

GYNECOLOGY

Use of fertility preservation services in female reproductive-aged cancer patients



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OBJECTIVE: The objective of the study was to determine the rates and predictors of fertility preservation services among reproductive-aged women with common cancers in the United States.

STUDY DESIGN: We used the MarketScan database to identify women 18–45 years of age with lung, breast, colorectal, or cervical cancer who underwent surgery and chemotherapy from 2009 through 2016. Services from 3 months before to 3 months after chemotherapy for evaluation for fertility preservation, laboratory testing for fertility evaluation, and fertility-preserving procedures were captured. Multivariable models were used to assess the factors associated with the use of fertility-preservation services.

RESULTS: A total of 18,781 women, including 386 cervical, 1372 colorectal, 246 lung, and 16,777 with breast cancer, were identified. In women 18–35 years old, 11.7% underwent evaluation for fertility preservation, 13.7% underwent laboratory testing, and 6.3% pursued fertility-preserving procedures. The rates of office evaluation, laboratory testing, and performance of procedure were 3.3%, 7.5%, and 1.9% in women aged 36–40 years and 0.5%, 7.2%, and 0.3% in those

aged 41–45 years, respectively. The rate of fertility preservation evaluation rose from 1.0% in 2009 to 5.5% in 2016 (risk ratio, 4.66, 95% confidence interval, 2.38–9.11) while use of fertility-preserving procedures increased from 1.0% to 4.6% (risk ratio, 3.84, 95% confidence interval, 1.94–7.59) during the same time period. In a multivariable model, use of any fertility-preserving interventions were more common in patients with breast cancer (adjusted risk ratio, 2.30, 95% confidence interval, 1.30–4.06), those in the Northeast (adjusted risk ratio, 1.24, 95% confidence interval, 1.10–1.40), and in younger women (18–35 years) (adjusted risk ratio, 2.59, 95% confidence interval, 2.32–2.89).

CONCLUSION: Although limited by lack of information regarding cancer stage and desire for future fertility, only a small fraction of reproductive-aged female cancer patients receiving chemotherapy are evaluated in a nationwide sample for fertility preservation or undergo fertility-preserving procedures.

Key words: fertility preservation, reproductive-aged cancer patients

Advances in cancer treatment over the past 2 decades have resulted in significant improvements in survival for young adults with cancer.¹ However, cancer treatments in young adults, particularly chemotherapy and pelvic radiotherapy, often have detrimental effects on reproductive function.¹ Cytotoxic chemotherapy, particularly alkylating agents, are gonadotoxic and can lead to DNA damage through DNA cross-linkage and DNA strand breaks.² These agents lead to a depletion of the pool of primordial and small antral follicles.³ Pelvic radiotherapy can cause

increased ovarian follicular atresia, uterine scarring, and reduced uterine blood flow, all factors that can have a significant impact on future fertility.⁴

Young cancer patients and their families report significant concern about infertility following gonadotoxic therapy.⁵ Decreased reproductive function and infertility in young cancer patients often results in emotional distress and can lead to psychological sequelae, such as posttraumatic stress disorder.⁶ Additionally, cancer survivors with higher levels of reproductive concerns are more likely to experience moderate to severe depression.⁷

Given the increasing number of reproductive-aged patients undergoing and surviving cancer treatment, as well as the concern for reproductive sequelae, fertility preservation has become a key quality-of-life issue in oncological care. The American Society of Clinical Oncology and the American Society of Reproductive Medicine have developed guidelines that recommend that

oncologists discuss fertility-preserving options with their reproductive-age cancer patients and recommend referral to reproductive endocrinology specialists.^{8,9}

Although these guidelines have been in place since 2006, there are few data describing the use of fertility-preserving services among young cancer patients. The objective of this study was to assess the use of fertility preservation services nationally in female reproductive-aged patients with common solid tumors.

Materials and Methods

Data

We utilized the Truven Health MarketScan database from January 2009 to December 2016. The MarketScan data set includes approximately 350 payers and captures claims from >50 million privately insured patients and 6 million Medicaid enrollees.¹⁰ The database includes claims for inpatient and outpatient services as well as prescription drug claims. Data were deidentified

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AJOG at a Glance

Why was the study conducted?

The study was conducted to evaluate the rates and predictors of fertility preservation services in a nationwide sample.

What are the key findings?

Use of fertility services has increased over time, but there are continued clinical and regional disparities in access to services.

What does the study add to what is already known?

This study characterizes population-based rates for the use of fertility preservation services for young female cancer patients.

and deemed exempt by the Columbia University Institutional Review Board.

Study population

Women ≤ 45 years of age with breast, cervical, lung, and colorectal cancer were identified (Table 1). *International Classification of Diseases (ICD)-9/ICD10* and *Current Procedural Terminology* codes for cancer diagnosis (Supplemental Table 1) were used to search the Truven database for the patient population. We included only women who had cancer claims within 30 days of the first cancer-directed surgery claim for the respective primary tumor sites and who had at least 2 claims for cancer ≥ 30 days apart.¹¹⁻¹³

A sensitivity analysis was performed, the window for diagnostic claims was increased from 30 days to 90 days (Supplemental Table 2). Patients were also excluded if they did not have consecutive insurance coverage from 6 months before to 6 months after the date of the first surgery claim. To capture women most likely to utilize fertility-preserving services, the cohort was limited to women who also received chemotherapy within 6 months of the date of the surgical procedure (Supplemental Tables 3-5).

Clinical and demographic characteristics analyzed included age (18–35, 36–40, and 41–45 years), cancer type (lung, breast, cervical, and colorectal), year of surgery (2009–2016), use of radiation (yes vs no), payer information (commercial insurance [non-health maintenance organization [HMO]], commercial [HMO insurance, and Medicaid), region of residence (Northeast, North Central, South, and West), and residence in a metropolitan

statistical area (metropolitan statistical area, nonmetropolitan statistical area, and unknown). Comorbidity was estimated using the Elixhauser comorbidity index and classified as 0, 1, and ≥ 2 .^{14,15}

Outcomes

The primary outcomes of our study were the use of fertility-preserving services including fertility evaluation, laboratory testing for the evaluation of fertility, and fertility preservation procedures within 3 month of chemotherapy.¹⁶ Fertility evaluation was defined as the occurrence of any billing code (*Current Procedural Terminology/ICD9/ICD10*) for the office evaluation of fertility preservation counseling (Supplemental Table 1).

Laboratory testing for the evaluation of fertility included codes for testing for luteinizing hormone, follicle-stimulating hormone, estradiol, progesterone, and antimullerian hormone (Supplemental Table 1). Fertility preservation procedures included any codes for in vitro fertilization, ovarian transposition, oocyte/embryo cryopreservation, or ovarian tissue cryopreservation (Supplemental Table 1).

