Prior oral contraception and postmenopausal fracture: a Women's Health Initiative observational cohort study

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Objective: To test for the possible association of past oral contraceptive (OC) use and incident fracture after menopause.
Design: A prospective cohort of 93,725 postmenopausal women.
Setting: Forty Women's Health Initiative (WHI) clinical centers across the United States.
Patient(s): Ethnically diverse 93,725 volunteer postmenopausal women, 50 to 79 years old.
Intervention(s): None.
Main Outcome Measure(s): The main outcome was self-reported incident first fracture assessed prospectively by annual questionnaire.
Result(s): The adjusted relative hazard (HR) for fracture among past OC users was 1.07 (95% CI, 1.01–1.15). Among women without any postmenopausal hormone treatment, past OC use for ≤5 years led to an HR of 1.15 (95% CI, 1.04–1.27) and for past OC use >5 years led to an HR of 1.09 (95% CI, 0.97–1.23) compared with never users.
Conclusion(s): This study does not support the idea that past OC use protects against later fracture. (Fertil Steril® 2005;84:374–83. ©2005 by American Society for Reproductive Medicine.)

Key Words: Osteoporotic fracture, oral contraceptive metabolic effects, menopause, cohort study, Women's Health Initiative

Hormone treatment after menopause can preserve bone density and reduce the risk of fracture (1). However, evidence that premenopausal use of oral contraceptives (OC) has a positive effect on bone density is conflicting, and the association of OC with the risk of fracture after menopause remains unclear (2, 3).

Healthy women with normal ovarian estrogen production achieve peak bone mass by their third decade of life. Thereafter, bone resorption begins to outpace accumulation (4), resulting in slow but progressive loss of bone mineral content during later reproductive years (5, 6) and rapid loss after menopause. For young women, ovulatory disturbances that lower estrogen production can result in premature bone mineral loss (7–9) and increased risk of fracture (10, 11). Even among healthy young women, lower estradiol levels are associated with reduced bone mass (11–13). Among adult reproductive age women, OC use is associated with evidence of decreased bone turnover (14, 15).

Oral contraceptives have been reported to have beneficial effects (16–19) or no effect (20–23) on bone mineral density (BMD). For late reproductive age women who may already be estrogen deficient, OC use might increase estrogen exposure and help prevent bone loss (24). There is substantial evidence that OC use is associated with increased bone density among women over the age of 30 years (17–19, 25); however, there are few data concerning the effect of OC on bone density in younger women (22, 26).

Oral contraceptives suppress ovarian hormone production with synthetic estrogen and progestin that are different from endogenous hormones. This ovarian suppression could lead to decreased estrogen exposure, loss of bone mineral content, and increased risk of fractures in later life. Longitudinal studies have found decreased BMD in young women using depo-medroxyprogesterone acetate (Depo-Provera) contra-

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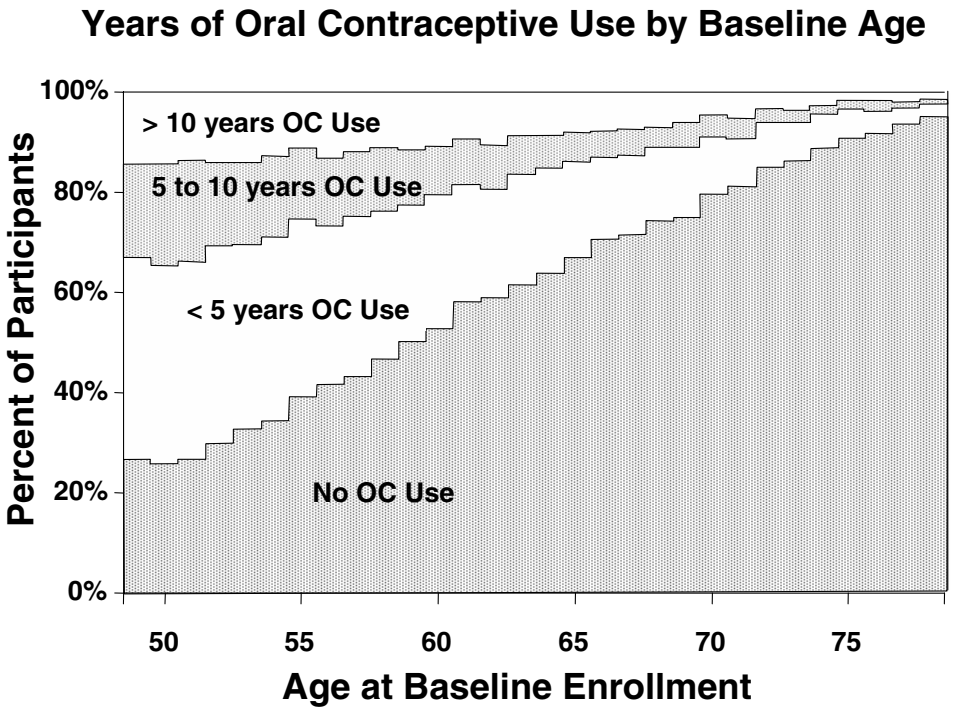
FIGURE 1

