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Associations of Parity, Breastfeeding, and Fractures in the Women's Health Observational Study

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Abstract

Objective—To examine associations of several aspects of parity and history of lactation with incident hip fractures and clinical fractures and, in a subset of women, with bone mineral density.

Methods—In this observational study, we analyzed data from 93,676 postmenopausal women participating in the Women's Health Initiative Observational Study, and all bone density data from the subset of participants who underwent bone density testing at 3 clinical centers. At baseline,

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For a list of investigators and academic centers participating in this study, see Appendix 1 online at <http://links.lww.com/xxx>.

participants were aged 50–79 years. Using Cox proportional hazards regression analysis, we examined associations of fracture incidence and bone density with several aspects of parity (number of pregnancies, age at first pregnancy lasting ≥ 6 months, and number of pregnancies lasting < 6 months) and breastfeeding (number of episodes of breastfeeding for at least one month, number of children breastfed, age when first breastfed, age when last breastfed, total number of months breastfed).

Results—The mean baseline age (SD) of participants was 64 (+/– 7.4) years (mean follow-up 7.9 years. During follow-up, incident rate of hip fracture was 1.27%. Ten percent of participants were nulligravid. In fully-adjusted models, number of pregnancies, parity, age at first birth, number of children breastfed, age at first breastfeeding, age at last breastfeeding, and total duration of breastfeeding were not statistically significantly associated with hip fracture incidence. There were no consistent associations of parity or lactation characteristics with overall clinical fracture risk or bone density. However, compared with never breastfeeding, a history of breastfeeding for at least one month was associated with a decreased risk of hip fracture (yes vs. no, hazard ratio 0.84, 95% confidence interval 0.73 – 0.98).

Conclusions—Patterns of parity and history of lactation were largely unrelated to fracture risk or bone density.

Introduction

An estimated one in two postmenopausal women in the United States will experience an osteoporotic fracture in their remaining lifetimes.(1) Osteoporotic fractures are associated with substantial increases in morbidity and mortality.(2)

Although not considered by current osteoporosis clinical guidelines, pregnancy and lactation have effects on maternal bone health.(3) The calcium demand of pregnant and lactating women is similar in magnitude.(4) During pregnancy, intestinal calcium absorption more than doubles, whereas during lactation, the maternal skeleton resorbs to provide the majority of the calcium contained in breast milk.(5) During lactation, the nursing infant requires that the breast milk contain sufficient calcium to allow for continued skeletal growth. During pregnancy and lactation, parathyroid hormone-related protein levels increase.(5)

The maternal skeleton has to compensate for the calcium requirements associated with breastfeeding; consequently, the mother's intestinal calcium absorption increases.(6) Other adaptations include increased bone resorption and decreased calcium excretion.(7–9) Bone loss is typically restored within 6–12 months after cessation of lactation.(3) Osteoporosis can occasionally present as fracture during late pregnancy or the first months of lactation, and transient osteoporosis of the hip can occur in late pregnancy or early postpartum.(5, 10, 11)

Few prospective U.S. studies have evaluated long-term associations of parity and lactation with incident fracture risk in postmenopausal women.(13–18) Published studies often did not have long-term follow-up(15), or did not examine lactation (13, 14, 16), age at first childbirth (13, 14, 16), or hip fracture outcomes.(13, 15) It is of great importance to

understand whether pregnancy- and lactation-associated bone loss have long-term adverse effects on the skeleton.

The objectives of this study were to examine associations of parity and lactation history with incident hip fractures, clinical fractures, and bone mineral density. (20)

Materials and Methods

This study is a secondary data analysis from an observational cohort study. The Women's Health Initiative Observational Study, initiated in 1992 at 40 U.S. clinical centers, was designed to examine the predictors and natural history of important causes of morbidity and mortality in postmenopausal women.(21) The study enrolled postmenopausal women aged between 50 and 79 years.

Details of the study design and enrollment, data quality assurance, and outcome adjudication methods, were described previously.(21–23) In brief, inclusion criteria included an expectation of remaining in the study recruitment area for at least 3 years. Exclusion criteria included medical conditions predictive of survival less than 3 years, alcoholism, drug dependency, and dementia. For the present analysis, we used data from the main study, which occurred between 1993 and 2005. Study questionnaires were administered at baseline and annually. All participants provided informed consent and the study was approved by institutional review boards at each clinical center.

