Lactation in Relation to Postmenopausal Breast Cancer

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A modest inverse association between lactation and breast cancer risk has most consistently been observed in premenopausal women, and certain breastfeeding patterns, such as prolonged duration and early age at first lactation, may be important determinants of risk. However, these associations have not generally been observed in relation to postmenopausal breast cancer. As part of a multicenter population-based case-control study, the authors examined postmenopausal breast cancer risk according to breastfeeding characteristics. Breast cancer patients aged 50–79 years were identified from statewide tumor registries in Massachusetts, New Hampshire, and Wisconsin from July 1992 through July 1995. Similarly aged control women were randomly selected from population lists. Information regarding lactation history and breast cancer risk factors was obtained through telephone interviews. This analysis included only data on parous postmenopausal women (3,633 cases and 3,790 controls). After adjustment for age, parity, age at first birth, and other breast cancer risk factors, breastfeeding for at least 2 weeks was associated with a slightly reduced risk of breast cancer in comparison with women who had never lactated (relative risk = 0.87, 95% confidence interval 0.78–0.96). There was only a modest suggestion that increasing cumulative duration of lactation was inversely associated with breast cancer risk; the relative risk for women who had breastfed for ≥24 months was 0.73 (95% confidence interval 0.56–0.94) (p-trend for duration = 0.10). Age at first lactation was not consistently associated with risk. Modest inverse associations appeared to persist even up to 50 years since first lactation. Use of hormones to suppress lactation was not associated with postmenopausal breast cancer, nor was inability to breastfeed related to risk. These results suggest that lactation may have a slight and perhaps long-lasting protective effect on postmenopausal breast cancer risk. Am J Epidemiol 1999;150:174–82.

MATERIALS AND METHODS

Identification of breast cancer cases

All female residents of Wisconsin, Massachusetts (excluding greater Boston), and New Hampshire aged 50–79 years with a new diagnosis of breast cancer reported between January 1992 and December 1994 were eligible for this study. Information on cancer site, histology, extent of disease, demographic factors, and follow-up physician was available from each state’s cancer registry. According to an institutionally approved protocol in each state, the physician of record for each potentially eligible case was contacted by mail for permission to approach the subject. Only cases with listed telephone numbers were considered among contemporary US women of childbearing age (8), such patterns are more common in older US women (9). We used data from a large population-based case-control study to clarify the relations between lactation and breast cancer incidence in postmenopausal US women.
eligible. At interview, cases aged 50–64 years who did not have a driver’s license (as verified by self-report; n = 186), cases aged 65–79 years who were not enrolled in the Medicare program (n = 52), and cases with previous breast cancer (n = 208) were excluded. Of the 6,839 eligible cases, physicians refused contact for 158 (2.3 percent); 293 (4.3 percent) were deceased; 83 (1.2 percent) could not be located; and 620 (9.1 percent) refused to participate. Thus, data for 5,685 women were available for general analysis, for an overall response rate of 83.1 percent. Response rates varied somewhat between the three states (78 percent (n = 1,624) for Massachusetts, 79 percent (n = 595) for New Hampshire, and 87 percent (n = 3,466) for Wisconsin). Of these cases, 98 percent had confirmation of invasive breast carcinoma through histologic or cytopathologic analysis or another means. The median elapsed time between diagnosis and interview was slightly over 1 year.

Identification of population controls

In each state, community controls were randomly selected from two sampling frames: Women aged 50–64 years were selected from lists of licensed drivers, and women aged 65–79 years were selected from a roster of Medicare beneficiaries compiled by the Health Care Financing Administration. Updated computer files of potential controls were obtained annually. Controls were selected at random within age strata to yield an age distribution similar to that of the cases within each state, and had to meet the eligibility criterion of having a listed telephone number. Control women were excluded if they reported a previous diagnosis of breast cancer (n = 311). Of the 7,655 potential controls, 183 had died (2.4 percent), 124 (1.6 percent) could not be located, 1,397 (18.2 percent) refused to participate, and 5,951 completed the study interview. Thus, the overall response rate was 78 percent (70 percent) for Massachusetts, 69 percent (n = 604) for New Hampshire, and 84 percent (n = 3,564) for Wisconsin).

