# Cigarette Smoking and Bone Mineral Density in Older Men and Women


## ABSTRACT

*Objectives.* The association between cigarette smoking and bone mineral density was examined prospectively in a population-based study of older Caucasian men and women.

*Methods.* Smoking patterns were determined at a 1972–1974 baseline evaluation and, again, 16 years later when 544 men and 822 women had bone mineral density measurements taken.

*Results.* Men and women who were cigarette smokers at baseline demonstrated significantly reduced bone mineral density of the hip compared with nonsmokers. Baseline smoking was not associated with significantly lower bone density at nonhip sites. Women demonstrated a significant dose–response relationship between baseline smoking status at all hip sites measured. Both sexes exhibited significant dose–response relationships between hip bone mineral density and change in smoking status between baseline and follow-up, demonstrating that smoking cessation in later life was beneficial in halting bone density loss associated with smoking.

*Conclusions.* Smoking was positively and significantly associated with decreased hip bone mineral density in old age. Bone loss associated with smoking would be expected to predict an increased risk of hip fracture in those who do not succumb earlier to another complication of tobacco use. (*Am J Public Health.* 1993;83:1265–1270)



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## Introduction

Studies investigating the association between cigarette smoking and osteoporosis have reported conflicting results.[1–14] Potential reasons for these differences include variations in bone sites examined and methods of bone density measurement, end points of interest, age and menopausal status of subjects, source of subjects, and adjustment for confounding variables. In addition, most studies of bone density have been conducted only in women, and most have not examined the hip, the site of most serious fractures in the elderly. Depending on the mechanism of bone loss associated with smoking, the effects in men could be equally deleterious.

Since smoking might influence fracture risk through several mechanisms unrelated to osteoporosis, studies of bone density theoretically provide a less confounded measure of the effect of cigarette smoking on osteoporosis. Using a population-based cohort of older men and women, we describe the association between cigarette smoking reported between 1972 and 1974 and again between 1988 and 1991 with bone mineral density measured at four sites during a clinic visit scheduled between 1988 and 1991. Examination of bone mineral density by smoking status collected at these two points in time provides insight into the influence of smoking cessation on bone mineral density later in life.

## Methods

Subjects were participants in the Rancho Bernardo Heart and Chronic Disease Study (described elsewhere).[15] Briefly, 82% of upper-middle-class Caucasian adults living in Rancho Bernardo, Calif, participated in a population-based heart disease risk factor screening survey between 1972 and 1974. Information about demographic variables, medical history, medication use, and past and current cigarette smoking behavior was obtained by standardized interview. Height and weight were measured with subjects in light clothing without shoes, and body mass index (kg/m$^2$) was calculated.

Over 99% of this cohort has been followed for vital status to the present time. Beginning in February 1988, all surviving ambulatory subjects 60 years of age or older were invited to participate in a follow-up study of osteoporosis. Subjects seen through April 1991 form the basis of this report. Dual energy x-ray absorptiometry (Hologic QDR model 1000, Waltham, Mass) was used to measure bone mineral density at the spine (lumbar 1 through lumbar 4) and hip (femoral neck, greater trochanter, intertrochanter), and single photon absorptiometry (Lunar model SP2B, Madison, Wis) was used to measure bone mineral density at the midshaft of the radius and the ultradistal radius of the nondominant arm. Cigarette smoking behavior, alcohol use, and exercise were assessed by standardized self-administered questionnaires and reviewed by clinic staff. Body mass index was calculated in the same manner as at baseline.

The Statistical Analysis System[16] was used in data analysis. Sex-specific


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**TABLE 1—Characteristics of the Study Cohort, by Sex and Baseline Smoking Status, Rancho Bernardo, Calif, 1972 through 1991**

