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Disparities in Fertility-Sparing Treatment and Use of Assisted Reproductive Technology After a Diagnosis of Cervical, Ovarian, or Endometrial Cancer

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Abstract

OBJECTIVE: To assess the presence of sociodemographic and clinical disparities in fertility-sparing treatment and assisted reproductive technology (ART) use among patients with a history of cervical, endometrial, or ovarian cancer.

METHODS: We conducted a population-based cohort study of patients aged 18–45 years who were diagnosed with cervical (stage IA, IB), endometrial (grade 1, stage IA, IB), or ovarian (stage IA, IC) cancer between January 1, 2000, and December 31, 2015, using linked data from the California Cancer Registry, the California Office of Statewide Health Planning and Development, and the Society for Assisted Reproductive Technology. The primary outcome was receipt of *fertility-sparing treatment*, defined as surgical or medical treatment to preserve the uterus and at least one ovary. The secondary outcome was *fertility preservation*, defined as ART use after cancer diagnosis. Multivariable logistic regression analysis was used to estimate odds ratios and 95% confidence intervals for the association between fertility-sparing treatment and exposures of interest: age at diagnosis, race and ethnicity, health insurance, socioeconomic status, rurality, and parity.

RESULTS: We identified 7,736 patients who were diagnosed with cervical, endometrial, or ovarian cancer with eligible histology. There were 850 (18.8%) fertility-sparing procedures among 4,521 cases of cervical cancer, 108 (7.2%) among 1,504 cases of endometrial cancer, and 741 (43.3%) among 1,711 cases of ovarian cancer. Analyses demonstrated non-uniform patterns of sociodemographic disparities by cancer type for fertility-sparing treatment and ART. Fertility-sparing treatment was more likely among young patients overall, and of those in racial and ethnic minority groups among survivors of cervical and ovarian cancer. ART use was low (n=52) and was associated with non-Hispanic White race and ethnicity, younger age (18–35 years), and private insurance.

CONCLUSION: This study demonstrates that clinical and sociodemographic disparities exist in the receipt of fertility-sparing treatment and ART use among patients with a history of cervical, endometrial, or ovarian cancer.

Precis

Disparities exist in fertility-sparing treatment and the use of assisted reproductive technology among patients with gynecologic malignancies.

INTRODUCTION

Gynecologic malignancies account for over 10,000 cancer diagnoses among reproductive-aged women in the United States each year. Fertility preservation may improve the ability of reproductive-aged patients to cope with cancer^{2–5} and improve survivors' quality of life. While definitive surgical resection is indicated for many, national guidelines recommend that physicians discuss fertility at the time of cancer diagnosis to allow for counseling about options. Fertility-sparing treatment is underused in early-stage gynecologic malignancies, despite being a reasonable and safe alternative to hysterectomy or bilateral-salpingooophorectomy. 11–14

Prior studies demonstrate disparities in cancer-related treatment by geography, ^{15–17} race and ethnicity, ^{15,18–21} and insurance status; ^{22,23} however, few examine disparities specifically related to fertility-sparing treatment. ²⁴ Reproductive-age patients face disparities accessing assisted reproductive technology (ART) services due to socioeconomic status (SES), geographic location, and race and ethnicity despite state mandates to offer insurance coverage for ART services, ^{25–27} however there are few studies of cancer survivors' use of ART. ²⁸

This study sought to assess the presence of disparities in fertility-sparing treatment and ART use among patients with a history of cervical, endometrial, or ovarian cancer. We hypothesized that fertility-sparing treatments are more likely to be covered by insurance than ART, resulting in fewer disparities. Disparity was defined using the Institute of Medicine definition: a difference in health care quality not due to differences in the health care needs of the patient.²⁹

METHODS

This population-based study used data linked between the California Cancer Registry (CCR), the California Office of Statewide Health Planning and Development (OSHPD), and the Society for Assisted Reproductive Technology Clinic Outcome Reporting System (SART CORS). We obtained approval for this study from the MD Anderson Institutional Review Board, the California OSHPD, CCR, the State of California Committee for the Protection of Human Subjects, and SART. The linked data set included CCR data from January 1, 2000, to December 31, 2015, and OSHPD data files for patients treated from January 1, 2000, through December 31, 2012 (Appendix 1, available online at http://links.lww.com/xxx). The data files included diagnostic and procedure codes using the International Classification of Diseases, 9th Clinical Modification and 10th Revisions.³⁰

The data from CCR and OSHPD were linked to SART CORS to identify patients with a gynecologic malignancy who underwent ART treatment between January 1, 2004 (earliest available data from SART), and December 31, 2015, using the woman's birth date, first and last name, social security number, and infant's birth date (when applicable). SART CORS includes more than 80% of clinics that provide ART, 90% of ART cycles in the United States, and is subject to annual review and verification. 31,32

In the linked database, we identified patients aged 18–45 years at the time of diagnosis with cervical cancer (stage IA, IB), endometrial cancer (grade 1, stage IA or IB), and ovarian cancer (stage IA, IC) between January 1, 2000, and December 31, 2015. The primary outcome analysis used the maximal date range of data available, 2000–2015. Secondary analyses utilized date ranges pending availability of data, described below. All stages were based on available data and defined by the American Joint Committee on Cancer (3rd edition for 2000–2004, 6th edition for 2004–2009, and 7th edition for 2010–2015). We included histologies eligible for fertility-sparing procedures using the International Classification of Diseases for Oncology codes (Appendix 2, available online at http://links.lww.com/xxx). 34

The primary outcome, receipt of fertility-sparing treatment, was defined as interventions that allowed for the retention of at least one ovary and the uterus for all three cancer types. Treatment included: loop electrosurgical excisional procedure, conization, and trachelectomy, with or without ovarian transposition or lymph node evaluation for cervical cancer; 11 hormonal management with progestin via intrauterine devices or oral medications for endometrial cancer; 35 and unilateral oophorectomy without hysterectomy, with or without additional biopsies for ovarian cancer. 11 This outcome was investigated using data from 2000–2015.

