

*Original Research Article*

# Reproductive Effects on Skeletal Health in Shuar Women of Amazonian Ecuador: A Life History Perspective

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**Objective:** Clinical and epidemiological research suggest that bone mineral density (BMD) in women is shaped by various reproductive factors such as parity and lactation patterns. However, the extent of these effects on BMD remains unclear because of contradictory findings and a focus on industrialized populations. Because fertility patterns in these groups are vastly different than those of women from non-Western, subsistence populations, our current understanding of the reproductive effects on skeletal health is incomplete. Using a life history perspective, this study examines the relationship between reproductive factors and bone density among women from the Indigenous Shuar population, an Amazonian Ecuadorian forager-horticulturalist group.

**Methods:** This preliminary, cross-sectional study included 130 premenopausal and postmenopausal women (14–86 years old) from the Morona-Santiago region of Ecuador. Anthropometrics were recorded, as was estimated BMD using a calcaneal ultrasonometer. A reproductive history questionnaire was administered that included questions regarding menarche, parity, lactation patterns, and menopause.

**Results:** Among postmenopausal women, early menarche and greater stature were significantly associated with higher bone density values. Among premenopausal women, few significant relationships between bone values and reproductive variables were documented; effects of lactation appeared to be transient and restored following weaning.

**Conclusions:** Although preliminary and not based on longitudinal data, these findings suggest that the effects of reproduction are transient as the system of calcium homeostasis in premenopausal women efficiently restores the bone loss that results from metabolically active reproductive states. Further, this research suggests that the timing of early life history events may canalize bone density phenotype. *Am. J. Hum. Biol.* 00:000–000, 2012. © 2012 Wiley Periodicals, Inc.

Bone mineral density (BMD) fluctuates over the life-span in response to various endogenous and exogenous factors such as diet and physical activity (Bartl and Frisch, 2004; IOF, 2010). Among reproductive-aged females, the effects of age and lifestyle on the skeletal system throughout the life-course may be further affected by reproductive factors, a consequence of heightened mobilization of calcium as well as shifts in the levels of sex steroids (e.g., estrogens and progesterone) and other hormones (e.g., parathyroid) essential for bone formation and maintenance (Agarwal and Stuart-Macadam, 2003; Bartl and Frisch, 2004; Galloway, 1997; Guyton and Hall, 2011; Pacifici, 2007). Despite our understanding of the mechanisms of bone turnover, clinical and epidemiological data are inconsistent regarding the extent to which female reproductive factors shape bone loss and accretion in both the immediate and long-term (i.e., premenopause and postmenopause, respectively). These inconsistencies may be partly attributed to the interrelated nature of developmental and reproductive stages (Agarwal and Glencross, 2011; Leidy, 1996; Pike, 2001). That is, the timing of each reproductive stage is closely linked to developmental factors as well as other characteristics of the reproductive cycle such as lactation patterns. These developmental factors, themselves, are further shaped by local ecological, environmental, and social variables (e.g., Piperata, 2009). Approaching skeletal health using a life history perspective is a potential remedy to this issue as it acknowledges that every life stage represents a point along a cumulative

progression, and that the dynamic interaction between developmental phases across the lifecycle is largely fueled by the availability of energetic resources necessary to modulate these stages (Leidy, 1996).

A second and arguably greater limitation to our current understanding of how reproduction affects skeletal health is that few studies have examined maternal bone status in non-Western, nonclinical populations. Even fewer data are available for subsistence-based, natural fertility groups. This is a critical oversight given that reproductive patterns and the associated hormonal cycles of women living in nonindustrialized populations are distinct from those of women in industrialized nations (Ellison et al., 1993; Sperling and Beyene, 1997; Whitten, 2008). For example, women in nonindustrialized groups often experi-

A version of this manuscript was presented at the 2011 Human Biology Association meeting and was awarded the E.E. Hunt Student Prize for Exceptional Student Presentation.

Contract grant sponsor: Wenner-Gren Foundation for Anthropological Research; Contract grant number: 7970; Contract grant sponsor: NSF; Contract grant number: BCS-0925910; Contract grant sponsors: Evonuk Foundation, Leakey Foundation, NIH; Contract grant number: 5DP1OD000516-5 via UCSB Center for Evolutionary Psychology, University of Oregon.

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Received 8 November 2011; Revision received 7 August 2012; Accepted 29 August 2012

DOI 10.1002/ajhb.22329

Published online in Wiley Online Library (wileyonlinelibrary.com).

ence relatively late menarche followed by an early first birth, greater lifetime parity, ~ 3–4 years of lactating per child, and relatively few lifetime menstrual cycles (Sperling and Beyene, 1997; Weaver, 1998). In comparison, women in industrialized Western nations typically experience early age at menarche, a later age at first parturition, reduced parity, limited breastfeeding periods, and a greater number of menstrual cycles (Eaton et al., 1994; Strassman, 1997; Whitten, 2008). These reproductive differences are accompanied by differences in hormonal levels (e.g., estrogens and progesterone) and, in turn, are predicted to shape bone integrity differently in Western and non-Western populations. Because contemporary subsistence populations have reproductive patterns more characteristic of most of our evolutionary past than those of Western groups, studies in subsistence populations can improve our understanding of the conditions under, which life history trade-offs in skeletal metabolism and reproduction evolved. Furthermore, research in subsistence-based groups may provide new insights into the complexities of bone loss that may be obscured by the confounding effects of the sedentary lifestyles and Westernized diets characteristic of industrialized populations. Given the enormous health and societal costs of osteoporosis and the severity of the problem, particularly for women, information from non-Western, natural fertility populations may be useful for the reevaluation and development of clinical guidelines and public health policies for osteoporosis prevention.

This study uses a life history perspective to investigate the relationship between bone density and reproductive factors among premenopausal and postmenopausal women from the Indigenous Shuar forager-horticulturalist population of Amazonian Ecuador, and tests several hypotheses suggested by the clinical and epidemiological literature.

#### REPRODUCTION AND SKELETAL HEALTH: LITERATURE REVIEW

The influence of reproductive factors on skeletal health is shaped primarily by fluctuations in sex steroids such as estrogens and progesterone (Galloway, 1997). Estrogens influence collagen formation and mineral deposition, and increase intestinal absorption and retention of calcium; progesterone promotes bone accrual through proliferation of osteoblastic activity (Agarwal and Stuart-Macadam, 2003; Galloway, 1997; Guyton and Hall, 2011). Additional circulating hormones that help to maintain the equilibrium of the central calcium pool and, therefore, are critical to bone integrity include parathyroid hormone, vitamin D, and calcitonin; modulations in these hormone levels also occur during various reproductive phases (Dawson-Hughes, 2004; Forwood, 2001). The reproductive variables that are most often linked to bone integrity in clinical and epidemiological literature, and are investigated in this study, include age at menarche, age at first parturition, patterns of breastfeeding (e.g., duration), and age at menopause.

