RESEARCH

Multiple sclerosis is associated with low bone mineral density and osteoporosis

Etienne J. Bisson, PhD, Marcia L. Finlayson, PhD, Okechukwu Ekuma, MSc, William D. Leslie, MD, and Ruth Ann Marrie, MD, PhD

Correspondence
Dr. Marrie
rmarrie@hsc.mb.ca

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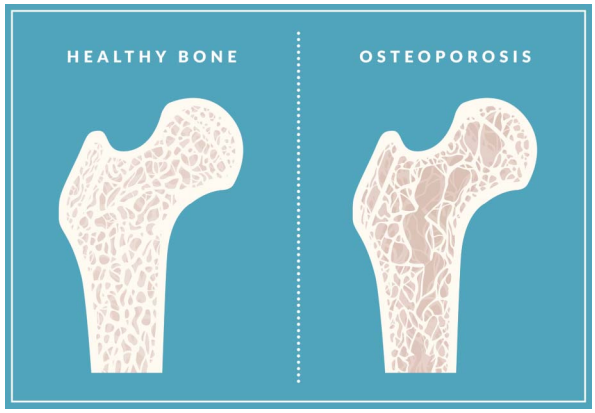
Abstract



Objective

To compare measures of bone mineral density (BMD) between people with and without MS.

Methods

Using population-based administrative data from Manitoba, Canada, we identified people with MS who received BMD screening and controls who received BMD screening matched 5:1 on age, sex, region of residence, and date of BMD screening. We determined the BMD T-scores for the femoral neck, total hip, and lumbar spine and frequency of osteoporosis (defined as T-score −2.5 or lower). We compared the groups with respect to the femoral neck T-score using multivariable linear regression, adjusting for age, sex, region, disability, continuity of care, recent previous fracture, falls history, medication use, and comorbidities. We compared the odds of osteoporosis between groups using multivariable logistic regression analysis.

Results

We identified 783 MS cases who underwent BMD screening and 3,915 matched controls. The mean (SD) femoral BMD T-score was lower in MS cases (−1.48 [1.08]) than in matched controls (−1.12 [0.98], $p < 0.001$), and the prevalence of osteoporosis was higher among the MS cases (range across BMD sites: 16%–26%) vs controls (6%–15%). MS was associated with a lower femoral neck BMD T-score after accounting for covariates ($\beta = -0.24$; 95% CI: −0.32 to −0.17) and more than 2-fold increased odds of osteoporosis (covariate-adjusted OR 2.41; 95% CI: 1.82–3.19).

Conclusions

People with MS have lower BMD and a higher prevalence of osteoporosis compared with people of similar age and sex without MS. These findings indicate the importance of addressing bone health as part of comprehensive MS care.

Osteoporosis is a highly prevalent metabolic bone disease characterized by low bone mineral density (BMD) and deterioration of bone tissue predisposing to fragility fractures. These fractures often lead to hospitalization, reduced quality of life, loss of independence, and even death.[1] In the general population, health care costs remained elevated 5 years after an osteoporosis-related fracture.[2] Given the high rate of falls among people with MS[3] and the

School of Rehabilitation Therapy (EJB, MLF), Faculty of Health Sciences, Queen's University, Kingston, Ontario; Manitoba Centre for Health Policy (OE), Max Rady College of Medicine, Rady Faculty of Health Sciences; Departments of Internal Medicine (Endocrinology) and Radiology (Nuclear Medicine) (WDL), Max Rady College of Medicine, Rady Faculty of Health Sciences; and Departments of Internal Medicine and Community Health Sciences (RAM), Max Rady College of Medicine, Rady Faculty of Health Sciences, Winnipeg, Manitoba, Canada.

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Our primary outcome, based on the results of the first BMD screening, was femoral neck T-score because this is the World Health Organization reference site used to diagnose osteoporosis.

association between falls and fractures, a greater understanding of low BMD and osteoporosis among people with MS is needed.

