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Trends in Periodic Surveillance Testing for Early-Stage Uterine Cancer Survivors

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Abstract

Objective—To examine the use of periodic surveillance testing for early-stage endometrial cancer survivors.

Methods—We performed a population-based analysis using the Surveillance, Epidemiology, and End Results-Medicare database, which was used to identify patients with stage I-II endometrioid endometrial cancer treated from 1992-2011. Three surveillance periods (7-18, 19-30, 31-42 months) after hysterectomy were examined. Use of vaginal cytology and imaging were quantified.

Results—We identified 17,638 patients. From 1992 to 2011, the use of chest radiography decreased (46.3% to 34.2%) during the first surveillance period, while imaging with chest CT (computed tomography) (0.9% to 12.6%), abdominopelvic CT (11.7% to 24.8%) and PET (0% to 2.9%) increased ($P<0.001$ for all). The use of cytology increased from 68.5% in 1992 to 72.3% in 2007, then decreased to 66.9% in 2011 ($P=0.02$). The mean number of cytologic samples obtained per-patient increased from 1.3 in 1992 to 1.6 in 2008 then declined to 1.3 in 2011, while the mean per-patient number of chest CTs (0.02 to 0.2), abdominopelvic CTs (0.2 to 0.4) and PETs (positron emission tomography) (0 to 0.03) rose from 1992 to 2011. In 2011, 49.3% underwent radiologic surveillance 7-18 months after diagnosis, while 11.9% underwent 2 or more radiologic

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assessments in combination with cytology. These findings were similar for surveillance periods 2 and 3.

Conclusions—The use of chest radiography has decreased and use of cytology has started to decline. However, the use of more costly imaging modalities is increasing despite a lack of evidence for the efficacy of these tests for early-stage endometrial cancer survivors.

Introduction

The majority of women with uterine cancer are diagnosed with early-stage disease and have a favorable prognosis.¹ Treatment typically consists of hysterectomy sometimes followed by adjuvant radiation or chemotherapy. After treatment, patients enter a period of surveillance that may include periodic follow-up, vaginal cytologic screening, and perhaps radiologic testing.²

Surveillance for cancer survivors has a number of goals. Foremost is the early detection of recurrent disease.^{3,4} While an important goal, the value of detecting asymptomatic recurrences in which effective salvage therapies can be administered has been difficult to demonstrate not only for uterine cancer, but also the majority of solid tumors.^{3,5,6} In addition, surveillance and follow-up play an important role in providing psychological support to survivors who often experience significant anxiety post treatment.⁷⁻¹⁰ Lastly, oncologists may also facilitate access to the healthcare system for the management of patients' comorbid conditions and other ongoing care requirements.¹¹

Although the Society of Gynecologic Oncology (2011) and National Comprehensive Cancer Network (ongoing) have published surveillance guidelines for endometrial cancer, data for many recommendations is lacking.^{2,4} Vaginal cuff cytology is commonly utilized despite multiple studies suggesting that cytologic follow-up is of little value.^{3,4,12-14} Likewise, while a number of radiologic imaging modalities are now frequently used for other tumor sites, little is known about the use and efficacy of these tests in endometrial cancer survivors.^{3,4} Given the limited data describing the use of surveillance testing, we performed a population-based analysis to examine the patterns of surveillance testing and in patients with early-stage, endometrial carcinomas.

Materials and Methods

The linked Surveillance, Epidemiology, and End Results-Medicare database was analyzed.¹⁵⁻¹⁷ This data source is a population-based tumor registry maintained by the National Cancer Institute. The Surveillance, Epidemiology, and End Results registry captures data on date of diagnosis, tumor histology, location, stage, treatment, and survival, as well as demographic and selected census tract-level information. The Medicare database includes information on patients with Medicare part A (inpatient) and part B (outpatient), including billed claims, services, and diagnoses. These two files are linked and provide data on initial services and all follow-up care. All data was de-identified and exemption from the Columbia University Institutional Review Board was obtained.

Women 65 years of age or older with stage I-II, endometrioid endometrial adenocarcinoma of the uterus were selected. Patients who underwent primary treatment with a hysterectomy between January 1, 1992, and December 31, 2011, were included in the analysis. Women who received chemotherapy or radiation prior to hysterectomy and those who survived 6 months after hysterectomy were excluded from the surveillance analysis. To exclude women with incomplete claims, patients enrolled in a non-Medicare health maintenance organization, those receiving Medicare for a reason other than age, and patients with other primary cancers were excluded.

