Original Contribution

Tubal Sterilization and Breast Cancer Incidence: Results From the Cancer Prevention Study II Nutrition Cohort and Meta-Analysis

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Tubal sterilization is a common form of contraception in the United States and is hypothesized to be associated with a lower risk of breast cancer. However, prior observational studies have reported inconsistent results. We investigated the association between tubal sterilization and breast cancer risk among 77,249 postmenopausal, cancer-free women in the Cancer Prevention Study II (CPS-II) Nutrition Cohort, enrolled in 21 states in the United States during 1992–1993. During 15 years of follow-up through June 30, 2007, 4,084 invasive breast cancer cases were diagnosed. Multivariable Cox proportional hazard regression was used to estimate hazard ratios and 95% confidence intervals. A meta-analysis including the CPS-II Nutrition Cohort results with other published results from 4 case-control studies and 3 prospective studies was conducted to provide a summary estimate for the association between tubal sterilization and breast cancer risk. In the CPS-II Nutrition Cohort, tubal sterilization was not associated with breast cancer incidence (multivariable-adjusted hazard ratio = 1.08, 95% confidence interval: 0.97, 1.20). Associations stratified by year of tubal sterilization, age, and time since surgery were also null. The meta-analysis also found no association between tubal sterilization and breast cancer risk (odds ratio = 0.97, 95% confidence interval: 0.84, 1.09). Tubal sterilization does not appear to be associated with breast cancer risk.

breast neoplasms; case-control studies; cohort studies; meta-analysis; tubal sterilization

Abbreviations: CI, confidence interval; CPS-II, Cancer Prevention Study II; HR, hazard ratio.

Editor’s note: An invited commentary on this article appears on page 500.

Tubal sterilization, the surgical disruption of the Fallopian tubes, is one of the most common methods of contraception in the United States (1). In US women aged 15–44 years, use of tubal sterilization as a method of birth control increased dramatically from 3.9% in the mid-1960s to 16.2% in 2002 (2, 3). Specifics of the surgical procedure have evolved over time with defined secular trends in the methods for accessing the tubes, occlusion or ligation of the tubes, in the degree of surrounding tissue damage, and possible side effects (4). The Pomeroy ligation technique was the predominant procedure prior to 1970, unipolar electrocautery and the Pomeroy technique were used in the early 1970s, and several other procedures have been used since the mid-1970s (4, 5).

Tubal sterilization has been hypothesized to be associated with a lower risk of breast cancer. However, results from 4 case-control (6–9) and 5 prospective (10–14) studies have been inconsistent. One (14) of the 9 studies on breast cancer and tubal sterilization was conducted in the Cancer Prevention Study II (CPS-II) Mortality Cohort. That study reported the strongest inverse association with tubal sterilization but was the only study among the 9 that used mortality, rather than incidence, as the outcome. Interpretation of these results must be done cautiously because mortality reflects both incidence and survival, which is particularly high for breast cancer, and thus is not useful for the study of etiology. Herein, we report on the association between tubal ligation and breast cancer incidence in the CPS-II
Nutrition Cohort, a subset of the CPS-II Mortality Cohort followed for cancer incidence, and our meta-analysis of published data.

**MATERIALS AND METHODS**

**Description of the CPS-II Nutrition Cohort**

Women in this analysis were drawn from the 97,786 female participants in the CPS-II Nutrition Cohort, a prospective study of cancer incidence and mortality established by the American Cancer Society in 1992–1993 (15) as a subgroup of the 1982 CPS-II Mortality Cohort (16, 17). At enrollment, CPS-II Nutrition Cohort participants resided in the 21 US states with population-based state cancer registries and were 50–74 years of age. In 1982 and 1992–1993, the participants completed a mailed questionnaire on demographic, medical, behavioral, environmental, and occupational factors. Starting in 1997, follow-up questionnaires were sent to cohort members every 2 years to update exposure information and to ascertain newly diagnosed cancer outcomes. Among the participants who received a follow-up questionnaire, the response rates for each follow-up questionnaire through 2005 were at least 91%.