Several studies have suggested that people with MS have lower BMD and higher rates of osteoporosis compared with healthy adults.[4–7] However, confidence in these findings is limited by the use of small clinical samples and methodological heterogeneity. Self-report studies suggest that the prevalence of low bone mass among persons with MS ranges from 26% to 73%, whereas the prevalence of osteoporosis ranges from 5% to 29%.[4] In the few studies using population-based data, actual measures of BMD have not been available. Therefore, we aimed at identifying and describing differences in measures of BMD generated through dual-energy x-ray absorptiometry (DXA) between people with and without MS using population-based data. We hypothesized that people with MS would have lower BMD and a higher prevalence of osteoporosis compared with people without MS.

Methods

Study design

We conducted a matched cohort study using administrative (health claims) data from Manitoba, Canada, over the period 1998–2012. The provincial health department maintains records of all health services claims for 98% of residents of the province (~1.3 million). We accessed these data through the Population Health Research Data Repository at the Manitoba Centre for Health Policy (MCHP). We used 6 databases (data elements used) including (1) Population Registry (sex, postal code, and dates of birth, death, and health care coverage); (2) Medical (physician) services (date of service, 1 diagnosis recorded using the *International Classification of Diseases, Ninth Revision, Clinical Modification* [*ICD-9-CM*]); (3) Hospital discharge abstract database (dates of admission and discharge, up to 25 diagnoses recorded using *ICD-9-CM* or *International Classification of Disease, 10th Revision, Canadian Modification* depending on the year); (4) Drug Program Information Network (DPIN; all prescriptions dispensed in the community (but not in hospitals) including date of dispensation, days supplied, and drug identification number); (5) Home Care (dates for starting and stopping services); and (6) the Manitoba Bone Mineral Density Database (MBMDD). All data sets were available from April 1, 1984, through March 31, 2012, except for DPIN (available as of April 1, 1995) and the MBMDD (available as of January 1, 1990). We linked these data sets using an encrypted unique personal health identification number.

Standard protocol approvals, registrations, and patient consents

We obtained ethics approvals from the Queen's University and University of Manitoba Research Ethics Boards and approval for administrative data access from Manitoba's Health Information Privacy Committee.

Source population

We identified people with MS using a validated administrative case definition, which required ≥3 hospital, physician, or prescription claims for a disease-modifying therapy in any combination ever (n = 5,810).[8] We defined the date of MS diagnosis as the first demyelinating disease claim.[9] We excluded individuals aged <20 years at MS diagnosis (n = 91) and those who underwent BMD screening before MS diagnosis (n = 81).

Identifying BMD screening

DXA is used to measure BMD and diagnose low bone mass and osteoporosis. The WHO defines low bone mass as a BMD value (T-score) between 1 and 2.5 SDs below young adult normative values. Osteoporosis is defined as a BMD value ≥2.5 SDs below young adult normative values.[10,11] The WHO diagnostic standard for the description of osteoporosis is DXA measurement at the femoral neck with BMD T-scores derived from the Third National Health and Nutrition Examination Survey (NHANES III) for white women aged 20–29 years.[10,12]

DXA testing of BMD has been managed as an integrated clinical program in Manitoba since 1997.[13] All scans are performed on a small number of cross-calibrated instruments (Lunar DPX, Prodigy, iDXA; GE Healthcare). Quality assurance and control is closely supervised by a designated medical physicist and reviewed triennially by the Manitoba BMD Program Committee. Measurements are routinely obtained from the femoral neck, total hip, and each of the first 4 lumbar vertebrae (with exclusions for artifact). The MBMDD also captures clinical risk factor scores, height, and weight.

We used the date of the first BMD screening to identify individuals with MS who had received BMD screening. For each MS case who underwent BMD screening, we identified 5 BMD controls who were matched based on age (±5 years), sex, area of residence (rural/urban), and date of first BMD screening (±1 year).

Outcomes

Our primary outcome, based on the results of the first BMD screening, was femoral neck T-score because this is the WHO

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reference site used to diagnose osteoporosis. To provide a more comprehensive skeletal assessment, we also examined the lumbar spine T-score, total hip T-score, and the minimum T-score of all 3 sites. Finally, we determined the proportion with osteoporosis based on a BMD value ≥2.5 SDs below young adult normative values at the femoral neck.[10,11]