##### *Age at menarche*

Several studies have documented associations between age at menarche and bone density, as well as with risk of osteoporosis later in life. A later age at menarche may lead to a heightened risk of osteoporosis in the postmenopausal period, whereas an earlier menarcheal age may reduce this possibility by increasing the peak bone mass achieved ear-

lier in life. Earlier menarcheal age may have a stimulating effect on bone development by increasing the osteoblastic activity that coincides with circulating estrogens, thereby establishing higher peak bone mass attainment, which provides a foundation for better bone health in later adulthood (Ito et al., 1995; Jaffe and Dell'Acqua, 1985; Roy et al., 2003). Additionally, early menarche may be related to larger body size, thereby increasing mechanical loading of the skeleton, as well as greater adiposity, which elevates the production of estrogen; both characteristics may function to stimulate bone accretion (Eastell, 2005). For these reasons, menarcheal age may be more strongly related to postmenopausal bone mass than age at menopause (e.g., Gerdhem and Obrant, 2004; Roy et al., 2003; Silman, 2003). However, not all studies of bone density and age at menarche are consistent, as several studies have shown no significant relationship (Ito et al., 1995; Ozdemir et al., 2005; Sioka et al., 2010; Varenna et al., 1999).

##### *Age at first parturition*

A later age at first birth has been linked with better skeletal health in both premenopausal and postmenopausal women. Bone density typically continues to increase into the mid-twenties when peak bone mass is achieved, but pregnancy and lactation during this period can disrupt bone formation and negatively influence long-term bone mass (Hayslip et al., 1989; Kent et al., 1990, 1993; Schnatz et al., 2010; Sowers et al., 1993). In addition to effects on postmenopausal bone health, a younger age at first pregnancy may have a negative impact during subsequent premenopausal years. In several studies, women who were younger at first parturition (<20 years old) demonstrated an impaired ability to gain in height when compared with other women, suggesting disruptions during early bone development (Allal et al., 2004; Gigante et al., 2006; Sear et al., 2004). Although associations between height and age at first parturition have been documented among Western industrialized groups and non-Western rural populations alike, the effect of the timing of first pregnancy on bone mass itself is not consistent across studies, with some research finding no significant relationship between age of first pregnancy and bone mass (e.g., Sowers et al., 1985).

##### *Pregnancy and parity*

Similarly, the literature is inconsistent regarding the long-term effects of pregnancy and parity on skeletal health. Several studies that have compared bone status of nulliparous and multiparous premenopausal and perimenopausal women have concluded that nulliparous females have lower bone density values (e.g., Sowers et al., 1992). Similarly, Forsmo et al. (2001) found that among early postmenopausal women, nulliparity predicted lower bone density values. However, several studies have reached the opposite conclusion, documenting a negative relationship between number of pregnancies and bone density (Allali et al., 2007; Gur et al., 2003). Further, other studies have found no significant associations between bone density and number of pregnancies (Ensom et al., 2002; Hillier et al., 2003; Lenora et al., 2009; Melton et al., 1993), including studies of Omani (Bererhi et al., 1996) and Finnish-American (Henderson et al., 2000) women, groups characterized by repeated, closely spaced pregnancies.

The inconsistencies in the literature are actually unsurprising given the multiple, complex pathways of calcium turnover during pregnancy. For example, pregnancy can decrease maternal bone density through heightened calcium demand associated with fetal growth. Yet, despite this draw on calcium, the maternal skeleton typically exhibits an increase in bone mass during pregnancy, most likely due to increased estrogen levels that inhibit bone loss and, in some cases, will promote bone accretion (Lees et al., 1998). Pregnancy also entails characteristics such as weight gain, which increases mechanical loading and the efficiency of intestinal calcium absorption, both of which contribute to the protective effect that being pregnant has on bone mass (Nguyen et al., 1995; Streeten et al., 2005). At present, it is not clear whether total number of offspring is an important factor in long-term skeletal health, or whether the influence of pregnancy on bone density is complicated by the effects of lactation patterns.

#### Lactation

The duration, timing, and intensity of lactation all appear to influence bone density, with some studies showing a protective effect of breastfeeding behaviors (Hreschchyn et al., 1988; Pearce, 2006) and others showing a negative effect (Affinito et al., 1996; Drinkwater and Chestnut, 1991; Kent et al., 1993; Lamke et al., 1977; Sowers, 1996). These seemingly contradictory results are again unsurprising given variation in lactation characteristics (e.g., intensity and duration), and how different studies were designed to assess the effects of lactation on bone health. For instance, several longitudinal studies that document changes in bone status during lactation and postweaning periods report that bone loss is transient and is later restored to prepregnancy values (Pearce, 2006; Sowers, 1996). Other studies, however, have shown that complete bone recovery never occurs, and that long-term breastfeeding can lead to progressive bone loss over the life-course (Chowdhury et al., 2002; Grimes and Wimalawansa, 2003; Lopez et al., 1996; Melton et al., 1993; Popivanov and Boianov, 2002; Sowers, 1996); other research has found no associations between lactation variables and bone density (Feldblum et al., 1992; Johnell and Nilsson, 1984).

The intensity of nursing may be a key variable that influences the extent of bone density loss. Pearce (2006), for example, found that a US cohort of women who lactated more intensively (i.e., the infant was exclusively breastfed and nursed frequently) had greater bone density values than those women who did not, suggesting that greater breastfeeding intensity may in fact serve to maintain bone integrity.

Although maternal bone status appears to be influenced by lactation patterns, the extent to which multiple reproductive cycles, coupled with other characteristics of lactation such as duration and intensity, impact long-term skeletal health is still largely unknown. The differences in results from the aforementioned studies may be largely attributed to the heterogeneity of lactation behaviors across study populations.