Statistical analysis

The rates of the use of fertility evaluation, laboratory testing, and procedures are presented descriptively. The change in utilization rates over time were evaluated using Cochran-Armitage tests for trend. The associations between the outcomes of interest and the clinical and demographic characteristics were analyzed using χ^2 tests. Evaluation by a gynecologist was included as a secondary outcome.

Multivariable log linear regression models with a Poisson distribution and log link function were developed to explore predictors associated with fertility evaluation, laboratory testing, and fertility-preserving procedures. The models included all of the clinical and demographic characteristics of interest. The results are reported as adjusted risk ratios (aRRs) with 95% confidence intervals (CIs). All hypothesis tests were 2 sided. A value of $P < .05$ was considered statistically significant. All analyses were conducted using SAS, version 9.4 (SAS Institute Inc, Cary, NC).

Results

A total of 18,781 women, including 386 cervical cancer (2.1%), 1372 colorectal cancer (7.3%), 246 lung cancer (1.3%), and 16,777 breast cancer (89.3%) patients, treated with chemotherapy, were identified (Figure 1). Overall, 2888 were aged 18–35 years (15.4%), 5083 were 36–40 years (27.1%), and 10,810 were 41–45 (57.6%) years. The clinical and demographic characteristics of the cohort are displayed in Table 1.

Overall, a medical evaluation for infertility was performed in 3.0% of women, laboratory testing was ordered in 8.3% of patients, a fertility-conserving procedure was undertaken in 1.7%, and 43.4% underwent evaluation by a gynecologist (Table 1). The rate of fertility evaluation rose from 1.0% in 2009 to 5.5% in 2016 ($P < .0001$). Similarly, over the same time period, the rate of laboratory testing rose from 8.6% to 10.0% ($P = .013$), the rate of fertility-conserving procedures increased from 1.0% to 4.6% ($P < .0001$), and the rate of evaluation by a gynecologist increased from 41.6% to 50.0% ($P < .0001$) (Figure 2).

Utilization of fertility-preserving services was more common in younger patients (Table 1). Among women 18–35 years of age, a fertility evaluation was performed in 11.7%, laboratory testing in 13.7%, a procedure in 6.3%, and gynecological evaluation in 53.6%. The corresponding rates in women aged 36–40 years were 3.3%, 7.5%, 1.9%, and 47.1%, respectively, while the rates in

TABLE 1
Rates of fertility evaluation, laboratory test, and procedure among young cancer patients

Variables	Overall cohort		Fertility evaluation		Pvalue	Fertility laboratory testing		Pvalue	Fertility preservation procedure		Pvalue	Gynecology visit		Pvalue
	n	%	n	%		n	%		n	%		n	%	
n	18,781		561	3.0		1554	8.3		307	1.6		8159	43.4	
Age group					< .0001			< .0001			< .0001			< .0001
18–35	2888	15.4	337	11.7		395	13.7		181	6.3		1549	53.6	
36–40	5083	27.1	166	3.3		381	7.5		97	1.9		2392	47.1	
41–45	10,810	57.6	58	0.5		778	7.2		29	0.3		4218	39.0	
Cancer type					.27			< .0001			.27			< .0001
Breast	16,777	89.3	513	3.1		1460	8.7		284	1.7		7315	43.6	
Cervix	386	2.1	6	1.6		31	8.0		3	0.8		308	79.8	
Colorectal	1372	7.3	36	2.6		54	3.9		17	1.2		478	34.8	
Lung	246	1.3	6	2.4		9	3.7		3	1.2		58	23.6	
Health insurance					< .0001			< .0001			.0018			< .0001
Non-HMO	15,709	83.6	509	3.2		1351	8.6		283	1.8		7133	45.4	
HMO	2475	13.2	52	2.1		181	7.3		24	1.0		933	37.7	
Medicaid	597	3.2	0	0.0		22	3.7		0	0.0		93	15.6	
Region					< .0001			< .0001			< .0001			< .0001
Northeast	3419	18.2	181	5.3		326	9.5		124	3.7		1564	45.7	
North Central	3734	19.9	109	2.9		265	7.1		55	1.5		1612	43.2	
South	7448	39.7	169	2.3		626	8.4		69	0.9		3578	48.0	
West	3294	17.5	100	3.0		301	9.1		59	1.8		1204	36.6	
Unknown	886	4.7	2	0.2		36	4.1		0	0.0		201	22.7	
Metropolitan statistical area					< .0001			< .0001			< .0001			< .0001
Non-MSA	2081	11.1	18	0.9		141	6.8		6	0.3		776	37.3	
MSA	15,813	84.2	541	3.4		1377	8.7		301	1.9		7178	45.4	
Unknown	887	4.7	2	0.2		36	4.1		0	0.0		205	23.1	

Selter et al. Fertility preservation services in reproductive-aged cancer patients. *Am J Obstet Gynecol* 2019.

(continued)

TABLE 1
Rates of fertility evaluation, laboratory test, and procedure among young cancer patients (continued)

Variables	Overall cohort		Fertility evaluation		Pvalue	Fertility laboratory testing		Pvalue	Fertility preservation procedure		Pvalue	Gynecology visit		Pvalue
	n	%	n	%		n	%		n	%		n	%	
Elixhauser comorbidity					.02			.77			.04			< .0001
0	14,110	75.1	449	3.2		1167	8.3		248	1.8		6257	44.3	
1	3292	17.6	82	2.5		279	8.5		45	1.4		1363	41.4	
≥2	1379	7.3	30	2.2		108	7.8		14	1.0		539	39.1	
Surgery year					< .0001			.013			< .0001			< .0001
2009	988	5.3	10	1.0		85	8.6		10	1.0		411	41.6	
2010	2256	12.0	45	2.0		179	7.9		20	0.9		941	41.7	
2011	2727	14.5	54	2.0		205	7.5		39	1.4		1140	41.8	
2012	3412	18.2	82	2.4		266	7.8		36	1.1		1385	40.6	
2013	3238	17.2	103	3.2		266	8.2		54	1.7		1421	43.9	
2014	2832	15.1	99	3.5		220	7.8		41	1.5		1237	43.7	
2015	2236	11.9	108	4.8		224	10.0		57	2.6		1078	48.2	
2016	1092	5.8	60	5.5		109	10.0		50	4.6		546	50.0	
Radiation within 6 months prior or after surgery					.4			.21			.47			.01
No	9164	48.8	264	2.9		782	8.5		143	1.6		3895	42.5	
Yes	9617	51.2	297	3.1		772	8.0		166	1.7		4264	44.3	

HMO, health maintenance organization; MSA, metropolitan statistical area.

