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Fertility-related experiences after breast cancer diagnosis in the Sister and Two Sister Studies

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Abstract

Background: Commonly-used chemotherapies can be toxic to the ovaries. Most studies evaluating receipt of fertility counseling for women in their reproductive years were performed in specific settings, limiting generalizability.

Methods: A nationwide sample of US women diagnosed with breast cancer before age 45 completed a survey assessing the prevalence of fertility counseling. Age-adjusted log-binomial

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regression was used to estimate prevalence ratios (PRs) and 95% confidence intervals (CIs) for fertility counseling.

Results: Among 432 survivors diagnosed during 2004–2011, 288 (67%) had not discussed the effects of treatment on fertility with a healthcare provider before or during treatment. Fertility discussion was associated with younger age (for <35 vs 40+ years, PR: 3.49, CI: 2.66–4.58) and lower parity (for parity 1 vs. 2, PR: 1.81, CI: 1.29, 2.53). Twenty percent of respondents reported that they were interested in future fertility (87/432) at the time of their diagnosis, but not all (66/87) received counseling on the impact of treatment on their fertility, and few (8/87) utilized fertility preservation strategies. Among women with a fertility interest who provided reasons for not taking steps to preserve fertility (N=68), reasons cited included concern for adverse impact on cancer treatment (56%), lack of knowledge (26%), decision to not have a child (24%), and cost (18%).

Conclusions: Across multiple treatment settings, most reproductive-age women diagnosed with breast cancer did not discuss fertility with a healthcare provider or use fertility preservation strategies. Discussing the potential impact of cancer treatment on future fertility is an important aspect of patient education.

Precis:

In this nationwide sample, a higher proportion of reproductive-age women diagnosed with breast cancer did not receive counseling or utilize fertility preservation compared to published reports in fertility-focused studies in a cancer population. Decisions about fertility preservation were not based on informed discussion and suggest opportunity for improved patient education and outreach.

Keywords

fertility; fertility counseling; fertility preservation; breast cancer

Introduction

Every year, over 23,000 American women aged <45 years are diagnosed with breast cancer.¹ The majority of these women receive chemotherapy that can impair fertility and/or endocrine therapy that can delay pregnancy attempts until older ages when fertility declines.² The overall 5-year relative survival rate for female breast cancer diagnosed before age 45 years is 87.6%.^{3, 4} Early detection and therapeutic advances permit most younger women to survive their initial diagnosis but also to realize the potential adverse impact of gonadotoxic therapies on fertility.⁵

In female cancer survivors of reproductive age, pretreatment counseling on the potential fertility-related complications of cancer treatment and options for fertility preservation has been associated with higher quality of life.^{6–8} However, many young women diagnosed with breast cancer report that they were not informed about infertility risks before initiating cancer treatment.^{9–11} Since 2006, national guidelines from the American Society of Clinical Oncology (ASCO)^{12–14}, the National Comprehensive Cancer Network,¹⁵ and the American

Society of Reproductive Medicine¹⁶ have recommended fertility counseling for reproductive-age patients with a cancer diagnosis.

Receipt of fertility counseling ranges from 34–81% across prior studies.^{17–28} Fertility counseling is more often received by women who are younger¹⁸, have lower parity,^{17, 18, 22, 29, 30} higher education,^{17, 18} higher income,^{22, 31} non-Hispanic White ethnicity,^{21, 32} and insurance coverage.²² Among women who do receive counseling, lower use of fertility preservation has been associated with concerns about cost,^{9, 33} treatment delay,^{11, 33} and/or an adverse impact on their cancer treatment.^{19, 33} In prior studies of reproductive-age women diagnosed with cancer who wanted to retain their fertility, 40–50% of women did not utilize fertility preservation.^{18, 34, 35}

Most literature on fertility counseling, interest, and preservation is derived from academic centers or studies specifically designed to address fertility.^{22, 36, 37} It is unclear whether findings accurately reflect the experience of women seen outside of an academic setting. To address this gap, participants across the U.S. from the Sister Study³⁸ and Two Sister Study³⁹ were surveyed on their fertility-related experiences following a breast cancer diagnosis.