Covariates

We selected covariates based on the literature or relevant contextual factors that may influence referral to DXA testing for BMD, including age, sex, region of residence (urban/rural based on postal code), body mass index (BMI), continuity of care, greater disability, recent fracture (in the last 12 months), history of falls, medication use (prolonged glucocorticoid therapy, antidepressants, and antispasmodics), and presence of specific comorbidities.[14–16] The BMI variable, drawn from the MBMDDB, was missing in <1% of subjects; these missing values were imputed using the mean BMI of the group. We defined prolonged glucocorticoid therapy as ≥90 days cumulative use over 1 year[17] Antidepressants and antispasmodics users were defined as 3-level categorical variables: nonusers, long-term users (≥180 days cumulative use), and short-term users (<180 days cumulative use). Continuity of primary care was deemed present if >50% of outpatient visits were to 1 physician group/clinic in a particular year.[18] Disability was considered to be present based on an open home care file of ≥90 days because impaired activities of daily living are required to qualify for home care. As detailed elsewhere, recent previous osteoporotic fractures of the hip, forearm, vertebra, or humerus were identified based on the presence of ≥1–2 physician claims or ≥1 hospitalization with relevant diagnostic codes (depending on the fracture site).[19] Based on their high prevalence in MS, or their association with altered BMD, specific comorbidities of interest included diabetes, ischemic heart disease, hypertension, chronic lung disease, rheumatoid arthritis, substance abuse, dementia, autoimmune thyroid, mood and anxiety disorder, and hyperlipidemia.[14,20–22] These were identified using validated case definitions and approaches used in previous work on osteoporosis (table e1, links.lww.com/CPJ/A102).[19,20,23–26] All covariates were defined as present or absent at the time of BMD screening unless otherwise specified.

Statistical analysis

We computed mean (SD) for continuous variables and frequency (percent) for categorical variables. First, we compared MS cases and controls using Student *t* tests, χ^2 tests, and Fisher exact tests as appropriate. Second, we compared the femoral neck BMD T-scores between groups using multivariable linear regression analysis, adjusting for covariates as described above. This allowed us to evaluate factors that may be associated with lower BMD without necessarily meeting the threshold for osteoporosis. Third, we compared the likelihood of osteoporosis at the femoral neck between groups using multivariable logistic regression analysis, adjusting for the same covariates. We examined potential interactions between groups (MS vs controls) and covariates. Model assumptions were tested and met.

Secondary analyses

We conducted logistic regression analyses to predict osteoporosis at the other sites and repeated all analyses without imputing BMI. Statistical analyses were conducted using SAS V9.4 (SAS Institute Inc, Cary, NC).

Data availability

As we are not the data custodians, we are not authorized to make the data available. With the necessary approvals, the data can be accessed through the MCHP.

Results

Study populations

We identified 783 persons with MS who underwent BMD screening postdiagnosis and 3,915 controls. Cases and controls were well matched with respect to age, sex, and region (table 1). Compared with controls, MS cases had a lower BMI, greater continuity of care, greater disability, and were more likely to have diabetes and hyperlipidemia. They were also more likely to use antidepressants and antispasmodics.

Compared with controls, MS cases had lower mean BMD T-scores at the 3 sites (femoral neck, total hip, and lumbar spine) (table 2). Among the MS cases, the prevalence of osteoporosis ranged from 15.9% to 17.3% across the 3 sites and was 26.1% based on the minimum T-score. The prevalence of osteoporosis was lower among controls at all sites.

Factors associated with femoral neck BMD and with osteoporosis

On multivariable linear regression analysis, MS was associated with a lower femoral neck BMD T-score (table 3). Other factors that were associated with lower BMD T-scores included increasing age, being female, greater disability, recent fracture, prolonged use of glucocorticoid therapy, and long-time use of antispasmodics. Chronic lung disease, rheumatoid arthritis, and substance abuse were also associated with lower BMD. Higher BMI, diabetes, and hypertension were associated with higher BMD. All other factors examined were not associated with low BMD. We did not observe any interactions between MS diagnosis and covariates on femoral BMD T-score.

