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## Induced Abortion and Breast Cancer Risk [Original Articles]

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### Abstract

Results from case-control studies suggest that induced abortion may be associated with a small increase in risk of breast cancer. While risk estimates from cohort studies have generally not observed such an association, these studies have had limited information regarding abortion and possible confounding variables. Therefore, we conducted a study among a cohort of post-menopausal women from whom detailed information regarding pregnancy outcomes as well as risk factors for breast cancer had been collected. The study sample included 37,247 Iowa Women's Health Study participants, 55-64 years of age at baseline in 1986, who reported no history of breast, or other, cancer (except non-melanoma skin cancer), and for whom information

regarding pregnancy outcomes (that is, live birth, stillbirth, spontaneous abortion, ectopic pregnancy or induced abortion) was available. We used linkage with records of the State Health Registry of Iowa, part of the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) program, to estimate the incidence of breast cancer among cohort members through 1995. We calculated age-adjusted relative risks and 95% confidence intervals using Cox proportional hazards regression. Only 653 women (1.8%) reported an induced abortion. The age-adjusted relative risk of breast cancer among women with prior induced abortion compared with those without was 1.1 (95% CI = 0.8–1.6). Relative risks were higher among women whose age at first abortion was less than 20 or at least 30 years, for those whose abortion took place after their first birth or who never gave birth, and for those with early termination (0–2 months). These estimates varied from 1.3–1.7, but the confidence intervals around each were wide. Since most women in this cohort were beyond their reproductive years when abortion became legal in 1973, the low prevalence of induced abortion argues for a cautious interpretation.

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Because an estimated 24% of all recognized pregnancies in the United States are terminated as induced abortions, <sup>1</sup> the possibility that induced abortion increases a woman's risk of breast cancer is a public health concern. Some, but not all, case-control studies have found a higher proportion of women with breast cancer than controls to have had an induced abortion. <sup>2–5</sup> This inconsistency may be due to differences in methods of case and control ascertainment, variation in the definition of the reference group, and the lack of information regarding parity in relation to the time the abortion was performed. In addition, recall bias may be a factor in these studies. <sup>6–8</sup> Although cohort studies avoid the problems of recall bias, only a few have examined the breast cancer-abortion relation. <sup>9–12</sup> Two that did, however, did not distinguish type of abortion (spontaneous or induced), <sup>9,10</sup> and none had information regarding breast cancer risk factors, other than age and limited reproductive characteristics.

An earlier analysis from the Iowa Women's Health Study, a prospective cohort study of postmenopausal women, examined the relation between spontaneous abortion and breast cancer and found no association. <sup>13</sup> Here, we present additional analyses to determine whether induced abortion increased the risk of breast cancer among these women. The Iowa Women's Health Study cohort differs from other cohorts that examined this issue in that women provided detailed information regarding the timing of induced abortion in relation to other pregnancies, as well as age, length of pregnancy at the time of the induced abortion, and risk factors for breast cancer which could confound the relation of interest.

## Methods <sup>†</sup>

### Description of Cohort <sup>†</sup>

The Iowa Women's Health Study cohort was formed in 1986 from among 99,929 women, ages 55 to 69 years, who were randomly selected from the 1985 Iowa driver's license list, and asked to complete a mailed questionnaire. A total of 41,836 women (42.7%) returned the baseline questionnaire. Breast cancer rates were similar for responders and non-responders. <sup>14</sup> To assess the risk of postmenopausal breast cancer associated with induced abortion, we excluded 4,185 (10%) women from the analysis based on their self-report at baseline of a history of breast cancer or other non-skin cancer, or a total or partial mastectomy.

