



Full Length Article

Longitudinal changes in hip geometry in relation to the final menstrual period: Study of Women's Health Across the Nation (SWAN)



Nayana Nagaraj^a, Robert M. Boudreau^a, Michelle E. Danielson^a, Gail A. Greendale^b,
Arun S. Karlamangla^b, Thomas J. Beck^c, Jane A. Cauley^{a,*}

^a Department of Epidemiology, Graduate School of Public Health, University of Pittsburgh, Pittsburgh, PA, USA

^b Division of Geriatrics, Geffen School of Medicine at UCLA, University of California, Los Angeles, CA, USA

^c Beck Radiological Innovations Inc., Cantonsville, MD, USA

ARTICLE INFO

Keywords:

Hip structure analysis
Final menstrual period
Menopausal transition
Hip geometry
Hip strength
Bone mineral density

ABSTRACT

Background: In SWAN, we showed that accelerated loss of bone mineral density (BMD) begins 1 year before the final menstrual period (FMP) to 2 years after the FMP and slows thereafter. However, the risk of fracture depends on both BMD and bone geometry. The hip structural analysis (HSA) measures important geometric properties of bone. Changes in HSA parameters across the menopausal transition have not been previously assessed.

Methods: The current analysis uses data from SWAN, 5 years before to 5 years after FMP ($N = 900$, Age (mean (SD)) = 46.85(2.60), 44% White). HSA parameters at the femoral narrow neck were obtained from 2D DXA scans and normalized to baseline values. FMP was determined from annual interviews. Changes in HSA were assessed over 3 periods, 5 to 2 years before FMP (pre-transmenopausal), 2 years before to 1 years after FMP (transmenopausal), 1 to 5 years after FMP (postmenopausal). Mixed linear models with random slopes were used to estimate the rate of change in HSA parameters relative to FMP.

Results: Loss of BMD, cross-sectional area (CSA), and section modulus (SM) and increases in outer diameter (OD) were greatest in the transmenopausal period (p for all < 0.05). Changes continued in the postmenopausal period but were not statistically significant. The cumulative percentage changes over 10 years in BMD (-10.67%), CSA (-9.01), SM (-7.03) and OD ($+1.95$) were statistically significant.

Conclusion: Changes in hip geometry across the menopause transition parallel changes in BMD and provide insight into mechanisms that may increase risk of fragility fracture.

1. Introduction

Menopause is a critical time in a woman's health, especially with respect to her skeletal health. Approximately half of the bone mineral density (BMD) loss is said to occur during the first 10 years after menopause [1]. However, the exact timing of this BMD loss with respect to menopause has been difficult to assess. Pinkerton et al., suggested a "critical time window" to assess the changes during reproductive aging [2]. In 2000, a prospective study demonstrated that accelerated decline in BMD begins about 2–3 years before the final menstrual period (FMP) and continues for 3–4 years after [3]. Similarly, other large longitudinal studies have shown significant peri-menopausal BMD loss at the femoral neck (FN) and the lumbar spine [4–6]. However, in the Study of Women's Health across the Nation (SWAN), the largest and longest study of the menopausal transition, there was little premenopausal BMD loss (5 years to 1 year before FMP); the rate of BMD loss at the FN

was highest between 1 years before to 2 years after the FMP [7].

While BMD measurements using DXA scanners are the most clinically useful measures of fracture risk, the higher risk is due to loss of bone mechanical strength to resist forces on the bone that occur in certain traumas (e.g., falls). In the simplest terms, bone strength can decline when there is no longer enough bone tissue in the right places to withstand traumatic forces or that bone tissue itself becomes less able to withstand forces that would otherwise not cause fractures. These two bone characteristics are termed geometry and material strength. Bone material strength requires an invasive measurement such as nanoindentation at a superficial location and cannot currently be measured using imaging methods [8]. Geometry can be measured from x-ray CT scans in 3D although complex finite element algorithms are needed to extract the geometry and to estimate strength from that data [9]. Another method is based on dimensional information (i.e., geometry) present in the digital image provided by the DXA scan. The hip

* Corresponding author at: Department of Epidemiology, Graduate School of Public Health, 130, DeSoto St, Pittsburgh, PA 15261, USA.

E-mail address: jcauley@pitt.edu (J.A. Cauley).

<https://doi.org/10.1016/j.bone.2019.02.016>

Received 25 July 2018; Received in revised form 6 February 2019; Accepted 15 February 2019

Available online 03 March 2019

8756-3282/ © 2019 Elsevier Inc. All rights reserved.

structural analysis (HSA) method uses file format information provided by scanner manufacturers together with image analysis algorithms to extract the limited geometric information evident in the frontal plane image [10]. HSA measures have been shown to predict fractures [11] in some [12] but not all studies [13]. This relationship was found to be independent of aBMD levels [12,14]. HSA parameters have also been shown to respond favorably to osteoporotic treatments [15,16].

To the best of our knowledge, no previous study has assessed changes in hip geometry using the HSA methods to evaluate the dimensional changes underlying BMD decline in relation to the FMP or whether there are racial variations in rates of change. For the present study, we aimed to first define the time of onset and offset of our hypothesized accelerated changes in hip geometry in relation to the FMP, and subsequently quantify the rate of change of these parameters during the 5 years before to 5 years after FMP. In addition, we assessed if this rate differed by race and was independent of other risk factors like age at FMP, smoking and physical activity.

2. Methods

2.1. Study population

SWAN is an ongoing, multi-site, community based, longitudinal cohort study of women aimed to examine the physiological and psychological changes during their transition through the midlife [17]. Between 1996 and 1997, 3302 participants from 7 sites across the US (Boston, MA; Oakland, CA; Los Angeles, CA; Detroit, MI; Chicago, IL; Pittsburgh, PA & Newark, NJ) were recruited. The eligibility criteria for the SWAN study included (1) an intact uterus and at least 1 ovary; (2) not pregnant or breast feeding; (3) at least 1 menstrual period within the past 3 months; (4) no hormone therapy use within the past 3 months.

BMD data was collected in five of the seven SWAN sites (Boston, MA; Oakland, CA; Los Angeles, CA; Detroit, MI; & Pittsburgh, PA). The Boston, Detroit and Pittsburgh sites recruited Black women. The Los Angeles and Oakland sites recruited Japanese and Chinese women, respectively. All the sites enrolled White women. At baseline, the BMD cohort consisted of 2335 participants from the 5 sites. Participants of the current study were from an ancillary study to SWAN – Hip strength across the menopausal transition study. For the current study, data from baseline to visit 10 was used. Only women who had a determinable natural FMP (non-surgical) were included. The women who remained pre- or peri-menopausal after 10 years were excluded from the analysis. In addition, women missing FMP data, on hormone therapy, or having only one DXA scan were excluded; final sample = 900 women (Supplementary Fig. 1). Written informed consent was obtained and all protocols were approved by the institutional review boards of the participating institutions.