#### Interbirth interval

A relatively short interbirth interval (IBI) may be a risk factor for low bone density in premenopausal and postmenopausal women, as in theory it compromises the ability for maternal calcium stores to restore to prepregnancy val-

ues, and may therefore lead to a substantial drain of bone from the maternal skeleton (Affinito et al., 1996). This phenomenon may follow a pattern similar to the maternal depletion syndrome in which insufficient spacing between pregnancy and lactation cycles in energy-restricted environments can result in a deterioration of fat and lean muscle stores (Miller et al., 1994; Vallengia and Ellison, 2001). While the maternal depletion syndrome is often used to explain the effects of repeated reproductive cycles on soft tissue reserves, it can provide a useful framework for examining the relationship between reproduction and bone quantity and quality. Interestingly though, the few longitudinal studies that have investigated IBIs have found that bone health is not compromised by reduced birth spacing (Henderson et al., 2000; Sowers et al., 1993).

#### Age at menopause

Several studies have documented a connection between age at menopause and postmenopausal bone health, with an earlier menopausal age linked to lower BMD (Sioka et al., 2010). This is expected since menopause is marked by a cessation of ovarian function and a consequent reduction in the production of estrogens. Because of menopause-related declines in estradiol, women who experience earlier menopause spend more time in a hypoestrogenic state that may place them at greater risk for poor bone health (Gallagher, 2007; Kritz-Silverstein and Barrett-Connor, 1993; Ohta et al., 1996; Pouillès et al., 1994).

### RESEARCH OBJECTIVES AND HYPOTHESES

This study focuses on Indigenous Shuar women of Ecuadorian Amazonia and evaluates four hypotheses:

1. *Women who experienced an earlier menarche will have higher bone density values.* This hypothesis is based on the premise that a relatively early menarcheal age increases lifetime exposure to estrogens and may reflect better juvenile energetic conditions and, hence, greater early bone mass.
2. *Women with an older age at first parturition will have higher bone density values.* This hypothesis is based on the logic that an older age at first parturition means the woman has greater time to accumulate bone tissue before any pregnancy-related disruptions of bone formation occur.
3. *Women with longer lactation durations will have lower bone density values.* This hypothesis is predicated on the high rates of bone turnover that occur during lactation and, thus, extended periods of breastfeeding will result in lower bone density values.
4. *Women with longer IBIs will have greater bone density values.* This hypothesis is based on longer IBIs permitting a greater period during which maternal bone density can restore to prepregnancy values.

### MATERIALS AND METHODS

#### The population

The Shuar are a large Indigenous population concentrated in the southeastern region of the Ecuadorian Amazon. Shuar participants in this study came from four small, rural Upano Valley communities located ~ 40 min

to 1 h by truck and 3–4 h by foot from the nearest market center (Sucua). Members of these communities continue to depend on subsistence horticulture for daily dietary needs, while also engaging in a small-scale agro-pastoralist production for market sale.

### Participants

Participants in this cross-sectional study initially included 141 Shuar women between 14 and 86 years old. However, women who were pregnant at the time of the study ( $n = 11$ ) were not included in the statistical analyses since bone density would likely reflect the acute influence of their pregnant state. No women in the study reported ever using hormonal contraception. Therefore, the analyses presented here include a total of 130 women.

Currently lactating women ( $n = 41$ ) were considered in the statistical analyses as they comprised half the reproductive age women in the sample, and can provide critical insights into effects of lactation on bone density. However, several analyses reported herein treat them as a separate group. Participants were also separated into premenopausal and postmenopausal cohorts for analyses. Because many of the reproductive variables are influenced by current age (e.g., older women typically have had more births), for some analyses, premenopausal women were further divided into  $\sim 10$ -year age subcategories (14–24, 25–34, 35–44, and >45) based on standard age divisions in the clinical and epidemiological literature. Participants were considered postmenopausal ( $n = 22$ ) if they were neither pregnant nor lactating at the time of the study and reported not having experienced a menstrual cycle within the last year.

All participants gave individual informed verbal consent and the study protocol was approved by community leaders, the *Federación Interprovincial de Centro Shuar (FISCH)*, and the Office for Protection of Human Subjects at the University of Oregon.

### Calcaneal ultrasound: BMD measurements

BMD values were estimated using calcaneal ultrasonometry, a technique that has proven to be clinically useful as a screening tool for early signs of low BMD (Nayak et al., 2006). The calcaneus is a weight-bearing site rich in trabecular bone and, although there is typically variation in bone density among various skeletal regions, the calcaneus is an ideal single-site measure of bone density (Barkmann et al., 2007; Nayak et al., 2006). Correlations between ultrasound parameters and dual-energy X-ray absorptiometry (DXA), the gold-standard in bone density measures, range from a low of 0.28–0.44 in some studies (e.g., He et al., 2000) to as high as 0.86 in others (e.g., Trimpou et al., 2010). Although DXA tests are preferred before administering hormonal treatment for osteoporosis, portable calcaneal ultrasonometer units can be used in remote settings without access to DXA and may be used to predict fracture risk in epidemiological studies (Krieg and Hans, 2009).

BMD measures of the right heel of each participant were made using a gel-based Sahara® bone ultrasonometer (Hologic, Waltham, MA). Instrumental quality control scans of the manufacturer-provided phantoms were performed daily. The device generates three skeletal health parameters: (1) broadband ultrasound attenuation (BUA; decibels per megahertz), which is the slope of the ultra-

sonic attenuation versus frequency as it passes through bone; (2) speed of sound (SOS; meters per second), a value determined by the width of the heel and time delay between initial transmission and subsequent receipt of sound waves; and (3) calculated heel BMD, which is a device-generated estimate determined by linearly combining BUA and SOS values and is based on the following equation:  $0.002592 \times (\text{BUA} + \text{SOS}) - 3.687$  ( $\text{g}/\text{cm}^2$ ) (Frost et al., 2000). BUA is more closely related to the micro-architecture of bone (e.g., trabecular connectivity) and, because trabecular bone has a greater surface to volume ratio, it is generally subject to greater metabolic activity and faster rates of turnover than cortical bone. SOS, however, is greatly influenced by the elasticity and mineral constituents of the bone matrix (Bartl and Frisch, 2004; Lee et al., 2011). All three parameters are presented in the text separately as they represent different components of bone density and health. Significant relationships are presented in figures using estimated heel BMD except in circumstances where BMD was not significantly associated; in these cases, results for BUA or SOS are shown.

### Anthropometric variables

Participant stature [measured to the nearest millimeter (mm)] and weight [measured to the nearest 0.1 kilogram (kg)] were recorded using a field stadiometer (Seca, Hanover, MD) and digital scale (Tanita BF-558 electronic scale, Tokyo, Japan), respectively. Body mass index (BMI) was calculated as weight (kg)/height ( $\text{m}^2$ ).