The secondary outcome, ART use following cancer diagnosis, was defined as one or more autologous embryo- or oocyte-freeze cycles or embryo transfer cycles after the date of cancer diagnosis. This outcome was investigated using ART data from 2004–2015 for individuals diagnosed from 2000–2015.

The exposures of interest included age (18–35 or 36–45 years) at diagnosis, race and ethnicity (American Indian, Asian or Pacific Islander, Hispanic, non-Hispanic Black, non-Hispanic White, and none of the above), insurance status at diagnosis (public, private, uninsured or self-pay, and other or unknown), rurality (urban or rural, according to medical service study area by census tract), and socioeconomic status (SES, Yost SES index at the census tract level, ³⁶ by quintiles). The additional variables collected for multivariable analysis included parity (0, 1, or 2 or more prior births), Charlson comorbidity scores at the time of diagnosis, marital status, year of diagnosis (2000–2005, 2006–2010, 2011–2015), cancer stage, and receipt of adjuvant chemotherapy, radiotherapy, or hormonal therapy. Histology was collected for all cancer types but only included in multivariate analysis for ovarian cancer due to exclusion of histologies contraindicated for fertility-sparing treatment limiting this variable's impact on endometrial and cervical cancer outcomes. Race and ethnicity data were used as exposures of interest given the results of prior studies demonstrating differences in fertility-sparing treatment among patients with a history of gynecologic cancer²⁴ and access to ART overall²⁵ by race and ethnicity.

Descriptive statistics of sociodemographic variables were performed among those who received fertility-sparing treatment and had a subsequent live birth after excluding those who received radiation. *Live births* were defined as the first birth whose fertilization occurred 3 or more months following a cancer diagnosis and fertility-sparing treatment. The fertilization date for each live birth was estimated using the infant's date of birth and gestational age at delivery. ³⁷ Live birth outcomes were available through the OSHPD database for births between January 1, 2000, and December 31, 2012, and were assessed for diagnoses from the same time period.

Categorical variables were assessed using Chi-squared tests or Fisher's exact tests. An analysis of the primary outcome was performed using multivariable logistic regression to assess the association between fertility-sparing treatment and the exposures of interest by cancer type. Due to the limited number of ART instances in the linked dataset, the variables of interest were collapsed to binary categories. Given overall limited number of ART procedures, univariable logistic regression analysis was performed for the secondary

outcome to assess the association of exposures of interest and ART use by cancer type. Odds ratios were calculated with 95% confidence intervals.

All statistical tests were two-sided, and differences were considered statistically significant at P < 0.05 and a 95% confidence interval not inclusive of the null (1.0). SAS Enterprise Guide software version 7.11 (SAS Institute, Inc.) was used for all statistical analyses.

We performed a sensitivity analysis of our primary outcome using the E-value, a measure which describes the robustness of estimates to possible unmeasured confounders using minimal assumptions. ³⁸ We used the E-value to quantify the magnitude of the association an unmeasured confounder would need with the exposures (sociodemographic and clinical variables) and primary outcome (fertility-sparing treatment) to explain away the calculated estimate, the E-value required to explain the confidence limit that was closest to the null, and to shift the confidence limit to a significant result.

RESULTS

We identified 7,736 patients aged 18–45 years who were diagnosed with a gynecologic malignancy in California between January 1, 2000, and December 31, 2015, and were eligible by histology to receive fertility-sparing treatment. Of these, 4,521 (58.4%) were diagnosed with cervical cancer (stage IA or IB), 1,504 (19.4%) with endometrial cancer (stage IA, IB), and 1,711 (22.1%) with ovarian cancer (stage IA, IC) (Figure 1).

There were 1,699 (22.0%) fertility-sparing procedures. Of the 4,521 patients with a history of cervical cancer 850 (18.8%) received fertility-sparing procedures, of the 1,504 patients with a history of endometrial cancer 108 (7.2%) received fertility-sparing treatment, and of the 1,711 patients with a history of ovarian cancer 741 (43.3%) received fertility-sparing procedures (Table 1). There were 52 (0.7%) instances of ART, and 228 (17.6%) patients had a live birth between 2000 and 2012 following fertility-sparing treatment (Table 2).

Among patients with cervical cancer who received fertility-sparing surgery versus those who did not, there were significant differences in all clinical and sociodemographic variables (Table 1). Multivariable regression (Table 3, Figure 2) demonstrated that younger age (18–35 vs 36–45 years), Asian or Pacific Islander (vs non-Hispanic White), single status (vs married), year of diagnosis (2006–2010 and 2011–2015 vs 2000–2005), and cancer stage IA (vs 1B) were associated with higher odds of fertility-sparing treatment.

