Impact of lifetime lactation on the risk and duration of frequent vasomotor symptoms: A longitudinal dose-response analysis

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Abstract

Objective: To examine the association between lifetime lactation and risk and duration of frequent vasomotor symptoms (VMS).

Design: Prospective cohort.

Setting: USA, 1995-2008.

Sample: 2,356 parous midlife women in the Study of Women's Health Across the Nation.

Methods: Lifetime lactation was defined as the duration of breastfeeding across all births in months. We used generalized estimating equations to analyze risk of frequent VMS and Cox regression to analyze duration of frequent VMS in years.

Main Outcome Measures: Frequent VMS (hot flashes and night sweats) were measured annually for 10 years, defined as occurring ≥6 days in the past 2 weeks.

Results: Overall, 57.1% of women reported hot flashes and 43.0% reported night sweats during follow-up. Lifetime lactation was inversely associated with hot flashes plateauing at 12 months

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of breastfeeding (6 months: adjusted odds ratio [AOR] 0.85, 95% CI 0.75-0.96; 12 months: AOR 0.78, 95% CI 0.65-0.93), and was inversely associated with night sweats in a downward linear fashion (6 months: AOR 0.93, 95% CI 0.81-1.08; 18 months: AOR 0.82, 95% CI 0.67-1.02; 30 months: AOR 0.73, 95% CI 0.56-0.97). Lifetime lactation was associated with shorter duration of hot flashes and night sweats in a quadratic (bell-shaped) fashion. The association was strongest at 12-18 months of breastfeeding and significant for hot flashes (6 months: adjusted hazard ratio [AHR] 1.35, 95% CI 1.11-1.65; 18 months: AHR 1.54, 95% CI 1.16-2.03; 30 months: AHR 1.18, 95% CI 0.83-1.68).

Conclusions: Longer lifetime lactation is associated with decreased risk and duration of frequent VMS.

Tweetable Abstract:

Longer lifetime #breastfeeding is associated with decreased risk and duration of frequent #hotflashes and #nightsweats in midlife.

Keywords

Hot Flashes; Sweating; Menopause; Breast Feeding; Middle Aged; Women's Health; Prospective Studies

INTRODUCTION

Vasomotor symptoms (VMS) of hot flashes and night sweats are hallmark symptoms of menopause. VMS arise from dysfunction in the thermoregulatory system that coordinates the brain and peripheral vasculature regarding target body temperature range.[1] Approximately 80% of women experience VMS during the menopausal transition, of which one third report frequent or bothersome symptoms.[2,3] VMS negatively impact quality of life due to depressive symptoms, disruptions to sleep and daily life activities, and increased healthcare use.[4,5] VMS are associated with higher risk for cardiometabolic diseases, with stronger effects observed when VMS are frequent or prolonged.[6-9] Prevention of VMS through identification of modifiable risk factors is therefore paramount to improve women's midlife health.

Breastfeeding has lasting beneficial effects on women's endocrine and cardiovascular health, which generally operate in a dose-response manner with cumulative breastfeeding duration over the lifetime.[10] Breastfeeding resets the extensive hypermetabolic changes from pregnancy and delays ovulation return through prolactin's suppressive effect on circulating estrogen.[11,12] Most women (>85%) form prenatal intentions to breastfeed for an average of 10-11 months,[13-15] yet earlier than desired breastfeeding cessation is common due to lactation difficulties and inadequate support.[16-18]

Whether breastfeeding influences the menopausal transition has not been comprehensively explored. Existing research suggests that breastfeeding may be protective against early menopause before age 45,[19-21] but has limited influence on age at natural menopause more broadly.[22,23] The possible impact of breastfeeding on VMS has not been investigated; evidence on this relationship would elucidate the value of breastfeeding promotion as a

preventative strategy for VMS. We therefore examined the association between lifetime lactation and the risk and duration of frequent VMS in midlife women.

METHODS

Data Source

We conducted a prospective cohort study using data from the Study of Women's Health Across the Nation (SWAN), a multi-ethnic longitudinal study of 3,302 women.[24] Beginning 1995-1997, women of Asian (Japanese and Chinese), Black, Hispanic, and White race/ethnicity were enrolled across 7 sites (Boston, Chicago, Detroit, Los Angeles, Newark, Pittsburgh, and Oakland). Women were eligible if they were aged 42-52 years, had an intact uterus and at least one ovary, experienced at least one menstrual period and had not used oral contraceptives or hormone replacement therapy (HRT) in the preceding 3 months, and were not pregnant. Data on physical and mental health, reproductive history, lifestyle, social determinants, and biomarkers were collected at baseline and annually for 15 years with clinical interviews, standardized questionnaires, physical examinations, and blood tests. Institutional review boards at each site approved the study protocol and all participants gave written, informed consent.

Analytic Sample

We accessed publicly available data from the baseline and first 10 follow-up visits (up to 2008).[25] We included parous women with complete data on lifetime lactation (n=2,718), excluding those who reported hysterectomy with ovary conservation (n=77) or participated in fewer than 2 follow-up visits (n=285). The analysis for risk of VMS included 2,356 women. The analysis for duration of VMS was restricted to women who reported symptoms at least one during follow-up and were thus at risk for the event of VMS cessation, excluding those who reported surgical menopause (bilateral oophorectomy) before symptom onset or using HRT within 2 years before symptom onset, resulting in 1,096 women for hot flashes and 828 women for night sweats.

