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

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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 cancer (stage IA, IB), endometrial cancer (grade 1, stage IA, IB), or ovarian cancer (stage IA, IC) between January 1, 2000, and December 31, 2015, using linked data from the CCR (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% CIs 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 nonuniform 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

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survivors of cervical and ovarian cancer. Use of ART was low (n=52) and was associated with a non-Hispanic White race and ethnicity designation, being of younger age (18–35 years), and having 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.
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Gynecologic malignancies account for more than 10,000 cancer diagnoses among reproductive-aged women in the United States each year.[1] Fertility preservation may improve the ability of reproductive-aged patients to cope with cancer[2–5] and improve survivors' quality of life.[6] Although 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.[7–10] 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-aged patients face disparities in 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 (now known as the National Academy 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 CCR (California Cancer Registry), the OSHPD (California Office of Statewide Health Planning and Development, now known as the California Department of Health Care Access and Information), and SART CORS (Society for Assisted Reproductive Technology Clinic Outcome Reporting System). We obtained approval for this study from the MD Anderson IRB, the OSHPD, the CCR, the State of California Committee for the Protection of Human Subjects, and the Society for Assisted Reproductive Technology. 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/AOG/C985). The data files included diagnostic and procedure codes using the International Classification of Diseases, Ninth and Tenth Revisions, Clinical Modification.[30]

The data from the CCR and the OSHPD were linked to SART CORS to identify patients with gynecologic malignancy who underwent ART treatment between January 1, 2004 (earliest available data from the Society for Assisted Reproductive Technology), and December 31, 2015, using the woman's birth date, first and last name, social security number, and child'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 used date ranges pending availability of data, described below. All stages were based on available data and defined by the American Joint Committee on Cancer (third edition for 2000–2004, sixth edition for 2004–2009, and seventh edition for 2010–2015).[33] 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/AOG/C985).[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 (LEEP), conization, and trachelectomy, with or without ovarian transposition or lymph node evaluation for cervical cancer[11]; hormonal management with progestin using 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 to 2015.

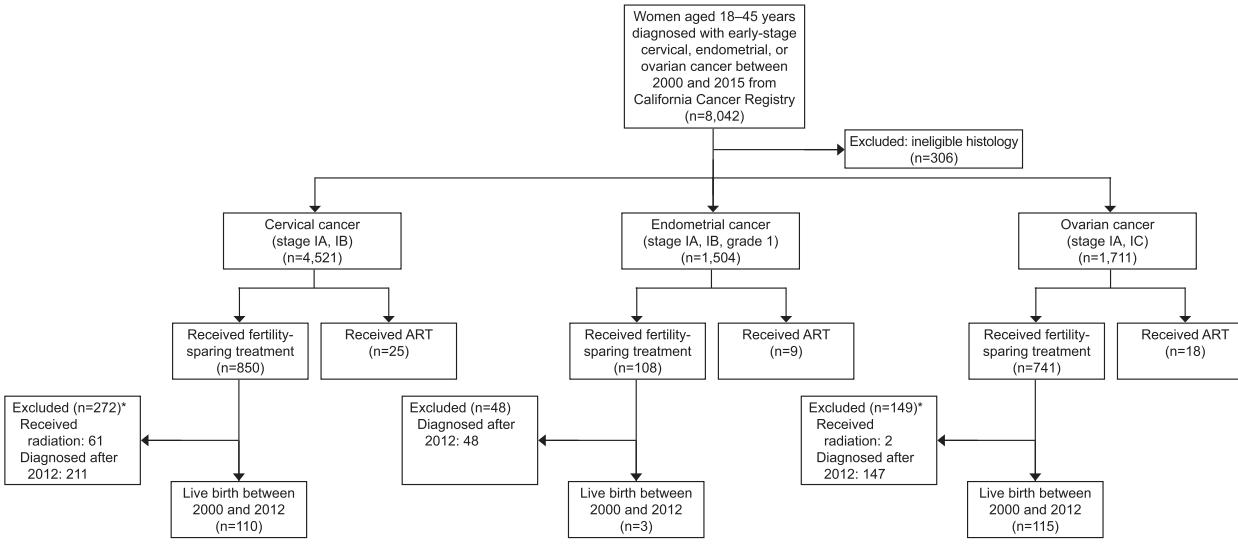

Fig. 1. Selection of cases. Assisted reproductive technology (ART) use was assessed for women diagnosed between 2000 and 2015, based on available ART data from 2004 to 2015. Live births were assessed for those with available data (diagnoses from 2000 to 2012). Included histologies are listed in Appendix 2, available online at http://links.lww.com/AOG/C985. *Not mutually exclusive

