Hormone Predictors of Bone Mineral Density Changes during the Menopausal Transition

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Objective and Context: Our objective was to examine predictability of reproductive hormone concentrations for bone mineral density (BMD) loss during the menopausal transition.

Design: We conducted a longitudinal (five annual examinations), multiple-site (n = 5) cohort study, the Study of Women’s Health Across the Nation (SWAN).

Participants: Participants included, at baseline, 2311 premenopausal or early perimenopausal African-American, Caucasian, Chinese, and Japanese women.

Main Outcome Measures: We assessed annual dual-energy x-ray absorptiometry lumbar spine and total hip BMD measures, with endogenous estradiol (E2), FSH, androgens, and self-reported menstrual bleeding patterns.

Results: Over the 4-yr period, lumbar spine BMD loss was 5.6% in natural postmenopause, 3.9% in surgical postmenopause, or 3.2% in late perimenopause. Baseline FSH concentrations, subsequent FSH levels, and their interaction predicted 4-yr BMD loss. If baseline FSH was less than 25 mIU/ml, higher follow-up FSH (>70 mIU/ml) predicted a 4-yr spine BMD loss of ~0.05 g/cm². If baseline FSH values were more than 35–45 mIU/ml, lower follow-up FSH (i.e. 40–50 mIU/ml) predicted a ~0.05 g/cm² 4-yr spine BMD loss. Charts show amounts of predicted BMD losses with combinations of baseline FSH values and FSH levels over time. E2 concentrations less than 35 pg/ml were associated with lower BMD, but annual E2 measures and changes did not predict BMD loss. Testosterone, free androgen index, and dehydroepiandrosterone sulfate concentrations were not significantly associated with BMD loss.

Conclusions: Spine and hip BMD losses during the menopause transition were most strongly related to the interaction between initial FSH levels and longitudinal FSH changes and not to E2 or androgen levels or changes. (J Clin Endocrinol Metab 91: 1261–1267, 2006)
(12%) women. These proportions remained relatively constant through the subsequent examinations. The protocol was approved by each study site’s Institutional Review Board, and a written informed consent was obtained from each participant.

**Measurements**

Lumbar spine, femoral neck, and total hip BMD (g/cm²) measurements were made with Hologic (Hologic, Inc., Bedford, MA) 2000 (Pittsburgh and Oakland sites) or 4500A (Boston, Detroit area, and Los Angeles sites) densitometers. Osteodensity (Research Triangle Park, NC) positioning devices were used to optimize reproducibility of hip measurements (22). The study-wide quality control program included a daily measurement of an anthropomorphic spine phantom, cross-site, and cross-time calibrations with a Hologic spine phantom and an on-site review of all scans for specified criteria. Synarc, Inc. (Waltham, MA) reviewed 5% of all scans as well as those scans with potential problems and defined the ultimate status of these scans as acceptable, requiring reanalysis, or rejected.

**Hormones and assays.** The phlebotomy protocol specified a blood draw after a 12-h fast and in the 2- to 5-d window of the early follicular phase of the menstrual cycle. If a blood sample could not be obtained in the 2- to 5-d window in the 60 d after the anniversary visit date (usually because of irregular menstrual cycles), blood was obtained in the subsequent 30 d without respect to menstrual bleeding. Serum was analyzed for E2, FSH, and testosterone concentrations as well as SHBG and DHEA-S. The off-line E2 assay is a semiautomated, competitive ACS:180 (E2–6) immun assay with manual steps and an off-line incubation (23). Inter- and intraassay coefficients of variation averaged 10.6 and 6.4%, respectively, at an E2 level of 50 pg/ml. Serum FSH concentrations were measured with a two-site chemiluminescent immun assay using constant amounts of two monoclonal antibodies. Each antibody is directed to different regions on the β-subunit [one coupled to paramagnetic particles and the other labeled with dimethylaminoethanol (DMAE)] with specificity for intact FSH. Inter- and intraassay coefficients of variation were 12.0 and 6.0%, respectively, at an FSH level of 15 IU/liter. The absolute concentrations of FSH in this study are somewhat higher than values from some clinical laboratories because of different antibody specificities.