There were 25 (0.6%) instances of ART among patients with a history of cervical cancer. There were no instances of ART among non-Hispanic Black patients, American Indian patients, those in the lowest SES quintile, or those with public insurance. Univariable logistic regression demonstrated higher odds of ART among patients who were younger (18–35 vs 36–45 years), non-Hispanic White (vs all non-White races or ethnicities), nulliparous (vs 1), of high SES (vs low) or diagnosed between 2000–2007 (vs 2008–2015) (Figure 3). Women with a history of cervical cancer accounted for 48.2% (n=110) of patients who had a live birth outcome following cancer diagnosis and fertility-sparing treatment (Table 2).

There were significant differences in age, year of diagnosis, Charlson comorbidity score, race or ethnicity, and cancer stage between patients with endometrial cancer who received fertility-sparing treatment versus those who did not (Table 1). Multivariable regression analysis (Table 3, Figure 2) found that age 18–35 years (vs 36–45 years) was associated with increased odds of fertility-sparing treatment.

There were 9 instances (0.6%) of ART, which was associated with high SES (vs low and middle) on univariable analysis (Figure 3). There were no instances of ART among non-Hispanic Black patients, American Indian patients, or publicly insured patients. Patients with a history of endometrial cancer accounted for 1.3% (3) of those who had a live birth outcome following their cancer diagnosis and fertility-sparing treatment.

Among patients with ovarian cancer who received fertility-sparing treatment versus those who did not, significant differences existed in age, Charlson comorbidity scores, marital status, race or ethnicity, rurality, cancer stage, histology, and receipt of chemotherapy (Table 1). Multivariable logistic regression models identified age 18–35 years (vs 36–45 years), middle, upper-middle, and highest SES (vs lowest SES), stage IA (vs IC), non-Hispanic Black and Hispanic (vs non-Hispanic White), and germ cell or sex cord stromal histology (vs epithelial) were associated with increased odds of fertility-sparing treatment (Table 3, Figure 2).

A total of 18 instances (1.1%) of ART occurred after diagnosis. On univariable analysis, ART use was associated with diagnosis between 2000–2007 (vs 2008–2015) (Figure 3). No ART instances were observed among non-Hispanic Black, American Indian, or publicly insured patients. Patients with a history of ovarian cancer accounted for the half of those who experienced a live birth following a cancer diagnosis and fertility-sparing treatment (115 of 228 [50.4%]) (Table 2).

Sensitivity analysis demonstrated our data were robust to moderate unmeasured confounders related to both exposure and outcome for most exposure variables. Our results appear to be robust to strong confounders with respect to age and diagnosis year (all cancer types) (Appendix 3, available online at http://links.lww.com/xxx).

DISCUSSION

We found differing patterns of sociodemographic disparities by cancer type for fertility-sparing treatment and ART that did not always follow anticipated patterns based on prior studies. Fertility-sparing treatment was more likely among patients in racial and ethnic minority groups for cervical and endometrial cancers and younger patients for all three cancers. ART was more likely among those diagnosed earlier in the cohort and those with private insurance across all three cancer types, and also among younger and non-Hispanic White patients with a history of cervical cancer.

Patients in racial and ethnic minority groups had higher odds of receiving fertility-sparing treatment than did non-Hispanic White patients among those with cervical and ovarian cancer, with no difference among those with a history of endometrial cancer. This result contrasts prior studies demonstrating racial disparities in access to, and receipt of,

guideline-based treatments for ovarian, ¹⁹ endometrial, ²¹ and cervical cancer. ²³ Although the baseline cohort could be affected by higher rates of prior hysterectomy or unilateral salpingo-oophorectomy among patients in racial and ethnic minority groups compared to non-Hispanic White patients, the overall rate of these procedures in the ages selected for this study is low. ^{39–41} Furthermore, while differences in ovarian histology by race or ethnicity could explain our findings, ^{42,43} race and ethnicity remained significant predictors of fertility-sparing procedures after controlling for histology. Lastly, incidental diagnoses of cancer at the time of surgery, while not different by race or ethnicity, accounted for the majority of cases for cervical and ovarian cancer in our study, which could affect interpretation of our findings.

The fertility-sparing treatments investigated in this analysis should be covered by both public and private insurance as they are guideline-based therapies; this is reflected in our findings of no significant disparities by insurance status. In contrast, prior studies have demonstrated that patients with public or no insurance are less likely to receive guideline-based treatment for gynecologic malignancies. ^{22,44–46} Our study had a high overall percentage of patients with insurance, thus possibly limiting generalizability and partially explaining the findings.

The lack of geographic disparities in fertility-sparing treatments differ from prior studies among patients with gynecologic malignancies that demonstrated a lower likelihood of receiving guideline-adherent care if they live farther from urban centers. ¹⁶ It is possible our study found different results due to a high percentage of fertility-sparing treatments (LEEP, cone, unilateral oophorectomy) being feasible in rural settings and by non-gynecologic oncologists.

There was overall low utilization of ART among patients in our study. The majority of instances of ART were noted in the earlier half of the study years, which may reflect lack of follow-up time for those diagnosed after 2007. The type of treatment patients in this cohort received may have variably impacted their fertility, from limited impact after a LEEP to more substantial impact after trachelectomy or oophorectomy, particularly if they had received prior gynecologic surgery.