### Reproductive history questions

Retrospective information on participant reproductive patterns was obtained through structured interviews. Each participant answered a series of questions regarding their reproductive histories. These included the following: (1) age at menarche (age at first menses); (2) age at first parturition; (3) number of births; (4) number of offspring breastfed (in rare instances, not all children were breastfed, which accounts for the difference between number of parturitions and number of offspring breastfed); (5) average duration of lactation per birth (women provided either a specific estimate of lactation duration for each child or an average estimate for all children); (6) total lifetime lactation months (this variable represents a sum total of months spent lactating during a participant's lifetime but does not account for the intensity of lactation); and (7) amount of time between each successive birth (i.e., IBI). Only five postmenopausal women were able to recall their age at menopause onset; this was too small a participant sample to perform meaningful statistical analyses.

### Data analyses

A preliminary ANCOVA test was performed to establish differences in bone density values between women who were either nulliparous or multiparous. This analysis was followed by a one-way ANOVA to determine differences in anthropometric and bone health values by menopausal status. Stepwise multiple linear regression analyses were performed to test hypotheses and investigate the relationships between bone density values, anthropometrics, and reproductive variables. As there are significant hormonal differences between premenopausal and postmenopausal women, it is standard in studies of bone health to analyze

TABLE 1. Anthropometric, bone density values, and reproductive profiles for premenopausal and postmenopausal Shuar women (including lactating women)

	Premenopausal (n = 108)				Postmenopausal (n = 22)				P
	Mean	SD	Min	Max	Mean	SD	Min	Max	
Age (years)	29.82	10.80	14.07	52.55	58.34	10.35	48.04	85.98	**
Height (cm)	148.74	4.53	136.00	158.67	144.32	6.07	134.50	153.10	**
Weight (kg)	56.01	10.13	24.90	97.40	52.64	11.16	36.70	81.20	Ns
BMI (kg/m <sup>2</sup> )	25.30	4.05	10.62	41.07	25.11	4.07	20.29	34.64	Ns
BUA (dB/MHz)	81.3	16.9	37.4	123.0	58.9	16.1	26.0	89.1	**
SOS (m/sec)	1574.8	28.2	1524.7	1661.9	1527.6	20.7	1475.9	1567.1	**
Estimated heel BMD	0.608	0.112	0.411	0.944	0.427	0.095	0.207	0.607	**
Menarche Age (years)	13.07	1.16	9.00	16.00	13.29	0.92	12.00	15.00	Ns
Age at First Parturition (years)	17.45	3.33	12.00	35.00	17.64	5.68	14.00	39.00	Ns
Number of Births	4.07	3.58	0.00	13.00	8.81	3.40	0.00	15.00	**
IBI (months)	31.10	12.96	12.00	73.64	31.58	8.02	20.90	49.07	Ns
Number of Offspring Breastfed	3.94	3.52	0.00	13.00	8.81	3.40	0.00	15.00	**
Average Lactation per Birth (months)	15.11	7.09	0.00	44.00	16.05	5.28	8.57	25.33	Ns
Lifetime Lactation (months)	66.14	67.73	0.00	312.00	137.24	72.15	0.00	240.00	**

Ns, not significant; \*\*  $P < 0.001$  (significant difference between menopausal states).

Abbreviations: BMI, Body mass index; BUA, Broadband ultrasound attention; IBI, Interbirth interval; SOS, Speed of sound.

TABLE 2. Anthropometric and bone density values for premenopausal women by age cohort (including lactating women)

	14–24 (n = 47)			25–34 (n = 25)			35–44 (n = 22)			45 > (n = 14)		
	Mean (SD)	Min	Max	Mean (SD)	Min	Max	Mean (SD)	Min	Max	Mean (SD)	Min	Max
Height (cm)	149.19 (4.94)	136.0	158.67	148.9 (4.11)	140.55	155.1	148.01 (4.36)	139.8	156.4	147.95 (4.13)	140.6	155.0
Weight (kg)	51.23 (7.34)	24.9	65.5	61.65 (12.42)	49.4	97.4	58.28 (6.82)	49.7	76.1	60.01 (11.38)	47.6	90.9
BMI (kg/m <sup>2</sup> )	22.99 (2.81)	10.62	28.87	27.96 (4.74)	22.77	41.07	26.59 (2.77)	22.66	33.38	27.26 (3.87)	23.26	37.84
BUA (dB/MHz)	79.4 (17.0)	44.7	120.9	82.5 (18.6)	37.4	122.5	83.8 (17.3)	55.3	123.0	82.1 (13.7)	64.2	113.8
SOS (m/sec)	1575.9 (27.0)	1524.9	1629.3	1576.9 (31.3)	1524.7	1649.6	1575.3 (27.8)	1535.8	1661.9	1567.0 (28.6)	1529.7	1613.9
Estimated heel BMD	0.604 (0.108)	0.411	0.848	0.618 (0.125)	0.426	0.878	0.614 (0.115)	0.438	0.944	0.592 (0.104)	0.445	0.792

Abbreviations: BMI = Body mass index; BUA = Broadband ultrasound attention; SOS = Speed of sound

these groups separately. Therefore, to determine the role of age and isolate it from other factors that shape BMD, an initial regression was performed separately for the premenopausal and postmenopausal groups. Moreover, because association between age and many of the reproductive variables may differ across the lifespan, comparing the effects of these variables on skeletal parameters from females of different age groups could be problematic. For this reason, an additional stepwise analysis was performed for each age cohort. Each bone density parameter (BUA, SOS, and BMD) was included separately as a dependent variable in regression models and age, height, weight, and BMI were used as the independent variables. Reproductive variables used in multivariate models included age at menarche, age at first parturition, number of live births, average duration of lactation per birth, total lifetime months spent lactating, and IBI. For both sets of analyses, lactating women were analyzed separately from nonlactating women. All statistical analyses were performed using SPSS 17.0 (SPSS).

## RESULTS

A total of 89 (82.4%) premenopausal and 21 (95.5%) postmenopausal women reported having at least one child. An ANCOVA comparing BUA, SOS, and BMD between nulliparous and parous women by menopausal status, controlling for age, indicated no significant differences between the groups in these values.

Table 1 presents the descriptive statistics for anthropometric variables, bone density values, and reproductive

profiles for participants, including lactating women, by menopausal status. Most anthropometric dimensions and all bone density measures were significantly higher among premenopausal than postmenopausal women. Anthropometric, bone density, and reproductive profiles for premenopausal women are shown in Tables 2 and 3, with data presented by age group. A reduced height was apparent with increasing age. However, all other body size and most bone health values were progressively higher with age until the mid-30s; weight, BMI, SOS, and BMD peak in the 25–34 year age category. BUA was the sole bone measure that did not show a similar trend and, rather, peaks in the 35–44 year age group.