Cross-sectional depiction of percent of participants by categories of past contraceptive use by baseline age. The prevalence and duration of self-reported past use of oral contraceptives became progressively less with advancing baseline age.



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ception (27, 28) or ultra-low dose OC (29); however, BMD appears to recover after stopping contraceptive use.

We examined the association of self-reported past OC use and the first occurrence of fracture in a prospective cohort of postmenopausal women to investigate how premenopausal OC use may be associated with the incidence of fracture after menopause.

MATERIALS AND METHODS

Study Population

The Women's Heath Initiative (WHI) is a multicenter study of U.S. women composed of a set of four partly overlapping clinical trials and an observational study (OS). The OS is a prospective cohort study designed to assess the impact of biological, lifestyle, biochemical, and genetic factors on the risk of heart disease, cancer, osteoporosis, fracture, and other major health events.

Women aged 50 to 79 years were recruited to the WHI at 40 clinical centers in the United States, mostly through mass mailings to age-eligible women. A detailed description of the WHI design is reported elsewhere (30). Women were either directly recruited to the OS or were offered OS enrollment because they were ineligible or unwilling to participate in the clinical trials. Exclusions for enrollment in the OS were participation in a clinical trial, less than 3 years predicted survival, alcohol or drug dependency, mental illness, dementia, or other inability to participate in the study. This analysis is of participants who enrolled in the OS between September 1994 and February 1997.

Fracture occurrence in women participants was ascertained annually after enrollment through February 28, 2000, with a mean follow-up time of 2.5 years. Of the 93,725 participants recruited into the observational study, 2,428 were excluded because no outcome data were available. In an effort to decrease confounding factors, we excluded 59 participants (7 fractures) who had a history of bone cancer, 2,338 participants (162 fractures) who reported use of bisphosphonates at baseline, and 7,953 (641 fractures) with missing information on key covariates. The remaining cohort consisted of 80,947 observational study participants. In these, 4,674 reported an incident fracture during the prospective follow-up period.

Each investigator obtained approval from their institutional review boards. Each of the participants signed written informed consent to participate in the WHI observational study.

Assessment

A detailed interview to assess past use of hormonal medications was conducted at the baseline visit. Past OC use was measured by asking, "Did you ever take birth control pills (oral contraceptives) for any reason?" If the participant answered "Yes," the timing and duration of OC use were determined by asking, "At what age did you start taking birth control pills?", "At what age did you stop taking birth control pills?", and "How many total years and months (between first age started and age stopped) did you take birth control pills?" The questionnaire did not ask about the indication for OC use. The WHI observational study cohort reported prior history of OC use at baseline before the initiation of the prospective follow-up to assess incident fracture.

Fracture incidence was assessed annually each year after baseline enrollment. Each subsequent year after enrollment the observational study participants were asked, "Since the date on the front of this form, has a doctor told you for the first time that you had new broken, fractured, or crushed bone?" If the participant answered yes, they were asked, "Which bones did you break, fracture or crush? (Mark all that apply) Hip, upper leg (not hip) pelvis, knee, lower leg or ankle, foot (not toe) tailbone (coccyx) spine or back (vertebra), lower arm or wrist, hand (not finger), elbow, upper area or shoulder or other." Further questions documented any hospitalization or diagnostic procedures associated with the fracture and the date of the fracture.