2.2. Study measures

2.2.1. Dual energy X-ray absorptiometry (DXA) scans

The scans of the FN were obtained annually from Hologic QDR scanners (Hologic, Inc., Bedford, MA) using the Osteodyne's Hip Positioner System (Osteodyne Inc., NC). The Osteodyne positioner was instituted to reduce positioning errors, important in longitudinal studies [18]. While 3 sites used the 4500A model from baseline throughout follow up, 2 sites upgraded from 2000 to 4500A models starting at visit 8. Both the 2000 and 4500A models were fan-beam scanners. A cross calibration study of 40 women who were scanned on the old and new machines was carried out to develop calibration regression equations. The HSA conversion/calibration software that converts the scan data into a format usable by HSA uses the same corrections used by Hologic. A quality control program was conducted in collaboration with Synarc, Inc., through the daily phantom measurements, cross site calibration every 6-months with an anthropomorphic spine standard, central

review of any scans that met the criteria for problem flagging, central review of 5% random sample of scans and local review of scans in all sites. The short-term measurement variability in vivo for FN BMD was noted to be 0.016 g/cm² (2.2%) [19].

2.2.2. Hip geometry (HSA)

The HSA method extracts the dual energy data present in the DXA scan file to produce a digital frontal image of the bone. The software developed at the Johns Hopkins School of Medicine, uses the principle that lines of pixels across the axis of the bone from edge to edge are a projection of the mineral in a cross-section from which some geometric properties can be measured [20]. All scans were de-identified prior to analysis by the HSA software. HSA parameters were assessed at the narrow neck (NN), shaft and intertrochanteric regions of the femur. For our current analyses, we examined the HSA parameters at the NN to allow for comparisons to published femoral neck aBMD changes. The NN represents the narrowest point in the FN. Geometry was assessed in 5 profiles which were 1 pixel apart and then averaged at each region. Bone mineral density (BMD) was calculated as the average of pixels in the region profiles. Cross-sectional area (CSA) was assessed as the integral of the pixel profile derived by the mean mineral density of adult bone mineral content (BMC) tissue (1.053 g/cm³). This is equivalent to the surface area of bone in the cross-section excluding soft tissue voids i.e., the total available surface to supporting forces directed along the bone axis. Although expressed in different units, CSA is similar to BMC in that a change in CSA would be interpreted as a change in the actual amount of bone (unlike BMD). Section modulus (SM) is an indicator of the ability of a structure to resist bending in a plane and is strongly dependent on the distribution of bone material away from the center of mass. Section modulus was computed as cross-sectional moment of inertia (CSMI) divided by the maximum distance from the section center of mass to the cortical surface in the image plane (d_{max}). The outer diameter (OD) is measured as the blur-corrected width of the bone measured along the bone mass profile.

The accuracy and precision of the HSA parameters has previously been evaluated using a specially constructed hip geometry phantom by Khoo et al. [21]. The phantom contained 6 different sized bone-simulating neck segments incorporating a trabecular core and an outer cortical shell. Pearson Correlation coefficients between DXA and phantom geometry were 1.00 for all parameters. Precision error (% CV) ranged between 0.3 and 3.9% over 10 repetitions. Accuracy tended to show positive errors for the narrowest region and negative errors for the widest region. Measurement errors over all six segments (max, min) were between 0.06 and -0.03 g/cm² for BMD, 0.20 and -0.23 cm² for CSA, 0.04, -0.14 cm for OD, and 0.11 and -3.75 cm³ for section modulus.

Significant differences in geometry were evident in adjusted comparisons between QDR 2000 and QDR 4500 models. Since the HSA software is independent of the DXA manufacturer's software, an adjustment was necessary. A linear correction in the DXA image pixel value (g/cm²) was derived as follows: given that the NN region BMD is an average of pixel value in a region, the correction was derived as the ratio of NN BMD from study participants scanned prior to visit 8 on the QDR2000 over those scanned on the QDR4500. There were no significant differences in age, height and weight between the two scanner subgroups used for the adjustment. The resulting linear correction was applied only to data from subjects scanned on the QDR2000. Additional adjustment for scanner was included in the analysis to account for any residual error. Finally, in supplementary analyses, we limited our analysis to the three clinics that used a Hologic 4500 scanner throughout the study.

2.2.3. Final menstrual period (FMP)

FMP was assessed using annual standardized interviews and defined as the last menstrual date reported at the visit immediately prior to being classified as postmenopausal (12 months of amenorrhea).

Changes in HSA parameters from 5 years before to 5 years after the FMP were assessed.

2.2.4. Other covariates

We measured the age at FMP, race, smoking status and physical activity. Age (years), race and smoking were obtained from interviews at baseline. Weight (kilograms) and height (meters) were obtained annually using calibrated scales. Physical activity at baseline was assessed using modified Baecke interview which included active living, occupational activity and home activity [22].

3. Statistical analysis

FMP was considered as time zero and we studied 5 years before to 5 years after FMP. Mixed effect spline models were used to estimate changes over time. The analyses consisted of 3 stages: 1) Non-parametric locally weighted scatterplot smoothing (LOESS) based heuristic assessment of the functional form of outcome trajectories in relation to FMP; 2) Determination of the fixed knots of the trajectories for modeling piecewise linear regression and 3) Piecewise linear regression with the fixed knots from step 2 to determine the rate of change of these parameters during the different phases of the trajectory (mixed effects regression models).

The HSA parameters were divided by their baseline values and percent change was calculated. LOESS smoothing was fit to the repeated measures of each HSA measure using all individuals combined. Best placement of the knots was assessed in 6-month using the Akaike Information Criterion (AIC) values. Based on the LOESS curves and the AIC values, we determined good fitting knots at 2 years before FMP and at 1 year after FMP. Thus, we identified 3 linear segments or phases – (i) Baseline to –2 years (Pre-transmenopausal) (ii) –2 to +1 years (Transmenopausal) (iii) +1 years to +5 years (Postmenopausal). We then used mixed effects spline regression models that included heterogeneous auto-regressive person-level random effects for the slopes (allowing the three slopes within an individual to be correlated yet vary between participants) combined with different residual error variances during each of the three menopausal phases. The models were subsequently adjusted for age at FMP, race, body weight, smoking status, physical activity, scanner and the baseline value of the parameter. Weight, physical activity and smoking were entered as time varying covariates. In addition to phase-specific slopes, the cumulative effect from –5 to 5 years was estimated to obtain the cumulative change in hip geometry over the 10 years. The results were expressed as percentage rate of change of the parameters with 95% confidence intervals. All analyses were conducted using SAS 9.3 (SAS Institute, Cary, NC, USA).

4. Results

At baseline, the mean age of these women was 46.85 years with an average body mass index of 27.36 kg/m². Most of these women were White (44.11%) or Black (29%) and about 17% were current smokers (Table 1).

The longitudinal changes in the HSA parameters 5 years before to 5 years after the FMP are shown in Fig. 1a–d. All the parameters showed little change during the pre-transmenopausal period up to 2 years before the FMP but showed accelerated changes during the transmenopausal period with a tapering off during the postmenopausal period. While BMD, CSA (BMC) and SM levels declined in relation to FMP, the OD increased.

The mean cumulative change of NN BMD over 10 years was –10.67% with the greatest loss observed in the transmenopausal period (–1.84%/year) (Table 2). The annualized percentage decline in BMD during the postmenopausal period was slower (–1.66%/year). Compared to Whites, Black (+1.79%/year) women lost significantly less BMD over 10 years. Chinese (+0.58%/year) and Japanese

Table 1
Baseline characteristics of the study population.