For inclusion in the current analysis, we required complete information regarding pregnancy and lactation history and incident fractures. Of the 93,676 women enrolled in the Observational Study, we excluded data from 696 participants who did not provide information regarding pregnancy and lactation history or incident fractures (Figure 1). Therefore, the analytic sample for the current study consisted of 92,980 participants. A subset (6,193 women) underwent bone density testing (described below); of those women, we had complete information for 5,919 women regarding pregnancy and lactation history and bone density.

On annual follow-up questionnaires, women self-reported incident fractures. Hip fractures were physician-adjudicated; non-hip fractures were self-reported.(24, 25) The average confirmation rate for all single-site fractures in our study is high, 71%.(25) *Incident clinical fractures* were defined as any clinical fracture, excluding fractures of the fingers and toes, ribs, sternum/chest, skull/face, and cervical vertebrae.

In the Bone Substudy, at baseline and annual visits 1, 3, 6, and 9, all participants at 3 of the 40 clinical centers at Pittsburgh (PA), Birmingham (AL), and Tucson/Phoenix (Az) were invited to undergo *bone density measurement* of the hip and lumbar spine by dual-energy X-ray absorptiometry (DXA) on Hologic QDR machines (models 2000, 200+, or 4500 Fan-beam, Hologic, Inc., New Bedford, MA, USA).(26) Standardized protocols were used for scan positioning and analysis by trained technicians. Quality assurance included review of a random sample of all scans, flagging of scans with specific problems, and calibration of phantoms across instruments and clinical sites.(27, 28)

Using information from questionnaires administered to all participants at the screening visit, we obtained information from each participant about the following *parity and lactation* characteristics: number of pregnancies, number of pregnancies lasting at least 6 months, age at first pregnancy lasting 6 months, breastfed a child for at least one month (yes/no), number of children breastfed, age when first breastfed a child, total number of months breastfeeding children, and number of months breastfeeding children for at least one month.

Using baseline questionnaires, we obtained demographic and socioeconomic information (age, race/ethnicity, education), medical history (including fracture prior to baseline), history of falls in the past 12 months, reproductive history (hysterectomy, oophorectomy, years since menopause), family history (including parental hip fracture), medication use, alcohol consumption, cigarette smoking, weight at age 35, and use of calcium and vitamin D supplements(20, 21, 23, 29), and physical activity.(30, 31) Height and weight were directly measured at baseline using a standardized protocol for calculation of body mass index.

We used Cox proportional hazards regression models to examine the associations of parity and lactation with incident fractures. Covariates included baseline age, race/ethnicity, education, smoking, alcohol consumption, hysterectomy, bilateral oophorectomy, years since menopause, history of fracture at age 55+, history of parental fracture, number of falls in the past 12 months, estrogen use, estrogen route of delivery, recency of estrogen use, body mass index, total weekly energy expenditure from physical activities (log-transformed), total (dietary plus supplemental) calcium intake (log-transformed), total vitamin D intake (log-transformed), and weight change since age 35. We adjusted for use at baseline of osteoporosis medications: risedronate, ibandronate, alendronate, zoledronic acid, raloxifene, calcitonin, parathyroid hormone/teriparatide, denosumab. We also adjusted for use at baseline of other medications that influence fracture risk: aromatase inhibitors, tamoxifen, antidepressants, corticosteroids, proton pump inhibitors, anti-epileptics, anti-neoplastics, thiazolidinediones. In sensitivity analyses, we censored data from participants reporting use of these medications at any time during study follow-up, beginning at the time they first reported using the medications. Covariates with skewed distributions were log-transformed as appropriate.

Next, we used multivariate repeated measures regression models to examine associations between parity and history of lactation and bone density among the subset of women in the bone density sample (n = 5,919). Lumbar spine bone density and femoral neck bone density were outcomes of separate regression models. Predictors and covariates were handled as in the Cox proportional hazards regression models described above. In pre-specified secondary analyses, we determined whether associations of parity and history of lactation with fracture and bone density outcomes varied according to age group, race/ethnicity, or body mass index. We also stratified by current/past/never use of menopausal hormone therapy at the time of study enrollment.