On multivariable logistic regression, MS was associated with increased odds of osteoporosis (table 4). Similar to the findings for mean BMD T-score, older age, female sex, greater disability, and use of antispasmodics were also associated with increased odds of osteoporosis. Of the comorbidities examined, only chronic lung disease was associated with osteoporosis. Higher BMI was associated with decreased odds of osteoporosis. All other factors examined

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Table 1 Characteristics of the MS cases and controls at the time of BMD screening

Characteristics	MS cases (n = 783)	Controls (n = 3,915)	*p* Value
Demographic			
Age (y), mean (SD)	56.4 (9.60)	56.4 (9.61)	0.977
Female sex, n (%)	723 (92.3)	3,615 (92.3)	1.000
Urban region of residence, n (%)	519 (66.3)	2,595 (66.3)	1.000
Clinical			
BMI (kg/m^2), mean (SD)	26.1 (5.72)	27.0 (5.74)	**<0.001**
Continuity of care, n (%)	106 (13.5)	50 (1.28)	**<0.001**
Greater disability, n (%)	58 (7.41)	47 (1.20)	**<0.001**
Recent previous fracture, n (%)	47 (6.00)	237 (6.05)	1.000
History of falls, n (%)	15 (1.92)	67 (1.71)	0.655
Medication use			
Prolonged glucocorticoid therapy use, n (%)	39 (4.98)	183 (4.67)	0.712
Antidepressant use, n (%)			**<0.001**
Short term (<180 d)	59 (7.54)	324 (8.28)	
Long term (≥180 d)	195 (24.9)	489 (12.5)	
Antispasmodic use, n (%)			**<0.001**
Short term (<180 d)	56 (7.15)	59 (1.51)	
Long term (≥180 d)	134 (17.1)	49 (1.25)	
Comorbidities, n (%)			
Hypertension	291 (37.2)	1335 (34.1)	0.100
Mood and anxiety disorder	145 (18.5)	671 (17.1)	0.353
Autoimmune thyroid disease	116 (14.8)	613 (15.7)	0.589
Hyperlipidemia	82 (10.5)	581 (14.8)	**0.001**
Diabetes	52 (6.64)	348 (8.89)	**0.042**
Chronic lung disease	43 (5.49)	202 (5.16)	0.725
Rheumatoid arthritis	27 (3.45)	198 (5.06)	0.054
Dementia	44 (5.62)	183 (4.67)	0.273
Substance abuse	23 (2.94)	145 (3.70)	0.926
Ischemic heart disease	20 (2.55)	131 (3.35)	0.317

Abbreviations: BMD = bone mineral density; BMI = body mass index.
Characteristics not used in the models due to low numbers are not shown.
Bold indicates statistical significance.

were not associated with osteoporosis. We identified an interaction between group (MS vs controls) and recent fracture (p = 0.02). A recent previous fracture was associated with increased odds of osteoporosis (OR 2.70; 95% CI: 1.28–5.70) in MS cases but not in controls (OR 1.07; 95% CI: 0.62–1.85). Compared with controls with no previous fracture, MS cases with a recent previous fracture had more than 5-fold increased odds of osteoporosis at the femoral neck (OR 5.58; 95% CI: 2.35–13.3).

Secondary analyses

Models predicting osteoporosis in the total hip, lumbar spine, or at any of the sites were largely similar to those for the femoral neck in magnitude and direction (table e2, links.lww.com/CPJ/A102). Notable differences were that the association between MS and greater disability with osteoporosis in the lumbar spine was not statistically significant. Findings were similar when participants with missing BMI (<1%) were excluded (table e3, links.lww.com/CPJ/A102).

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We found that BMD in people with MS was more affected at the femoral neck than in the lumbar region.

Discussion

In this population-based study, we compared BMD measurements among MS cases and matched controls. We found that people with MS who undergo BMD screening have lower BMD and a higher prevalence of osteoporosis than people without MS after accounting for multiple potential confounders. Multiple factors were associated with low BMD and the likelihood of osteoporosis.

We compared BMD measurements among people with MS and people without MS who were referred for BMD screening. Thus, our control group was not a healthy control group. Previous studies have generally compared BMD measurements among people with MS and healthy controls. The number of individuals with MS included in each of these studies was relatively small, ranging from 31 to 99.[4] In a meta-analysis of 7 studies, the mean difference in BMD (g/cm^2) between people with MS and healthy controls at the femoral neck was −0.11 (95% CI: −01.6 to −0.06).[4] This result is not strictly comparable to our findings as we reported T-scores, but the implications are the same.

