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Association of lifetime lactation and characteristics of menopause: a longitudinal cohort study

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Abstract

Background Lactation has many established benefits for women's long-term health; however, its influence on menopause is less clear. This study investigated the association between lifetime duration of lactation and the timing and type of menopause in midlife women.

Methods We analyzed survey data on 19,783 parous women aged 40 to 65 years at enrollment in the Alberta's Tomorrow Project (2000–2022), a prospective community-based cohort study in Alberta, Canada. Duration of lifetime lactation across all births was categorized as: <1 month (reference group; 19.8% of women), 1–3 months (12.1%), 4–6 months (11.7%), 7–12 months (18.8%), and ≥ 13 months (37.7%). Women were classified as premenopause, natural menopause (age at 1 year after the final menstrual period), surgical menopause (age at bilateral oophorectomy), or indeterminate menopause (age at premenopausal hysterectomy with ovarian preservation). Flexible parametric survival analysis and multinomial logistic regression were used to analyze menopause timing and type, respectively, according to lactation status and controlling for birth year, education, parity, hormonal contraceptive use, and smoking.

Results In a dose-response manner, longer lactation was associated with reduced risk of natural menopause before age 50 (for ≥ 13 months of lactation, adjusted hazard ratio at age 45: 0.68, 95% CI 0.59–0.78), surgical menopause before age 55 (age 45: 0.56, 0.50–0.63), and indeterminate menopause before age 50 (age 45: 0.75, 0.69–0.82). Longer lactation was associated with lower odds of surgical (adjusted odds ratio 0.54, 95% CI 0.45–0.66) and indeterminate menopause (0.63, 0.55–0.73), compared to natural menopause.

Conclusions Optimizing the timing of natural menopause and reducing risks of early surgical and indeterminate menopause may be novel maternal benefits of breastfeeding.

Keywords Breastfeeding, Menopause, Oophorectomy, Hysterectomy, Childbirth, Longitudinal study, Alberta's Tomorrow Project

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Background

Breastfeeding has positive life course effects on maternal health. Cumulative duration of lactation is associated with lowered risk of cardiometabolic disease [1, 2] and reproductive cancers [3, 4], generally in an inverse dose-response manner. Women's health benefits of breastfeeding are thought to be facilitated by the distinct endocrine profile of lactation and its broader systemic impacts. High prolactin levels inhibit the release of gonadotropins and sex steroid hormones, which modulate several reproductive (e.g., ovulation) and metabolic (e.g., glucose homeostasis) functions [5, 6]. Robust evidence on the lasting impacts of lactation on maternal health can therefore bolster public health promotion of breastfeeding and guide clinical risk stratification of women as they age.

The impact of lifetime lactation duration on menopause is less clear. Menopause demarcates the end of female reproductive function and typically occurs with a final menstrual period in the absence of obvious medical cause between 45 and 58 years, termed natural menopause [7]. Menopause can also be induced medically through removal of the ovaries (oophorectomy) or uterus (hysterectomy).

Given that the female ovarian reserve is fixed at birth, the prevailing "follicle sparing" hypothesis posits that breastfeeding-related changes in endogenous hormones which suppress ovulation and ovarian activity leading to lactational amenorrhea may slow the rate of follicle decline and delay the onset of natural menopause [8–10]. However, studies investigating lactation history among a set of potential factors related to timing of natural menopause have yielded mixed findings [11–19]. Recent prospective studies on lactation as a primary exposure suggest its influence on natural menopause may change as women age; lifetime duration of lactation appears to be associated with reduced risk of early natural menopause before age 45 [20], but not with differences in menopausal timing more broadly (i.e., 45 to 60 years) [21]. These contrasting findings signify a need for evidence on the possible time-varying impact of lactation history across the full continuum of natural menopause and aging. There is also a lack of evidence on medical types of menopause, despite biological pathways between lactation and estrogen-sensitive gynecologic conditions such as endometriosis [22], adenomyosis [23], and uterine fibroids [24] that are frequently treated with oophorectomy or hysterectomy. We sought to generate this evidence by investigating the association between lifetime duration of lactation and the timing and type of menopause in midlife women using a flexible survival analysis approach.

Methods

Study sample

We conducted a secondary analysis of the Alberta's Tomorrow Project (ATP), a province-wide prospective cohort study investigating chronic disease etiology [25]. In total, 52,810 English-speaking Albertans ($n=34,950$ females) aged 35–69 years with no cancer history were recruited in two phases: two-stage telephone random digit dialing mapped to regional health authorities (2000–2009); and volunteer sampling through targeted communication and advocacy strategies (2009–2015). Comprehensive health and demographic data were collected through standardized questionnaires approximately every 3–5 years with response rates of 70–80%; questionnaires can be found at https://myatpresearch.ca/survey-questions/. For this analysis, we used self-report data from all questionnaires completed by August 2022, representing a median of 2 study contacts (interquartile range 2 to 4 contacts) and 6 years of follow-up (interquartile range 2.7 to 10.7 years) over midlife and beyond per participant. The ATP Study was approved by the Health Research Ethics Board of Alberta at Alberta Innovates (HREBA.CC-17-0461 and HREBA.CC-17-0494) and all participants provided written informed consent. This secondary analysis of ATP data was approved by the Conjoint Health Research Ethics Board at the University of Calgary (REB22-0742) in accordance with the Canadian Tri-Council Policy Statement on Ethical Conduct for Research Involving Humans.

We included parous females aged 40–65 years at baseline who provided data on lifetime lactation duration and menopausal status, excluding those who were pregnant at baseline, reported an extreme age at menopause (≤35 or >65 years) or unspecified menopause type, or were missing covariate data (Fig. 1).

Measures

Lifetime lactation duration, defined as the total number of months spent breastfeeding across all live births, was self-reported retrospectively at baseline and categorized into: not at all or <1 month (reference group), 1–3 months, 4–6 months, 7–12 months, and ≥13 months.

Menopause characteristics were measured at baseline and each follow-up through self-report of final menstrual period, hysterectomy, or oophorectomy. We defined menopause type as: premenopause; natural menopause from a final menstrual period with no medical cause; surgical menopause induced through bilateral oophorectomy; indeterminate menopause from a final menstrual period induced through hysterectomy, whereby loss of menstruation with ovarian preservation renders the clinical timing of menopause inconclusive. We defined timing of natural menopause as age at one full year after the