**Population for analysis**

Individuals were excluded from the present analysis if they did not return any follow-up surveys and were alive as of December 31, 1997 (n = 3,122), reported a history of cancer in 1992–1993 (except nonmelanoma skin cancer, n = 13,091), or were premenopausal or did not know their menopausal status and were less than 55 years of age in 1992–1993 (n = 4,259; these women were excluded because tubal sterilization status was not updated after the 1982 questionnaire).

**Breast cancer cases**

Incident breast cancer diagnoses through June 30, 2007, were self-reported on follow-up questionnaires and subsequently verified by obtaining medical records (n = 3,131) or through linkage with state registries when complete medical records could not be obtained (n = 809) (15). A small number of cases (n = 111) were identified during confirmation of another reported cancer diagnosis. Interval deaths between the biennial questionnaires were obtained through automated linkage of the cohort with the National Death Index, in which the death certificate listed breast cancer as a primary or contributory cause of death (International Classification of Diseases, Tenth Revision, codes 174.0–174.9) (n = 33) (18). A self-reported breast cancer diagnosis could not be verified for 65 women who were excluded from the present analysis. Invasive breast cancer was the outcome of interest for these analyses. A total of 4,084 invasive breast cancers were diagnosed among 77,249 women included in the analytical cohort.

**Exposure data**

Details about tubal sterilization were reported on the 1982 CPS-II Mortality Cohort questionnaire that included a table that queried “birth control methods.” “Tubal ligation” was listed as a separate item in the table. Participants were asked to indicate their age when first used and number of years of use [of tubal ligation]. On the basis of these data, we created 5 major tubal sterilization variables. First, we defined women as having or not having a tubal sterilization. Women with tubal sterilizations were defined as “yes” if they reported an age at or years since tubal sterilization. Women who did not respond to the questions about age at or years since tubal sterilization were defined as “no.” Second, we created a calendar year of tubal sterilization by adding age at procedure to the participant’s year of birth and categorized into 3 groups: before 1970, 1970–1974, and 1975 or later. These categories were used in previous papers (10) including the previously reported CPS-II mortality analysis (14), and they approximate the secular trends in tubal sterilization procedures. Third, we calculated women’s age at tubal sterilization, which was categorized as <30, 30–34, 35–39, and ≥40 years. Fourth, reported years since tubal sterilization were categorized as <15, 15–19, 20–24, 25–29, and ≥30 years. Finally, we combined age and year at tubal sterilization and categorized as follows: <35 years and before 1975, <35 years and 1975 or later, ≥35 years and before 1975, and ≥35 years and 1975 or later.

Age at menarche, parity, age at first birth, age at menopause, alcohol intake, smoking status, education, family history of breast cancer in a mother or sister, personal history of breast cysts, body mass index, hysterectomy, oophorectomy, use of postmenopausal hormones, recent mammographic screening, and use of oral contraceptives were reported on the questionnaires in 1982 or 1992–1993. Information on use of mammographic screening and use of postmenopausal hormones was updated in follow-up questionnaires.