Selter et al. Fertility preservation services in reproductive-aged cancer patients. *Am J Obstet Gynecol* 2019.

women aged 41–45 years were 0.5%, 7.2%, 0.3%, and 39.0%, respectively ($P < .0001$ for all).

In a series of multivariable models, age, tumor type, and region were the factors most consistently associated with fertility-preserving services (Table 2). Examining a composite of use any fertility-preserving evaluation, laboratory testing, or procedures, compared with women aged 40–45 years, the risk ratio (RR) for women aged 18–35 years was 2.56 (95% CI, 2.29–2.86), while the risk ratio for those aged 36–40 years was 1.22 (95% CI, 1.08–1.36). Breast cancer patients were most likely to receive services (RR, 2.30; 95% CI, 1.30–4.06 vs lung cancer).

Compared with patients in the South, those in the Northeast (RR, 1.24; 95% CI, 1.04–1.40) and West (RR, 1.17; 95% CI, 1.03–1.33) were more likely to use services as were those who lived in metropolitan statistical areas (RR, 1.35, 95% CI, 1.14–1.60).

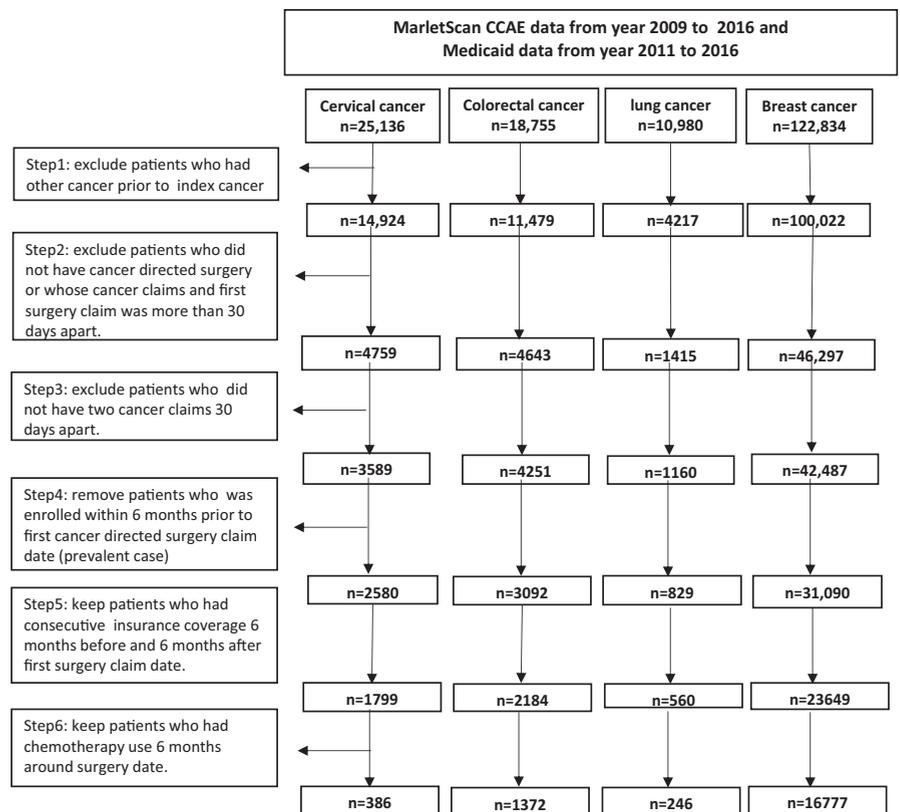
There was no association between year of diagnosis and the composite outcome, although fertility evaluation was significantly more frequently utilized during later years of the study. There were also no differences in the composite outcome and comorbidity score. Similarly, there was no difference in the composite between women with non-HMO commercial insurance plans compared with Medicaid, while HMO patients had a lower likelihood to undergo fertility evaluation and procedure as well as laboratory testing (RR, 0.83; 95% CI, 0.72–0.96). These results were largely unchanged in a sensitivity analysis in which the window for diagnostic claims was expanded from 30 to 90 days (Supplemental Table 2).

Comment

Principal findings

These findings demonstrate that only a small percentage of reproductive-aged women who underwent chemotherapy for cancer treatment received fertility-conserving services or treatments. Encouragingly, the use of these services has increased over time. A number of clinical and nonclinical factors were

FIGURE 1
Flow chart for study selection of the cohort



Selter et al. Fertility preservation services in reproductive-aged cancer patients. *Am J Obstet Gynecol* 2019.

associated with the allocation of fertility-preserving services.

Results

Prior studies of regional data have also found a low use of fertility-preserving services for young cancer patients. A 2012 study of the California cancer registry study found that only 4% of reproductive-aged women pursued fertility preservation.¹⁷ A nationwide study in The Netherlands between 2002 and 2008 found a rate of fertility preservation of only 2%.¹⁸ Using a broad definition of tests and procedures to evaluate and preserve fertility, we noted a slightly higher rate of use of services and found that use has increased over time. These findings suggest that reproductive health is beginning to become a more important aspect of oncological care in reproductive-aged women.

Although the use of reproductive services was low, studies suggest that

young cancer patients are interested in these services and that fertility preservation is often an unmet need.¹⁹ In one report of young adult cancer survivors, 76% of patients reported concern about having children following a diagnosis of cancer.²⁰ When providers overlook fertility concerns, cancer patients report feeling significant distress, with poorer quality of life and depression.^{19,21} Some cancer patients even report that the loss of fertility can be as significant as the diagnosis of cancer.¹⁹ Importantly, patients referred for reproductive fertility preservation services report high levels of satisfaction and better coping with their diagnosis.¹⁹

Not surprisingly, we noted that the use of fertility-preserving services was more common in younger women. This finding is consistent with other studies showing that older patients are less likely to receive fertility counseling, regardless of parenting desires or parity.^{17,22}

We also found that patients with commercial non-HMO insurance were more likely to receive fertility services than those with HMO plans. This is likely because fertility preservation services are expensive and differ in coverage based on different insurance plans. For example, fertility preservation services are not mandatory under federal Medicaid regulation.²³ Some states, such as Connecticut, Rhode Island, Maryland, Delaware, Illinois, and New York, have enacted legislation to cover fertility preservation services, but cost will continue to be an issue for many cancer patients.

Finally, patients with breast cancer were more likely than other cancer types to undergo fertility services. It is possible that because breast cancer is more common, particularly among young women, breast oncologists may be more aware of the reproductive challenges associated with treatment, suggesting that education of all types of oncologists is needed to increase referral services for patients with other cancer types.