The testosterone assay is a competitive chemiluminescent ACS-180 immun assay. The SWAN reporting range for the testosterone assay is 10–100 ng/dl (actual assay range, 2–478 ng/dl). The ACS testosterone assay is standardized analytically and confirmed by gas chromatography–mass spectrometry. The assay has an interassay coefficient of variation of 13.8% and an intraassay coefficient of variation of 6.5%. The de novo two-site chemiluminescent assay for SHBG involved competitive binding of DMAE-labeled SHBG to a commercially available rabbit anti-SHBG antibody and a solid phase of goat antirabbit IgG conjugated to paramagnetic particles. Inter- and intraassay coefficients of variation were 9.9 and 6.1%, respectively. Total testosterone (T) was indexed to SHBG to calculate the free androgen index [FAI = 100 × T (ng/dl)/28.84 × SHBG (nm)].

The DHEA-S assay is a competitive chemiluminescent ACS-180 immun assay. This assay was developed de novo for SWAN and uses rabbit polyclonal anti-DHEA-S antibody, goat antirabbit IgG labeled with paramagnetic particles, and DHEA-S labeled with DMAE. The SWAN reporting range for the DHEA-S assay is 1.52–450 μg/dl (actual assay range, 1.52–1020 μg/dl). The assay is standardized against DHEA-S obtained from Steraloids (Newport, RI) and has an interassay coefficient of variation of 19.0% and an intraassay coefficient of variation of 13.6%.

**Menopausal status and other measures.** Menopausal status assignment was based on annual reports about menstrual bleeding and its regularity. Premenopause was identified as no decreased regularity in menstrual bleeding during the last year. Other classifications were early perimenopause (decreased menses regularity in the 3 months before interview), late perimenopause (no menses for 3–11 months), and postmenopause (no menses for 12 or more months). Surgical menopause was defined by report of either hysterectomy or oophorectomy.

At the baseline examination, 53% (n = 1244) of women were classified as premenopausal, and the remaining 47% of women were classified as early perimenopausal. The number of women classified as premenopausal declined progressively from baseline for each of the follow-up years (26, 18, 13, and 8%, respectively). Conversely, the number of women who became postmenopausal (and without hormone therapy use) rose progressively from 1% at the first follow-up examination to 15% at the fourth follow-up examination.

Hormone therapy (HT) use and medication use was identified from interviews and, when possible, confirmed by observing the medication packaging. There was no use of HT at the baseline examination as a condition of study eligibility, although by the fourth follow-up visit, cumulatively, 20.4% of women had reported HT use. Data from women reporting HT use were censored from subsequent analyses at the first reported use.

Weight and height were measured with calibrated electronic or balance beam scales and stadiometers, and those data were used to calculate body mass index (BMI, kg/m²). Means and variances were back-transformed for presentation (27). Hormone data were described according to time of phlebotomy in relation to menstrual bleeding (in or out of the 2- to 5-d period after menstrual bleeding). At baseline, 79% of specimens were drawn in 2–5, but this proportion declined to 37% by the fourth follow-up examination as women’s menses became increasingly irregular. Values for 19 extreme but biologically plausible hormone values from the five annual visits (four E2, one FSH, eight testosterone, three SHBG, and three DHEA-S values) were imputed by shifting them closer to the main body of their distributions while retaining their ranks. There were 19 women with missing data about menstrual bleeding status at one of the five examinations whose menopause status was imputed based on FSH values. Analyses including or excluding these imputed data indicated that there was no difference in the primary findings of this report. Data from women using oral glucocorticoids or bone antiresorptive therapy were censored at the first report of use.