We found that BMD in people with MS was more affected at the femoral neck than in the lumbar region. This would be consistent with reduced mobility in MS, and mechanical loading on the lumbar spine associated with prolonged sitting or wheelchair use.[27] Previous smaller studies have been inconsistent as to whether BMD is more affected at the femoral neck or in the lumbar region. In 80 females with MS who were hospitalized and underwent BMD screening, BMD was more affected at the femoral neck than at the lumbar spine.[28] A study of 31 men and women with MS found that BMD at the lumbar spine was lower than in age-matched controls, but was not reduced at the femoral neck.[7] Previous studies have reported the prevalence of osteoporosis in MS to vary from 5% to 29% based on self-report. Of 142 women recruited to undergo BMD screening, 20.4% had osteoporosis.[29] Our estimate lies near the upper bound of these earlier estimates.

Several factors were associated with low BMD apart from MS. Consistent with findings in the general population, older age and female sex were associated with low BMD.[14] Several comorbidities were associated with low BMD, consistent with expectations.[14] The association between low BMD and osteoporosis in chronic obstructive pulmonary disease likely reflects the history of smoking, poor nutrition, and reduced physical activity. Even after accounting for smoking, greater disease duration and severity are associated with lower bone mass.[30] Substance abuse in general, as we did not distinguish between types of substances, was associated with lower BMD. Chronic alcohol abuse is associated with low bone mass and increased fracture risk through multiple mechanisms including reduced bone formation.[22] Heavy cannabis use is also associated with low bone mass and increased fracture risk due to increased bone turnover and indirect effects via low BMI.[21] Multiple classes of medications may affect BMD including glucocorticoids, anticonvulsants, antidepressants, and benzodiazepines. In our population, antispasmodics were also associated with low BMD. These medications are used to manage spasticity, which is often associated with ambulatory disability, a factor known to be associated with low BMD. Diabetes and hypertension were associated with higher BMD. This is

Table 2 Bone mineral density and osteoporosis in MS cases and controls

Characteristics	MS cases (n = 783)	Controls (n = 3,915)	*p* Value
Bone mineral density T-score, mean (SD)			
Femoral neck	−1.48 (1.08)	−1.12 (0.98)	<0.001
Total hip	−1.18 (1.38)	−0.63 (1.18)	<0.001
Lumbar spine	−1.04 (1.50)	−0.88 (1.46)	0.009
Minimum score[a]	−1.76 (1.20)	−1.43 (1.11)	<0.001
Osteoporosis[b]**, n (%)**			
Femoral neck	129 (17.3)	246 (6.48)	<0.001
Total hip	115 (15.9)	178 (4.83)	<0.001
Lumbar spine	122 (17.2)	471 (13.0)	0.004
Minimum T-score[a]	197 (26.1)	605 (15.8)	<0.001

[a] Lowest T-score measurement available from all 3 sites.
[b] Defined as T-score ≤−2.5.

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Table 3 Factors associated with femoral neck T-score[a] on multivariable linear analysis (n = 4542)

		95% CI		
	Estimate (β)[b]	Lower	Upper	*p* Value
MS cases (ref: controls)	−0.24	−0.32	−0.17	**<0.0001**
Age (per decade)	−0.40	−0.50	−0.30	**<0.0001**
Sex (ref: male)	−0.31	−0.41	−0.21	**<0.0001**
Urban region of residence (ref: rural)	0.046	−0.0082	0.010	0.096
Continuity of care (ref: no)	−0.072	−0.22	0.078	0.35
Diabetes (ref: no)	0.10	0.005	0.20	**0.040**
Hypertension (ref: no)	0.077	0.017	0.14	**0.013**
Chronic lung disease (ref: no)	−0.25	−0.37	−0.14	**<0.0001**
Autoimmune thyroid disease (ref: no)	0.045	−0.026	0.12	0.21
Mood and anxiety disorder (ref: no)	0.025	−0.054	0.10	0.54
Hyperlipidemia (ref: no)	0.036	−0.039	0.11	0.34
Rheumatoid arthritis (ref: no)	−0.13	−0.26	−0.012	**0.032**
Recent fracture (ref: no)	−0.32	−0.43	−0.21	**<0.0001**
Substance abuse (ref: no)	−0.14	−0.26	−0.020	**0.022**
Dementia (ref: no)	−0.058	−0.19	0.077	0.40
Ischemic heart disease (ref: no)	0.10	−0.048	0.25	0.18
Greater disability (ref: no)	−0.27	−0.45	−0.085	**0.0041**
Prolonged glucocorticoid use (ref: no)	−0.18	−0.31	−0.058	**0.0040**
Antidepressant use (ref: no)				
Short term (<180 d)	−0.13	−0.30	0.034	0.11
Long term (≥180 d)	0.018	−0.062	0.099	0.66
Antispasmodic users (ref: no)				
Short term (<180 d)	−0.13	−0.30	0.034	0.12
Long term (≥180 d)	−0.30	−0.44	−0.16	**<0.0001**
History of falls (ref: no)	−0.20	−0.40	0.002	0.052
BMI (per 5 kg/m^2)	0.30	0.25	0.30	**<0.0001**