| | Men | | | | Women | | | |
|---|---|---|---|---|---|---|---|---|
| | Smokers (n = 87) | | Nonsmokers (n = 417) | | Smokers (n = 181) | | Nonsmokers (n = 573) | |
| | No. | % | No. | % | No. | % | No. | % |
| Age, y[a] | | | | | | | | |
| 60–69 | 30 | 34.5 | 99 | 23.7 | 71 | 39.2 | 130 | 22.7 |
| 70–79 | 35 | 40.2 | 137 | 32.9 | 75 | 41.4 | 234 | 40.8 |
| 80–89 | 22 | 25.3 | 169 | 40.5 | 35 | 19.3 | 198 | 34.6 |
| 90–99 | 0 | ... | 12 | 2.9 | 0 | ... | 11 | 1.9 |
| Alcohol use[a] | | | | | | | | |
| None | 11 | 12.6 | 79 | 18.9 | 24 | 13.3 | 169 | 29.5 |
| 1–3 d/wk | 22 | 25.3 | 118 | 28.1 | 53 | 29.4 | 217 | 37.9 |
| 4+ d/wk | 54 | 62.1 | 221 | 25.3 | 103 | 57.2 | 187 | 32.6 |
| Estrogen use[b] | ... | ... | ... | ... | 95 | 52.5 | 268 | 46.8 |
| Antihypertensive use[b] | 6 | 6.9 | 42 | 10.1 | 20 | 11.1 | 61 | 10.7 |
| Exercise[a] | 58 | 66.7 | 321 | 77.0 | 104 | 57.5 | 392 | 68.5 |
| Body mass index,[b] mean (SD) | 25.6 (3.2) | | 25.8 (2.8) | | 22.9 (3.3) | | 23.6 (3.0) | |

*Note.* One female smoker had missing alcohol use information, and one female nonsmoker had missing exercise information.
[a]Osteoporosis follow-up.
[b]Baseline.

**TABLE 2—Mean Bone Mineral Density Measurements, by Site and Baseline Smoking Status, Rancho Bernardo, Calif, 1972 through 1991**

| | Smokers,[a] Mean ± SE | Nonsmokers,[b] Mean ± SE |
|---|---|---|
| Men | | |
| Total spine (n = 496) | 1.055 ± 0.022 | 1.070 ± 0.010 |
| Ultradistal radius (n = 490) | 0.320 ± 0.011 | 0.333 ± 0.005 |
| Midradius (n = 486) | 0.748 ± 0.011 | 0.754 ± 0.005 |
| Total hip (n = 491) | 0.895 ± 0.016 | 0.935 ± 0.008* |
| Femoral neck (n = 494) | 0.708 ± 0.014 | 0.740 ± 0.006* |
| Trochanter (n = 494) | 0.669 ± 0.014 | 0.696 ± 0.007 |
| Intertrochanter (n = 491) | 1.039 ± 0.019 | 1.087 ± 0.009* |
| Women | | |
| Total spine (n = 743) | 0.882 ± 0.013 | 0.885 ± 0.007 |
| Ultradistal radius (n = 711) | 0.232 ± 0.006 | 0.229 ± 0.003 |
| Midradius (n = 719) | 0.567 ± 0.007 | 0.582 ± 0.004 |
| Total hip (n = 732) | 0.741 ± 0.010 | 0.780 ± 0.005** |
| Femoral neck (n = 733) | 0.608 ± 0.008 | 0.632 ± 0.005** |
| Trochanter (n = 733) | 0.531 ± 0.008 | 0.564 ± 0.004** |
| Intertrochanter (n = 732) | 0.864 ± 0.011 | 0.910 ± 0.004** |

*Note.* Measurements were adjusted for follow-up age, alcohol use, and exercise and baseline body mass index, antihypertensive use, and estrogen use (in women).
[a]For men, n = 87; for women, n = 181.
[b]For men, n = 417; for women, n = 573.
*$P < .05$ (differences between smokers and nonsmokers).
**$P < .01$ (differences between smokers and nonsmokers).