Data collection

Cases and controls were sent letters briefly describing the study before they were contacted by telephone. The 45-minute telephone interview, conducted between July 1992 and July 1995, elicited information on known or suspected risk factors for breast cancer. Questions on breastfeeding were included in the questionnaire from July 1992 through November 1994. The subjects were queried about whether they had ever breastfed any of their children for at least 2 weeks, which child had been breastfed first, the total cumulative duration of lactation, and use of any medication to inhibit lactation. For women interviewed between July 1992 and June 1993, information was also collected on length of lactation for each live birth, number of children breastfed, and reasons for cessation of nursing. The interview also covered exogenous hormone use, physical activity, alcohol-use history, selected dietary elements, height and weight, medical history, and demographic factors. To maintain blinding, information on the woman’s screening practices as well as on her personal and family history of breast cancer was not obtained until the end of the interview. For 87 percent of cases and 96 percent of controls, the interviewer remained unaware of the case/control status of the subject until the end of the interview.

Analysis

Only lactation occurring before an assigned reference date was included in this analysis. For case subjects, this was the date of diagnosis of breast cancer. For control subjects, this was the date that corresponded to the frequency of the cases’ dates of diagnosis within 5-year age strata (on average, this was 1 year prior to interview and varied slightly between study sites).

Lifetime duration of lactation was defined as the cumulative total of the periods of lactation (≥2 weeks) after each live birth. Insufficient milk was defined as an insufficient milk supply within the first 3 months after any of the first three pregnancies.

Age was defined as age at diagnosis (for cases) or age at the reference date (for controls). Parity was the number of full term pregnancies (defined as pregnancies of >6 months’ gestation resulting in live birth or stillbirth). A woman was considered postmenopausal if she reported having undergone natural menopause or a bilateral oophorectomy before the reference date. Women reporting hysterectomy alone were classified as postmenopausal if their reference age was greater than or equal to 55 years, the 90th percentile for age at natural menopause in the control group (among both smokers and nonsmokers). In cases of hysterectomy without bilateral oophorectomy, menopausal status was considered unknown if the woman’s reference age was less than 55 years.

A subject with a mother, sister, or daughter who had had breast cancer was considered to have a positive family history of breast cancer. Recent alcohol consumption was defined as the total number of drinks of beer, wine, and hard liquor consumed per week 5 years before the reference date. Quartiles of body mass index (weight (kg)/height (m)²) at the reference date were calculated on the basis of the distribution of control values.
Odds ratios and 95 percent confidence intervals from logistic regression models were used to estimate relative risks (10). Conditional models stratified according to age and state were used to accommodate the slightly different age distribution of the case subjects and the controls in each state. Multiplicative interactions of lactation (ever/never and total duration) with other risk factors were evaluated by incorporating product terms into multivariate models. Subjects with unknown values for any variables in the multivariate analyses were incorporated as a separate category.

Subjects for analysis

Analysis was restricted to parous postmenopausal women who were interviewed before November 1994 (3,712 cases and 3,930 controls). We excluded six cases with breast cancer and seven controls who could not provide a complete lactation history, and an additional 73 cases and 133 controls with unknown menopausal status. Thus, 3,633 cases and 3,790 controls remained for this analysis.

RESULTS

Compared with the controls, women with breast cancer were more likely to have a first degree relative with breast cancer, older age at first full term pregnancy, lower parity, older age at menopause, greater body mass index, and slightly higher educational attainment (table 1). These variables were therefore included as potential confounders in all regression models, although adjusted estimates differed slightly from estimates adjusted only for age and study site.

Breastfeeding for at least 2 weeks was reported by 47 percent of the women with breast cancer and 48 percent of controls. The multivariate-adjusted relative risk of breast cancer among women who had breastfed for at least 2 weeks compared with those who had never breastfed was 0.87 (95 percent confidence interval 0.78–0.96) (table 2). There was a suggestion that a longer total duration of breastfeeding was inversely associated with risk of breast cancer (p-trend = 0.10); for women reporting having breastfed for 2 or more years, the relative risk was 0.73 (95 percent confidence interval 0.56–0.94). Number of children breastfed and duration of breastfeeding for the first child were not related to risk.

Timing of lactation was not consistently associated with risk, yet all risk estimates were below 1, including several that were significantly reduced (table 3). There were no clear trends in risk by age at first initiation of lactation (p-trend = 0.69). However, since age at first lactation was highly correlated with age at first birth (r = 0.88), it was difficult to distinguish between the effects of these two factors. Years since first lactation was also not related to risk (p-trend = 0.79), although some remote lactation experiences remained inversely associated with risk. For example, the relative risk for women who had first lactated 45–49 years previously was 0.66 (95 percent confidence interval 0.54–0.82).