Use of surveillance testing typically decreases with time since diagnosis.¹⁸ To account for this change over time, we developed a conceptual framework including three surveillance periods as previously described by Keating and colleagues.¹⁸ Within this framework, the start of evaluation (time point 0) is hysterectomy. Patients are assumed to receive any adjuvant therapy (chemotherapy or radiation) during the 6 month period after hysterectomy. After this period of primary treatment, we defined three surveillance periods: period 1 (months 7 to 18), period 2 (months 19 to 30), and period 3 (months 31 to 42). Women were censored from a given surveillance period and all subsequent surveillance periods if they received radiation, chemotherapy, or died (from any cause) during a surveillance period. In addition, we also excluded patients who were alive but did not have follow-up for the surveillance period.

Age at diagnosis was stratified into 5-year intervals and race was recorded as white, black, Hispanic and other. The marital status variable was recorded as married, not married, and unknown. An aggregate socioeconomic status (SES) score was calculated from education, poverty level, and income data from the 2000 census tract data, as previously reported by Du and co-workers.¹⁹ Patient scores were ranked on a scale of 1-5 by use of the formula that incorporated education, poverty, and income weighted equally, with 1 being the lowest value. The prevalence of comorbid medical diseases was assessed using the Klabunde adaptation of the Charlson comorbidity index (ie, the Klabunde–Charlson index).^{20,21} Medicare claims were examined for diagnostic codes of the International Classification of Disease, Ninth Revision, Clinical Modification (ICD-9-CM). Each condition was weighted, and patients were assigned a score that was based on the Klabunde–Charlson index.²¹ Area of residence was categorized as metropolitan or nonmetropolitan. The registries were grouped as: Eastern, Western and Midwest. Stage was captured using the American Joint Cancer Commission staging criteria and reported extent of disease codes to classify patients based on the 2009 FIGO staging criteria. Patients with cervical involvement for whom the nature of cervical involvement was unknown were categorized as stage IINOS. Tumor grade was grouped as well, moderately or poorly differentiated or unknown. Use of adjuvant vaginal brachytherapy, whole pelvic radiation and chemotherapy were noted.

Outcomes of interest were use of cytologic and radiologic follow-up testing. The following tests were examined: vaginal cytology, chest radiography, computed tomography of the chest (chest CT), computed tomography of the abdomen and/or pelvis (abdomen/pelvic CT), and positron emission tomography (with or without computed tomography). To identify testing, we extracted claims from the Medicare files by searching the Level II Healthcare Common Procedure Coding System (HCPCS), Current Procedural Terminology (CPT)

codes, and International Classification of Disease, Ninth Revision, Clinical Modification (ICD-9-CM) diagnostic and procedure codes from the physician claims files, the hospital outpatient claims files, or the Medicare provider review files.

In addition to the individual tests, we developed three composite endpoints to explore use of resource intensive surveillance. Active surveillance was defined as use of any of the following tests during a surveillance period: cytology, chest radiography, chest CT, abdomen/pelvic CT, or PET. Radiologic surveillance was defined as any imaging test (chest radiography, CT chest, abdomen/pelvic CT, or PET) during a given surveillance period. Lastly, high-intensity surveillance was characterized as vaginal cytology in combination with some form of chest imaging (chest radiograph or CT chest) and imaging of the abdomen/pelvis (abdomen/pelvic CT or PET).

Cost was estimated as the direct cost attributable to the five tests of interest. To estimate cost, we utilized the Centers for Medicare and Medicaid Services (CMS) published fee schedules.²² Medicare reimbursement for PET scan is highly variable and dependent on the local Medicare carrier. As such, estimates for the cost of PET were based on publically available reimbursement schedules.²³ For each code, we estimated the global fee for the diagnostic service of interest based on the national payment amount. All costs are reported in 2014 dollars. As each test has multiple billing costs, costs were estimated using the median reimbursement amount. Sensitivity analyses were performed using the lowest price adjustment and the primary findings of the study were largely unchanged.