**Statistical analyses**

Participants contributed person-time to the analysis until they were censored at the date of diagnosis for those diagnosed with invasive breast cancer (or in situ carcinoma of the breast), date of death for those who died before the end of follow-up, date of last survey returned for those lost to follow-up before the end of follow-up, or June 30, 2007, for those that reached the end of the follow-up period. Multivariable-adjusted Cox proportional hazard regression models (19) were used to calculate hazard ratios and 95% confidence intervals for the associations of tubal sterilization with invasive breast cancer incidence. All models were stratified on exact year of age at enrollment. Multivariable-adjusted models included age at menarche (<12, 12, 13, ≥14 years, missing); parity combined with age at first birth (nulliparous, 1–2 livebirths and ≤25 years at first birth, 1–2 livebirths and 25–29 years at first birth, 1–2 livebirths and ≥30 years at first birth, ≥3 livebirths and ≤25 years at first birth, ≥3 livebirths and 25–29 years at first birth, ≥3 livebirths and ≥30 years at first birth, unknown); age at...
menopause (<50, 50–54, ≥55 years, missing); alcohol intake (never drinker, <1, 1, ≥2 drinks/day, former, missing/unknown); smoking status (never, current, former); education (some high school plus those with missing education, high school graduate, some college, college graduate, missing); family history of breast cancer in mother or sister (yes, no); history of breast cysts (yes, no); body mass index defined as weight (kg)/height (m)² (<18.5, 18.5–24.9, 25.0–29.9, ≥30.0, missing); hysterectomy/oophorectomy (none, uterus only, uterus plus 1 ovary, uterus plus 2 ovaries, 1 ovary only, both ovaries only, uterus plus unknown ovary(ies), unknown); use of postmenopausal hormone therapy (never, current, former, other/ever/missing); use of screening mammography (never or not recent, current, missing); and use of oral contraceptives (never, ever, missing). Use of screening mammography and use of postmenopausal hormones were treated as time-dependent covariates. The Cox proportional hazards assumption was evaluated by testing for an interaction with time in the model; no violations of the assumption were observed. Associations of tubal sterilization with breast cancer incidence were examined for effect modification by parity (0, 1, ≥2 livebirths), hysterectomy (yes, no), and oophorectomy (yes, no), comparing the −2 log likelihood of models with and without interaction terms. Reported P values are 2 sided and were considered statistically significant if P < 0.05. P values for linear trend were calculated on the basis of the median values of the stratum within each variable category treated as an ordinal variable.

To further evaluate the role of exposure misclassification among women who did not report tubal sterilization on the 1982 baseline survey but may have undergone surgery after completion of the survey, we performed sensitivity analyses that excluded women who were premenopausal in 1982 but postmenopausal in 1992–1993.

The aforementioned analyses were conducted by using Statistical Analysis System, version 9.2, software (SAS Institute, Inc., Cary, North Carolina).

**Meta-analysis**

Nine epidemiologic studies investigating the association between tubal sterilization and breast cancer, published in English peer-reviewed journals through September 2011, were identified in PubMed searches and references of identified papers. One article was excluded from the meta-analysis because the results were based on mortality and not incidence (14). A retrospective review of medical records in Ontario, Canada (11), also was excluded because insufficient data were provided. Study-specific crude hazard ratios or odds ratios and the corresponding 95% confidence intervals were abstracted from published results of the remaining 7 studies, as well as our own from the CPS-II Nutrition Cohort (described above). These studies included 4 case-control studies: the Women’s Interview Study of Health (WISH) (8), the Women’s Contraceptive and Reproductive Experiences (CARE) Study (7), a Korean study (9), and the Cancer and Steroid Hormone (CASH) Study (6). The CPS-II Nutrition Cohort and 3 additional studies published from established cohorts also were selected: the Shanghai Women’s Health Study (SWHS) (13), the Royal College of General Practitioners’ Oral Contraceptive Study (RCGPOCS) (12), and the Nurses’ Health Study (NHS) (10).

Summary relative risks and 95% confidence intervals for tubal sterilization (ever compared with never) were calculated by using a random-effects model with each study result weighted by the within- and between-study variances (20). The presence of study heterogeneity was assessed by estimating I² (the proportion of variation in the relative risks attributable to heterogeneity) (21), and publication bias was assessed by the Begg (22) and Egger (23) tests. The meta-analysis statistical analyses were performed with Stata/SE, version 11.0, software (StataCorp LP, College Station, Texas).

**RESULTS**

**CPS-II Nutrition Cohort**

Overall, 8.8% of the study participants had a tubal sterilization (Table 1), which ranged from 2.8% among women born in 1903–1920 to 21.5% among women born in 1941–1952. Of the women who had a tubal sterilization, more than half of the women had the procedure at age 35 years or older and before 1974. Women who had a tubal sterilization were more likely to be younger at enrollment, to have more children, to have their first birth before age 25 years, and to have used oral contraceptives than were women who did not have a tubal sterilization (Table 1).