Unlike trends seen in fertility-sparing treatment, we found that racial and ethnic minority patients were less likely to use ART after a diagnosis of cervical cancer. This finding is consistent with prior studies' findings of lower ART use in the general non-Hispanic Black and Hispanic populations.⁴⁷

Insurance type may mediate the race and ethnicity disparity as Medicaid does not cover fertility treatment, disproportionately affecting patients in racial and ethnic minority groups, as the program covers 30% of Black patients and 25% of Hispanic patients versus 15% of non-Hispanic White patients. Additionally, during the study period, California had a mandate to offer coverage for infertility services that applied differentially to private insurances, did not apply to Medicaid or public insurances, and specifically excluded in vitro fertilization. 49

In the general population, geographic disparity is demonstrated by the unequal distribution of access to ART services nationwide, as nearly 30% of reproductive-age patients do not have access to a local ART clinic based on census data.⁵⁰ The lack of geographic disparity in ART services in this study may be due to low overall numbers, California's above-national average ART use rates, or the abundance of ART clinics.⁵¹ Despite the high use of ART in California among the general population, our findings suggest that ART use among patients after treatment for cervical, endometrial, or ovarian cancers is low.

Live births were overall infrequent (228 births among 1,293 cases from 2000–2012). Half of live births were to patients with a history of ovarian cancer. This may be related to increased rates of infertility⁵² and increased likelihood of preterm birth⁵³ among those undergoing fertility-sparing treatment for endometrial and cervical cancer, respectively. In comparison, prior studies of fertility-sparing treatment for ovarian cancer did not find an association with adverse pregnancy outcomes.³⁷ The low number of live births may be related to recurrence or ongoing disease, as patients who receive fertility-sparing treatment are at risk for further infertility-inducing procedures or treatments in these circumstances.

The strengths of this study include a large database created by unique linkages that were robust in sample size and granularity. California is a state with a large population and relatively high access to medical centers, which allowed for a large number of outcomes compared to prior studies. Restricting the analysis to one state decreased possible confounding by insurance mandates or practice patterns. Additionally, though state demographics changed during the study period, the demographics of our cohort remained constant.

The limitations of our study include inability to verify registry data, data misclassification or underreporting, and inaccuracies in the linkage process. Women may have received fertility-sparing treatment or ART in California and subsequently left the state. A lack of knowledge of the surgeon's intent was mitigated by selecting a cohort for whom fertility-sparing treatment represented guideline-concordant care. We could not address patient-, health care professional-, or intuition-specific barriers to fertility-sparing treatment or ART, nor individuals' desire for such interventions. We were limited by the years of data available in each dataset, with possible ART use or live births following a cancer diagnosis not yet published, and by missing or unknown data regarding oncologic or sociodemographic variables. Lastly, there were very few outcomes of interest for ART and live births, limiting the certainty of the statistical conclusions.

The results of this study for the primary outcome of fertility-sparing treatment did not follow anticipated race or ethnicity disparities. In addition, the results demonstrated no insurance-based disparities for fertility-sparing treatments, in contrast to the significant findings of insurance-based disparities for ART. There were few ART instances overall and zero instances among non-Hispanic Black and publicly insured patients, highlighting a need to address these disparities in clinical practice. The results of this study will improve health care professionals' awareness of existing disparities and emphasize the need for equitable access to fertility-related care among survivors of gynecologic malignancies.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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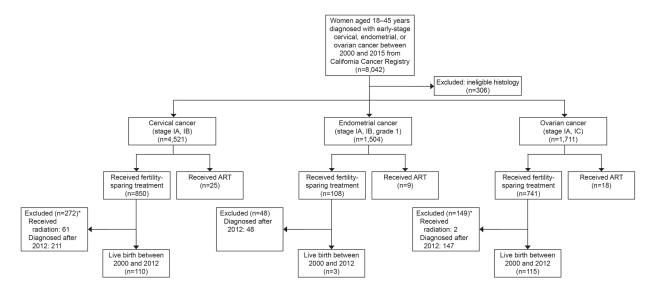


Figure 1. Selection of cases. Assisted reproductive technology (ART) use was assessed for women diagnosed 2000–2015, based on available ART data from 2004 to 2015. Live births were assessed for those with available data (diagnoses from 2000–2012). Included histologies are listed in Appendix 2 (http://links.lww.com/xxx) *Not mutually exclusive.

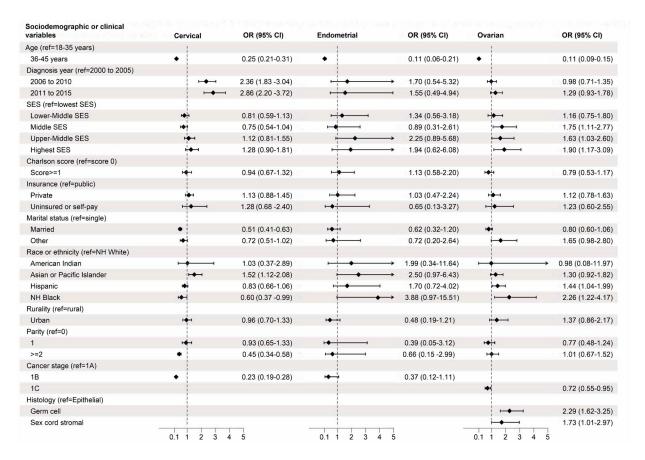


Figure 2. Multivariable analysis of adjusted odds ratio of fertility-sparing treatment by cancer type and variables of interest. All variables presented were included in multivariable analysis. Rows without adjusted odds ratios presented were not applicable to that cancer type (stage IB for ovarian, stage IC and histology type for cervical, endometrial). aOR, adjusted odds ratio; SES, socioeconomic status; NH, non-Hispanic.