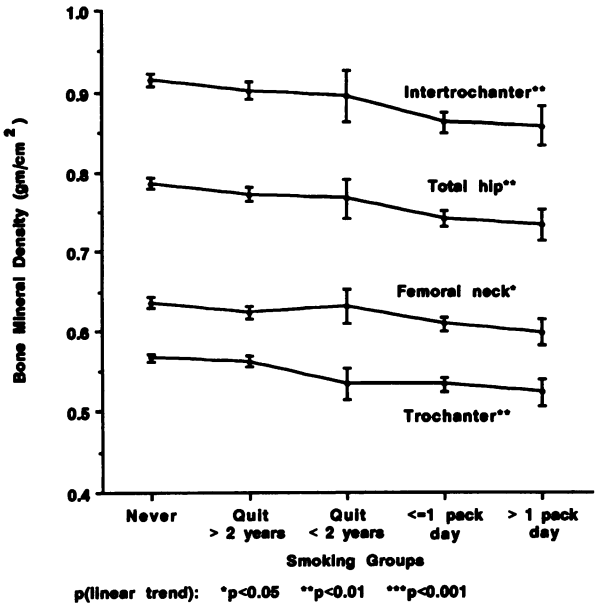
comparisons were made between subjects who, at baseline, reported themselves as current smokers, past smokers, and never smokers. Dose–response relationships were assessed by comparing bone mineral density for never smokers, long-term (more than 2 years) and recent (less than 2 years) quitters, and two levels of current smokers (less than one pack per day and one or more packs per day) as reported at baseline. Sex-specific comparisons were also made between subjects who, at the osteoporosis follow-up study, reported themselves to be never smokers, quitters before baseline, quitters after baseline but prior to the osteoporosis follow-up, and current smokers. Analysis of covariance was used to determine adjusted mean bone mineral density differences between baseline smokers and nonsmokers and across both sets of smoking categories. Potentially confounding variables considered in these analyses included baseline and follow-up measures of body mass index (continuous), baseline estrogen and antihypertensive use (dichotomous), follow-up age (continuous), follow-up exercise (dichotomous: current exercise three or more times per week), follow-up alcohol use (trichotomous: none, light [1 to 3 days per week], moderate–heavy [4 or more days per week]), and age when smoking began. Linear contrasts in the analysis of covariance models were used to test for linear trends in multiply adjusted bone mineral densities across the five smoking categories from baseline and across the four smoking categories from the osteoporosis follow-up. All $P$ values were two-tailed, and statistical significance was defined as $P < .05$. No adjustment was made for multiple comparisons; rather, detailed $P$ values are presented.

## Results

Characteristics of the 1258 ambulatory subjects who were 60 years of age or older when they completed the bone density follow-up study are shown in Table 1. Men and women who reported smoking at baseline were younger and leaner and tended to use more alcohol than those who did not smoke.

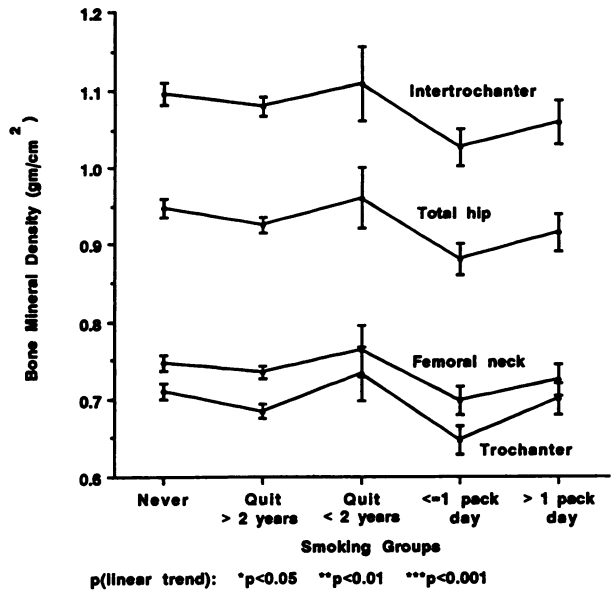
Both men and women who were current smokers at baseline had significantly lower bone density at the hip ($P < .01$) than nonsmokers before and after adjustment for the confounding effects of follow-up age, exercise, and alcohol use and baseline body mass index, antihypertensive use, and estrogen use (in women) (Table 2). When individual hip sites were examined, men and women who were smokers at baseline had significantly lower bone mineral density levels at the femoral neck ($P < .05$) and intertrochanter ($P < .05$). Bone density of the greater trochanter was significantly lower ($P < .05$) in female but not male cigarette smokers. Bone density at the spine, ultradistal radius, and midradius did not differ significantly by smoking status in either men or women.