### Data Collection <sup>†</sup>

Women completed a self-administered questionnaire about known and suspected risk factors for breast cancer, including demographics, family history of breast cancer, body measurements (height, weight, waist, hip), physical activity, smoking, diet, alcohol consumption, medical history and medication use, including hormone use, and reproductive history. Women who reported having ever been pregnant also provided detailed information for up to 10 pregnancies. This information included the age at pregnancy, the number of months pregnant, and the pregnancy outcome (that is, live birth, stillbirth, miscarriage, ectopic pregnancy or induced abortion). We classified women according to whether they had ever had an induced abortion, and if so, we then calculated the number of abortions, age at first abortion, time since first abortion, timing of first induced abortion in relation to first birth, and gestational length (in months) of first aborted pregnancy. Women with missing pregnancy outcomes ( $N = 404$ ) were excluded, leaving 37,247 women for analysis.

We used the State Health Registry of Iowa, part of the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) program, to identify incident breast cancers (ICD-O codes 174.0–174.9) occurring among cohort members through 1995. We obtained vital status from the State Health Registry for deaths occurring in Iowa, from follow-up questionnaires for non-Iowa residents and from the National Death Index for non-respondents. We calculated person-years from the date of completion of the baseline questionnaire in 1986 until one of the following events (in order of priority): (1) date of diagnosis of breast cancer; (2) date of death (if death occurred in Iowa); (3) date moved out of Iowa (if date of move known); (4) mid-point of interval between last follow-up date and December 31, 1995 (if date of move out of Iowa unknown); or (5) mid-point of interval between date of last contact and date of death (for deaths in cohort members who moved from Iowa). Person-years were counted through December 1995 for women otherwise presumed to be alive and living in Iowa.

### Analysis $\pm$

We calculated the relative risk of breast cancer among women reporting a history of induced abortion, and for various characteristics associated with their first induced abortion, compared with women without a history of induced abortion, using proportional hazards regression.<sup>15</sup> We present relative risks and corresponding 95% confidence intervals after adjusting for age only, since the results were unchanged by the addition of other potential confounders, including education, marital status, religion, family history of breast cancer, body mass index, waist-to-hip ratio, smoking status, alcohol consumption, age at menarche, parity, age at first birth, number of live births, history of breast feeding, and oral contraceptive and estrogen use. We also repeated the analyses after excluding women who had never been pregnant.

### Results $\pm$

The distribution of lifestyle characteristics and breast cancer risk factors among women with and without a history of induced abortion are summarized in Table 1. A total of 653 women (1.8%) were identified as having had an abortion prior to 1986. Women who did or did not report an induced abortion were similar for most characteristics shown in Table 1, except women reporting an induced abortion were less likely to be married or to be Catholic, Mormon, or 7th Day Adventist, and more likely to report alcohol use, current smoking, and ever use of estrogens than women without an induced abortion. They also tended to be younger at the time of their first birth than women who did not report an induced abortion.

**TABLE 1. Distribution of Breast Cancer Risk Factors at Baseline According to History of Induced Abortion, Iowa Women's Health Study, 1986**