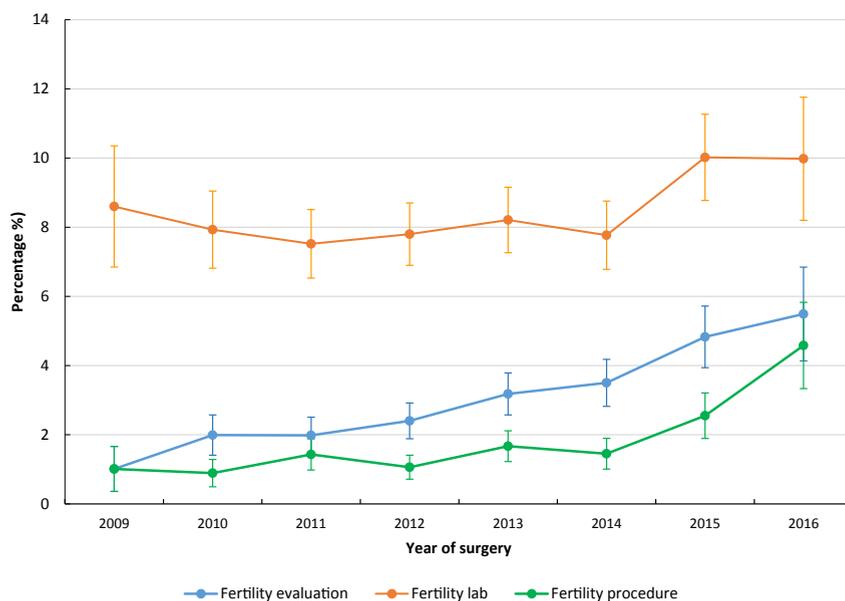
Clinical implications

Even though the use of fertility preservation services has increased over time, there still remain significant barriers. The fact that our study found differences in utilization in different regions, metropolitan vs nonmetropolitan areas, suggests that cancer patients may not be receiving the same access to services, depending on where they live. Studies have shown that the lack of an integrated referral system, limited resources or reproductive endocrinology specialists, and time constraints can limit oncologists' referral patterns in certain parts of the country.^{19,24,25} Oncologists can also feel an urgency to start cancer treatment and do not perceive fertility as a priority, which can decrease their education of patients regarding fertility preservation services.^{19,26} These barriers further highlight the need to raise awareness for both patients and providers.

Strengths and limitations

While this study benefits from the inclusion of a large sample of women, we

FIGURE 2
Rates of fertility evaluation, testing, and procedures over time



Rates of fertility evaluation, testing, and procedures over time with 95% confidence intervals.

Selter et al. Fertility preservation services in reproductive-aged cancer patients. *Am J Obstet Gynecol* 2019.

recognize a number of important limitations. First, administrative data may undercapture utilization of some services. In particular, fertility preservation services obtained using out-of-pocket expenditures without insurance would not be captured. However, most commercial insurances provide coverage for laboratory testing and office evaluation; thus, these services would likely have been captured.

Second, MarketScan lacks specific coding to identify office visits to reproductive endocrinologists. We used specific billing codes for the evaluation for fertility preservation as a surrogate. We also reported visits to gynecologists, although this measure undoubtedly includes evaluations for a variety of conditions aside from management of infertility.

Third, some of the testing used for the evaluation of fertility is nonspecific and may have been ordered for other indications (such as follicle-stimulating hormone and estradiol for breast cancer). A priori, we chose a broad definition of fertility testing, evaluations, and procedures. Rates of individual

interventions and a composite are included for comparison. Furthermore, we lack data on tumor characteristics such as stage as well as obstetric characteristics such as prior pregnancies.

As with any study of administrative data, we cannot capture the patient's reproductive desires. Therefore, the study would undercapture those patients who discussed fertility with oncologists but were not referred for fertility services either because of severity of disease or lack of desire for fertility. Germline testing was not included in this study, which could have an impact on patients' desires for future fertility. Furthermore, while using a large administrative database, to ensure we were including only incident cases, we used only claims within 30 days of first cancer-directed surgery claim for the respective primary tumor sites, which did not allow us to examine other cancers such as lymphoma/leukemia in which surgery was not a part of treatment.

Also, we are unable to capture fertility counseling provided by oncologists and other care providers not associated with a billing claim. Discussion of fertility-conserving options by oncologists is an

TABLE 2
Multivariable models of factors associated with fertility preservation services

Variables	Fertility evaluation aRR (95% CI)	Fertility laboratory test aRR (95% CI)	Fertility preservation procedure aRR (95% CI)	Any fertility service ^a aRR (95% CI)
Age group, y				
18–35	23.10 (17.47–30.54) ^b	1.98 (1.75–2.23) ^b	25.24 (17.04–37.39) ^b	2.56 (2.29–2.86) ^b
36–40	6.14 (4.55–8.28) ^b	1.05 (0.93–1.18)	7.18 (4.74–10.87) ^b	1.22 (1.08–1.36) ^c
41–45	Referent	Referent	Referent	Referent
Cancer type				
Lung	Referent	Referent	Referent	Referent
Breast	1.52 (0.68–3.40)	2.63 (1.36–5.07) ^c	1.73 (0.55–5.41)	2.30 (1.30–4.06) ^c
Cervix	0.52 (0.17–1.61)	2.25 (1.07–4.73) ^c	0.55 (0.11–2.73)	1.71 (0.88–3.33)
Colorectal	1.21 (0.51–2.89)	1.14 (0.56–2.31)	1.22 (0.36–4.19)	1.15 (0.62–2.12)
Health insurance				
Non-HMO	Referent	Referent	Referent	Referent
HMO	0.71 (0.53–0.95) ^c	0.83 (0.71–0.97) ^c	0.56 (0.37–0.86) ^c	0.83 (0.72–0.96) ^c
Medicaid	NA	0.70 (0.35–1.37)	NA	0.58 (0.30–1.12)
Region				
Northeast	2.32 (1.88–2.87) ^b	1.14 (0.99–1.30)	4.03 (3.00–5.42) ^b	1.24 (1.10–1.40) ^c
North Central	1.32 (1.04–1.68) ^c	0.85 (0.74–0.99) ^c	1.63 (1.15–2.33) ^c	0.89 (0.78–1.02)
South	Referent	Referent	Referent	Referent
West	1.35 (1.05–1.74) ^c	1.10 (0.96–1.27)	2.02 (1.42–2.87) ^b	1.17 (1.03–1.33) ^c
Unknown	0.87 (0.06–12.84)	0.79 (0.20–3.16)	NA	0.83 (0.23–2.96)
Metropolitan statistical area				
Non-MSA	Referent	Referent	Referent	Referent
MSA	3.41 (2.13–5.47) ^b	1.24 (1.04–1.48) ^c	5.02 (2.23–11.29) ^b	1.35 (1.14–1.60) ^c
Unknown	1.17 (0.08–17.86)	0.90 (0.22–3.63)	NA	0.95 (0.26–3.42)
Elixhauser comorbidity				
0	Referent	Referent	Referent	Referent
1	0.84 (0.66–1.07)	1.08 (0.95–1.23)	0.84 (0.61–1.15)	1.06 (0.94–1.20)
≥2	0.86 (0.59–.24)	1.07 (0.88–1.31)	0.73 (0.42–1.25)	1.03 (0.85–1.24)
Surgery year				
2009	Referent	Referent	Referent	Referent
2010	1.84 (0.92–3.64)	0.91 (0.71–1.18)	0.79 (0.37–1.70)	0.93 (0.73–1.19)
2011	1.97 (1.00–3.87) ^c	0.90 (0.70–1.15)	1.39 (0.70, 2.79)	0.94 (0.74–1.20)
2012	2.32 (1.20–4.48) ^c	0.92 (0.72–1.18)	0.98 (0.48–1.97)	1.00 (0.79–1.26)
2013	2.89 (1.51–5.53) ^c	0.97 (0.76–1.23)	1.44 (0.73–2.84)	1.04 (0.82–1.31)
2014	3.10 (1.61–5.94) ^c	0.89 (0.69–1.14)	1.21 (0.60–2.42)	1.03 (0.81–1.31)
2015	4.48 (2.34–8.58) ^b	1.13 (0.88–1.46)	2.29 (1.17–4.50) ^c	1.25 (0.98–1.59)
2016	4.66 (2.38–9.11) ^b	1.10 (0.83–1.46)	3.82 (1.94–7.55) ^c	1.19 (0.91–1.56)