Age did not appear to modify the association between lactation and risk of breast cancer (table 4), nor did time since menopause or family history of breast cancer. However, there was a suggestion that the weak association between duration of lactation and breast cancer risk was modified by age at first birth, such that women with older age at first birth (≥30 years) had a nonsignificantly greater protection from increasing duration of lactation than women with an early first birth (p for interaction = 0.07). Results were similar when interactions were assessed on the additive scale.

The use of medication to suppress lactation was not associated with risk of postmenopausal breast cancer, regardless of age at first use (table 5). In addition, women who cited insufficient milk supply as the reason for not nursing did not have an increased risk of breast cancer compared with women with a sufficient milk supply, after adjustment for total duration of lactation.

DISCUSSION

In this large study of postmenopausal women, lactation was associated with a very modest reduction in risk of breast cancer. There was a suggestion that certain breastfeeding practices—specifically, longer total duration of lactation—were associated with a slightly greater reduction in risk. The weak inverse association appeared to persist throughout the postmenopausal period.

Overall, for pre- and postmenopausal women combined, the epidemiologic literature does not support a consistent association between lactation and breast cancer risk (7). However, when attention is focused on premenopausal women, a fairly consistent inverse association emerges: Overall, studies suggest a 20–30 percent reduction in risk among women who have ever breastfed (1–6, 11–17). Most consistently, a longer duration of total breastfeeding has been associated with breast cancer risk reductions as great as 40–60 percent (1, 3, 5, 12–15, 18, 19). Recently, age at first lactation has been identified as a possible arbiter of risk, with an earlier age at initiation being associated with a stronger reduction in risk for premenopausal women (11, 19) and possibly for postmenopausal women (17). However, because of the very strong correlation between age at first birth and age at first lacta-
It is notable that in countries with low breast cancer risk, the protection conferred by lactation appears to be stronger and to be sustained throughout the postmenopausal period as well (1–6). For example, in Mexico, Romieu et al. (1) found a relative risk of 0.31 (95 percent confidence interval 0.16–0.57) for lactation of >60 months (an uncommon experience in the US population) in both premenopausal and postmenopausal women. This risk profile may reflect variation in breastfeeding practices—e.g., early lactation,
TABLE 2. Relative risk of postmenopausal breast cancer according to lactation experience among parous breast cancer cases and controls from three US states, 1992–1995

<table>
<thead>
<tr>
<th>Lactation</th>
<th>No. of cases</th>
<th>No. of controls</th>
<th>Relative risk*</th>
<th>95% confidence interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Never lactated†</td>
<td>1,925</td>
<td>1,988</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>Ever lactated</td>
<td>1,708</td>
<td>1,802</td>
<td>0.87</td>
<td>0.78–0.96</td>
</tr>
<tr>
<td>p value</td>
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<td></td>
<td></td>
<td>0.01</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Total duration of lactation (months)</th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;3</td>
<td>719</td>
<td>775</td>
<td>0.89</td>
<td>0.78–1.02</td>
</tr>
<tr>
<td>3–6</td>
<td>322</td>
<td>367</td>
<td>0.77</td>
<td>0.64–0.93</td>
</tr>
<tr>
<td>7–12</td>
<td>305</td>
<td>275</td>
<td>1.06</td>
<td>0.87–1.28</td>
</tr>
<tr>
<td>13–23</td>
<td>175</td>
<td>182</td>
<td>0.81</td>
<td>0.63–1.04</td>
</tr>
<tr>
<td>≥24</td>
<td>151</td>
<td>170</td>
<td>0.73</td>
<td>0.56–0.94</td>
</tr>
<tr>
<td>Continuous‡ (per 3 months)</td>
<td></td>
<td></td>
<td></td>
<td>0.99</td>
</tr>
<tr>
<td>p value</td>
<td></td>
<td></td>
<td></td>
<td>0.01</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Duration of lactation (months) for first child breastfed§</th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Never breastfed†</td>
<td>651</td>
<td>658</td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>&lt;3</td>
<td>297</td>
<td>296</td>
<td>0.98</td>
<td>0.76–1.27</td>
</tr>
<tr>
<td>3–6</td>
<td>166</td>
<td>157</td>
<td>0.84</td>
<td>0.62–1.15</td>
</tr>
<tr>
<td>≥7</td>
<td>98</td>
<td>75</td>
<td>1.05</td>
<td>0.69–1.58</td>
</tr>
<tr>
<td>Continuous‡ (per 3 months)</td>
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<td></td>
<td></td>
<td>1.00</td>
</tr>
<tr>
<td>p value</td>
<td></td>
<td></td>
<td></td>
<td>0.98</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>No. of children breastfed§,$ $</th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>0†</td>
<td>926</td>
<td>844</td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>364</td>
<td>354</td>
<td>0.92</td>
<td>0.74–1.14</td>
</tr>
<tr>
<td>2</td>
<td>221</td>
<td>186</td>
<td>0.99</td>
<td>0.74–1.33</td>
</tr>
<tr>
<td>3</td>
<td>122</td>
<td>96</td>
<td>1.06</td>
<td>0.70–1.59</td>
</tr>
<tr>
<td>≥4</td>
<td>124</td>
<td>122</td>
<td>0.95</td>
<td>0.59–1.50</td>
</tr>
<tr>
<td>Continuous‡ (per one child)</td>
<td></td>
<td></td>
<td></td>
<td>0.98</td>
</tr>
<tr>
<td>p value</td>
<td></td>
<td></td>
<td></td>
<td>0.62</td>
</tr>
</tbody>
</table>