The aim of this analysis is to examine the prevalence of fertility interest, discussion, and use of preservation options among premenopausal, reproductive-age women with a breast cancer diagnosis in the Sister Study and Two Sister Study.

Methods

The Sister Study recruited a cohort of U.S. women whose sister had been diagnosed with breast cancer but who themselves had never had breast cancer at enrollment (2003–2009). Sister Study participants were recruited in the United States and Puerto Rico using brochures, flyers, mail, email, as well as free and paid media campaigns in English and Spanish as previously described.³⁸ Between 2008 and 2010, the Two Sister Study enrolled the sisters (of Sister Study participants) who had been diagnosed with young-onset (<50 years) breast cancer.³⁵ Data for the current analysis come from a survivor survey sent to Sister Study and Two Sister Study participants diagnosed with breast cancer prior to October 2012. Participants who had undergone tubal ligation, hysterectomy, or bilateral oophorectomy (permanent sterilization), or reported experiencing menopause prior to breast cancer diagnosis were excluded. The sample included 52 women from the Sister Study with breast cancer diagnosed at ages 35–44 and 474 women from the Two Sister Study with breast cancer diagnosed at ages 28–44 years. Study participants received treatment in both academic and community settings across the United States.^{38, 39} Parity was defined as number of children birthed prior to cancer diagnosis and the referent group was defined by the most prevalent parity.

Outcomes assessed included the prevalence of fertility interest, discussion, and use of preservation prior to breast cancer treatment. Fertility interest was defined as answering “Yes” to the question “Before your breast cancer diagnosis, did you think you wanted to get pregnant at some point in the future?” Fertility discussion was defined as answering “Yes” to the question “Did you ever have a discussion with a health care provider about the effect

your treatment could have on your future fertility or ability to have children?” The use of fertility preservation was defined as answering “Yes” to “Before you began treatment, or during your treatment, did you take any additional steps to lessen your chances of becoming infertile as a result of your cancer treatment?” Women who responded “Yes” then selected one or more of the following response options: cryopreservation of embryos, cryopreservation of unfertilized eggs, cryopreservation of ovarian tissue, and/or GnRH agonist. Information on breast cancer diagnosis, tumor characteristics, and treatment data were abstracted from medical records as previously described.^{39–41} Endocrine therapy non-adherence was defined as non-initiation or reporting taking endocrine therapy most of the time, sometimes, rarely or never (rather than always) among women with estrogen receptor positive breast cancer.

Age-adjusted (<40/40+ years) log-binomial regression was used to estimate prevalence ratios (PRs) and 95% confidence intervals (CIs) for fertility discussion. All tests were two-sided, and p-values <0.05 were considered statistically significant. Analyses were performed using Statistical Analysis Software (SAS) version 9.4 (SAS Institute, Inc, Cary, NC). This analysis uses information from Data Release 6.0.

Results

In total, 526 women aged <45 years at breast cancer diagnosis completed the survivor survey. Of these, 432 (82%) were premenopausal and had not undergone permanent sterilization and were included in analyses. Most women were non-Hispanic White with an annual household income \$50,000 (Table 1).^{41, 42} Breast cancer stage was distributed such that 15% of women were Stage 0, 39% Stage I, 32% Stage II, 14% Stage III, and 1% were Stage IV at diagnosis. A minority (25%) of patients were diagnosed with breast cancer prior to 2006, the year that the ASCO guidelines about Fertility and Cancer were first published (Table 1).¹² The majority of women (89%) completed the survey 5–8 years after diagnosis; years since diagnosis was not significantly associated with reported receipt of fertility counseling (Table 1). The prevalence of fertility counseling did not differ between the Sister Study (31%) and Two Sister Study (33%) in age-adjusted models (PR: 1.08, CI: 0.68, 1.72) (Table 1).

Overall, 67% of women (288/432) did not discuss the fertility impact of treatment with a healthcare provider before or during their cancer treatment (Figure 1). Across both the Sister Study and the Two Sister Study, 20% of women (87/432) reported having an interest in future fertility prior to their breast cancer diagnosis (Figure 1). A similar proportion (21%) reported that before treatment they were unaware that cancer treatment could affect a woman’s fertility (*data not shown*).

