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RESEARCH ARTICLE

# The association between fracture risk and bone mineral density in black postmenopausal women living with human immunodeficiency virus

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**Background:** South African urban postmenopausal women have an increased risk for the development of low bone mineral density (BMD) and consequently osteoporosis. Osteoporosis and fractures are also a concern in people living with HIV (PLHIV).
**Objectives:** This study aimed to determine the 10-year fracture risk probability (major osteoporotic and hip) using the Fracture Risk Assessment Tool (FRAX®) and the association with BMD in Black postmenopausal women living with HIV on highly active antiretroviral therapy (HAART).
**Methods:** This study is a cross-sectional analysis that forms part of a prospective cohort study in South Africa. Baseline data from 120 Black postmenopausal women living with HIV were used. BMD was measured by dual X-ray absorptiometry (DXA) at the spine, left femoral neck of the hip, total hip, and total body. The fracture risk was determined using a validated online fracture risk instrument for South African populations. Multivariate linear regression models were applied to assess the associations of 10-year risk of major osteoporotic fracture or hip fracture, respectively, with site-specific BMDs, adjusting for calcium intake, serum vitamin D, duration of HIV infection, and physical activity.
**Results:** The median 10-year risk of major osteoporotic and hip fracture (1.3%, 95% CI 1.0, 2.1%, and 0.2%, 95% CI 0.1, 0.4%) was low. Risk of major osteoporotic fracture and hip fracture was negatively associated with site-specific BMDs ($p < 0.05$). Duration of diagnosed HIV infection showed a trend for an association with spine BMD ($p = 0.058$).
**Conclusions:** In settings with no access to DXA, fracture risk calculated using FRAX® will be a useful indicator of site-specific BMD among Black postmenopausal women living with HIV. Although the FRAX tool is not validated in individuals living with HIV, both FRAX fracture risk estimates and DXA-derived BMD assessments independently predicted a similarly low probability of fracture.

**Keywords:** Africa, bone mineral density, fracture risk, HIV, osteoporosis, postmenopausal

## Introduction

Osteoporosis is a multifactorial skeletal disease presenting most often in postmenopausal women.[1] Osteoporosis is characterised by reduced bone mass and deterioration of the micro-architecture of the bone. As a result, bone strength is reduced and vulnerability to fractures increases.[2,3] This disease has become a global epidemic with an estimated 1.4 million females over the age of 50 years suffering from osteoporosis.[2]

In South Africa, the incidence of osteoporosis is similar to that of high-income countries; however, fracture data are limited.[4] A recent multicentre study reported that the incidence rate of hip fractures was higher in women than men in the older age groups among all ethnic groups.[5] Furthermore, a 10-fold increase in hip fracture incidence in Black people has been reported in KwaZulu-Natal and 113 cases of fragility fractures of the hip in Cape Town have been reported.[6,7] Currently, South Africa is experiencing rapid urbanisation, the driving force being increased work opportunities and improved living conditions in cities.[8] Environmental factors influencing the risk of lower bone mineral density (BMD) may be attributed to changes in diet and physical activity (PA) as a result of urbanisation.[9] Dietary changes associated with urbanisation such as a shift from traditional foods consumed in rural areas towards consumption of Western foods low in calcium and vitamin D negatively influence BMD.[9–11] Postmenopausal women can benefit from regular PA as it may contribute towards increasing bone formation, improving bone structure, and maintaining BMD.[12,13] Kruger and colleagues found that Black urban women have low PA levels, especially women older than 70 years.[8]

Osteoporosis and associated fractures are also becoming a concern in people living with HIV (PLHIV).[14–19] It is estimated that 15% of PLHIV will be diagnosed with osteoporosis.[20] Women who are living with HIV are especially at risk as they are more likely to experience early menopause, increasing their risk of developing osteoporosis.[21,22] Various studies have shown a marked increase in the prevalence of bone demineralisation in PLHIV.[23–26] In comparison with the general population, PLHIV are 6.4 times more likely to develop low BMD and have a fracture risk as high as 58%.[20,27] Fractures are likely to occur 10 years earlier in PLHIV than in HIV-uninfected individuals.[28] Globally an estimated 39 million individuals were living with HIV at the end of 2022, of whom two-thirds are living in Africa.[29] South Africa reports the highest prevalence in the world, with 8.2 million PLHIV in 2021.[30] HIV infection is not the only factor that leads to increased bone loss. Antiretroviral therapy (ART) is also known to decrease BMD by various mechanisms and has also been associated with poor vitamin D status.[31–33] Upon initiation of ART, bone demineralisation occurs rapidly but stabilises after 24 months.[34–36] A recent randomised controlled trial showed that vitamin $D_2$ and calcium supplementation may reduce this bone loss among PLHIV receiving ART.[37] Despite the fact that highly active antiretroviral therapy (HAART) has been proved to improve survival and

