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Disparities in the Use of Assisted Reproductive Technologies after Breast Cancer: A Population-Based Study

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Abstract

Purpose: Equitable access to oncofertility services is a key component of cancer survivorship care, but factors affecting access and use remain understudied.

Methods: To describe disparities in assisted reproductive technology (ART) use among women with breast cancer in California, we conducted a population-based cohort study using linked oncology, ART, and demographic data. We identified women age 18–45 years diagnosed with invasive breast cancer between 2000 and 2015. The primary outcome was ART use—including oocyte/embryo cryopreservation or embryo transfer—after cancer diagnosis. We used

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Author Contributions

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Competing Interests

The authors have no relevant financial or non-financial interests to disclose.

log-binomial regression to estimate prevalence ratios (PRs) and 95% confidence intervals (CIs) to identify factors associated with ART use.

Results: Among 36,468 women with invasive breast cancer, 206 (0.56%) used ART. Women significantly less likely to use ART were age 36–45 years at diagnosis (vs. 18–35 years: PR = 0.17, 95% CI = 0.13 to 0.22); non-Hispanic Black or Hispanic (vs. non-Hispanic White: PR = 0.31, 95% CI = 0.21 to 0.46); had at least one child (vs. no children: adjusted PR [aPR] = 0.39, 95% CI = 0.25 to 0.60); or lived in non-urban areas (vs. urban: aPR = 0.28, 95% CI = 0.10 to 0.75), whereas women more likely to use ART lived in high-SES areas (vs. low-/middle-SES areas: aPR = 2.93, 95% CI = 2.04 to 4.20) or had private insurance (vs. public/other insurance: aPR = 2.95, 95% CI = 1.59 to 5.49).

Conclusion: Women with breast cancer who are socially or economically disadvantaged, or who already had a child, are substantially less likely to use ART after diagnosis. The implementation of policies or programs targeting more equitable access to fertility services for women with cancer is warranted.

Keywords

Breast Cancer; Assisted Reproductive Technology; Fertility Preservation; Disparities

INTRODUCTION

Women diagnosed with breast cancer during their reproductive years may have to make complex decisions about parenthood and reproductive health while navigating the physical, psychological, and financial effects of cancer and its treatment.[1,2] The risk or realization of medically induced (iatrogenic) infertility can influence cancer treatment decisions[3,4] and subsequent quality of life.[5] Importantly, as more women delay childbirth,[6] fertility concerns are becoming increasingly relevant to women who have not started or completed building their families at the time of diagnosis. For women with breast cancer, receipt of chemotherapy can accelerate the natural decline of a woman's ovarian reserve, or reproductive potential, and may result in immediate ovarian failure (i.e., menopause) or premature ovarian failure (i.e., menopause before age 40)—highlighting the urgency in access to fertility preservation for this population.[7,8] The need to undergo months or years of cancer treatment during one's reproductive years can also result in reduced fertility after completion of cancer treatment due to the natural age-related decline of the ovarian reserve.[7,9] Although the appropriateness of oncofertility services varies based on patient and clinical factors, the use of assisted reproductive technology (ART) to cryopreserve oocytes or embryos before cancer treatment, or to attempt pregnancy using embryo transfer post-treatment, are established methods of fertility preservation and family-building for women with cancer.[1,10]

Ensuring equitable access to oncofertility services is key to addressing cancer care disparities. Access to fertility preservation specifically among underserved populations has emerged as an important area of widening disparity in health care.[11,12] Fertility services often are not covered by health insurance in the United States, and with costs of up to $15,000 for the cryopreservation of oocytes or embryos, many women find the option of

paying out-of-pocket for ART to be prohibitively expensive.[13] In the few prior studies that have examined patient-level factors associated with ART use after cancer diagnosis, disparities in use were observed by age at diagnosis, race/ethnicity, socioeconomic status (SES), and rurality.[12,14–17] However, most studies to date have been limited by the lack of generalizability of their study populations, including the use of convenience samples, patients recruited from single academic institutions, or patients who had ART covered by insurance. Because of these limitations, critical gaps remain in our understanding of the disparities in access to and use of oncofertility services among a population-based sample of women with cancer, which limits the development of targeted interventions to improve accessibility.