Results

Of the 93,676 participants of the Women's Health Initiative Observational Study, we excluded data from 696 women for whom information was lacking regarding fracture

outcomes and key exposures, resulting in an analytic sample of 92,980 participants (Figure 1). Of the 6,193 participants of the bone mineral density subset, we excluded data from 274 women for whom information was missing regarding bone density or key exposures, resulting in an analytic sample of 5,919 participants for the bone density analyses.

At baseline, the mean age $\pm$ standard deviation (SD) of the participants was 63.6 ($\pm$ 7.4 years and mean $\pm$ (SD) body mass index was 27.3 $\pm$ (5.9) kg/m² (Table 1). 17% of participants were non-white. The majority of participants were non-smokers. At baseline, mean total intake of calcium was 1241 mg/d; mean total intake of vitamin D (dietary plus supplement use) was 390 IU/d. The prevalence of osteoporosis medication use at baseline was 2.5%. Thirteen percent of participants were nulliparous (Table 2). The mean age at first birth was between 20 and 29 years in 64.9% of participants and 30 years in 8.6% of participants. Fifty-seven percent of the parous participants had breastfed for at least one month, and 5.9% of the parous participants had breastfed for 24 months. Thirty-two percent of participants were younger than age 25 when they first breastfed. The mean (median, interquartile range [IQR]) duration of follow-up was 7.88 (Median 8.1, IQR 6.9–9.0) years. 1,928 clinical fractures and 1,185 hip fractures occurred in the study participants during the study follow-up period. During follow-up, the incident rate of hip fracture was 1.27%.

In unadjusted models, nearly every parity and lactation characteristic was significantly associated with lower risk of incident hip fractures (Table 3). However, after adjustment for covariates, the only characteristic that was statistically significantly associated with hip fracture risk was breastfeeding for at least 1 month (incidence 1.2% vs. 1.28% for never breastfeeding). Among 83,563 participants who had a prior pregnancy, ever breastfeeding for at least 1 month was associated with a 16% lower risk of hip fracture (odds ratio [OR] 0.84, 95% confidence interval [CI] 0.73–0.98. This association between breastfeeding for at least 1 month and lower risk of hip fracture did not differ by ever-use vs. never-use of estrogen therapy ($p_{\text{interaction}}$ 0.78). Magnitudes of associations after additional adjustment for duration of menopausal hormone therapy use among women who were current or past users of menopausal hormone therapy were similar to those of the original analyses (data not shown). None of the parity and lactation characteristics were associated with incident clinical fractures (Table 4). Associations between parity and fracture risk did not differ by number of children breastfed ($p_{\text{interaction}}$ = 0.97 for hip fracture, $p_{\text{interaction}}$ = 0.93 for clinical fracture).

Associations of parity and lactation characteristics with incident hip fractures (Appendix 2, **available online at** <http://links.lww.com/xxx>) and overall clinical fractures (Appendix 3, **available online at** <http://links.lww.com/xxx>) did not differ by baseline age category. However, associations between breastfeeding for at least one month (vs. never breastfeeding) and decreased hip fracture risk were statistically significant among white women (incidence 1.35% vs. 1.46%, OR 0.83, 95% CI 0.72–0.97, p = 0.02), but not among black women or women of other race/ethnicity ($p_{\text{interaction}}$ 0.59) (Appendix 4, **available online at** <http://links.lww.com/xxx>). No other associations varied by race/ethnicity for hip fractures or for incident clinical fractures (Appendix 5, **available online at** <http://links.lww.com/xxx>). Associations of parity and lactation characteristics with clinical

fractures and with hip fractures did not vary by baseline use of menopausal hormone therapy or body mass index (data not shown).

In repeated measures analysis of serial bone density measurements, few parity or lactation characteristics were significantly associated with femoral neck bone density (Appendix 6, **available online at** <http://links.lww.com/xxx>) or lumbar spine bone density (Appendix 7, **available online at** <http://links.lww.com/xxx>). Age at first birth ($p = 0.006$) and number of children breastfed ($p = 0.004$) were significantly associated with femoral neck bone density, but no clear directions of associations or “dose-response” patterns emerged across categories of increasing age at first birth or increasing numbers of children breastfed.

