Osteoporos Int (1998) 8:282–290

Osteoporosis International

Original Article

A Prospective Study of Bone Loss in Menopausal Australian-Born Women

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Abstract. Two hundred and twenty-four women (74 pre-, 90 peri-, 60 post-menopausal), aged 46–59 years, from a population-based cohort participated in a longitudinal study of bone mineral density (BMD). BMD was measured by dual-energy X-ray absorptiometry (DXA) at the lumbar spine and femoral neck and the time between bone scans was on average 25 (range 14–41) months. The aim of the study was to assess changes in BMD in relation to changes in normal menopausal status. During the study period women who were between 3 and 12 months past their last menstrual period (n = 22, late perimenopausal) at the time of the second bone scan had a mean (SE) annual change in BMD of -0.9% (0.4%) at the lumbar spine and -0.7% (0.6%) at the femoral neck (both $p<0.05$ compared with women who remained premenopausal). In the women who became postmenopausal (n = 42) the mean annual changes in BMD were -2.5% (0.2%) at the lumbar spine and -1.7% (0.2%) at the femoral neck (both $p<0.0005$), and in the women who remained postmenopausal (n = 60) they were -0.7% (0.2%) per year and -0.5% (0.3%) per year respectively (both $p<0.05$), compared with women who remained premenopausal. In the 1–3 years after the final menstrual period (FMP) there was greater bone loss from the lumbar spine than the femoral neck ($p<0.05$). In women who were menstruating at the time of the second bone scan and whose FMP could be dated prospectively (n = 35), higher baseline oestradiol levels were associated with less lumbar spine bone loss ($p<0.005$). In the women who remained postmenopausal there was an association between baseline body mass index (BMI) and percentage change per year in femoral neck BMD ($p<0.05$), such that women with higher BMI had less bone loss. In conclusion, during the time of transition from peri- to post-menopause, women had accelerated BMD loss at both the hip and spine.

Keywords: Bone density; Bone loss; Hip; Menopause; Perimenopause; Spine

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Introduction

Although low bone mineral density (BMD) attributed to oestrogen deficiency is an important determinant of postmenopausal osteoporotic fractures [1], relatively few prospective studies have followed a population-based sample of women through the menopausal transition to examine the effect of this transition on BMD, and none has been reported of an Australian-born population. Vertebral bone loss has been reported to accelerate in some perimenopausal women [2–6], but results are contradictory about the existence of accelerated loss at the hip, probably because the precise methods for measurement of hip BMD have only recently been introduced. Variations in the definition of the perimenopause may also be a reason for inconsistencies across studies in BMD changes during this period of life [7,8].

In a cross-sectional study of a subset of this cohort we were unable to show any association between BMD and calcium intake or physical activity [9]. However, as there is uncertainty about the relation of dietary calcium intake [10,11] and physical activity [12] to rates of change in bone in the axial and appendicular skeleton, particularly around the time of the menopause, it was important to monitor these and other lifestyle variables to see whether they make a contribution to variation in bone loss of the time of the menopausal transition.

In this paper we report the rates of bone loss in 224 women aged 46–59 years who had two bone density scans separated by a period of approximately 2 years. The rate of BMD loss at the lumbar spine (LS) and femoral neck (FN) was examined according to six menopausal transition categories: *remaining* (i) premenopausal, i.e. continuing to have regular menstrual cycles; (ii) early perimenopausal, i.e. continuing to report changes in frequency of menses, or (iii) postmenopausal, i.e. continuing to have no menstrual cycles; or *becoming* (iv) early perimenopausal, i.e. reporting change from regular to irregular menstrual cycles, (v) late perimenopausal, i.e. reporting amenorrhoea of at least 3 but less than 12 months, or (vi) postmenopausal, i.e. reporting amenorrhoea for 12 consecutive months with no identifiable cause.

Bone densitometry undertaken in the Melbourne Women's Midlife Health Project was approved by the Human Ethics Committees of the University of Melbourne and the Royal Melbourne Hospital.