In this study, we examined sociodemographic disparities in the use of ART and ART-associated live birth among women with invasive breast cancer in California using a novel linkage of population-based data sources that were linked by our study team for research purposes. Informed by prior literature,[12,14–17] we hypothesized that women with breast cancer least likely to use ART after diagnosis would be older, non-Hispanic Black or Hispanic, not married, parous at diagnosis (had at least one child), lack private health insurance, have comorbidities, or live in areas with lower SES or non-urban areas.

METHODS

Data sources

We conducted a population-based cohort study using data from the California Cancer Registry, the Society for Assisted Reproductive Technology Clinic Outcome Reporting System (SART CORS), and the California Office of Statewide Health Planning and Development (OSHPD; now known as the Department of Health Care Access and Information). We obtained approval from the MD Anderson Cancer Center Institutional Review Board, California Cancer Registry, SART CORS, OSHPD, and State of California Committee for the Protection of Human Subjects.

The California Cancer Registry—a statewide population-based cancer surveillance system—was linked to the SART CORS to identify women who were diagnosed with invasive breast cancer between 2000 and 2015, and who received oncofertility services between 2004 and 2015 at SART-member fertility clinics. The data linkage used women's social security numbers, first and last names, and birth dates. SART CORS contains data from 94% of all ART cycles conducted in the United States between 2004 and 2015, and 80% of all ART cycles performed at fertility clinics in California.[18,19] Women receiving ART at SART-member clinics sign clinical consent forms that include a request for permission to use their deidentified data for research. Approximately 10% of the clinics are audited each year to validate the accuracy of the reported data.[18]

The California Cancer Registry and SART CORS data were then linked to OSHPD birth files, which have been used in previous studies of live births and birth outcomes among women with cancer.[20–25] The OSHPD does not gather data for deliveries in military facilities, home deliveries, out-of-state deliveries, or deliveries at birthing centers not

reporting to the California OSHPD. The data linkage was conducted by OSHPD using maternal date of birth, social security number, and ZIP code.

In the linked databases, we identified women age 18–45 years who were diagnosed with stage I-III breast cancer between 2000 and 2015. These age and stage criteria were applied so that our cohort included reproductive-age women with relatively high rates of cancer survival and who were potentially at risk of infertility from receipt of chemotherapy.

Outcome and exposure assessment

The primary outcome was any ART use, including oocyte or embryo cryopreservation (i.e., oocyte or embryo freezing/banking for fertility preservation) or embryo transfer to attempt pregnancy (involving the transfer of at least one embryo to the uterus), after cancer diagnosis. Given known disparities in ART outcomes among the general population,[26,27] we performed a secondary analysis of live births with the use of ART among women who had at least one transfer cycle to attempt pregnancy. The conception date for each live birth was estimated using the infant date of birth and gestational age from the OSHPD. A birth for which the conception date was within 30 days of a transfer cycle was categorized as a birth resulting from ART.

Informed by sociodemographic characteristics associated with ART use after cancer in previous studies and the availability of covariates in our linked database, we examined multiple factors associated with ART use, including age at diagnosis; race and ethnicity; Charlson comorbidity score[28]—a weighted index of comorbidities summed into a single comorbidity score, with a score of 0 representing no comorbidities; marital status; parity at diagnosis; health insurance at diagnosis; SES (defined using the Yost SES index[29]—a composite score constructed using seven SES-related variables at the census tract-level) at diagnosis; and geographic area of residence at diagnosis. Parity data were obtained from the OSHPD. All other factors were obtained from the California Cancer Registry; census tract–level factors were determined using a woman's address at the time of cancer diagnosis. Race and ethnicity are social constructs and were interpreted together in this analysis as an indicator of the extent to which historical and structural factors, including racism, may affect access to cancer survivorship care.[30,31]