In sensitivity analyses, after we excluded data from women taking osteoporosis medication at baseline or at any time during follow-up, results were nearly identical to those of the main analysis for hip fractures (Appendix 8, **available online at** <http://links.lww.com/xxx>) and incident overall clinical fractures (Appendix 9, **available online at** <http://links.lww.com/xxx>). The OR for hip fracture in women who had breastfed children for at least 1 month (vs. never breastfeeding) was 0.85 (95% CI 0.72–1.00) after censoring, and 0.84 (0.73–0.98) before censoring. Results were very similar after further exclusion of women who were prior users of estrogen before baseline, who initiated estrogen during study follow-up, or who experienced menopause before age 40 (data not shown).

Discussion

In this large multi-ethnic postmenopausal cohort study with 7.9 years of follow-up, we examined multiple aspects of parity and lactation history in relation to fracture risk and bone density. Parity and lactation history were not associated with risk of hip fracture or clinical fracture, and there were no consistent associations with bone density over time. Results were generally similar across racial/ethnic categories.

Our results fill knowledge gaps in the previously-published literature regarding parity, lactation, and bone health in postmenopausal women, because previous studies often lacked long-term follow-up(15), did not evaluate lactation behaviors as a risk (or protective) factor(13, 14, 16), did not consider age at first childbirth(13, 14, 16), or did not analyze incident hip fracture outcomes(13, 15) or serial BMD bone density measurements by DXA. (19)

Our multivariable-adjusted findings differ from those of previous prospective studies in the U.S. In the Study of Osteoporotic Fractures, a cohort in which mean participant age was older than our present study, nulliparity was associated with increased risk of hip fractures over the 10-year follow-up duration(14, 16), and in the Leisure World cohort study with 20 years of follow-up, nulliparity was associated with increased risk of hip fracture.(17)

On the other hand, our finding of an absence of association between age at first childbirth or number of pregnancies and hip fracture risk is consistent with the multivariate-adjusted results of the Leisure World Cohort study.(17) The statistical models in our study were adjusted for a more extensive, fixed set of covariates selected *a priori* from previously-published studies (age, race/ethnicity, education, smoking, alcohol consumption, prior

hysterectomy, prior oophorectomy, years since menopause, previous fracture, parental history of fracture, frequency of falls, estrogen use, use of medications that influence bone, body mass index, physical activity level, calcium and vitamin D intake, and weight change since age 35), which may explain the different findings between the previous studies and our study. The findings described above from the Study of Osteoporotic Fractures and Leisure World Study were produced by stepwise methods for selection of covariates that were significantly associated with the outcome in the specific cohort examined.(14, 16, 17) Future research is necessary to further pinpoint the time course of pregnancy- and lactation-associated changes in bone metabolism.

These findings extend the findings from our prior study of pre- or early peri-menopausal women, in which parity and lactation history were not associated with fracture risk during a 15-year follow-up period.(12)

Strengths of this study include the large sample size, prospective fracture assessment, detailed assessment of osteoporosis risk factors and reproductive histories, and long duration of follow-up. The importance of the covariates that we assessed is evident in the differences between results of the univariate and the multivariate models. Limitations include possible recall bias of breastfeeding history and the self-report of non-hip fractures. However, the average confirmation rate for all single-site fractures in the our study is high, 71%.(25) Also, study participants may have been more healthy than women in the general population. We suspect that the association between breastfeeding for at least 1 month and decreased hip fracture risk was spurious (due to multiple statistical comparisons), especially because there was no association of fracture risk with total duration of breastfeeding. Finally, we may not have had sufficient statistical power to detect associations in the smaller bone density subset.

In conclusion, patterns of parity and history of lactation were largely unrelated to fracture risk or bone density. The results of this study may inform clinical counseling regarding osteoporosis risk and may provide reassurance about the lack of long-term persisting harmful effects of childbearing and lactation on postmenopausal bone health.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1.
Flow diagram of analytic cohorts. Fracture cohort (**A**) and bone mineral density cohort (**B**).