Selter et al. Fertility preservation services in reproductive-aged cancer patients. *Am J Obstet Gynecol* 2019.

(continued)

TABLE 2

Multivariable models of factors associated with fertility preservation services (continued)

Variables	Fertility evaluation aRR (95% CI)	Fertility laboratory test aRR (95% CI)	Fertility preservation procedure aRR (95% CI)	Any fertility service ^a aRR (95% CI)
Radiation within 6 months before or after surgery				
No	Referent	Referent	Referent	Referent
Yes	1.13 (0.96–1.34)	0.92 (0.83–1.02)	1.12 (0.89–1.40)	0.95 (0.87–1.05)

aRR, adjusted risk ratio; CI, confidence interval; HMO, health maintenance organization; MSA, metropolitan statistical area.

^a Includes fertility evaluation, laboratory testing, or procedure; ^b $P < .0001$; ^c $P < .05$.

Selter et al. Fertility preservation services in reproductive-aged cancer patients. *Am J Obstet Gynecol* 2019.

important first step in fertility preservation.

Finally, we evaluated a number of cancer types. For each tumor the individual treatments will effect fertility and ovarian function differently.

Research implications

While the results of our study suggest that rates of fertility preservation referrals for reproductive-aged women are low, further research is needed to elucidate the specific reasoning behind these low rates. Future studies addressing both oncologist and patients' knowledge/views on fertility preservation could help to determine specific barriers to implementation of fertility preservation services.

Conclusion

In summary, these data demonstrate that despite American Society of Clinical Oncology and the American Society of Reproductive Medicine recommendations for oncologists to initiate fertility preservation options for their reproductive-age cancer patients, the rate of referral for services remains low. While it is encouraging that the use of fertility services has increased over time, the clinical, socioeconomic, and regional disparities in access to services suggest that interventions to promote access to fertility-preserving services are greatly needed. ■

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SUPPLEMENTAL TABLE 1

ICD and CPT codes for cancer diagnosis, cancer-directed surgeries, fertility evaluation, fertility procedure, and fertility laboratory test

Variables	ICD9 diagnosis/ procedure codes	ICD10 diagnosis/ procedure codes	CPT
Cancer diagnosis			
Colorectal cancer	153–154.8	C18, C18.0–C18.9, C19, C20, C21, C21.0, C21.1, C21.2, C21.8	
Lung cancer	162–162.9	C34, C34.0, C34.00, C34.01, C34.02, C34.1, C34.10, C34.11, C34.12, C34.2, C34.3, C34.30, C34.31, C34.32, C34.8, C34.80, C34.81, C34.82, C34.9, C34.90, C34.91, C34.92	
Breast	174–174.9	C50	
Cervix	180–180.9	C53, C53.0, C53.1, C53.8, C53.9	
Cancer-directed surgery			
Lung lobectomy	32.59, 32.29, 32.39, 32.49, 32.20, 32.50, 32.30, 32.41,	0BBK,* 0BBL,* 0BDM,* 0BTK,* 0BTL,* 0BTM,* 0BBK*	32100, 32110, 32124, 32140, 32141, 32150, 32610, 32440, 32442, 32445, 32480, 32482, 32484, 32486, 32488, 32491, 32500, 32503, 32504, 32505, 32506, 32507, 32540, 32657, 32661, 32662, 32663, 32666, 32667, 32668, 32669, 32670, 32671, 32672, 32673, 32674
Colectomy	17.3, 17.31, 17.32, 17.33, 17.34, 17.35, 17.36, 17.39, 45.7, 45.71, 45.72, 45.73, 45.74, 45.75, 45.76, 45.79, 45.8, 45.81, 45.82, 45.83, 45.94, 48.4, 48.40, 48.41, 48.42, 48.43, 48.49, 48.50, 48.52, 48.59, 48.51, 48.6, 48.61, 48.62, 48.63, 48.64, 48.65, 48.69,	0DBE,* 0DBF,* 0DBG,* 0DBK,* 0DBL,* 0DBM,* 0DBN,* 0DBP,* 0DBQ,* 0DBR,* 0DTE,* 0DTF,* 0DTG,* 0DTK,* 0DTL,* 0DTM,* 0DTN,* 0DTP,* 0DTQ,* 0DTR*	44140, 44141, 44143, 44144, 44145, 44146, 44147, 44150, 44151, 44153, 44155, 44156, 44157, 44158, 44160, 44204, 44205, 44206, 44207, 44208, 44210, 44211, 44212, 44213, 45110, 45111, 45112, 45113, 45114, 45116, 45119, 45120, 45121, 45123, 45126, 45160, 45717, 45172, 45190, 45395, 45397, 45402
Hysterectomy	68.3, 68.31, 68.39, 68.4, 68.41, 68.49, 68.5, 68.51, 68.59, 68.6, 68.61, 68.69, 68.7, 68.71, 68.79, 68.9	OUT9	58150, 58152, 58180, 58200, 58210, 58240, 58950, 58951, 58953, 58956, 58594, 58825, 58260, 58262, 58263, 58267, 58270, 58275, 58280, 58285, 58290, 58291, 58292, 58293, 58294, 58541, 58542, 58543, 58544, 58548, 58550, 58552, 58553, 58554, 58570, 58571, 58572, 58573
Breast mastectomy/ lumpectomy/ lymphadenectomy	85.3, 85.31, 85.32, 85.33, 85.34, 85.36, 85.4, 85.41, 85.42, 85.43, 85.44, 85.45, 85.46, 85.47, 85.48, 85.2, 85.20, 85.21, 85.22, 85.23, 85.24, 85.25, 85.1, 85.11, 85.12, 85.19, 40.3, 40.29, 40.50, 40.51, 40.23	0HTT,* 0HTU,* 0HTV,* 0HBT,* 0HBU,* 0HBV,* 07B5,* 07B6,* 07B8,* 07B9,* 07T5,* 07T6,* 07T8,* 07T9*	19303, 19304, 19305, 19306, 19307, 19180, 19182, 19200, 19220, 19240, 19110, 19120, 19125, 19126, 19160, 19162, 19301, 19302, 38792, 38900, 78195, 78800, 78801, 38740, 38745, 19305, 19306, 19307, 38500, 38525, 19302