After adjustment for the above covariates, significant baseline tobacco use dose–response relationships were seen for each individual hip site and for the total hip among women (Figure 1) and at the



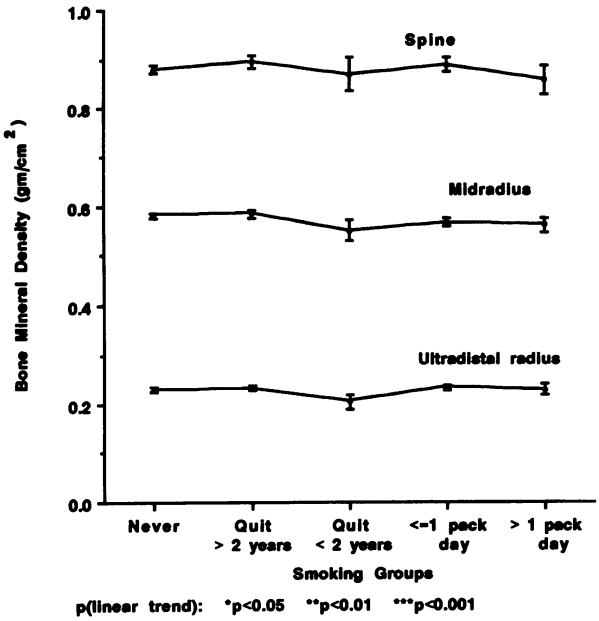

*Note.* Results have been adjusted for baseline body mass index, antihypertensive use, and estrogen use and follow-up age, alcohol use, and exercise.

**FIGURE 1—Mean bone mineral density at individual hip sites for women, by 1972–1974 smoking status.**



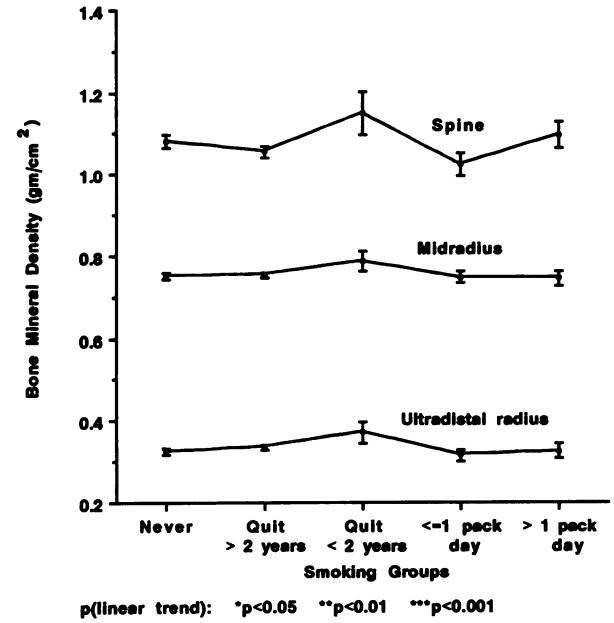

*Note.* Results have been adjusted for baseline body mass index and antihypertensive medication use and follow-up age, alcohol use, and exercise.

**FIGURE 2—Mean bone mineral density at individual hip sites for men, by 1972–1974 smoking status.**




*Note.* Results have been adjusted for baseline body mass index, antihypertensive medication use, and estrogen use and follow-up age, alcohol use, and exercise.

**FIGURE 3—Mean bone mineral density at the spine and radial sites for women, by 1972–1974 smoking status.**

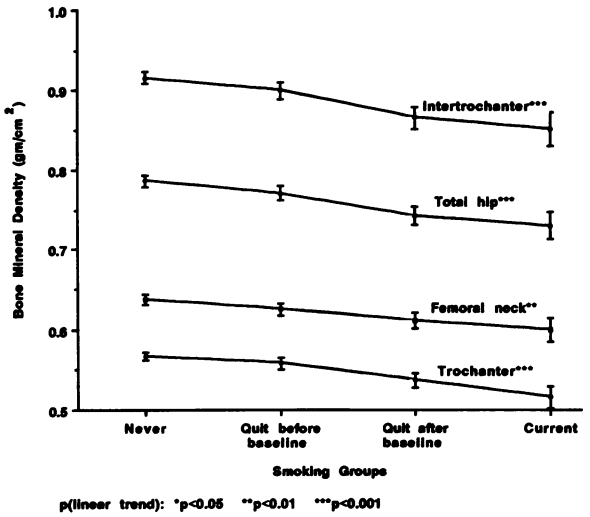



*Note.* Results have been adjusted for baseline body mass index and antihypertensive medication use and follow-up age, alcohol use, and exercise.