Subjects and Methods

Study Population

The subjects of this report were identified from a cross-sectional survey of a randomly selected population sample of 2001 Melbourne women [13] who were Australian-born and aged 45–55 years at the time of the first interview in May 1991. Women who were prepared to be contacted again, had menstruated in the last 3 months, and were not taking hormone therapy (n = 779) were invited to take part in a longitudinal study on women's health during mid-life; 438 (56%) accepted. All the 438 participants in the longitudinal cohort were eligible for the BMD study, and an additional, randomly selected 46 naturally postmenopausal women from the original cohort of 2001 were included. Of these, 333 women (68%) participated in the cross-section BMD study. The main reason given by the women who refused to attend the bone denistometry unit was 'lack of time'. The mean age at baseline was 51.5 (range 46–59) years.

Menopausal status was determined by menstrual history reported at the time of the BMD measurement, and date of final menstrual period (FMP) was verified with the aid of prospectively kept menstrual diaries [14]. At the time of the first BMD measurements, 112 women were premenopausal (i.e. having regular menstrual cycles), 114 were 'early' perimenopausal (i.e. experiencing changes in frequency of their menses), 20 were 'late' perimenopausal (i.e. amenorrhoea of at least 3 but less than 12 months) and 87 were naturally postmenopausal (amenorrhoea for 12 consecutive months with no identifiable cause) with mean (SE) time since final menstrual period of 3.5 (0.3) years.

A total of 274 women (82%) returned for a second bone scan an average of 25 (range 14–41) months later. The average time between scans was 23 (range 14–37) months for the pre- and perimenopausal women and 30 (range 15–41) months for the postmenopausal group. At the time of the second bone density scan 40 women were taking hormone therapy and 4 had undergone a surgical menopause. These 44 women were excluded from the longitudinal bone study. A further 6 women were also excluded: 3 due to bone densitometer failure and 3 because of osteoarthritis causing over estimation of BMD. Therefore 224 women were included in this longitudinal bone study.

Bone Density, Physical, Lifestyle and Hormone Measurements

BMD of the lumbar spine (second to fourth lumbar vertebrae) and the femoral neck were measured by dual-energy X-ray absorptiometry (DXA) using a Hologic QDR-1000 W densitometer in the Bone Densitometry Unit, Department of Medicine, the Royal Melbourne Hospital. The within-subject coefficient of variation was 1% at the lumbar spine and 1.7% at the femoral neck [15]. The long-term in vitro precision was 0.37% for the lumbar spine and 0.47% for the proximal femur using Hologic anthropomorphic phantoms.

For each subject the following were recorded at the time of each BMD measurement: body height, measured to the nearest 0.1 cm with subjects in the erect position without shoes; body weight, measured to the nearest 0.1 kg with subjects wearing indoor clothes but no shoes; body mass index (BMI), calculated as weight/height^2 (kg/m^2); waist circumference, measured at the narrowest part of the trunk; hip circumference, measured at the widest circumference over the great trochanters; age; self-reported changes in menstrual frequency in the past 12 months; and time since the last menstrual period. At baseline a self-administered short food frequency questionnaire [9] was used to estimate calcium intake and a physical activity questionnaire [16] measured the total physical activity of participants during the previous 12 months. The short food frequency questionnaire accounts for 60% of the total calcium intake in Australian women [17]. The same questionnaires were repeated at the time of the second bone scan. Current and past smoking habits were obtained at the initial baseline survey.

Blood was taken during the follicular phase (between days 4 and 8 of the cycle) if the women were having regular menses, and for irregularly cycling women the number of days since their last menstrual period were recorded at the time of venipuncture. In the pre- and perimenopausal women blood samples were taken a mean (SD) of 2.5 (0.1) months from the time of their BMD measurements. Blood samples were taken from the postmenopausal women at the time of their BMD measurements. FSH and oestradiol levels were measured as previously described [9,18].