For participants in the WHI OS, only hip fractures were subject to both local and central adjudication. Other fracture sites were adjudicated only for a subset of the OS participants who were recruited at one of three WHI BMD centers. Others have found that self-report of fracture among postmenopausal women agrees well with medical record review. Investigators for the European Prospective Osteoporosis Study found a 9% false-positive rate of self-reported fracture among their women participants and that fracture of the hip and forearm are reported more accurately than fractures at other sites (31). The WHI investigators found agreement between self-reports for single-site fractures and medical records were high for hip (78%) and forearm/wrist (81%) but relatively lower for clinical spine fractures (51%) in a subset of the WHI clinical trial and OS cohorts (32).

Exercise such as aerobics, aerobic dancing, jogging, tennis, and swimming were examples of strenuous exercise; biking outdoors, use of an exercise machine, calisthenics, easy swimming, or popular or folk dancing were defined as moderate exercise. Smokers were defined as participants who smoked at least 100 cigarettes at some time in their lives. Calcium supplementation and use of medications such as corticosteroid, anticonvulsants, thiazide diuretics, and thyroid hormones were determined at baseline and after 3 years of follow-up, although only baseline data were used in this analysis. A history of amenorrhea was defined as having more than 1 year without menstrual bleeding before menopause.

TABLE 1

All self-reported fractures experienced by participants—September 1994 to February 1997.

	OC use	
	Ever use[a] n (%)	Never use n (%)
Hip	160 (0.32)	60 (0.18)
Upper arm or shoulder	60 (0.12)	28 (0.08)
Pelvis	94 (0.19)	45 (0.13)
Elbow	128 (0.26)	60 (0.18)
Lower arm/wrist	647 (1.31)	348 (1.03)
Knee (patella)	146 (0.30)	82 (0.24)
Upper leg (not hip)	235 (0.48)	130 (0.39)
Spine/back (vertebra)	254 (0.51)	145 (0.43)
Other	637 (1.29)	410 (1.22)
Lower leg/ankle	485 (0.98)	359 (1.07)
Hand (not finger)	76 (0.15)	61 (0.18)
Foot (not toe)	381 (0.77)	344 (1.02)
Tailbone (coccyx)	23 (0.05)	22 (0.07)

[a] *Note:* These are all incident fractures that were self-reported by participants. In our analysis we used only the first self-reported fracture.

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Data Analysis

Oral contraceptive use was divided a priori into nonusers, short-term users (≤5 years of use), and long-term users (>5 years of use) based on the assumption that an association of OC use with fracture prevention would be most apparent with increasing exposure.

We used age-adjusted (1-year interval) logistic regression to compare OC users and nonusers with respect to baseline characteristics. We performed multivariate analyses of OC use and self-reported postmenopausal fractures using a Cox proportional hazards model. The model was stratified for age at baseline (1-year intervals), hormone therapy use (never, past, and current), and duration of hormone therapy use (5-year intervals) adjusted for race/ethnicity, smoking, and parity. We retained several covariates in our model that may affect bone metabolism such as calcium supplement use, corticosteroid, thiazide diuretics, thyroid hormone, vitamin D supplementation, and alcohol use. We also retained reproductive factors such as irregular menses, hysterectomy, age at menopause, and history of menopausal symptoms in the model.

We used the approach of Freedman (33) and the actual sample sizes and incidence rates observed to estimate power.

TABLE 2

Description of study population by history of oral contraceptive (OC) use (adjusted for age).