* Adjusted for study site, age, number of births, age at first birth, family history of breast cancer, age at menopause, body mass index, and education.
† Reference category.
‡ Continuous model included women who had never lactated.
§ Data were available for subjects interviewed between July 1992 and June 1993.
¶ Relative risk was also adjusted for duration of lactation.

long duration, and exclusive breastfeeding—but may also reflect different etiologic pathways in these generally low risk populations.

A number of large and well conducted studies have failed to observe a reduction in risk associated with lactation (19–26). In these studies, the association of lactation with breast cancer risk may have been constrained by recent changes in breastfeeding practices among US women. While early and prolonged lactation appears to be most strongly associated with risk, even among women reporting this history, there may be important differences in practice. London (27) noted that "on-demand" breastfeeding is a relatively recent practice and is perhaps more likely to result in deferred ovulation than a regimen of scheduled feedings. At the same time, supplemental use of formula has become more common, and with supplemental foods the return to ovulation is more rapid (28). In a sample of our case and control subjects, we found a modest correlation between duration of lactation and months of postpartum amenorrhea (Spearman's $r = 0.44$ for cases and 0.46 for controls). Thus, depending on the detailed characteristics of breastfeeding, similar total durations of breastfeeding may be qualitatively different and lead to discordant results. In one study, a high proportion of premenopausal women but not postmenopausal women reported employment outside the home during the childbearing years, with substantive differences between the groups in lactation practices (29). In our earlier case-control study (11), an analysis restricted to lifetime homemakers found similar inverse associations in premenopausal and postmenopausal women. This suggests that some specific lactation behaviors, represented in this case
TABLE 3. Relative risk of postmenopausal breast cancer according to age and timing of lactation among parous breast cancer cases and controls from three US states, 1992-1995