Statistical Analysis

Participants and non-participants were compared using chi-square and Student's *t*-tests. The change in BMD was divided by the time between measurements and expressed as an annual rate in terms of grams per centimetre per year and as a percentage of the baseline value per year. These two expressions were highly correlated ($r = 0.99$) and we have used percentage change per year (% change/yr) for simplicity. Weighting in analyses to compensate for the differences in follow-up lengths among subjects did not affect the results and is not reported. Rates of loss in the menopausal transition groups were tested against zero using Student's *t*-test. Statistical comparisons between menopausal and menopausal transition groups were made using analysis of variance. Multiple linear regression was used to assess the effect of the independent variables (lifestyle, hormonal, gynaecological and anthropomorphic factors) on the rate of bone loss, by estimating regression coefficients, β. Cases were excluded from linear regression analyses if the standardized residual was greater than an absolute value of 3. Years since FMP and hormone levels were log transformed and physical activity measures were square root transformed for all analyses. Unless otherwise noted, a nominal level of significance of $p < 0.05$ was used and all statistical tests were two-tailed. The Lowess curve was used to fit a line to the scatterplot of percentage change data and time to/since FMP; this curve uses a locally weighted regression smoothing using an iterative weighted least-squares method [19]. SPSS [19] software was used for all analyses.

Results

Subjects

There were small differences between participants in the longitudinal bone density study and eligible non-participants in that participants were more likely: to be in paid employment (full- or part-time) (75% vs 61%, $p < 0.0005$), to have more than 12 years of education (37% vs 24%, $p < 0.0001$), to exercise at least once per week (70% vs 62%, $p < 0.05$) and to have children living at home (82% vs 72%, $p < 0.005$). Participants were less likely to be current smokers (15% vs 24%, $p < 0.05$). Thiazide diuretics were taken at some stage by 5 (2%) of the women in the longitudinal bone study.

The baseline age, BMI and lifestyle variables of the 224 women who participated in the longitudinal bone study are shown in Table 1. Early and late perimenopausal and postmenopausal women were on average 1.4 years, 3.9 years and 4.6 years older ($p < 0.0005$), respectively, than premenopausal women. There was no difference in BMI or any lifestyle variable between menopausal groups.

Baseline Bone Density, Hormone Levels and Gynaecological Characteristics

Table 2 shows the baseline BMD and hormonal levels and gynaecological characteristics by menopausal status. Using the premenopausal group as the reference category, the postmenopausal group had lower mean BMD at the lumbar spine (by 11.5%) and femoral neck (by 9.3%; both $p < 0.0005$). Compared with the premenopausal women, FSH levels were higher in the early peri-, late peri- and postmenopausal women (all $p < 0.0005$) and oestradiol levels were lower in the late peri- ($p < 0.05$) and postmenopausal women ($p < 0.0005$). The perimenopausal women had fewer

Table 1. Mean (SE) of baseline characteristics by menopausal status

Variable	Premenopausal (*n*=74)	Perimenopausal		Postmenopausal (*n*=60)
		'Early' (*n*=78)	'Late' (*n*=12)	
Age (years)	49.3 (0.2)	50.7 (0.3)***	53.2 (0.7)***	53.9 (0.3)***
BMI (kg/m^2)[a]	25.3 (0.5)	24.9 (0.6)	25.4 (1.4)	26.5 (0.6)
Physical activity (h/week)	7.1 (0.9)	5.4 (0.6)	7.8 (1.9)	6.6 (0.8)
Calcium intake (mg/day) by SFF[b]	515 (43)	573 (53)	656 (97)	552 (60)
Caffeine intake (mg/day)	380 (26)	313 (25)	296 (54)	395 (36)
Current smokers (%)	14%	14%	25%	15%
Years smoked	22 (2)	22 (2)	34 (2)	22 (3)
Pack-years	24 (4)	20 (3)	17 (6)	19 (3)
Alcohol users (%)	66%	68%	58%	42%
Alcohol consumption by users (units/week)	7 (1)	7 (1)	7 (2)	6 (1)

***$P < 0.0005$ compared with the premenopausal group.
[a]Body mass index (weight/height^2).
[b]Calcium intake assessed by short food frequency questionnaire (SFF) accounts for on average 60% of total calcium intake in Australian women.

