–1.51)**	1.04 (0.76–1.41)
>+2 cm	**1.28 (1.09–1.51)**	**1.30 (1.09–1.54)**	1.20 (0.70–2.03)	**2.29 (1.65–3.18)**	1.10 (0.90–1.33)	**1.20 (1.00–1.46)**	1.28 (0.90–1.81)
p value, between categories	**<0.001**	**<0.001**	0.531	**<0.001**	**0.048**	**<0.001**	**0.002**
p value, interaction			0.453		**<0.001**		**<0.001**

Note: Data from regression models with competing mortality. Significant effects in boldface.
Abbreviation: CI = confidence interval.

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Table 4. Hazard Ratios (HR, 95% CI) for Incident Major Osteoporotic Fracture (MOF) and Incident Hip Fracture (HIP) Per cm Increase in Abdominal Thickness Index (ATI), Adjusted for FRAX Probability

ATI	Incident MOF HR (95% CI)	Incident HIP HR (95% CI)
Total population	**1.07 (1.05–1.09)**	**1.09 (1.05–1.13)**
Women	**1.08 (1.05–1.10)**	**1.10 (1.06–1.14)**
Men	1.01 (0.95–1.08)	1.06 (0.94–1.18)
p value, interaction	0.066	0.560
Age <65 years	**1.13 (1.09–1.16)**	**1.29 (1.19–1.39)**
Age >65 years	**1.04 (1.02–1.07)**	**1.04 (1.00–1.08)**
p value, interaction	**0.001**	**<0.001**
Diabetes absent	**1.07 (1.04–1.09)**	**1.09 (1.05–1.14)**

Note: Data from regression models with competing mortality. Significant effects in boldface. Diabetes present is not shown because of a nonlinear relationship.

Abbreviation: CI = confidence intervals.

women with ATI in the highest category, where observed probability significantly exceeded predicted probability. Findings in men showed a similar but generally weaker trend (calibration slope 1.50 for MOF and 1.62 for hip fracture). Although all points estimates for observed probability exceeded predicted probability, confidence limits still included the line of identity.

Discussion

We found that greater BMI-discordant abdominal thickness predicted greater risk for incident fracture when adjusted for conventional FRAX probability. This effect was significant in women but not in men. Whether this reflects a true sex difference or an underpowered analysis for men is unclear, as the sex-interaction terms did not show significant effect modification. However, there was a clear age-interaction, with much larger effects in younger versus older individuals, and also a significant diabetes interaction, with a bimodal increase in risk for those in the lowest and highest ATI categories. It is worth noting that BMI is a primary input variable in the FRAX algorithm, is worthwhile where high BMI is protective, but this protection all but disappears when adjusted for BMD.[39] The present study indicates that distribution of soft tissue beyond BMI is a further modifier of fracture risk.