Statistical analysis

The primary analysis examined disparities in any ART use after cancer diagnosis. Log-binomial regression was used to estimate prevalence ratios (PRs) and 95% confidence intervals (CIs) for the likelihood of ART use by sociodemographic characteristics. We calculated unadjusted and adjusted estimates for each sociodemographic factor after controlling for all other covariates identified as confounders with the use of a directed acyclic graph; confounders were covariates that we hypothesized could affect both the predictor of interest and ART use. Only unadjusted estimates are presented for age at diagnosis and race and ethnicity, as the other sociodemographic covariates were considered mediators of ART use (affected by age or race/ethnicity and influencing ART use) and adjusting for these covariates could minimize or hide true disparities.[32,33] Given the potential influence of cancer characteristics on disease prognosis and the decision to use

ART, we conducted a sensitivity analysis limited to women who received chemotherapy (i.e., potentially at risk of infertility from cancer treatment) and further described hormone receptor status by ART use among that subset of patients. Covariate categories within adjusted regression models were collapsed as needed given small sample sizes.

The secondary analysis examined live birth with the use of ART after cancer diagnosis by sociodemographic characteristics. Women who had a live birth resulting from ART were compared with women who had at least one ART transfer cycle to attempt pregnancy but did not have a live birth resulting from ART, including women with no live births or births resulting from natural conception only. Small sample sizes precluded regression analysis. All statistical tests were two-sided, and differences were considered statistically significant at $p < .05$. SAS Enterprise Guide version 7.1 was used for all analyses.

Sensitivity analysis for unmeasured confounding

We used E-values to assess the robustness of our results to unmeasured confounding.[34] To quantify the minimum strength of association an unmeasured confounder must have with both the exposure (sociodemographic characteristics) and the outcome (ART use) to fully explain the observed associations, we calculated the E-values needed to shift the observed PR to the null value of 1.0; to shift the CI to include the null (for observed CIs that excluded the null); and to shift the CI to exclude the null (for observed CIs that included the null).[34]

RESULTS

Sample characteristics

Among 36,468 women age 18–45 years diagnosed with stage I-III breast cancer in California between 2000 and 2015, 206 (0.56%) used ART after diagnosis, and 18 had an ART-associated live birth (Figure 1). Ninety-three women used ART for oocyte or embryo cryopreservation only; 82 women used ART for embryo transfer only; and 31 women used ART for both cryopreservation and embryo transfer.

The sociodemographic and clinical characteristics of women who used ART after cancer diagnosis are summarized in Table 1. Compared with women who did not use ART, women who used ART were more likely to be age 18–35 years (54.9% vs. 16.5%); be non-Hispanic White (66.0% vs. 49.3%); be single (38.3% vs. 23.3%); have no children (85.4% vs. 71.5%); have private health insurance (85.4% vs. 71.8%); live in high-SES areas (79.1% vs. 51.2%); and live in urban areas (98.1% vs. 88.6%). Notably, 71.6% of the overall sample had no children at the time of diagnosis. The groups had similar distributions of cancer stages and treatments; however, women who used ART were more likely to be diagnosed in 2011–2015 (38.8% vs. 30.0%) and diagnosed with estrogen receptor (ER)–positive (72.3% vs. 69.2%), progesterone receptor (PR)–positive (65.0% vs. 61.5%), or HER2-negative cancer (62.1% vs. 54.5%).

ART use after cancer diagnosis

The regression analysis revealed disparities in ART use after breast cancer diagnosis for all sociodemographic characteristics examined except Charlson comorbidity score (Table 2).

In the unadjusted analysis, women age 36–45 years at diagnosis had a significantly lower prevalence of ART use compared with women age 18–35 years (PR = 0.17, 95% CI = 0.13 to 0.22); and non-Hispanic Black and Hispanic women had a significantly lower prevalence of ART use compared with non-Hispanic White women (PR = 0.31, 95% CI = 0.21 to 0.46). In analyses of other exposures (with adjustment for all other sociodemographic variables, including parity), significantly lower rates of ART use after breast cancer diagnosis were observed among women who were married (vs. single/other: adjusted PR [aPR] = 0.64, 95% CI = 0.47 to 0.86); women with at least one child (vs. no children: aPR = 0.39, 95% CI = 0.25 to 0.60); and women living in non-urban areas (vs. urban: aPR = 0.28, 95% CI = 0.10 to 0.75). Women with private health insurance had 2.89 (95% CI = 1.56 to 5.38) times the prevalence of ART use compared with women with public or other health insurance; and women living in high-SES areas had 2.96 (95% CI = 2.07 to 4.25) times the prevalence of ART use compared with women living in low- or middle-SES areas.