quality of life meaningfully, the higher incidence of osteoporosis and associated fractures has become a significant concern.[38,39] Other risk factors for low BMD in patients with HIV include low weight, older age, smoking, and female sex.[16,23,31,32] The Fracture Risk Assessment Tool (FRAX®) developed by the University of Sheffield in the United Kingdom is recommended to predict the 10-year fracture risk probability in individuals and the assessment tool has been adapted for the South African population. However, the tool lacks validation in PLHIV.[40,41]

Urbanisation combined with increasing life expectancy and prevalence of HIV and ART use has detrimental effects on the bone health of South Africans.[8,20] The main objectives of this study were to determine the number of risk factors for fracture in Black postmenopausal PLHIV on HAART and the association between 10-year fracture risk probability (major osteoporotic and hip) using FRAX® and BMD of the total body, spine, and left femoral neck, respectively.

## Method

### Study design and setting

This study was a cross-sectional analysis using baseline results from a prospective cohort study from the North-West province with Black postmenopausal PLHIV on HAART. Participants were recruited from an outpatient clinic for PLHIV at Potchefstroom Hospital. All measurements were performed at the Metabolic Unit of North-West University (NWU).

### Study population

Black postmenopausal HIV-positive women aged ≥ 45 years on HAART were studied, because limited data exist on bone health in PLHIV in Southern Africa.[5] The HAART consisted mainly of tenofovir, emtricitabine, and efavirenz combined in a fixed-dose tablet ($n = 103$, 85.8%). The remainder of participants received combinations of the following: tenofovir, with emtricitabine, nevirapine, or lamivudine as well as combinations including abacavir, zidovudine, or lopinavir/ritonavir.

The available sample size for the study was 120 women. This study may be underpowered to assess the association between traditional risk factors for adverse bone health and BMD in this older cohort of women living with HIV. The number of women living with HIV is limited and, in our experience, it is not feasible to recruit large numbers of older (≥ 45 years) HIV-positive women, because most women living with HIV are younger than 45 years. This study will be considered as an exploratory study, and the results will be interpreted with caution.

### Ethics approval and consent to participate

Written informed consent was obtained from all participants. Approval from the Human Research Ethical Committee of the NWU (NWU-00061-17-A1-01) and the Department of Health to conduct the study was also obtained.

Inclusion criteria included Black postmenopausal South African women, ≥45 years living with well-controlled HIV and on HAART. Exclusion criteria for the cross-sectional study included use of anti-osteoporotic agents; history of metabolic bone disease; habitual use of calcium and/or vitamin D supplementation. The data were collected from August to November 2017.

## Measures

### Sociodemographic and health information

The sociodemographic and health information of the participants was determined by an interviewer-administered structured questionnaire. Information that was collected included: age, educational status, housing, occupation, smoking, alcohol consumption, chronic medication use, diagnosis of type 2 diabetes mellitus, year of first diagnosis of HIV infection, and year of initiation of HAART.

### Anthropometric measurements

Anthropometric measurements were performed by trained fieldworkers, postgraduate students, and registered dietitians. Anthropometric measurements included height and weight. Participants were weighed without shoes and wore minimal clothing. Height and weight were measured using a calibrated digital scale with stadiometer (Seca 264, Hamburg, Germany) following standard procedures.