**FIGURE 4—Mean bone mineral density at the spine and radial sites for men, by 1972–1974 smoking status.**

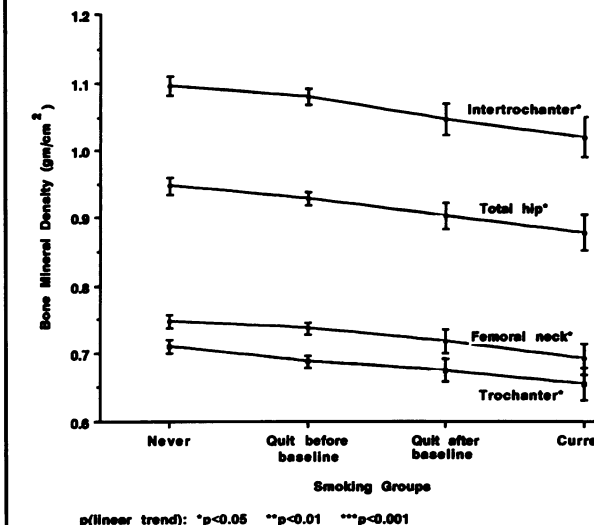
total hip and intertrochanter among men (Figure 2). No such trends were observed among men for the other hip sites (Figure 2) or among either sex at the spine, ultradistal radius, or midradius (Figures 3 and 4).

When we analyzed the data using smoking status as defined at the osteoporosis follow-up, both men and women demonstrated significant multiply adjusted dose–response relationships between smoking and bone mineral density at each of the hip sites examined (Figures 5 and 6). Women also exhibited a significant dose–response relationship at the midradius (Figure 7) and men at the spine



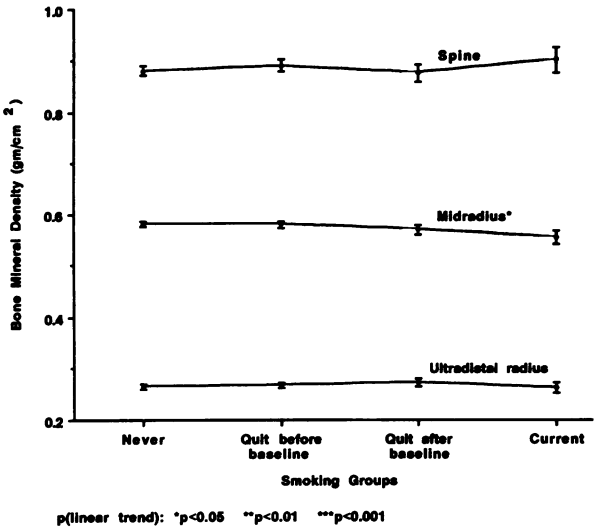

*Note.* Results have been adjusted for baseline body mass index, antihypertensive medication use, and estrogen use and follow-up age, alcohol use, and exercise.

**FIGURE 5—Mean bone mineral density at individual hip sites for women, by 1988–1991 smoking status.**



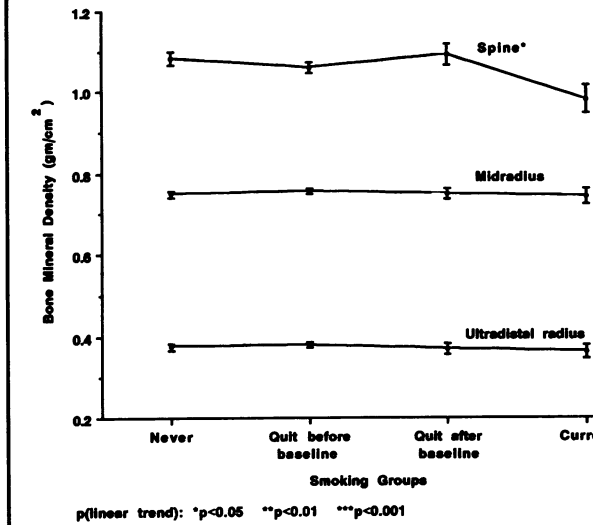

*Note.* Results have been adjusted for baseline body mass index and antihypertensive medication use and follow-up age, alcohol use, and exercise.