In sensitivity analysis restricted to women with breast cancer who received chemotherapy (i.e., potentially at risk of infertility from cancer treatment), ART use remained low (0.60%) (Table 1) and sociodemographic disparities by age, race and ethnicity, parity, rurality, insurance status, and SES persisted (Table 2). Among the subset who received chemotherapy, distribution of hormone receptor status was similar between patients who did vs. did not use ART: ER-positive, 67% vs. 66%; PR-positive, 59% vs. 57%; HER-2 positive, 21% vs. 22%; and triple negative, 17% vs. 16%, respectively.

ART-associated live birth after cancer diagnosis

Among the 206 women who used ART after diagnosis, 113 had at least one embryo transfer cycle. Of these women, 18 (15.9%) had an ART-associated live birth, including 4 women who had previously cryopreserved oocytes or embryos (mean time to conception after diagnosis, 4.0 years [standard deviation (SD) = 2.2 years]) and 14 women who had not previously cryopreserved oocytes or embryos (mean time to conception after diagnosis, 4.7 years [SD = 2.2 years]) (Table 3). No significant differences in sociodemographic characteristics were observed between women who did or did not have an ART-associated live birth after diagnosis. A lower proportion of women with an ART-associated live birth lived in urban areas (88.9% vs. 98.9%), but this difference was not significant (data not presented owing to restrictions in reporting small cell sizes per the California Cancer Registry).

Sensitivity analysis for unmeasured confounding

For factors significantly associated with ART use, E-values to shift the PR to 1.0 ranged from 2.5 to 11.2, and E-values to shift the CI to include the null ranged from 1.6 to 8.6 (Table 4). Using age at diagnosis as an example, we can interpret these values as follows: Among women age 36–45 years at diagnosis, the observed association (PR = 0.17) could be explained by an unmeasured confounder that was associated with both age at diagnosis and ART use by a risk ratio of 11.2. Moving the CI to include the null value of 1 would require an unmeasured confounder that was associated with both age at diagnosis and ART use by a risk ratio of 8.6.

DISCUSSION

In this population-based cohort study of women with invasive breast cancer in California, we observed a low overall rate of ART use and substantial disparities in ART use by sociodemographic characteristics. Only 0.56% of all women with breast cancer in California—and a similarly low percentage (0.6%) among women who received potentially gonadotoxic chemotherapy—used ART after diagnosis, which may be attributed to, in part, the lack of mandated health insurance coverage for oncofertility services in California during the study period and the prohibitive cost of paying for services out-of-pocket.[13] Similarly low use of ART has been observed in a population-based sample of women with any type of cancer in North Carolina (1.2% overall use),[12] and across the country among the general population (1.2%–1.8% of all births in the U.S. during 2004–2015 resulted from ART).[35] Further, women who were older at diagnosis, were non-Hispanic Black or Hispanic, were married, had at least one child at diagnosis, or were living in non-urban areas were significantly less likely to use ART after cancer diagnosis, whereas women who had private health insurance or were living in high-SES areas were significantly more likely to use ART. These population-based data provide important evidence that oncofertility services are underutilized and that their use is largely limited to the most socially and economically advantaged women. Such findings support the need to take steps to ensure more equitable access to oncofertility services in the United States, such as improving insurance coverage for such procedures.

Although racial and ethnic minoritized groups and rural and low-SES populations have suboptimal access to and quality of cancer survivorship care,[36–38] only a few studies have examined patient-level factors contributing to the post-diagnosis use of ART specifically. One 2010 survey of women with cancer in California reported lower rates of fertility preservation among those age 36–40 years at diagnosis and among Latina/Hispanic women, which may have been driven in part by less access to fertility counseling.[14] A second study of the medical records of women diagnosed with breast cancer between 2005 and 2010 at three academic medical centers found that women who used fertility preservation were slightly older and lived in higher-income areas.[15] A third study that identified fertility preservation procedures among women diagnosed with lung, breast, colorectal, or cervical cancer between 2009 and 2016 using administrative claims data (capturing privately insured and Medicaid patients) found lower rates of fertility preservation among women age 36–45 years, those with Medicaid, and those living in non-urban areas.[16] However, the findings of these previous studies are limited by their lack of generalizability, as the study populations were self-selected women who responded to a survey focused on fertility,[14] women receiving cancer care at one of three large academic medical centers,[15] and women with private insurance or Medicaid whose fertility-preserving procedures were at least partially covered by their insurance provider.[16]