	OC use		
	Never use	Ever use	*P*[a]
N	47,922	33,025	
Years of follow-up	2.5 ± 1.2	2.6 ± 1.1	NS
Fracture history at baseline			
Fracture history before age 55[b]	7533 (15.7%)	2998 (9.1%)	NS
Years of OC use			
First use of OC			
≤30 years	—	20,732 (62.8%)	—
31–39 years	—	9,028 (27.3%)	—
≥40 years	—	3,265 (9.9%)	—
Last use of OC			
≤30 years	—	10,817 (32.8%)	—
31–39 years	—	12,572 (38.1%)	—
≥40 years	—	9636 (29.2%)	—
Demographic			
Body mass index	27.3 ± 5.8	26.9 ± 5.8	NS
Age	65.9 ± 6.9	60.0 ± 6.5	
Race/ethnicity			
White	40,206 (83.9%)	28,532 (86.4%)	
African-American	3797 (7.9%)	2144 (6.5%)	<.01
Hispanic	1560 (3.3%)	1097 (3.3%)	NS
Asian	1429 (3.0%)	780 (2.4%)	<.01
Native American	213 (0.4%)	111 (0.3%)	<.01
Other/unspecified	717 (1.5%)	361 (1.1%)	<.01
Medications			
Postmenopausal hormones			
Never	21,424 (44.7%)	10,655 (32.3%)	
Past	7160 (14.9%)	4002 (12.1%)	NS
Current	19,338 (40.4%)	18,368 (55.6%)	<.05
Duration of hormone use			
Never	21,424 (44.7%)	10,655 (32.3%)	
<5 years	9106 (19.0%)	8875 (26.9%)	<.05
5–9 years	5424 (11.3%)	5806 (17.6%)	<.05
10–14 years	4440 (9.3%)	3792 (11.5%)	<.05
≥15 years	7528 (15.7%)	3897 (11.8%)	<.05
Total calcium intake (mg)	1154 ± 750	1192 ± 744	NS
Corticosteroid use	689 (1.4%)	301 (0.9%)	NS
Vitamin D supplements	24,397 (50.9%)	17,373 (52.6%)	NS
Thiazide diuretic use	779 (4.2%)	589 (4.0%)	NS
Thyroid hormone use	2670 (14.5%)	1847 (12.6%)	NS
Habits			
Smoking			
Never	25,431 (53.1%)	15,572 (47.2%)	
Past	19,778 (41.3%)	15,219 (46.1%)	<.05
Current	2713 (5.7%)	2234 (6.8%)	NS
Alcohol			
Non drinker	5957 (12.4%)	2674 (8.1%)	
Past drinker	9188 (19.2%)	5581 (16.9%)	NS
Current drinker	32,777 (68.4%)	24,770 (75.0%)	NS

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TABLE 2

Continued.

	OC use		
	Never use	Ever use	*P*[a]
Reproductive history			
Pregnancy			
Never pregnant	5835 (12.2%)	2336 (7.1%)	
No live birth	1222 (2.5%)	940 (2.8%)	<.05
Any live birth	40,865 (85.3%)	27,260 (82.5%)	<.05
Irregular menses	2232 (4.7%)	1978 (6.0%)	NS
Hysterectomy	20,478 (42.7%)	13,342 (40.4%)	NS
Age at menopause	49 ± 7.1	48.8 ± 5.9	NS
Menopausal symptoms	32,532 (67.9%)	25,169 (76.2%)	NS

Note: NS = not statistically significant.
[a] Comparisons adjusted for age (1-year intervals).
[b] Fractures reported at baseline before entering the study.

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Our sample provided a 94% (alpha 0.05) power to detect a 10% and a 99% (alpha 0.05) power to detect a 20% difference in fracture rates among OC users versus never users.

RESULTS

Previous OC use and occurrence of incident fractures during the study period were confounded by baseline age. Self-reported fracture rate was constant among women with baseline ages of 50 to 60 years but increased sharply for older baseline ages. The prevalence and duration of self-reported past use of OC became increasingly less with advancing baseline age (Fig. 1).

Without adjusting for baseline age of the participants, the crude rate of first self-reported fracture was 24 fractures per 1000 women years for never users, 22 fractures per 1000 women years for women with <5 years of OC use, and 20 fractures per 1000 women years for women with a history of ≥5 years of OC use. Crude fracture rates for past OC users were nominally greater for all common sites of osteoporotic fractures (Table 1).