Patients and the public were not involved in the development of this secondary analysis study.

Lifetime Lactation Duration

At baseline, women answered retrospective questions on gravidity and breastfeeding duration in months for each live birth, with 0 representing no initiation of breastfeeding or breastfeeding for less than 1 month. We defined lifetime lactation as the sum of breastfeeding durations across all births, truncated at the 90th percentile (30 months) to reduce the influence of extreme values.[26]

Vasomotor Symptoms

At baseline and annual follow-up visits, women answered standardized questions on the frequency with which they experienced hot flashes and night sweats in the preceding 2 weeks: not at all, 1-5 days, 6-8 days, 9-13 days, or daily. We derived variables for hot flashes and night sweats separately, given their differential risk factors and effects on women's

quality of life.[4,27] Frequent VMS were defined as those occurring 6 days in the past 2 weeks. Duration of VMS was defined as years elapsed between the visit dates of first and last report of VMS. VMS cessation was defined as two consecutive visits without HRT use or frequent VMS.[28,29] To account for VMS reported at a single visit, we added a random standard normal deviate to the total duration for all observations. This technique was used instead of uniformly adding 0.5 years,[28,29] to reduce the number of ties at 0.5 years duration.

Covariates

In order to estimate the total effect of lifetime lactation on VMS risk and duration (i.e., through all potentially causal pathways), we included potential confounders, but not mediators, as covariates;[30] these included education, race/ethnicity, parity, smoking, and body mass index (BMI).[31-36] Covariates were measured at baseline using questionnaires and clinical interviews. Educational level (college degree, less than college degree), race/ethnicity (Asian, Black, Hispanic, White), parity (1, 2, 3, 4+), and smoking (past/never, current) were self-reported. Height and weight were measured using standardized protocols to calculate BMI (kg/m^2). Menopause was staged annually using self-reported bleeding patterns and surgical history (premenopausal, perimenopausal, natural postmenopausal, or surgical postmenopausal).

Statistical Analysis

For the association between lifetime lactation and risk of frequent VMS, we used generalized estimating equations (GEE) for binary repeated measures with an unstructured correlation structure to estimate odds ratios (OR) and 95% confidence intervals (CI). Models were separately constructed for hot flashes and night sweats. Lifetime lactation is often modelled as a continuous linear variable or reduced from its full distribution to categories of 3, 6, or 12-month intervals. These approaches may improve coefficient interpretability, but are often statistically inefficient and can distort the true relationship.[37] To use all available data and permit flexible modelling of the relationships under study, we modelled lifetime lactation continuously using a restricted cubic spline with 3 knots at the recommended 10th, 50th, and 90th percentiles of the sample (Table S1).[26] Multivariable models controlled for race/ethnicity, parity, smoking, education, and BMI as time-fixed covariates, and age as a time-varying covariate. Recognizing the sociodemographic barriers to HRT access and variability in how HRT use is handled in epidemiological analyses of VMS,[38,39] our main analysis included visits where HRT use was reported to produce results reflective of the real world population average association between lifetime lactation and risk of frequent VMS.[40]

We conducted three sensitivity analyses for the GEE models. First, we censored (excluded) visits where HRT use was reported. Second, we restricted to women with a parity of 2 (the largest category). Third, we adjusted for menopause stage as a time-varying covariate.

For the association between lifetime lactation and duration of frequent VMS, we used Cox proportional hazards regression to estimate hazard ratios (HR) and 95% CIs. Models were constructed separately for hot flashes and night sweats and lifetime lactation was modelled using a restricted cubic spline with 3 knots (Table S1). The event was cessation of frequent VMS. An HR>1 indicated shorter duration of VMS compared to the reference group,

which was lifetime lactation of 0 months. Women who did not experience VMS cessation were right censored at last completed study visit where frequent VMS were reported, HRT initiation, or end of follow-up, whichever came first. We additionally right censored women who experienced surgical menopause. Multivariable models controlled for race/ethnicity, parity, smoking, education, BMI, and age at first report of VMS as time-fixed covariates. Proportional hazards were assessed using smoothed plots and statistical tests of Schoenfeld residuals, time-by-covariate interactions, and log-log plots. Both models were stratified on race/ethnicity and adjusted for BMI categorized as under/normal weight (24.9 kg/m^2), overweight (25.0-29.9 kg/m^2), or obese (30 kg/m^2), and models for night sweats were additionally stratified on education, given evidence of non-proportional hazards for these covariates.

Using the adjusted model, we calculated the predicted survival functions across all lifetime lactation values for a fixed covariate profile representing the average SWAN participant.[26] From these functions, we plotted the median duration of frequent VMS according to lifetime lactation to support clinical interpretation of HRs.

Lastly, we conducted four sensitivity analyses for the Cox models. First, we used age as the underlying time scale.[41] Second, we restricted to women with a parity of 2. Third, we adjusted for menopause stage at first report of VMS. Fourth, we used a competing risks framework to account for HRT. A competing risk is an event whose occurrence precludes the occurrence of the event of interest; in this setting, HRT use precludes naturally occurring VMS cessation and may be more appropriately modelled as a competing risk than through right-censoring. To explore this, we used Fine and Gray's proportional subdistribution hazards model to estimate the subhazard ratio (SHR) and 95% CI, specifying HRT use within 2 years of the last report of VMS as a competing risk.