Abbreviation: BMI = body mass index.
[a] A T-score is a standardized score, which compares bone mineral density with young adult normative values, where the units are SDs.
[b] Unless otherwise specified, β (regression coefficient) reflects the effect of a 1 unit change in the variable. Thus, β = −0.24 for MS indicates that persons with MS have a BMD T-score, which is 0.24 SDs lower than persons without MS. Goodness of fit (scaled deviance) = 1.0055.
Bold indicates statistical significance.

consistent with the literature suggesting that increased fracture risk in diabetes is due to poor bone quality rather than low BMD.[31] Some antihypertensive agents (e.g., thiazide diuretics) improve bone health and reduce fracture risk, although further study of this issue is needed.[32]

Greater disability, as measured by the EDSS, is associated with lower BMD in MS.[7] We did not have information regarding the EDSS among persons with MS in our study population; however, we used home care services use as a proxy for disability. In Manitoba, access to home care services is predicated on demonstrated impairment in activities of daily living. Thus, this measure is specific for disability but will miss some cases of disability when family or friends are able to support disabled individuals without home care services. Consistent with these previous studies, our proxy measure of disability was associated with lower BMD.

Our findings have important implications for the care of people with MS. People with MS should be referred for BMD

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Table 4 Adjusted ORs and 95% CIs for factors associated with osteoporosis at the femoral neck[a]

		95% CI		
	OR	Lower	Upper	*p* Value
MS cases (ref: controls)	2.41	1.82	3.19	<0.0001
Age (per decade)	1.08	1.06	1.09	**<0.0001**
Sex (ref: male)	1.64	1.03	2.63	**0.035**
Urban region of residence (ref: rural)	0.91	0.71	1.16	0.43
Continuity of care (ref: no)	1.15	0.68	1.93	0.61
Diabetes (ref: no)	1.04	0.64	1.69	0.86
Hypertension (ref: no)	0.91	0.70	1.20	0.51
Chronic lung disease (ref: no)	2.41	1.63	3.56	**<0.0001**
Autoimmune thyroid disease (ref: no)	0.77	0.55	1.08	0.13
Mood and anxiety disorder (ref: no)	0.90	0.62	1.30	0.58
Hyperlipidemia (ref: no)	0.88	0.63	1.24	0.47
Rheumatoid arthritis (ref: no)	1.31	0.76	2.26	0.34
Recent fracture (ref: no)	1.42	0.92	2.21	0.12
Substance abuse (ref: no)	1.44	0.87	2.38	0.15
Dementia (ref: no)	0.60	0.29	1.24	0.17
Ischemic heart disease (ref: no)	0.91	0.46	1.78	0.78
Greater disability (ref: no)	2.87	1.65	5.00	**0.0002**
Prolonged glucocorticoid use (ref: no)	1.15	0.63	2.10	0.64
Antidepressant use (ref: no)				
Short term (<180 d)	0.90	0.58	1.40	0.63
Long term (≥180 d)	0.93	0.65	1.35	0.72
Antispasmodic use (ref: no)				
Short term (<180 d)	1.36	0.74	2.48	0.32
Long term (≥180 d)	2.44	1.53	3.88	**0.0002**
History of falls (ref: no)	1.65	0.79	3.45	0.18
BMI (per 5 kg/m^2)	0.84	0.82	0.86	**<0.0001**