Fertility discussion was positively associated with younger age, Hispanic ethnicity (compared to non-Hispanic whites), residing in the Western United States, lower parity, and more intensive cancer therapy (Table 2). Compared to women over 40 years old at the time of diagnosis, fertility discussion was more than three times as likely to occur in women aged 28–35 years (PR: 3.49, CI: 2.66–4.58) and nearly twice as likely in women aged 35–39 years (PR: 1.89, CI: 1.41–2.52). Fertility discussion was more prevalent in Hispanic women

(PR: 2.01, CI: 1.25–3.24) compared to non-Hispanic White women. Receipt of fertility counseling varied by geographical location, determined by U.S. Census Bureau regional definitions.⁴³ Compared to the 39% prevalence of fertility counseling among women residing in the Western U.S., fewer women (23%) in the Midwest region received counseling (PR: 0.59, CI: 0.41–0.86). Hispanic ethnicity was related to geographic region whereby most Hispanic women lived in the South or West regions (South: N=10, 42%, West: N=10, 42%, Northeast: N=2, 8%, Midwest: N=2, 8%). Compared to women with two children, those with one child were more likely to receive fertility counseling (PR: 1.81, CI: 1.29–2.53). Compared to those who received chemotherapy or endocrine therapy, women who did not receive chemotherapy or endocrine therapy were 44% less likely to discuss fertility (PR: 0.56, CI: 0.32–0.99). Estrogen receptor status was not associated with receipt of fertility discussion whereby women with ER+ tumors were similarly likely to receive fertility counseling compared to their ER- counterparts (OR: 1.20, CI: 0.86–1.11). Rural or urban setting was associated with lower prevalence of receipt of fertility counseling in sensitivity analyses excluding women with Stage 0 disease (PR: 0.64, CI: 0.41–0.98, Supplementary Table 1) but was not significant when considering the entire cohort (Table 2).

Among women diagnosed with breast cancer before, in the same year, or after the first publication of ASCO guidelines in 2006, the proportion who received fertility counseling was 32%, 31% and 35%, respectively. Calendar year of diagnosis was not associated with receipt of fertility counseling in age-adjusted models (Table 2). Sensitivity analysis excluding women with Stage 0 breast cancer (N=64) yielded similar findings (Supplementary Table 1).

Among women who discussed fertility with a provider, 73% (102/140) of conversations were initiated by a physician. In the subset of women interested in future fertility, 24% (21/87) reported that they did not receive fertility counseling and 9% (8/87) took steps to preserve fertility. Of the eight women who reported taking steps to preserve fertility, five received gonadotropin-releasing hormone (GnRH) agonists alone, one cryopreserved embryos only, one cryopreserved oocytes only, and one cryopreserved both oocytes and embryos.

Women were allowed to select multiple reasons that they did not take steps to preserve fertility. Among women who reported an interest in future fertility prior to breast cancer diagnosis but did not take steps to preserve fertility (N=79), 68 women provided responses. Among these 68 women, the most common reasons cited included concern for adverse effect on cancer treatment (56%), lack of knowledge (26%), decision to not have children (24%), and cost (18%) (Figure 2).

Among 340 women who did not report a fertility interest before their breast cancer diagnosis, eight (2%) changed their mind after cancer treatment about trying to conceive in the future. Among all 432 women, since cancer diagnosis sixteen women overall reported consulting with a fertility specialist, four women underwent infertility treatments, five adopted a child, and two women fostered a child. Of women prescribed endocrine therapy (N=305), 71% reported 100% adherence. Non-adherence appeared to be more common in

women with an interest in future fertility (33 vs. 27%, respectively) but associations were not statistically significant (age-adjusted PR: 1.25, CI: 0.80–1.94, *data not shown*).

Discussion

Results from this nationwide sample demonstrate that most reproductive-age women diagnosed with breast cancer did not receive counseling on the potential impact of cancer treatment on fertility and did not utilize fertility preservation strategies. Fertility-related discussions were reported by a modest proportion (33%) of women overall, suggesting an area where improvements are needed in breast cancer care delivery.⁴⁴ Approximately 1 in 5 women in our sample reported that they had hoped to become pregnant in the future before receiving their cancer diagnosis.