OR and HR results with a 95% CI that did not include the null value of 1 were considered statistically significant. All data cleaning and analyses were conducted in Stata MP V17.

RESULTS

Sample Characteristics

One third of women reported 0 months of lifetime lactation. Among those who reported 1 month of breastfeeding, the median lifetime lactation was 11 months (interquartile range, 4-22). Demographic and health gradients across lifetime lactation were evident for most characteristics, except for parity and HRT use (Table 1). Women with longer lifetime lactation were slightly more likely to be premenopausal at the end of follow-up. The proportions of women who reported never/past smoking, a college degree, and self-identified as White were higher in longer lactation groups, whereas the proportion with baseline obesity decreased. Overall, 57.1% of women (n = 1,346) reported frequent hot flashes and 43.0% (n = 1,012) reported frequent night sweats during follow-up.

Lifetime Lactation and Risk of Frequent VMS

Prevalence of hot flashes generally decreased as lifetime lactation increased (Table 1), with the highest prevalence in the 0 month group (61.4%, n = 489) and the lowest prevalence

in the 18-23 month group (41.8%, n = 59). In the GEE models, lifetime lactation was associated frequent hot flashes in a non-linear fashion (Figure 1). This association was attenuated toward the null following adjustment for covariates, but remained statistically significant across nearly all lifetime lactation values. Compared to 0 months of lactation, duration of lifetime lactation was inversely associated with odds of hot flashes up to approximately 12 months after which we observed a plateau (6 months: AOR 0.85, 95% CI 0.75-0.96; 12 months: AOR 0.78, 95% CI 0.65-0.93).

Prevalence of night sweats generally decreased as lifetime lactation increased (Table 1), with the highest prevalence in the 0 month group (48.2%, n = 384) and the lowest prevalence in the 18-23 month group (32.6%, n = 46). In the GEE models, lifetime lactation was associated with frequent night sweats in a linear fashion (Figure 2). This association was attenuated toward the null following adjustment for covariates; 95% CIs shifted to enclose the null for lifetime lactation values at 1 through 18 months, however the downward trend remained intact. Compared to 0 months of lactation, duration of lifetime lactation was inversely associated with odds of night sweats (6 months: AOR 0.93, 95% CI 0.81-1.08; 18 months: AOR 0.82, 95% CI 0.67-1.02; 30 months: AOR 0.73, 95% CI 0.56-0.97).

Results were robust to sensitivity analyses censoring visits with HRT, adjusting for menopause stage, and restricting to women with a parity of 2 (Figure S1 and S2).

Lifetime Lactation and Frequent VMS Duration

In the Cox models, lifetime lactation was associated with duration of frequent hot flashes in a quadratic (bell-shaped) fashion (Figure 3). This association was unchanged following adjustment for covariates. Compared to 0 months of lactation, duration of lactation was associated with shorter duration of hot flashes up to approximately 12 months where we observed a plateau until 18 months, followed by a decrease in the magnitude of this association trending towards the null (6 months: AHR 1.35, 95% CI 1.11-1.65; 18 months: AHR 1.54, 95% CI 1.16-2.03; 30 months: AHR 1.18, 95% CI 0.83-1.68). Median duration of frequent hot flashes for the average participant was 6.6 years at 0 months of lactation, which decreased as lifetime lactation increased to as low as 4.5 years at 8 through 20 months of lactation (Figure S3).

Lifetime lactation was associated with duration of frequent night sweats in a similar quadratic (bell-shaped) fashion (Figure 4). This association was attenuated following adjustment for covariates; 95% CIs shifted to enclose the null for lifetime lactation values at 1 through 20 months, however the bell-shaped trend remained intact. Compared to 0 months of lactation, duration of lactation was associated with shorter duration of night sweats up to approximately 12 months where we observed a plateau until 18 months, followed by a decrease in the magnitude of this association trending towards (and reaching) the null; at no point was this association statistically significant (6 months: AHR 1.19, 95% CI 0.93-1.52; 18 months: AHR 1.22, 95% CI 0.88-1.68; 30 months: AHR 1.01, 95% CI 0.66-1.55). Median duration of frequent night sweats for the average participant was 4.3 years at 0 months of lactation, which decreased as lifetime lactation increased to as low as 3.5 years at 4 through 24 months of lactation (Figure S4).

Results were robust to sensitivity analyses using age as the time scale, restricting to women with a parity of 2, adjusting for menopause stage at first report of VMS, and using a subdistribution hazards model to account for competing risks from HRT (Figures S5 and S6). Of note, the association between lifetime lactation and duration of night sweats was statistically significant at 1 through 18 months in the subdistribution hazards model (6 months: SHR 1.28, 95% CI 1.01-1.61; 12 months: SHR 1.40, 95% CI 1.03-1.91; 18 months: SHR 1.38, 95% CI 1.01-1.87).