### Dietary intakes

Dietary intakes over the period of a month were assessed using a standardised quantitative food frequency questionnaire (QFFQ) that was previously validated in this population.[42,43] The QFFQ was administered by trained fieldworkers in a language that the participant understood, namely English, Afrikaans, Tswana, or Xhosa. Food models and photographs in photo books with three portion sizes of the most commonly eaten foods were used to estimate portion sizes.[42,43] Dietary energy, macronutrients, and micronutrients were analysed using the South African Medical Research Council Food Finder software®, which is based on South African food composition tables.[44]

### Physical activity

PA was assessed using the Global Physical Activity Questionnaire (GPAQ) recommended by the World Health Organization (WHO).[45] The questionnaire gathers information on PA done in the previous seven days in the following domains: occupational PA, transport-related PA, and PA during leisure time.[45] The times spent during the various PA domains in terms of frequency (days per week) and duration (minutes per day) were estimated. The total PA level of each individual was calculated in metabolic equivalent-minutes (MET-minutes) per week by multiplying the MET intensity for each activity domain by minutes per week spent during each activity and according to reported day(s). The MET intensities used to score GPAQ were vigorous (8METs), moderate (4METs), and leisure time (4METs) PA as defined in the WHO guidelines. Participants were classified into GPAQ active or inactive categories according to the WHO cut-point of < 600 MET-minutes/week for inadequate vs. > 600 for adequate PA.[45]

### Bone mineral density

Bone mineral density (BMD) was measured by a registered radiographer through X-ray absorptiometry (DXA) with the default Hologic settings (Hologic Discovery W, APEX system software version 2.3.1) at the lumbar spine and left proximal hip regions including the total hip and femoral neck in g/cm$^2$. Participants were asked to change into cotton gowns with no metal buttons or zip-pull fasteners and asked to remove all jewellery and other personal item(s) that could interfere with the DXA scan.

### Risk factors for fracture

Risk of fractures was assessed using a checklist developed from information in the literature.[46] The checklist included 11 risk factors for fracture similar to the FRAX instrument such as: age, female sex, underweight, previous fragility fractures, parent fractured hip (fragility), current smoking, glucocorticoid therapy during the last six months, chronic proton pump inhibitor (PPI) use during the last six months, rheumatoid arthritis, secondary osteoporosis, and alcohol consumption of $\geq$ 3 units per day. The number of risk factors represents the sum of the conditions present in each participant, but risk factors were not weighted, and all contributed the same value to the final risk score (risk factor present = 1). Finally, the recently validated online fracture risk instrument for South African populations was used to generate a 10-year probability of a major osteoporotic fracture or hip fracture, respectively, for each study participant.[41] The 10-year probability of a major osteoporotic fracture or hip fracture, respectively, was calculated without the inclusion of left femoral neck of the hip BMD. The risk factors in this instrument are similar to the checklist, with the exception of PPI use, which is excluded from the FRAX online instrument.[46] These risk factors were based on a systematic set of meta-analyses of population-based cohorts worldwide and validated in independent cohorts with over 1 million patient-years of follow-up. The construct of the FRAX model for South Africa retained the beta coefficients of the risk factors in the original FRAX model with the incidence rates of hip fracture and mortality rates for South Africa.[41] The risk factors included in the risk instrument include the same variables used in the checklist compiled for the current study, except for PPI use during the last six months. The beta coefficients for each risk factor in the validated FRAX model equation represent the strength of the association of the individual risk factor with the 10-year probability of a major osteoporotic fracture or hip fracture.

### Serum vitamin D concentration

Fasting blood samples of 5 ml were collected by a registered nurse in serum tubes and centrifuged as soon as possible after sample collection. Serum was prepared and stored in a bio-freezer at −80°C until analyses were performed. Fasting serum concentrations of vitamin D (25OHD) were measured by an electrochemiluminescence immunoassay on the Elecsys 2010 (Roche, Basel, Switzerland).

## Statistical analysis

The distribution of the different variables was assessed using the Kolmogorov–Smirnov test and Q–Q plots. Descriptive statistics of sociodemographic data, dietary intakes, PA, and BMD at the different sites, as well as fracture risk scores, are presented as means and standard deviation (data with normal distribution) or median and interquartile range (non-normal distribution). The correlation between BMI and left femoral neck of the hip BMD was assessed using Spearman correlation analysis. To determine the association between fracture risk probability and BMD of the left femoral neck and spine, respectively, multivariable regression models were used with site-specific BMD as the dependent variable for each model, with adjustment for calcium intake, serum vitamin D concentration, duration of HIV infection, and PA. Participants were further categorised according to the WHO cut-offs for normal BMD, osteopenia, and osteoporosis based on BMD T-scores at the left femoral neck of the hip BMD.

The Statistical Package for the Social Sciences (SPSS version 30 program; IBM Corp, Armonk, NY, USA) was used to perform all statistical analyses and a $p$-value of $\leq 0.05$ was accepted as statistically significant.