In the present study, an overwhelming 90% of women with an interest in future fertility did not utilize fertility preservation and 24% never discussed fertility with a provider. The low incidence of receipt of fertility counseling in our nationwide cohort is similar to the previously reported 9% prevalence of fertility counseling in the community setting, and suggests that counseling rates outside of academic or major cancer centers may be suboptimal.⁴⁵ Among women who indicated they wanted a future pregnancy prior to their breast cancer diagnosis, few used fertility preservation in contrast to published reports of 40–50% utilization of fertility preservation.^{32, 34, 35} Our findings are more consistent with Canadian reports in which 46–9%²⁸ of young female cancer patients utilized preservation strategies. The proportion of women diagnosed with cancer before (2004–2005), in the same year (2006), and in the years after (2007–2011) publication of the ASCO guidelines in 2006 was similar. During these years, embryo cryopreservation was the only accepted, non-experimental fertility preservation option recommended.⁴⁷ However, only two women used this strategy, one of whom also preserved oocytes. Two women underwent oocyte cryopreservation which had an experimental designation until 2013.⁴⁷ The most common strategy reported (by five women) was use of a GnRH agonist, which may reduce susceptibility to gonadotoxic effects of chemotherapy but is likely to provide only a modest benefit⁴⁸ and was not a recommended fertility preservation strategy by ASCO at the time this survey was conducted.¹⁴ The most recent ASCO recommendations support the use of a GnRH agonist but not in lieu of a proven fertility method.¹⁴

Receipt of fertility discussion was associated with younger age in our cohort. Letourneau and colleagues reported that women over 35 years old at the time of cancer diagnosis during 1997 to 2007 were less likely to receive fertility counseling than younger women, but this difference did not achieve statistical significance.¹⁸ Our finding that women with higher parity are less likely to receive fertility counseling is consistent with prior reports in reproductive-age women with any cancer diagnosis between 1990 and 2009.¹⁷ In our study, both nulliparous and uniparous women were more likely to receive fertility counseling than women with 2 children. Previous investigations have often evaluated parity as a dichotomous variable (“having at least one child/children at diagnosis”).^{6, 17, 18, 25} Chin and colleagues demonstrated that desired family size is associated with fertility counseling whereby women with fewer children than desired were more likely to receive counseling.¹⁷ Though the comparison of nulliparous and uniparous women was limited by sample size, our results

could indicate that primiparous women have contemplated ideal family size and may be more likely to advocate for future fertility to complete their desired family size. Lower receipt of fertility discussion was associated with rural setting in sensitivity analyses excluding women with Stage 0 disease. This finding suggests that the lower prevalence of fertility counseling in the present work may be related to differences in counseling by population density, or more plausibly, proximity to major cancer or academic centers..

Frequently cited reasons for not using fertility preservation in our study and others are cancer treatment concerns, including concern for treatment delay and concern for an adverse impact of fertility preservation on cancer^{33, 49–51}, as well as lack of knowledge of options.¹¹ Assumptions that fertility preservation will delay and adversely affect cancer treatment are not supported by existing, albeit limited, evidence. Letourneau and colleagues demonstrated no difference in time to neoadjuvant chemotherapy in women with breast cancer who underwent fertility preservation compared to those who did not (38 vs. 39 days, respectively, $P=0.7$)⁵² and Chien et al. similarly found no difference (42 vs. 36 days, respectively, $P=0.5$).⁵³ Research also counters concerns that fertility preservation may impair long-term survival but current evidence is limited to one investigation.⁵⁴ Among 262 reproductive-age women diagnosed with breast cancer, Moravek et al. demonstrated no significant difference in mortality between those who underwent oocyte or embryo cryopreservation before treatment compared to those who did not (1.8 vs. 3.4%, respectively).⁵⁴ However, these findings were published only recently and were not available to address potential concerns at the time of breast cancer diagnosis among women in our analysis.