Frequency distributions between categorical variables were compared using χ^2 tests. Trends over time for the number of women who received each test and the per-patient number of each test are reported descriptively for each surveillance period. The association between demographic, clinical, and oncologic characteristics and testing were estimated using multivariable log-linear regression models using generalized estimating equations accounting for hospital-level clustering. Separate models to examine active, radiologic, and high-intensity surveillance were developed. Cost was calculated as the mean per-patient cost for all tests during a given period. All analyses were conducted with SAS, version 9.4 (SAS Institute, Cary, NC). All statistical tests were two-sided. A P-value of <0.05 was considered statistically significant.

Results

A total of 17,638 patients with stage I-II endometrial cancer who survived greater than 6 months and did not receive preoperative chemotherapy or radiation were identified. The clinical and demographic characteristics of the patients are displayed in Table 1. Within the cohort, 16,326 (92.6%) women had stage I neoplasms while the remaining 1312 (7.4%) had stage II tumors. Lymph node evaluation was performed in 9795 (55.5%) of the patients. Within the first 6 months after hysterectomy, brachytherapy was utilized in 3875 (22.0%), pelvic radiation in 4867 (27.6%), and adjuvant chemotherapy in 298 (1.7%) women.

Among the 15,957 women who entered surveillance period 1, cytology was performed in 70.4% (11,228), chest radiography in 39.9% (6374), chest CT in 7.6% (1211),

abdominopelvic CT in 21.0% (3353) and PET in 1.2% (185). From 1992 to 2011, the use of chest radiography declined from 46.3% to 34.2% ($P<0.001$) (Figure 1). Use of cytology increased from 68.5% to 72.3% for those treated in 2007 then declined to 66.9% in 2011, while performance of chest CT increased over time to 12.6% in 2011 ($P<0.001$). Similarly, abdominopelvic CT increased from 11.7% in 1992 to 24.8% in 2011 ($P<0.001$), and PET increased over time to 2.9% in 2011 ($P<0.0001$) all increased through 2011. The mean per-patient number of cytologic specimens increased from 1.3 in 1992 to a peak of 1.6 in 2008 then declined to 1.3 in 2011 ($P<0.001$), while the mean per patient chest radiographs decreased from 0.8 to 0.5 over the time period ($P<0.001$) (Figure 2). The mean number chest CTs (0.02 to 0.2), abdominopelvic CTs (0.2 to 0.4) and PETs (0 to 0.03) per patient all increased from 1992 to 2011 ($P<0.001$ for all).

During surveillance period 1, active surveillance increased from 82.2% to a peak of 85.8% in 2009, then decreased to 82.7% in 2011, radiologic surveillance rose from 48.6% to 50.6% in 2009, then decreased to 49.3% in 2011 and high-intensity surveillance increased from 6.9% to 14.4% in 2009, then declined to 11.9% in 2011. Table 2 displays the characteristics of patients receiving radiologic and high-intensity surveillance during surveillance period 1. Higher tumor grade and comorbidity score were associated with increased likelihood of both radiologic and high-intensity surveillance. Similarly, performance of lymphadenectomy and receipt of brachytherapy, pelvic radiation, and chemotherapy were associated with both radiologic and active surveillance. Patients who resided in non-metropolitan area were less likely to undergo radiologic (RR=0.93; 95% CI, 0.89-0.97) and high-intensity (RR=0.82; 95% CI, 0.72-0.93) surveillance, while residents of the Midwest were more likely to receive both. Finally, higher socioeconomic status was associated with increased use of high-intensity surveillance; compared to women in the lowest SES stratum, the relative risk for women in the highest SES category was 1.19 (95% CI, 1.02-1.40).

The same general trends applied during surveillance periods 2 ($n=14,262$) and 3 ($n=12,507$); cytologic follow-up remained relatively constant until around 2009 then declined, use of chest radiography declined throughout, while CT scans of the chest as well as abdomen and pelvis and PET increased with time (Figures 1 and 2). During surveillance period 2, from 1992 to 2011, use of cytology decreased from 62.8% to 53.3% ($P=0.04$), chest radiography dropped from 42.4% to 32.9% ($P<0.001$), while chest CT (peak in 11.4% in 2006 then 7.2% in 2011) ($P<0.001$), abdominopelvic CT (8.7% to 19.6%) ($P<0.001$), and PET (0% to 1.9%) ($P<0.001$) all increased.