Similar to our study, two recent population-based studies reported that the use of oncofertility services after diagnosis varies by sociodemographic characteristics[12,17]; however, one of these studies defined “use” as having a fertility-related discussion with a healthcare provider, and advice and infertility testing were the most common fertility services reported by the study participants.[17] To our knowledge, only one other study

has examined the actual use of fertility services in a population-based sample of women with cancer. Similar to the present study, the previous study, whose cohort was identified from the North Carolina Central Cancer Registry, found that fertility preservation was also lower among women who were age 35–39 years at diagnosis, non-Hispanic Black, parous, or living in non-urban or low-SES areas.[12] Neither this previous study nor the present study adjusted for other sociodemographic factors in analyses of race and ethnicity, as adjustment for covariates such as SES at the time of diagnosis (a mediator of ART use) could lead to bias in the estimate of the total effect of race and ethnicity on ART use.[32,33] The findings of the present study and those of the North Carolina study together suggest that historical and structural factors continue to disadvantage women of color in accessing equitable health care. Importantly, unlike the analysis of North Carolina data, our study additionally captured women who accessed ART after cancer diagnosis to attempt pregnancy without prior fertility preservation, suggesting that sociodemographic disparities persist when patients initiate ART use in the years following cancer diagnosis.

ART has enabled millions of women worldwide to overcome subfertility and infertility, and opportunities to preserve reproductive function have become increasingly available as established clinical practices. Among women with a history of cancer, access to ART may be the most important modifiable factor that can improve the chances of achieving pregnancy and giving birth. Thus, a logical step towards reducing family-building health disparities is to enhance access to ART, which involves disentangling the complex factors underlying these disparities, including patient-, provider-, and institutional-level barriers.[39–43] Geographic barriers may be targeted through clinical interventions that improve the design and implementation of telehealth platforms; for instance, by providing oncofertility consultations to patients receiving care at an institution that does not have on-site oncofertility support and is remote from the nearest fertility clinic. The creation of regional oncofertility centers could also help to improve geographic access for more of the cancer patient population. Arguably most important, though, are the continued efforts among advocacy groups, clinicians, and state and federal legislatures to mandate coverage for fertility preservation and fertility treatment for individuals facing medically induced infertility. Aligning with policies such as the Women’s Health and Cancer Rights Act (which mandates insurance coverage for breast reconstruction after breast cancer treatment) and extending coverage to oncofertility services would represent a powerful policy commitment to addressing existing health disparities in reproductive health and help ensure equitable, comprehensive cancer survivorship care.[44–46]

Our study had several limitations related to the use of linked population-based data and the lack of availability of certain relevant variables. Because we did not have data on reproductive interest, we could not determine the extent to which observed associations between sociodemographic characteristics and ART use were driven by differences in patient desire for future family-building (e.g., lower desire among older women or those who already had at least one child). Some women included in our analyses may not have used ART due to lack of access, but rather due to lack of need for such services. The E-value sensitivity analysis was conducted in an attempt to quantify the magnitude of unmeasured confounding (including patient desire) that would explain the observed associations; we found that substantial confounding beyond that of the variables adjusted

for in the present analysis would need to be present to fully explain our results for most of the sociodemographic characteristics examined. However, given the strength of association that patient desire likely has on the use of elective ART, future studies should examine whether sociodemographic disparities persist among a sample of women who desired future family building after cancer diagnosis. In addition, we could not determine the extent to which specific patient-, provider-, or institution-level barriers influenced a woman's ability to access ART information or services after cancer diagnosis. Further, although the SART CORS captured the large majority of ART procedures during the study period, it did not capture those of women who were diagnosed with cancer in California but used ART in another state, used ART at a non–SART-member fertility clinic, or used ART before 2004 or after 2015 (outside of the range of available ART data from SART CORS).