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The secondary outcome, *ART use after 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 to 2015 for individuals diagnosed from 2000 to 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 SES (Yost SES index at the Census tract level,[36] by quintile). The additional variables collected for multivariable analysis included parity (zero, one, or two 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 effect 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 cancer[24] and access to ART, overall,[25] 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 birth* was defined as the first birth in which fertilization occurred 3 or more months after a cancer diagnosis and fertility-sparing treatment. The fertilization date for each live birth was estimated using the child'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 χ^2 tests or Fisher 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 data set, the variables of interest were collapsed to binary categories. Given the 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% CIs.

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

Sociodemographic and Clinical Characteristics	Cervical Cancer (n=4,521)			Endometrial Cancer (n=1,504)			Ovarian Cancer (n=1,711)		
	Fertility-Sparing (n=850)	Non–Fertility-Sparing (n=3,671)	*P**	Fertility-Sparing (n=108)	Non–Fertility-Sparing (n=1,396)	*P**	Fertility-Sparing (n=741)	Non–Fertility-Sparing (n=970)	*P**
Age (y)			<.01			<.01			<.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			<.01			.04			.22
2000–2005	296 (16.4)	1,508 (83.6)		17 (6.8)	233 (93.2)		255 (42.6)	344 (57.4)	
2006–2010	292 (19.5)	1,208 (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			<.01			.52			.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)	
CCI score			<.01			<.01			.01
0	621 (16.6)	3,121 (83.4)		70 (6.8)	966 (93.2)		648 (44.4)	813 (55.6)	
1 or higher	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			.01			.31			.92
Public	162 (15.5)	880 (84.5)		21 (9.5)	199 (90.5)		110 (44.5)	137 (55.5)	
Private	558 (19.4)	2,313 (80.6)		74 (6.9)	997 (93.1)		519 (42.8)	694 (55.6)	
Uninsured or 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			<.01			.34			<.01
Single	397 (26.9)	1,079 (73.1)		49 (8.8)	510 (91.2)		396 (53.4)	345 (46.6)	
Married	337 (14.0)	2,064 (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 and ethnicity			<.01			.01			<.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)	1,348 (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)	1,688 (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)		†	†	
Rurality			.02			.67			<.01
Rural	91 (15.2)	506 (84.8)		11 (6.4)	161 (93.6)		49 (29.2)	119 (70.8)	
Urban	759 (19.3)	3,165 (80.7)		97 (7.3)	1,235 (92.7)		692 (44.8)	851 (55.2)	
Parity§			<.01			.22			.19
0	632 (19.6)	2,590 (80.4)		102 (7.4)	1,276 (92.6)		597 (43.2)	785 (56.8)	
1	89 (31.2)	196 (68.8)		†	†		64 (50.0)	64 (50.0)	
2 or more	129 (12.7)	883 (87.3)		†	†		80 (39.8)	121 (60.2)	
Cancer stage			<.01			<.01			<.01
1A	641 (30.4)	1,469 (69.6)		66 (6.3)	987 (93.7)		545 (47.0)	614 (53.0)	
1B	209 (8.7)	2,202 (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‖			<.01			.08			<.01
Adenocarcinoma	215 (15.7)	1,158 (84.3)		23 (9.9)	210 (90.1)		NA	NA	
Adenosquamous carcinoma	15 (6.9)	201 (93.1)		NA	NA		NA	NA	

(*continued*)

Table 1. Patient Characteristics by Fertility-Sparing Treatment and Cancer Type (*continued*)

