

Factors Associated with Bone Mineral Density in Healthy African Women

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Background

- Healthy women generally achieve peak bone mass at approximately 30 years of age.
- The process of bone accumulation may continue slowly until 50 years of age.
- Factors traditionally associated with lower Bone Mineral Density (BMD) include:
 - Pregnancy
 - Lactation
 - Use of depo –medroxy progesterone acetate (DMPA) for contraception
 - Low body mass
 - Low physical activity (PA)
 - Low socio-economic status
 - A sedentary lifestyle
- Environmental, nutritional and genetic factors have also been shown to contribute to variations in bone metabolism.

BMD in SSA Women

- Nearly all prior studies establishing normative BMD levels have been conducted in middle to high resource settings.
- Relatively little data exist on the BMD of healthy women in Sub-Saharan Africa (SSA), especially in countries other than South Africa.
- Women from Zimbabwe had higher BMD than those from Brazil, Bangladesh, China, Egypt Mexico, and Thailand. (Petitti et al, Obst Gyn 2000)
- The CDC TDF2 study demonstrated a higher than expected prevalence of low BMD (6.8%, CI 3.4 - 11.0) in young Batswana adults. (Kasonde et al, PLoS ONE 2014)
- Normative reference levels for these subpopulations have not been established.

BMD in SSA Women

- Factors affecting BMD in healthy African women have not been well studied.
- High rate of fertility, extended lactation, frequent use of DMPA and nutritional deficiencies are common among Sub-Saharan African women and could affect BMD.
- The VOICE study, which evaluated oral Tenofovir Disoproxil Fumarate (TDF), oral Tenofovir Disoproxil Fumarate - Emtricitabine (TDF-FTC) and Tenofovir gel for HIV-1 prevention.
- The study provided us a unique opportunity to conduct a cross-sectional baseline evaluation of BMD among Zimbabwean and Ugandan women.

MTN-003B

- From Sep 2009 -June 2012, 5,029 women aged 18 - 45 years were enrolled and followed up in the VOICE study at 15 sites in South Africa, Uganda and Zimbabwe.
- HIV-negative, sexually active women, with no laboratory evidence of renal, hepatic or haematological disease were enrolled.
- Additional exclusion criteria were current or recent pregnancy or current breastfeeding, any history of non-traumatic bone fracture, current injection drug use, chronic Hepatitis B, or any ongoing medical condition/medication known to affect bone.
- All women enrolled into the VOICE oral arms in Uganda and Zimbabwe were offered participation in the BMD Sub-study.

Methods

- At sub-study entry, the following information was recorded for all participants:
 - Self-reported contraceptive and lactation history
 - Anthropometric measurements (height and weight)
 - Abbreviated food frequency questionnaire for estimation of dietary calcium
 - Physical activity (PA) assessment using the International Physical Activity Questionnaire
- Baseline BMD of the lumbar spine (LS) and total hip (TH) were measured at study entry by dual-energy x-ray absorptiometry (DXA). T- and Z- scores were derived from the National Health and Nutrition Examination Survey (NHANES) reference database.
- 25'hydroxy-Vitamin D was measured from stored sera.

Statistical Analysis

- Demographic characteristics and other factors of interest were summarized descriptively.
- Distributions of these factors for each site were compared and p-values were provided from chi-squared test for categorical variables and from Wilcoxon two-sample test for continuous variables.
- Independent factors associated with baseline BMD were identified using an analysis of covariance model.
- Logistic regression models were used to identify independent factors associated with low T-scores (< -1.0) for BMD.

Baseline Demographics

	Overall	Uganda	Zimbabwe	P-value
N	518	187	331	
Median age (IQR)	29 (25,32)	28 (24, 31)	29 (25, 32)	0.452
Physical Activity [Total MET hours/week] (IQR)	57.9 (29.4, 107.0)	48.8 (23.7, 107.0)	63.1 (32.6, 107.1)	0.051
Median Parity (IQR)	2 (2, 3)	3 (2, 4)	2 (2, 3)	0.0001
Earns own income (N,%)	279 (54%)	138 (74%)	141 (43%)	<0.0001
Married (N, %)	410 (79%)	100 (53%)	310 (94%)	<0.0001
Median BMI* [kg/m ²] (IQR)	24.8 (22.2, 28,6)	24.5 (22.2, 29.0)	24.9 (22.2, 28.6)	0.984
Lifetime Breastfeeding duration (N, %)				<0.0001
>5years	151 (30%)	89 (49%)	62 (19%)	
2 - 5 years	252 (49%)	60 (33%)	192 (59%)	
<2 years	107 (21%)	33 (18%)	74 (23%)	