Conclusions

We observed low use of ART (<0.6%) among women diagnosed with invasive breast cancer in California between 2000 and 2015. Our findings additionally suggest significant sociodemographic disparities in the use of fertility preservation and fertility treatment after diagnosis. The implementation of policies or programs that target these disparities is warranted; this may entail in-depth studies aimed at identifying and understanding the specific barriers that prevent the delivery of fertility information and services to certain cancer patient populations and obtaining a deeper understanding of factors that influence ART use among women with breast cancer. In particular, future studies should investigate the degree to which state-legislated mandates for fertility preservation and fertility treatment, including the fertility preservation bill (Senate Bill No. 600) enacted in California in 2019, have impacted ART use among women with cancer.[13] Equitable access to fertility services for cancer patient populations should be standard practice in comprehensive, evidence-based survivorship care.

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Data Availability

The data underlying this article cannot be shared publicly owing to the need to protect the privacy of the study participants. Researchers with appropriate IRB approval can contact the corresponding author to obtain a deidentified dataset.

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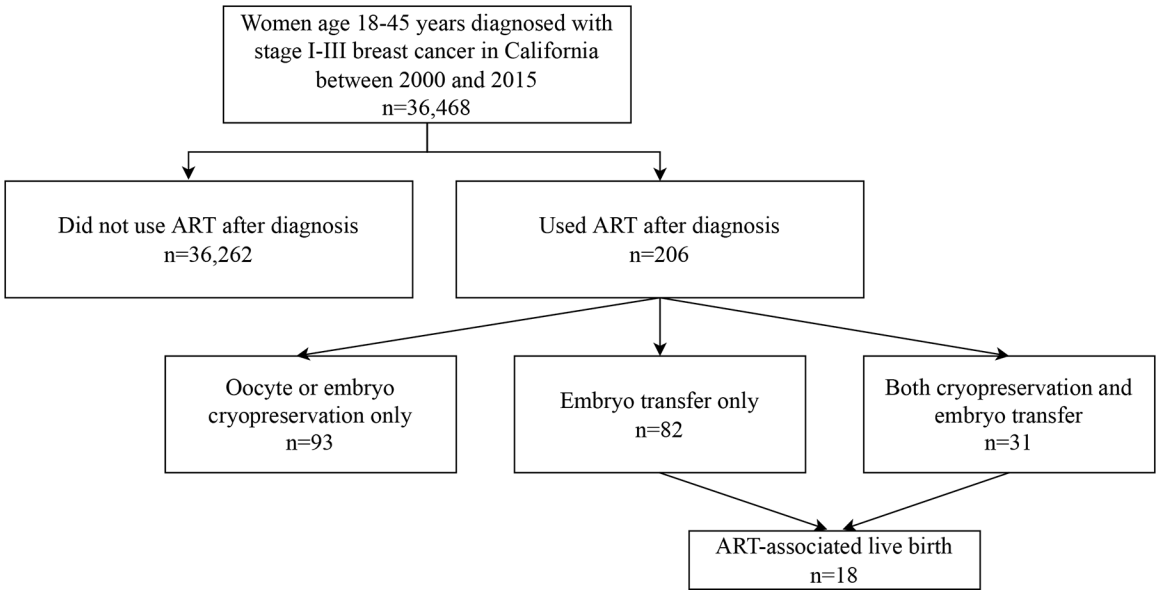

Figure 1.

Cohort selection flow diagram

Abbreviations: ART, assisted reproductive technology

Table 1.