<table>
<thead>
<tr>
<th>Age (years) at which subject first breastfed</th>
<th>No. of cases</th>
<th>No. of controls</th>
<th>Relative risk*</th>
<th>95% confidence interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Never breastfed†</td>
<td>1,925</td>
<td>1,988</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>&lt;20</td>
<td>191</td>
<td>243</td>
<td>0.96</td>
<td>0.73-1.27</td>
</tr>
<tr>
<td>20-24</td>
<td>689</td>
<td>766</td>
<td>0.83</td>
<td>0.71-0.96</td>
</tr>
<tr>
<td>25-29</td>
<td>404</td>
<td>415</td>
<td>0.79</td>
<td>0.66-0.96</td>
</tr>
<tr>
<td>≥30</td>
<td>164</td>
<td>146</td>
<td>0.76</td>
<td>0.57-1.01</td>
</tr>
<tr>
<td>Continuous†§</td>
<td></td>
<td></td>
<td>0.99</td>
<td>0.97-1.02</td>
</tr>
<tr>
<td>p-trend</td>
<td></td>
<td></td>
<td>0.69</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Years since subject first breastfed</th>
<th>No. of cases</th>
<th>No. of controls</th>
<th>Relative risk*</th>
<th>95% confidence interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Never breastfed†</td>
<td>1,925</td>
<td>1,988</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>8-29</td>
<td>101</td>
<td>143</td>
<td>0.86</td>
<td>0.63-1.17</td>
</tr>
<tr>
<td>30-34</td>
<td>149</td>
<td>217</td>
<td>0.91</td>
<td>0.71-1.17</td>
</tr>
<tr>
<td>35-39</td>
<td>232</td>
<td>353</td>
<td>0.75</td>
<td>0.61-0.92</td>
</tr>
<tr>
<td>40-44</td>
<td>351</td>
<td>333</td>
<td>0.95</td>
<td>0.79-1.15</td>
</tr>
<tr>
<td>45-49</td>
<td>299</td>
<td>291</td>
<td>0.68</td>
<td>0.54-0.82</td>
</tr>
<tr>
<td>50-65</td>
<td>316</td>
<td>233</td>
<td>0.88</td>
<td>0.69-1.12</td>
</tr>
<tr>
<td>Continuous†‡</td>
<td></td>
<td></td>
<td>1.00</td>
<td>0.99-1.01</td>
</tr>
<tr>
<td>p-trend</td>
<td></td>
<td></td>
<td>0.79</td>
<td></td>
</tr>
</tbody>
</table>

* Adjusted for study site, age, number of births, age at first birth, family history of breast cancer, age at menopause, body mass index, and education. Excludes 260 cases and 232 controls with missing age at first lactation.
† Reference category.
‡ Continuous model included women who had never lactated.
§ With adjustment for all terms except age at first lactation, relative risk = 1.01 (95% confidence interval 1.00-1.03); p = 0.12.

by "homemakers," may be necessary to achieve a protective effect.

It seems unlikely, based upon the results of this study and those from other reports (11, 17, 20, 30), that the apparent protective effect of lactation is attributable to an increased risk among women who are unable to lactate, as first suggested by Byers et al. (13). Furthermore, an increased risk of breast cancer among users of lactation suppressants has not been supported by this study or by several other recent studies (11, 15, 17, 20, 21). Thus, other reasons must be considered as explanations for the inverse association between lactation and breast cancer risk.

Of the several mechanisms proposed for beneficial effects of lactation on breast cancer risk, it remains unclear which best explain the epidemiologic observations. The ovulatory suppression that occurs with prolonged breastfeeding may reduce exposure to the cyclic hormones of reproductive life (31). Indeed, a long duration of lactation appears to be the strongest predictor of breast cancer risk in studies which have found an effect for lactation. However, one study that examined lactational amenorrhea found that lactation per se was more strongly associated with risk than was duration of amenorrhea (20). In addition to lactation's transient effect on ovulation, other hormones and autocrine and paracrine growth factors directly produced by the mammary gland are also germane (32, 33). In particular, there is evidence that transforming growth factor-β, which is expressed during lactation, is a hormonally regulated negative growth factor in human breast cancer cells (34, 35). Behavioral and environmental influences on the expression of these factors may be important because of their relation with oncogenes, proto-oncogenes, and tumor suppressor expression (32). Direct physical changes in the breast that accompany milk production may also contribute to the observed protective effect (12, 36). Having lactated may beneficially affect the relation between the mammary epithelium and the stroma (37, 38). There is some evidence to suggest that breast tissue may be especially sensitive to these lactational changes in early reproductive life (36). Lactating rats and mice have been found to be relatively resistant to the effects of chemical carcinogens, as compared with nonlactating controls (39, 40), reflecting low rates of DNA synthesis during lactation (41, 42) or increased elimination of carcinogens by the secretory mammae (39, 40, 43). Concentrations of toxic organochlorines in human breast milk decrease with increasing cumulative duration of lactation (44). It may be that some of the beneficial effects of lactation wane over time, perhaps explaining the attenuated association in postmenopausal women.
TABLE 4. Relative risk of postmenopausal breast cancer according to selected risk factors and their interaction with lactation among parous breast cancer cases and controls from three US states, 1992–1995