No significant secular trend in age at menarche or age at first parturition was seen in this sample. Across all Shuar participants, IBI varies from 1 to 6 years, with the longest average duration between births reported among the oldest premenopausal cohort [3.25 years (39 months)]. While most women reported breastfeeding all of their children, the total number of offspring breastfed was not necessarily identical to the total number of parturitions since some infants died immediately following birth and, in one instance, a teenage mother did not produce breast milk. On average, children were completely weaned at ~ 1 year, 3 months old, although some participants continued to lactate for up to 3.6 years (44 months). The total duration of lactation across the individual's lifetime was age-dependent as it is related both to number of offspring and breastfeeding practices. Older women, therefore, tended to have higher total lifetime lactation, with one 45-year old participant nursing for ~ 26 years (312 months).

TABLE 3. Reproductive profile of Shuar women by age cohort

	14–24 ( <i>n</i> = 47)			25–34 ( <i>n</i> = 25)			35–44 ( <i>n</i> = 22)			45 > ( <i>n</i> = 14)		
	Mean (SD)	Min	Max	Mean (SD)	Min	Max	Mean (SD)	Min	Max	Mean (SD)	Min	Max
Menarche Age (years)	13.24 (1.23)	10.0	16.0	13.05 (1.05)	11.0	15.0	12.77 (1.19)	9.0	14.0	13.08 (1.08)	11.0	15.0
Age at First Parturition (years)	17.07 (2.21)	13.0	22.0	16.90 (2.47)	14.0	22.0	18.10 (4.46)	13.0	35.0	18.14 (4.44)	12.0	28.0
Number of Births	1.17 (1.18)	0	4.0	4.96 (2.75)	0	10.0	7.09 (3.26)	1.0	13.0	7.29 (3.29)	0	13.0
IBI (months)	25.27 (10.22)	14.92	48.0	26.13 (9.39)	12.0	51.93	35.25 (14.61)	12.89	66.18	39.10 (12.59)	21.85	73.64
Number of Offspring Breastfed	1.15 (1.19)	0	4.0	4.72 (2.56)	0	10.0	7.05 (3.24)	1.0	13.0	6.86 (3.57)	1.0	13.0
Average Lactation per Birth (months)	13.54 (6.97)	0	28.0	16.10 (7.22)	9.0	44.0	15.32 (6.12)	1.0	24.0	15.90 (8.73)	4.0	36.0
Lifetime Lactation (months)	17.44 (22.23)	0	84.0	69.43 (32.84)	0	132.0	116.64 (75.0)	1.0	288.0	117.04 (87.34)	8.0	312.0

Abbreviations: IBI = Interbirth interval

TABLE 4. Stepwise multiple regression results for estimated heel BMD, SOS, and BUA and reproductive variables

Model	Estimated heel BMD				SOS				BUA				
	Coefficient (SE)	$\beta$	<i>P</i>	Adj ( <i>r</i> <sup>2</sup> )	Coefficient (SE)	$\beta$	<i>P</i>	Adj ( <i>r</i> <sup>2</sup> )	Coefficient (SE)	$\beta$	<i>P</i>	Adj ( <i>r</i> <sup>2</sup> )	
<b>Premenopausal</b>													
Entire group (lactating)													
Mean lactation per birth													
14–24 year olds (lactating)													
Height <sup>a</sup>	1	0.016 (0.006)	0.006	0.033	0.349	3.774 (1.644)	0.608	0.047	0.299	2.424 (0.909)	0.664	0.026	0.379
Height	2	0.002 (0.007)	0.069	0.818		0.216 (1.930)	0.035	0.914					
Age at first parturition		0.061 (0.023)	0.780	0.028	0.615	15.178 (6.066)	0.778	0.037	0.558	8.388 (3.358)	0.732	0.037	0.608
35–44 year olds (nonlactating)													
Mean lactation (per birth)		0.020 (0.004)	0.832	0.001	0.658	5.080 (1.064)	0.847	0.001	0.685	2.577 (0.703)	0.774	0.005	0.555
<b>Postmenopausal</b>													
Menarche age <sup>b</sup>		–0.58 (0.023)	–0.576	0.025	0.281								
Height <sup>c</sup>	1									1.511 (0.699)	0.514	0.050	0.208
Height <sup>c</sup>	2									1.384 (0.518)	0.471	0.020	
Menarche age										–10.738 (3.122)	–0.606	0.005	0.568

Only significant results are presented.

<sup>a</sup>In this model, height was only significant when reproductive variables were not considered.

<sup>b</sup>Menarche age was only significantly associated with estimated heel BMD.

<sup>c</sup>In Model 1, height was significant when reproductive variables were not considered; this significance was maintained when reproductive factors were included in Model 2.

Premenopausal lactating women were analyzed as a separate group from nonlactating individuals in the initial regression analyses. Table 4 shows the results from the regression analyses for each skeletal parameter according to menopausal status, age cohort, and lactation status. Among lactating women as a group, the only significant relationships were that BUA and SOS were negatively related to the average number of breastfeeding months per child; that is, the longer duration a female spent breastfeeding each offspring, the lower her skeletal health values ( $P < 0.05$ ). Subsequent regression analyses were performed on each premenopausal age cohort and revealed that only among 14–24 year olds were anthropometric variables and reproductive parameters significantly associated with BUA, SOS, and BMD. When body size variables were considered separately in the model, there were significant positive associations between stature and BMD, SOS, and BUA with ~ 35, 30, and 38% of the variation in these values attributable to height, respectively. Weight and BMI showed no significant relationship with any bone parameter. Upon inclusion of reproductive variables in the model, height was no longer a significant predictor of bone density; BMD, SOS, and BUA values were more strongly associated with age at first parturition. Females who were older at age of first parturition had significantly higher bone density values (BMD, SOS, BUA:  $P < 0.05$ ). No similar trends in bone

density for premenopausal lactating women in other age cohorts were found. The positive association between BMD and age at first parturition among lactating 14–24 year olds is shown in Figure 1.

In the nonlactating, premenopausal group, the first stepwise analysis performed on the entire nonlactating cohort revealed no significant relationship between age, the reproductive variables, and the bone parameters. When each nonlactating age cohort was analyzed separately, the only significant predictor of bone health parameters was average duration of lactation per birth, and this relationship was only found among 35–44 year olds (Table 4). Women from this age group who reported having longer bouts of nursing per child also had significantly higher BMD ( $P = 0.001$ ), SOS ( $P = 0.001$ ), and BUA ( $P = 0.005$ ) values. No significant relationship among anthropometrics, reproductive variables, and bone density were documented for any other age group of nonlactating women.