## Results

Participant characteristics are summarised in Table 1. A small proportion of the participants (5%) had a PA level of > 600 MET-minutes/week (adequate PA), 22% were overweight, 38% were obese, and 8.3% were underweight. The median 10-year probabilities of major osteoporotic fracture and hip fracture without the addition of BMD of the study participants were low (1.3%, 95% CI 1.0, 2.1%, and 0.2%, 95% CI 0.1, 0.4%).

Self-reported risk factors for fracture are given in Table 2. All participants were postmenopausal females and aged $\geq$ 45 years. About one-third of these women had no additional risk factor or just one added risk factor (39.2% and 37.5% respectively). Self-reported previous fragility fracture occurred in 19.2%. The highest number of risk factors in an individual was five and was present in 6/120 of the participants (5%).

There was a positive correlation between BMI and left femoral neck of the hip BMD ($r = 0.55$, $p < 0.001$), spine BMD ($r = 0.43$, $p < 0.001$), and total body BMD ($r = 0.39$, $p < 0.001$). The association between major osteoporotic and hip fracture risk, respectively, was calculated with the FRAX tool without BMD, and BMD was assessed in two ways. First, the association between individual fracture risk probability and total, spine, and left femoral neck of the hip BMD was assessed in multivariable linear regression models. Participant fracture risk probability was entered as a continuous variable. In an additional model the association between fracture risk probability and BMD was assessed with further adjustment for serum vitamin D concentration, calcium intake, reported duration of HIV infection, duration of HAART therapy, and PA as additional covariates. Results of fully adjusted models are presented in Table 3. Final models with only fracture risk probability and with additional adjustment are reported and only variables included in the final adjusted models are shown.

Higher probability of major osteoporotic as well as hip fracture predicted lower total, spine, and left femoral neck BMD in the unadjusted and adjusted models ($p < 0.05$), with the exception of major osteoporotic probability in the spine BMD model, which was not significant ($p = 0.13$). Hip fracture probability explained the highest variance of 15% in total BMD ($p < 0.001$). Duration of HIV infection showed a trend for negative association with spine BMD ($p = 0.05$).

Participants were further categorised according to the WHO cut-offs for normal BMD, osteopenia, and osteoporosis based on the T-score calculated from femoral neck of the left hip BMD (Table 4).

More than 50% of the women had normal BMD, while 37% had osteopenia, and 10% met DXA-BMD criteria for osteoporosis. Participants with osteopenia or osteoporosis were significantly older and had lower BMI compared with those with normal BMD ($p < 0.01$). Although the FRAX-calculated 10-year risks for major osteoporotic and hip fractures without BMD were uniformly low across all BMD categories, the calculated absolute fracture risk was significantly higher in those with osteopenia or osteoporosis. Previous fragility fractures were reported only by women with either normal BMD (12/64: 19%) or those with osteopenia (11/44: 25%). Timing and anatomical sites of these fractures are not known.

**Table 1:** Characteristics of the study participants

| Characteristics | *n* (%) | Median | Interquartile range |
|---|---|---|---|
| Age (years) | | 50 | 48, 55 |
| Hypertension | 55 (45.8%) | | |
| Type 2 diabetes mellitus | 10 (8.3%) | | |
| Current smokers | 12 (10%) | | |
| Alcohol intake (g/day) | | 0.0 | 0, 1 |
| Physical activity moderate (minutes/week) | | 145.0 | 45, 300 |
| Physical activity vigorous (minutes/week) | | 0.0 | 0, 0 |
| Sedentary time (minutes/day) | | 240.0 | 120, 360 |
| Duration of HIV infection (years) | | 10 | 7, 14 |
| Duration of HAART (years) | | 9 | 5, 13 |
| Weight (kg) | | 66.7 | 54.1, 80.0 |
| Height (cm) | | 156.0 | 151.5, 161.1 |
| BMI (kg/m$^2$) | | 27.1 | 22.4, 32.6 |
| Lean mass (kg) | | 36.2 | 32.5, 42.1 |
| Body fat (%) | | 38.6 | 33.8, 43.6 |
| Calcium intake (mg/day) | | 724 | 462, 1040 |
| Serum vitamin D concentration (ng/ml) | | 36.6 | 28.1, 44.0 |
| FRAX MOF (%) | | 1.3 | 1.0, 2.1 |
| FRAX HF (%) | | 0.2 | 0.1, 0.4 |