Previous studies have been inconsistent for adverse effects of central obesity on osteoporotic fracture risk. In an early prospective study of 766 women and 360 men from Australia, Yang and colleagues[13] reported that lower abdominal fat measured with DXA was independently associated with higher fracture risk (especially clinical vertebral fractures) in women adjusted for BMD but not BMI (inconclusive in men because of the small numbers of fractures observed). The US Nurses' Health Study and Health Professionals Follow-up Study (61,677 postmenopausal women and 35,488 men aged >50 years) found a significant BMI-independent association of hip fracture with increasing waist circumference (relative risk [RR] per 10 cm increase 1.13, 95% CI 1.04–1.23) and increasing waist-to-hip ratio (RR per 0.1 unit increase 1.14, 95% CI 1.04–1.23) in women but not in men.[14] A meta-analysis of nine studies to February 2017 found that abdominal obesity based upon waist circumference was associated with a higher risk of hip fracture (RR = 1.40, 95% CI 1.25–1.58) in both women and men, especially in studies with <10 years' follow-up, non-US countries, and when BMI was a covariate in the analysis.[15] A separate meta-analysis that also appeared in 2017 confirmed the positive relationship between increasing risk of hip fracture and increasing waist circumference.[16] These studies were unable to study the independent or modifying effects of BMD or associations between abdominal obesity and fractures at other bone sites. Subsequently, positive associations between waist circumference and vertebral fracture risk have been reported from a nationwide cohort study in South Korea (352,095 participants aged ≥40 years) in both women and men (obese versus non-obese adjusted HR = 1.26, 95% CI 1.19–1.34 and 1.26, 95% CI 1.11–1.23, respectively). Although analyses were not adjusted for BMI and BMD, similar HRs were observed when stratified by BMI category. Abdominal obesity has even been associated with a higher risk of secondary vertebral fracture after percutaneous vertebral augmentation.[18] In the UK Biobank, visceral adipose tissue (VAT), estimated from a prediction model, showed an inverted U-shaped association with heel ultrasound in men (*p* for nonlinearity <0.001) but a monotonic increase in women (*p* for nonlinearity 0.28) when adjusted for lean mass from bioelectrical impedance and other covariates.[19] Estimated VAT was associated with lower (not greater) risk of hip fracture in men and women; total fractures showed no significant relationship with VAT in women but a bimodal effect in men that increased above and below 1.25 kg (*p* for nonlinearity <0.001). Significant VAT-BMI interactions were found in men but not women. Evidence of causality was not observed in two-sample Mendelian randomization analyses, raising the possibility that observational associations could be the result of confounding. Greater DXA-measured VAT was associated with lower BMD in middle-aged Australian men and women after adjustment for age, body mass, and other covariates.[17] A cross-sectional analysis of US National Health and Nutrition Examination Survey data (*N* = 1979 participants aged ≥65 years, 2017–2020) found that greater weight-adjusted waist circumference was associated with osteoporosis.[21] Most recently, a population-based study of 18,236 men and women aged 40–70 years from Canada reported that greater BMI-adjusted waist circumference (adjusted for multiple covariates but not BMD) was associated with increased risk of distal lower limb fractures (but only for BMI within the normal and overweight ranges) and distal upper limb fractures (only for BMI in the overweight range) and was not significantly associated with risk for all fractures or MOF.[20,22] The biological mechanism underlying this association is unclear but may in part relate to associations of visceral adiposity with diabetes and systemic inflammation.[7–9] Waist circumference is positively correlated with the inflammatory markers interleukin-6 and tumor necrosis factor-α, consistent with the hypothesis that central obesity is a biomarker from the inflammatory state.[40] Type 2 diabetes is strongly associated with central obesity and increased fracture risk, despite BMD measurements that are not reduced or are even higher than expected.[41,42]

Strengths of this study include a large well-characterized cohort and longitudinal assessment of incident fractures using validated data sources and definitions.[35,36] To our knowledge, this is the first study that has directly examined fracture outcomes using DXA-derived tissue thickness adjusted for BMI. Limitations are also acknowledged. As noted earlier, our findings were inconclusive for men, perhaps because of their relatively small proportion of the study population. Additional studies with larger numbers of men would be required to clarify this question. Fracture outcomes were assessed from administrative health care data rather than direct X-ray review, but the definitions used