Although this study was cross-sectional, a scatter plot of BMD by years since last birth offers insight into how BMD may fluctuate through time with lactation status (Fig. 2). Among nonlactating women, there is minor variability in BMD values; conversely, among lactating women, BMD is highly variable. Although an ANOVA did not reveal significant differences in bone density values between lactating and nonlactating women by age cohort, the minor fluctuations in BMD among nonlactating women is noteworthy.

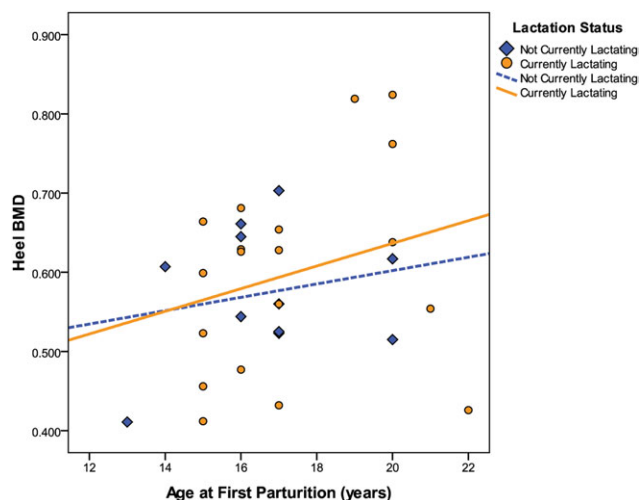


Fig. 1. Estimated heel BMD and age at first parturition by lactation status among premenopausal women. A significant relationship was determined for women who were lactating at the time of the study. (Not Currently Lactating:  $R^2 = 0.046$ ; Currently Lactating:  $R^2 = 0.069$ ). [Color figure can be viewed in the online issue, which is available at [wileyonlinelibrary.com](http://wileyonlinelibrary.com).]

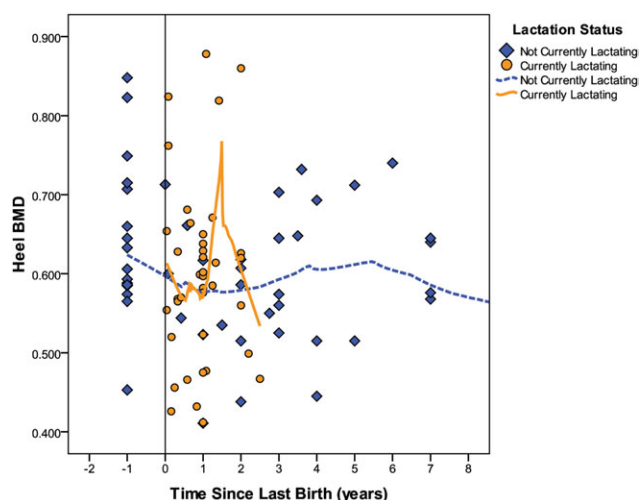


Fig. 2. Scatter plot of estimated heel BMD and time since last birth (years) by lactation status among premenopausal women with Loess smoothing lines. Individuals to the left of the black line (zero) are nulliparous. (Not Currently Lactating:  $R^2 = 0.046$ ; Currently Lactating:  $R^2 = 0.069$ ). [Color figure can be viewed in the online issue, which is available at [wileyonlinelibrary.com](http://wileyonlinelibrary.com).]

Stepwise regression analyses of reproductive variables and bone health among postmenopausal women indicated that the only reproductive variable that significantly predicts bone health values later in life was age at menarche (BMD:  $P < 0.05$ ). The younger the age at first menses, the higher the bone density values in postreproductive life (Table 4); this relationship is illustrated in Figure 3. Of the anthropometric variables, current height, but not weight or BMI, was significantly related to postmenopausal BUA. Taller postmenopausal women have higher BUA values, but this relationship was not apparent for SOS or BMD. Approximately 36% of the variation in BUA can be attributed to current height (Fig. 4). While taller women were, also the youngest of the postmenopausal age

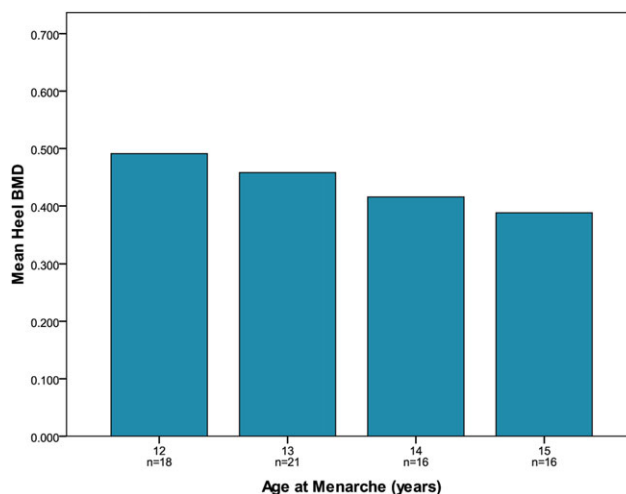


Fig. 3. Estimated heel BMD by age at menarche among postmenopausal women (with 95% confidence intervals). [Color figure can be viewed in the online issue, which is available at [wileyonlinelibrary.com](http://wileyonlinelibrary.com).]

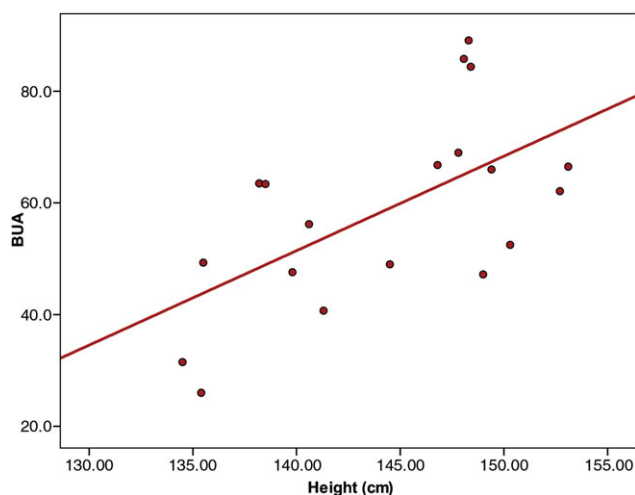


Fig. 4. Scatter plot of BUA by height among postmenopausal women with linear best fit line ( $R^2 = 0.36$ ). A similar trend was not determined for SOS and estimated BMD. [Color figure can be viewed in the online issue, which is available at [wileyonlinelibrary.com](http://wileyonlinelibrary.com).]

cohort, the relationship between greater height and higher BUA values remained significant when controlling for age. Additionally, Table 4 illustrates that the interaction between height and age at menarche was significant for BUA only ( $P = 0.005$ ). Taller women who reported an earlier age at menarche had higher bone density values when compared with other postmenopausal women.