Table 1

Selected Baseline Characteristics of the Study Participants (n=92,980) *

Characteristic	Number (%)
Age, years	
50–59	29457 (31.68%)
60–69	40926 (44.02%)
70–79	22597 (24.30%)
Age (years) [†]	63.62 +/-7.37
Race / ethnicity	
White	77607 (83.47%)
Black	7516 (8.08%)
Hispanic	3499 (3.76%)
Other	4358 (4.69%)
Education	
High school/GED or less	19725 (21.39%)
School after high school	33700 (36.54%)
College Degree or higher	38800 (42.07%)
Body mass index (kg/m2) [‡]	27.26+/- 5.86
Smoking status	
Never	46736 (50.93%)
Past	39303 (42.83%)
Current	5735 (6.25%)
Alcohol consumption	
Non/past drinker	27757 (30.04%)
<1 drink/week	29263 (31.67%)
1–14 drinks/week	31374 (33.95%)
>14 drinks/week	4016 (4.35%)
Total calcium (mg/d) [§]	1241.6 +/- 769.8
Total vitamin D (IU/d) ^{**}	389.85 +/-286.7
Total energy expenditure/week from physical activities (MET-hours) ^{††}	13.71 +/-14.36
History of fracture age 55+	
Under age 55 when filled out the form	12568 (14.60%)
No	61046 (70.90%)
Yes	12490 (14.51%)
Parental history of fracture	
None	58798 (63.24%)
One parent	31177 (33.53%)
Both parents	3005 (3.23%)
Number of falls in the past 12 months	

Characteristic	Number (%)
None	62235 (67.68%)
1 time	18306 (19.91%)
2 times	7533 (8.19%)
3 or more times	3879 (4.22%)
Menopausal Hormone Use	
Never used	37655 (40.53%)
Past user	13846 (14.90%)
Current user	41395 (44.56%)
Route of estrogen delivery	
Never used	37655 (43.67%)
Former	13840 (16.05%)
Oral E+P	13145 (15.24%)
Oral CEE alone	16412 (19.03%)
Oral estradiol	3007 (3.49%)
Transdermal estradiol	2176 (2.52%)
Recency of estrogen use (years)	
Non User	37655 (40.53%)
Past, < 5	5532 (5.96%)
Past, 5–<10	2557 (2.75%)
Past, >10	5757 (6.20%)
Current	41395 (44.56%)
Bisphosphonates	2318 (2.49%)
Selective estrogen receptor modulators	38 (0.04%)
Calcitonin	355 (0.38%)
Aromatase inhibitors	7 (0.01%)
Tamoxifen	1021 (1.10%)
Antidepressants	6978 (7.50%)
Glucocorticoid	1256 (1.35%)
Proton Pump Inhibitors	2109 (2.27%)
Anti-epileptics	1041 (1.12%)
Anti-neoplastics	1525 (1.64%)
Thiazolidinediones	88 (0.09%)
Weight history	
Weight at age 35 (lbs) ^{††}	131.95 +/-20.41
Weight change since age 35 (lbs) ^{§§}	26.02 +/-29.75
Maximum adult weight (lbs) ^{***}	163.43 +/-35.34
Minimum adult weight (lbs) ^{†††}	118.10 +/-16.86

* Baseline characteristics unless otherwise stated

[†]Values are mean $\pm$ standard deviation (SD).

[‡]Values are mean $\pm$ SD.

^{\$}Includes total intake from both diet and supplements. Values are mean $\pm$ SD.

^{**}Includes total intake from both diet and supplements. Values are mean $\pm$ SD.

^{††}Values are mean $\pm$ SD.

^{‡‡}Values are mean $\pm$ SD.

^{\$\$}Values are mean $\pm$ SD.

^{***}Values are mean $\pm$ SD.

^{†††}Values are mean $\pm$ SD.