Selter et al. Fertility preservation services in reproductive-aged cancer patients. Am J Obstet Gynecol 2019.

(continued)

SUPPLEMENTAL TABLE 1

ICD and CPT codes for cancer diagnosis, cancer-directed surgeries, fertility evaluation, fertility procedure, and fertility laboratory test (continued)

Variables	ICD9 diagnosis/ procedure codes	ICD10 diagnosis/ procedure codes	CPT
Fertility evaluation	V26.4, V26.42, V26.49	Z31.6, Z31.62, Z3.169	
Fertility preservation procedure	V26.82, V26.8, V26.81, V26.89, 659.2, 651.9	Z31.8, Z31.83, Z31.84, Z31.89, UY00Z0, OUY00Z1, OUY00Z2, OUI10Z0, OUI10Z1, OUI10Z2, OUI00ZZ, OUI04ZZ, OUI08ZZ, OUI10ZZ, OUI14ZZ, OUI18ZZ, OUI20ZZ, OUI24ZZ, OUI28ZZ	58970, 58974, 76948, 89250, 89251, 89290, 89291, 89252, 89253, 89254, 89255, 89256, 89257, 89260, 89261, 89264, 89268, 89272, 89280, 89281, S4011, S4020, S4025, S4021, S4015, 58825, 89258, 0058T, 0357T, 89337, 89335, 89259, 89342, 89343, 89344, 89346, 89352, 89353, 89354, 89356
Fertility testing	V26.1, V26.2, V26.21, V26.22, V26.29	Z31.41, Z31.4, Z31.49, Z318, Z31.84, Z31.89, Z31.9	83001, 83002, 84144, 82670, 82367,

CPT, Current Procedural Terminology; ICD9, International Classification of Diseases, ninth revision; ICD10, International Classification of Diseases, 10th revision.

Selter et al. Fertility preservation services in reproductive-aged cancer patients. Am J Obstet Gynecol 2019.

SUPPLEMENTAL TABLE 2

Multivariable models of use of fertility preservation services within 90 days of the diagnosis of cancer

Variables	Fertility evaluation aRR (95% CI)	Fertility laboratory test aRR (95% CI)	Fertility procedure aRR (95% CI)	Fertility evaluation/procedure and laboratory test aRR (95% CI)
Age group				
18–35	23.10 (17.47–30.54) ^a	1.98 (1.75–2.23) ^a	25.24 (17.04–37.39) ^a	2.56 (2.29–2.86) ^a
36–40	6.14 (4.55–8.28) ^a	1.05 (0.93–1.18)	7.18 (4.74–10.87) ^a	1.22 (1.08–1.36) ^b
41–45	Referent	Referent	Referent	Referent
Cancer type				
Lung	Referent	Referent	Referent	Referent
Breast	1.52 (0.68–3.40)	2.63 (1.36–5.07) ^b	1.73 (0.55–5.41)	2.30 (1.30–4.06) ^b
Cervix	0.52 (0.17–1.61)	2.25 (1.07–4.73) ^b	0.55 (0.11–2.73)	1.71 (0.88–3.33)
Colorectal	1.21 (0.51–2.89)	1.14 (0.56–2.31)	1.22 (0.36–4.19)	1.15 (0.62–2.12)
Health insurance				
Non-HMO	Referent	Referent	Referent	Referent
HMO	0.71 (0.53–0.95) ^b	0.83 (0.71–0.97) ^b	0.56 (0.37–0.86) ^b	0.83 (0.72–0.96) ^b
Medicaid	NA	0.70 (0.35–1.37)	NA	0.58 (0.30–1.12)
Region				
Northeast	2.32 (1.88–2.87) ^a	1.14 (0.99–1.30)	4.03 (3.00–5.42) ^a	1.24 (1.10–1.40) ^b
North Central	1.32 (1.04–1.68) ^b	0.85 (0.74–0.99) ^b	1.63 (1.15–2.33) ^b	0.89 (0.78–1.02)
South	Referent	Referent	Referent	Referent
West	1.35 (1.05–1.74) ^b	1.10 (0.96–1.27)	2.02 (1.42–2.87) ^a	1.17 (1.03–1.33) ^b
Unknown	0.87 (0.06–12.84)	0.79 (0.20–3.16)	NA	0.83 (0.23–2.96)

Selter et al. Fertility preservation services in reproductive-aged cancer patients. Am J Obstet Gynecol 2019.

(continued)

SUPPLEMENTAL TABLE 2

Multivariable models of use of fertility preservation services within 90 days of the diagnosis of cancer (continued)