In Tables 2 and 3, we list selected covariates categorized by OC use and duration. Oral contraceptive usage was as follows: 47,922 women reported never using OC, 18,406 women reported short-term (1.5 ± 1 year) OC use, and 14,619 reported long-term (10 ± 4.5 years) OC use.

Oral contraceptive users differed significantly from women who had never used OC in many ways. Past OC users were more likely to be current users of hormone therapy after menopause, to be past smokers, and to be nulliparous and less likely to belong to a minority population. The majority of users began OC use before age 31. Short-term users (48%) were more likely than long-term users (13%) to have started and stopped OC before the age of 31 years ($P<.001$). There was no evidence of a statistically significant association of previous OC use with a history of amenorrhea, and no statistically significant difference in the association of a history of amenorrhea with long-term or short-term OC use.

We found no evidence of a decrease in relative hazard (HR) of fracture associated with past OC use (Table 4). Prior OC use was associated with a small increased relative hazard of fracture (HR 1.07; 95% CI, 1.01, 1.15). A history of irregular menses before menopause was associated with a 16% increased relative hazard of fracture (HR 1.16; 95% CI, 1.02–1.32). Previous reported fracture before the age of 55 was a strong predictor of future fracture, increasing the relative hazard to 1.76 (95% CI, 1.63–1.89). Current smoking and corticosteroid use were both associated with increased while non-white race was associated with decreased hazard of fracture (data not shown).

We performed a few exploratory subgroup analyses. Women who were younger at baseline and closer to the time of OC use might be expected to demonstrate the greatest protection from fracture based on increased premenopausal calcium stores. However, when we restricted the data set to participants 50 to 64 years old at baseline, we found no evidence of decreased fracture rate among past OC users. Among women who had ≤5 years of postmenopausal hormone treatment, prior OC use for ≤5 years was associated with 15% increased relative hazard of fracture ($P<.01$), and OC use for >5 years was not associated with a statistically significant increase in relative hazard of fracture. Excluding a history of prior fracture from our main model did not result in a statistically significantly change in the relative hazard of fracture associated with OC use. When restricting the anal-

TABLE 3

Description of study population by duration of oral contraceptive (OC) use (adjusted for age).

	OC use		
	≤5 years	>5 years	*P*[a]
N	18,406	14,619	
Years of follow-up	2.6 ± 1.1	2.6 ± 1.2	NS
Fracture history at baseline			
Fracture history before age 55[b]	1695 (9.2%)	1303 (8.9%)	NS
Years of OC use			
First use of OC			
≤30 years	10,711 (58.2%)	10,021 (68.5%)	.01
31–39 years	5361 (29.1%)	3667 (25.1%)	
≥40 years	2334 (12.7%)	931 (6.4%)	.01
Last use of OC			
≤30 y	8873 (48.2%)	1944 (13.3%)	
31–39 years	6567 (35.7%)	6005 (41.1%)	
≥40 years	2966 (16.1%)	6670 (45.6%)	<.05
Demographic			
Body mass index	27.3 ± 6	26.8 ± 5.6	NS
Age	60.1 ± 6.5	59.9 ± 6.5	
Race/ethnicity			
White	15,945 (86.6%)	12,587 (86.1%)	
African-American	1050 (5.7%)	1094 (7.5%)	NS
Hispanic	649 (3.5%)	448 (3.1%)	NS
Asian	479 (2.6%)	301 (2.1%)	NS
Native American	64 (0.3%)	47 (0.3%)	NS
Other/unspecified	219 (1.2%)	142 (1.0%)	NS
Medications			
Postmenopausal hormone use			
Never	6391 (34.7%)	4264 (29.2%)	
Past	2329 (12.7%)	1673 (11.4%)	NS
Current	9686 (52.6%)	8682 (59.4%)	
Duration of hormone use			
Never	6391 (34.7%)	4264 (29.2%)	
<5 years	5021 (27.3%)	3854 (26.4%)	NS
5–9 years	3030 (16.5%)	2776 (19.0%)	NS
10–14 years	1897 (10.3%)	1895 (13.0%)	NS
≥15 years	2067 (11.2%)	1830 (12.5%)	NS
Total calcium intake (mg)	1193 ± 775	1190 ± 703	NS
Corticosteroid use	182 (1.0%)	119 (0.8%)	NS
Vitamin D supplements	9584 (52.1%)	7789 (53.3%)	NS
Thiazide diuretic use	779 (4.2%)	589 (4.0%)	NS
Thyroid hormone use	2670 (14.5%)	1847 (12.6%)	NS
Habits			
Smoking			
Never	8750 (47.5%)	6822 (46.7%)	
Past	8426 (45.8%)	6793 (46.5%)	NS
Current	1230 (6.7%)	1004 (6.9%)	NS
Alcohol			
Non drinker	1616 (8.8%)	1058 (7.2%)	
Past drinker	3300 (17.9%)	2281 (15.6%)	NS
Current drinker	13,490 (73.3%)	11,280 (77.2%)	NS