Longitudinal modeling using SAS PROC MIXED incorporated a random intercept term to account for the correlated errors among repeated measures of the same woman. Three longitudinal models were used to estimate contribution to bone density change (20, 22). The first model, shown in Table 1, was a mixed-effects model that included the baseline and follow-up FSH level as a time-varying variable and included a quadratic term to describe change with time. A second longitudinal model related menopause status to bone density measures. The third model included baseline BMD values and hormone concentrations as well as subsequent annual hormone values in relation to bone density change. For FSH, but not E2, there was a significant interaction between the baseline hormone levels and subsequent hormone differences in relation to BMD levels. Building upon this information, the longitudinal models used in Tables 3 and 4 are as follows: BMD = baseline BMD, baseline hormone concentration, follow-up hormone concentrations, and time × follow-up hormone interaction (plus time main effects and covariates). The predictive information from the longitudinal models for the lumbar spine and the total hip was used to estimate the contribution of baseline and follow-up FSH to BMD change. Data are shown according to baseline FSH values corresponding to the 50th, 75th, 90th, and 95th percentiles of that distribution; subsequent FSH data values correspond approximately to the 25th, 50th, 75th, and 80th percentiles of the distribution of follow-up FSH values. Covariates included ethnicity, clinical site, BMI (time-varying), as well as low dō as a time-varying covariate. The dō value is an estimate of x-ray attenuation and is related to body thickness. Age, physical activity index, and smoking status were held fixed at their baseline levels.

Only P values less than 0.01 were considered relevant because of the large sample size and the number of comparisons that were made.

**Results**

Table 1 summarizes the unadjusted BMD values at baseline and at each of the subsequent four follow-up examina-
BMD change

Over a 4-yr period, there was statistically significant BMD loss at the total hip and spine bone sites, particularly the lumbar spine, as shown with fitted lines from longitudinal models (Fig. 1). Cumulative lumbar spine BMD decreased 3.2, 3.9, and 5.6%, respectively, among pre- and perimenopausal women who transitioned to late perimenopausal, postmenopausal (surgical), and postmenopausal (natural) status. At the total hip, cumulative BMD decreased 1.8, 1.9, and 2.9%, respectively, as women progressed to the late perimenopausal or postmenopausal (surgical or natural) stages.

Higher baseline FSH concentrations were associated with lower BMD at the spine and total hip, as has been previously reported (20). Both baseline FSH and subsequent annual FSH levels were required to predict lumbar spine and total hip BMD loss over the 4-yr period. Furthermore, there was an interaction between the baseline and follow-up FSH levels so that the baseline FSH levels influenced the level of follow-up FSH in relation to bone loss. If baseline FSH was lower (<25 mIU/ml), then statistical modeling indicated that more lumbar spine change occurred only when the follow-up FSH concentrations were higher (40–70 mIU/ml), and as shown in Fig. 2, the greatest amount of spine BMD loss (~0.05 g/cm²) was projected when the follow-up FSH values were greater than 70 mIU/ml. However, if the baseline FSH was higher (i.e. 35–45 mIU/ml), then modeling indicated that lower levels of follow-up FSH (i.e. 40–50 mIU/ml) are associated with a ~0.05 g/cm² spine BMD change over the 4-yr period (see heavy line in Fig. 2).

Because BMD loss predicted from the β-coefficients of baseline FSH, FSH over time, and their interaction are complex, Tables 3 and 4 are provided as charts to show the