Variables	Fertility evaluation aRR (95% CI)	Fertility laboratory test aRR (95% CI)	Fertility procedure aRR (95% CI)	Fertility evaluation/procedure and laboratory test aRR (95% CI)
Metropolitan statistical area				
Non-MSA	Referent	Referent	Referent	Referent
MSA	3.41 (2.13–5.47) ^a	1.24 (1.04–1.48) ^b	5.02 (2.23–11.29) ^a	1.35 (1.14–1.60) ^b
Unknown	1.17 (0.08–17.86)	0.90 (0.22–3.63)	NA	0.95 (0.26–3.42)
Elixhauser comorbidity				
0	Referent	Referent	Referent	Referent
1	0.84 (0.66–1.07)	1.08 (0.95–1.23)	0.84 (0.61–1.15)	1.06 (0.94–1.20)
≥2	0.86 (0.59–1.24)	1.07 (0.88–1.31)	0.73 (0.42–1.25)	1.03 (0.85–1.24)
Surgery year				
2009	Referent	Referent	Referent	Referent
2010	1.84 (0.92–3.64)	0.91 (0.71–1.18)	0.79 (0.37–1.70)	0.93 (0.73, 1.19)
2011	1.97 (1.00–3.87) ^b	0.90 (0.70–1.15)	1.39 (0.70–2.79)	0.94 (0.74–1.20)
2012	2.32 (1.20–4.48) ^b	0.92 (0.72–1.18)	0.98 (0.48–1.97)	1.00 (0.79–1.26)
2013	2.89 (1.51–5.53) ^b	0.97 (0.76–1.23)	1.44 (0.73–2.84)	1.04 (0.82–1.31)
2014	3.10 (1.61–5.94) ^b	0.89 (0.69–1.14)	1.21 (0.60–2.42)	1.03 (0.81–1.31)
2015	4.48 (2.34–8.58) ^a	1.13 (0.88–1.46)	2.29 (1.17–4.50) ^b	1.25 (0.98–1.59)
2016	4.66 (2.38–9.11) ^a	1.10 (0.83–1.46)	3.82 (1.94–7.55) ^b	1.19 (0.91–1.56)
Radiation within 6 months before or after surgery				
No	Referent	Referent	Referent	Referent
Yes	1.13 (0.96–1.34)	0.92 (0.83–1.02)	1.12 (0.89–1.40)	0.95 (0.87–1.05)

aRR, adjusted risk ratio; CI, confidence interval; HMO, health maintenance organization; MSA, metropolitan statistical area.

^a $P < .0001$; ^b $P < .05$.

Selter et al. Fertility preservation services in reproductive-aged cancer patients. Am J Obstet Gynecol 2019.

SUPPLEMENTAL TABLE 3

Chemotherapy codes

ICD9/ICD10	CPT	HCPCS
ICD9 diagnosis: V58.1, V58.11, V58.12, E93.31, E93.07	0519F, 96401, 96405, 96408, 96409, 96410,	C8953, C8954, C8955, C9025, C9027, C9214, C9257, C9414, C9415, C9418
ICD10 diagnosis: Z51.11, Z51.12	96411, 96412, 96413, 96414, 96415, 96416	C9420, C9421, C9425, C9431, C9432, C9440, C9442, C9449, C9453, C9455
ICD9 procedure: 00.10, 99.25	96417, 96420, 96422, 96423, 96425, 96440,	G0355, G0359, G0361, G0498, G0360, G0362, G8372
ICD10 procedure: 3E00X05, 3E0230, 3E02305, 3E02305, 3E0300, 3E0330, 3E03305, 3E0400, 3E04005, 3E0430, 3E04305, 3E0500, 3E05005, 3E0530, 3E05305, 3E0600, 3E06005, 3E0630, 3E06305, 3E0930, 3E09305, 3E0970, 3E09305, 3E09X0, 3E09X05, 3E0A05, 3E0B30, 3E0B305, 3E0B70, 3E0B705, 3E0BX0, 3E0BX05, 3E0C70, 3E0C705, 3E0CX0, 3E0CX05, 3E0D30, 3E0D305, 3E0D30, 3E0D305, 3E0D70, 3E0D705, 3E0DX0, 3E0DX05, 3E0F30, 3E0F305, 3E0F70, 3E0F705, 3E0F80, 3E0F805, 3E0G30, 3E0G305, 3E0G70, 3E0G705, 3E0H30, 3E0H305, 3E0H70, 3E0H705, 3E0H80, 3E0H805, 3E0J30, 3E0J305, 3E0J70, 3E0J705, 3E0J80, 3E0J805, 3E0K30, 3E0K305, 3E0K70, 3E0K705, 3E0K80, 3E0K805, 3E0L30, 3E0L305, 3E0L70, 3E0L705, 3E0M30, 3E0M305, 3E0M70, 3E0M705, 3E0P30, 3E0P305, 3E0P70, 3E0P705, 3E0P80, 3E0P805, 3E0Q30, 3E0Q305, 3E0Q70, 3E0Q705, 3E0Q00, 3E0Q005, 3E0R30, 3E0R305, 3E0S30, 3E0S305, 3E0V30, 3E0V305, 3E0W30, 3E0Y30, 3E0Y305, 3E0Y70, 3E0Y705	96445, 96446, 96450, 96542, 96545, 96549	J8510, J8515, J8520, J8521, J8530, J8540, J8560, J8562, J8565, J8600, J8610, J8670, J8700, J8705, J8999, J9000, J9001, J9002, J9010, J9015, J9017, J9019, J9020, J9022, J9023, J9025, J9027, J9031, J9032, J9033, J9034, J9035, J9039, J9040, J9041, J9042, J9043, J9045, J9047, J9050, J9055, J9060, J9062, J9065, J9070, J9080, J9090, J9091, J9092, J9093, J9094, J9095, J9096, J9097, J9098, J9100, J9120, J9130, J9145, J9150, J9151, J9155, J9160, J9165, J9170, J9171, J9175, J9176, J9178, J9179, J9180, J9181, J9182, J9185, J9190, J9200, J9201, J9203, J9205, J9206, J9207, J9208, J9209, J9211, J9212, J9213, J9214, J9215, J9216, J9217, J9228, J9230, J9245, J9250, J9260, J9261, J9262, J9263, J9264, J9265, J9266, J9267, J9268, J9270, J9271, J9280, J9285, J9290, J9291, J9293
		J9295, J9299, J9300, J9301, J9302, J9303, J9305, J9306, J9307, J9308, J9310, J9315, J9320, J9325, J9328, J9330, J9340, J9351, J9352, J9354, J9355, J9357, J9360, J9370, J9371, J9390, J9395, J9400, J9600, J9999, Q0081, Q0083, Q0084, Q0085, Q2017, Q2024, Q2049, Q2050, Q5102, S0116, S5019, S5020, S9329, S9330, S9331

CPT, Current Procedural Terminology; HCPCS, Healthcare Common Procedure Coding System; ICD9, International Classification of Diseases, ninth revision; ICD10, International Classification of Diseases, 10th revision.

Selter et al. Fertility preservation services in reproductive-aged cancer patients. *Am J Obstet Gynecol* 2019.