The mean per-patient cost of cytologic surveillance for those who underwent testing during surveillance period 1 was \$62 in 1992 and remained relatively stable to \$63 in 2011 (Figure 3). Similarly, the mean per patient cost of chest radiography among those who underwent the test was \$117 in 1992 and remained relatively constant to \$114 in 2011. However, the mean per-patient cost of CT and/or PET increased substantially from \$509 in 1992 to 750 in 2011.

Discussion

Our findings suggest that the use of surveillance testing among women with early-stage endometrial cancer is widespread. While the use of chest radiography has decreased and use of cytology has started to decline, the use of more costly imaging modalities is increasing. These tests are not only being used in a greater number of women, but are also being performed more frequently in those women who are being tested.

The majority of women with endometrial cancer who recur do so within 3 years of diagnosis, and approximately 80% are symptomatic at the time of recurrence.³ Most studies to date have been unable to detect a difference in survival between symptomatic and asymptomatic recurrences, raising doubt about the value of screening asymptomatic women.³ The National Comprehensive Cancer Network (NCCN) has long published surveillance guidelines and currently recommends periodic physical examination every 3-6 months while imaging is only recommended as clinically indicated.² The Society of Gynecologic Oncology published surveillance recommendations in 2011.¹⁴

In our cohort, vaginal cytology was the most frequently utilized surveillance test. Prior work has consistently shown that cytologic surveillance is of little value given that the majority of women with a vaginal cuff recurrence experience symptomatic vaginal bleeding and have a mass on examination.^{4,12-14,24-32} In one report of 433 women, abnormal Pap results were common (13% of women and 3% of all specimens), although no cases of recurrent endometrial cancer were diagnosed based on abnormal cytology alone.¹³ One observational study estimated that the detection of each asymptomatic vaginal recurrence would require 1067 cytologic tests at a cost of over \$44,000.¹²

Given that most radiologic tests are for the detection of metastatic disease, prior work has shown these tests to be of little benefit for asymptomatic patients.^{3,4,27,28} Historically, chest radiography has been used to detect pulmonary recurrences; 0-14% of asymptomatic patients will have abnormalities.³ More recently, CT and PET have been used for the surveillance of women with endometrial cancer. While these tests are more costly, both modalities appear to be more sensitive for the detection of recurrent disease.^{3,33-35} The major concern for use of any radiologic test is that patients with metastatic disease are unlikely to be salvaged and the benefit of the early detection of recurrent disease has not been demonstrated.^{3,4}

There are likely numerous factors that contributed to the increased use of surveillance testing we noted. Cancer survivors often have substantial anxiety and desire testing even with the knowledge that testing may not alter survival.^{7-10,36} A survey of colorectal cancer survivors found that 99% of patients wanted follow-up with serum tumor marker testing irrespective of its ability to change outcome.³⁶ For oncologists, developing surveillance strategies for individual patients is complicated by the availability of numerous guidelines, many of which differ between professional societies, and the majority of which are based on expert opinion and not high-quality data.

We acknowledge a number of limitations. First, we are unable to distinguish between tests ordered for surveillance and those ordered for symptomatic evaluation. To limit this bias, we

developed a classification schema to exclude patients who died or began treatment for a recurrence. However, it is likely that a small number of tests were performed for evaluation of a complaint and not surveillance. In particular, patients with comorbidities are more likely to undergo testing to examine other primary diseases. Our analysis of cost only examines the direct costs of the tests and would be higher if office evaluations and the cost of downstream evaluation of abnormalities were included. Some small, statistically significant findings we demonstrated may not necessarily be clinically significant. Finally, we did not evaluate the effect of surveillance testing on survival.

Our data suggests that strategies to improve the follow-up care of women with endometrial cancer are needed. A prior cohort study noted that women with localized endometrial tumors were 6 times more likely to die from cardiovascular disease than from endometrial cancer.³⁷ These data, along with the fact that current surveillance testing is largely ineffective in prolonging survival from endometrial cancer, suggest that the follow-up care of women with endometrial cancer may be improved if greater focus is placed on the diagnosis and management of medical comorbidities, lifestyle modification, and preventive care.^{11,38} Initiatives to develop more thoughtful follow-up strategies for women with endometrial cancer may not only improve patient satisfaction and long-term outcome, but also help reduce unneeded medical expenditures.