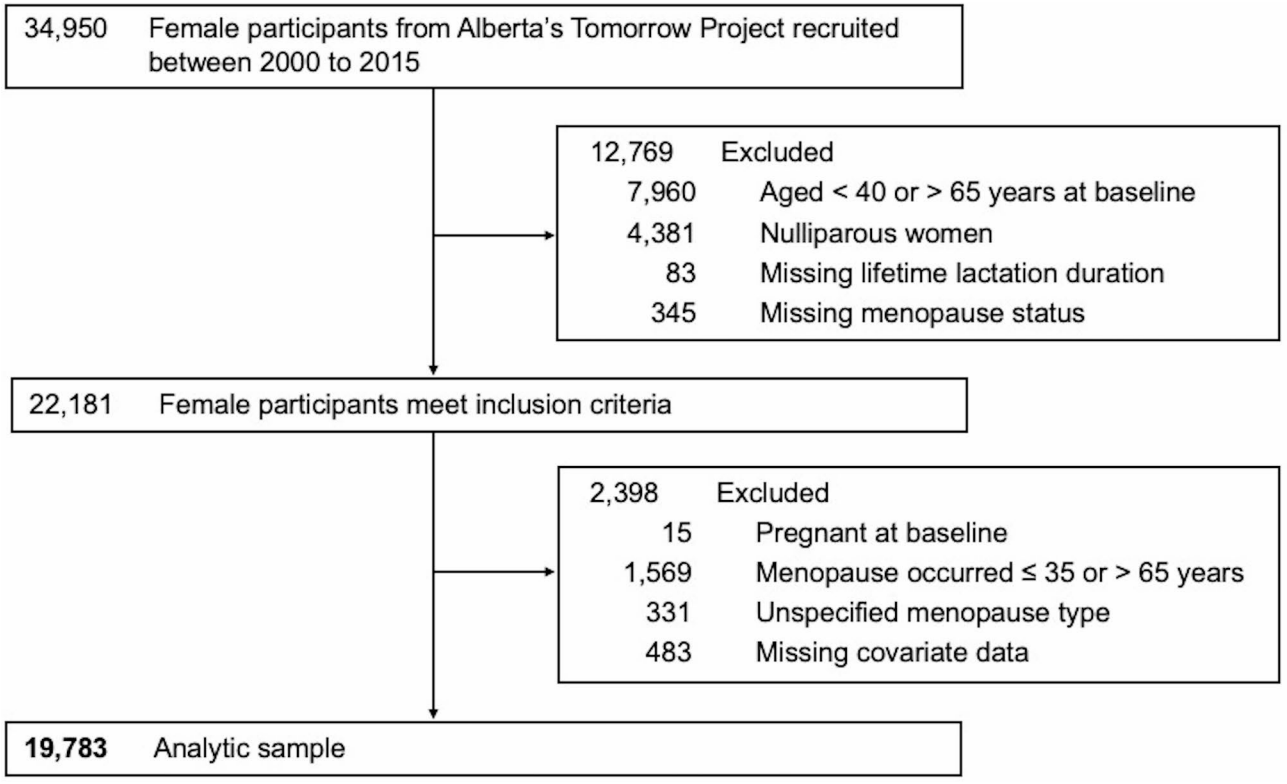

Fig. 1 Flow diagram of included female participants from Alberta's Tomorrow Project

final menstrual period; and surgical and indeterminate menopause as age at surgery.

To estimate the total effect of lifetime lactation on timing of menopause, covariates were selected based on known or suspected associations with lactation duration [26–28] and timing of menopause (including gynecologic indications for iatrogenic menopause) [29–33], based on dataset availability, and using measurements at baseline and thus as proximal to the childbearing years as possible to represent potential confounding variables as opposed to mediating (pathway) variables. Demographic characteristics were participant year of birth and highest level of education. Health-related factors were parity, lifetime duration of hormonal contraceptive use, past or current smoking, body mass index (BMI), and physician-diagnosed diabetes, cardiovascular disease (including hypertension), and autoimmune disease. Menopausal hormone therapy (MHT) was measured at baseline and most follow-up contacts and defined as lifetime use and timing of initiation relative to menopause.

Statistical analysis

We analyzed the association between lifetime lactation duration and timing of menopause using flexible parametric survival analysis. We modelled menopause type-specific hazards to account for competing risks given that menopause can only occur from one cause [34]. With age as the underlying time scale, person-time at risk was counted in years from age 35 to age at menopause or censoring due to the earliest of end of study follow-up, attrition, occurrence of a competing menopause type, or reaching either age 65 for natural menopause or age 60 for surgical or indeterminate menopause (owing to small event counts thereafter). We allowed this association to vary over time using restricted cubic splines with 4 degrees of freedom (3 internal knots) for the baseline hazard and 1 degree of freedom (no internal knots) for the effect of lactation. First, we estimated cumulative incidence functions with simulation-based 95% confidence intervals (CIs) [35]. Next, we estimated hazard ratios (HRs) and 95% CIs for earlier menopause, unadjusted and then adjusted for birth year, education, parity, duration of hormonal contraceptive use, and smoking to represent the total effect of lactation on menopause (i.e., controlling for confounding but inclusive of potential mediating pathways). An HR greater than 1 indicated earlier menopause in the group of interest (1–3, 4–6, 7–12, or ≥13 months) compared to the reference group (<1 month) among those who were still premenopausal up to a given time point. To aid with interpretation of natural menopause HRs, we calculated the predicted age at natural menopause for participants in each lactation group using the adjusted survival model and plotted these values; this approach was not feasible for surgical

or indeterminate menopause due to heavy censoring of natural menopause as a competing risk.

Among women who experienced menopause between 35 and 65 years, we analyzed the association between lifetime lactation duration and type of menopause using multinomial logistic regression, with natural menopause as the reference outcome group. We estimated odds ratios (ORs) and 95% CIs, unadjusted and adjusted for birth year, education, parity, duration of hormonal contraceptive use, and smoking.

We conducted five sensitivity analyses. First, we explored whether associations differed when restricted to women with 2 births (the largest parity group) to distinguish the effects of lactation from that of underlying number of births. Second, we accounted for the potential influence of MHT use prior to menopause by adding premenopausal MHT as a censoring event for the survival models and excluding women reporting premenopausal MHT from the multinomial models. Third, we further adjusted for baseline BMI and chronic medical conditions, which may have represented potential mediators (i.e., causal pathway variables that are influenced by lactation and in turn influence menopause timing) instead of confounders in the associations studied depending on each woman's health trajectory and age at enrollment. Fourth, we explored potential reverse causation, wherein a shorter reproductive window given early onset of menopause could have systematically reduced lifetime lactation duration, by restricting to women who experienced menopause > 40 years, at which point most parous women have completed childbearing [36]. Fifth, for survival models only, we accounted for potential informative censoring using stabilized inverse probability of censoring weights estimated using exposure and covariate data [37, 38].

Data were cleaned in Stata MP version 17 and analyzed and visualized in R version 4.2.2 [39, 40].

Results

We analyzed 19,783 females aged 40–65 at ATP Study baseline (Fig. 1). For lifetime lactation duration, 19.8% of women reported < 1 month, 12.1% reported 1–3 months, 11.7% reported 4–6 months, 18.8% reported 7–12 months, and 37.7% reported ≥ 13 months. Demographic and health gradients across lifetime lactation were evident for most characteristics (Table 1). A later year of birth, university or post-graduate degree, higher order parity, and never smoking were more frequent in longer lactation groups. Conversely, mean BMI was lower and chronic medical conditions and MHT were less frequent in longer lactation groups.

By study end, 74.8% of women experienced menopause; natural menopause was most common (57.4%), followed by indeterminate (12.1%) and surgical menopause (5.4%). For age at natural menopause, there was a positive gradient with higher cumulative incidence curves among longer lactation groups and noticeable separation amongst curves beginning at age 55 (Fig. 2). Conversely, for age at surgical and indeterminate menopause, there was a negative gradient with lower cumulative incidence curves among longer lactation groups and noticeable separation amongst curves across nearly all ages (Fig. 2).