SUPPLEMENTAL TABLE 4

National Drug Code number for chemotherapy

68158014901, 68158014951, 68185014951, 54016413, 93753656, 310020130, 310020137, 378603405, 378603477, 378603493, 781535631, 904619546, 904622961, 12280034630, 16571042103, 16729003510, 16729003515, 16729003516, 21695099030, 33261095700, 33261095730, 33261095760, 33261095790, 35356027030, 42043018003, 42254016130, 42291010530, 51079032301, 51079032306, 51655063853, 51991062010, 51991062033, 54569573100, 54569619800, 54868500000, 54868613000, 54868613001, 55111064730, 55175550503, 60258086603, 60429028630, 60429028690, 60505298503, 60687011211, 60687011221, 62033037606, 62756025013, 62756025083, 63323012930, 66336053330, 66336053390, 66435041530, 67877017110, 67877017130, 68001015504, 68001015508, 68084044821, 68382020906, 68382020910, 418880210, 11793088001, 11793880201, 49281088001, 49281088003, 49281088058, 68152010809, 55566830100, 55566830101, 55566830102, 55566830301, 55566840100, 55566840101, 55566840102, 55566840301, 2145301, 13013202, 54569575100, 9766304, 54008013, 378500193, 47781010830, 49999098630, 54569573200, 54868526100, 59762285801, 60687013211, 60687013221, 63629126201, 85052503, 85052504, 85052505, 85052506, 93712005, 93712086, 172496058, 172496070, 185112505, 185112518, 185112588, 555087004, 555087063, 591222718, 591246618, 49884075305, 49884075313, 54569394200, 54868462800, 58016017000, 58016017030, 58016017060, 58016017090, 58016017099, 60429027205, 60429027218, 69097091591, 310072010, 310072025, 310072050, 310095036, 310095130, 310096036, 310096130, 54569394300, 4198701, 4199309, 4200709, 4200909, 4201009, 4201109, 4201209, 4201507, 4201509, 4201607, 4201609, 4201707, 4201709, 4690033, 85012002, 85012003, 85012004, 85028502, 85053901, 85057102, 85064703, 85064704, 85064705, 85068901, 85076901, 85092301, 85111001, 85113301, 85116801, 85117901, 85117902, 85118401, 85118402, 85119101, 85119102, 85123501, 85124201, 85125401, 85435001, 85435101, 85435201, 339650099, 339650199, 339650299, 339650399, 339650499, 339650599, 339650699, 339650799, 339650899, 339650999, 339651099, 339651199, 339651299, 339651399, 339651499, 339651599, 339651699, 339651799, 54868308500, 54868308501, 54868334100, 34101901, 54746000101, 50242005214, 50242005223, 7326101, 7326201, 67800011110, 67800012110, 54026913, 78024915, 93762056, 378207105, 378207193, 603418016, 16729003410, 16729003415, 35356040930, 42254024330, 42291037490, 51991075910, 51991075933, 53217010830, 54569571400, 54868415100, 54868625200, 55111064630, 60505325503, 60505325508, 62756051183, 63323077230, 68084080311, 68084080321, 68258595503, 24022205, 24059707, 24059722, 24060545, 24061030, 24079375, 26971101, 74210803, 74228203, 74244003, 74334603, 74347303, 74364103, 74364203, 74366303, 74368303, 74377903, 74969403, 182315499, 185740014, 185740085, 300210601, 300210801, 300228201, 300243701, 300244001, 300333601, 300334301, 300334601, 300361224, 300361228, 300362624, 300362628, 300362630, 300362901, 300362906, 300363901, 300363906, 300364101, 300364201, 300366301, 300367301, 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SUPPLEMENTAL TABLE 5
ICD and CPT codes for radiation

Variables	ICD9	ICD10	CPT/HCPCS
Beam	92.23, 92.24, 92.25, 92.26	D00, D70, DDO, DP0, DU0, DW0	CPT: 55876, 77401, 77402, 77403, 77404, 77406, 77407, 77408, 77409, 77411, 77412, 77413, 77414, 77416, 77399, 77417, 77421, 77422, 77423, 77425 HCPCS: G6001, G6002, G6003, G6004, G6005, G6006, G6007, G6008, G6009, G6010, G6011, G6012, G6013, G6014
IMRT			CPT: 77418, 77301, 0073T, 77338, 77385, 77386 HCPCS: G0174, G0178, G6015, G6016
Brachytherapy	92.20, 92.27	D01, D71, DD1, DU1, DW1	CPT: 76965, 77316, 77317, 77318, 77326, 77327, 77328, 77750, 79403, 79101, 77761, 77762, 77763, 77776, 77777, 77778, 77781, 77782, 77783, 77784, 77785, 77786, 77787, 77789, 77790, 77799, 57155, 57156, 77770, 77771, 77316, 77317, 77318, 0182T, 77767, 77768, 77770, 77771, 77772 HCPCS: C1164, C1174, C1325, C1700, C1701, C1702, C1703, C1704, C1705, C1707, C1709, C1711, C1712, C1715, C1716, C1717, C1719, C1720, C1728, C1790, C1791, C1792, C1793, C1794, C1795, C1796, C1797, C1798, C1799, C1800, C1801, C1802, C1803, C1804, C1805, C1806, C2616, C2634, C2635, C2636, C2637, C2638, C2639, C2640, C2641, C2642, C2643, C2644, C2645, C2698, C2699, C9725, S2270, G0458, Q3001
Proton			CPT: 77520, 77522, 77523, 77525, 77380, 77381
SBRT		D02, D72, DD2, DU2, DW2	CPT: 77377, 0082T, 0083T, 77435 HCPCS: G0173, G0243, G0251, G0339, G0340
Simulation			CPT: 77280, 77285, 77290
Plan			CPT: 76370, 77014, 77261, 77262, 77263, 77295, 77299, 77300, 77301, 77305, 77310, 77315, 77321, 77331, 77332, 77333, 77334, 77336, 77338, 77370, 77371, 77372, 77373, 77399, 77470, 0197T HCPCS: G0338

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(continued)

SUPPLEMENTAL TABLE 5
ICD and CPT codes for radiation (continued)

Variables	ICD9	ICD10	CPT/HCPCS
Radiation management			CPT: 77427, 77431, 77420, 77435, 77470, 77499, 77419, 77420, 77425, 77430
Radiation unknown	92.21, 92.22, 92.29, 92.20, 92.28		CPT: 77424, 77432, 77435, 77469, 77499, 77520, 77522, 77523, 77525, 77326, 77327, 77328, 77336, 77014, 76950, 77421, 0197T, 77385, 77386, 77387, 77306, 77307, 76370, 76375, 76376, 77790, 19296, 20555, 58346, 55920, 77280, 77332, 77295, 77300, 79900, 78265, 78266
Other radiation		D0Y, D7Y, DDY, DPY, DUY, DWY	

CPT, Current Procedural Terminology; HCPCS, Healthcare Common Procedure Coding System; ICD9, International Classification of Diseases, ninth revision; ICD10, International Classification of Diseases, 10th revision.

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