Table 2. Baseline mean (SE) bone mineral density measurements, geometric mean (95% confidence interval) for FSH and oestradiol levels, and mean (SE) of gynaecological variables, by menopausal status

Variable	Premenopausal (*n*=74)	Perimenopausal		Postmenopausal (*n*=60)
		'Early' (*n*=78)	'Late' (*n*=12)	
Lumbar spine BMD (g/cm^2)	1.104 (0.015)	1.110 (0.015)	1.124 (0.035)	0.980 (0.018)***
Femoral neck BMD (g/cm^2)	0.840 (0.012)	0.829 (0.014)	0.812 (0.028)	0.772 (0.011)***
FSH (iu/l)	9.6 (7.9–11.8)	19.5*** (15.0–25.2)	60.9*** (36.4–101.9)	80.3*** (69.8–92.3)
Oestradiol (pmol/l)	216.5 (174.2–269.2)	228.1 (180.8–287.8)	87.4* (40.0–191.4)	28.4*** (24.2–33.4)
% OCP past users	77%	75%	83%	81%
OCP (years take by past users)	6.2 (0.8)	6.4 (0.8)	5.9 (1.3)	6.6 (0.9)
Parity	3.1 (0.2)	2.5 (0.2)*	2.0 (0.4)*	2.6 (0.2)
Ever breast-fed (% yes)[a]	88%	86%	80%	90%
Months breast-fed[a]	14 (2)	11 (1)	7 (3)	12 (2)
Age at menarche (years)	13.2 (0.2)	13.1 (0.1)	13.3 (0.3)	13.0 (0.2)
History of short menstrual cycles	4%	12%	18%	10%
History of 6 months or more of amenorrhoea[b]	3%	12%	8%	16%

OCP, oral contraceptive pill.
$^{***}P < 0.0005$, $^{*}p < 0.05$ compared with the premenopausal group.
[a]Ever breast-fed and months breast-fed were computed only among women who reported one or more live births.
[b]Excluding pregnancy and menopausal years.

children than the premenopausal women but there were no differences between the means of the four groups with respect to any of the other variables.

Changes in Bone Density and Menopausal Status

Table 3 shows the change in menopausal status of the cohort over the period of the study. Table 4 shows that the mean (SE) annual percentage change in BMD of the lumbar spine and femoral neck, in the women who became postmenopausal during the study, was different compared with zero (both $p < 0.0005$). The change in lumbar spine BMD (LS-BMD) was greater than that in femoral neck BMD (FN-BMD) in this group ($p < 0.05$). Figure 1 illustrates these annual percentage changes for each of the six menopausal transition groups and shows that changes in the women who became late peri- or postmenopausal, or remained postmenopausal were different from the premenopausal women ($p < 0.05$).

Changes in Bone Density and Baseline BMD and BMI

The lumbar spine and femoral neck changes in BMD were independent of baseline BMD in all menopausal groups, except for FN-BMD in the group that became postmenopausal ($\beta = -0.04$, SE 0.016, $p < 0.05$), such that the larger the initial bone mass the greater the bone loss.

Table 3. Change in menopausal status of the cohort over the period of the study, baseline median age (years) of menopausal transition groups and median time (months) between scans

Menopausal status at second bone scan	*n*	Baseline median age (range)	Baseline menopausal status	*n*	Median time (months) between scans (range)
Remained premenopausal	31	48 (46–52)	Premenopausal	31	19 (14–41)
Pre- to early perimenopausal	36	49 (46–55)	Premenopausal	36	24 (15–34)
Remained early perimenopausal	33	49 (46–55)	Early perimenopausal	33	19 (15–34)
Became late perimenopausal	22	50 (47–55)	Premenopausal	4	29 (18–33)
			Early perimenopausal	18	26 (15–36)
Became postmenopausal	42	53 (47–56)	Premenopausal	3	29 (18–35)
			Early perimenopausal	27	27 (15–37)
			Late perimenopausal	12	27 (22–32)
Remained postmenopausal	60	54 (48–59)	Postmenopausal	60	34 (15–41)

Table 4. Mean (SE) annual percentage changes in lumbar spine bone mineral density (LS-BMD) and femoral neck bone mineral density (FN-BMD), by menopausal transition group

Menopausal transition group	*n*	LS-BMD (% change/year)	*p*[a]	FN-BMD (% change/year)	*p*[a]
Remained premenopausal	31	0.31 (0.34)	0.4	0.72 (0.44)	0.1
Pre- to early perimenopausal	36	−0.13 (0.30)	0.7	0.52 (0.31)	0.1
Remained early perimenopausal	33	−0.20 (0.27)	0.3	0.08 (0.44)	0.9
Became late perimenopausal	22	−0.92 (0.42)	0.07	−0.71 (0.64)	0.3
Became postmenopausal	42	−2.48 (0.24)	<0.0005	−1.74 (0.23)	<0.0005
Remained postmenopausal	60	−0.74 (0.21)	<0.005	−0.50 (0.28)	0.08

[a]*p* value to test rate of change with zero.