Characteristics	Analysis sample (N = 900)
Age (years)*	46.85 ± 2.60
Race/ethnicity	
White N (%)	397 (44.11)
Black N (%)	260 (29.00)
Chinese N (%)	123 (13.67)
Japanese N (%)	119 (13.22)
Height (cm)*	161.73 ± 6.67
Weight (kg)*	71.91 ± 19.57
Body mass index (kg/m ²)*	27.36 ± 6.92
Smoking status	
Current smokers N (%)	149 (16.67)
Past smokers N (%)	217 (24.27)
Never smokers N (%)	528 (59.06)
Physical activity score (range 3–14)	7.70 ± 1.75
Narrow neck bone mineral density (g/cm ²)*	1.05 ± 0.18
Narrow neck section modulus (cm ³)*	1.33 ± 0.29
Narrow neck cross sectional area (cm ²)*	2.94 ± 0.53
Narrow neck outer diameter (cm)*	2.96 ± 0.21

* Mean ± SD.

(+0.99%/year) women lost significantly less BMD in the postmenopausal period but not cumulatively.

The cumulative loss in CSA (BMC) over 10 years was –9.01%/year (Table 3). The greatest loss in CSA (BMC) occurred during the transmenopausal period (–1.45%/year) and in the postmenopausal period (–1.59%/year). Compared to White women, Japanese women lost significantly greater CSA (BMC) in the pre-transmenopausal (–0.29%/year) and the transmenopausal (–0.62%/year) periods. However Japanese women lost significantly less during the postmenopausal periods (+1.02%/year). Weight had a protective effect on CSA (BMC) in the transmenopausal (+0.03%/year) period and cumulatively over 10 years (+0.11%/year). Age at FMP, smoking or physical activity were unrelated to change in CSA(BMC).

The cumulative loss in SM over 10 years was –7.03%/year with significant loss in the trans (–1.09%/year) and postmenopausal (–1.33%/year) periods (Table 4). No significant ethnic differences were noted cumulatively. Compared to the White women, the Japanese women experienced greater loss of SM in the pre-transmenopausal (–0.50%/year) period but significantly less in the postmenopausal period (+1.58%/year). Greater body weight was protective in the transmenopausal (+0.04%/year) period and cumulatively over 10 years (+0.17%/year).

Over the 10-year period, OD increased by +1.95%/year (Table 5). Both the transmenopausal (+0.44%/year) and postmenopausal (+0.11%/year) periods showed significant increases in OD. Compared to White women, Black women had significantly lower rates of increase in OD transmenopausally (–0.19%/year) and cumulatively over 10 years (–0.79%/year). Current smoking had a detrimental effect on the rate of change of OD in the transmenopausal (+0.25%/year) and a protective effect in the postmenopausal period (–0.15%/year). Weight and physical activity had no significant effect on the rate of change of OD.

We repeated our analyses limiting the sample size to only those sites that consistently used the Hologic 4500 Hologic scanner and results were similar, although our sample size was reduced by 40% and excluded the Chinese women recruited in Oakland, CA, (Supplemental tables 1–4).

5. Discussion

We found that cumulative 10-year changes in hip geometry across the menopausal transition were significant at the NN BMD (–10.67%), CSA (similar to BMC), (–9.01), SM (–7.03) and OD (+1.95). For the most part, the greatest change occurred during the transmenopausal

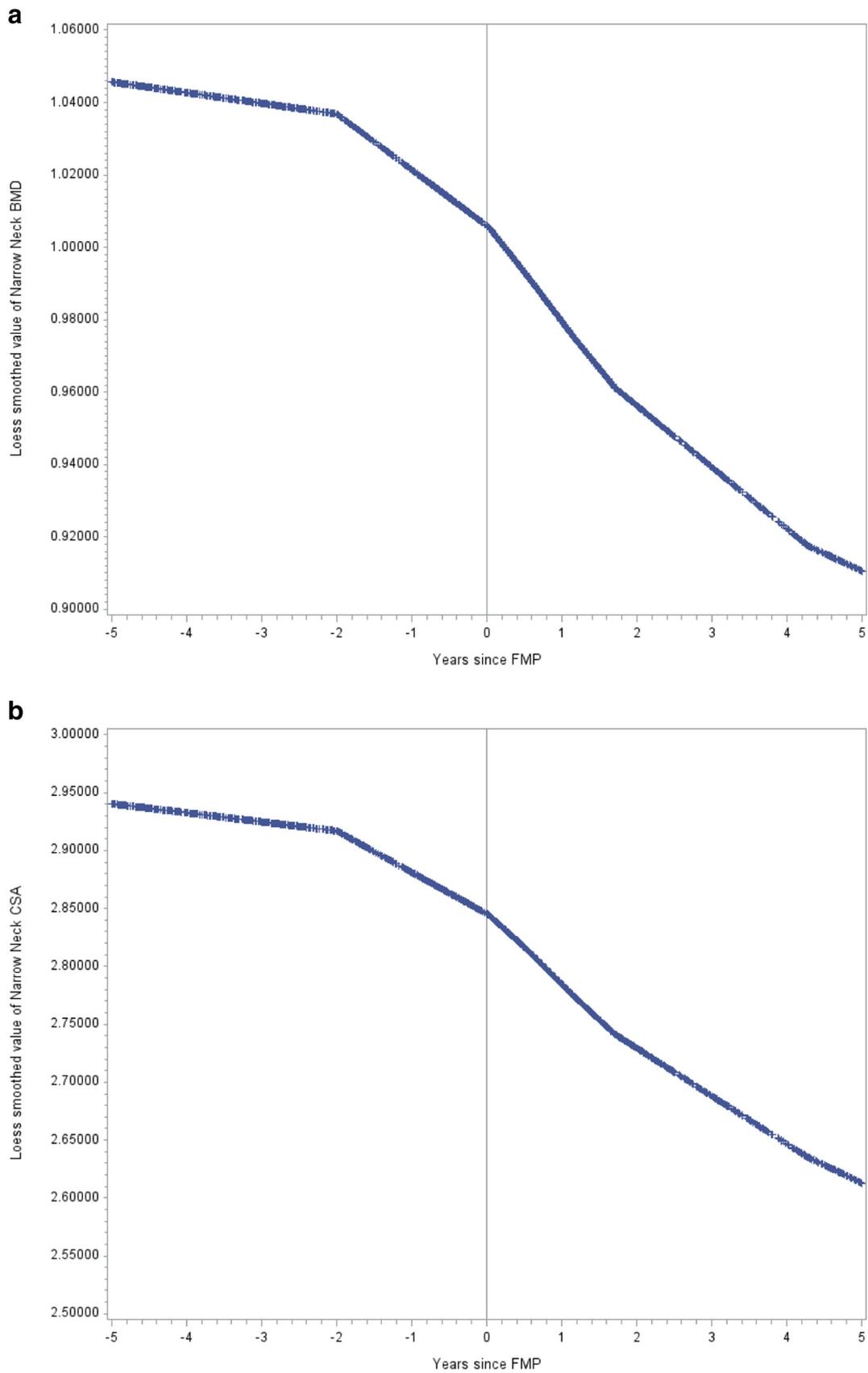


Fig. 1. The longitudinal trajectory of changes in hip geometry relative to time before or after the final menstrual period (FMP) (time zero). The x-axis is labeled as years since the FMP. The y-axis is labeled as LOESS smoothed value of each parameter.
 a: Longitudinal trajectory of the narrow neck (NN) bone mineral density (BMD) in relation to FMP.
 b: Longitudinal trajectory of the NN Cross Sectional Area (CSA) in relation to FMP.
 c: Longitudinal trajectory of the NN Outer Diameter (OD) in relation to FMP.
 d: Longitudinal trajectory of the NN Section Modulus (SM) in relation to FMP.