| TABLE 1. Cross-sectional lumbar spine and total hip BMD values for five annual visits, according to menopause status |
|---------------------------------------------------------------|
|                  | Baseline | Visit 1 | Visit 2 | Visit 3 | Visit 4 |
| No. with BMD     |          |         |         |         |         |
| Age (yr)         | 2311     | 1951    | 1854    | 1780    | 1735    |
| Total hip BMD (g/cm²) | 0.963 ± 0.146 | 0.960 ± 0.145 | 0.957 ± 0.145 | 0.956 ± 0.145 | 0.956 ± 0.145 |
| Premenopause     | 0.963 ± 0.148 | 0.975 ± 0.147 | 0.976 ± 0.142 | 0.968 ± 0.139 | 0.958 ± 0.130 |
| Early perimenopause | 0.964 ± 0.144 | 0.955 ± 0.147 | 0.955 ± 0.146 | 0.965 ± 0.148 | 0.960 ± 0.147 |
| Late perimenopause | 0.961 ± 0.144 | 0.944 ± 0.151 | 0.948 ± 0.150 | 0.951 ± 0.157 | 0.951 ± 0.157 |
| Postmenopause without HT | 0.892 ± 0.117 | 0.912 ± 0.144 | 0.907 ± 0.149 | 0.913 ± 0.141 | 0.913 ± 0.141 |
| Lumbar spine BMD (g/cm²) | 1.078 ± 0.139 | 1.076 ± 0.142 | 1.069 ± 0.143 | 1.063 ± 0.146 | 1.056 ± 0.149 |
| Premenopause     | 1.081 ± 0.139 | 1.091 ± 0.139 | 1.084 ± 0.133 | 1.085 ± 0.136 | 1.082 ± 0.146 |
| Early perimenopause | 1.076 ± 0.139 | 1.073 ± 0.143 | 1.074 ± 0.145 | 1.079 ± 0.145 | 1.082 ± 0.142 |
| Late perimenopause | 1.066 ± 0.157 | 1.044 ± 0.146 | 1.038 ± 0.152 | 1.034 ± 0.161 | 1.034 ± 0.161 |
| Postmenopause w/o HT | 1.010 ± 0.117 | 1.016 ± 0.162 | 0.992 ± 0.145 | 0.988 ± 0.140 | 0.988 ± 0.140 |

Results are presented as mean ± SD.
predicted bone losses for various levels of baseline FSH and subsequent FSH measures over a 4-yr period. For example, the Table 3 chart shows that in the second-year follow-up, there was a predicted lumbar spine BMD loss of 0.025 g/cm² when the baseline and follow-up FSH concentrations were 70 mIU/ml and 15 mIU/ml, respectively. The greatest predicted loss in 4-yr of follow-up was 0.069 g/cm² among those whose baseline and follow-up FSH concentrations were 70 and 75 mIU/ml, respectively.

Measures of baseline E2 and its 4-yr variation during this transitional period were poor predictors of incremental BMD change. Significant lumbar spine BMD loss (≥0.040 g/cm²) was associated with E2 concentrations that were less than 35 pg/ml, regardless of the baseline FSH 2 levels.

There was no association of lumbar spine, total hip, or femoral neck BMD change with change in levels of testosterone, FAI, DHEA-S, or SHBG concentrations (data not shown).

**Discussion**

To our knowledge, this is the first study to longitudinally characterize BMD loss at the spine and hip in women during the menopausal transition and relate that loss to levels of change in reproductive hormone concentration. Statistical modeling of the baseline FSH values combined with the 4-yr levels of annual FSH concentrations and their interaction were predictive of amount of BMD loss. In contrast, variation in baseline and follow-up changes in annual E2 concentrations were not predictive of the amount of BMD loss; however, absolute E2 values less than 35 pg/ml were associated with BMD loss. These data suggest that serial FSH levels measured in pre- or early perimenopausal women, aged 42–52 yr, may help clinicians predict rates of bone loss during the menopause transition, but the relationship is complex, requires at least two FSH values, and may be challenging to apply in a busy clinical setting. Because our data are based on annual assessments, we cannot determine whether more frequent hormone assessment would be as predictive. E2 levels may be useful as predictors only when they become sufficiently low.

Few studies have examined BMD change prospectively during the menopausal transition, incorporating information about hormone patterns and bleeding patterns. An initial cross-sectional report from the Melbourne’s Women Health Study showed that FSH levels were incrementally higher in Caucasian women classified as pre-, peri-, and postmenopausal and that BMD levels were lower in each menopausal stage (28). By the time of the second BMD measure, about 50% (102 of 224) of the Melbourne Study population had experienced menopause (17, 28), compared with 25% of SWAN women by the end of yr 4 in this report (409 of 1678) (20). The second report of the Melbourne’s Women Health Study did not describe how hormone changes were associated with BMD change (17). In a Swedish cohort of 152 women (with a baseline age of 48 yr), there was a rise is FSH commencing 4.75 yr before the menopause; however, the investigators did not relate their FSH or E2 measures to the concurrently collected BMD measures of the forearm (29). A subsequent report of the same cohort excluded bone and hormone measures in the pre- and perimenopausal period (30). A study of 75 women living in Nebraska showed that, on average, FSH concentrations were rising at least 4 yr before the last menstrual period; however, estimates of bone