## DISCUSSION

The primary goal of this study was to test hypotheses related to the association between bone health and reproduction among a natural fertility population of Shuar women from Ecuadorian Amazonia. As reported

elsewhere (Madimenos et al., 2011a), Shuar females have modestly higher premenopausal bone density values when compared to industrialized populations including U.S., German, and Korean reference populations, but similar values were found among postmenopausal women.

#### *Age at menarche*

Hypothesis 1. Women who experienced an earlier menarche will have higher bone density values. This study found support for the first hypothesis. Among Shuar postmenopausal women, earlier menarche was associated with higher bone density values, although a similar trend was not documented among premenopausal women. Postmenopausal women who were younger at first menses (12 or 13 years old) had significantly greater skeletal health values compared to women who reported first menses at 14 or 15 years old. Earlier menarcheal age was the primary predictor of postmenopausal bone mass, suggesting that the timing of this developmental stage and the factors that influence its onset, including nutrition and disease burden, canalizes bone density phenotype.

From a mechanistic perspective, the secretion of estrogens at menarche contributes to bone accretion processes and, thus, an early first menses expands the female reproductive life and increases cumulative exposure to these hormones. Additionally, early menarcheal age is related to larger body size and greater fat content, both of which serve to increase overall bone quantity (Eastell, 2005).

From a life history perspective, the age at which a female experiences her first menses reflects a suite of early environmental and social factors that influence endocrine function regulating trade-offs between growth and reproduction (Sloboda et al., 2010). Following life history theory, a developing organism will allocate energetic resources to growth, and these resources will only become essential for reproduction at the time of sexual maturity. In an energy-deficient environment, organisms will delay reproductive maturation until a time when resources are adequate and reproductive activities will be successful; in an energy-sufficient environment they will begin reproduction earlier because the costs of delaying reproduction are not outweighed by the benefits of continued growth (Coall and Chisholm, 2010; Ellison, 1982). Girls with better nutritional status thus tend to mature earlier than girls with poorer nutritional status (Ellison 1982, 1990). In this study, a younger age at first menses therefore may indicate better early environmental and energetic states. Postmenopausal Shuar women who experienced early menarche were arguably in better phenotypic condition than those who experienced first menses later, that is, they were within a “healthy” range for the timing of this developmental stage at an earlier age. Women who were older at menarche may reflect more compromised early phenotypic quality that then may resonate into postmenopausal life.

The notion that key developmental events can serve as an indirect proxy for early energetic conditions with effects on phenotypic quality in later life is further supported by the positive association between height and skeletal health. Height is frequently used as a marker of early environmental and nutritional conditions (Benefice et al., 2006; Bogin, 1999; Bogin and Loucky, 1997; Bronte-Tinkew and DeJong, 2004), and in this study height is the one anthropometric variable that recurrently demonstrates relationships with bone health across premeno-

pausal and postmenopausal women. As with the mechanisms governing menarche onset, shorter stature can reflect poor nutrition or adverse circumstances that lead to the devotion of energy towards a competing physiological domain (e.g., immune function) and inhibit skeletal growth in the process (Blackwell et al., 2010; Ellison et al., 1993; Gluckman and Hanson, 2004; Jasienska et al., 2006). Results from this study indicate that both greater stature and earlier age at menarche may serve as indicators of early energetic conditions, and they remain important predictors of phenotypic quality, in this case bone quality and quantity, across the lifespan. In line with this reasoning, we previously demonstrated that a significant proportion of Shuar children (~40%; between 2 and 18 years old) were short for their age (i.e., stunted), although low weight for age or height (e.g., wasting) was rare; this earlier finding suggests that among Shuar, height-for-age is a more accurate proxy of early phenotypic condition, even when measured during childhood (Blackwell et al., 2010).

#### *Age at first parturition*

Hypothesis 2. Women with an older age at first parturition will have higher bone density values. Partial support was demonstrated for the second hypothesis; only among young, premenopausal lactating women were the positive effects of age at first parturition on estimated BMD documented. A similar relationship was not observed among nonlactating women. Pregnancy and lactation are periods of extensive bone turnover and, if normal growth patterns are disrupted to accommodate reproduction, this may result in lower peak bone mass. A later age at first parturition, therefore, may provide a protective effect for early bone health. Being young (<18-years-old) at first pregnancy is also linked to poorer pregnancy outcomes and greater risk of fetal deaths (Kline et al., 1989; Kramer, 1987; Wood, 1994), an association that may suggest an evolutionary advantage to a later age at first parturition for both optimal maternal and offspring fitness. However, one should also consider that a later age at first pregnancy shortens the reproductive life span, which reduces the potential number of offspring a female may have and can lower her completed fertility. Therefore, results here may reflect a quantity/quality trade-off between maternal condition and the number or quality of her offspring.

#### *Lactation*

Hypothesis 3. Women with longer lactation durations will have lower bone density values. Results provided partial support for the third hypothesis. The findings did show that, among the Shuar, average weaning is relatively early (~15 months) compared with many other subsistence populations including the Yanomamo (24–36 months; Early and Peters, 1990), and the !Kung (36–48 months; Lee, 1979); the average duration of breastfeeding among subsistence populations is ~29 ± 10 months (Sellen, 2001).

Among the significant findings, women who were lactating at the time of the study and reported breastfeeding for longer periods with each child had significantly lower BMD values than other lactating women. These results are similar to those of other studies that suggest lactating women will experience a loss in bone mass during the first few months of breastfeeding, typically coinciding with the



period of lactational amenorrhea. Upon resumption of menses with weaning, these women typically will completely regain their bone mass (Kalkwarf and Specker, 1995; Kolthoff et al., 1998; Lopez et al., 1996; Sowers et al., 1996). Studies have also shown that women who do not breastfeed do not experience fluctuations in postpartum bone integrity (Hayslip et al., 1989; Laskey et al., 1998).