Characteristic	Induced Abortion			
	Yes (N = 653)		No (N = 36,594)	
	N	%	N	%
Age, years				
55-59	222	34.0	13,208	36.0
60-64	220	33.7	12,798	35.0
65-74	211	32.3	10,588	29.0
Marital status				
Married	456	69.8	27,984	76.5
Widowed, divorced, or separated	189	28.9	7,476	20.4
Never married	7	1.1	854	2.3
Unknown	1	0.2	280	0.8
Education				
Less than high school	129	19.8	7,034	19.2
High school	236	36.1	15,259	41.7
Some college	182	27.9	9,679	26.5
College graduate	105	16.1	4,534	12.4
Unknown	1	0.2	88	0.2
Catholic, Mormon, or Seventh Day Adventist	96	14.7	7,479	20.4
Family history of breast cancer				
None	490	75.0	26,763	73.1
Second degree only	84	12.9	3,946	10.8
First degree only	52	8.0	3,589	9.8
First and second degree	6	0.9	723	2.0
Unknown	21	3.2	1,573	4.3
Body mass index (kg/m <sup>2</sup> )				
1st tertile	207	31.7	12,188	33.3
2nd tertile	225	34.5	12,125	33.1
3rd tertile	221	33.8	12,281	33.6
Waist-to-hip ratio				
1st tertile	221	33.8	12,228	33.4
2nd tertile	203	31.1	12,196	33.3
3rd tertile	224	34.3	12,017	32.9
Unknown	5	0.8	153	0.4
Alcohol				
<1 Serving/week	345	52.8	21,916	59.9
1-6 Servings/week	171	26.2	8,455	23.1
≥7 Servings/week	94	14.4	3,162	8.6
Unknown	43	6.6	3,061	8.4
Smoking				
Never	315	48.2	23,865	65.2
Former	176	27.0	6,889	18.8
Current	150	23.0	5,285	14.4
Unknown	12	1.8	555	1.5
Ever used oral contraceptives	143	21.9	6,933	19.0
Ever used estrogen	306	46.9	13,936	38.1
Nulligravid	0	0.0	2,879	7.9
Nulliparous	49	7.5	3,253	8.9
Age at menarche, years				
<13	298	45.6	15,397	42.1
≥13	350	53.6	20,811	56.9
Unknown	5	0.8	386	1.0
Age at first birth among parous women, years				
<20	189	31.3	7,353	22.1
20-24	275	45.5	16,744	50.2
25-29	109	18.1	7,128	21.4
≥30	31	5.1	2,071	6.2
Unknown	0	0.0	45	0.1
Number of births among parous women				
1-2	226	37.4	11,358	34.1
≥3	378	62.6	21,983	65.9
History of breast feeding among parous women	291	48.2	14,706	44.1
Ever had miscarriage	197	30.2	9,766	26.7

Table 1. Distribution of Breast Cancer Risk Factors at Baseline According to History of Induced Abortion, Iowa Women's Health Study, 1986

We observed no excess risk of breast cancer among women who reported having an induced abortion compared with those who did not (age-adjusted RR = 1.1, 95% CI = 0.8-1.6), nor did risk increase with increasing number of reported induced abortions (Table 2). We observed an increased risk of breast cancer among women reporting a younger age (less than 20 years) or older age (30 years or older) at the time of first abortion, among those who remained nulliparous after their first abortion or whose first abortion took place after their first birth, or among women with abortions in the earliest months of gestation. These estimates varied from 1.3 to 1.7, but the

confidence intervals were wide. Only one case among the exposed women reported an induced abortion since 1973, precluding an examination in this cohort of the risk of breast cancer associated with induced abortion before and after its legalization. There was no change in the risk estimates when we excluded women who had never been pregnant from the analysis.

TABLE 2. Relative Risk of Breast Cancer Associated with Prior Induced Abortion, Iowa Women's Health Study, 1986-1995

Exposure	No. of Cases	Person-Years	Age-Adjusted Relative Risk	Age-Adjusted 95% Confidence Interval
Never had induced abortion*	1,317	336,211	1.0	
Induced abortion				
Ever	26	5,931	1.1	0.8-1.6
1 abortion	22	4,981	1.1	0.7-1.7
2 or more	4	950	1.0	0.6-1.7
Age at first abortion, years				
<20	7	1,207	1.5	0.7-3.1
20-24	8	1,690	1.2	0.6-2.4
25-29	1	722	0.4	0.1-2.5
30+	7	1,076	1.7	0.8-3.6
Unknown	3	1,236	0.6	0.2-1.9
Timing of first induced abortion				
Nulliparous	3	430	1.7	0.6-5.4
Before first birth	7	1,764	1.0	0.5-2.1
After first birth	13	2,630	1.3	0.7-2.2
Unknown	3	1,107	0.7	0.2-2.1
Gestational length of first aborted pregnancy, months				
0-2	14	2,644	1.3	0.8-2.3
3+	8	1,943	1.1	0.5-2.1
Unknown	4	1,344	0.8	0.3-2.0

\* Referent category.