Table 2

Reproductive Characteristics of the Study Participants (n=92,980)

Characteristic	Number (%)
Parity	
Never pregnant	9318 (10.07%)
Never had pregnancy lasting $\geq$ 6 months	2568 (2.77%)
1	8443 (9.12%)
2	24305 (26.26%)
3	22303 (24.09%)
4	13396 (14.47%)
5+	12234 (13.22%)
How many times pregnant	
0	9318 (10.05%)
1	6741 (7.27%)
2	18959 (20.45%)
3	20953 (22.60%)
4	15611 (16.84%)
5	9466 (10.21%)
6	5279 (5.70%)
7	2865 (3.09%)
8+	3501 (3.78%)
Age at first birth, years	
Never pregnant/No pregnancy lasting $\geq$ 6 months	11886 (14.14%)
<20	10458 (12.44%)
20–29	54529 (64.86%)
30+	7195 (8.56%)
Had hysterectomy	38847 (41.82%)
Had bilateral oophorectomy	18792 (20.62%)
Years since menopause	
< 10	27241 (30.54%)
10 – <20	32647 (36.60%)
20	29317 (32.86%)
Among women who were pregnant at least once (n=83,563)	
Breastfed for at least one month	46777(56.51%)
How many children breastfed	
None	35994(43.53%)
1–2	29407(35.57%)
3–5	15629(18.90%)
6+	1652(2.00%)
How old when first breastfed? (years)	

Characteristic	Number (%)
Never breastfed	35994(43.56%)
<20	6065(7.34%)
20 – 24	20592(24.92%)
25 – 29	14092(17.06%)
30 – 34	4314(5.22%)
35 – 39	1327(1.61%)
40 – 44	227(0.27%)
45+	11(0.01%)
How old when last breastfed? (years)	
Never breastfed	35994(43.63%)
<20	1975(2.39%)
20 – 24	9372(11.36%)
25 – 29	14270(17.30%)
30 – 34	12659(15.34%)
35 – 39	6358(7.71%)
40 – 44	1727(2.09%)
45+	143(0.17%)
Number of months breastfed	
Never breastfed	35994(43.64%)
1–6	23713(28.75%)
7–12	10196(12.36%)
13–23	7730(9.37%)
24+	4852(5.88%)

Table 3Associations of parity and lactation history with incident hip fractures^{*}

Predictor	Unadjusted model [†]		Multivariable-adjusted model [‡]	
	HR (95% CI) [§]	p	HR (95% CI)	p
Parity characteristics				
# pregnancies lasting ≥ 6 months		0.005		0.15
Never pregnant	Reference ^{**} (1.00)		Reference (1.00)	
Never had pregnancy lasting ≥ 6 months	0.74 (0.50–1.11)		0.79 (0.46–1.34)	
1	0.96 (0.75–1.22)		1.14 (0.85–1.52)	
2	0.75 (0.61–0.92)		0.87 (0.68–1.11)	
3	0.75 (0.61–0.92)		0.80 (0.62–1.02)	
4	0.79 (0.63–0.99)		0.85 (0.65–1.11)	
5+	0.98 (0.78–1.22)		0.90 (0.68–1.18)	
How many times pregnant		0.03		0.34
None	Reference (1.00)		Reference (1.00)	
1	0.93 (0.71–1.20)		1.10 (0.81–1.50)	
2	0.84 (0.68–1.03)		0.94 (0.73–1.20)	
3	0.72 (0.59–0.89)		0.81 (0.63–1.04)	
4	0.77 (0.62–0.96)		0.88 (0.68–1.14)	
5	0.79 (0.62–1.01)		0.85 (0.63–1.14)	
6	0.97 (0.74–1.28)		0.85 (0.60–1.21)	
7	0.77 (0.53–1.13)		0.63 (0.39–1.03)	
8+	1.07 (0.78–1.46)		0.91 (0.61–1.35)	
Age at first birth (years)		<.0001		0.21
Never pregnant/No pregnancy lasting ≥ 6 months	Reference (1.00)		Reference (1.00)	
<20	0.56 (0.43–0.73)		0.86 (0.62–1.20)	
20 – 29	0.85 (0.72–1.01)		0.87 (0.71–1.07)	
30+	1.14 (0.90–1.44)		1.08 (0.82–1.42)	
Lactation pattern among participants who had been pregnant (n=83,563)				
Breastfed for at least 1 month		0.27		0.03
No	Reference (1.00)		Reference (1.00)	
Yes	0.93 (0.83–1.06)		0.84 (0.73,0.98)	
How many children breastfed?		0.30		0.14
None	Reference (1.00)		Reference (1.00)	
1–2	0.89(0.77–1.02)		0.83(0.70–0.99)	
3–5	1.00(0.84–1.18)		0.85(0.69–1.04)	
6+	1.14(0.75–1.74)		1.00(0.60–1.65)	
How old when first breastfed? (years)		0.09		0.39
Never breastfed	Reference (1.00)		Reference (1.00)	