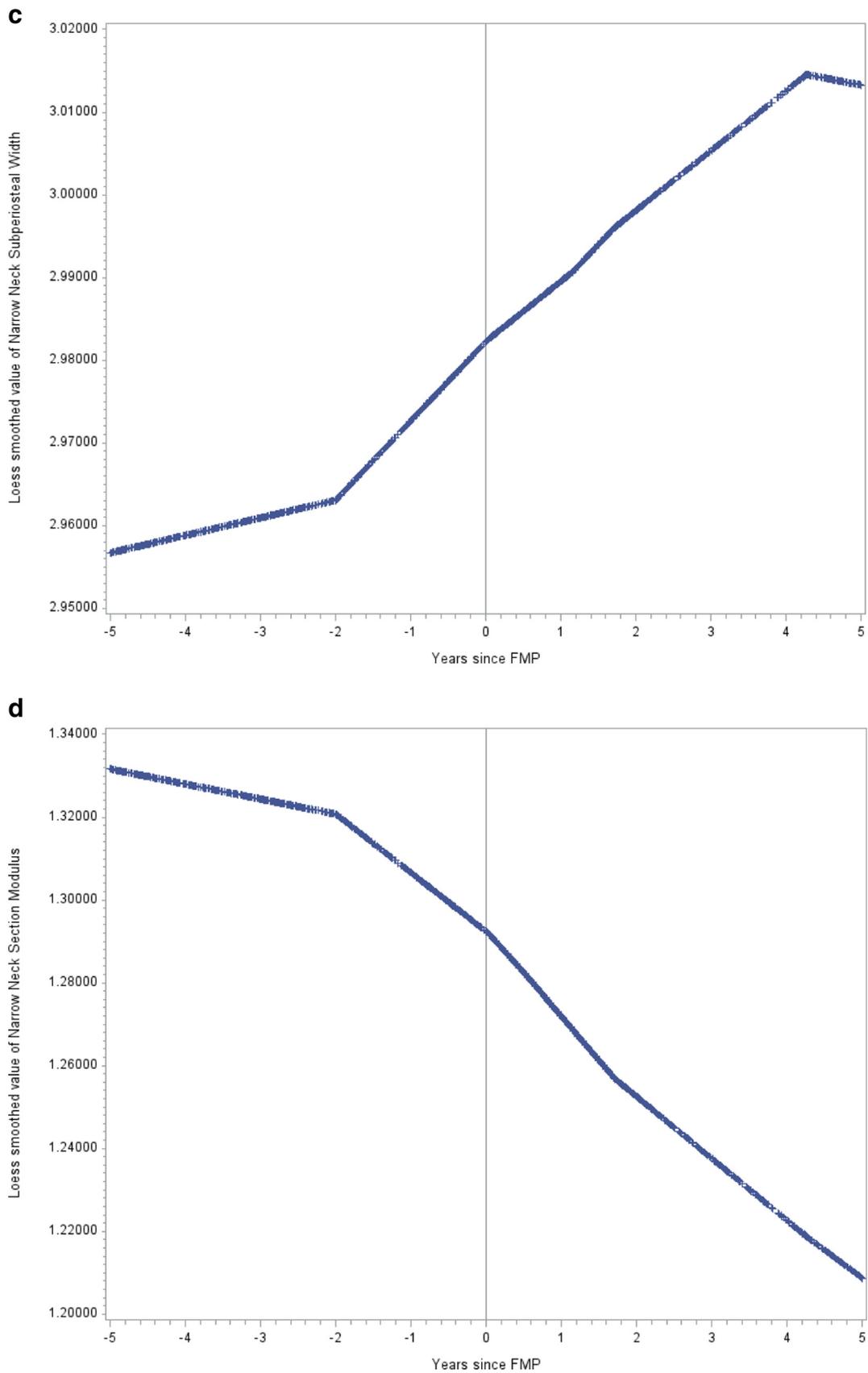


Fig. 1. (continued)

period (2 years before to 1 year after FMP). The trajectories of BMD, CSA (BMC) and SM showed 3 distinct phases – minimal nonsignificant decline in the pre-transmenopausal period, greatest decline in

transmenopausal period and continued decline in the postmenopausal period. OD showed similar patterns of change across the 3 periods. The OD increased greatly in the transmenopausal period. However, OD

Table 2
Rate of change of baseline normalized NN BMD in relation to FMP.

NN BMD ^a	Rate of change (slope ^b) in each FMP-defined phase (%/year)			
	Pre-transmenopause (Prior to 2 years before FMP) Mean ^c (95% CI), −0.001(−0.07, 0.07)	Transmenopause (2 years before to 1 years after FMP) Mean ^c (95% CI), −1.84(−2.01, −1.66)	Postmenopause (1 years after FMP and beyond) Mean ^c (95% CI), −1.66(−1.82, −1.49)	Cumulative change ^c (%) Mean ^d (95% CI), −10.67(−11.29, −10.05)
Age at FMP (years)	0.005(−0.03, 0.04)	−0.05(−0.12, 0.01)	0.02(−0.04, 0.08)	−0.17(−0.40, 0.06)
Race ^e				
Black	0.08(−0.16, 0.33)	0.40(0.01, 0.79)	0.02(−0.35, 0.39)	1.79(0.37, 3.31)
Chinese	0.09(−0.16, 0.33)	−0.05(−0.57, 0.47)	0.58(0.10, 1.05)	1.13(−0.78, 3.04)
Japanese	−0.30(−0.53, −0.07)	0.02(−0.35, 0.39)	0.99(0.44, 1.53)	−0.82(−2.75, 1.12)
Weight	0.0001(−0.003, 0.005)	0.02(0.01, 0.03)	0.002(−0.01, 0.01)	0.10(0.07, 0.14)
Smoking status ^f				
Current smoker	−0.02(−0.24, 0.20)	−0.18(−0.63, 0.27)	−0.01(−0.43, 0.41)	−0.78(−2.40, 0.84)
Ex-smoker	0.08(−0.10, 0.25)	−0.01(−0.44, 0.33)	0.11(−0.25, 0.47)	0.15(−1.22, 1.51)
Physical activity at baseline	0.09(−0.05, 0.24)	−0.13(−0.44, 0.19)	−0.20(−0.49, 0.10)	−0.70(−1.85, 0.44)

^a Adjusted for all the variables listed in the table along with site, scanner, and baseline value.
^b Rate of change (slope) in percentage of baseline value of the index of interest. Negative values mean faster decline, and positive values mean slower decline.
^c The mean values of trajectory parameters are from a null model (with no predictors) that fit a single common trajectory to the sample.
^d Cumulative change during the years spanning the final menstrual period [Median time (years) of first visit – Median time (years) of last visit].
^e REF- White.
^f REF- Non-smoker. Bold = statistically significant.

Table 3
Rate of change of baseline normalized narrow neck cross sectional area in relation to final menstrual period (FMP).