Sociodemographic and Clinical Characteristics	Cervical Cancer (n=4,521)			Endometrial Cancer (n=1,504)			Ovarian Cancer (n=1,711)		
	Fertility-Sparing (n=850)	Non–Fertility-Sparing (n=3,671)	*P**	Fertility-Sparing (n=108)	Non–Fertility-Sparing (n=1,396)	*P**	Fertility-Sparing (n=741)	Non–Fertility-Sparing (n=970)	*P**
Squamous carcinoma	577 (21.5)	2,110 (78.5)		NA	NA		NA	NA	
Endometrioid adenocarcinoma	NA	NA		85 (6.7)	1,186 (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 (0.0)	
Chemotherapy			<.01			1.00			<.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)	1,370 (92.7)		482 (48.7)	508 (51.3)	
Unknown	†	†		†	†		14 (38.9)	22 (61.1)	
Radiotherapy§			<.01			.25			.84
Yes	61 (8.2)	682 (91.8)		0 (0.0)	26 (100)		†	†	
No	789 (20.9)	2,988 (79.1)		108 (7.3)	1,370 (92.7)		739 (43.4)	965 (56.6)	
Hormonal therapy§			.20			<.01			.72
Yes	†	†		108 (100)	0 (0.0)		†	†	
No	848 (18.8)	3,656 (81.2)		0 (0.0)	1,393 (100)		736 (43.3)	965 (56.7)	

SES, socioeconomic status; CCI, Charlson Comorbidity Index; NA, not applicable.
Data are n (row %) unless otherwise specified.
* *P* values calculated using χ^2 and Fisher exact tests.
† Values not shown to protect confidentiality of the individuals summarized in the data.
‡ Includes separated, divorced, widowed, unmarried, or in a domestic partnership.
§ Among patients in the data set who received non–fertility-sparing treatment, parity was unknown for two, radiotherapy was unknown for two, and hormonal therapy was unknown for four. These rows were excluded from the table for conciseness.
‖ Specific histology codes are listed in Appendix 2, available online at http://links.lww.com/AOG/C985.

All statistical tests were two-sided, and differences were considered statistically significant at $P<.05$ and a 95% CI not inclusive of the null (1.0). SAS Enterprise Guide 7.11 was used for all statistical analyses.

We performed a sensitivity analysis of our primary outcome using the E-value, a measure that 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 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%) were diagnosed with endometrial cancer (stage IA, IB), and 1,711 (22.1%) were diagnosed with ovarian cancer (stage IA, IC) (Fig. 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 after fertility-sparing treatment (Table 2).

Among patients with cervical cancer who received fertility-sparing surgery compared with those who did not, there were significant differences in all clinical and sociodemographic variables (Table 1). Multivariable regression (Table 3 and Fig. 2) demonstrated that younger age (18–35 years vs 36–45 years), Asian or Pacific Islander (vs non-Hispanic White), single status (vs married), year of diagnosis (2006–

Table 2. Analysis of Live-Birth Outcomes After Cancer Diagnosis and Fertility-Sparing Surgery by Cancer Type*

Sociodemographic and Clinical Characteristics	Cervical Cancer (n=639)			Ovarian Cancer (n=594)		
	Live Birth (n=110)	No Live Birth (n=529)	*P*	Live Birth (n=115)	No Live Birth (n=479)	*P*
Age (y)			<.01			<.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			<.01			<.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			.42			.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)	
CCI score			<.01			.35
0	62 (13.7)	389 (86.3)		105 (20.2)	414 (79.8)	
1 or higher	†	†		†	†	
Unknown	44 (28.8)	109 (71.2)		†	†	
Insurance			.90			.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 or self-pay	†	†		†	†	
Other or unknown	17 (20.0)	68 (80.0)		14 (18.2)	63 (81.8)	
Marital status			.02			.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 and ethnicity			.03			.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			.46			.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			<.01			.01
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 or more	15 (16.9)	74 (83.1)		†	†	
Cancer stage			.03			.37
1A	96 (18.8)	414 (81.2)		91 (20.2)	360 (79.8)	
1B	14 (10.9)	115 (89.1)		NA	NA	
1C	NA	NA		24 (16.8)	119 (83.2)	
Histology§			.97			.01
Adenocarcinoma	29 (17.6)	136 (82.4)		NA	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)	

(*continued*)

Table 2. Analysis of Live-Birth Outcomes After Cancer Diagnosis and Fertility-Sparing Surgery by Cancer Type* (*continued*)

Sociodemographic and Clinical Characteristics	Cervical Cancer (n=639)			Ovarian Cancer (n=594)		
	Live Birth (n=110)	No Live Birth (n=529)	*P*	Live Birth (n=115)	No Live Birth (n=479)	*P*
Chemotherapy			1.00			.97
Yes	0 (0.0)	†		38 (19.5)	157 (80.5)	
No	110 (17.4)	522 (82.6)		75 (19.2)	315 (80.8)	
Unknown	0 (0.0)	†		†	†	
Hormonal therapy			.83			.48
Yes	0 (0.0)	†		†	†	
No	110 (17.2)	528 (82.8)		114 (19.3)	477 (80.7)	
Unknown	0 (0.0)	†		0 (0.0)	0 (0.0)	

SES, socioeconomic status; CCI, Charlson Comorbidity Index; NA, not applicable.
Data are n (row %) unless otherwise specified.
* *Live birth* was defined as a live birth of a neonate who 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.
† Values not shown to protect the confidentiality of the individuals summarized in the data.
‡ Includes separated, divorced, widowed, unmarried, or in a domestic partnership.
§ Specific histology codes are listed in Appendix 2, available online at http://links.lww.com/AOG/C985.