**FIGURE 6—Mean bone mineral density at individual hip sites for men, by 1988–1991 smoking status.**




*Note.* Results have been adjusted for baseline body mass index, antihypertensive medication use, and estrogen use and follow-up age, alcohol use, and exercise.

**FIGURE 7—Mean bone mineral density at the spine and radial sites for women, by 1988–1991 smoking status.**




*Note.* Results have been adjusted for baseline body mass index and antihypertensive medication use and follow-up age, alcohol use, and exercise.

**FIGURE 8—Mean bone mineral density at the spine and radial sites for men, by 1988–1991 smoking status.**

(Figure 8). In the subset of men and women who had ever smoked, these relationships were not altered when adjusted for the age when smoking began (data not shown).

## *Discussion*

In this older, population-based cohort followed prospectively, cigarette smoking reported 16 to 18 years earlier significantly predicted lower bone mineral density at the hip in both men and women. This finding was not observed at the other sites examined. In women, a dose–response relationship between number of cigarettes smoked and bone mineral density was observed at all hip sites, supporting a causal association. When smoking status at the osteoporosis follow-up was used for analysis, both men and women exhibited significant dose–response relationships between smoking and bone mineral density at each of the hip sites examined. The significant dose–response relationships seen in men at the spine and in women at the midradius may be due to chance or may be real.

Our findings of significant dose–response relationships at the hip in women parallel those reported by other investigators. La Vecchia et al.[17], in a case-control study, identified a dose–response risk of

hip fracture in women by both number of cigarettes smoked and duration of years smoking. Similarly, Rundgren and Mellstrom[18] found ex-smokers to have bone densities between those of current and never smokers. In a prospective study, also conducted in Southern California, Paganini-Hill et al.[2] identified a nonsignificant dose–response relationship between hip fracture and past smoking in women.

In the present study, cigarette smoking predicted osteopenia at the hip. These results contradict other studies that have shown lower bone density at the calcaneus, forearm, or metacarpal sites in currently smoking men[11,19,20] and in currently smoking women who were at least 8 years postmenopausal.[1,12,13,20] In a study of postmenopausal but not elderly women, Krall and Dawson-Hughes[1] found bone density at the hip, spine, and radius to be inversely related to pack-years, although the rate of loss was statistically significant only at the radius. To date, too few studies of smoking and bone density of the proximal femur have been published to conclude whether the elderly hip is particularly vulnerable to the effects of cigarette smoking. This would be an important finding, given the public health impact of hip fracture in an aging society.

The mechanism whereby cigarette smoking leads to increased hip fracture and osteopenia is unknown. Since cigarette smokers typically are leaner and exercise less than nonsmokers, some protection in nonsmokers could be mediated by greater body mass or bone strength. Only one of three short-term prospective studies of smoking and bone density has found bone loss to be related to cigarette smoking independent of obesity.[1,12,17] The bone density–smoking association observed here was independent of both body mass index and exercise. However, when the analysis of long-term smoking was adjusted for body mass index at follow-up, the difference between bone mineral density in current smokers and recent quitters was minimized, and at some sites negated. This may be due, in part, to weight gain in recent quitters, which may be beneficial in halting the bone loss process associated with smoking. In fact, body mass index at follow-up of both men and women who quit smoking between baseline and follow-up approached or exceeded that of never smokers in our data. Furthermore, smokers may differ from nonsmokers with regard to diet and alcohol use, which are rarely measured with sufficient precision to be entirely excluded as confounders. In contrast, smoking histories have been found to be surprisingly reliable, with excellent agreement between self-reported past smoking and medical record information.[21]

As reviewed elsewhere,[22] many studies have found that women who smoke cigarettes often become postmenopausal 1 to 2 years earlier than women who have never smoked. Postmenopausal estrogen deficiency is an important cause of osteoporosis in women, but estrogen deficiency seems unlikely to explain the parallel decrease in bone density observed in men. In fact, men in this cohort who smoked cigarettes had higher levels of endogenous estrogen than did nonsmokers.[23] Smoking is associated with a variety of other metabolic effects, several of which suggest plausible mechanisms for smoking-related changes in bone density, including altered levels of calcitonin,[4] androstenedione,[23,24] and serum steroid hormones.[25]