**FIG. 2.** Fitted lines representing projections of 4-yr spine BMD loss in pre- and early perimenopausal women based on initial FSH concentrations, subsequent annual follow-up FSH concentrations, and their interaction.
loss were annualized from a transmenopause statistical model and not related to hormone concentrations or their change (31). Finally, in a study of 231 women aged 32–77 yr with multiple measures of sex steroids and BMD, bone loss was associated with lower estrogen and SHBG levels (11). FSH levels were not evaluated in these women.

Postmenopausal bone loss has been attributed to a state of relative E2 deficiency (18), so it may appear incongruous that FSH concentrations were more predictive of bone loss during the menopause transition than were E2 values. There are potential explanations for this observation, however. First, FSH may serve as a proxy measure of ovarian dynamics involving E2. During the menopausal transition, FSH values may better characterize ovarian status than do E2 values because of the cyclic interaction of E2 and progesterone in the luteal phase represented by progressively irregular menstrual cycles. Second, FSH may have direct effects on bone. It has been reported that FSHβ (ligand) and FSH receptor

TABLE 3. Lumbar spine BMD loss predicted with baseline and follow-up FSH levels

| Follow-up FSH (mIU/ml) | Predicted lumbar spine BMD (g/cm²) loss | Baseline FSH, 15 mIU/ml | Baseline FSH, 25 mIU/ml | Baseline FSH, 45 mIU/ml | Baseline FSH, 70 mIU/ml |
|------------------------|----------------------------------------|-------------------------|-------------------------|-------------------------|-------------------------|
| yr 1                   |                                        |                         |                         |                         |                         |
| 15                     | -0.005                                 | -0.008                  | -0.012                  | -0.015                  |                         |
| 25                     | -0.002                                 | -0.006                  | -0.009                  | -0.012                  |                         |
| 50                     | -0.001                                 | -0.003                  | -0.006                  | -0.009                  |                         |
| 75                     | -0.003                                 | -0.001                  | -0.004                  | -0.007                  |                         |
| yr 2                   |                                        |                         |                         |                         |                         |
| 15                     | -0.025                                 | -0.028                  | -0.032                  | -0.035                  |                         |
| 25                     | -0.026                                 | -0.030                  | -0.033                  | -0.036                  |                         |
| 50                     | -0.028                                 | -0.032                  | -0.035                  | -0.038                  |                         |
| 75                     | -0.030                                 | -0.033                  | -0.037                  | -0.039                  |                         |
| yr 3                   |                                        |                         |                         |                         |                         |
| 15                     | -0.038                                 | -0.041                  | -0.045                  | -0.048                  |                         |
| 25                     | -0.042                                 | -0.045                  | -0.049                  | -0.052                  |                         |
| 50                     | -0.047                                 | -0.050                  | -0.054                  | -0.057                  |                         |
| 75                     | -0.050                                 | -0.053                  | -0.057                  | -0.060                  |                         |
| yr 4                   |                                        |                         |                         |                         |                         |
| 15                     | -0.044                                 | -0.047                  | -0.050                  | -0.053                  |                         |
| 25                     | -0.049                                 | -0.052                  | -0.055                  | -0.058                  |                         |
| 50                     | -0.055                                 | -0.059                  | -0.062                  | -0.065                  |                         |
| 75                     | -0.059                                 | -0.062                  | -0.066                  | -0.069                  |                         |

Baseline FSH levels correspond to the 50th, 75th, 90th, and 95th percentiles of the FSH distribution. Follow-up FSH levels correspond to the 25th, 50th, 75th, and 80th percentiles of 4-yr FSH values. Estimated effects shown are based on the β-coefficients associated with baseline FSH, time-varying FSH, and the FSH × linear and quadratic time interactions, from the longitudinal model of lumbar spine BMD. The model was adjusted for site, ethnicity, body size, and baseline age.