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 years vs 36–45 years), non-Hispanic White (vs all non-White races or ethnicities), nulliparous (vs one or more), of high SES (vs low) or diagnosed between 2000 and 2007 (vs 2008–2015) (Fig. 3). Patients with a history of cervical cancer accounted for 48.2% (n=110) of those who had a live birth after 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 and those who did not (Table 1). Multivariable regression analysis (Table 3 and Fig. 2) found that being aged 18–35 years (vs 36–45 years) was associated with increased odds of fertility-sparing treatment.

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

Among patients with ovarian cancer who received fertility-sparing treatment compared with 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 being aged 18–35 years (vs 36–45 years); being in the middle, upper-middle, and highest SES (vs lowest SES); being stage IA (vs IC); being of non-Hispanic Black and Hispanic (vs non-Hispanic White) racial and ethnic designation; and having germ cell or sex cord stromal histology (vs epithelial) were associated with increased odds of fertility-sparing treatment (Table 3 and Fig. 2).

A total of 18 instances (1.1%) of ART occurred after diagnosis. On univariable analysis, ART use was associated with diagnosis between 2000 and 2007 (vs 2008–2015) (Fig. 3). No ART instances were observed among non-Hispanic Black patients, American Indian patients, or patients with public insurance. Patients with a history of ovarian cancer accounted for the half of those who had a live birth after 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

Table 3. Multivariable* Logistic Regression of Fertility-Sparing Treatment by Cancer Type

Sociodemographic and Clinical Characteristics	Cervical Cancer		Endometrial Cancer		Ovarian Cancer	
	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 (y)						
18–35	Ref	Ref	Ref	Ref	Ref	Ref
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	Ref	Ref	Ref	Ref	Ref	Ref
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	Ref	Ref	Ref	Ref	Ref	Ref
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)
CCI score						
0	Ref	Ref	Ref	Ref	Ref	Ref
1 or higher	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	Ref	Ref	Ref	Ref	Ref	Ref
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	Ref	Ref	Ref	Ref	Ref	Ref
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†	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 and ethnicity						
Non-Hispanic White	Ref	Ref	Ref	Ref	Ref	Ref
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)
Hispanic	0.74 (0.62–0.88)	0.83 (0.66–1.06)	1.55 (0.92–2.63)	1.70 (0.72–4.02)	1.61 (1.29–2.03)	1.44 (1.04–1.99)
Non-Hispanic Black	0.97 (0.69–1.37)	0.60 (0.37–0.99)	2.94 (1.13–7.65)	3.88 (0.97–15.51)	1.93 (1.23–3.03)	2.26 (1.22–4.17)
Rurality						
Rural	Ref	Ref	Ref	Ref	Ref	Ref
Urban	1.33 (1.05–1.69)	0.96 (0.70–1.33)	1.14 (0.60–2.19)	0.48 (0.19–1.21)	1.97 (1.39–2.79)	1.37 (0.86–2.17)
Parity						
0	Ref	Ref	Ref	Ref	Ref	Ref
1	1.86 (1.43–2.43)	0.93 (0.65–1.33)	1.22 (0.43–3.48)	0.39 (0.05–3.12)	1.32 (0.92–1.89)	0.77 (0.48–1.24)

(*continued*)

Table 3. Multivariable* Logistic Regression of Fertility-Sparing Treatment by Cancer Type (*continued*)