Longer lifetime lactation was associated with timing of natural, surgical, and indeterminate menopause in crude and adjusted models; associations were dose-response in nature, reflected by increasing magnitude with longer lactation, and varied over time based on underlying age. For natural menopause (Fig. 3, Supplemental Table S1), adjusted HR curves displayed a positive slope beginning at 4–6 months of lactation that traversed the null around ages 50 to 55 and steepened with longer lifetime lactation. For example, adjusted HRs for ≥ 13 months of lactation indicated that risk of natural menopause was lower between ages 35 to 50 (age 45: 0.68, 95% CI 0.59–0.78), similar between ages 50 to 55 (age 55: 1.11, 95% CI 0.98–1.24), and elevated between ages 55 to 65 (age 60: 1.48, 95% CI 1.26–1.73), compared to < 1 month of lactation. The distributions of predicted mean age at natural menopause from the adjusted survival model were indeed centered at slightly older ages and had less variability with longer lifetime lactation (Supplemental Figure S1). For surgical menopause (Fig. 4, Supplemental Table S1), the adjusted HR curve at 1–3 months of lactation was fairly flat and showed a protective effect (age 50: 0.71, 95% CI 0.61–0.80), whereas the adjusted HR curves from 4 to 6 months of lactation onward displayed a positive slope that enclosed the null around age 52 and steepened with longer lifetime lactation. Adjusted HRs for ≥ 13 months of lactation indicated that risk of surgical menopause was lower risk between ages 35 to 55 (age 45: 0.56, 95% CI 0.50–0.63) and similar between ages 55 to 60 (age 55: 0.82, 95% CI 0.63–1.04), compared to < 1 month of lactation. For indeterminate menopause (Fig. 5, Supplemental Table S1), the adjusted HR curve at 1–3 months of lactation was fairly flat and showed a null effect (age 50: 1.03, 95% CI 0.82–1.27), whereas the adjusted HR curves from 4 to 6 months of lactation onward displayed a positive slope that traversed the null around age 50 and steepened with longer lifetime lactation. Adjusted HRs for ≥ 13 months of lactation indicated that risk of indeterminate menopause was lower between ages 35 to 50 (age 45: 0.75, 95% CI 0.69–0.82) and elevated between ages 50 to 60 (age 55: 1.84, 95% CI 1.36–2.72), compared to < 1 month of lactation. However, 95% CI width increased rapidly after age 50.

Among women who experienced menopause, lifetime lactation had an inverse and dose-response association with surgical and indeterminate menopause in crude and

Table 1 Baseline characteristics of Alberta's Tomorrow Project female participants by lifetime lactation duration

Characteristic	Lifetime Lactation Length									
	< 1 month *N* = 3,911		1–3 months *N* = 2,386		4–6 months *N* = 2,307		7–12 months *N* = 3,716		≥ 13 months *N* = 7,463	
	n	%	*n*	%	*n*	%	*n*	%	*n*	%
Birth year										
1930s	97	2.5	59	2.5	35	1.5	34	0.9	52	0.7
1940s	1403	35.9	628	26.3	528	22.9	553	14.9	759	10.2
1950s	1711	43.7	1068	44.8	1093	47.4	1779	47.9	3494	46.8
1960s	666	17.0	568	23.8	587	25.4	1207	32.5	2730	36.6
1970s	34	0.9	63	2.6	64	2.8	143	3.8	428	5.7
Age at baseline, mean (SD)	54.2	(6.7)	52.9	(6.9)	52.8	(7.0)	51.6	(6.7)	50.7	(6.6)
Education										
High school or less	2275	58.2	1125	47.2	949	41.1	1249	33.6	2013	27.0
College degree	1062	27.2	766	32.1	730	31.6	1212	32.6	2143	28.7
University degree	431	11.0	371	15.5	456	19.8	942	25.3	2505	33.6
Post-graduate degree	143	3.7	124	5.2	172	7.5	313	8.4	802	10.7
Parity										
1	884	22.6	622	26.1	505	21.9	501	13.5	275	3.7
2	1936	49.5	1115	46.7	1231	53.4	2182	58.7	3231	43.3
≥ 3	1091	27.9	649	27.2	571	24.8	1033	27.8	3957	53.0
Smoking status										
Never	1484	37.9	944	39.6	1039	45.0	1903	51.2	4418	59.2
Former	1661	42.5	1009	42.3	922	40.0	1437	38.7	2514	33.7
Current	766	19.6	433	18.1	346	15.0	376	10.1	531	7.1
Hormonal contraceptive use										
Never used	312	8.0	204	8.5	194	8.4	281	7.6	702	9.4
Ever used	3599	92.0	2182	91.5	2113	91.6	3435	92.4	6761	90.6
Years of use, mean (SD)	6.3	(4.7)	6.8	(5.3)	7.0	(5.3)	7.5	(5.5)	7.1	(5.4)
Body mass index, mean (SD)	28.3	(6.2)	27.9	(6.2)	27.2	(5.6)	26.9	(5.6)	26.3	(5.4)
Chronic medical conditions										
Diabetes	251	6.5	140	5.9	110	4.8	187	5.1	332	4.5
Cardiovascular disease	1280	32.8	673	28.3	556	24.1	803	21.7	1339	18.0
Autoimmune	318	8.2	212	9.0	184	8.0	326	8.8	590	7.9
Menopausal hormone therapy										
Never used	2111	54.0	1383	58.0	1399	60.7	2436	65.6	5287	70.9
Ever used	1798	46.0	1000	42.0	907	39.3	1280	34.4	2174	29.1
Premenopausal initiation	628	34.9	362	36.2	361	39.8	516	40.3	910	41.9
Postmenopausal initiation	814	45.3	448	44.8	414	45.6	608	47.5	1067	49.1
Initiation timing unknown	356	19.8	190	19.0	132	14.6	156	12.2	197	9.1

SD: standard deviation

adjusted models using natural menopause as the reference outcome group (Table 2). For example, ≥ 13 months of lactation was associated with lower odds of surgical (adjusted OR 0.54, 95% CI 0.45–0.66) and indeterminate menopause (adjusted OR 0.63, 95% CI 0.55–0.73) compared to < 1 month of lactation.

Results from the survival (Supplemental Figures S2, S3, S4) and multinomial logistic (Supplemental Table S2) models were robust to sensitivity analyses restricting to women with 2 births, censoring or excluding women at initiation of premenopausal MHT, additionally adjusting for baseline BMI and chronic medical conditions, restricting to women with menopause > 40 years, and inverse probability of censoring weighting. Of note, restricting to women with menopause > 40 years attenuated point estimates and decreased precision for the associations between lifetime lactation and indeterminate menopause.

Discussion

This longitudinal cohort study detected a dose-response and time-dependent relationship between lifetime lactation and menopausal characteristics. Longer lactation was associated with a slight narrowing of the distribution for timing of natural menopause centered around 50 to 55 years. Risk of surgical menopause through