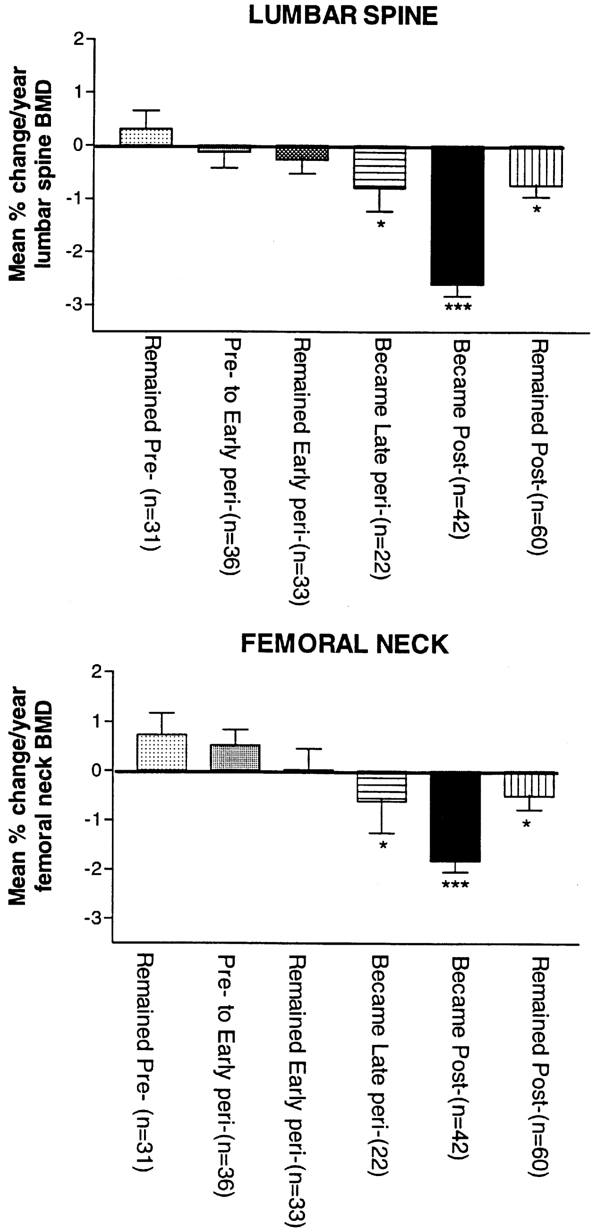

Fig. 1. Mean (*vertical lines* indicate ± SE) annual percentage change in BMD at the lumbar spine and femoral neck for each of the six menopausal transition groups (*n*, number of women in each group). *$p < 0.05$, ***$p < 0.0005$ compared with 'remained premenopausal' women.

All changes in BMD were independent of baseline BMI, with the exception of the women who remained postmenopausal: LS-BMD ($\beta = 0.08$, SE 0.04, $p = 0.07$), FN-BMD ($\beta = 0.13$, SE 0.06, $p < 0.05$). That is, postmenopausal women with larger baseline BMI had less bone loss. The differences in the annual percentage change in BMD between menopausal transition groups reported in Table 4 remained significant with minimal difference in the rates of change estimates, after adjustment for baseline BMD and BMI.

In the women who became postmenopausal, the percentage change per year in FN-BMD was associated with weight change per year ($\beta = 0.26$, SE 0.10, $p < 0.05$) and with waist circumference change per year ($\beta = 0.33$, SE 0.13, $p < 0.05$) after adjusting for baseline FN-BMD, such that women who gained weight or who increased their waist circumference had less bone loss. Change in LS-BMD was independent of changes in weight or waist circumference.