Narrow neck cross sectional area ^a	Rate of change (slope ^b) in each FMP-defined phase (%/year)			
	Pre-transmenopause (Prior to 2 years before FMP) Mean ^c (95% CI), −0.003 (−0.07, 0.0)	Transmenopause (2 years before to 1 years after FMP) Mean ^c (95% CI), −1.45 (−1.63, −1.27)	Postmenopause (1 years after FMP and beyond) Mean ^c (95% CI), −1.59 (−1.76, −1.42)	Cumulative change ^d (%) Mean ^c (95% CI), −9.01 (−9.63, −8.39)
Age at FMP (years)	−0.004 (−0.04, 0.03)	−0.03 (−0.10, 0.04)	0.02 (−0.05, 0.08)	−0.09 (−0.33, 0.14)
Race ^e				
Black	0.03 (−0.15, 0.22)	0.24 (−0.17, 0.66)	0.001 (−0.41, 0.42)	1.05 (−0.35, 2.45)
Chinese	0.09 (−0.16, 0.34)	−0.18 (−0.74, 0.38)	0.54 (−0.01, 1.09)	0.54 (−1.37, 2.45)
Japanese	−0.29 (−0.53, −0.06)	−0.62 (−1.21, −0.04)	1.02 (0.42, 1.62)	−1.03 (−2.98, 0.92)
Weight	0.0002 (−0.004, 0.005)	0.03 (0.01, 0.04)	0.001 (−0.01, 0.02)	0.11 (0.08, 0.15)
Smoking status ^f				
Current smoker	−0.07 (−0.29, 0.16)	−0.004 (−0.49, 0.48)	−0.08 (−0.56, 0.40)	−0.30 (−1.92, 1.32)
Ex-smoker	0.07 (−0.11, 0.26)	−0.11 (−0.52, 0.30)	0.14 (−0.27, 0.55)	−0.01 (−1.37, 1.36)
Physical activity at baseline	0.08 (−0.07, 0.23)	−0.10 (−0.45, 0.24)	−0.18 (−0.51, 0.16)	−0.61 (−1.75, 0.53)

^a Adjusted for all the variables listed in the table along with site, scar, and baseline value.
^b Rate of change (slope) in percentage of baseline value of the index of interest. Negative values mean faster decline, and positive values mean slower decline.
^c The mean values of trajectory parameters are from a null model (with no predictors) that fit a single common trajectory to the sample.
^d Cumulative change during the years spanning the final menstrual period [Median time (years) of first visit – Median time (years) of last visit].
^e REF- White.
^f REF- Non-smoker. Bold = statistically significant.

increase slowed in the postmenopausal period.

With age, subperiosteal apposition occurs [20,23], resulting in expansion of the femoral diameter. Conventional BMD is proportional to BMC/region area, so BMD ‘loss’ can occur by actual bone loss (BMC decline) or by expansion of the region area. For example, a study using both conventional BMD with region area and the HSA analysis on the NHANES III sample of the US population showed that one third of the femoral neck BMD loss in both men and women from ages 20–29 to 80+ was due to expansion of the femoral neck region not bone loss [24]. Using HSA parameters, BMD of a cross-section is proportional to CSA/OD. This results in reduction of BMD while preserving the SM [20,23,25]. In a study of Swedish women transitioning through menopause (N = 108, mean postmenopausal follow up period over 15 years), the distal radius BMD loss was partially due to an increase in the outer diameter [25], suggesting that changes in bone geometry may compensate for the loss of aBMD to maintain strength. However, the study population was small and their measurements were estimated

manually from radial scans using an early low resolution scanner. However, the results from our study are consistent with these findings where the cumulative loss of BMD was greater than loss of SM or increase in OD. This supports the theory that the changes in bone geometry over time, may compensate for the loss of BMD and the increase in the OD reflects periosteal apposition.

Fractures result from an imbalance between bone strength and load on the bone [26]. Despite the strong and consistent ability of aBMD to predict fractures even after 25 years [27], it does not completely explain fractures in women who do not meet the BMD criteria for osteoporosis [28]. Studies have demonstrated that accounting for the structural properties of the bone in addition to aBMD can better quantify bone strength [29]. The menopausal transition and increasing age are associated with increased risk of fractures [30,31]. However, the exact mechanism is still not clearly understood. Although aBMD is the clinical gold standard for predicting fracture risk [32], the risk of fracture depends on not just the bone density but also the bone

Table 4
Rate of change of baseline normalized narrow neck section modulus in relation to final menstrual period (FMP).

Narrow neck section modulus ^a	Rate of change (slope ^b) in each FMP-defined phase (%/year)			
	Pre-transmenopause (Prior to 2 years before FMP) Mean ^c (95% CI), -0.01 (-0.11, 0.09)	Transmenopause (2 years before to 1 years after FMP) Mean ^c (95% CI), -1.09 (-1.32, -0.86)	Postmenopause (1 years after FMP and beyond) Mean ^c (95% CI), -1.33 (-1.54, -1.11)	Cumulative change ^d (%) Mean ^c (95% CI), -7.03 (-7.80, -6.25)
Age at FMP (years)	0.003 (-0.05, 0.05)	-0.02 (-0.11, 0.07)	0.02 (-0.07, 0.10)	-0.05(-0.34, 0.25)
Race ^e				
Black	0.06 (-0.20, 0.33)	-0.26 (-0.80, 0.28)	-0.12 (-0.63, 0.40)	-1.16(-2.91, 0.60)
Chinese	0.13 (-0.23, 0.49)	-0.68 (-1.42, 0.05)	0.68 (-0.01, 1.38)	-1.10(-3.53, 1.33)
Japanese	-0.50 (-0.84, -0.16)	-0.61 (-1.49, 0.16)	1.58 (0.81, 2.35)	-0.30(-2.81, 2.22)
Weight	0.001 (-0.01, 0.01)	0.04 (0.02, 0.05)	0.01 (-0.01, 0.02)	0.17(0.12, 0.21)
Smoking status ^f				
Current smoker	-0.09 (-0.42, 0.23)	0.07 (-0.57, 0.70)	0.05 (-0.56, 0.70)	0.18(-1.88, 2.24)
Ex-smoker	0.10 (-0.16, 0.36)	-0.21 (-0.75, 0.32)	0.26 (-0.25, 0.78)	-0.13(-1.86, 1.61)
Physical activity at baseline	0.08 (-0.14, 0.30)	-0.11 (-0.56, 0.34)	-0.23 (-0.66, 0.19)	-0.74(-2.19, 0.71)

^a Adjusted for all the variables listed in the table along with site, scanner, and baseline value.

^b Rate of change (slope) in percentage of baseline value of the index of interest. Negative values mean faster decline, and positive values mean slower decline.

^c The mean values of trajectory parameters are from a null model (with no predictors) that fit a single common trajectory to the sample.

^d Cumulative change during the years spanning the final menstrual period [Median time (years) of first visit - Median time (years) of last visit].

^e REF- White.

^f REF- Non-smoker. Bold = statistically significant.

geometry. Most hip fractures in the elderly occur due to sideways falls and are believed to occur due to bending and axial compression on the bone [11]. The HSA combines these two factors and estimates a comprehensive representation of bone geometry [33,34]. Previous research has shown that HSA parameters are associated with the risk of fractures. The risk of incident hip fracture increased by 44–55%, 36–41%, 28–63% with 1 SD decrease in BMD, CSA (BMC) and SM [32]. By extension, the cumulative change of the HSA parameters from our results suggests that these changes could lead to clinically significant increased risk of fractures.