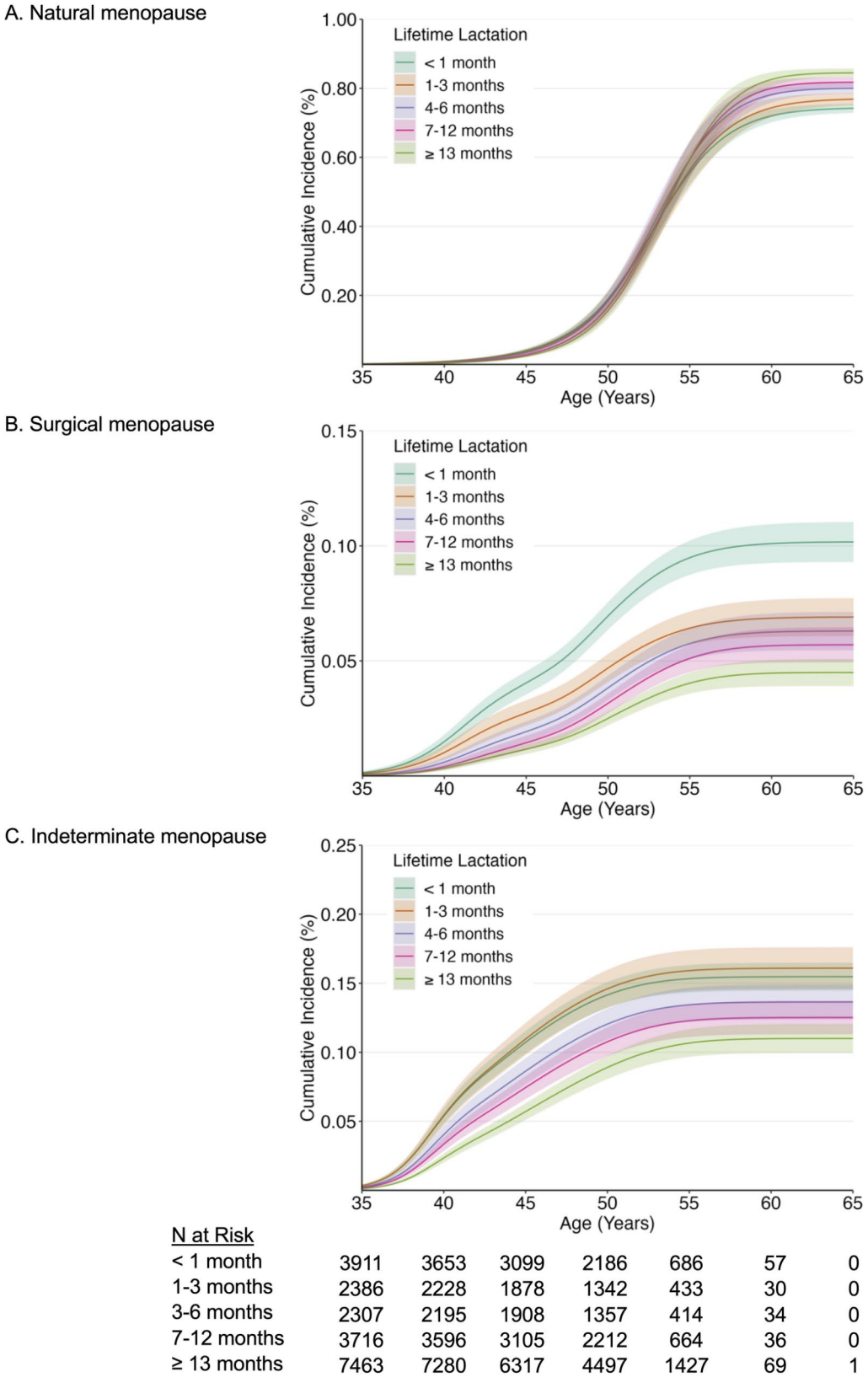

Fig. 2 Cumulative incidence of natural, surgical, and indeterminate menopause by lifetime lactation. Y-axes of panel B and C were re-sized for better visualization. The number of participants at risk at each time point excludes participants who experienced menopause and participants who were censored before menopause

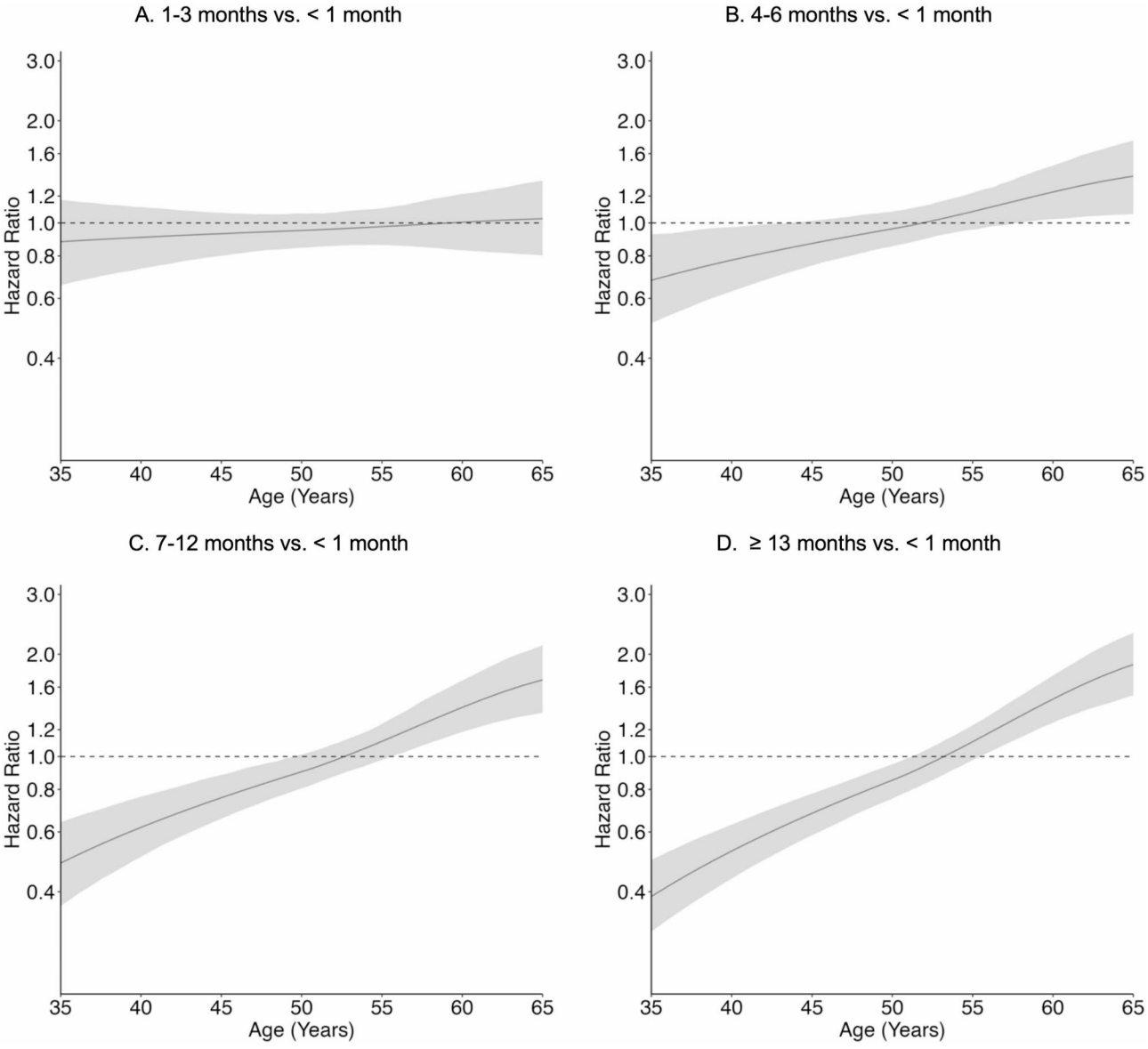

Fig. 3 Adjusted association of lifetime lactation and timing of natural menopause. Models controlled for birth year, education, parity, duration of hormonal contraceptive use, and smoking

bilateral oophorectomy decreased with increasing lactation, particularly before age 55. Longer lactation was also associated with decreased risk of indeterminate menopause through premenopausal hysterectomy with ovarian preservation before age 50 but increased risk of indeterminate menopause thereafter; however, this association was attenuated in sensitivity analysis restricting to menopause after 40 years and may thus have been partly induced through reverse causation. Findings suggest that optimizing the timing of natural menopause to the biological norm of 50 to 55 years and reducing the risk of early surgical and indeterminate menopause may be novel maternal benefits associated with breastfeeding.

Our finding of a time-dependent effect of lactation on natural menopause aligns with existing evidence. An analysis of 2,377 parous women in the Study of Women's Health Across the Nation found no association between lactation duration and timing of natural menopause after controlling for social factors [21], however the study's selection criteria systematically excluded women with early natural menopause (i.e., <45 years) [41]. Conversely, an analysis of 59,388 parous women in the Nurses' Health Study II focused solely on the outcome of early natural menopause and reported that longer lactation was protective [20].