Sociodemographic and Clinical Characteristics	Cervical Cancer		Endometrial Cancer		Ovarian Cancer	
	Unadjusted OR (95% CI)	Adjusted OR (95% CI)	Unadjusted OR (95% CI)	Adjusted OR (95% CI)	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
2 or more	0.60 (0.49–0.73)	0.45 (0.34–0.58)	0.38 (0.08–1.31)	0.66 (0.15–2.99)	0.87 (0.64–1.18)	1.01 (0.67–1.52)
Cancer stage						
1A	Ref	Ref	Ref	Ref	Ref	Ref
1B	0.22 (0.18–0.26)	0.23 (0.19–0.28)	0.25 (0.09–0.68)	0.37 (0.12–1.11)	NA	NA
IC	NA	NA	NA	NA	0.62 (0.50–0.76)	0.72 (0.55–0.95)
Histology						
Epithelial	NA	NA	NA	NA	Ref	Ref
Germ cell	NA	NA	NA	NA	5.50 (4.18–7.23)	2.29 (1.62–3.25)
Sex cord stromal	NA	NA	NA	NA	1.88 (1.25–2.83)	1.73 (1.01–2.97)

OR, odds ratio; Ref, reference; SES, socioeconomic status; CCI, Charlson Comorbidity Index; NA, not applicable.
* 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.
† Includes separated, divorced, widowed, unmarried, or in a domestic partnership.

confounders with respect to age and diagnosis year (all cancer types) (Appendix 3, available online at http://links.lww.com/AOG/C985).

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 was more likely among younger patients for all three cancers. Use of ART was more likely among those diagnosed earlier in the cohort and those with private insurance across all three cancer types, and also was more likely 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 with non-Hispanic White patients, the overall rate of these procedures in the ages selected for this study is low.[39–41] Furthermore, although 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, although 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, 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.