TABLE 4. Predicted total hip BMD change from baseline and follow-up FSH from longitudinal models in pre- and perimenopausal women

| Follow-up FSH (mIU/ml) | Predicted total hip BMD (g/cm²) loss | Baseline FSH, 15 mIU/ml | Baseline FSH, 25 mIU/ml | Baseline FSH, 45 mIU/ml | Baseline FSH, 70 mIU/ml |
|------------------------|----------------------------------------|-------------------------|-------------------------|-------------------------|-------------------------|
| yr 1                   |                                        |                         |                         |                         |                         |
| 15                     | -0.004                                 | -0.005                  | -0.006                  | -0.006                  |                         |
| 25                     | -0.004                                 | -0.005                  | -0.006                  | -0.006                  |                         |
| 50                     | -0.004                                 | -0.005                  | -0.006                  | -0.007                  |                         |
| 75                     | -0.005                                 | -0.005                  | -0.006                  | -0.007                  |                         |
| yr 2                   |                                        |                         |                         |                         |                         |
| 15                     | -0.009                                 | -0.009                  | -0.010                  | -0.011                  |                         |
| 25                     | -0.010                                 | -0.010                  | -0.011                  | -0.011                  |                         |
| 50                     | -0.011                                 | -0.012                  | -0.012                  | -0.013                  |                         |
| 75                     | -0.012                                 | -0.013                  | -0.015                  | -0.014                  |                         |
| yr 3                   |                                        |                         |                         |                         |                         |
| 15                     | -0.017                                 | -0.017                  | -0.018                  | -0.019                  |                         |
| 25                     | -0.019                                 | -0.020                  | -0.020                  | -0.020                  |                         |
| 50                     | -0.022                                 | -0.022                  | -0.023                  | -0.024                  |                         |
| 75                     | -0.024                                 | -0.025                  | -0.026                  | -0.026                  |                         |
| yr 4                   |                                        |                         |                         |                         |                         |
| 15                     | -0.027                                 | -0.028                  | -0.029                  | -0.029                  |                         |
| 25                     | -0.032                                 | -0.033                  | -0.033                  | -0.033                  |                         |
| 50                     | -0.037                                 | -0.038                  | -0.038                  | -0.039                  |                         |
| 75                     | -0.041                                 | -0.042                  | -0.043                  | -0.044                  |                         |

Baseline FSH levels correspond to the 50th, 75th, 90th, and 95th percentiles of the FSH distribution. Follow-up FSH levels correspond to the 25th, 50th, 75th, and 80th percentiles of 4-yr FSH values. Estimated effects shown are based on the β-coefficients associated with baseline FSH, time-varying FSH, and the FSH × linear and quadratic time interactions, from the longitudinal model of hip BMD. The model was adjusted for site, ethnicity, body size, and baseline age.
null mice have normal bone mass despite severe hypogonadism (32), and high FSH concentrations augment estrogen's effect on osteoclast formation in a nongenomic manner by stimulating osteoclast activity and survival (33, 34). Our findings that FSH levels, but not baseline E2 concentrations or their 4-yr variation, predicted bone loss in midlife women are consistent with a possible direct effect of FSH on bone. The observation that BMD loss was detectable in women whose E2 levels were less than 35 pg/ml is consistent with an important effect of E2 itself on bone, although levels may need to fall below some threshold value before this effect is apparent.

Bone loss was related to the passage of time, baseline FSH levels, and FSH levels over time even among women classified as premenopausal. This highlights the need to reconsider definitions of the early stages of the menopause transition (35). This could be done by incorporating FSH measures into definitions of bleeding regularity, reconsidering the number of menses used to define the reproductive stages, or employing greater rigor in defining the duration of time spent in the transitional stages. This refinement appears to be particularly relevant to bone and the timing and rate of loss because, as we had previously reported, pre- and early perimenopausal women with FSH levels above 26 mIU/ml had, on average, a 2.5% lower BMD than pre- and early perimenopausal women with baseline FSH levels less than 10 mIU/ml (20). We speculate that BMD loss had already been occurring among those with higher baseline FSH concentrations, a speculation that would be consistent with a recent report in premenopausal women (36).