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TABLE 3

Continued.

	OC use		
	≤5 years	>5 years	*P*[a]
Reproductive history			
Pregnancy			
Never pregnant	1273 (6.9%)	1063 (7.3%)	
No live birth	486 (2.6%)	454 (3.1%)	NS
Any live birth	14,158 (76.9%)	13,102 (89.6%)	NS
Irregular menses	1124 (6.1%)	854 (5.8%)	NS
Hysterectomy	7763 (42.2%)	5579 (38.2%)	NS
Age at menopause	48.8 ± 6.1	48.9 ± 5.6	NS
Menopausal symptoms	14,050 (76.3%)	11,119 (76.1%)	NS

Note: NS = not statistically significant.
[a] Comparisons adjusted for age (1-year intervals).
[b] Fractures reported at baseline before entering the study.

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ysis to participants who had no history of previous fracture, there was no statistically significant association of OC and fracture.

DISCUSSION

Major strengths of our study are large sample size, and diverse ethnic, geographic, and socioeconomic status of the participants. After adjusting for age, postmenopausal hormone use, history of premenopausal irregular menstrual periods, and other significant covariates, previous use of OC was not associated with protection against fracture after menopause. Among women without previous postmenopausal hormone treatment, 5 years or less of OC use statistically significantly increased the relative hazard of fracture compared with never users. Our study demonstrates that careful consideration of age as a covariate is necessary when conducting studies of past OC use and later fracture.

Our finding of a small, but statistically significant, increased risk of fracture among previous OC users was unexpected. It may be that women with a history of irregular menstrual cycles or amenorrhea who were already at risk for poor bone formation were preferentially prescribed OC to help regulate their menstrual bleeding. However, the observed association of increased risk of fracture remained even after adjusting our multivariate model for a history of amenorrhea. This clinical relevance of such a modest increase in risk can be debated.

In this analysis, exposure to OC was determined at baseline by participant recall. As a result our estimate of timing and duration of exposure to OC is not very precise. Even so, it is possible that use of OC in youth, when women should have been forming bone, may have resulted in a net decrease in bone mineralization. This is contrary to published information regarding BMD among young OC users (34).

Relatively few studies have been published on the association of prior OC use with fracture in postmenopausal women. In those studies, fracture risk among women who used OC after age 35 or 40 was decreased (35, 36). These studies may suggest that the effect of OC use on bone stores and later fracture risk will depend on a woman's age at the time of OC use.

Bone density is an intermediate factor that has been studied in relation to OC use. Reports of the effect of OC use on BMD have been conflicting. Current OC use was associated with increased BMD in young women (25, 34, 37, 38), and prior OC use was associated with increased BMD after menopause (17). Others found that women who used steroid contraception had either no difference in BMD (39), lower BMD (40), evidence of reduced bone formation and resorption (41, 42), or decreased femoral neck strength (43).

Oral contraceptive use was found to inhibit positive effects of exercise on BMD among women age 20 to 35 years old (44). Among perimenopausal and mid-reproductive age women, OC use is associated with decreased bone turnover (24) and higher BMD among OC users than among those who do not use OC (19, 45–47). In the WHI, information on BMD was only available for a subsample of participants, and was not assessed in this analysis.