Tubal sterilization was not associated with risk of invasive breast cancer (Table 2). Multivariable-adjusted estimates did not meaningfully vary from the estimates based on age-adjusted models. In sensitivity analyses, exclusion of women who were premenopausal in 1982 did not appreciably alter results (hazard ratio (HR) = 1.06, 95% confidence interval (CI): 0.89, 1.27). The association between tubal sterilization and breast cancer risk was similar by year of tubal sterilization, age at tubal sterilization, years since tubal sterilization, and by combined age and year at tubal sterilization with no clear linear trend (Table 2).

The associations between tubal sterilization and breast cancer risk were similar for women who had undergone hysterectomy (HR = 1.14, 95% CI: 0.94, 1.39) and for women who did not (HR = 1.03, 95% CI: 0.90, 1.18; Pinteraction = 0.78), as well as for women who had undergone oophorectomy (HR = 1.11, 95% CI: 0.88, 1.40) and for women who had not (HR = 1.07, 95% CI: 0.94, 1.21; Pinteraction = 0.69). Parity also did not modify the association between tubal sterilization and breast cancer risk (nulliparous women: HR = 1.51, 95% CI: 0.70, 3.28; parous women: HR = 1.06, 95% CI: 0.94, 1.18; Pinteraction = 0.37).

**Meta-analysis**

We performed a meta-analysis of the association between tubal sterilization and breast cancer risk that included our study as well as 4 case-control studies and 4 prospective studies. Based on the case-control studies, with a total of 11,548 breast cancer cases and 11,493 controls, the summary estimate for tubal sterilization compared with no tubal sterilization was relative risk = 0.91 (95% CI: 0.64, 1.18) with significant between-study heterogeneity (I² test: Am J Epidemiol. 2013;177(6):492–499
After exclusion of the Korean study that appeared to be an outlier, the relative risk was 1.06 (95% CI: 0.88, 1.25), but the between-study heterogeneity remained statistically significant ($I^2 = 78.8\%$, $P = 0.009$). Based on the prospective studies with 11,569 breast cancer cases in 224,222 participants, the summary relative risk was 1.00 (95% CI: 0.90, 1.10) with no evidence of between-study heterogeneity ($I^2$ test: $P = 0.17$).

The overall summary relative risk for all 9 studies was also null (relative risk = 0.97, 95% CI: 0.84, 1.09); however, there was a lack of homogeneity across the study-specific results ($I^2$ test: $P \leq 0.0001$). No publication bias was evident (Egger’s test: $P = 0.47$; Begg’s test: $P = 0.81$).

**DISCUSSION**

In our study of 4,084 invasive breast cancer cases diagnosed among 77,249 postmenopausal women in the CPS-II...
Nutrition Cohort, tubal sterilization was not associated with invasive breast cancer risk. Similarly, there were no associations with age at tubal sterilization, year of tubal sterilization, and the combined age and year at tubal sterilization. The summary estimate from the accompanying meta-analysis of 8 observational studies, including the CPS-II Nutrition Cohort, also showed no association between tubal sterilization and breast cancer risk.

Results from the CPS-II Nutrition Cohort were consistent with those from the 3 published cohort studies (the Shanghai Women’s Health Study (13), the Royal College of General Practitioners’ Oral Contraceptive Study (12), and the Nurses’ Health Study (10)), and no evidence of between-study heterogeneity was observed (Figure 1). The strength of these studies is their large sample size, the long follow-up time, and the prospective collection of exposure information.

In the CPS-II Nutrition Cohort, we were able to comprehensively control for known and suspected breast cancer risk factors, although adjustment for these factors did not appear to confound the association. In our cohort, tubal sterilization surgeries were not updated over the follow-up period, in which premenopausal women might have undergone surgery after the 1982 questionnaire. To minimize the potential for misclassification bias, we excluded the women who were still premenopausal in 1992–1993 and further excluded the women who went through the menopausal transition between 1982 and 1992–1993 in sensitivity analyses and found no difference in the hazard ratio.