Changes in Bone Density and Time since Last Menstrual Period

The 22 women who were late perimenopausal at the time of their second bone scan were on average 6 (range 3–11) months past their last menopausal period. Prospective data subsequently showed that 6 of these women went on to experience at least one more menstrual period. The 42 women who had become postmenopausal prior to the time of their second bone density scan were on average 2.2 (range 1.0–3.4) years past their FMP. The 60 women who remained postmenopausal during the study were on average 6.0 (range 2.6–17.1) years past their FMP at the time of the second bone scan.

The greatest mean percentage loss, at both the lumbar spine and femoral neck, occurred in the women who at the time of their second bone scan were between 2 and 3 years past their FMP. At the lumbar spine, bone loss was lower in women who were less than 1 year or more than 3 years past their FMP compared with women who were 2–3 years past their FMP ($p < 0.005$). At the femoral neck, bone loss was lower in women who were more than 5 years past their FMP compared with women 2–3 years past their FMP ($p < 0.05$).

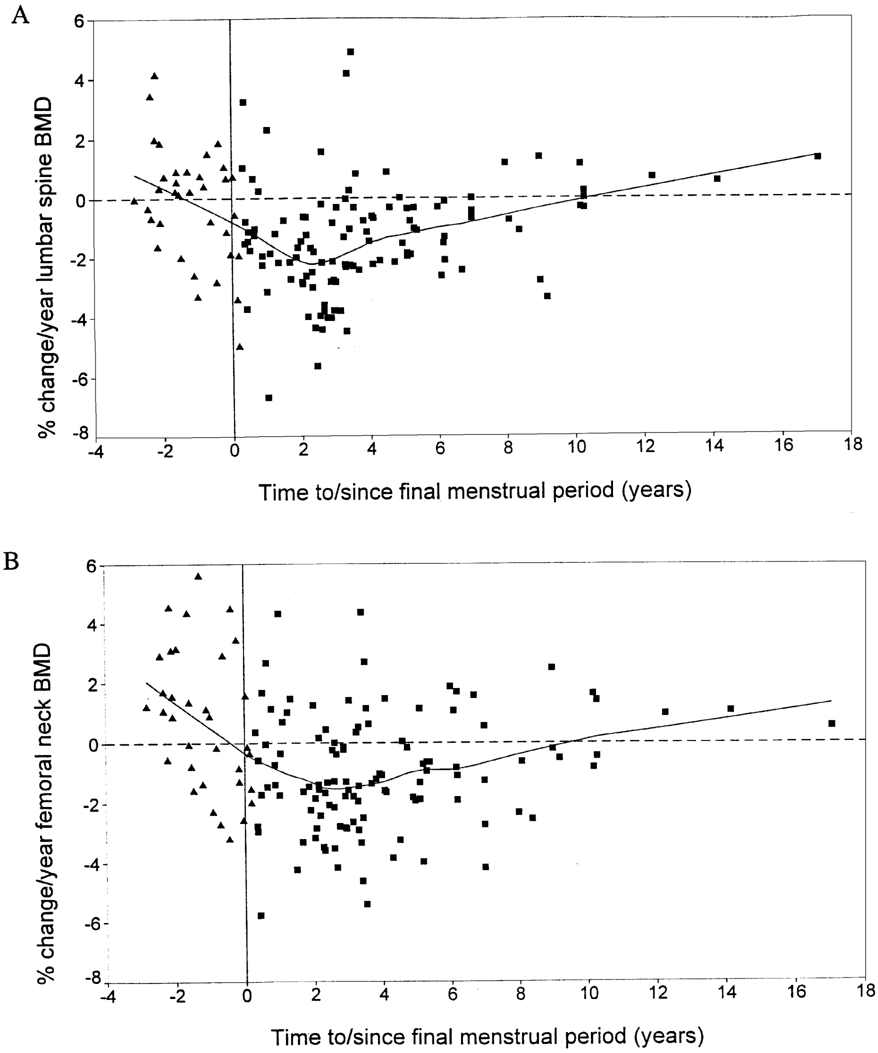

Fig. 2. Individual BMD changes (%/year) measured longitudinally at the lumbar spine (**A**) and femoral neck (**B**), in women whose date of final menstrual period (FMP) was known. On the *x*-axis, 0 is the time of final menstrual period, negative values refer to years before FMP and positive values refer to years after FMP. *Triangles* represent the women who had menstruated in the 3 months prior to their second bone scan and whose FMP was documented prospectively (n = 35). The *line* drawn is a Lowess curve.