BMI: body mass index; BMD: bone mineral density; HAART: highly active antiretroviral therapy; FRAX MOF: 10-year probability of major osteoporotic fracture without BMD; FRAX HF: 10-year probability of hip fracture without BMD

**Table 2:** Risk factors for fracture identified among women

| Risk factors | *n* (%) |
|---|---|
| Female | 120 (100%) |
| Age > 45 years | 120 (100%) |
| Underweight | 10 (8.3%) |
| Smoking current | 12 (10%) |
| Alcohol consumption ≥ 3 units per day | 6 (5.0%) |
| Previous fragility fracture | 23 (19.2%) |
| Parent fracture hip (fragility) | 14 (11.7%) |
| Glucocorticoid therapy (> 3 months) | 0 (0.0%) |
| Rheumatoid arthritis | 0 (0.0%) |
| Proton pump inhibitor[a] | 8 (6.7%) |
| Secondary osteoporosis | 0 (0.0%) |

[a]Risk factor not included in the fracture risk instrument for South Africans.

## Discussion

There was a strong, positive association between site-specific DXA-BMD and fracture risk estimated by the FRAX tool. Although the overall fracture risk was low, women with DXA-BMD criteria for osteopenia and osteoporosis had significantly higher risk. These results indicate that calculated fracture risk may be a useful indicator of site-specific BMD among Black postmenopausal women living with HIV in settings with no access to DXA. In South Africa and other low-to middle-income countries with a relatively high prevalence of HIV infection, few PLHIV have access to DXA and those with an increased fracture risk may remain unidentified if the FRAX tool is not utilised.[47]

Self-reported fragility fractures and parental hip fracture history could not be verified and should be interpreted with caution.

**Table 3:** Multiple regression models for the association between fracture risk probability and BMD with site-specific BMD

| Variables | Adjusted $R^2$ | Standardised ß coefficient | *p*-value |
|---|---|---|---|
| Total BMD model with major osteoporotic fracture risk probability: | | | |
| Major osteoporotic fracture probability | 0.05 | −0.30 | 0.01 |
| Total BMD model with hip fracture risk probability: | | | |
| Hip fracture risk probability | 0.15 | −0.44 | < 0.001 |
| Spine BMD model with major osteoporotic fracture probability: | | | |
| Major osteoporotic fracture probability | 0.05 | −0.17 | 0.13 |
| Duration of HIV infection | | −0.23 | 0.05 |
| Spine BMD model with hip fracture risk probability: | | | |
| Hip fracture risk probability | 0.12 | −0.32 | 0.004 |
| Left femoral neck BMD model with major osteoporotic fracture probability: | | | |
| Major osteoporotic fracture probability | 0.05 | −0.27 | 0.02 |
| Left femoral neck BMD model with hip risk probability: | | | |
| Hip fracture risk probability | 0.12 | −0.37 | < 0.001 |

BMD: bone mineral density; MET- minutes: metabolic equivalent-minutes. Regression models adjusted for calcium intake (mg/day), serum vitamin D, duration of HIV infection, and PA level; FRAX calculations done without left femoral neck BMD.

**Table 4:** Characteristics according to the WHO cut-offs for normal BMD, osteopenia and osteoporosis

| Characteristics | Normal BMD[¥] *T* score ≥ −1 (*n* = 64, 53.3%) | Osteopenia[¥] *T*-score −1 to −2.5 (*n* = 44, 36.7%) | Osteoporosis[¥] *T*-score ≤ −2.5 (*n* = 12, 10%) | *p*-value |
|---|---|---|---|---|
| Age (years) | 49 (47,51) | 54 (49, 58)[a] | 52 (48, 59) | < 0.001 |
| Weight (kg) | 75.3 (61.1, 87) | 56.3 (52.7, 68.5)[a] | 50.9 (42.4, 61.4)[a] | < 0.001 |
| Height (m) | 157.7 (153, 161.4) | 155.2 (151.2, 160.8) | 157.6 (151.3, 160.9) | 0.42 |
| BMI (kg/m$^2$) | 30,7 (25.9, 33.8) | 23.9 (21.8, 29)[a] | 20.2 (16.8, 24.6)[a] | < 0.001 |
| Duration of HIV infection (years) | 9 (5, 13) | 11 (8, 14) | 8 (8, 14) | 0.44 |
| Duration of HAART (years) | 8 (5, 13) | 10 (8, 12) | 8 (8, 14) | 0.42 |
| Calcium intake (mg/day) | 707.6 (444.4, 891.2) | 746.1 (462.8, 1157.8) | 711.3 (589, 806.9) | 0.51 |
| Serum vitamin D concentration (ng/ml) | 35.4 (26.6, 42.5) | 36.9 (29.1, 46.8) | 37.4 (25, 45.7) | 0.89 |
| Self-reported previous fragility fracture (n) | 12 | 11 | 0 | |
| FRAX MOF (%) | 1.1 (0.9, 1.6) | 1.7 (1.3, 2.3)[a] | 1.5 (1.2, 2.2) | < 0.001 |
| FRAX HF (%) | 0.1 (0.1, 0.2) | 0.4 (0.2, 0.6)[a] | 0.3 (0.2, 0.7)[a] | < 0.001 |