DISCUSSION

Main Findings

In this longitudinal dose-response analysis of the SWAN cohort, we found that lifetime lactation may be modestly protective against frequent VMS during midlife. While the shape of this association varied by VMS type, it was generally observed that longer lifetime lactation was linked to reduced likelihood of frequent hot flashes and night sweats. Women with lifetime lactation around 12 months had roughly 20% lower relative odds of both VMS types after adjusting for demographic and lifestyle factors. Among women who experienced frequent VMS, lifetime lactation was associated with VMS duration in a bell-shaped fashion with the shortest duration of hot flashes and night sweats observed at 12 to 18 months of lactation. This association remained significant for hot flashes, but not night sweats, after adjustment. On average, women reporting lifetime lactation between approximately 6 to 20 months experienced a 2.1-year reduction in hot flash duration and 0.8- year reduction in night sweat duration across 10 years of prospective follow-up. Lactation-related reductions in risk and duration of frequent VMS were similar in magnitude to those observed for other lifestyle and behavioural factors, such as smoking and obesity, that are emphasized for VMS prevention in clinical practice guidelines.[42]

While benefits of breastfeeding for maternal cardiometabolic health and cancer risk are widely acknowledged,[10,43] evidence related to menopausal health is limited. Findings from a recent comprehensive review on risk factors for VMS suggest that breastfeeding has been overlooked entirely to date.[44] Our study addressed this knowledge gap by demonstrating a clinically important reduction in risk and duration of frequent VMS with cumulative months of lifetime lactation and highlights a potential role for breastfeeding promotion in primary prevention of VMS.

Strengths and Limitations

A key limitation is the possibility that our results are attributable to confounding. Breastfeeding behaviours are highly socially patterned due to structural socioeconomic barriers and cultural factors. For example, Black American women report the lowest breastfeeding rates among any racial group,[31] and nuanced barriers to breastfeeding include historical trauma related to wet nursing during slavery as well as inadequate and racially biased healthcare support.[45] Breastfeeding disparities have also been observed in women with low socioeconomic status.[46-48] VMS vary across these demographic groups and according to lifestyle behaviours such as smoking.[36,44] We controlled for race/ethnicity, education, smoking, parity, and BMI at study baseline, and lactation effects were attenuated

but not eliminated. However, these characteristics can change over the life course and may have differed during the reproductive years, resulting in some residual confounding.

We lacked data on birth spacing, oral contraceptive use, and breastfeeding intensity. Breastfeeding can continue during conception of a subsequent pregnancy and initiation of oral contraceptives following birth, and can vary in intensity from exclusive in the first 6 months to partial breastfeeding up to 2 years and beyond; all of which markedly influence reproductive hormones and maternal physiology. Unmeasured confounding from these factors could explain the non-linear relationships we observed, specifically the plateauing or attenuation of effects with longer lifetime lactation.

Breastfeeding was measured through retrospective self-report. Recall of breastfeeding duration is generally valid and reliable several decades after birth,[49,50] yet recall bias or memory error is possible. SWAN participants lost to follow-up have tended to be less healthy, smokers, less educated, or self-identify as Black or Hispanic.[51] This may have given rise to selection bias since these factors are associated with shorter breastfeeding duration and higher risk of VMS, in which case we under-estimated the true association; however, we adjusted for several of these factors.[52] For women who reported VMS at the first or last study visit, exact start and end dates of VMS are unknown thus our estimates of median duration are likely conservative.

Finally, we acknowledge statistical limitations pertaining to precision and type 1 error. The 95% CIs we observed ranged from a null or very small protective effect to a large protective effect, and larger replication studies are needed to determine the true effect size for the impact of lifetime lactation on frequent VMS with greater precision. Given the large number of models and point estimates reported in our main and sensitivity analyses, it is possible that some significant results are attributable to type 1 error.

Interpretation

The pathophysiology of VMS is not well understood. Leading hypotheses describe how declining estrogen levels around menopause narrow the thermoneutral zone and interfere with peripheral vasculature response to body temperature fluctuations.[53,54] Increasing evidence has highlighted a group of hypothalamic neurons–kisspeptin, neurokinin B and dynorphin (KNDy neurons)–which hypertrophy with waning levels of estrogen and gonadotropins and contribute to the generation of VMS.[55-57] Importantly, gradual cessation of VMS suggests that the thermoregulatory system eventually adapts to menopausal changes and restores normal function.

Our results showed that duration of lifetime lactation could have a significant and positive impact on the female body's capacity to adapt to midlife changes in the thermoneutral zone. Lactation bears similarities to menopause in that both are hypoestrogenic states. During lactation, high levels of prolactin exert an antagonistic effect on estrogen production,[12] and women have reported hypoestrogenic symptoms like VMS and vaginal dryness during the early postpartum.[58,59] It is possible that breastfeeding acclimates the thermoregulatory system and KNDy neurons to uncharacteristically low levels of estrogen in advance of menopause, which renders a more robust adaptation to similar circumstances during midlife.

Lactation also facilitates sustained improvements in vascular function and anthropometry. Midlife women who breastfed exhibit better subclinical vascular health and lower BMI than women who did not, even after accounting for cardiovascular and social risk factors.[60,61] These differences are thought to partly underpin the dose-response reductions in cardiovascular morbidity observed in women who have breastfed.[43,62] Breastfeeding may therefore improve vascular reactivity in the context of thermoregulation, reducing the onset and persistence of VMS in midlife. Additional studies on the impact of lactation and hypoestrogenic exposures on VMS and that explore mediation through vascular and anthropometric health markers would help corroborate these interpretations.

