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## Cost of cancer management by stage at diagnosis among Medicare beneficiaries

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### ABSTRACT

**Objective:** Estimate the annual cost of care in the 5 years following a cancer diagnosis for 17 invasive cancer types, by stage at diagnosis.

**Methods:** We used 2012–2016 data from the Surveillance, Epidemiology, and End Results (SEER) registry-Medicare claims database to examine cost of care among Medicare beneficiaries with a confirmed cancer diagnosis based on International Classification of Diseases for Oncology, Third Edition histology codes reported in SEER. Beneficiaries contributed to the annual cost calculations (Years 1–5) using their observed time after diagnosis. Beneficiaries were continuously enrolled in fee-for-service Medicare Parts A/B and Part D during follow-up. Total, inpatient, outpatient, and pharmacy cancer-related service costs were calculated.

**Results:** From 2012 to 2016, we identified 597,778 Medicare beneficiaries with incident cancer diagnosis within 5 years (Stage I, II, III, and IV: 32.6%, 33.4%, 15.9%, and 18.0%, respectively). In Year 1, mean (standard deviation) total costs for Stage I diagnoses varied from \$7640 (\$17,378) (prostate) to \$94,636 (\$117,636) (pancreas). Total costs increased by stage and reached \$58,783 (\$92,344) (prostate) to \$156,982 (\$175,009) (stomach) for Stage IV diagnoses in Year 1. Costs in Year 1 were significantly higher for Stage IV diagnoses than for earlier stages across all cancer types. In Years 2–5, total costs were lower than in Year 1 but continued to increase by stage.

**Conclusions:** Beneficiaries diagnosed at later stages of cancer have higher costs of care (up to 7 times as much) than those diagnosed at earlier stages. Earlier cancer diagnosis may lead to more efficient treatment and decreased management cost.

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## Introduction

Cancer is a major contributor to disease burden worldwide and is the second leading cause of death in the United States (US)<sup>1</sup>, with a lifetime cancer risk in men and women of 40.1% and 38.7%, respectively<sup>2</sup>. Cost estimates for cancer care in 2020 ranged from \$174 billion to over \$1 trillion, depending on the inclusion of indirect costs<sup>3</sup>.



Stage at diagnosis is an important determinant of cancer mortality for all cancer types<sup>4</sup> and may also be a key determinant of cost. Commercially-insured patients diagnosed with advanced breast and lung cancer have higher monthly costs than those diagnosed earlier<sup>5</sup>. A similar pattern has been seen in younger Medicaid beneficiaries with breast cancer<sup>6</sup> and older commercially-insured patients with breast, colorectal, lung, or prostate cancer<sup>7</sup>. A study using linked Surveillance, Epidemiology, and End Results (SEER)-Medicare data found increased end-of-life costs for cancer survivors but did not report cost by stage<sup>8</sup>.

Early diagnosis and screening can reduce mortality, in large measure by identifying curable cancers at earlier stages<sup>9–11</sup>. Although decision analyses have been used to model the impact of screening on costs<sup>12</sup>, we found no comprehensive measurement of the cost of cancer by stage in the US. Among Medicare beneficiaries with confirmed cancer diagnoses, we estimated the annual cost of care in the 5 years following a cancer diagnosis for 17 invasive cancer types, by stage at diagnosis, with the goal of improving future estimates of the cost and benefit of early cancer detection.

## Methods

### Study design and data source

We employed a retrospective cross-sectional design using 2012–2016 data from the linked SEER registry-Medicare

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claims database to estimate annual cost of care following a cancer diagnosis, by stage at diagnosis.

SEER-Medicare data are a linked data set derived from the linkage between the National Cancer Institute's SEER program of cancer registries and Medicare Research Identifiable Files claims. SEER is a surveillance program that collects clinical, demographic, and cause of death information on all persons with a confirmed case of cancer in one of the 18 SEER regions<sup>13</sup>. The Medicare portion of the SEER-Medicare linkage includes all claims paid by Medicare for each covered beneficiary. These claims report the actual amount paid rather than charges. Medicare Parts A and B claims data include payments and dates of service for beneficiaries with fee-for-service (FFS) coverage for inpatient hospitalizations, skilled nursing facility care, outpatient hospital services, physician/supplier services, infusion/injectable drugs or their oral equivalent, durable medical equipment, hospice, and home health care. Medicare Part D claims data include payments and dates of service for oral prescription drugs.