In these analyses, there was no clearly identified role for androgens, including total testosterone, SHBG, FAI, and DHEA-S. This absence of such associations is consistent with a cross-sectional study that found no relationship between BMD and total testosterone in early postmenopausal women (37). In contrast, however, a longitudinal study of women followed for 2–8 yr reported that bone loss was associated with lower androgen concentrations (11).

Our study has limitations. First, although we have bone turnover markers measured in specimens from the SWAN baseline, turnover markers have not been measured concurrently with BMD and hormone levels. At baseline, we found FSH concentrations were positively correlated with both n-telopeptides and osteocalcin (38), but we cannot relate the longitudinal FSH measures to bone turnover (39). Second, although the SWAN protocol specified phlebotomy in the early follicular phase to enhance the interpretability of steroid hormone levels, this strategy precluded having information about hormone levels in the luteal phase. Furthermore, as women progressed through the transitional process, it became increasingly difficult to index phlebotomy to a menstrual bleed, thus obscuring whether specimens reflected the follicular or luteal phase of the menstrual cycle.

In conclusion, we found a significant BMD loss throughout the menopausal transition that could be predicted by having at least two serial FSH measures. Statistical modeling of baseline FSH values, annual follow-up FSH levels, and their interaction allowed us to build prediction models of bone loss and present the information in charts that can be used as a nomogram. This information may be useful in identifying transitioning women who may experience greater bone loss. Our results are consistent with the growing body of evidence that FSH may have direct effects on bone. Finally, we did not identify a significant association of BMD loss with changes in androgens over time.

Acknowledgments

Clinical Centers: University of Michigan, Ann Arbor, MI (MaryFran Sowers, PI); Massachusetts General Hospital, Boston, MA (Robert Neer, PI 1985–1989; Joel Finkelstein, PI 1990–1999; Jon A. P. McGoey, PI 1999 to present); Rush University, Chicago, IL (Lynda Powell, PI); University of California, Davis/Kaiser, Davis, CA (Ellen Gold, PI); University of California, Los Angeles, Los Angeles, CA (Gail Greendale, PI); University of Medicine and Dentistry, New Jersey Medical School, Newark, NJ (Gerson Weiss, PI 1995–2004; Nanette Santoro, PI 2004 to present); and the University of Pittsburgh, Pittsburgh, PA (Karen Matthews, PI).

National Institutes of Health (NIH) Program Office (Program Officers): National Institute on Aging, Bethesda, MD (Marcia Orly, 1994–2001; Sherry Sherman, 1994 to present); National Institute of Nursing Research, Bethesda, MD (Yvonne Bryan).

Central Laboratory: University of Michigan, Ann Arbor, MI (Daniel McConnell, PI) (CLASS, Central Ligand Assay Satellite Services). Endocrine Center, New England Research Institutes, Watertown, MA (Sonia McKinlay, PI 1995–2001); University of Pittsburgh, Pittsburgh, PA (Kim Sutton-Tyrrell, PI 2001 to present).

Received August 15, 2005. Accepted January 4, 2006.

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The Study of Women's Health Across the Nation (SWAN) has grant support from the National Institutes of Health, Department of Health and Human Services, through the National Institute on Aging, the National Institute of Nursing Research, and the NIH Office of Research on Women's Health (Grants RR004061, AG012505, AG012535, AG012539, AG012546, AG012553, AG012554, and AG012495). M.R.S. is a consultant to Merck Co. M.J., D.M., and R.L. have nothing to declare. G.A.G. is a consultant to Wyeth. J.S.F., J.J., and B.E. have nothing to declare. R.M.N. is a consultant to Amgen, Inc. and is on the speakers bureau for Merck.

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