CONCLUSIONS

Breastfeeding is associated with reduced risk and duration of frequent VMS in midlife. Protective effects were strongest around 12 months of lifetime lactation and were pronounced for hot flashes. VMS are a significant concern for women with far-reaching impacts on quality of life and health service use, thus primary prevention strategies are needed. Scaling up healthcare policies and practices shown to improve population breastfeeding rates may help reduce the burden of VMS.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

FUNDING

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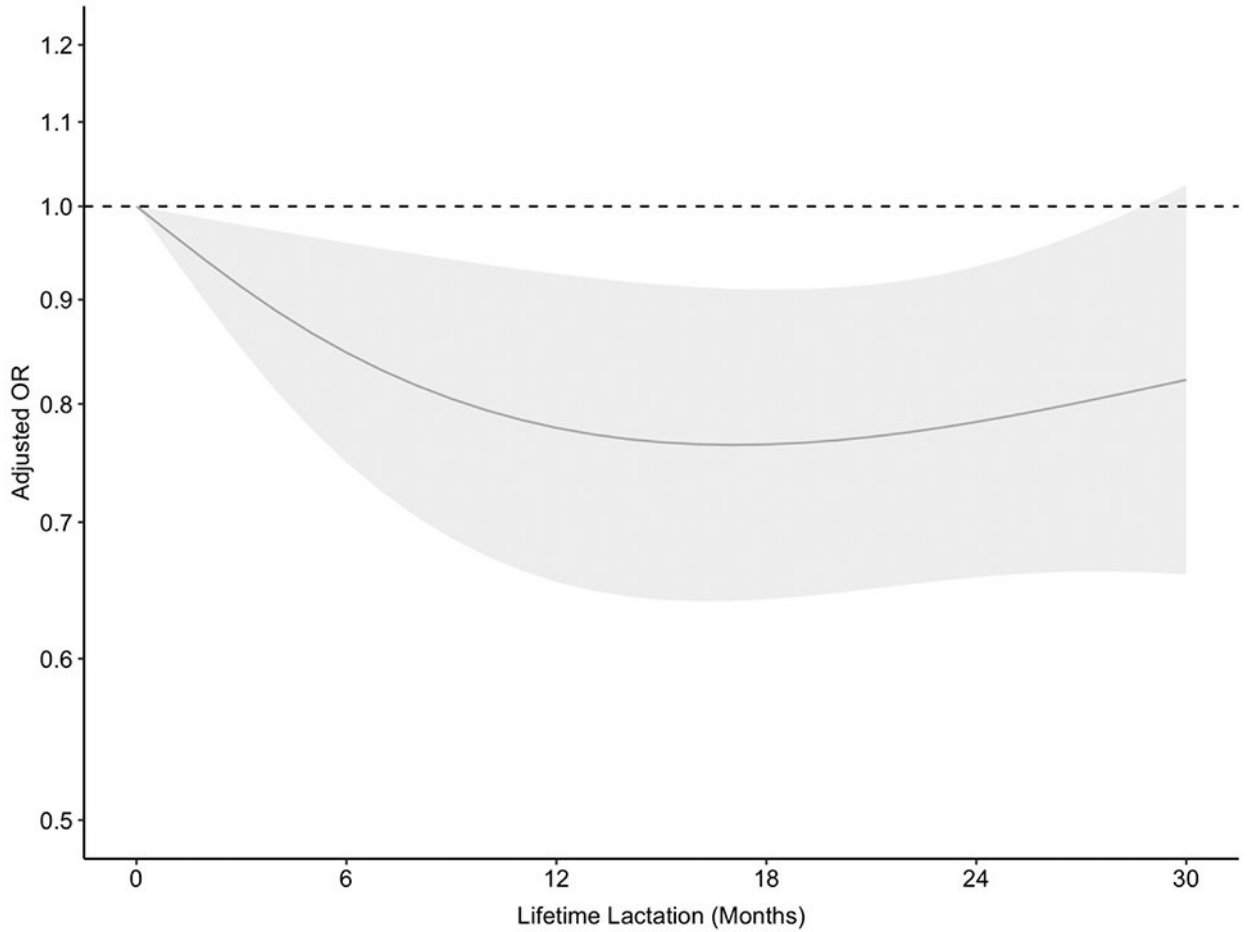| Lactation (Months)	6	12	18	24	30
Crude OR 95% CI	0.70 (0.62-0.79)	0.58 (0.49-0.69)	0.54 (0.46-0.64)	0.55 (0.47-0.65)	0.59 (0.48-0.72)
Adjusted OR 95% CI	0.85 (0.75-0.96)	0.78 (0.65-0.93)	0.76 (0.64-0.91)	0.78 (0.66-0.93)	0.82 (0.66-1.02)

Figure 1.

Association of lifetime lactation and frequent hot flashes [Caption: OR, odds ratio. CI, confidence interval. Adjusted models controlled for education, race/ethnicity, parity, smoking, and body mass index at baseline as time-fixed covariates, and age as a time-varying covariate.]