Predictor	Unadjusted model [†]		Multivariable-adjusted model [‡]	
	HR (95% CI) [§]	p	HR (95% CI)	p
<20	0.66(0.49–0.88)		0.83(0.57–1.20)	
20 – 24	0.91(0.78–1.06)		0.81(0.67–0.99)	
25 – 29	1.03(0.87–1.22)		0.83(0.67–1.02)	
30 – 34	1.12(0.86–1.46)		1.00(0.74–1.36)	
35 – 39	0.94(0.57–1.55)		0.97(0.57–1.66)	
40 – 44	0.34(0.05–2.44)		0.40(0.06–2.87)	
45+	NA		NA	
How old when last breastfed? (years)		0.001		0.39
Never breastfed	Reference (1.00)		Reference (1.00)	
<20	0.69(0.43–1.12)		0.93(0.51–1.71)	
20 – 24	0.79(0.63–0.98)		0.78(0.59–1.03)	
25 – 29	0.77(0.64–0.93)		0.79(0.63–0.99)	
30 – 34	1.12(0.95–1.33)		0.92(0.75–1.13)	
35 – 39	1.03(0.82–1.30)		0.81(0.61–1.06)	
40 – 44	1.42(0.99–2.04)		0.99(0.65–1.50)	
45+	1.79(0.57–5.56)		0.93(0.23–3.76)	
Number of months breastfed		0.68		0.19
Never breastfed	Reference (1.00)		Reference (1.00)	
1–6	0.95(0.82–1.10)		0.85(0.71–1.01)	
7–12	0.88(0.71–1.07)		0.77(0.60–0.99)	
13–23	0.99(0.79–1.23)		0.88(0.68–1.15)	
24+	0.88(0.66–1.16)		0.92(0.67–1.27)	

* Cox proportional hazards regression models

[†] Includes predictor only without any covariates

[‡] Includes the following covariates: age, race/ethnicity, education, smoking status, alcohol consumption, hysterectomy, bilateral oophorectomy, years since menopause, previous fracture, parental history of fracture, number of falls in the past 12 months, estrogen use, estrogen route of delivery, recency of estrogen use, use of prescription osteoporosis medication, use of aromatase inhibitors, tamoxifen use, antidepressant use, corticosteroid use, proton pump inhibitor use, anti-epileptic use, anti-neoplastic use, thiazolidinedione use, body mass index, total energy expenditure per week from physical activities (log-transformed), total calcium intake (log -transformed), total vitamin D intake (log-transformed) at baseline, and weight change since age 35.

[§] HR denotes hazard ratio; CI denotes confidence interval.