Our work, in conjunction with prior studies [20, 42, 43], do not support the follicle sparing hypothesis as the

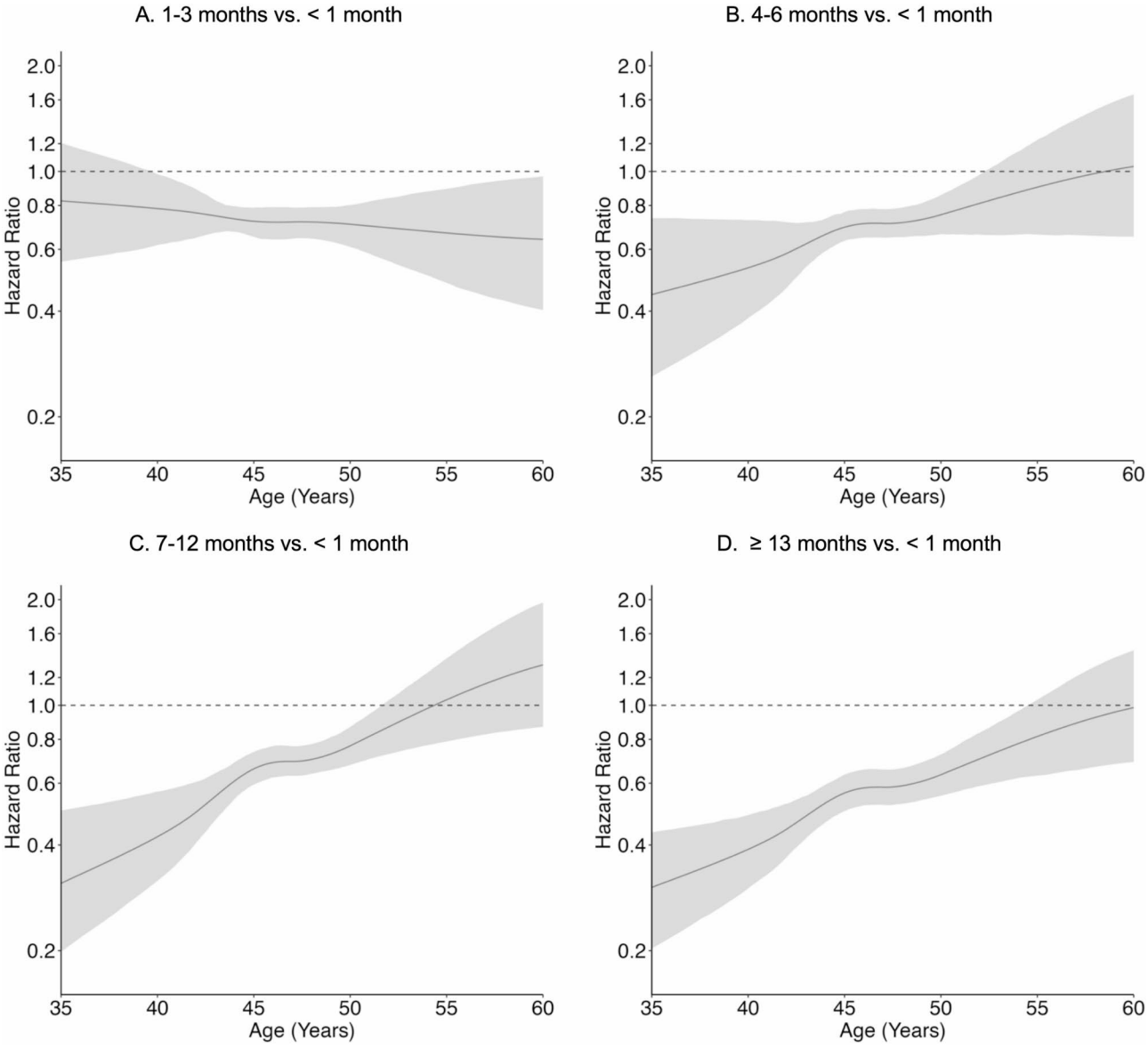

Fig. 4 Adjusted association of lifetime lactation and timing of surgical menopause. Models controlled for birth year, education, parity, duration of hormonal contraceptive use, and smoking

sole mechanism between lactation and natural menopause; there is evidence of a dose-response effect of lactation, but it does not appear unidirectional towards delayed menopause. Rather, our HR curves displayed an intriguing trend wherein longer lactation was associated with a slight narrowing of the distribution for timing of menopause centered around 50 to 55 years. The population mean age of natural menopause at 50 to 53 years is fairly consistent across geographies and generations [7, 44], suggesting a biological norm in the rate of follicular decline underpinned perhaps by genetics or evolution [45–47]. This biological norm is also reflected in epidemiologic data showing that early natural menopause (<45 years) has numerous potential harms, but also that late natural menopause (>55 years) bears risks for breast, uterine, ovarian cancer [29]. It is possible that homeostatic mechanisms exist in the ovaries to permit follicle sparing up to this biological norm, but not thereafter. This would explain the diminishment of effect we observed for lactation around age 50 for natural menopause, which has been similarly observed in studies of other follicle sparing exposures such as parity where effects appear exclusively in relation to early menopause [20, 21, 42, 48]. Future biomedical research is needed to elucidate the precise physiologic impacts of lactation intensity and duration on ovarian activity and explore a potential point of diminished returns on follicle sparing activity. In terms of increased onset of menopause