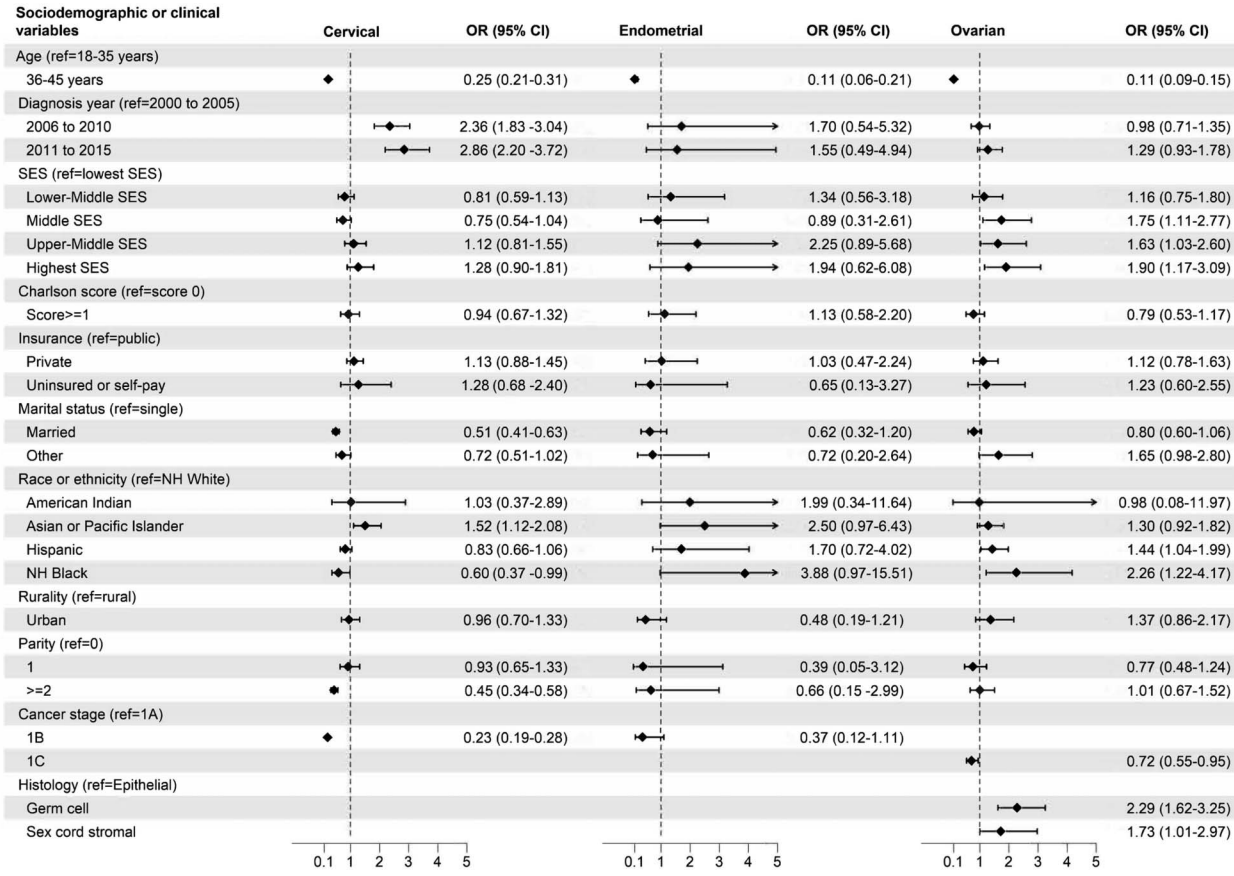

Fig. 2. Multivariable analysis of adjusted odds ratio (OR) of fertility-sparing treatment by cancer type and variables of interest. All variables presented were included in multivariable analysis. Rows without adjusted ORs presented were not applicable to that cancer type (stage IB for ovarian, stage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

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There was overall low use 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 affected their fertility, from limited effect after LEEP to more substantial effect after trachelectomy or oophorectomy, particularly if they had undergone prior gynecologic surgery.

Unlike trends seen in fertility-sparing treatment, we found that patients in racial and ethnic minority groups 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; Medicaid does not cover fertility treatment, disproportionately affecting patients in racial and ethnic minority groups, because the program covers 30% of Black patients and 25% of Hispanic patients compared with 15% of non-Hispanic White patients.[48] Additionally, during the study period, California had a mandate to offer coverage for infertility services that applied differentially to private insurance, did not apply to Medicaid or public insurance, 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-aged 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

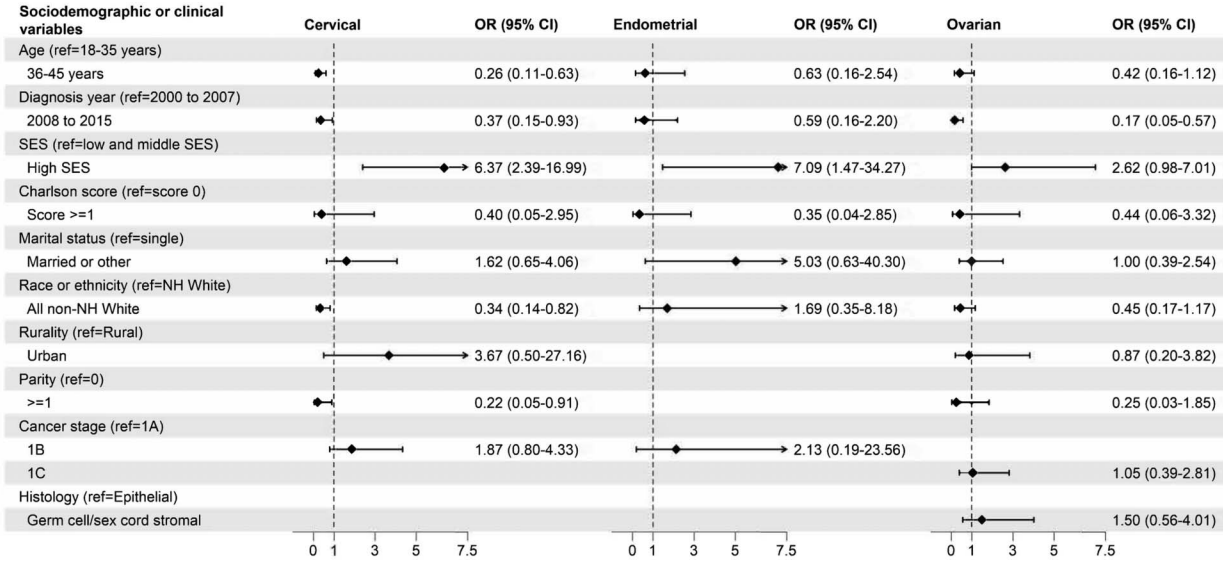

Fig. 3. Univariable analysis of odds ratio (OR) of assisted reproductive technology by cancer type and variables of interest. Rows without ORs presented were not applicable to that cancer type (stage IB for ovarian, stage IC and histology type for cervical, endometrial) or could not be calculated (rurality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

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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 patients from 2000 to 2012). Half of live births were to patients with a history of ovarian cancer. This may be related to increased rates of infertility[52] and increased likelihood of preterm birth[53] 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 with 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 data set, with possible ART use or live births after a cancer diagnosis not yet published, and we were limited 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 patients and patients with public insurance, highlighting the 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.

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