*BMI = Body Mass Index

Baseline Contraceptive History

	Overall	Uganda	Zimbabwe	P-value
N	518	187	331	
Contraceptive Method ever Used** (N,%)				
DMPA	367 (71%)	149 (80%)	218 (66%)	0.0006
COCP	420 (81%)	100 (54%)	320 (97%)	<0.0001
Implant	139 (27%)	12 (6%)	127 (38%)	<0.0001
Duration of Use in All (months)***				
DMPA	3(0, 24)	15 (1, 37)	0 (0, 12)	<0.0001
COCP	29.5 (2.0, 72.0)	1 (0, 14)	51 (24, 84)	<0.0001
Implant	0 (0, 0)	0 (0,0)	0 (0,0)	0.0002
Duration of Use in those indicating method (months) ***				
DMPA	12(1, 36)	24 (12, 48)	6 (0, 28)	<0.0001
COCP	38.5 (18.0,84.0)	12.5 (3, 33)	53.5 (25, 87)	<0.0001
Implant	0.5 (0, 11)	14 (1, 36)	0 (0, 7)	0.0011

**Percent of women reporting history of specific method

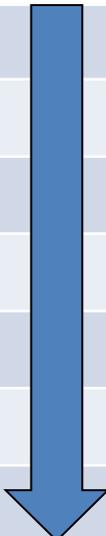
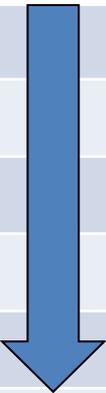
*** Median (IQR)

Baseline BMD

- The median lumbar spine (LS) BMD was 0.97 g/cm² (IQR: 0.90, 1.04).
- The median total hip (TH) BMD was 0.96 g/cm² (IQR: 0.88, 1.03)

	Zimbabwe	Uganda	P value
LS BMD (g/cm ²)	1.00	0.93	<0.0001
TH BMD (g/cm ²)	0.98	0.93	<0.0001

Univariate Analysis

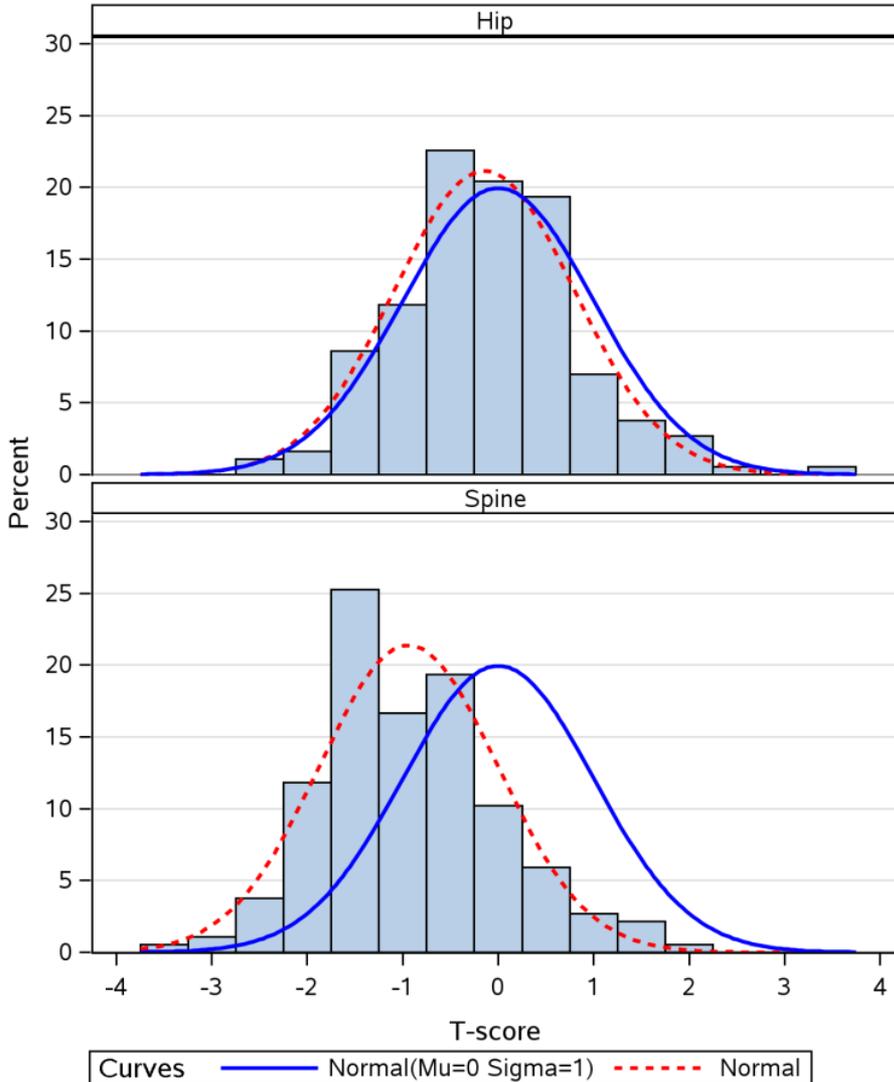
Parameter	Lumbar Spine	Total Hip
Enrolment in Uganda		
Lower BMI		
Lower categorical PA		
Less education		
History of and duration of DMPA use		
Longer duration of breastfeeding		-----
Higher parity		-----
Longer history of and duration of use of COCP and contraceptive		
Higher Serum vitamin D concentration	-----	
Lower Calcium Intake	-----	-----
Age	-----	-----