Changes in Bone Density and Time to Final Menstrual Period

Figure 2 shows the individual BMD changes (%/year), at the lumbar spine and femoral neck, in women whose date of FMP was known. Thirty-five women, who had menstruated in the 3 months prior to their second bone scan, had their date of menopause (time to FMP) documented prospectively and these women were between -2.8 and +0.2 years to/since their FMP. The mean (SE) change per year in BMD for these women was a loss of -0.16 (0.3)% at the lumbar spine and a gain of 0.96 (0.5)% at the femoral neck ($p<0.05$ compared with zero). There was an association between the percentage change per year in LS-BMD of these 35 women and baseline oestradiol levels (β = 1.06, SE 0.29, $p<$;0.005), such that women who had higher oestradiol levels at baseline had less bone loss. Baseline FSH levels were also associated with percentage change per year in LS-BMD and FN-BMD (β = -0.96, SE 0.38, $p<0.05$ for LS; β = -1.10, SE 0.52, $p<0.05$ for FN), higher FSH levels being associated with more bone loss. No other physical or lifestyle variables were associated with bone changes in these 35 women.

Figure 2 also illustrates the variation in BMD changes that occur as women pass through the menopause transition. As there were limited numbers of women who were more than 10 years since menopause the smoothed curve is weighted by only a few points at the far right of the graph.

Changes in Bone Density and Lifestyle Variables

There was no association between BMD loss and calcium intake or change in calcium intake. Calcium intake increased during the study period, the mean (SE) intake at baseline being 522 (20) mg/day compared with 690 (31) mg/day at follow-up ($p<0.0005$). There was no association between annual change in BMD and physical activity at baseline or during the study period. In the women who became postmenopausal during the study 6 were current smokers and their means (SE) annual change in LS-BMD was -3.3% (0.5%) compared with the 36 non-smokers whose LS-BMD loss was −2.3% (0.3%)/year ($p=0.1$).

Discussion

In this sample, which was drawn from a population-based cohort of Australian-born women, those who remained pre- or early perimenopausal had little or no bone loss at the hip or spine. However, those women who became postmenopausal between BMD measurements, i.e. 1 year without menses, had more bone loss at the hip and spine than women who had already experienced the menopause with their FMP an average of 3.5 years earlier. In those women who had experienced more than 3 months but less than 12 months of amenorrhoea (late perimenopausal group), the rate of bone loss at the hip and spine was also greater than that of the women who had remained premenopausal, and was similar to the loss in women who had remained postmenopausal.

For LS-BMD, the mean annual rate of change of −2.5% (95% confidence interval, CI, from −2.0% to −3.0%) in those women who became postmenopausal is similar to that of −2.3% (95% CI from −1.9% to −2.8%) reported by Pouilles et al. [6] for a similar menopausal status group. We found no evidence of bone loss at the lumbar spine in those women who remained early perimenopausal during the study period, but evidence of bone loss in those women who were late perimenopausal at the time of their second BMD scans. These results are in agreement with some previous studies [6,20], but others have shown pre- and perimenopausal loss at the lumbar spine in longitudinal studies [21,22]. These reported differences in bone loss may be accounted for by differences in the methods, such as definitions used to characterize the perimenopause, or differences in variables such as hormone levels [23,24], calcium intake [25] or physical activity levels [26].

For the femoral neck, we found evidence of no bone loss in those women who remained pre- or early perimenopausal. In women who became postmenopausal, the mean annual rate of bone loss was −1.7% (95% CI from −1.3% to −2.2%). No other studies appear to have reported change in FN-BMD across the menopausal transition. However, this rate of bone loss is similar to the rates of early postmenopausal loss reported by Stevenson et al. [27] (−1.5%/year, CI not reported) and Pouilles et al. [28] (−1.8%/year, 95% CI from −1.5%/year to −2.2%/year). We also found evidence of bone loss in the femoral neck in the late perimenopausal women.