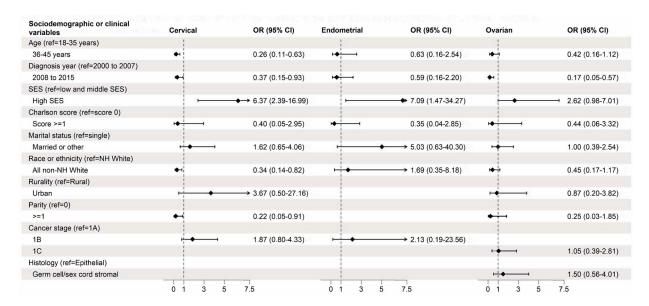


Figure 3.
Univariable analysis of odds ratio of assisted reproductive technology by cancer type and variables of interest. Rows without odds ratios presented were not applicable to that cancer type (stage IB for ovarian, stage IC and histology type for cervical, endometrial), or unable to be calculated (rurality and parity for endometrial cancer). OR, odds ratio; SES, socioeconomic status; NH, non-Hispanic.

Table 1.Patient Characteristics by Fertility-Sparing Treatment and Cancer Type

Sociodemographic and clinical characteristics	Cervical (n=4,521)			Endometrial (n=1,504)			Ovarian (n=1,711)		
	Fertility- Sparing (n=850)	Not Fertility- Sparing (n=3,671)	P Value	Fertility- Sparing (n=108)	Not Fertility- Sparing (n=1,396)	P Value	Fertility- Sparing (n=741)	Not Fertility- Sparing (n=970)	<i>P</i> Value
Age (years), n (%)			< 0.01			< 0.01			< 0.01
18–35	573 (31.3)	1,260 (68.7)		66 (18.2)	296 (81.8)		552 (70.5)	231 (29.5)	
36–45	277 (10.3)	2,411 (89.7)		42 (3.7)	1,100 (96.3)		189 (20.4)	739 (79.6)	
Diagnosis year, n (%)			< 0.01			0.04			0.22
2000–2005	296 (16.4)	1508 (83.6)		17 (6.8)	233 (93.2)		255 (42.6)	344 (57.4)	
2006–2010	292 (19.5)	1208 (80.5)		32 (5.3)	571 (94.7)		229 (41.2)	327 (58.8)	
2011–2015	262 (21.5)	955 (78.5)		59 (9.1)	592 (90.9)		257 (46.2)	299 (53.8)	
SES, n (%)			< 0.01			0.52			0.96
Lowest	160 (17.8)	738 (82.2)		24 (7.2)	309 (92.8)		106 (42.1)	146 (57.9)	
Lower-middle	154 (16.5)	780 (83.5)		21 (5.6)	355 (94.4)		151 (43.8)	194 (56.2)	
Middle	156 (16.7)	778 (83.5)		20 (6.8)	274 (93.2)		165 (44.7)	204 (55.3)	
Upper-middle	206 (20.6)	794 (79.4)		26 (8.2)	293 (91.8)		163 (43.1)	215 (56.9)	
Highest	174 (23.0)	581 (77.0)		17 (9.3)	165 (90.7)		156 (42.5)	211 (57.5)	
Charlson comorbidity score, n (%)			< 0.01			< 0.01			0.01
Score=0	621 (16.6)	3121 (83.4)		70 (6.8)	966 (93.2)		648 (44.4)	813 (55.6)	
Score 1	63 (14.0)	386 (86.0)		22 (5.2)	399 (94.8)		70 (33.8)	137 (66.2)	
Unknown	166 (50.3)	164 (49.7)		16 (34.0)	31 (66.0)		23 (53.5)	20 (46.5)	
Insurance, n (%)			0.01			0.31			0.92
Public	162 (15.5)	880 (84.5)		21 (9.5)	199 (90.5)		110 (44.5)	137 (55.5)	
Private	558 (19.4)	2313 (80.6)		74 (6.9)	997 (93.1)		519 (42.8)	694 (55.6)	
Uninsured/self-pay	28 (24.6)	86 (75.4)		*	*		25 (45.5)	30 (54.5)	
Other or unknown	102 (20.6)	392 (79.4)		11 (7.4)	137 (92.6)		87 (44.4)	109 (55.6)	
Marital status, n (%)			< 0.01			0.34			< 0.01
Single	397 (26.9)	1079 (73.1)		49 (8.8)	510 (91.2)		396 (53.4)	345 (46.6)	
Married	337 (14.0)	2064 (86.0)		49 (6.2)	738 (93.8)		283 (34.7)	532 (65.3)	
Other †	68 (13.8)	425 (86.2)		*	*		45 (39.1)	70 (60.9)	
Unknown	48 (31.8)	103 (68.2)		*	*		17 (42.5)	23 (57.5)	
Race or ethnicity, n (%)			< 0.01			0.01			< 0.01
American Indian	*	*		*	*		*	*	
Asian or Pacific Islander	110 (22.1)	388 (77.9)		34 (11.4)	263 (88.6)		161 (43.8)	207 (56.3)	
Hispanic	246 (15.4)	1348 (84.6)		44 (6.9)	597 (93.1)		262 (49.0)	273 (51.0)	
Non-Hispanic Black	46 (19.3)	192 (80.7)		*	*		46 (53.5)	40 (46.5)	
Non-Hispanic White	416 (19.8)	1688 (80.2)		22 (4.5)	464 (95.5)		264 (37.3)	444 (62.7)	
None of the above	23 (50.0)	23 (50.0)		0 (0.0)	10 (100.0)		*	*	
Rurality, n (%)			0.02			0.67			< 0.01