Multivariable Analysis

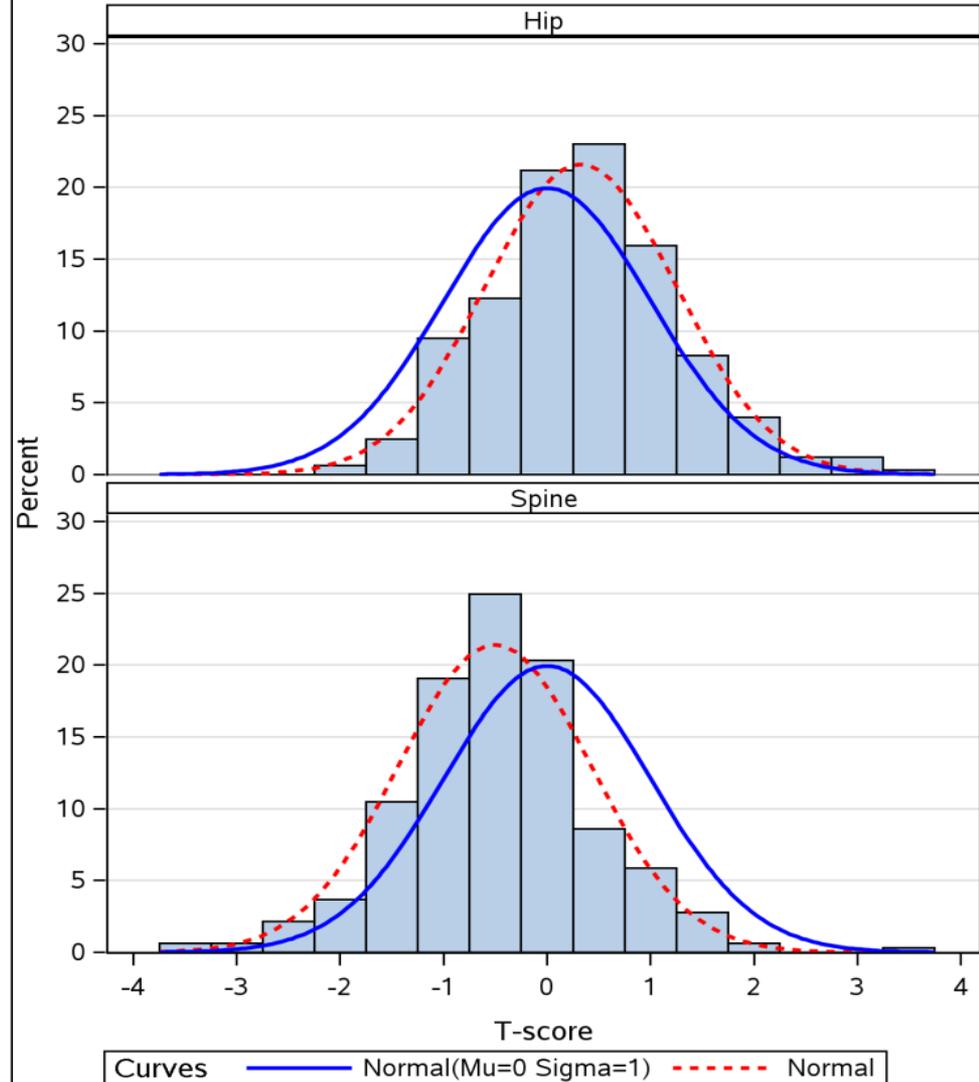
	Total Hip		Lumbar Spine	
	Parameter Estimate (SE)	p-value	Parameter Estimate (SE)	p-value
Country (Uganda vs. Zimbabwe)	-0.0437 (0.0106)	<0.001	-0.0260 (0.0098)	0.009
Age (years)	-0.0001 (0.0011)	0.962		
BMI (kg/m ²)	0.0060 (0.0009)	<0.001	0.0037 (0.0008)	<0.001
Duration of DMPA (months)	-0.0003 (0.0002)	0.081	-0.0004 (0.0002)	0.005
Duration of Implant Use (months)	0.0006 (0.0004)	0.182	0.0013 (0.0004)	<0.001
Categorical Physical Activity		0.007		0.011
High (vs. Low)	0.0446 (0.0210)	0.026	0.0347 (0.0191)	0.071
High (vs. Moderate)	0.0277 (0.0104)	0.008	0.0252 (0.0094)	0.007
Ever Breastfed	-0.0907 (0.0389)	0.020		
Lifetime Duration of Breastfeeding				0.069
>5 years (vs. < 2 years)			-0.0251 (0.0128)	0.051
>5 years (vs. 2-5 years)			-0.0223 (0.0106)	0.035
Vitamin D Total Concentration		0.111		
Deficiency (vs. Sufficiency)	-0.0366 (0.0244)	0.151		
Insufficiency (vs. Sufficiency)	-0.0174 (0.0090)	0.079		