The timing of bone loss at the spine and femoral neck were similar, although the rate of loss was greater at the lumbar spine in those women who became postmenopausal (−2.48% compared with −1.74%, $p<0.05$; see Table 4). At both sites the rate of bone loss increased for the first 3 years post-menopause and then slowed with increasing years since menopause, in agreement with other studies [27,28]. Due to the age of the population sample we have limited numbers of women who were more than 10 years since menopause and the graphs shown in Fig. 2 are weighted by few data points.

The months before and after the final menstrual period are characterized by significant ovarian and gonadotrophin hormonal variability and change [18,29–31]. In one longitudinal study, a marked decrease in oestradiol levels occurred during the 6-month period around the menopause [31]. In the present study, women who were still menstruating at the time of their second bone scan, but in whom the final menstrual period could be dated prospectively, showed a significant association between rate of BMD change at the spine and baseline oestradiol levels as well as rate of BMD change at the spine and hip and baseline FSH levels. Thus, time prior to the final menstrual period, when the hormonal milieu is unstable [32], accounts for variability in bone changes among perimenopausal women. Slemenda et al. [33] also found that oestrogen concentrations were lower in perimenopausal women losing radial bone mass at a greater rate, but they did not find oestradiol to predict bone loss at the spine or hip. They did not prospectively date the final menstrual period.

We did not detect any influence of calcium intake or physical activity on variation in bone changes either across the menopausal transition or postmenopausally, as has been found in other studies [34,35]. In postmenopausal women high BMI was protective against bone loss, as has been shown in other studies [36]. This protective effect of excess weight may be explained by a combination of hormonal and mechanical factors [37]. In our women, however, there was no effect of weight on bone loss from the lumbar spine in the late peri- to early postmenopausal period. Increasing waist circumference, which was associated with an increase in weight, was protective against bone loss from the femoral neck. The over-riding effect of hormonal changes on rates of bone loss, particularly in the early postmenopause, may mask any effects that anthropomorphic or lifestyle variables may have on changes in bone mass.

Some limitations of our study include, firstly, the problem with self-reported calcium intake and physical activity, secondly, the fact that the ranges or levels of calcium intake and physical activity in the cohort may not be sufficient to detect associations, and, thirdly, that the cohort is biased in that the women studied were more likely to be regularly exercising than those who were not measured for bone density. Further, the physical activity profile of the cohort was not at the level of resistance training that has been shown in intervention studies to improve bone mass to postmenopausal women [38,39]. In addition calcium intake levels of the cohort were not as high as those in the calcium intervention trial of Reid et al. [40]. There is evidence for a link between smoking and BMD in both cross-sectional and longitudinal studies [41,42]. The small number of smokers in this cohort limits our ability to show a smoking effect. This study was also limited by the uptake of hormone therapy; 15% of the cohort who returned for their second bone scan were using hormone therapy, which reduced the numbers available for analysis of bone changes during the normal menopause transition.

In conclusion, these data show accelerated bone loss at both the lumbar spine and femoral neck in the months after the final menstrual period. Our data support the benefit of active intervention being initiated in the late perimenopausal period or as early as possible after the final menstrual period in women identified as having low bone mass at that time.

Acknowledgements. This study was supported by grants from the Australian Dairy Corporation, the Victorian Health Promotion Foundation, the Public Health Research and Development Committee, the Australian National Health and Medical Research Council, the Percy Baxter Trust, the H. & L. Hecht Trust, the Estate of the late Daniel Scott, the Ian Potter Foundation, the Smorgon Family Trust, the Leigh and Majorie Bronwen Murray Charitable Trust and the Helen M. Schutt Trust. The research team would like to thank Corry Garamszegi, Liz River and the field workers in the Melbourne Women's Midlife Health Project for their help, Bahtiyar Kaymakci and Sue Kantor from the Bone Densitometry Unit at the The Royal Melbourne Hospital, and Nick Balazs and the staff of the Department of Chemical Pathology at the Monash Medical Centre. The Prince Henry's Institute of Medical Research received a grant in aid from Organon (Aust) Pty Ltd. towards the cost of hormone assays. The research team would also like to thank all the women who participated in this study.

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Received for publication 23 June 1997
Accepted in revised form 5 November 1997