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Figure 1.

Percentage of women who underwent surveillance testing. **A.** Surveillance period 1 (7–18 months), change in use over time. Chest radiograph ($P<.001$), chest computed tomography (CT) ($P<.001$), abdominopelvic CT ($P<.001$), positron emission tomography (PET) ($P<.0001$), cytology ($P=.017$). **B.** Surveillance period 2 (19–30 months), change in use over time. Chest radiograph ($P<.001$), chest CT ($P<.001$), abdominopelvic CT ($P<.001$) and PET ($P<.001$); while no significant change for cytology ($P=.695$). **C.** Surveillance period 3 (31–42 months), change in use over time. Chest radiograph ($P<.001$), chest CT ($P<.001$), abdominopelvic CT ($P<.001$), PET ($P<.001$); while no significant change for cytology ($P=.474$).

Figure 2.

Tests per patient. **A.** Surveillance period 1 (7–18 months), change in use over time. Chest radiograph ($P<.001$), chest computed tomography (CT) ($P<.001$), abdominopelvic CT ($P<.001$), positron emission tomography (PET) ($P<.001$), cytology ($P<.001$). **B.** Surveillance period 2 (19–30 months), change in use over time. Chest radiograph ($P=.001$), chest CT ($P<.001$), abdominopelvic CT ($P<.001$), PET ($P<.001$), cytology ($P<.001$). **C.** Surveillance period 3 (31–42 months), change in use over time. Chest radiograph ($P=.001$), chest CT ($P<.001$), abdominopelvic CT ($P<.001$), PET ($P<.001$); while no significant change for cytology ($P=.075$).

Figure 3.
Cost of surveillance testing for women during surveillance period 1. CT, computed tomography; PET, positron emission tomography.

Table 1

Clinical and demographic characteristics of women with stage I-II endometrial cancer.

	N	(%)
	17,638	
<i>Age (years)</i>		
65-69	4701	(26.7)
70-74	5214	(29.6)
75-79	4056	(23.0)
80	3667	(20.8)
<i>Race</i>		
White	16,114	(91.4)
Black	784	(4.4)
Hispanic	180	(1.0)
Other/missing	560	(3.2)
<i>Year of diagnosis</i>		
1992	731	(4.1)
1993	695	(3.9)
1994	657	(3.7)
1995	682	(3.9)
1996	631	(3.6)
1997	637	(3.6)
1998	573	(3.3)
1999	539	(3.1)
2000	1152	(6.5)
2001	1143	(6.5)
2002	1088	(6.2)
2003	1086	(6.2)
2004	1051	(6.0)
2005	1055	(6.0)
2006	1070	(6.1)
2007	988	(5.6)
2008	952	(5.4)
2009	988	(5.6)
2010	961	(5.5)
2011	959	(5.4)
<i>Marital status</i>		
Married	8235	(46.7)
Unmarried	8779	(49.8)
Unknown	624	(3.5)
<i>Area of residence</i>		
Metropolitan	14,684	(83.3)
Non-metropolitan	2954	(16.8)

	N	(%)
<i>Registry</i>		
Eastern	3844	(21.8)
Midwest	6838	(38.8)
West	6956	(39.4)
<i>Socioeconomic status</i>		
Lowest (first) quintile	3509	(19.9)
Second quintile	4055	(23.0)
Third quintile	2988	(16.9)
Fourth quintile	4387	(24.9)
Highest (fifth) quintile	2680	(15.2)
Unknown	19	(0.1)
<i>Comorbidity score</i>		
0	10,591	(60.1)
1	4496	(25.5)
2	2551	(14.5)
<i>Stage</i>		
IA	11,441	(64.9)
IB	3551	(20.1)
INOS	1334	(7.6)
IIB	358	(2.0)
IINOS	954	(5.4)
<i>Tumor grade</i>		
1	7398	(41.9)
2	6463	(36.6)
3	2601	(14.8)
Unknown	1176	(6.7)
<i>Lymphadenectomy</i>		
No	7843	(44.5)
Yes	9795	(55.5)
<i>Adjuvant brachytherapy</i>		
No	13,763	(78.0)
Yes	3875	(22.0)
<i>Adjuvant external beam radiation</i>		
No	12,771	(72.4)
Yes	4867	(27.6)
<i>Adjuvant chemotherapy</i>		
No	17,340	(98.3)
Yes	298	(1.7)
<i>Patients entering surveillance period</i>		
Period 1 (7-18 months)	15,957	(90.5)
Period 2 (19-30 months)	14,262	(80.8)