We have shown similar timelines for the changes in aBMD and composite strength indices during the menopausal transition. The loss in areal FN BMD was highest during 1 year before the FMP to 2 years after FMP [7]. Composite indices of FN strength (compression, bending, and impact) have been shown to predict hip fracture risk [35]. The decline in compression and bending strength indices also started 1 year before the FMP [36] to 1 year after. In contrast, the accelerated changes in HSA that we observed started 2 years before FMP and continued up

until 5 years after. Therefore, changes in hip geometry may precede loss of aBMD and FN strength. Put together, the loss of BMD, and changes in geometry may both contribute to an increased loss of bone micro and macro architecture during the transmenopausal period, thereby increasing a woman's susceptibility to fracture.

In a subset of 198 women from the Pittsburgh SWAN site, Jepson et al. showed 14-year longitudinal changes in aBMD and bone area [37]. Changes in BMC and bone area were not reflected in changes in aBMD highlighting the need to examine changes in bone parameters beyond BMD. However, this analysis did not align these changes with the final menstrual period and therefore, could not identify which stage of the menopausal transition changes began or to quantify the changes within each menopausal stage. In addition, this study calculated changes in bone parameters using only the baseline and final scans and did not include the annual scans at each clinic visit and thus, ignored the variability and non-linear changes in aBMD.

Chinese women have lower aBMD levels compared to the White women [38] but have lower hip fracture rates [39]. This paradox has

Table 5
Rate of change of baseline normalized narrow neck outer diameter in relation to final menstrual period (FMP).

Narrow neck outer diameter ^a	Rate of change (slope ^b) in each FMP-defined phase (%/year)			
	Pre-transmenopause (Prior to 2 years before FMP) Mean ^c (95% CI), -0.01 (-0.03, 0.01)	Transmenopause (2 years before to 1 years after FMP) Mean ^c (95% CI), 0.44 (0.38, 0.50)	Postmenopause (1 years after FMP and beyond) Mean ^c (95% CI), 0.11 (0.06, 0.16)	Cumulative change ^d (%) Mean ^c (95% CI), 1.95 (1.73, 2.18)
Age at FMP (years)	-0.01 (-0.02, -0.0003)	0.01 (-0.01, 0.04)	0.003 (-0.02, 0.02)	0.04(-0.04, 0.13)
Race ^e				
Black	-0.04 (-0.09, 0.01)	-0.19 (-0.33, -0.05)	0.03 (-0.10, 0.16)	-0.79(-1.31, -0.26)
Chinese	0.01 (-0.07, 0.08)	-0.07 (-0.27, 0.13)	0.02 (-0.15, 0.19)	-0.23(-0.96, 0.50)
Japanese	0.003 (-0.06, 0.07)	-0.04 (-0.25, 0.16)	-0.04 (-0.20, 0.19)	-0.18(-0.90, 0.54)
Weight	-0.001 (-0.002, 0.001)	-0.001 (-0.004, 0.002)	0.0004 (-0.003, 0.004)	-0.005(-0.02, 0.01)
Smoking status ^f				
Current smoker	-0.06 (-0.12, 0.01)	0.25 (0.09, 0.42)	-0.15 (-0.30, -0.002)	0.61(-0.004, 1.21)
Ex-smoker	-0.01 (-0.06, 0.05)	-0.01 (-0.16, 0.13)	-0.03 (-0.16, 0.10)	-0.14(-0.65, 0.38)
Physical activity at baseline	-0.02 (-0.06, 0.03)	0.03 (-0.09, 0.14)	-0.01 (-0.11, 0.10)	0.06(-0.37, 0.49)

^a Adjusted for all the variables listed in the table along with site, scanner, and baseline value.

^b Rate of change (slope) in percentage of baseline value of the index of interest. Negative values mean faster decline, and positive values mean slower decline.

^c The mean values of trajectory parameters are from a null model (with no predictors) that fit a single common trajectory to the sample.

^d Cumulative change during the years spanning the final menstrual period [Median time (years) of first visit - Median time (years) of last visit].

^e REF- White.

^f REF- Non-smoker. Bold = statistically significant.

been largely explained by the differences in hip geometry between the Whites and Chinese women. Of interest, compared to White women, Japanese women demonstrated unfavorable changes in the pre-trans and transmenopausal periods for CSA (BMC) but fared better in the postmenopausal periods. Japanese women also showed significantly slower changes in the postmenopausal period for BMD and SM as well. These slower rates of change in the postmenopausal period may contribute to greater cortical stability in later life and lower fracture rates.

Compared to White women, the risk of fractures in Black women is shown to be 50% lower [40]. The lower fracture risk among Black women may reflect their significantly higher BMD [20,41], higher CSA (BMC) and SM [42]. In addition, Black women have previously been shown to experience slower rates of loss of BMD [7] and the FN strength indices [36] during the menopausal transition. Our study extends these findings to hip geometry, demonstrating slower rates of change of bone geometry during the menopausal transition in Black women compared to White women, further contributing to their lower rates of fractures.

Age at FMP, smoking and physical activity showed no effect on the cumulative change of the HSA parameters. In the transmenopausal period, higher body weight was associated with significantly lower change in all HSA parameters, except OD. Similar associations were noted with change of BMD [7] and FN strength indices [36]. In addition, use of medications affecting bone metabolism (calcium, vitamin D, antidiabetics, antiepileptics, corticosteroids) also had no significant effect on the overall change of HSA parameters (results not shown).

Strengths of our study include the large multiethnic population, and long duration of follow up, which allowed for multiple longitudinal assessments. The use of mixed effects models provided greater statistical power. The analysis used the FMP which is shown to be a more accurate and valid representation of menopausal status than reliance on bleeding characteristics [2]. However, the study is not without limitations. The HSA parameters derived in this study were measured directly from 2-dimensional (2D) digital DXA images using algorithms for extracting the pixel data provided by the manufacturers under non-disclosure agreements [10]. The principle limitation of the HSA method is the uncertainty in positioning of the hip such that the dimensions reflected in measured geometry will vary depending on how the femur is projected into the 2D DXA image plane. However, this would be minimal in SWAN because we used the OsteoDyne's positioner which reduced positioning errors. Since DXA images are 2 dimensional, the measurements cannot provide information relevant to resistance of bending forces out of the image plane. Nevertheless, HSA geometry has previously shown to correspond well with that of 3D QCT in analysis of load stress [36]. Finally, the sample sizes for the Chinese and Japanese women were relatively small and our results may not be generalizable to those populations.

Despite these limitations, to our knowledge, no studies have assessed the timing and the rate of change of these HSA parameters across the menopausal transition. The changes in these parameters were greatest in the transmenopausal period suggesting greater skeletal vulnerability around FMP. Changes in hip geometry across the menopause transition parallel changes in BMD and provide insight into mechanisms that may increase risk of fragility fracture. If, however, the cumulative changes in HSA parameters around menopause predict future fracture risks, short-term treatment of women e.g., a single infusion of zoledronic acid, may be warranted at the time of menopause to preserve skeletal strength.

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.bone.2019.02.016>.

Disclosures

Thomas J. Beck is CEO of Beck Radiological Innovations, Inc. Cantonville, MD. The other authors have no disclosures.