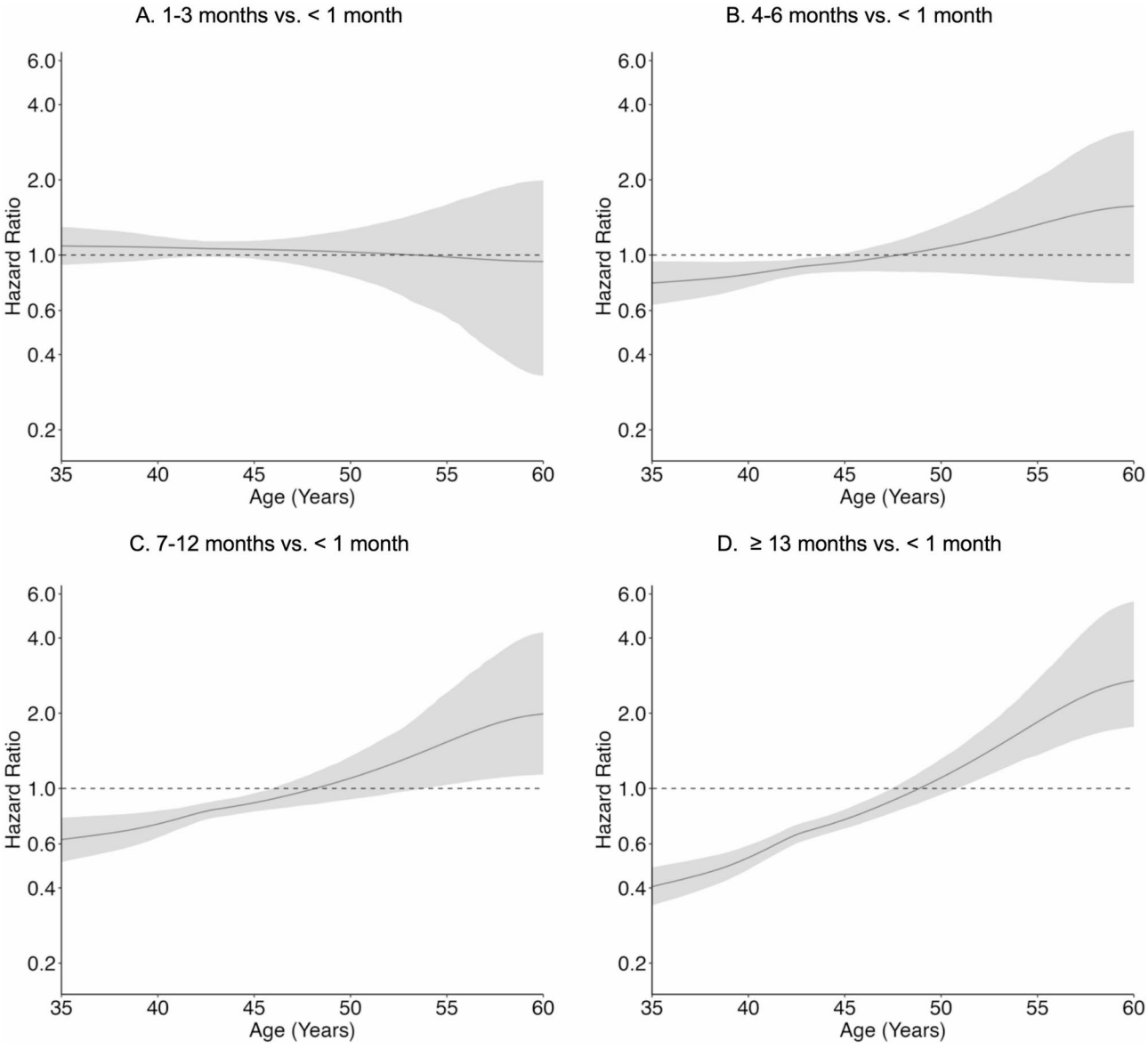

Fig. 5 Adjusted association of lifetime lactation and timing of indeterminate menopause (premenopausal hysterectomy). Models controlled for birth year, education, parity, duration of hormonal contraceptive use, and smoking

after age 50, broader positive health effects of lactation may play a role. Obesity is one of the few known risk factors for late menopause [49, 50] and is less common in women who have longer breastfeeding duration as lactation is bidirectionally associated with lower adiposity [51, 52]. Our findings persisted after controlling for baseline BMI, but residual confounding or mediating effects are possible without longitudinal measurement spanning back to preconception.

To our knowledge, our analysis of lactation in relation to iatrogenic menopause is a novel addition to the literature. Our finding of decreased risks of surgical menopause and premenopausal hysterectomy before age 50 with longer lactation is consistent with evidence showing that lactation is associated with reduced incidence and symptom severity of uterine fibroids and endometriosis [22–24, 53, 54], which are indicated in approximately 20% of bilateral oophorectomies and 60% of hysterectomies in early adulthood [55–57]. Importantly, these data suggest a novel sequelae of lactation-related health benefits for women through reducing early oophorectomy and hysterectomy and their downstream risks of cardiovascular disease and dementia [58–60].

Our finding of increased risk of premenopausal hysterectomy after age 50, albeit partly explained by possible reverse causation, was unexpected and hypothesis-generating on the potential role of lactation in common indications for hysterectomy without oophorectomy after 50

Table 2 Association of lifetime lactation and menopause type among women who experienced menopause

Lifetime Lactation (months)	No. (%) with the outcome					Odds Ratio 95% CI						
	Natural (ref)		Surgical		Indeterminate	Surgical				Indeterminate		
						Crude		Adjusted		Crude		Adjusted
< 1 (Ref)	2281	(70.9)	357	(11.1)	580 (18.0)	1	–	1	–	1	–	1 –
1–3	1362	(72.9)	144	(7.7)	362 (19.4)	0.68	(0.55–0.83)	0.73	(0.60–0.90)	1.05	(0.90–1.21)	1.03 (0.89–1.20)
4–6	1385	(76.8)	124	(6.9)	294 (16.3)	0.57	(0.46–0.71)	0.66	(0.53–0.82)	0.83	(0.71–0.98)	0.85 (0.73–1.00)
7–12	2128	(78.1)	172	(6.3)	426 (15.6)	0.52	(0.43–0.63)	0.64	(0.53–0.79)	0.79	(0.69–0.90)	0.78 (0.68–0.91)
≥ 13	4197	(80.9)	266	(5.1)	725 (14.0)	0.40	(0.34–0.48)	0.54	(0.45–0.66)	0.68	(0.60–0.77)	0.63 (0.55–0.73)

Adjusted models controlled for birth year, education, parity, duration of hormonal contraceptive use, and smoking

years of age. For example, pelvic organ prolapse is indicated in up to 50% of hysterectomies performed at age 50 or older [55, 57, 61], and is an anatomic condition arising from deterioration of pelvic floor muscles and ligaments through pregnancy, birth, aging, and other load-bearing exposures [62]. One possible interpretation is that breastfeeding may interfere with tissue remodelling through supressing estrogen and its regenerative effects on pelvic floor connective tissue [63]. This theoretical mechanism has received limited attention in population research, with only two clinical studies reporting no evidence of an association between breastfeeding and pelvic floor dysfunction though limited by lack of statistical power [64, 65]. Another possible interpretation involves systematic differences in mode of delivery across lactation groups. Compared to Cesarean birth, vaginal birth is associated with fewer breastfeeding difficulties and longer breastfeeding duration [66, 67], but is also a causal factor for pelvic organ prolapse as women age [32]. Future research should revisit the association of lactation and hysterectomy in conjunction with data on clinical indication for this procedure, and explore the underlying roles (if any) of pelvic floor disorders and mode of delivery.

This study has limitations to consider. Data were measured through self-report, with retrospective collection of lactation data and a combination of retrospective and prospection collection of menopause data depending on women's ages at enrollment. Recall of lactation duration and menopause characteristics generally exhibits moderate-to-high accuracy up to 20 years later [68–73], yet the possibility of memory error and thus random misclassification bias cannot be ruled out. Residual confounding is probable given baseline measurement of covariates in midlife, as some characteristics (e.g., education, BMI) are often dynamic and may have differed during the childbearing years. Temporal and cultural changes in breastfeeding determinants, hysterectomy patterns, and opportunistic oophorectomy recommendations are well-documented; [74–76] given that we lacked data on the calendar years a women breastfed and, where applicable, underwent gynecologic procedures, analysis of the impact of historical trends in women's health on reproductive associations could be a valuable area of future inquiry. The ATP Study is largely representative of the Alberta female population; however, unintentionally low sampling from diverse race/ethnic groups and individuals with post-secondary education places some limits on the external validity of results [25].

Conclusion

This cohort study found a dose-response relationship between lifetime lactation and menopause characteristics that is dynamic over the continuum of aging. Longer lactation was associated with delayed onset of

natural menopause before age 50 and quicker onset of natural menopause after age 55, thus concentrating natural menopause during the biological norm of 50 to 55 years. Longer lactation was also associated with reduced risks of early surgical menopause (bilateral oophorectomy) and indeterminate menopause (premenopausal hysterectomy with ovarian preservation) before age 50, with possible evidence of slightly increased risk of indeterminate menopause after age 50. Additional studies are needed to better understand how lactation and associated obstetric and health factors may impact gynecologic physiology, conditions, and surgery rates as women age. Findings suggest that scaling up healthcare policies and practices shown to improve population breastfeeding rates could help optimize the type and timing of menopause women experience in midlife.

Abbreviations

ATP	Alberta's Tomorrow Project
BMI	Body mass index
CI	Confidence interval
HR	Hazard ratio
MHT	Menopausal hormone therapy

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12889-024-20508-7.

Supplementary Material 1

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Author contributions

NVS and EAB conceptualized the study, secured project funding, and obtained project approvals and dataset access from the Alberta's Tomorrow Project team. NVS and BH drafted the analysis plan and conducted the analysis. NVS wrote the initial manuscript draft. MB, HKB, and EAB contributed to data interpretation and critically reviewed the manuscript. All authors approved the final version of the manuscript and submission.

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Data availability

Requests to access the data used in this study can be directed to the Alberta's Tomorrow Project team at ATP.Research@albertahealthservices.ca.

Declarations

Ethics approval and consent to participate

The ATP Study was approved by the Health Research Ethics Board of Alberta at Alberta Innovates (HREBA.CC-17-0461 and HREBA.CC-17-0494). This secondary analysis of ATP data was approved by the Conjoint Health Research Ethics Board at the University of Calgary (REB22-0742).