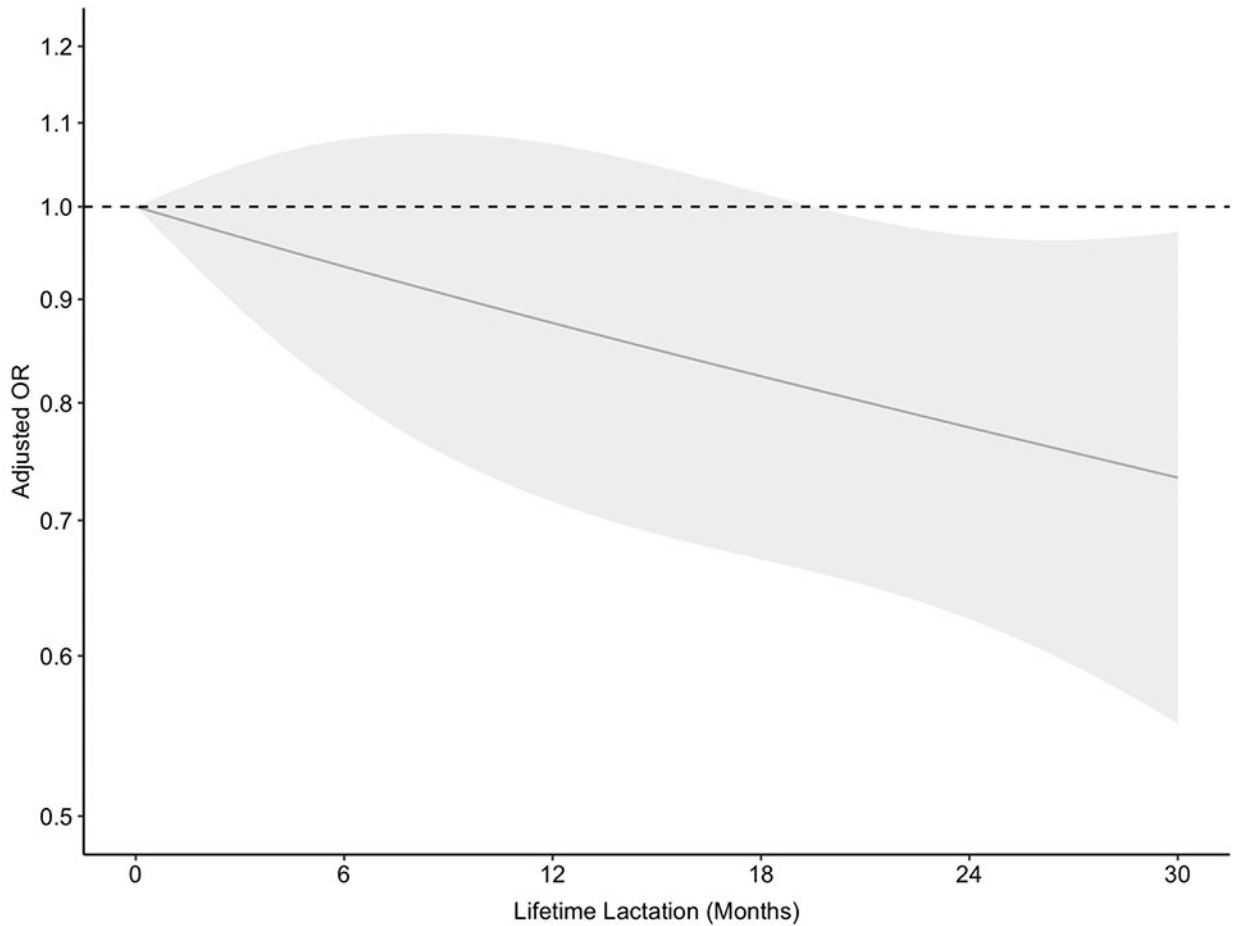| Lactation (Months)	6	12	18	24	30
Crude OR 95% CI	0.74 (0.64-0.86)	0.61 (0.50-0.74)	0.54 (0.45-0.66)	0.51 (0.42-0.62)	0.50 (0.38-0.64)
Adjusted OR 95% CI	0.93 (0.81-1.08)	0.88 (0.71-1.07)	0.82 (0.67-1.02)	0.78 (0.63-0.97)	0.73 (0.56-0.97)

Figure 2.
Association of lifetime lactation and frequent night sweats [Caption: OR, odds ratio. CI, confidence interval. Adjusted models controlled for education, race/ethnicity, parity, smoking, and body mass index at baseline as time-fixed covariates, and age as a time-varying covariate.]