	Cervical (n=4,521)			Endometrial (n=1,504)			Ovarian (n=1,711)		
Sociodemographic and clinical characteristics	Fertility- Sparing (n=850)	Not Fertility- Sparing (n=3,671)	P Value	Fertility- Sparing (n=108)	Not Fertility- Sparing (n=1,396)	P Value	Fertility- Sparing (n=741)	Not Fertility- Sparing (n=970)	P Value
Rural	91 (15.2)	506 (84.8)		11 (6.4)	161 (93.6)		49 (29.2)	119 (70.8)	
Urban	759 (19.3)	3165 (80.7)		97 (7.3)	1235 (92.7)		692 (44.8)	851 (55.2)	
Parity, n (%) [‡]			< 0.01			0.22			0.19
0	632 (19.6)	2590 (80.4)		102 (7.4)	1276 (92.6)		597 (43.2)	785 (56.8)	
1	89 (31.2)	196 (68.8)		*	*		64 (50.0)	64 (50.0)	
2	129 (12.7)	883 (87.3)		*	*		80 (39.8)	121 (60.2)	
Cancer stage, n (%)			< 0.01			< 0.01			< 0.01
1A	641 (30.4)	1469 (69.6)		66 (6.3)	987 (93.7)		545 (47.0)	614 (53.0)	
1B	209 (8.7)	2202 (91.3)		*	*		NA	NA	
1C	NA	NA		NA	NA		196 (35.5)	356 (64.5)	
1, unknown	NA	NA		38 (18.7)	165 (81.3)		NA	NA	
Histology, n (%) $^{\mathcal{S}}$			< 0.01			0.08			< 0.01
Adenocarcinoma	215 (15.7)	1158 (84.3)		23 (9.9)	210 (90.1)		NA	NA	
Adenosquamous carcinoma	15 (6.9)	201 (93.1)		NA	NA		NA	NA	
Squamous carcinoma	577 (21.5)	2110 (78.5)		NA	NA		NA	NA	
Endometrioid adenocarcinoma	NA	NA		85 (6.7)	1186 (93.3)		NA	NA	
Germ cell	NA	NA		NA	NA		246 (74.5)	84 (25.5)	
Sex cord stromal	NA	NA		NA	NA		50 (50.0)	50 (50.0)	
Epithelial	NA	NA		NA	NA		445 (34.7)	836 (65.3)	
None of the above	43 (17.6)	202 (82.4)		0.0)	0 (0.0)		0 (0.0)	0 (0.0)	
Chemotherapy, n (%)			< 0.01			1.00			< 0.01
Yes	47 (9.6)	444 (90.4)		*)	*		245 (35.8)	440 (64.2)	
No	799 (19.9)	3,216 (80.1)		107 (7.2)	1370 (92.7)		482 (48.7)	508 (51.3)	
Unknown	*	*		*	*		14 (38.9)	22 (61.1)	
Radiotherapy, n (%)			< 0.01			0.25			0.84
Yes	61 (8.2)	682 (91.8)		0 (0.0)	26 (100.0)		*	*	
No	789 (20.9)	2,988 (79.1)		108 (7.3)	1370 (92.7)		739 (43.4)	965 (56.6)	
Hormonal therapy, n $(\%)^{\frac{1}{T}}$			0.20			< 0.01			0.72
(70)			0.20	108		<0.01			0.72
Yes	*	*		(100.0)	0 (0.0)		*	*	
No	848 (18.8)	3,656 (81.2)		0 (0.0)	1393 (100.0)		736 (43.3)	965 (56.7)	

Abbreviations: SES, socioeconomic status, NA, not applicable.

Cells are n (row percentage). P values were calculated by chi-squared and Fisher's exact tests.

 $^{^*}$ Values are not shown to protect confidentiality of the individuals summarized in the data.

 $[\]dot{\tau}_{\text{"Other"}}$ marital status included separated, divorced, widowed, unmarried, or in a domestic partnership.

There were 2 unknown cases of parity, 2 unknown cases of radiotherapy, and 4 unknown cases of hormonal therapy among patients who received non-fertility sparing treatment in the dataset. These rows were excluded from the table for conciseness.

 $[\]ensuremath{\mathcal{S}}$ Specific histology codes are listed in Appendix 2 (http://links.lww.com/xxx).

Jorgensen et al. Page 19

Table 2.Analysis of live birth outcomes after cancer diagnosis and fertility-sparing surgery by cancer type