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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References

1. Tschiderer L, Seekircher L, Kunutsor S, Peters S, O'Keeffe L, Willeit P. Breastfeeding is associated with a reduced maternal cardiovascular risk: systematic review and meta-analysis involving data from 8 studies and 1 192 700 parous women. J Am Heart Assoc. 2022;10:e022746.
2. Rameez RM, Sadana D, Kaur S, Ahmed T, Patel J, Khan MS, et al. Association of maternal lactation with diabetes and hypertension: a systematic review and Meta-analysis. JAMA Netw Open. 2019;2:e1913401.
3. Chowdhury R, Sinha B, Sankar M, Taneja S, Bhandari N, Rollins N, et al. Breastfeeding and maternal health outcomes: a systematic review and meta-analysis. Acta Paediatr. 2015;104(Supplement 467):99–113.
4. Jordan SJ, Na R, Johnatty SE, Wise LA, Adami HO, Brinton LA, et al. Breastfeeding and endometrial cancer risk: an analysis from the epidemiology of endometrial cancer consortium. Obstet Gynecol. 2017;129:1059–67.
5. Strauss J, Barbieri R, Yen. Jaffe's reproductive endocrinology: physiology, pathophysiology, and clinical management. 7th ed. Philadelphia, PA: Elsevier Saunders; 2014.
6. Stuebe AM, Rich-Edwards JW. The reset hypothesis: lactation and maternal metabolism. Am J Perinatol. 2009;26:81–8.
7. InterLACE Study Team. Variations in reproductive events across life: a pooled analysis of data from 505 147 women across 10 countries. Hum Reprod. 2019;34:881–93.
8. McGee EA, Hsueh AJW. Initial and cyclic recruitment of ovarian follicles. Endocr Rev. 2000;21:200–14.
9. Cramer DW, Xu H, Harlow BL. Does incessant ovulation increase risk for early menopause? Am J Obstet Gynecol. 1995;172:568–73.
10. Cramer DW, Xu H. Predicting age at menopause. Maturitas. 1996;23:319–26.
11. Zamaniyan M, Moosazadeh M, Peyvandi S, Jaefari K, Goudarzi R, Moradinazar M, et al. Age of natural menopause and related factors among the Tabari cohort. J Menopausal Med. 2020;26:18.
12. Whelan EA, Sandler DP, Mcconnaughey DR, Weinberg CR. Menstrual and reproductive characteristics and age at natural menopause. Am J Epidemiol. 1990;131:625–32.
13. Dasgupta D, Pal B, Ray S. Factors that discriminate age at menopause: a study of Bengali Hindu women of West Bengal. Am J Hum Biology. 2015;27:710–5.
14. Özdemir O, Çöl M. The age at menopause and associated factors at the health center area in Ankara, Turkey. Maturitas. 2004;49:211–9.
15. Shobeiri F, Nazari M. Age at menopause and its main predictors among Iranian women. Int J Fertil Steril. 2014;8:267–72.
16. Nagel G, Altenburg HP, Nieters A, Boffetta P, Linseisen J. Reproductive and dietary determinants of the age at menopause in EPIC-Heidelberg. Maturitas. 2005;52:337–47.
17. Kaczmarek M. The timing of natural menopause in Poland and associated factors. Maturitas. 2007;57:139–53.
18. Zsakai A, Mascie-Taylor N, Bodzsar EB. Relationship between some indicators of reproductive history, body fatness and the menopausal transition in Hungarian women. J Physiol Anthropol. 2015;34:35.
19. Dvornyk V, Long JR, Liu PY, Zhao LJ, Shen H, Recker RR, et al. Predictive factors for age at menopause in Caucasian females. Maturitas. 2006;54:19–26.
20. Langton CR, Whitcomb BW, Purdue-Smithe AC, Sievert LL, Hankinson SE, Manson JE, et al. Association of parity and breastfeeding with risk of early natural menopause. JAMA Netw Open. 2020;3:e1919615.