Acknowledgement

The Study of Women's Health Across the Nation (SWAN) has grant support from the National Institutes of Health (NIH), DHHS, through the National Institute on Aging (NIA), the National Institute of Nursing Research (NINR) and the NIH ORWH (Grants NR004061; AG012505, AG012535, AG012531, AG012539, AG012546, AG012553, AG012554, AG012495). The Hip Strength Through the Menopausal Transition has grant support from the NIA (AG026463). Additional support for this project provided by NIA through P30-AG028748. Dr. Nagaraj was supported by the Bone Strength Through the Menopausal Transition: Trabecular Bone Score from the NIA (AG026463). The content of this article is solely the responsibility of the authors and does not necessarily represent the official views of the NIA, NINR, ORWH or the NIH. Clinical Centers: University of Michigan, Ann Arbor – Siobán Harlow, PI 2011, MaryFran Sowers, PI 1994–2011; Massachusetts General Hospital, Boston, MA – Joel Finkelstein, PI 1999 – present; Robert Neer, PI 1994–1999; Rush University, Rush University Medical Center, Chicago, IL – Howard Kravitz, PI 2009 – present; Lynda Powell, PI 1994–2009; University of California, Davis/Kaiser – Ellen Gold, PI; University of California, Los Angeles – Gail Greendale, PI; Albert Einstein College of Medicine, Bronx, NY – Carol Derby, PI 2011, Rachel Wildman, PI 2010–2011; Nanette Santoro, PI 2004–2010; University of Medicine and Dentistry – New Jersey Medical School, Newark – Gerson Weiss, PI 1994–2004; and the University of Pittsburgh, Pittsburgh, PA – Karen Matthews, PI. NIH Program Office: National Institute on Aging, Bethesda, MD – Sherry Sherman 1994 – present; Marcia Ory 1994–2001; National Institute of Nursing Research, Bethesda, MD – Program Officers. Central Laboratory: University of Michigan, Ann Arbor – Daniel McConnell (Central Ligand Assay Satellite Services). Coordinating Center: University of Pittsburgh, Pittsburgh, PA – Kim Sutton-Tyrrell, PI 2001 – present; New England Research Institutes, Watertown, MA - Sonja McKinlay, PI 1995–2001. Steering Committee: Susan Johnson, Current Chair; Chris Gallagher, Former Chair. We thank the study staff at each site and all the women who participated in SWAN.

Author roles

Study concept and design: JAC, GAG, ASK
 Data collection: JAC, GAG, MED
 Data analysis and interpretation: JAC, NN, RMB, TJB
 Drafting manuscript: NN, JAC
 Critical review and final approval of manuscript content: JAC, RMB, MED, GAG, ASK, TJB.

Statistical Analysis: NN and RMB performed the statistical analyses and are independent of any commercial funder. They had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analyses.

References

- [1] J.S. Finkelstein, *Osteoporosis: Cecil Textbook of Medicine*, (2000), pp. 1366–1373.
- [2] J.V. Pinkerton, D.W. Stovall, Reproductive aging, menopause, and health outcomes, *Ann. N. Y. Acad. Sci.* 1204 (1) (2010) 169–178.
- [3] R. Recker, J. Lappe, K. Davies, R. Heaney, Characterization of perimenopausal bone loss: a prospective study, *J. Bone Miner. Res.* 15 (10) (2000) 1965–1973.
- [4] J.R. Buchanan, C. Myers, T. Lloyd, R.B. Greer 3rd, Early vertebral trabecular bone loss in normal premenopausal women, *J. Bone Miner. Res.* 3 (5) (1988) 583–587.
- [5] C.C. Johnston Jr., S.L. Hui, R.M. Witt, R. Appledorn, R.S. Baker, C. Longcope, Early menopausal changes in bone mass and sex steroids, *J. Clin. Endocrinol. Metab.* 61 (5) (1985) 905–911.
- [6] M.E. Arlot, E. Sornay-Rendu, P. Garnero, B. Vey-Marty, P.D. Delmas, Apparent pre- and postmenopausal bone loss evaluated by DXA at different skeletal sites in women: the OFELY cohort, *J. Bone Miner. Res.* 12 (4) (1997) 683–690.
- [7] Greendale GA, Sowers MF, Han W, M.H. H, Finkelstien JS, Crandall CJ, Lee JS, Karlamangla AS. Bone mineral density loss in relation to the final menstrual period in a multiethnic cohort: results from the study of Women's Health Across the Nation (SWAN). *J. Bone Miner. Res.* 2012;27(1): 111–118.
- [8] T.D. Rozental, K.C. Walley, S. Demissie, S. Kaska, A. Martinez-Betancourt,