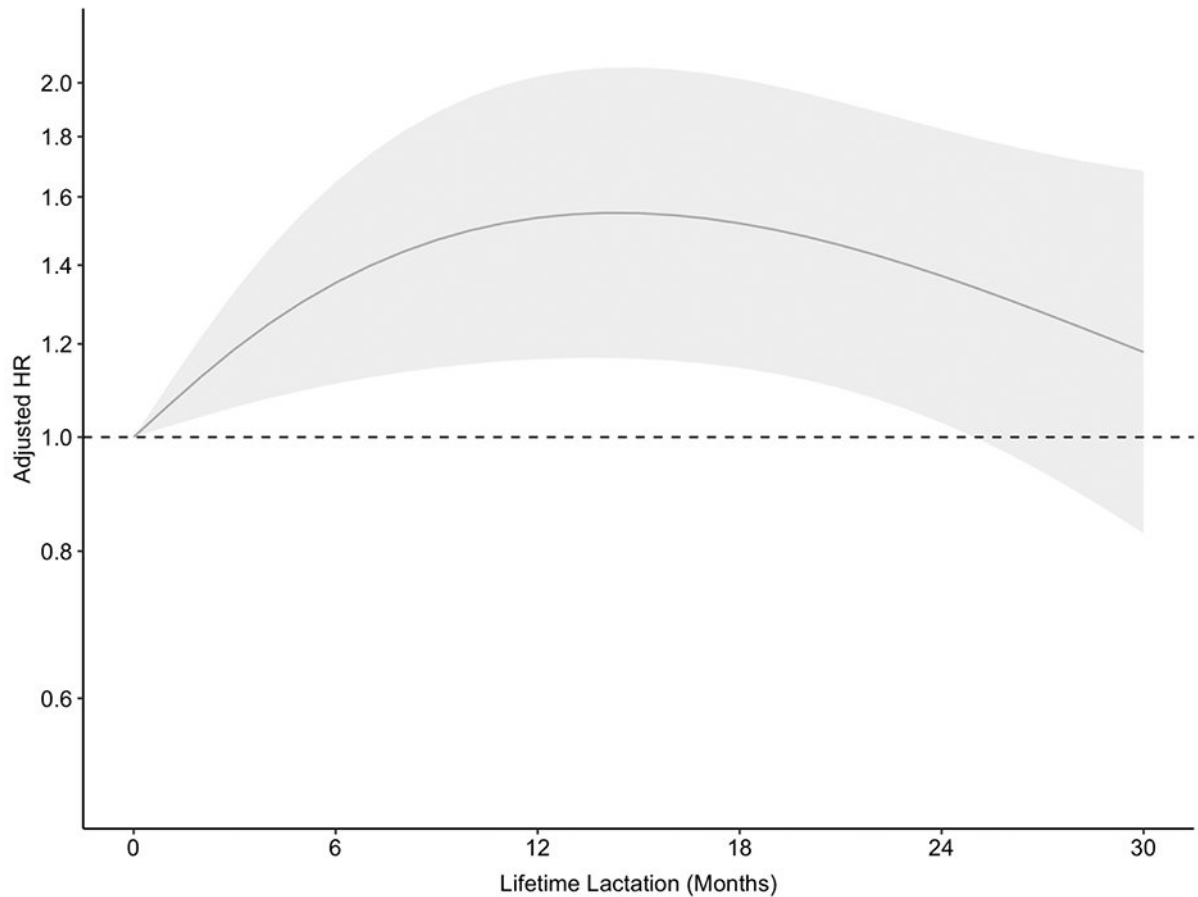| Lactation (Months)	6	12	18	24	30
Crude HR **95% CI**	1.44 (1.20-1.73)	1.67 (1.29-2.15)	1.62 (1.26-2.09)	1.40 (1.09-1.81)	1.15 (0.84-1.58)
Adjusted HR **95% CI**	1.35 (1.11-1.65)	1.54 (1.16-2.03)	1.52 (1.15-2.02)	1.37 (1.03-1.83)	1.18 (0.83-1.68)

Figure 3.

Association of lifetime lactation and duration of frequent hot flashes [Caption: HR, odds ratio. CI, confidence interval. Adjusted models controlled for education, race/ethnicity, parity, smoking, and body mass index at baseline and age at first report of hot flashes. An HR>1 indicated shorter duration of frequent hot flashes compared to the reference group, which was lifetime lactation of 0 months.]