BMD: bone mineral density; WHO: World Health Organization; BMI: body mass index; FRAX MOF: 10-year probability of major osteoporotic fracture without BMD; FRAX HF: 10-year probability of hip fracture without BMD. [¥] WHO BMD categories were determined using left femoral neck BMD T-scores; values are reported as median (25th, 75th percentiles); Kruskal–Wallis with multiple comparison rank tests were used to compare between three groups of continuous, non-normally distributed data. [a] Compared against normal BMD, [b]compared against osteopenia, 0.05/3 = 0.0167, adjusted by the Bonferroni correction for multiple comparisons: 0.05/3 = 0.0167.

The timing of fractures relative to HIV onset was unknown and cannot be used to explain the high reported prevalence (19.2%) despite the low calculated fracture risk. Fractures may have occurred early in the disease course, before effective disease control, and during initial HAART. Neither previous nor parental fracture history was associated with BMD. This is noteworthy as previous research has suggested an association between increased risk of another fracture and previous fracture history.[23,48,49]

Race plays a modifying role in the relationship between HIV and fracture risk. A meta-analysis and systematic review found higher risk of fractures in non-Black population groups than in Black groups.[18] Previously, studies reported that Black populations have a reduced risk of osteoporosis and skeletal fragility due to their enhanced BMD; however, these findings from the United States of America and Europe may not be relevant to South Africa's Black population.[50,51] Limited data on BMD are available on non-White population groups living in low- to middle-income countries such as South Africa.[52] Changes in diet and PA as a result of urbanisation increase the risk of lower BMD in Black South African women.[9] The fracture rate among Black South Africans has been increasing.[6] Johansson et al.[41] compared the lifetime probability of hip fracture in various countries. They found that the probability for hip fracture in Black South African women is still among the lowest of all countries (4.5%).[41] The low background fracture risk in South African Black women may in part explain the very low fracture probability documented in this study. Conradie et al.[53] compared BMD between otherwise healthy adult Black and White South African women and documented site-specific differences in BMD. Higher femoral neck BMD in the Black women possibly explains the lower hip fractures prevalence in this ethnic group. The ethnic differences in BMD were mostly explained by significant bodyweight differences between the two groups.[53]

HIV and HAART, especially tenofovir disoproxil fumarate use, have been shown to decrease BMD and consequently increase the risk of osteoporosis and associated fractures by various mechanisms.[15,20,27,31–33,38,39] A South African study demonstrated that exposure to ART is associated with lower total hip BMD in a young group of PLHIV.[32] The present study confirms the negative association between duration of HIV infection and spine BMD, but not femoral neck BMD. The 10-year probability of hip fracture among the women from the current study was low at 0.2% with BMD included in the calculations.

The high prevalence of obesity (38%) and overweight (22%) as well as the low prevalence of underweight in only 10 of the participants (8.3%) may have contributed to the low probability of hip fracture among the women from the current study. Low BMI is a known risk factor for osteoporosis and fracture, whereas a high BMI has a strong positive association with BMD.[54,55] BMI was not included in the regression models as underweight was included as a fracture risk factor in the FRAX tool. Low BMI is a known risk factor for osteoporosis and fracture, whereas a high BMI has a strong positive association with BMD.[23,46]

The median calcium intake of the women was 724 mg, which is higher than has previously been reported for this population group.[8] Kruger and colleagues reported a low calcium intake (200–450 mg/day) in both rural and urban Black women older than 45 years.[8] In this study no association between calcium intake and total BMD, spine BMD, and left femoral neck BMD was demonstrated. The high self-reported calcium intake may be explained by possible over-reporting by the participants and/or the influence of previous nutrition counselling, which has resulted in participants consuming more dairy foods than previously during early life.