Table 2. Relative Risk of Breast Cancer Associated with Prior Induced Abortion, Iowa Women's Health Study, 1986-1995\*  
Referent category.

## Discussion <sup>±</sup>

Our study was limited to post-menopausal women who entered the cohort in 1986, when they were 55 to 69 years old. Consequently, nearly all Iowa Women's Health Study participants had completed their reproductive years before abortion was legalized in 1973 in the United States. Only 1.8% of the cohort reported at least one induced abortion, which raises the possibility that women may have either underreported abortions occurring before legalization or falsely reported the outcome of their pregnancy if it had been terminated by that procedure during that era. An historical accounting of abortion in the 20th century <sup>16</sup> suggests that abortions were not an uncommon occurrence before legalization in this country; certainly the procedure was available in some states and in Europe before 1973. The frequency of induced abortion before the early 1970s is difficult to determine, however. Based on current national data, <sup>17</sup> abortion rates in Iowa are considerably lower than that of other states; presumably pre-1973 rates would also be expected to have been low. Others have shown that women may underreport induced abortion by as much as 50%. <sup>18</sup>

Given the concern that Iowa Women's Health Study participants may have inaccurately reported a history of induced abortion, we calculated the amount of misclassification that would need to be present to yield a true relative risk of breast cancer of at least 1.5. In the cohort, we observed breast cancer rates of 438 and 392 per 100,000 person-years, among women who reported they did and did not have induced abortions, respectively (crude RR = 1.12). To obtain a relative risk of 1.2, for example, the true rate of breast cancer among the non-exposed would need to equal 365/100,000 ( $0.00438 \div 1.5 = 0.00365$ ). Assuming that women who reported an induced abortion were truthful, then the observed rate of breast cancer among the non-exposed

(392/100,000) is a weighted average of the rate among exposed women who falsely reported no abortion (438/100,000) plus the rate among women who accurately reported no abortion (365/100,000) [ $0.00392 = x(0.00438) + (1-x)(0.00365)$ ]. Solving for  $x$ , the proportion of women with abortion who reported otherwise, the relative risk of 1.1 estimated from these data would require that more than one third of the women who reported no abortion were, in fact, misclassified. This unlikely scenario leads us to conclude that our null finding is not likely to be explained by this bias.

The Iowa Women's Health Study provides a relatively complete assessment of reproductive history and outcomes. These data allowed us to calculate relative risks adjusted for known confounders, which was possible only to a limited extent in other cohort studies.<sup>9-12</sup> Adjustment, however, made little difference in our finding of no association between induced abortion and breast cancer risk. In addition, our results are consistent with the few cohort<sup>10,12</sup> and all but one of the case-control studies<sup>8,23,24,27,31,33</sup> to have examined the relation between induced abortion and breast cancer risk according to menopausal status. The consistency of the results among postmenopausal women is surprising given the degree of uncertainty, based on some positive case-control studies, as to whether induced abortion increases the risk of breast cancer, at least among some groups of women.<sup>19-33</sup> Methodologic differences among the case-control studies, highlighted in recent reviews, may explain these inconsistencies.<sup>2-5</sup> Of particular concern is recall bias for which strong evidence has been reported to support some of the positive findings.<sup>6-8</sup> In the absence of an increased risk for breast cancer among postmenopausal women who reported an induced abortion, however, recall bias would not appear to be a factor in those case-control studies which have reported on the effect of menopausal status on the relation of induced abortion and breast cancer.

The mechanism by which induced abortion is thought to affect breast cancer risk—the interruption of cell differentiation in proliferating tissue due to pregnancy—is biologically plausible and supported by limited data from animal studies.<sup>34-36</sup> Our data do not provide support for this hypothesis and our results are strengthened by the consistency of the findings for postmenopausal women in both cohort and case-control studies.

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