The effect of OC use on bone mineralization may be different for women taking OC today than it was for our study cohort. Over the years, OC formulations have changed, and there is evidence that various OC preparations have different effects on BMD (48). One weakness of our analysis

TABLE 4

Hazard ratio of fracture by oral contraceptive (OC) use.

	Hazard ratio	95% CI
Any OC use (base model)[a]		
No OC use	1.00	
Any OC use	1.07	(1.01, 1.15)
By 5 years OC use[b]		
No OC use	1.00	
≤5 years OC use	1.09	(1.01, 1.18)
5 to 10 years OC use	1.07	(0.96, 1.20)
>10 years OC use	1.02	(0.91, 1.15)
Participants <64 years[c]		
No OC	1.00	
≤5 years OC use	1.08	(0.98, 1.19)
>5 years OC use	1.02	(0.91, 1.14)
No or past HT use for <5 years[d]		
No OC use	1.00	
≤5 years OC use	1.15	(1.04, 1.27)
>5 years OC use	1.09	(0.97, 1.23)
Excluding prior fractures as a covariate[e]		
No OC use	1.00	
≤5 years OC use	1.10	(1.02, 1.18)
>5 years OC use	1.05	(0.96, 1.14)
Excluding participants with prior fracture[f]		
No OC use	1.00	
≤5 years OC use	1.08	(0.99, 1.18)
>5 years OC use	1.05	(0.96, 1.16)

[a] Adjusted for baseline age (1-year intervals), hormone therapy (HT) use (never, past, current), and duration (5-year intervals), follow-up time, calcium intake (mg), corticosteroid use, vitamin D use, thiazide use, thyroid hormone use, age, race/ethnicity, smoking, alcohol use, moderate/strenuous exercise (hours/week) body mass index, parity, history of irregular menses for more than 1 year before menopause, hysterectomy, age at menopause, menopausal symptoms, prior fracture before age 55, length of OC use, age of last OC use, age of first OC use, HT use, and duration of HT use.

[b] As above, with duration of OC use in categories of 5-year intervals (excluding adjustment for duration of OC use as covariate).

[c] Base model with restriction to participants <64 years old.

[d] Base model restricted to participants with no history of HT use or past use for <5 years.

[e] Base model excluding prior fractures.

[f] Base model excluding participants with prior fractures.

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is that we do not know the dose or composition of the OC used by our participants.

Another weakness of this analysis is that the history of exposure to OC is dependent on accurate participant recall. Although others have shown that recall of OC use, duration of use, and first and last use is accurate when compared with existing medical records (49, 50), some of the apparent decrease in previous use of OC among older women in the present study may be attributed to poor recall. It seems unlikely that the results of this study were affected by recall bias associated with incident fracture because OC history was obtained at baseline well before the fractures occurred and were reported. Ascertainment bias in this study was also unlikely because the history of previous OC use was just one of many historical factors obtained at study baseline. Furthermore, the prevailing wisdom at the time was that OC use would protect against future fracture.

The WHI study population consists of healthy volunteers, so our findings may not be generalizable to all women. We did not have sufficient power in this analysis to test for a possible significant association of OC use on individual fracture sites. Fracture risk may be related to some other factor that made it more likely for a woman both to use OC pills and to sustain a traumatic fracture. It is also possible that women with lower premenopausal BMD were more likely to use OC (i.e., to "regulate" their menstrual bleeding) and thus started out with lower calcium stores.

We found no evidence that premenopausal OC use is associated with a decreased risk of osteoporotic fracture for menopausal women. The absence of evidence of protection against fracture in this large prospective observational cohort allows us to infer that increased bone stores and decreased future risk of fracture cannot be presumed to be a benefit of OC use. However, oral contraceptives have many proven benefits. These findings of an absence of decreased fracture risk associated with OC use should have no clinical impact because fracture protection is not a primary indication for OC use. As such, we do not believe that these observed differences should discourage women from using OC.

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