Previous studies of young women with breast cancer show that fertility-related concerns impact treatment decisions.^{23, 34, 37} In an academic center, women who endorsed concern about the gonadotoxic impact of cancer treatment or who desired future childbearing were one-fifth as likely to initiate endocrine therapy as their counterparts.⁵⁵ This association was not apparent in our sample. Similarly, our data support the lower end of the range of previous reports of how often reproductive-age women diagnosed with cancer receive fertility counseling (34–81%).^{17–26} The low prevalence (33%) of fertility counseling in our sample may reflect practice differences in our geographically diverse sample.¹⁵ Uptake of in vitro fertilization services may also vary based on state-mandated insurance coverage.^{56, 57}

Our findings may be limited by recall, whereby some women who discussed fertility do not recall this discussion³⁶ due to the overwhelming gravity, complexity, or sheer volume of medical information shared with patients around the time of cancer diagnosis.¹⁶ The majority of participants (68%) were over age 40 at the time of breast cancer diagnosis such that practitioners may have been less likely to discuss fertility preservation due to lower success rates with oocyte cryopreservation in older women.⁵⁸ Selection bias in this volunteer cohort is possible; however a low prevalence of receipt of fertility counseling among a relatively well-educated and high-resourced sample is additionally concerning for what prevalence may be among women with fewer resources. Our study population was largely non-Hispanic White and estimates were adjusted for age only, leaving the potential for residual confounding or incomplete assessment of the experience of minority women. A higher prevalence of fertility counseling in the West and South regions of the U.S., which contain higher concentrations of Hispanic women relative to the Midwest may confound

assessment of the Hispanic woman's experience. Whether women received their fertility counseling, cancer diagnosis and/or treatment at an academic or community setting was not assessed. The low proportion that recalled discussing fertility with their doctor in our cohort may partially reflect the inclusion of diagnosis years that pre-dated the ASCO guideline recommending fertility discussion for all reproductive-age cancer patients.^{12, 59} However, the proportion of women who reported fertility counseling varied only slightly before and after 2006 (32–35%). Strengths of this investigation include using a sample that was not recruited to the study based on fertility interests and was treated in diverse settings across the country. Tumor hormone receptor status, chemotherapy and endocrine therapy were abstracted directly from medical records.

A previous investigation of young women with breast cancer determined that the preferred method of obtaining fertility-related information is consultation with a fertility specialist followed by a decision aid, such as an information booklet.^{34, 60} Supplanting counseling with provision of an information booklet or referral to a web-based information or telehealth platform may help patients interpret data on the fertility-related impact of cancer treatment in a more convenient, memorable, and usable way.^{34, 37, 60, 61} In this nation-wide sample, the majority of reproductive-age women did not receive fertility counseling, and among those interested in future pregnancy before diagnosis, few utilized fertility preservation. Our findings reinforce the continued need to implement guideline-concordant care by providing fertility counseling regarding the potential impact of breast cancer treatment on fertility and available fertility preservation options.⁶² Additional investigation of disparities in provision of fertility counseling, as well as research to identify strategies that enhance receipt of recommended counseling, such as web-based or telehealth decision aids to augment in-office counseling sessions, is merited.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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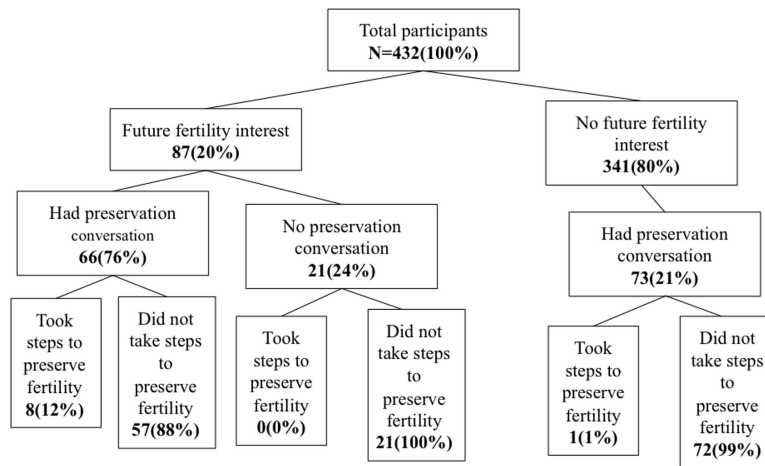


Figure 1. Fertility discussion and utilization of preservation among 432 NIEHS Sister Study and Two Sister Study participants who completed the breast cancer survivor survey.