Although questions remain about site vulnerability and the mechanism of the cigarette smoking–osteoporosis association, these prospective data demonstrate that cigarette smoking among primarily White, upper-middle-class elderly men and women is associated with reduced bone mineral density at the hip and parallel several studies of hip fracture.[1,8,10,13] They further suggest that smoking cessation, even in later life, may be beneficial in slowing or halting bone loss due to smoking. The mean ages of smoking cessation for women and men who stopped smoking during the 16- to 18-year period between baseline and follow-up were 64.1 (range = 45 to 84) and 62.8 (range = 32 to 81), respectively.

Our findings, as well as those from previously reported studies of bone loss and fracture, demonstrate that men and women who smoke are at increased risk for subsequent bone loss, which may place them at increased risk of fracture later in life. Furthermore, we found that smoking cessation, even in later life, may have a positive effect on limiting bone loss associated with smoking. □

## Acknowledgments

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## References

1. Krall EA, Dawson-Hughes B. Smoking and bone loss among postmenopausal women. *J Bone Miner Res.* 1991;6:331–338.
2. Paganini-Hill A, Chao A, Ross RK, Henderson BE. Exercise and other factors in prevention of hip fracture: the Leisure World study. *Epidemiology.* 1991;2:16–25.
3. Stevenson JC, Lees B, Devenport M, Cust MP, Ganger KF. Determinants of bone mineral density in normal women: risk factors for future osteoporosis? *Br Med J.* 1989;298:924–928.
4. Leino A, Impivaara O, Jarvisalo J, Helenius H. Factors related to risk of osteoporosis in 50 year old women. *Calcif Tissue Int.* 1991;49:S76–S77.
5. Hemenway D, Coldits GA, Willett WC, Stampfer MJ, Speizer FE. Fractures and lifestyle: effect of cigarette smoking, alcohol intake, and relative weight on the risk of hip and forearm fractures in middle-aged women. *Am J Public Health.* 1988;78:1554–1558.
6. Jensen J, Christiansen C, Rodbro P. Cigarette smoking, serum estrogens and bone loss during hormone-replacement therapy early after menopause. *N Engl J Med.* 1985;313:973–975.
7. Paganini-Hill A, Ross RK, Gerkins VR, Henderson BE, Arthur M, Mack TM. Menopausal estrogen therapy and hip fracture. *Ann Intern Med.* 1981;95:28–31.
8. Alderman BW, Weiss NS, Daling JR, et al. Reproductive history and postmenopausal risk of hip and forearm fracture. *Am J Epidemiol.* 1986;124:262–267.
9. Kreiger N, Kelsey JL, Holford TR, O'Connor T. An epidemiologic study of hip fracture in postmenopausal women. *Am J Epidemiol.* 1982;116:141–148.
10. Williams AR, Weiss NS, Ure CL, Ballard J, Daling JR. Effect of weight, smoking and estrogen use on the risk of hip and forearm fractures in postmenopausal women. *Obstet Gynecol.* 1982;60:695–699.
11. Seeman E, Melton LJ III, O'Fallon WM, Riggs BL. Risk factor for spinal osteoporosis in men. *Am J Med.* 1983;75:977–983.
12. Slemenda CW, Hui SL, Longcope C, Johnson CC. Cigarette smoking, obesity and bone mass. *J Bone Miner Res.* 1989;4:737–741.
13. Aloia JF, Cohn SH, Vaswani A, Yeh JK, Yuen K, Ellis K. Risk factors for postmenopausal osteoporosis. *Am J Med.* 1985;78:95–100.
14. Sparrow D, Beausoleil NI, Garvey AJ, Rosner B, Silbert JE. The influence of cigarette smoking and age on bone loss in men. *Arch Environ Health.* 1982;37:246–249.
15. Criqui MH, Barrett-Connor E, Austin M. Differences between respondents and nonrespondents in a population based cardiovascular disease study. *Am J Epidemiol.* 1978;108:367–372.
16. SAS Institute Inc. *SAS Procedures Guide, Version 6, Third Edition.* Cary, NC: SAS Institute Inc; 1990.
17. La Vecchia C, Negri E, Levi F, Baron JA. Cigarette smoking, body mass and other risk factors for fractures of the hip. *Int J Epidemiol.* 1991;20:671–677.
18. Rundgren A, Mellstrom D. The effect of tobacco smoking on the bone mineral content of the ageing skeleton. *Mech Age Dev.* 1984;28:272–277.
19. deVernejoul MC, Bielakoff J, Herve M, et al. Evidence for defective osteoblastic function. A role for alcohol and tobacco