In contrast to the cohort studies, significant between-study heterogeneity was observed among the 4 case-control studies. The Cancer and Steroid Hormone Study, the largest case-control study, reported the strongest positive association between tubal sterilization and breast cancer risk (Figure 1) (6), whereas 2 other large case-control studies (the Women’s Contraceptive and Reproductive Experiences Study (7) and the Women’s Interview Study of Health (8)) found no association. Conversely, a small Korean study reported the strongest inverse association (9). The small sample size of the Korean study (9), which included 155 cases and 204 controls, contributed to some of the heterogeneity observed among the case-control studies. Moreover, inconsistencies among the case-control studies might be due to inherent weaknesses of the study design, such as recall bias and biased selection of controls. In addition, inadequate control for oophorectomy and hysterectomy in some studies might play a role. The Cancer and Steroid Hormone Study that found the strongest positive association excluded women who had a hysterectomy and/or bilateral oophorectomy (6), whereas the Women’s Interview Study of Health did not control for these factors and reported no association (8). In the Korean study reporting the strongest inverse association, it is unclear whether they controlled for hysterectomy and oophorectomy, although they reported a strong inverse association for oophorectomy and risk of breast cancer (9). If the Korean investigators did not account for the potentially strong correlation between tubal sterilization and oophorectomy, it is possible that confounding by oophorectomy could explain their observed inverse association for tubal sterilization. For instance, in the Women’s Contraceptive and Reproductive Experiences Study, Press et al. (7) calculated the breast cancer association with tubal sterilization overall (odds ratio = 0.74, 95% CI: 0.66, 0.83) and excluding women who had undergone hysterectomy or oophorectomy (odds ratio = 0.93, 95% CI: 0.84, 1.03), demonstrating that other reproductive surgeries have the potential to confound the tubal sterilization and breast cancer association. Therefore, the between-study heterogeneity observed among the case-control studies is likely due to noncausal factors.

Overall estimates of the association between tubal sterilization and breast cancer risk might mask susceptible subgroups defined by time since surgery or type of surgery. It is possible that, if tubal sterilization were to have a biological effect on ovarian hormone levels shortly after surgery, the extended period between tubal sterilization and breast cancer diagnosis in some studies, like the CPS-II Nutrition Cohort, may have biased the estimates.
obscure an association. However, the Cancer and Steroid Hormone Study (6) and the Women’s Interview Study of Health (8) that examined categories of duration as short as <1 year and <5 years, respectively, among young women did not demonstrate stronger associations with breast cancer risk with shorter duration since tubal sterilization. The CPS-II

Table 2. Age- and Multivariable-adjusted Association Between Tubal Sterilization and Breast Cancer Risk Among 77,249 Female Participants From 21 States in the US Cancer Prevention Study II Nutrition Cohort With Follow-up From 1992–1993 to 2007