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>No. of cases</th>
<th>No. of controls</th>
<th>Relative risk</th>
<th>95% confidence interval</th>
<th>p for interaction†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Never breastfed‡</td>
<td>1,925</td>
<td>1,988</td>
<td>1.0</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Age (years)

| 50–59               | 278          | 485           | 0.85          | 0.69–1.05               |                  |
| 60–69               | 657          | 741           | 0.94          | 0.80–1.10               |                  |
| 70–79               | 737          | 543           | 0.80          | 0.66–0.96               | 0.99 (0.92)      |

Time (years) since menopause

| <10                 | 250          | 390           | 0.85          | 0.68–1.06               |                  |
| 10–15               | 288          | 340           | 0.99          | 0.78–1.25               |                  |
| 16–24               | 562          | 521           | 0.86          | 0.71–1.04               |                  |
| ≥25                 | 415          | 351           | 0.89          | 0.71–1.12               | 0.64 (0.95)      |

Family history of breast cancer

| Absent             | 1,283        | 1,521         | 0.86          | 0.76–0.96               |                  |
| Present            | 375          | 240           | 0.93          | 0.73–1.19               | 0.51 (0.95)      |

Age (years) at first birth

| <20                 | 264          | 324           | 1.07          | 0.82–1.39               |                  |
| 20–24               | 850          | 915           | 0.87          | 0.75–1.00               |                  |
| 25–29               | 422          | 424           | 0.79          | 0.64–0.96               |                  |
| ≥30                 | 135          | 103           | 0.87          | 0.62–1.22               | 0.41 (0.07)      |

* Adjusted for study site, age, number of births, age at first birth, family history of breast cancer, age at menopause, body mass index, and education.
† Interaction between an indicator of lactation (ever/never) and the risk factor; interaction for duration of lactation is shown in parentheses. Risk factors were evaluated in continuous form, except for family history.
‡ Reference category.

TABLE 5. Relative risk of postmenopausal breast cancer according to milk supply and use of lactation-suppressant hormones among parous breast cancer cases and controls from three US states, 1992–1995

<table>
<thead>
<tr>
<th>Use of lactation-suppressant hormones</th>
<th>No. of cases</th>
<th>No. of controls</th>
<th>Relative risk</th>
<th>95% confidence interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Never use†</td>
<td>2,229</td>
<td>2,103</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>Ever use</td>
<td>1,287</td>
<td>1,583</td>
<td>0.99</td>
<td>0.89–1.11</td>
</tr>
<tr>
<td>Once</td>
<td>475</td>
<td>551</td>
<td>0.97</td>
<td>0.83–1.13</td>
</tr>
<tr>
<td>More than once</td>
<td>812</td>
<td>1,032</td>
<td>1.01</td>
<td>0.88–1.15</td>
</tr>
</tbody>
</table>

Age (years) at first use

| 13–20                               | 116          | 199            | 0.97          | 0.72–1.31               |
| 20–24                               | 570          | 778            | 0.93          | 0.80–1.09               |
| 25–44                                | 596          | 604            | 1.05          | 0.90–1.21               |

Sufficiency of milk supply‡

| Sufficient                         | 331          | 317            | 1.00          |                         |
| Insufficient                       | 354          | 321            | 1.05          | 0.81–1.35               |
| Did not nurse for reasons other than insufficient milk supply | 530 | 540 | 0.91 | 0.72–1.15 |

* Adjusted for study site, age, number of births, age at first birth, family history of breast cancer, age at menopause, body mass index, education, and duration of lactation.
† Reference category.
‡ Determination of sufficiency was limited to women who reported an inadequate milk supply within the first 3 months after the first, second, or third delivery.
It is unlikely that our results are attributable to bias or confounding. The response rates in this study were quite high (83 percent for cases and 78 percent for controls), which suggests that selection bias, if any, would be limited. We relied on the retrospective recall of lactation and other early life experiences; however, reproductive histories tend to be reported with a high degree of validity (45). In our study, we reinterviewed a sample of cases and controls and found that lactation history was reliably recalled (Spearman correlations for ever lactating: \( r = 0.88 \) for cases and \( r = 0.90 \) for controls).

Some postmenopausal women in this large study reported lactation histories of long duration and early initiation. Despite this wide range of experiences, only a very modest association with breast cancer risk was observed, even among extreme categories of lactation experiences. However, this weak protective effect appeared to persist throughout the postmenopausal period. Our results suggest that lactation confers long-lasting benefits with regard to breast cancer risk, over and above childbearing itself.

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