	N	(%)
Period 3 (31-42 months)	12,507	(70.9)

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Table 2

Predictors of active, radiologic, and high-intensity surveillance during surveillance period 1.

	Radiologic Surveillance			High-intensity surveillance		
	N	(%)		N	(%)	
	7909	49.6		1833	11.5	
<i>Age (years)</i>						
65-69	2033	47.3	Reference	491	11.4	Reference
70-74	2381	49.6	1.04 (0.99- 1.08)	581	12.1	1.05 (0.94- 1.18)
75-79	1841	50.3	1.04 (1.00- 1.09)	447	12.2	1.06 (0.94- 1.19)
80	1654	51.7	1.08 (1.03- 1.13)**	314	9.8	0.86 (0.75- 0.98)*
<i>Race</i>						
White	7256	49.6	Reference	1674	11.5	Reference
Black	348	51.1	0.95 (0.88- 1.02)	94	13.8	1.00 (0.82- 1.22)
Hispanic	83	52.2	1.08 (0.92- 1.25)	15	9.4	0.97 (0.60- 1.57)
Other/missing	222	44.4	0.94 (0.85- 1.04)	50	10.0	1.04 (0.80- 1.37)
<i>Year of diagnosis</i>						
1992	324	48.6	Reference	46	6.9	Reference
1993	337	53.0	1.10 (0.99- 1.22)	44	6.9	1.02 (0.69- 1.50)
1994	284	47.3	0.99 (0.88- 1.11)	52	8.7	1.28 (0.88- 1.85)
1995	306	49.2	0.99 (0.89- 1.11)	48	7.7	1.05 (0.72- 1.55)
1996	279	49.2	1.00 (0.89- 1.12)	47	8.3	1.14 (0.78- 1.68)
1997	266	45.7	0.93 (0.83- 1.05)	51	8.8	1.26 (0.86- 1.84)
1998	265	51.7	1.04 (0.93- 1.16)	52	10.1	1.39 (0.96- 2.03)
1999	231	47.1	0.96 (0.85- 1.08)	45	9.2	1.27 (0.86- 1.88)
2000	504	48.2	0.97 (0.88- 1.08)	108	10.3	1.41 (1.02- 1.96)*
2001	499	47.4	0.96 (0.87- 1.06)	115	10.9	1.48 (1.07- 2.05)*
2002	499	49.6	1.00 (0.91- 1.11)	124	12.3	1.64 (1.19- 2.26)*
2003	510	51.7	1.03 (0.93- 1.14)	124	12.6	1.63 (1.18- 2.24)*
2004	446	47.5	0.94 (0.85- 1.04)	121	12.9	1.65 (1.20- 2.28)*
2005	487	52.1	1.04 (0.95- 1.15)	129	13.8	1.79 (1.30- 2.47)*
2006	491	51.2	0.96 (0.87- 1.06)	142	14.8	1.48 (1.07- 2.05)*
2007	449	50.6	1.00 (0.91- 1.11)	124	14.0	1.64 (1.19- 2.26)*
2008	446	52.4	1.03 (0.93- 1.14)	126	14.8	1.62 (1.18- 2.24)*
2009	450	50.6	0.94 (0.85- 1.04)	128	14.4	1.65 (1.20- 2.28)*
2010	405	47.5	1.04 (0.95- 1.15)	103	12.1	1.79 (1.30- 2.47)*
2011	431	49.3	1.04 (0.95- 1.15)	104	11.9	1.79 (1.30- 2.47)*
<i>Marital status</i>						
Married	3672	48.6	Reference	865	11.5	Reference
Unmarried	3964	50.6	1.01 (0.98- 1.04)	910	11.6	1.04 (0.95- 1.14)