Regular PA benefits postmenopausal women as it contributes towards increasing bone formation, improving bone structure, and maintaining BMD.[12] PA has been found to have a low but significant effect on BMD at the proximal femur and lumbar spine.[56] In this study only a small proportion of the participants had an adequate PA level of > 600 MET-minutes/week. Participants did not partake in vigorous activity, had a median moderate activity level of 145 minutes/week and spent a median of 240 minutes/day in sedentary activities. Similar low PA levels have been reported in this population group.[8] In this study only the current PA levels were measured, which is not reflective of the effects on BMD of PA during young adulthood.[57]

Smoking and excessive alcohol consumption are well-established risk factors for adverse bone health and fracture risk and may also contribute to skeletal fragility in PLHIV.[58,59] Smoking affects bone health by impairing osteoblast functioning as well as reducing intestinal calcium absorption, and is also associated with lower bodyweight and earlier onset of menopause.[59–61] A meta-analysis found that smoking in women increases vertebral and hip fracture risk by 13% and 31% respectively.[62] Kruger and colleagues found that smoking contributed to increased osteoporosis risk in urbanised Black postmenopausal women.[8] In this study only 12 participants (10%) were active smokers and the number of cigarettes smoked per day was very low, ranging from 1 to 11 cigarettes per day. No significant association was observed between smoking and BMD in this study. Data on the number of pack years smoked was not obtained. Given the implication of smoking on bone health, it is important that education regarding this subject be given.

Chronic alcohol intake may have direct and indirect toxic effects on bone and may result in increased bone resorption due to increased parathyroid hormone levels.[63] Prior studies have demonstrated that alcohol abuse is a risk factor for osteoporosis in urbanised Black postmenopausal women.[8] In our study only six participants (5%) reported that they consumed ≥ 3 units of alcohol per day, and may in part explain why an association between alcohol intake and BMD could not be established.

Medication use such as glucocorticoid drugs and PPI is associated with compromised bone health.[64–66] Prolonged use of glucocorticoid drugs adversely affects bone health by decreasing intestinal calcium absorption and renal reabsorption, and inhibiting osteoblast function, thereby increasing risk for osteoporosis-related fractures. Fracture incidence can be as high as 30% if these drugs are taken for an average of five years.[64,65] A cohort study found an increased risk of fractures in women currently using PPI as well as those with a prior fracture after the age of 40 years.[67] Similarly, a meta-analysis concluded that PPI use was associated with an increased risk of hip and vertebral fractures in elderly men and women.[68] In our study, none of the participants were on chronic glucocorticoid therapy, whilst 6.7% of the participants received PPI therapy. Participants could not recall the duration of PPI use, but the dose and duration were probably not sufficient to show an association with BMD.

## Limitations and strengths

To our knowledge this study is the first to investigate the association between fracture risk determined by the South African adapted FRAX® and BMD in Black postmenopausal women living with HIV on HAART.

The study had some limitations. It had a relatively small sample size and may be underpowered to assess the association between fracture risk and BMD. The number of postmenopausal women living with HIV is limited and, in our experience, it is not feasible to recruit large numbers of women aged ≥ 45 years, because most women living with HIV are younger. Other limitations include a possible over-reporting of calcium intake, and parental hip fracture was not confirmed but self-reported. Furthermore, previous fragility fractures were self-reported, and the location of these fractures was not recorded.

## Conclusions

Among Black postmenopausal PLHIV, the 10-year probability for major osteoporotic fractures and hip fractures was low. Higher probability of major osteoporotic as well as hip fracture was associated with lower spine and proximal BMD. Urbanisation combined with high prevalence of HIV and ARV use has detrimental effects on the bone health of South Africans and is a growing concern. The results of this study indicate that fracture risk probability determined by the South African adapted FRAX® is significantly associated with BMD in Black postmenopausal women living with HIV on HAART. The risk of fractures in ageing woman living with HIV must always be considered by the practitioner and can be calculated using the FRAX tool adapted for South African women. In settings with no access to DXA, fracture risk calculated using FRAX® will be a useful indicator of site-specific BMD among Black postmenopausal women living with HIV.

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