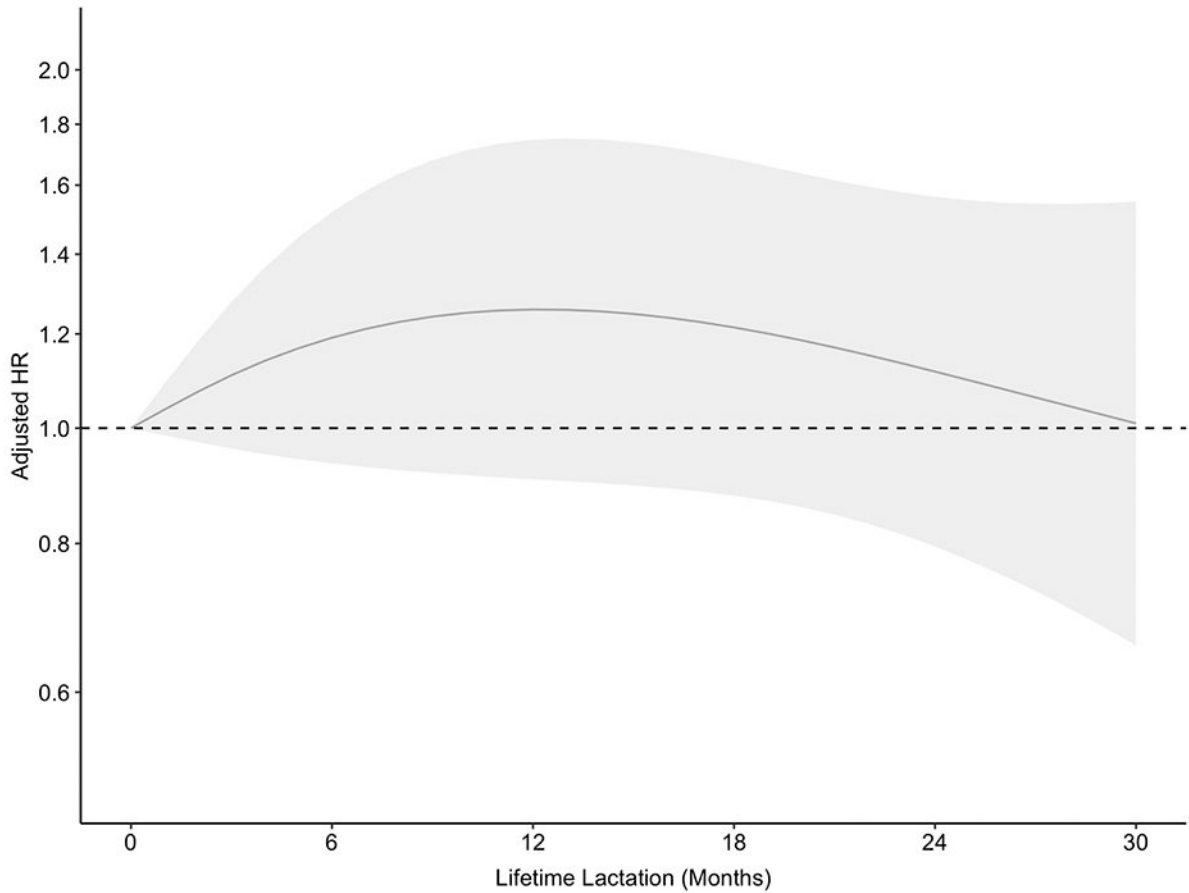| Lactation (Months)	6	12	18	24	30
Crude HR **95% CI**	1.30 (1.04-1.63)	1.43 (1.07-1.93)	1.40 (1.05-1.86)	1.27 (0.95-1.70)	1.13 (0.77-1.65)
Adjusted HR **95% CI**	1.19 (0.93-1.52)	1.26 (0.91-1.75)	1.22 (0.88-1.68)	1.12 (0.80-1.56)	1.01 (0.66-1.55)

Figure 4.

Association of lifetime lactation and duration of frequent night sweats [Caption: HR, odds ratio. CI, confidence interval. Adjusted models controlled for education, race/ethnicity, parity, smoking, and body mass index at baseline and age at first report of night sweats. An HR>1 indicated shorter duration of frequent night sweats compared to the reference group, which was lifetime lactation of 0 months.]

Table 1.

Sample characteristics (N=2,356)

	Lactation 0 months	Lactation 1-5 months	Lactation 6-11 months	Lactation 12-17 months	Lactation 18-23 months	Lactation 24 months
Number of participants, n	797	454	333	253	141	378
Baseline age, median (IQR)	46 (44-48)	46 (44-48)	46 (43-48)	46 (44-48)	46 (44-48)	45 (43-47)
Parity						
1	25.8	30.2	22.8	12.6	5.0	6.6
2	39.0	40.3	51.1	50.2	49.6	29.6
3	21.5	18.3	17.4	24.1	29.1	35.7
4+	13.7	11.2	8.7	13.0	16.3	28.0
Type of menopause						
None (pre-menopausal)	20.5	20.0	25.2	26.1	26.2	26.7
Natural	72.9	74.4	70.3	68.8	70.2	70.6
Surgical	6.6	5.5	4.5	5.1	3.5	2.6
Self-identified race/ethnicity						
Asian	9.5	24.2	20.4	23.3	24.8	19.8
Black	45.8	31.3	23.4	19.0	19.9	13.0
Hispanic	9.0	6.2	8.7	7.5	3.5	6.6
White	35.6	38.3	47.4	50.2	51.8	60.6
Baseline BMI category						
Under/normal weight	29.8	44.3	44.2	44.8	48.9	45.2
Overweight	27.9	25.4	27.9	30.6	24.1	31.1
Obese	42.3	30.3	27.9	24.6	27.0	23.7
Baseline smoking						
Never or past	75.2	82.1	88.9	89.7	90.1	91.0
Current	24.8	17.9	11.1	10.3	9.9	9.0
Educational level						
College degree	22.5	38.2	49.8	50.8	58.3	55.7
Less than college degree	77.5	61.8	50.2	49.2	41.7	44.3
HRT during follow-up	27.2	30.4	33.0	27.7	21.3	29.4

	Lactation 0 months	Lactation 1-5 months	Lactation 6-11 months	Lactation 12-17 months	Lactation 18-23 months	Lactation 24 months
VMS during follow-up						
Frequent hot flashes	61.4	63.0	58.9	51.0	41.8	49.5
Frequent night sweats	48.2	47.8	42.3	39.1	32.6	33.1

BMI, body mass index. IQR, interquartile range. HRT, hormone replacement therapy. VMS, vasomotor symptoms.