** Ref denotes reference group.

Table 4

Associations of parity and lactation patterns with incident clinical fractures *

Predictor	Univariate model [†]		Multivariable-adjusted model [‡]	
	HR (95% CI) [§]	p	HR (95% CI)	p
Parity characteristics				
# pregnancies lasting >6 months		0.02		0.14
Never pregnant	Reference ^{**} (1.00)		Reference (1.00)	
Never had term pregnancy lasting ≥ 6 months	0.81 (0.59–1.12)		0.69 (0.43–1.09)	
1	1.03 (0.84–1.25)		1.22 (0.96–1.55)	
2	0.87 (0.74–1.03)		1.01 (0.83–1.23)	
3	0.89 (0.76–1.05)		0.94 (0.77–1.16)	
4	0.92 (0.77–1.10)		0.97 (0.78–1.21)	
5+	1.10 (0.92–1.32)		1.00 (0.80–1.25)	
How many times pregnant		0.20		0.78
None	Reference (1.00)		Reference (1.00)	
1	1.00 (0.81–1.24)		1.17 (0.91–1.51)	
2	0.93 (0.79–1.10)		1.03 (0.84–1.27)	
3	0.86 (0.73–1.02)		0.97 (0.79–1.19)	
4	0.92 (0.77–1.09)		0.99 (0.80–1.23)	
5	0.93 (0.76–1.13)		0.98 (0.77–1.24)	
6	1.01 (0.81–1.27)		0.92 (0.69–1.23)	
7	0.96 (0.72–1.28)		0.86 (0.60–1.23)	
8+	1.22 (0.95–1.56)		0.98 (0.71–1.35)	
Age at first birth (years)		0.06		0.40
Never pregnant/No pregnancy lasting ≥ 6 months	Reference (1.00)		Reference (1.00)	
<20	0.82 (0.67–0.99)		1.08 (0.84–1.38)	
20 – 29	0.97 (0.85–1.12)		1.02 (0.86–1.22)	
30+	1.09 (0.89–1.32)		1.19 (0.94–1.50)	
Lactation pattern among participants who had been pregnant (n=83,563)				
Breastfed for at least 1 month		0.71		0.51
No	Reference (1.00)		Reference (1.00)	
Yes	1.02(0.92–1.12)		0.96 (0.86–1.08)	
How many children breastfed?		0.38		0.82
None	Reference (1.00)		Reference (1.00)	
1–2	0.99(0.89–1.10)		0.96(0.84–1.09)	
3–5	1.05(0.92–1.19)		0.95(0.81–1.11)	
6+	1.28(0.94–1.76)		1.10(0.74–1.62)	
How old when first breastfed? (years)		0.70		0.69
Never breastfed	Reference (1.00)		Reference (1.00)	

Predictor	Univariate model [†]		Multivariable-adjusted model [‡]	
	HR (95% CI) [§]	p	HR (95% CI)	p
<20	0.97(0.80–1.18)		1.02(0.80–1.30)	
20 – 24	1.03(0.91–1.16)		0.96(0.83–1.11)	
25 – 29	1.02(0.89–1.17)		0.91(0.77–1.08)	
30 – 34	1.13(0.91–1.39)		1.13(0.89–1.44)	
35 – 39	0.85(0.56–1.29)		0.87(0.55–1.40)	
40 – 44	0.22(0.03–1.53)		0.28(0.04–2.02)	
45+	NA		NA	
How old when last breastfed? (years)		0.29		0.91
Never breastfed	Reference (1.00)		Reference (1.00)	
<20	0.92(0.66–1.29)		1.03(0.69–1.56)	
20 – 24	0.99(0.85–1.17)		0.93(0.77–1.14)	
25 – 29	0.94(0.82–1.08)		0.98(0.83–1.16)	
30 – 34	1.07(0.93–1.23)		0.97(0.82–1.15)	
35 – 39	1.04(0.86–1.25)		0.87(0.70–1.09)	
40 – 44	1.39(1.04–1.86)		1.14(0.82–1.60)	
45+	1.50(0.56–4.00)		1.08(0.35–3.36)	
Total number of months breastfed		0.83		0.62
Never breastfed	Reference (1.00)		Reference (1.00)	
1–6	1.03(0.92–1.15)		0.96(0.84–1.10)	
7–12	0.98(0.84–1.14)		0.92(0.76–1.11)	
13–23	0.98(0.83–1.17)		0.93(0.76–1.15)	
24+	1.11(0.91–1.36)		1.12(0.88–1.42)	

* Cox proportional hazards regression models were used. Incident clinical fractures were defined as any clinical fracture with the exception of fractures of the fingers and toes, ribs, sternum/chest, skull/face, and cervical vertebrae.

[†] Includes predictor only without any covariates

[‡] Includes the following covariates: age, race/ethnicity, education, smoking status, alcohol consumption, hysterectomy, bilateral oophorectomy, years since menopause, previous fracture age 55+, parental history of fracture, number of falls in the past 12 months, estrogen use, estrogen route of delivery, recency of estrogen use, use of prescription osteoporosis medication, use of aromatase inhibitors, tamoxifen use, antidepressant use, corticosteroid use, proton pump inhibitor use, anti-epileptic use, anti-neoplastic use, thiazolidinedione use, body mass index, total energy expenditure per week from physical activities (log-transformed), total calcium intake (log -transformed), total vitamin D intake (log-transformed) at baseline, and weight change since age 35.

[§] HR denotes hazard ratio; CI denotes confidence interval.

** Ref denotes reference group.