Sociodemographic and cancer-related characteristics of women diagnosed with breast cancer in California between 2000 and 2015 by use of assisted reproductive technology (ART) after diagnosis (n=36,468)

	ART used, n=206	No ART used, n=36,262
Characteristic	**n (%)**	**n (%)**
Age at diagnosis, years		
18–35	113 (54.9)	5998 (16.5)
36–45	93 (45.1)	30264 (83.5)
Race and ethnicity		
Non-Hispanic White	136 (66.0)	17862 (49.3)
Non-Hispanic Asian/Pacific Islander	42 (20.4)	6254 (17.2)
Hispanic	22 (10.7)	9118 (25.1)
Non-Hispanic Black[a]	<11 (<5.3)	2698 (7.4)
Non-Hispanic American Indian	0 (0)	172 (0.5)
Unknown[a]	<11 (<5.3)	158 (0.4)
Charlson comorbidity score		
0	191 (92.7)	33109 (91.3)
≥1	15 (7.3)	3153 (8.7)
Marital status		
Single	79 (38.3)	8436 (23.3)
Married	115 (55.8)	23371 (64.5)
Other[a]	<11 (<5.3)	3592 (9.9)
Unknown	<11 (<5.3)	863 (2.4)
Parity at diagnosis		
0 children	176 (85.4)	25934 (71.5)
≥1 child	30 (14.6)	10325 (28.5)
Unknown	0 (0)	3 (.008)
Health insurance at diagnosis		
Public[a]	<11 (<5.3)	5916 (16.3)
Private	176 (85.4)	26041 (71.8)
Uninsured/self-pay[a]	<11 (<5.3)	412 (1.1)
Other/unknown	19 (9.2)	3893 (10.7)
Census tract–level SES		
Low or middle	43 (20.9)	17685 (48.8)
High	163 (79.1)	18577 (51.2)
Rurality		
Urban	202 (98.1)	32145 (88.6)
Rural[a]	<11 (<5.3)	3992 (11.0)
Other[a,b]	<11 (<5.3)	125 (0.3)

Characteristic	ART used, n=206 n (%)	No ART used, n=36,262 n (%)
Year of cancer diagnosis		
2000–2005	42 (20.4)	13830 (38.1)
2006–2010	84 (40.8)	11556 (31.9)
2011–2015	80 (38.8)	10876 (30.0)
Stage at diagnosis		
I	74 (35.9)	12889 (35.5)
II	104 (50.5)	17196 (47.4)
III	28 (13.6)	6177 (17)
Estrogen receptor status		
Negative	53 (25.7)	8986 (24.8)
Positive	149 (72.3)	25077 (69.2)
Unknown	4 (1.9)	2199 (6.1)
Progesterone receptor status		
Negative	68 (33.0)	11239 (31.0)
Positive	134 (65.0)	22297 (61.5)
Unknown	4 (1.9)	2726 (7.5)
HER2 status		
Negative	128 (62.1)	19747 (54.5)
Positive	37 (18.0)	6564 (18.1)
Unknown	41 (19.9)	9951 (27.4)
Triple-negative		
No	162 (78.6)	27810 (76.7)
Yes	28 (13.6)	4515 (12.4)
Unknown	16 (7.8)	3937 (10.9)
Surgery received		
Yes	204 (99.0)	35185 (97.0)
Lumpectomy	88 (42.7)	15971 (44.0)
Mastectomy	116 (56.3)	19214 (53.0)
No[a]	<11 (<5.3)	1049 (2.9)
Unknown[a]	<11 (<5.3)	28 (0.1)
Radiation received		
Yes	101 (49.0)	17560 (48.4)
No	105 (51.0)	18695 (51.6)
Unknown	0 (0)	7 (0)
Chemotherapy received		
Yes	149 (72.3)	24759 (68.3)
No	55 (26.7)	10810 (29.8)
Unknown	2 (1.0)	693 (1.9)

Abbreviations: SES, socioeconomic status.

[a] Exact number not reported because the California Cancer Registry requires suppression of cell sizes <11.

[b] Other rurality status includes census tracts with a population density <11 persons per square mile.

Table 2.