21. Scime NV, Shea AK, Faris PD, Brennand EA. Association of lifetime lactation and age at natural menopause: a prospective cohort study. Menopause. 2022;29:1161–7.
22. Farland LV, Eliassen AH, Tamimi RM, Spiegelman D, Michels KB, Missmer SA, et al. History of breast feeding and risk of incident endometriosis: prospective cohort study. BMJ. 2017;358:j3778.
23. Hall MS, Holt VL, Holzman C, Vazquez AI, Harris HR, As-Sanie S, et al. Breastfeeding history and adenomyosis risk using a novel case-control study design. Fertil Steril. 2023;119:644–52.
24. Terry KL, De Vivo I, Hankinson SE, Missmer SA. Reproductive characteristics and risk of uterine leiomyomata. Fertil Steril. 2010;94:2703–7.
25. Ye M, Robson PJ, Eurich DT, Vena JE, Xu JY, Johnson JA. Cohort profile: Alberta's tomorrow project. Int J Epidemiol. 2017;46:1097–l1098.
26. Scime NV, Lee S, Jain M, Metcalfe A, Chaput K. A scoping review of breastfeeding in women with chronic diseases. Breastfeed Med. 2021;16:851–62.
27. Scime NV, Metcalfe A, Nettel-Aguirre A, Tough SC, Chaput KH. Association of prenatal medical risk with breastfeeding outcomes up to 12 months in the all our families community-based birth cohort. Int Breastfeed J. 2021;16:69.
28. Vehling L, Chan D, McGavock J, Becker AB, Subbarao P, Moraes TJ, et al. Exclusive breastfeeding in hospital predicts longer breastfeeding duration in Canada: implications for health equity. Birth. 2018;45:440–9.
29. Gold EB. The timing of the age at which natural menopause occurs. Obstet Gynecol Clin North Am. 2011;38:425–40.
30. Shafrir AL, Farland LV, Shah DK, Harris HR, Kvaskoff M, Zondervan K, et al. Risk for and consequences of endometriosis: a critical epidemiologic review. Best Pract Res Clin Obstet Gynaecol. 2018;51:1–15.
31. Pavone D, Clemenza S, Sorbi F, Fambrini M, Petraglia F. Epidemiology and risk factors of uterine fibroids. Best Pract Res Clin Obstet Gynaecol. 2018;46:3–11.
32. Schulten SFM, Claas-Quax MJ, Weemhoff M, van Eijndhoven HW, van Leijsen SA, Vergeldt TF, et al. Risk factors for primary pelvic organ prolapse and prolapse recurrence: an updated systematic review and meta-analysis. Am J Obstet Gynecol. 2022;227:192–208.
33. Brennand EA, Scime NV, Huang B, McDonagh Hull P. Education level is associated with the occurrence and timing of hysterectomy: a cohort study of Canadian women. Acta Obstet Gynecol Scand. 2024;103:2211-2200.
34. Austin PC, Lee DS, Fine JP. Introduction to the analysis of survival data in the presence of competing risks. Circulation. 2016;133:601–9.
35. Mandel M. Simulation-based confidence intervals for functions with complicated derivatives. Am Stat. 2013;67:76–81.
36. Provencher C, Galbraith N. Statistics Canada. Fertility in Canada, 1921 to 2022. 2024.
37. Cole SR, Hernán MA. Constructing inverse probability weights for marginal structural models. Am J Epidemiol. 2008;168:656–64.
38. Robins JM, Finkelstein DM. Correcting for noncompliance and dependent censoring in an-AIDS clinical trial with inverse probability of censoring weighted (IPCW) log-rank tests. Biometrics. 2000;56:779–88.
39. Jackson CH, Flexsurv. A platform for parametric survival modeling in R. J Stat Softw. 2016;70 Latimer 2013.
40. Ripley B, Venables W. Package Nnet. R Package Version. 2016;7:700.
41. Gold EB, Crawford SL, Avis NE, Crandall CJ, Matthews KA, Waetjen LE, et al. Factors related to age at natural menopause: longitudinal analyses from SWAN. Am J Epidemiol. 2013;178:70–83.
42. Scime NV, Huang B, Brown HK, Brennand EA. Association of parity with the timing and type of menopause: a longitudinal cohort study. Am J Epidemiol. 2024;kwae320.
43. Gottschalk MS, Eskild A, Hofvind S, Bjelland EK. The relation of number of childbirths with age at natural menopause: a population study of 310147 women in Norway. Hum Reprod. 2022;37:333–40.
44. Te Velde ER, Pearson PL. The variability of female reproductive ageing. Hum Reprod Update. 2002;8:141-54.
45. Das A, Destouni A. Novel insights into reproductive ageing and menopause from genomics. Hum Reprod. 2023;38:195–203.
46. Kirkwood T, Austad S. Why do we age? Nature. 2000;408:233–8.
47. Faddy MJ, Gosden RG, Gougeon A, Richardson SJ, Nelson JF. Accelerated disappearance of ovarian follicles in mid-life: implications for forecasting menopause. Hum Reprod. 1992;7:1342–6.
48. Mishra GD, Pandeya N, Dobson AJ, Chung HF, Anderson D, Kuh D, et al. Early menarche, nulliparity and the risk for premature and early natural menopause. Hum Reprod. 2017;32:679–86.
49. Zhu D, Chung HF, Pandeya N, Dobson AJ, Kuh D, Crawford SL, et al. Body mass index and age at natural menopause: an international pooled analysis of 11 prospective studies. Eur J Epidemiol. 2018;33:699–710.
50. Oldfield AL, Vanden Brink H, Carter FE, Jarrett BY, Lujan ME. Obesity is associated with alterations in antral follicle dynamics in eumenorrheic women. Hum Reprod. 2023;38:459–70.
51. Cieśla E, Stochmal E, Głuszek S, Suliga E. Breastfeeding history and the risk of overweight and obesity in middle-aged women. BMC Womens Health. 2021;21.
52. Rasmussen KM. Association of maternal obesity before conception with poor lactation performance. Annu Rev Nutr. 2007;27:103–21.
53. Delli Carpini G, Morini S, Papiccio M, Serri M, Damiani V, Grelloni C, et al. The association between childbirth, breastfeeding, and uterine fibroids: an observational study. Sci Rep. 2019;9:1–8.
54. Porta RP, Sangiuliano C, Cavalli A, Pereira LCHM, Masciullo L, Piacenti I et al. Effects of breastfeeding on endometriosis-related pain: a prospective observational study. Int J Environ Res Public Health. 2021;18.
55. Jacobson G, Shaber R, Armstrong M, Hung Y-Y. Hysterectomy rates for benign indications. Obstet Gynecol. 2006;107:1278–83.
56. Erickson Z, Rocca WA, Smith CY, Gazzuola Rocca L, Stewart EA, Laughlin-Tommaso SK, et al. Time trends in unilateral and bilateral oophorectomy in a geographically defined American population. Obstet Gynecol. 2022;139:724–34.
57. Hakkarainen J, Nevala A, Tomas E, Nieminen K, Malila N, Auranen A. Decreasing trend and changing indications of hysterectomy in Finland. Acta Obstet Gynecol Scand. 2021;100:1722–9.
58. Rocca WA, Grossardt BR, Shuster LT, Stewart EA. Hysterectomy, oophorectomy, estrogen, and the risk of dementia. Neurodegener Dis. 2012;10:175–8.
59. Zhu D, Chung HF, Dobson AJ, Pandeya N, Brunner EJ, Kuh D, et al. Type of menopause, age of menopause and variations in the risk of incident cardiovascular disease: pooled analysis of individual data from 10 international studies. Hum Reprod. 2020;35:1933–43.
60. Ingelsson E, Lundholm C, Johansson ALV, Altman D. Hysterectomy and risk of cardiovascular disease: a population-based cohort study. Eur Heart J. 2011;32:745–50.
61. Jiang J, Ding T, Luo A, Lu Y, Ma D, Wang S. Comparison of surgical indications for hysterectomy by age and approach in 4653 Chinese women. Front Med. 2014;8:464–70.
62. DeLancey JO, Mastrovito S, Masteling M, Horner W, Ashton-Miller JA, Chen L. A unified pelvic floor conceptual model for studying morphological changes with prolapse, age, and parity. Am J Obstet Gynecol. 2023;230:476–e4842.
63. Koelbl H, Halpern-Elenskaia K. Biochemical properties and hormonal receptors of pelvic floor tissues. In: Santoro GA, Wieczorek AP, Sultan AH, editors. Pelvic Floor Disorders. 2nd Edition. Springer Nature; 2021.
64. Lovejoy DA, Roem JL, Blomquist JL, Pandya PR, Handa VL. Breastfeeding and pelvic floor disorders one to two decades after vaginal delivery. Am J Obstet Gynecol. 2019;221:333.e1-333.e8.
65. Shoham I, Baumfeld Y, Yohay Z, Pardo E, Glinter H, Erenberg M, et al. The impact of breastfeeding on pelvic floor recovery from pregnancy and labor. Eur J Obstet Gynecol Reproductive Biology. 2020;251:98–105.
66. Singh J, Scime NV, Chaput KH. Association of Caesarean delivery and breastfeeding difficulties during the delivery hospitalization: a community-based cohort of women and full-term infants in Alberta, Canada. Can J Public Health. 2023;114:104–12.
67. Prior E, Santhakumaran S, Gale C, Philipps LH, Modi N, Hyde MJ. Breastfeeding after cesarean delivery: a systematic review and meta-analysis of world literature. Am J Clin Nutr. 2012;95:1113–35.
68. Olson JE, Shu XO, Ross JA, Pendergrass T, Robison LL. Medical record validation of maternally reported birth characteristics and pregnancy-related events: a report from the children's cancer group. Am J Epidemiol. 1997;145:58–67.
69. Buka SL, Goldstein JM, Spartos E, Tsuang MT. The retrospective measurement of prenatal and perinatal events: accuracy of maternal recall. Schizophr Res. 2004;71:417–26.
70. Rödström K, Bengtsson C, Lissner L, Björkelund C. Reproducibility of self-reported menopause age at the 24-year follow-up of a population study of women in Göteborg, Sweden. Menopause. 2005;12:275–80.
71. Jung AM, Missmer SA, Cramer DW, Ginsburg ES, Terry KL, Vitonis AF, et al. Self-reported infertility diagnoses and treatment history approximately 20 years after fertility treatment initiation. Fertil Res Pract. 2021;7:1–13.
72. Promislow JHE, Gladen BC, Sandler DP. Maternal recall of breastfeeding duration by elderly women. Am J Epidemiol. 2005;161:289–96.
73. Natland ST, Andersen LF, Nilsen TIL, Forsmo S, Jacobsen GW. Maternal recall of breastfeeding duration twenty years after delivery. BMC Med Res Methodol. 2012;12:179.

74. Cusimano MC, Ferguson SE. Contemporary evidence mandates contemporary guidelines: opportunistic oophorectomy at non-malignant hysterectomy. BJOG. 2023;130:141–2.
75. Chen I, Choudhry AJ, Tulandi T. Hysterectomy trends: a Canadian perspective on the past, present, and future. J Obstet Gynaecol Can. 2019;41:S340–2.
76. Wright AL, Schanler RJ. The resurgence of breastfeeding at the end of the second millennium. J Nutr. 2001;131:S421–5.

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