### Patient population

We identified beneficiaries residing in a SEER region diagnosed with an invasive, primary cancer between 1 January 2007, and 31 December 2015. To be included in this study, the beneficiaries must have had an International Classification of Diseases for Oncology, Third Edition (ICD-O-3) SEER site recode for a primary cancer in one of the following sites: anus (includes anal canal and anorectum), bladder, breast (hormone receptor-positive [HR+] and hormone receptor-negative [HR-], separately), cervix, colon, esophagus, head and neck, kidney and renal pelvis, liver (includes intrahepatic bile duct), lung and bronchus, lymphoid, ovary, pancreas, prostate, stomach, and uterus. These represent a mix of the most common solid and hematologic malignancies and account for over 75% of new cancer cases<sup>14</sup>. Beneficiaries must also have been enrolled in Medicare Parts A/B FFS and Part D plans at one point within 5 years since diagnosis and within the study period (2012–2016). Beneficiaries with cancers *in situ* or with unknown cancer stage were excluded.

The start of observation was the date of cancer diagnosis, the beginning of the study period (1 January 2012), or the beginning of Medicare enrollment, whichever occurred latest. The first day of the diagnosis month was assigned as the date of diagnosis (i.e. index date). Beneficiaries were observed until one of the following endpoints was reached: disenrollment, diagnosis of a successive primary cancer, death, 5 years elapsed since diagnosis, or study end (31 December 2016), whichever occurred first. Follow-up time varied and no minimum length was required. Beneficiaries diagnosed with multiple primary cancers were eligible to be included in multiple cancer cohorts but were only included in 1 cohort at a time, with the diagnosis date for a successive primary cancer marked as the end of follow-up for the previous primary cancer. Beneficiaries in each cancer cohort were stratified according to the Derived American Joint Cancer Committee Stage Group, 6th edition, stage at diagnosis<sup>15</sup>.

### Study measures

Demographic characteristics were measured on the index date. The primary study outcome was the cost of cancer-related care. To isolate cancer-attributable costs, we identified claims that included a cancer diagnosis or treatment code, indicating the delivery of a cancer-related service. This included inpatient or outpatient medical claims from Medicare Parts A/B with an International Classification of Diseases, Ninth or Tenth Revision, Clinical Modification (ICD-9-CM or ICD-10-CM) diagnosis code for any cancer (ICD-9-CM: 140.x-239.x; ICD-10-CM: C00.x-D49.x) in any field. This broad approach assumed claims for cancer-related treatments such as chemotherapy and biological therapy were captured by a cancer diagnosis code. Cancer-related Medicare Part D outpatient pharmacy claims were defined as those with a National Drug Code (NDC) linked to the Generic Product Identifier (GPI) category for antineoplastic agents and adjunctive therapies (GPI 21) or with an NDC for a treatment approved by the US Food and Drug Administration for conditions caused by cancer or its treatment<sup>16</sup>.

Time after diagnosis was divided into 7 relevant periods: Months 1–6, Months 7–12, and each Year 1 through 5. Costs for each period, including inpatient, outpatient, and outpatient pharmacy services, were calculated as the combination of the Medicare payment amount to providers, deductible, copayment, and coinsurance during the relevant period. If the follow-up period for the beneficiary ended during one of the periods (e.g. due to death, or another primary cancer diagnosis) costs were annualized (or semi-annualized for the first and second 6-month periods). Beneficiaries who were diagnosed before our study period were included if the diagnosis occurred less than five years before the study period. For example, if a beneficiary were diagnosed on 1 September 2010, and died on 30 June 2015, their observation period would begin on 1 January 2012 (study start date). The beneficiary would contribute no time to Year 1 (because diagnosis was >1 year before study start); they would contribute 8 months of data to Year 2 (1 January 2012 to 31 August 2012); a full year of data to Year 3 (1 September 2012 to 31 August 2013) and to Year 4 (1 September 2013 to 31 August 2014); and 10 months of data to Year 5 (1 September 2014 to 30 June 2015 [date of death]). Costs were reported for each cancer type by stage, adjusted to 2016 US dollars.

### Statistical analysis

For each cancer cohort we performed descriptive analyses of cancer-related costs by stage and time period (cancer-related inpatient, outpatient, and pharmacy costs are reported in [Supplemental Tables](#)). Within each cohort we compared total cancer-related costs between each Stage I-III and Stage IV for each period and reported the cost difference. As a sensitivity analysis, we assessed the impact of annualization on costs by examining non-annualized versus annualized cancer-related costs in Year 1 for beneficiaries in the lung and prostate cancer cohorts. As another sensitivity analysis, we examined the

extent to which the two semi-annualized cost periods approximated annualized costs for each cancer. Analysis of possible effects on outcomes related to sex/gender or ethnic groups were beyond the study scope.