consumption in osteoporosis in middle-aged men. *Clin Orthop.* 1983;179:107–115.
20. Hollo I, Gergely I, Boross M. Influence of heavy smoking upon the bone mineral content of the radius of the aged and effect of tobacco smoke on the sensitivity to calcitonin of rats. *Aktuel Gerontol.* 1979;9:365–368.
21. Horwitz RI, Yu EC. Problems and proposals for interview data in epidemiologic research. *Int J Epidemiol.* 1985;14:463–467.
22. Baron JA. Cigarette smoking and age at natural menopause. In: Wald N, Baron J, eds. *Smoking and Hormone-Related Disorders.* New York, NY: Oxford University Press; 1990:57–63.
23. Barrett-Connor E, Khaw KT. Cigarette smoking and increased endogenous estrogen levels in men. *Am J Epidemiol.* 1987; 126:187–192.
24. Khaw KT, Tazuke S, Barrett-Connor E. Cigarette smoking and levels of adrenal androgens in postmenopausal women. *N Engl J Med.* 1988;318:1705–1709.
25. Friedman AJ, Favnikar VA, Barbieri RL. Serum steroid hormone profiles in postmenopausal smokers and non-smokers. *Fertil Steril.* 1987;47:398–401.

## *Call for Abstracts and Student Papers on Preventive Medicine*

### Call for Abstracts for PREVENTION 94

PREVENTION 94, the eleventh annual national disease prevention and health promotion meeting, will be held in Atlanta, Ga, from March 19 through 22, 1994. The meeting theme "Science, Skills and Strategies" will be the focus of 4 days of general sessions, concurrent sessions, poster sessions, and workshops. As policymakers, health care providers, scientists, and health care consumers strive to develop mechanisms to ensure that all Americans receive appropriate, adequate, and affordable health care, prevention has become a focal point. The preventive medicine community must be prepared to answer questions about the science of prevention, the skills needed to practice prevention, and the strategies required to meet the health needs of populations and individuals. "PREVENTION 94: Science, Skills and Strategies" will provide a forum where participants will learn of the latest scientific developments in the field while addressing the educational, programmatic, and philosophical issues related to disease prevention and health promotion.

Abstracts are sought for presentations at PREVENTION 94 that are directly linked to the meeting theme and conference focus. Abstracts should represent the results of scientific research, technological advances, innovations in program design, practice methods, or educational techniques.

Abstracts must be submitted on an original Abstract Form with one copy. No faxes. Abstracts must be received by *October 1, 1993.* No exceptions. Forms are available from PREVENTION 94 offices; call (202) 789-0006. Mail them to PREVENTION 94, 1015 15th St, NW, Suite 403, Washington, DC 20005.

### Award for Best Student Paper on Preventive Medicine

The American College of Preventive Medicine, the Association of Teachers of Preventive Medicine, the Association of Preventive Medicine Residents, and the Ulrich and Ruth Frank Foundation for International Health announce awards for the best paper on preventive medicine by a medical student. The prize for the best paper is $1000. Awardees will be honored at the PREVENTION 94 Conference, the annual meeting of the Association of Teachers of Preventive Medicine and the American College of Preventive Medicine. All prevention-oriented topics will be considered; papers concerned with women's health issues are encouraged.

Papers are due *October 27, 1993.* For more information, send a self-addressed, stamped envelope to Linda Mermelstein, MD, Preventive Medicine Resident, c/o Department of Preventive Medicine, HSC, Level 3, Room 086, State University of New York–Stony Brook, Stony Brook, NY 11794–8036.