<table>
<thead>
<tr>
<th>Variable</th>
<th>Person-Years</th>
<th>No. of Cases</th>
<th>Age Adjusted</th>
<th>Multivariable Adjusted*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>HR 95% CI</td>
<td>HR 95% CI</td>
</tr>
<tr>
<td>Tubal sterilization</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>865,599</td>
<td>3,703</td>
<td>1.00 Referent</td>
<td>1.00 Referent</td>
</tr>
<tr>
<td>Yes</td>
<td>86,939</td>
<td>381</td>
<td>1.09 0.98, 1.22</td>
<td>1.08 0.97, 1.20</td>
</tr>
<tr>
<td>Calendar year at tubal sterilization</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No tubal ligation</td>
<td>865,599</td>
<td>3,703</td>
<td>1.00 Referent</td>
<td>1.00 Referent</td>
</tr>
<tr>
<td>Tubal ligation year</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Before 1970</td>
<td>31,639</td>
<td>145</td>
<td>1.07 0.91, 1.26</td>
<td>1.08 0.91, 1.27</td>
</tr>
<tr>
<td>1970–1974</td>
<td>28,779</td>
<td>125</td>
<td>1.11 0.93, 1.33</td>
<td>1.09 0.91, 1.30</td>
</tr>
<tr>
<td>1975 or later</td>
<td>25,293</td>
<td>108</td>
<td>1.14 0.93, 1.38</td>
<td>1.09 0.90, 1.33</td>
</tr>
<tr>
<td>Age at tubal sterilization</td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>No tubal ligation</td>
<td>865,599</td>
<td>3,703</td>
<td>1.00 Referent</td>
<td>1.00 Referent</td>
</tr>
<tr>
<td>Tubal ligation age, years</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;30.0</td>
<td>11,230</td>
<td>51</td>
<td>1.11 0.84, 1.46</td>
<td>1.15 0.87, 1.52</td>
</tr>
<tr>
<td>30.0–34.9</td>
<td>19,712</td>
<td>72</td>
<td>0.94 0.74, 1.19</td>
<td>0.95 0.75, 1.21</td>
</tr>
<tr>
<td>35.0–39.9</td>
<td>29,327</td>
<td>138</td>
<td>1.19 1.00, 1.42</td>
<td>1.17 0.98, 1.39</td>
</tr>
<tr>
<td>≥40</td>
<td>26,316</td>
<td>119</td>
<td>1.10 0.91, 1.32</td>
<td>1.04 0.87, 1.26</td>
</tr>
<tr>
<td>P_trend</td>
<td></td>
<td></td>
<td>0.32 0.68</td>
<td></td>
</tr>
<tr>
<td>Years since tubal sterilization</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No tubal ligation</td>
<td>865,599</td>
<td>3,703</td>
<td>1.00 Referent</td>
<td>1.00 Referent</td>
</tr>
<tr>
<td>Tubal ligation, years prior</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;15</td>
<td>8,797</td>
<td>41</td>
<td>1.29 0.95, 1.76</td>
<td>1.23 0.90, 1.69</td>
</tr>
<tr>
<td>15.0–19.9</td>
<td>28,606</td>
<td>117</td>
<td>1.06 0.88, 1.28</td>
<td>1.03 0.85, 1.24</td>
</tr>
<tr>
<td>20.0–24.9</td>
<td>23,146</td>
<td>93</td>
<td>1.02 0.82, 1.25</td>
<td>1.00 0.81, 1.23</td>
</tr>
<tr>
<td>25.0–29.9</td>
<td>9,375</td>
<td>54</td>
<td>1.39 1.06, 1.82</td>
<td>1.39 1.06, 1.82</td>
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<tr>
<td>≥30.0</td>
<td>16,662</td>
<td>75</td>
<td>1.01 0.80, 1.27</td>
<td>1.02 0.81, 1.29</td>
</tr>
<tr>
<td>P_trend</td>
<td></td>
<td></td>
<td>0.75 0.95</td>
<td></td>
</tr>
<tr>
<td>Age combined with year at tubal sterilization</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No tubal ligation</td>
<td>865,599</td>
<td>3,703</td>
<td>1.00 Referent</td>
<td>1.00 Referent</td>
</tr>
<tr>
<td>&lt;35 years, before 1975</td>
<td>29,270</td>
<td>119</td>
<td>1.01 0.84, 1.21</td>
<td>1.03 0.86, 1.24</td>
</tr>
<tr>
<td>&lt;35 years, 1975 or later</td>
<td>1,273</td>
<td>3</td>
<td>0.99 0.31, 3.23</td>
<td>0.98 0.30, 3.18</td>
</tr>
<tr>
<td>≥35 years, before 1975</td>
<td>31,148</td>
<td>151</td>
<td>1.16 0.99, 1.37</td>
<td>1.13 0.95, 1.33</td>
</tr>
<tr>
<td>≥35 years, 1975 or later</td>
<td>24,020</td>
<td>105</td>
<td>1.14 0.93, 1.39</td>
<td>1.10 0.90, 1.34</td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence interval; HR, hazard ratio.
* Multivariable-adjusted models included age at menarche (<12, 12, 13, ≥14 years, missing); parity combined with age at first birth (nulliparous, 1–2 livebirths and <25 years at first birth, 1–2 livebirths and 25–29 years at first birth, 1–2 livebirths and ≥30 years at first birth, ≥3 livebirths and <25 years at first birth, ≥3 livebirths and 25–29 years at first birth, ≥3 livebirths and ≥30 years at first birth, unknown); age at menopause (<50, 50–54, ≥55 years, missing); alcohol intake (never drinker, <1, 1–2 drinks/day, former drinker, missing/unknown); smoking status (never, current, former, unclassifiable, missing); education (some high school, high school graduate, some college, college graduate, missing); family history of breast cancer in mother or sister (yes, no); history of breast cysts (yes, no); body mass index defined as weight (kg)/height (m)$^2$ (<18.5, 18.5–24.9, 25.0–29.9, ≥30.0, missing); hysterectomy/oophorectomy (none, uterus only, uterus plus 1 ovary, uterus plus 2 ovaries, 1 ovary only, both ovaries only, uterus plus unknown ovary(ies), unknown); use of postmenopausal hormone therapy (never, current, former, others/unclassifiable/missing); recent mammogram (never or not recent, within 2 years, missing); and use of oral contraceptives (never, ever, missing).
Nutrition Cohort and the Nurses’ Health Study (10) also did not find a clear pattern of breast cancer risk with years since surgery. Therefore, the variable, years since tubal sterilization, is unlikely to be associated with breast cancer risk.