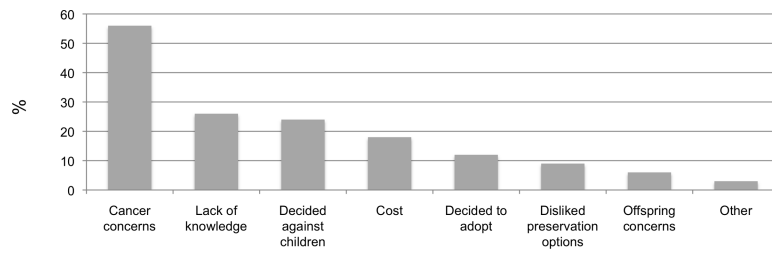


Figure 2.

Distribution of reported reasons for not taking steps to preserve fertility among 68 NIEHS Sister Study and Two Sister Study participants who had been interested in a future pregnancy prior to their breast cancer diagnosis. Twelve possible responses were collapsed to eight categories defined as: Cancer concerns (56%: “I wanted to start cancer treatment right away,” or “Was afraid it would affect my breast cancer or the treatment,”); Lack of knowledge (26%: “Did not know there were any options”); Decided against children (24%: “Did not wish to have children after cancer treatment;); Cost (18% “It was too expensive,” or “Health insurance didn’t cover it”); Decided to adopt (12%: “Decided to adopt in the future”); Disliked preservation options (9%: “Fertility treatment options were overwhelming or invasive,” or “Did not like available options”); Offspring concerns (6%: “Concerned about passing on disease”); and Other (3%: “Decided to use egg or embryo donation in the future,” or “Decided to try to get pregnant at that time”

Table 1.

Participant characteristics among 432 women enrolled in the NIEHS Sister Study and Two Sister Study.

Characteristic	N	%
Age at diagnosis, median (IQR)	41.9	(39.2, 43.5)
28.3–34.9	24	6%
35–39.9	112	26%
40–44.9	296	69%
Race		
Non-Hispanic White	383	89%
Non-Hispanic Black	15	3%
Hispanic	25	6%
Other	9	2%
Marital status		
Never married	36	8%
Legally married/living as married	362	84%
Widowed/divorced/separated	34	8%
Household income		
Less than \$20,000	5	1%
\$20,000-\$49,999	44	10%
\$50,000-\$99,999	152	35%
\$100,000-\$200,000	165	38%
More than \$200,000	56	13%
Don't know/refused	10	2%
Education		
High school or less	33	8%
Some college	92	21%
Bachelor's degree or higher	307	71%
Rural/urban (>50% of census tract population resides in rural/urban area)		
Rural	82	20%
Urban	337	80%
Region		
Northeast	86	20%
Midwest	141	33%
South	111	26%
West	89	21%
Calendar year of breast cancer diagnosis		
2004–2005	108	25%
2006	150	35%
2007–2011	174	40%

Characteristic	N	%
Time since diagnosis (years), median (IQR)	6.2	(5.5, 7.0)
1.3-<5	47	11%
5-<6	133	31%
6-<7	142	33%
7-8.2	110	25%
Study	N	%
Sister Study	39	9%
Two Sister Study	393	91%
Parity at breast cancer diagnosis		
0	131	30%
1	58	13%
2	159	37%
3+	83	19%
Stage		
0	64	15%
I	167	39%
II	137	32%
III/IV	63	15%
Missing	1	0%
ER status		
Negative	96	23%
Positive [†]	326	77%
Treatment		
No chemotherapy or endocrine therapy	49	11%
Endocrine therapy without chemotherapy	71	16%
Chemotherapy without endocrine therapy	83	19%
Chemotherapy and endocrine therapy	229	53%

[†] Includes 2 women with borderline ER+ status

Table 2.

Age-adjusted prevalence ratios (PR) and 95% confidence intervals (CI) for receipt of fertility counseling among 432 women enrolled in the NIEHS Sister Study and Two Sister Study.