T-scores

Histogram of Baseline Bone Mineral Density (BMD) T-scores
by Anatomical Location
Country Number=Uganda



Histogram of Baseline Bone Mineral Density (BMD) T-scores
by Anatomical Location
Country Number=Zimbabwe



Low T-scores

- Overall, the proportions of women with T-score between -1 and -2.5 were 35.3% for LS and 9.7% for TH
- The proportion of women with a T-score less than -2.5 was low:
 - 1.5% for LS and
 - 0.2% for TH.
- Compared with their Zimbabwean counterparts, participants from Uganda had a greater than 2-fold increased risk of having a baseline T-score of < -1.0 for LS ($p < 0.01$).
- Distributions of Z-scores were similar to those of T-scores.

Limitations

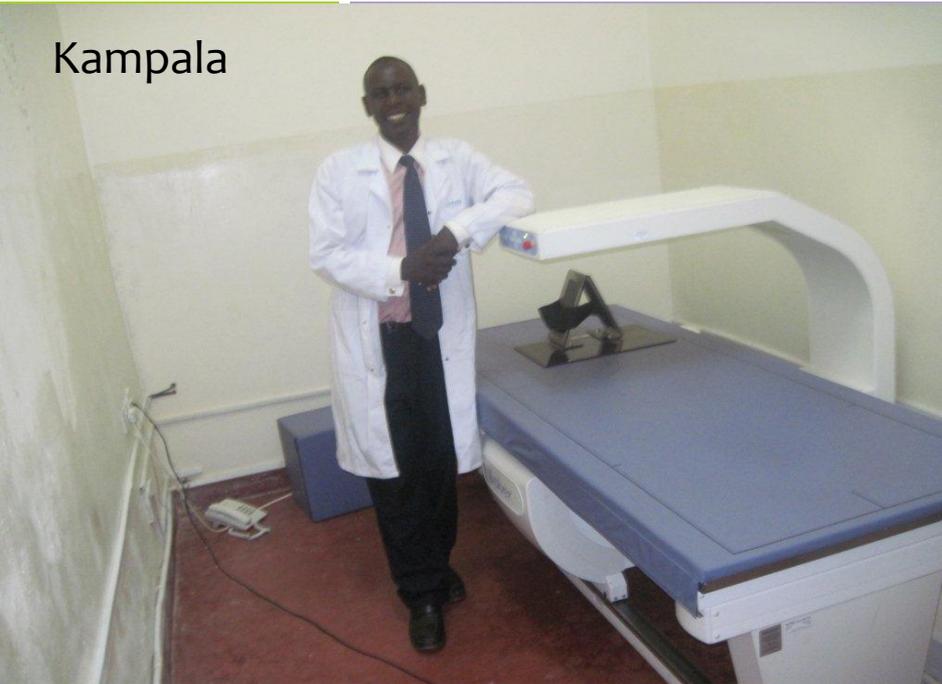
- Dietary calcium information collected was approximate due to lack of a validated tool for local foods available at the sites.
- Accuracy of the calcium intake may have been affected by:
 - translation of foods,
 - difficulty in calculating quantities by participant self-report.
- Our study did not measure some variables associated with BMD in prior studies such as:
 - Caffeine intake,
 - Smoking,
 - Detailed menstrual history (age at menarche).

Conclusion

- This large cross-sectional study showed that the BMD of healthy African women in Uganda and Zimbabwe is comparable to that of a US reference population.
- Lower TH and LS BMD was found to be independently associated with:
 - Lower levels of physical activity
 - Longer duration of DMPA use
 - Lower Body Mass Index
 - Uganda as country of residence
 - Lifetime duration of breastfeeding > 5 years
- To date, this study represents the largest report of BMD in black African women outside of South Africa.
- These data provide an important resource to define the normal ranges of BMD in healthy premenopausal African women.

Thank you

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