Prevalence ratio (PR) estimates of assisted reproductive technology (ART) use among women diagnosed with breast cancer in California between 2000 and 2015 (n=36,468)

		Full sample (n=36,468)	Received chemotherapy (n=24,908)
Characteristic	**Unadjusted PR (95% CI)**	**Adjusted PR (95% CI)[a]**	
Age at diagnosis, years			Unadjusted
18–35	1.00	n/a	1.00
36–45	0.17 (0.13 to 0.22)		0.18 (0.13 to 0.25)
Race and ethnicity			Unadjusted
Non-Hispanic White	1.00		1.00
Non-Hispanic			
Asian/Pacific	0.88 (0.63 to 1.25)	n/a	0.67 (0.43 to 1.04)
Islander			
Non-Hispanic Black or Hispanic	0.31 (0.21 to 0.46)		0.30 (0.19 to 0.47)
Charlson comorbidity score at diagnosis			
0	1.00	1.00	1.00
≥1	0.83 (0.49 to 1.39)	1.04 (0.60 to 1.79)	1.19 (0.63 to 2.25)
Marital status at diagnosis			
Single/other	1.00	1.00	1.00
Married	0.68 (0.52 to 0.90)	0.64 (0.47 to 0.86)	0.74 (0.52 to 1.06)
Parity at diagnosis			
0 children	1.00	1.00	1.00
≥1 child	0.43 (0.29 to 0.63)	0.39 (0.25 to 0.60)	0.42 (0.26 to 0.68)
Health insurance at diagnosis			
Public/other	1.00	1.00	1.00
Private	3.87 (2.11 to 7.11)	2.89 (1.56 to 5.38)	2.06 (1.07 to 3.97)
Census tract–level SES at diagnosis			
Low or middle	1.00	1.00	1.00
High	3.59 (2.56 to 5.01)	2.96 (2.07 to 4.25)	3.48 (2.18 to 5.55)
Rurality at diagnosis			
Urban	1.00	1.00	1.00
Non-urban	0.16 (0.06 to 0.42)	0.28 (0.10 to 0.75)	0.31 (0.10 to 0.97)

Abbreviations: CI, confidence interval; SES, socioeconomic status.

[a]Adjusted models included the following covariates: age at diagnosis, race and ethnicity, Charlson comorbidity score, marital status, parity, health insurance, census tract–level SES, and rurality.

Table 3.

Live births among women diagnosed with breast cancer in California between 2000 and 2015 who had at least one embryo transfer after diagnosis (n=113)

	Cryopreservation and transfer, n=31	Transfer only, n=82
Characteristic	**n (%)**	**n (%)**
Any live birth after cancer diagnosis	6 (19.4)	20 (24.4)
ART-associated live birth	4 (12.9)	14 (17.1)
Natural conception live birth	2 (6.5)	6 (7.3)
Mean (SD) time from diagnosis to first ART-associated live birth, years	4.0 (2.2)	4.7 (2.2)

Abbreviations: ART, assisted reproductive technology; SD, standard deviation.

Table 4.

Assessment of unmeasured confounding using the E-value[a]

Characteristic	Adjusted PR (95% CI)	E-value to shift PR to 1.0	E-value to shift CI to include the null[b]	E-value to shift CI to exclude the null[c]
Age 36–45 years at diagnosis	0.17 (0.13 to 0.22)	11.2	8.6	n/a
Non-Hispanic Asian/Pacific Islander	0.88 (0.63 to 1.25)	1.5	n/a	1.8
Non-Hispanic Black or Hispanic	0.31 (0.21 to 0.46)	5.9	3.8	n/a
Charlson comorbidity score ≥1	1.04 (0.60 to 1.79)	1.2	n/a	3.0
Married at diagnosis	0.64 (0.47 to 0.86)	2.5	1.6	n/a
At least one child at diagnosis	0.39 (0.25 to 0.60)	4.6	2.7	n/a
Private health insurance at diagnosis	2.89 (1.56 to 5.38)	5.2	2.5	n/a
Living in high census tract–level SES area at diagnosis	2.96 (2.07 to 4.25)	5.4	3.6	n/a
Living in non-urban area at diagnosis	0.28 (0.10 to 0.75)	6.6	2.0	n/a

Abbreviations: ART, assisted reproductive technology; CI, confidence interval; PR, prevalence ratio; SES, socioeconomic status.

[a]The E-value represents the strength of association an unmeasured confounder must have with both the exposure (sociodemographic characteristics) and the outcome (ART use) to fully explain the observed associations.[34]

[b]For observed CIs that excluded the null value of 1.

[c]For observed CIs that included the null value of 1.