Characteristic	Received fertility counseling † N=140 (100%)	No fertility counseling † N=288 (100%)	Age-adjusted PR (95% CI)
Age at diagnosis, median (IQR)			
28.3–34.9	20 (14)	4 (1)	3.49 (2.66, 4.58)
35–39.9	50 (36)	61 (21)	1.89 (1.41, 2.52)
40–44.9	70 (50)	223 (77)	1
Race			
Non-Hispanic White	116 (83)	264 (92)	1
Non-Hispanic Black	6 (4)	8 (3)	1.31 (0.76, 2.24)
Hispanic	12 (9)	13 (5)	2.01 (1.25, 3.24)
Other	6 (4)	3 (1)	1.65 (1.10, 2.48)
Marital status			
Never married	14 (10)	22 (8)	1
Legally married/living as married	115 (82)	244 (85)	0.85 (0.57, 1.26)
Widowed/divorced/separated	11 (8)	22 (8)	0.88 (0.49, 1.57)
Household income			
Less than \$20,000	1 (71)	4 (1)	0.51 (0.09, 2.86)
\$20,000-\$49,999	14 (10)	29 (10)	0.94 (0.60, 1.49)
\$50,000-\$99,999	50 (36)	101 (35)	1
\$100,000-\$200,000	52 (38)	111 (39)	0.98 (0.73, 1.32)
More than \$200,000	22 (16)	34 (12)	1.21 (0.85, 1.74)
Education			
High school or less	6 (4)	26 (9)	0.65 (0.32, 1.35)
Some college	31 (22)	59 (20)	1.00 (0.74, 1.36)
Bachelor's degree or higher	103 (74)	203 (70)	1
Rural/urban (>50% of census tract population resides in a rural/urban area)			
Rural	19 (14)	63 (22)	0.69 (0.46, 1.04)
Urban	114 (86)	219 (78)	1
Region			
Northeast	26 (19)	30 (35)	0.84 (0.59, 1.20)
Midwest	77 (55)	32 (23)	0.59 (0.41, 0.86)
South	27 (19)	42 (38)	0.93 (0.67, 1.28)
West	19 (14)	35 (39)	1
Calendar year of breast cancer diagnosis	Received fertility counseling †	No fertility counseling † N=288 (100%)	Age-adjusted PR (95% CI)

Characteristic	Received fertility counseling [†] N=140 (100%)	No fertility counseling [†] N=288 (100%)	Age-adjusted PR (95% CI)
	N=140 (100%)		
2004–2005	34 (24)	73 (25)	0.97 (0.68, 1.37)
2006	45 (32)	102 (35)	1
2007–2011	61 (44)	113 (39)	1.15 (0.85, 1.54)
Time between diagnosis and survey (years)			
1.3-<5	18 (13)	29 (10)	1.23 (0.82, 1.82)
5-<6	43 (31)	89 (31)	1
6-<7	45 (32)	95 (33)	0.97 (0.70, 1.34)
7	34 (24)	75 (26)	0.89 (0.62, 1.26)
Study			
Sister Study	12 (9)	27 (9)	1.08 (0.68, 1.72)
Two Sister Study	128 (91)	261 (91)	1
Parity at breast cancer diagnosis			
0	47 (34)	84 (29)	1.35 (0.97, 1.88)
1	29 (21)	29 (10)	1.81 (1.29, 2.53)
2	41 (29)	117 (41)	1
3+	23 (16)	58 (20)	1.17 (0.77, 1.77)
Stage			
0	14 (10)	50 (17)	0.66 (0.40, 1.09)
I	53 (38)	112 (39)	1
II	49 (35)	86 (30)	0.97 (0.72, 1.31)
III/IV	23 (16)	40 (14)	1.05 (0.73, 1.51)
ER status			
Negative	28 (20)	66 (23)	1
Positive	110 (79)	216 (75)	1.20 (0.86, 1.66)
Treatment			
No chemotherapy or endocrine therapy	10 (7)	39 (14)	0.56 (0.32, 0.99)
Endocrine therapy without chemotherapy	16 (11)	55 (19)	0.71 (0.45, 1.12)
Chemotherapy without endocrine therapy	25 (18)	56 (19)	0.79 (0.56, 1.11)
Chemotherapy and endocrine therapy	89 (64)	138 (48)	1

[†]Column totals may not sum to 100% due to missing and/or rounding