Abbreviation: BMI = body mass index.
Bold indicates statistical significance.
[a] No interaction terms included in this model; c-statistic = 0.805.

screening. The fracture risk assessment tool (FRAX) incorporates age, sex, BMI, prolonged use of glucocorticoids, parental hip fracture, current smoking, high alcohol intake, previous fragility fracture, and (optionally) femoral BMD.[33] Thus, the FRAX tool highlights relevant clinical factors that can be considered in screening. Some authors proposed indications for BMD screening in MS to be postmenopausal status (in women) and an EDSS score of 6.0 or more.[5] Among persons with MS with an EDSS score of <6.0, a previous fracture, prolonged glucocorticoid use, and use of anticonvulsants were also indications for screening. Our findings suggest that these recommendations are reasonable, but also suggest that the use of antispasmodics, substance use, and the presence of comorbid conditions associated with poor bone health should also be indications for BMD screening in the MS population. An important note of caution, however, is that the FRAX tool appears to underestimate the risk of osteoporotic fractures in MS, and adjustment to the tool may be needed to address this limitation and support optimal management of bone health.[34]

Once identified, osteoporosis can be managed as usual in the general population.[35] Ideally, however, low BMD would be

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identified early so that preventive efforts can target high-risk individuals to reduce their risk of fractures. To achieve this will require education of patients and health care providers regarding the risk of poor bone health in MS. Specific efforts to ensure appropriate nutrition and increase physical activity[36] will be needed to maximize bone strength throughout the disease course. Smoking cessation, moderation of alcohol intake, and prevention of comorbidities that increase fracture risk will also be needed. Given the role of falls in osteoporotic fractures, continued expansion of falls prevention efforts are needed.[37,38]

Study strengths included the population-based design, use of matched controls, and consideration of multiple factors that may influence bone health. This study also had limitations. We examined individuals who underwent BMD screening; thus, our findings may not be representative of those in the entire MS population. Because factors associated with BMD screening in Manitoba do not differ in the MS and non-MS populations,[39] and because we controlled for these factors, this potential selection bias is unlikely to affect the between-group comparisons. We did not use a formally validated, MS-specific measure of disability. Because of small numbers of individuals affected, we were not able to evaluate associations with fatigue, anticonvulsant use, and several conditions (inflammatory bowel disease, congestive heart failure, chronic kidney disease, chronic liver disease, glaucoma, and organ transplant). We could not capture IV glucocorticoid use, but their intermittent use was not associated with an increased risk of osteoporotic fracture in chronic obstructive pulmonary disease.[40] We also could not capture vitamin D status and its association with bone health.[7] We did not assess previous use of osteoporosis medications or estrogen, but this would tend to bias toward the null as more people with MS had osteoporosis and were thus more likely to be treated.

In a screened population, MS was associated with low BMD after accounting for factors commonly associated with BMD and was associated with over 2-fold increased odds of osteoporosis. These results indicate the importance of addressing bone health as part of comprehensive MS care. Given the high rate of falls among people with MS and the association between falls and fractures, the development of systematic approaches to BMD screening and to optimize bone health is needed.

TAKE-HOME POINTS

- → Persons with MS have lower BMD than people without MS.
- → Persons with MS have more than 2-fold increased odds of osteoporosis than people without MS.
- → Bone health should be addressed as part of comprehensive care in MS.

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Disclosure

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Appendix Authors

Name	Location	Role	Contribution
Etienne J. Bisson, PhD	Queen's University, Kingston, Canada	Author	Obtained study funding, responsible for study concept and design, and drafting and revision of the manuscript.
Marcia L. Finlayson, PhD	Queen's University, Kingston, Canada	Author	Obtained study funding, responsible for study concept and design, and drafting and revision of the manuscript
Ruth Ann Marrie, MD, PhD	University of Manitoba, Winnipeg, Canada	Author	Obtained study funding, responsible for study concept and design, and revision of the manuscript

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Appendix *(continued)*

Name	Location	Role	Contribution
Okechukwu Ekuma, MSc	University of Manitoba, Winnipeg, Canada	Author	Data analysis and revision of the manuscript
William D. Leslie, MD	University of Manitoba, Winnipeg, Canada	Author	Obtained study funding, responsible for study concept and design, and revision of the manuscript

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