- A.M. Parker, J.N. Tsai, E.W. Yu, M.L. Boussein, Bone material strength index as measured by impact microindentation in postmenopausal women with distal radius and hip fractures, *J. Bone Miner. Res.* 33 (4) (2018) 621–626.
- [9] D.L. Kopperdahl, T. Aspelund, P.F. Hoffmann, S. Sigurdsson, K. Siggeirsdottir, T.B. Harris, V. Gudnason, T.M. Keaveny, Assessment of incident spine and hip fractures in women and men using finite element analysis of CT scans, *J. Bone Miner. Res.* 29 (3) (2014) 570–580.
- [10] T.J. Beck, S.B. Broy, Measurement of hip geometry-technical background, *J. Clin. Densitom.* 18 (3) (2015) 331–337.
- [11] S. Kaptoge, T.J. Beck, J. Reeve, K.L. Stone, T.A. Hillier, J.A. Cauley, S.R. Cummings, Prediction of incident hip fracture risk by femur geometry variables measured by hip structural analysis in the study of osteoporotic fractures, *J. Bone Miner. Res.* 23 (12) (2008) 1892–1904.
- [12] A.Z. LaCroix, T.J. Beck, J.A. Cauley, C.E. Lewis, T. Bassford, R. Jackson, G. Wu, Z. Chen, Hip structural geometry and incidence of hip fracture in postmenopausal women: what does it add to conventional bone mineral density? *Osteoporos. Int.* 21 (6) (2010) 919–929.
- [13] P. Szulc, F. Duboeuf, A.M. Schott, P. Dargent-Molina, P.J. Meunier, P.D. Delmas, Structural determinants of hip fracture in elderly women: re-analysis of the data from the EPIDOS study, *Osteoporos. Int.* 17 (2) (2006) 231–236.
- [14] S.B. Broy, J.A. Cauley, M.E. Lewiecki, J.T. Schousboe, J.A. Shepherd, W.D. Leslie, Fracture risk prediction by non-BMD DXA measures: the 2015 ISCD official positions part I: hip geometry, *J. Clin. Densitom.* 18 (3) (2015) 287–308.
- [15] S.L. Bonnick, T.J. Beck, F. Cosman, M.C. Hochberg, H. Wang, A.E. de Papp, DXA-based hip structural analysis of once-weekly bisphosphonate-treated postmenopausal women with low bone mass, *Osteoporos. Int.* 20 (6) (2009) 911–921.
- [16] J. Takada, G. Katahira, K. Iba, T. Yoshizaki, T. Yamashita, Hip structure analysis of bisphosphonate-treated Japanese postmenopausal women with osteoporosis, *J. Bone Miner. Metab.* 29 (4) (2011) 458–465.
- [17] Sowers MR, Crawford SL, Sternfeld B, Morganstein D, Gold EB, Greendale GA, et al. Chapter 11: SWAN: A multicenter, multiethnic, community based cohort study of women and the menopausal transition. In: Lobo RA, Kelsey J, Marcus R, editors. *Menopause: Biology and Pathobiology*. New York: Academic Press; 2000, p. 175–88.
- [18] D. Hans, F. Duboeuf, A.M. Schott, S. Horn, L.V. Avioli, M.K. Drezner, P.J. Meunier, Effects of a new positioner on the precision of hip bone mineral density measurements, *J. Bone Miner. Res.* 12 (8) (1997) 1289–1294.
- [19] J.S. Finkelstein, S.E. Brockwell, V. Mehta, G.A. Greendale, M.R. Sowers, B. Ettinger, J.C. Lo, J.M. Johnston, J.A. Cauley, M.E. Danielson, R.M. Neer, Bone mineral density changes during the menopause transition in a multiethnic cohort of women, *J. Clin. Endocrinol. Metab.* 93 (3) (2008) 861–868.
- [20] T.J. Beck, A.C. Looker, C.B. Ruff, H. Sievanen, H.W. Wahner, Structural trends in the aging femoral neck and proximal shaft: analysis of the third National Health and nutrition examination survey dual-energy X-ray absorptiometry data, *J. Bone Miner. Res.* 15 (12) (2000) 2297–2304.
- [21] B.C. Khoo, T.J. Beck, K. Brown, R.I. Price, Evaluating accuracy of structural geometry by DXA methods with an anthropometric proximal femur phantom, *Australas. Phys. Eng. Sci. Med.* 36 (3) (2013) 279–287.
- [22] J.A. Baecke, J. Burema, J.E. Frijters, A short questionnaire for the measurement of habitual physical activity in epidemiological studies, *Am. J. Clin. Nutr.* 36 (5) (1982) 936–942.
- [23] R.P. Heaney, M.J. Barger-Lux, K.M. Davies, R.A. Ryan, M.L. Johnson, G. Gong, Bone dimensional change with age: interactions of genetic, hormonal, and body size variables, *Osteoporos. Int.* 7 (5) (1997) 426–431.
- [24] T.J. Beck, A.C. Looker, F. Mourrada, M.M. Daphtary, C.B. Ruff, Age trends in femur stresses from a simulated fall on the hip among men and women: evidence of homeostatic adaptation underlying the decline in hip BMD, *J. Bone Miner. Res.* 21 (9) (2006) 1425–1432.
- [25] H.G. Ahlborg, O. Johnell, C.H. Turner, G. Rannevik, M.K. Karlsson, Bone loss and bone size after menopause, *N. Engl. J. Med.* 349 (4) (2003) 327–334.
- [26] P. Tranquilli Leali, C. Doria, A. Zachos, A. Ruggiu, F. Milia, F. Barca, Bone fragility: current reviews and clinical features, *Clin Cases Miner Bone Metab* 6 (2) (2009) 109–113.
- [27] D.M.P.L. Black, T.F. Lang, B. Chan, S.R. Cummings, E.S. Orwoll, A prospective study of DXA and QCT at the hip and spine predicting clinical fractures in men: the MrOS study, *JBMR* 19 (Suppl. 1) (2004) S18.
- [28] S.A. Wainwright, L.M. Marshall, K.E. Ensrud, J.A. Cauley, D.M. Black, T.A. Hillier, M.C. Hochberg, M.T. Vogt, E.S. Orwoll, Study of osteoporotic fractures research G. Hip fracture in women without osteoporosis, *J. Clin. Endocrinol. Metab.* 90 (5) (2005) 2787–2793.
- [29] S.R. Cummings, J.A. Cauley, L. Palermo, P.D. Ross, R.D. Wasnich, D. Black, K.G. Faulkner, Racial differences in hip axis lengths might explain racial differences in rates of hip fracture. Study of osteoporotic fractures research group, *Osteoporos. Int.* 4 (4) (1994) 226–229.
- [30] E. Banks, G.K. Reeves, V. Beral, A. Balkwill, B. Liu, A. Roddam, Million Women Study C, Hip fracture incidence in relation to age, menopausal status, and age at menopause: prospective analysis, *PLoS Med.* 6 (11) (2009) e1000181.
- [31] R.S. Sterling, Gender and race/ethnicity differences in hip fracture incidence, morbidity, mortality, and function, *Clin. Orthop. Relat. Res.* 469 (7) (2011) 1913–1918.
- [32] U.S. Department of Health and Human Services, Bone Health and Osteoporosis: A Report of the Surgeon General, U.S. Department of Health and Human Services, Office of the Surgeon General, Rockville, MD, 2004 (In).
- [33] M.L. Boussein, Determinants of skeletal fragility, *Best Pract. Res. Clin. Rheumatol.* 19 (6) (2005) 897–911.
- [34] M.E. Ruppel, L.M. Miller, D.B. Burr, The effect of the microscopic and nanoscale structure on bone fragility, *Osteoporos. Int.* 19 (9) (2008) 1251–1265.
- [35] A.S. Karlamangla, E. Barrett-Connor, J. Young, G.A. Greendale, Hip fracture risk assessment using composite indices of femoral neck strength: the Rancho Bernardo study, *Osteoporos. Int.* 15 (1) (2004) 62–70.
- [36] S. Ishii, J.A. Cauley, G.A. Greendale, C.J. Crandall, M.H. Huang, M.E. Danielson, A.S. Karlamangla, Trajectories of femoral neck strength in relation to the final menstrual period in a multi-ethnic cohort, *Osteoporos. Int.* 24 (9) (2013) 2471–2481.
- [37] K.J. Jepsen, A. Kozminski, E.M. Bigelow, S.H. Schlecht, R.W. Goulet, S.D. Harlow, J.A. Cauley, C. Karvonen-Gutierrez, Femoral neck external size but not aBMD predicts structural and mass changes for women transitioning through menopause, *J. Bone Miner. Res.* 32 (6) (2017) 1218–1228.
- [38] E. Barrett-Connor, E.S. Siris, L.E. Wehren, P.D. Miller, T.A. Abbott, M.L. Berger, A.C. Santora, L.M. Sherwood, Osteoporosis and fracture risk in women of different ethnic groups, *J. Bone Miner. Res.* 20 (2) (2005) 185–194.
- [39] J.A. Cauley, D. Chalhoub, A.M. Kassem, Gel H. Fuleihan, Geographic and ethnic disparities in osteoporotic fractures, *Nat. Rev. Endocrinol.* 10 (6) (2014) 338–351.
- [40] J.A. Cauley, Defining ethnic and racial differences in osteoporosis and fragility fractures, *Clin. Orthop. Relat. Res.* 469 (7) (2011) 1891–1899.
- [41] M.S. Putman, E.W. Yu, H. Lee, R.M. Neer, E. Schindler, A.P. Taylor, E. Cheston, M.L. Boussein, J.S. Finkelstein, Differences in skeletal microarchitecture and strength in African-American and white women, *J. Bone Miner. Res.* 28 (10) (2013) 2177–2185.
- [42] M.E. Danielson, T.J. Beck, Y. Lian, A.S. Karlamangla, G.A. Greendale, K. Ruppel, J. Lo, S. Greenspan, M. Vuga, J.A. Cauley, Ethnic variability in bone geometry as assessed by hip structure analysis: findings from the hip strength across the menopausal transition study, *J. Bone Miner. Res.* 28 (4) (2013) 771–779.