Although significant associations between bone values and reproductive factors were not seen in the nonlactating group as a whole, when analyzed by age cohort, findings indicated that longer periods of breastfeeding per child may confer a protective effect on BMD in the 35–44 year old cohort. While several studies report a negative association between number of months of recalled lactation and bone status (e.g., Lissner et al., 1991), the vast majority of epidemiological studies of premenopausal and postmenopausal women have found no negative effect of lactational history on BMD (Feldblum et al., 1992; Kovacs and Kronenberg, 1997; Johnell and Nilsson, 1984; Sowers, 1996). The precise way that bone loss is experienced and subsequently restored during lactation is not clear, although our finding that longer nursing periods are related to higher BMD in the 35–44 year cohort, independent of quantity of offspring, is intriguing. It is worth noting that the benefits of breastfeeding on maternal and offspring health are well-established in the literature (e.g., Rasmussen and McGuire, 1996), and may help to prevent premenopausal breast cancer (Newcomb et al., 1994), obesity (Dewey et al., 1993), and ovarian cancer (Rosenblatt and Thomas, 1993). While our study results should be interpreted with caution because of small sample size, these data are consistent with other research that suggests potential protective mechanisms against bone loss may be associated with breastfeeding practices (e.g., Pearce, 2006).

Only a few associations between lactation variables and bone mass were documented in this study. Because of the heterogeneity in lactation duration and intensity within and across populations, the long-term effects of lactation on skeletal health remain unclear. Additional research into this relationship is necessary and should also consider the social and ecological factors that shape decisions about lactation duration and intensity (e.g., availability of social support) and the implications for skeletal health (e.g., Piperata, 2009).

#### *Interbirth interval*

Hypothesis 4. Women with longer IBIs will have greater bone density values. This study found no significant association between birth spacing and estimated BMD for premenopausal or postmenopausal women. In this study, as well as others (e.g., Bererhi et al., 1996; Sowers et al., 1995), the effects of the maternal depletion syndrome have not been demonstrated for skeletal reserves as they have for body fat. One hypothesis for this pattern involves the contribution of maternal fat stores to satisfy costs of offspring brain development. The mobilization of larger amounts of fat during pregnancy and lactation serves an adaptive function that helps meet the developmental needs of the fetal and neonatal brain (Lassek and Gaulin, 2006). Replenishing fat stores rapidly may therefore not be possible because of the continuous and critical need to satisfy the requirements of the growing infant's metabol-

ically expensive brain. While maternal skeletal calcium stores are drawn upon to support offspring skeletal growth in an analogous way, it may be the case that replenishing calcium stores is more easily achieved than maternal fat reserves, perhaps because of greater availability of calcium from the environment (e.g., Stini, 1995), thereby facilitating the recovery of bone loss between reproductive cycles. It remains to be seen whether shorter IBI is related to lower bone density in more nutritionally stressed populations, such as those with a higher prevalence of wasting, than what has been documented in the Shuar.

#### *Study limitations*

This study has several key limitations. First, participant sample sizes are small, particularly in the postmenopausal cohort, which restricts statistical power; therefore, these data should be considered preliminary. Future data collection is in progress to expand the size of the sample. Second, several postmenopausal women could not recall their age at menopause, which reduced the sample size and illustrates the limitation of retrospective studies. This study is limited by a reliance on memory for information about past reproductive patterns. Relatively close birth spacing, high fertility rates, and infant/childhood mortality can make it difficult for participants to accurately recall information such as offspring age and lactation patterns. These are common problems in human biology research that this study attempted to control by corroborating information with relatives. Third, diet and physical activity were not addressed in this study, although the influences of these factors on skeletal health are well documented (e.g., Adami et al., 2004; Bunker, 1994; Proctor et al., 2000). Information on diet was collected using food frequency questionnaires but these data were not considered in this study. This decision was made because the dietary variability in the sample Shuar villages was minimal (consisting primarily of yucca, plantains, and sometimes chicken). Additionally, we were not confident in the accuracy of food frequency data for quantifying nutritional variables that may contribute to skeletal integrity (e.g., calcium and protein). Further, because of high solar radiation near the equator, deficiencies in vitamin D, an essential nutrient for the intestinal absorption of calcium, are rarely found in these populations (e.g., da Rocha and Ribiero, 2003). Other lifestyle factors, including caffeine intake, cigarette smoking, and alcohol use, may also affect skeletal health yet such habits are rarely adopted among Shuar women in these rural communities. Physical activity data for all participants was not available, although data on a subset of rural Shuar women indicate that activity patterns among Shuar females do not vary significantly across reproductive states (Madimenos et al., 2011b). Instead, men with pregnant and lactating partners appear to increase their participation in subsistence work to compensate for the elevated energy needs of their wives. This suggests that there is less variability in physical activity levels among Shuar females who are pregnant and lactating than in sedentary, Westernized populations and, thus, controlling for this variable may not be as significant as for other groups. However, future research will include a measure of physical activity to determine how it relates to skeletal health. Finally, this study was cross-sectional which,

although useful for obtaining a larger participant sample, provides only a snapshot of bone health. This approach also impairs the ability to establish causality and to discern long-term changes in BMD.

### Summary

This study examined the relationship between female reproductive variables and skeletal health in the subsistence-based Shuar population. This research demonstrated that early menarche and greater stature are associated with higher bone density among postmenopausal Shuar women. This result highlights the importance of early life history events and conditions for establishing and maintaining phenotypic quality throughout the life course. This finding adds to the growing literature on the developmental origins of health and disease, which to date has documented an important role of developmental environment on chronic diseases such as cardiovascular disease, type 2 diabetes, and several cancers (Barker, 1995a,b; Gluckman and Hanson, 2004). Further, results suggest that the effects of lactation on skeletal health are transient during premenopausal years, and are typically restored during weaning. The fertility patterns of Shuar women are markedly different than those of Western females, from whom most of our current understanding of the relationship between reproduction and skeletal health are based. This study represents one of the few to investigate reproductive effects on patterns of bone loss in a non-Western population. In fact, to our knowledge these are among the only published data available on bone density for a subsistence-based, natural fertility population. Additional data from the Shuar are necessary to examine the trade-offs in this relationship in greater detail, and more cross-cultural studies approaching skeletal health using a life history perspective are needed.

### ACKNOWLEDGMENTS

The authors express gratitude to Ruby Fried, Michael Fernandez, Betsy Ruth, Paula Tallman, Cesar Kayap, Oswaldo Mankash, Luzmila Jempekat, Estela Jempekat, and Marilu Utitaj for their assistance with data collection. Finally, they wish to express our gratitude to the participants in this study.

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