Different birth cohorts also experienced secular trends in surgical methods that differed in their degree of surrounding tissue damage and possible side effects (4). Only 4 studies (7, 8, 10), including the CPS-II Nutrition Cohort, directly examined year at tubal sterilization as a proxy for surgical methods during that time. Results from the Nurses’ Health Study found a lower risk of breast cancer for women who had a tubal sterilization between 1970 and 1974 (HR = 0.84, 95% CI: 0.73, 0.97) (10)—years that correspond to the prevalent use of unipolar electrocautery and Pomeroy ligation techniques that have been associated with the greatest potential for destruction of the surrounding tissue (4, 5). However, the Women’s Interview Study of Health and the Women’s Contraceptive and Reproductive Experiences case-control studies (7, 8) and the CPS-II Nutrition Cohort that examined year at tubal sterilization did not find an inverse breast cancer association for tubal sterilization during these years. Therefore, year of surgery (as a proxy for surgical methods) is unlikely to be associated with breast cancer risk.

The lack of association between tubal sterilization and breast cancer risk in the CPS-II Nutrition Cohort and the meta-analysis is consistent with current evidence that tubal sterilization does not alter ovarian hormone levels as initially proposed. Early reports suggested that tubal sterilization, particularly the unipolar electrocautery and Pomeroy ligation procedures (4, 5), damaged the uterine artery, resulting in reduced blood supply to the ovary (limiting gonadotropin signaling to the ovary) and lower levels of ovarian hormones (24). However, a comprehensive review of the extensive literature on tubal sterilization and changes in hormone levels suggested that some of the early studies did not account for changes in use of oral contraceptives after tubal sterilization (25). Studies that measured hormone
levels before and after tubal sterilization in the same women found no changes in hormone levels associated with the tubal sterilization (25). The lack of association with breast cancer provides indirect support that the underlying mechanism for the consistent inverse association between tubal sterilization and ovarian cancer might be due to a mechanical barrier (26, 27).

On the basis of findings from the CPS-II Nutrition Cohort and the meta-analysis of more than 24,000 incident breast cancer cases, there is no evidence that tubal sterilization plays a role in breast cancer etiology.

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