	Cervi	cal Cancer (n=639)	Ovarian Cancer (n=594)			
Sociodemographic and clinical characteristics	Live Birth (n=110)	No Live Birth (n=529)	<i>P</i> Value	Live Birth (n=115)	No Live Birth (n=479)	<i>P</i> Value
Age (years), n (%)			< 0.01			< 0.01
18–35	99 (21.9)	354 (78.1)		109 (24.4)	338 (75.6)	
36–45	11 (5.9)	175 (94.1)		*	*	
Diagnosis year, n (%)			< 0.01			< 0.01
2000–2005	63 (23.3)	207 (76.7)		75 (29.4)	180 (70.6)	
2006–2012	47 (12.7)	322 (87.3)		40 (11.8)	299 (88.2)	
SES, n (%)			0.42			0.05
Lowest	14 (12.3)	100 (87.7)		22 (28.9)	54 (71.1)	
Lower-middle	18 (16.4)	92 (83.6)		29 (23.8)	93 (76.2)	
Middle	22 (18.5)	97 (81.5)		19 (13.7)	120 (86.3)	
Upper-middle	33 (21.2)	123 (78.8)		21 (16.4)	107 (83.6)	
Highest	23 (16.4)	117 (83.6)		24 (18.6)	105 (81.4)	
Charlson comorbidity score, n (%)			< 0.01			0.35
Score=0	62 (13.7)	389 (86.3)		105 (20.2)	414 (79.8)	
Score 1	*	*		*	*	
Unknown	44 (28.8)	109 (71.2)		*	*	
Insurance, n (%)			0.90			0.88
Public	17 (16.3)	87 (83.7)		16 (20.8)	61 (79.2)	
Private	72 (16.8)	356 (83.2)		79 (19.0)	337 (81.0)	
Uninsured/self-pay	*	*		*	*	
Other/unknown	17 (20.0)	68 (80.0)		14 (18.2)	63 (81.8)	
Marital status, n (%)			0.02			0.40
Single	41 (14.1)	250 (85.9)		53 (17.1)	257 (82.9)	
Married	57 (22.4)	198 (77.6)		51 (22.1)	180 (77.9)	
Other †	*	*		*	*	
Unknown	*	*		*	*	
Race or ethnicity, n (%)			0.03			0.23
American Indian	*	*		0 (0.0)	*	
Asian or Pacific Islander	*	*		29 (22.5)	100 (77.5)	
Hispanic	37 (21.0)	139 (79.0)		45 (22.8)	152 (77.2)	
Non-Hispanic Black	*	*		*	*	
Non-Hispanic White	54 (16.5)	273 (83.5)		33 (14.6)	193 (85.4)	
None of the above	*	13 (65.0)		*	*	
Rurality, n (%)			0.46			0.11
Rural	12 (20.7)	46 (79.3)		*	37 (90.2)	
Urban	98 (16.9)	483 (83.1)		111 (20.1)	442 (79.9)	
Parity, n (%)			< 0.01			0.01

Jorgensen et al.

Yes

No

Yes No

Unknown

Unknown

Hormonal therapy, n (%)

Cervical Cancer (n=639) Ovarian Cancer (n=594) Sociodemographic and clinical Live Birth No Live Birth Live Birth No Live Birth characteristics (n=110)(n=529) Value (n=115)(n=479) Value 0 71 (14.8) 409 (85.2) 100 (20.2) 396 (79.8) 1 24 (34.3) 46 (65.7) 13 (27.7) 34 (72.3) 2 15 (16.9) 74 (83.1) 0.03 Cancer stage, n (%) 0.37 1A 96 (18.8) 414 (81.2) 91 (20.2) 360 (79.8) 1B 14 (10.9) 115 (89.1) NA NA 119 (83.2) 1C NA NA 24 (16.8) Histology, n (%) 0.97 0.01 29 (17.6) NA Adenocarcinoma 136 (82.4) NA Adenosquamous carcinoma NA NA Squamous carcinoma 74 (17.1) 358 (82.9) NA NA Endometrioid adenocarcinoma NA NA NA NA Germ cell NA NA 54 (26.1) 153 (73.9) Sex cord stromal NA NA Epithelial NA NA 53 (15.4) 291 (84.6) None of the above 0(0.0)0(0.0)Chemotherapy, n (%) 1.00 0.97

Page 20

SES, socioeconomic status; NA, not applicable.

Live birth was defined as a live birth that had been conceived 3 months after the cancer diagnosis and fertility-sparing surgery. The three births that occurred among patients with a history of endometrial cancer are not presented because of the low number of results to protect the confidentiality of individuals represented in these data. Those who had prior radiation or were diagnosed after 2012 were excluded from analysis, due to contraindication to attempting a live birth and lack of data, respectively.

522 (82.6)

528 (82.8)

0.83

38 (19.5)

75 (19.2)

114 (19.3)

0(0.0)

157 (80.5)

315 (80.8)

477 (80.7)

0(0.0)

0.48

0(0.0)

110 (17.4)

0(0.0)

0(0.0)

110 (17.2)

0(0.0)

^{*}Values are not shown to protect the confidentiality of the individuals summarized in the data.

 $[\]dot{\tau}$, "Other" marital status included separated, divorced, widowed, unmarried, or in a domestic partnership.

[‡]Specific histology codes are listed in Appendix 2 (http://links.lww.com/xxx).

Table 3.Multivariable *logistic regression of fertility-sparing treatment by cancer type