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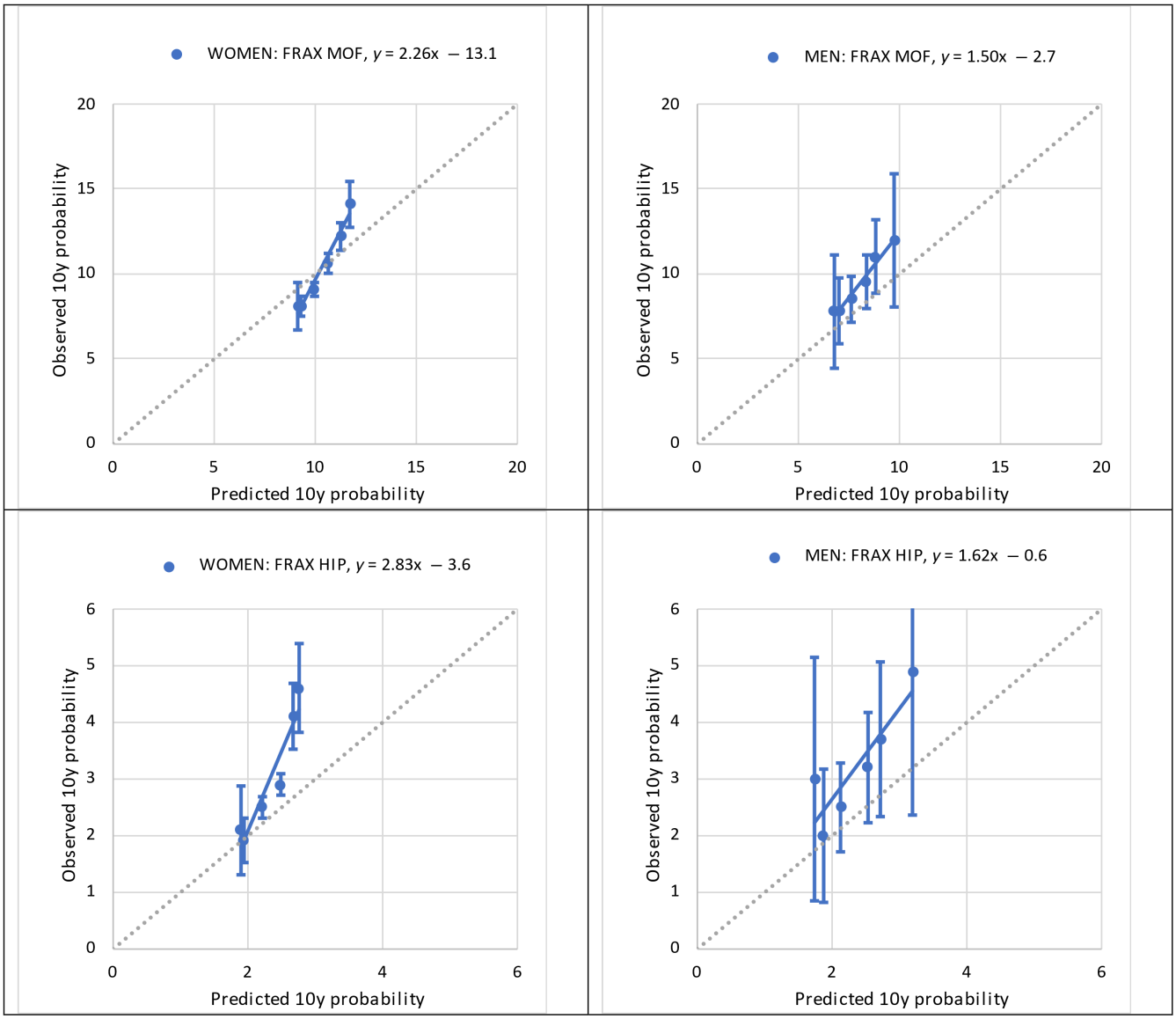

Fig. 1. Sex-stratified calibration plots by abdominal thickness index (ATI) category for predicted (*x* axis) versus observed (*y* axis, 95% confidence interval [CI] bars) 10-year probability of FRAX major osteoporotic fracture (MOF; upper panel) and hip fracture probability (hip; lower panel). Line of identity in solid gray.

have been validated against X-rays.[35] The current analysis was performed with a single DXA manufacturer, which has a direct output for tissue thickness. Whether the same relationships would be found with other manufacturers is unclear. Waist circumference is correlated closely with abdominal tissue thickness and could potentially serve as a valid proxy.[26] Abdominal tissue thickness fails to differentiate subcutaneous and visceral compartments. Finally, our subgroup analysis for individuals with diabetes was unable to differentiate type 1 from type 2, and this could potentially explain the observed bimodal effect because individuals with low abdominal tissue thickness may be more likely to have type 1 diabetes, which is associated with much higher fracture risk than type 2 diabetes.[43,44]

In conclusion, these data support the need to investigate increased abdominal thickness beyond that predicted by BMI and sex as a FRAX-independent risk factor fracture. This risk may be particularly important in individuals younger than 65 years. Among those with diabetes, risk appears to be bimodal with an increase among those within both the lowest and highest categories of BMI-discordant abdominal thickness.

Author Contributions

William D. Leslie: Conceptualization; data curation; formal analysis; writing – original draft; writing – review and editing; methodology; project administration. **Neil Binkley:** Writing – review and editing; conceptualization. **John T. Schousboe:** Conceptualization; writing – review and editing. **Eugene V. McCloskey:** Conceptualization; writing – review and editing. **Helena Johansson:** Writing – review and editing. **Nicholas C. Harvey:**

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Writing – review and editing. **John A. Kanis:** Writing – review and editing.

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Peer Review

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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.

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