	Radiologic Surveillance			High-intensity surveillance		
	N	(%)		N	(%)	
Unknown	273	47.2	0.96 (0.87- 1.04)	58	10.0	0.87 (0.68- 1.11)
<i>Area of residence</i>						
Metropolitan	6587	49.6	Reference	1548	11.7	Reference
Non-metropolitan	1322	49.5	0.93 (0.89- 0.97)**	285	10.7	0.82 (0.72- 0.93)**
<i>Registry</i>						
Eastern	1642	47.5	Reference	427	12.4	Reference
Midwest	3416	55.2	1.24 (1.18- 1.29)***	890	14.4	1.45 (1.30- 1.63)**
West	2851	45.2	1.01 (0.96- 1.06)	516	8.2	0.82 (0.72- 0.93)**
<i>Socioeconomic status</i>						
Lowest (first) quintile	1569	50.9	Reference	335	10.9	Reference
Second quintile	1842	50.0	1.00 (0.95- 1.05)	428	11.6	1.10 (0.96- 1.26)
Third quintile	1334	49.3	1.00 (0.95- 1.05)	318	11.7	1.12 (0.96- 1.30)
Fourth quintile	1942	48.5	1.00 (0.95- 1.06)	458	11.4	1.10 (0.95- 1.27)
Highest (fifth) quintile	1216	49.5	1.05 (0.99- 1.11)	293	11.9	1.19 (1.02- 1.40)*
<i>Comorbidity score</i>						
0	4525	46.5	Reference	1049	10.8	Reference
1	2095	51.9	1.11 (1.07- 1.15)***	509	12.6	1.11 (1.00- 1.22)*
2	1289	58.9	1.26 (1.20- 1.31)***	275	12.6	1.11 (0.98- 1.26)
<i>Stage</i>						
IA	4972	47.1	Reference	1020	9.7	Reference
IB	1724	54.8	1.02 (0.98- 1.07)	504	16.0	1.12 (1.00- 1.25)*
INOS	159	54.8	1.01 (0.95- 1.07)	48	16.6	0.91 (0.76- 1.08)
IIB	449	57.5	1.08 (0.98- 1.19)	123	15.8	1.18 (0.93- 1.49)
IINOS	430	48.0	1.05 (0.98- 1.13)	76	8.5	1.18 (0.99- 1.42)
<i>Tumor grade</i>						
1	3256	46.9	Reference	657	9.5	Reference
2	2939	50.4	1.02 (0.98- 1.06)	694	11.9	1.05 (0.95- 1.16)
3	1218	56.7	1.09 (1.04- 1.14)**	349	16.2	1.24 (1.10- 1.41)**
Unknown	496	47.7	0.99 (0.92- 1.06)	133	12.8	1.15 (0.96- 1.36)
<i>Lymphadenectomy</i>						
No	3409	47.5	Reference	605	8.4	Reference
Yes	4500	51.3	1.04 (1.00- 1.07)*	1228	14.0	1.35 (1.23- 1.49)***
<i>Brachytherapy</i>						
No	5890	46.8	Reference	1161	9.2	Reference
Yes	2019	59.7	1.07 (1.01- 1.13)*	672	19.9	1.20 (1.03- 1.39)*
<i>External beam radiation</i>						
No	5402	46.0	Reference	1033	8.8	Reference

	Radiologic Surveillance			High-intensity surveillance		
	N	(%)		N	(%)	
Yes	2507	59.4	1.18 (1.12- 1.25) ***	800	19.0	1.57 (1.34- 1.82) ***
<i>Chemotherapy</i>						
No	7833	49.4	Reference	1804	11.4	Reference
Yes	76	70.4	1.34 (1.18- 1.51) ***	29	26.9	1.84 (1.34- 2.53) **

Relative risk (95% confidence interval).

Surveillance period 1 spans months 7 to18 after hysterectomy. Radiologic surveillance was defined as any imaging test (chest radiography, CT chest, abdomen/pelvic CT, or PET), high-intensity surveillance was characterized as vaginal cytology in combination with some form of chest imaging (chest radiograph or CT chest) and imaging of the abdomen/pelvis (abdomen/pelvic CT or PET).

* P<0.05,

** P<0.01,

*** P<0.001