	Cerv	ical	Endom	etrial	Ovarian		
Sociodemographic and clinical characteristics	Unadjusted OR (95% CI)	Adjusted OR (95% CI)	Unadjusted OR (95% CI)	Adjusted OR (95% CI)	Unadjusted OR (95% CI)	Adjusted OR (95% CI)	
Age, years							
18–35	Reference	Reference	Reference	Reference	Reference	Reference	
36–45	0.25 (0.22–0.30)	0.25 (0.21– 0.31)	0.17 (0.11–0.26)	0.11 (0.06– 0.21)	0.11 (0.09-0.13)	0.11 (0.09– 0.15)	
Diagnosis year							
2000-2005	Reference	Reference	Reference	Reference	Reference	Reference	
2006–2010	1.23 (1.03–1.47)	2.36 (1.83– 3.04)	0.77 (0.42–1.41)	1.70 (0.54– 5.32)	0.95 (0.75–1.19)	0.98 (0.71– 1.35)	
2011–2015	1.40 (1.16–1.68)	2.86 (2.20– 3.72)	1.37 (0.78–2.39)	1.55 (0.49– 4.94)	1.16 (0.92–1.46)	1.29 (0.93– 1.78)	
SES							
Lowest	Reference	Reference	Reference	Reference	Reference	Reference	
Lower-middle	0.91 (0.71–1.16)	0.81 (0.59– 1.13)	0.76 (0.42–1.39)	1.34 (0.56– 3.18)	1.07 (0.77–1.49)	1.16 (0.75– 1.80)	
Middle	0.93 (0.73–1.18)	0.75 (0.54– 1.04)	0.94 (0.51–1.74)	0.89 (0.31– 2.61)	1.11 (0.81–1.54)	1.75 (1.11– 2.77)	
Upper-middle	1.20 (0.95–1.51)	1.12 (0.81– 1.55)	1.14 (0.64–2.04)	2.25 (0.89– 5.68)	1.04 (0.76–1.44)	1.63 (1.03– 2.60)	
Highest	1.38 (1.09–1.76)	1.28 (0.90– 1.81)	1.33 (0.69–2.54)	1.94 (0.62– 6.08)	1.02 (0.74–1.41)	1.90 (1.17– 3.09)	
Charlson comorbidity score							
Score=0	Reference	Reference	Reference	Reference	Reference	Reference	
Score 1	0.82 (0.62–1.09)	0.94 (0.67– 1.32)	0.76 (0.47–1.25)	1.13 (0.58– 2.20)	0.64 (0.47–0.87)	0.79 (0.53– 1.17)	
Insurance							
Public	Reference	Reference	Reference	Reference	Reference	Reference	
Private	1.31 (1.08–1.59)	1.13 (0.88– 1.45)	0.70 (0.42–1.17)	1.03 (0.47– 2.24)	0.93 (0.71–1.23)	1.12 (0.78– 1.63)	
Uninsured or self-pay	1.77 (1.12–2.80)	1.28 (0.68– 2.40)	0.30 (0.07–1.32)	0.65 (0.13– 3.27)	1.04 (0.58–1.87)	1.23 (0.60– 2.55)	
Marital status							
Single	Reference	Reference	Reference	Reference	Reference	Reference	
Married	0.44 (0.38-0.52)	0.51 (0.41– 0.63)	0.69 (0.46–1.04)	0.62 (0.32– 1.20)	0.46 (0.38–0.57)	0.80 (0.60– 1.06)	
Other $\dot{\tau}$	0.44 (0.33-0.58)	0.72 (0.51– 1.02)	0.71 (0.32–1.62)	0.72 (0.20– 2.64)	0.56 (0.38-0.84)	1.65 (0.98– 2.80)	
Race or ethnicity							
Non-Hispanic White	Reference	Reference	Reference	Reference	Reference	Reference	
American Indian	1.41 (0.54–2.41)	1.03 (0.37– 2.89)	2.22 (0.49– 10.14)	1.99 (0.34– 11.64)	2.52 (0.42– 15.20)	0.98 (0.08– 11.97)	
Asian or Pacific Islander	1.15 (0.91–1.46)	1.52 (1.12– 2.08)	2.73 (1.56–4.76)	2.50 (0.97– 6.43)	1.31 (1.01–1.69)	1.30 (0.92– 1.82)	

Jorgensen et al.

IC

Histology Epithelial

Germ cell

Sex cord stromal

Cervical Ovarian **Endometrial** Unadjusted OR Sociodemographic and Adjusted OR Unadjusted OR Adjusted OR Unadjusted OR Adjusted OR clinical characteristics (95% CI) (95% CI) (95% CI) (95% CI) (95% CI) (95% CI) 1.44 (1.04-0.83 (0.66-1.70 (0.72-Hispanic 0.74 (0.62-0.88) 1.06) 1.55 (0.92-2.63) 4.02) 1.61 (1.29-2.03) 1.99) 0.60 (0.37-3.88 (0.97-2.26 (1.22-Non-Hispanic Black 0.97 (0.69-1.37) 0.99) 2.94 (1.13-7.65) 15.51) 1.93 (1.23-3.03) 4.17) Rurality Rural Reference Reference Reference Reference Reference Reference 0.96 (0.70-0.48 (0.19-1.37 (0.86-Urban 1.33 (1.05-1.69) 1.33) 1.14 (0.60-2.19) 1.21) 1.97 (1.39-2.79) 2.17) Parity 0 Reference Reference Reference Reference Reference Reference 0.93 (0.65-0.39 (0.05-0.77 (0.48-1 1.86 (1.43-2.43) 1.33) 1.22 (0.43-3.48) 3.12) 1.32 (0.92-1.89) 1.24) 0.45 (0.34-0.66 (0.15-1.01 (0.67-2.99) 2 0.60 (0.49-0.73) 0.38 (0.08-1.31) 0.87 (0.64-1.18) 1.52) 0.58)Cancer stage 1A Reference Reference Reference Reference Reference Reference 0.23 (0.19-0.37 (0.12-1B 0.22 (0.18-0.26) 0.25 (0.09-0.68) NA NA 0.28)1.11)

Page 22

0.72 (0.55-

0.95)

Reference 2.29 (1.62–

3.25) 1.73 (1.01–

2.97)

Abbreviations: OR, odds ratio; CI, confidence interval; SES, socioeconomic status; NA, not applicable.

NA

0.62 (0.50-0.76)

Reference

5.50 (4.18-7.23)

1.88 (1.25-2.83)

Histology was included only for ovarian cancer. All other variables presented in the table were included in the multivariable logistic regression for all three cancer types.

 $^{^{\}dagger}$,"Other" marital status included separated, divorced, widowed, unmarried, or in a domestic partnership.