Means and standard deviations (SD) or 95% confidence intervals (95% CI) were reported for continuous measures, and frequencies and percentages for categorical measures. Statistical testing for comparing costs (each Stage I-III versus Stage IV) was conducted using analysis of variance (ANOVA) with Dunnett's method to adjust for multiple comparisons<sup>17</sup>. All tests were two-sided at a significance level of 0.05. Statistical analyses were conducted using SAS version 9.4.

## Results

### Patient identification and demographics by stage and cancer

We identified 2,122,639 Medicare beneficiaries diagnosed with a selected cancer between January 2007 and December 2015. Within this group, 1,777,856 beneficiaries had staging information; 597,778 met the continuous enrollment criteria and were included in the study (Table 1). The cancer-specific samples ranged from 2831 (anal cancer) to 124,058 (prostate cancer) beneficiaries. Eighty-two percent of cancers were diagnosed at Stages I-III, compared to 18.0% in Stage IV, although the distribution varied across cancer types, from 95.5% in Stages I-III in HR+ breast cancer to 53.2% in pancreatic cancer. The mean age at diagnosis varied by cancer and stage (Table 2).

### Total cancer-related costs by stage

For every cancer studied, beneficiaries diagnosed at Stage IV incurred the highest cost compared to those diagnosed at earlier stages for each of the first 5 years after diagnosis (Figures 1 and 2). In addition, beneficiaries diagnosed at Stage IV had the highest first 6-month costs compared to those diagnosed earlier, except for three cancers (esophagus,

pancreas, and stomach cancers) (Supplemental Tables). Costs were lowest among beneficiaries diagnosed at Stage I, and this was true for every year after diagnosis for all but one cancer: bladder cancer diagnosed at Stage I versus Stage III in Year 5 (Figure 1). This pattern was also evident during the first half of Year 1, as Stage I Months 1–6 costs were the lowest compared to other stages for all cancers (Supplemental Tables).

We estimated differences in cancer-related costs between beneficiaries diagnosed in Stage IV and those diagnosed earlier for all 7 time periods. For every period regardless of cancer type, beneficiaries diagnosed at Stage IV had statistically significantly higher costs than those diagnosed at Stage I (all  $p < .01$ ). Representative data for Months 1–6, Months 7–12, Year 1, and Year 5 are shown in Table 3; remaining data are shown in Supplemental Tables. In Months 1–6, the Stage IV to I difference in mean cancer-related costs ranged from \$21,839 (95% CI, \$16,735–\$26,942) in beneficiaries with pancreatic cancer to \$53,304 (\$50,192–\$56,415) in beneficiaries with bladder cancer. In Months 7–12, the Stage IV to I mean cancer-related cost difference ranged from \$14,627 (\$12,607–\$16,646) in beneficiaries with lymphoid cancer to \$38,574 (\$36,937–\$40,212) in beneficiaries with kidney cancer. In Year 1, the Stage IV to I mean cancer-related cost difference ranged from \$51,143 (\$47,016–\$55,270) in beneficiaries with prostate cancer to \$104,027 (\$99,018–\$109,036) in beneficiaries with kidney cancer, and in Year 5 from \$5894 (\$3939–\$7849) in beneficiaries with head and neck cancer to \$61,416 (\$59,498–\$63,335) in beneficiaries with HR+ breast cancer.

For nearly all cancers, there remained a statistically significant difference between costs among beneficiaries diagnosed at Stage IV and those diagnosed at Stage II or III (exceptions noted in Table 3). Cost differences were greatest between beneficiaries diagnosed at Stage IV and those diagnosed at Stage I, smaller for Stage IV versus Stage II, and smallest for Stage IV versus Stage III (with the exception of beneficiaries with pancreatic cancer in Year 1 and beneficiaries with bladder cancer in Year 5, where the difference between Stages IV and III was greater than the difference

**Table 1.** Patient counts by cancer type and stage at diagnosis.

Cancer Type	All Stages N	Stage I N (%)	Stage II N (%)	Stage III N (%)	Stage IV N (%)
All Cancers	597,778	195,055 (32.6)	199,744 (33.4)	95,323 (15.9)	107,656 (18.0)
Anus	2831	649 (22.9)	1114 (39.4)	852 (30.1)	216 (7.6)
Bladder	19,398	11,030 (56.9)	4818 (24.8)	1449 (7.5)	2101 (10.8)
Breast HR+	103,386	57,110 (55.2)	32,095 (31.0)	9556 (9.2)	4625 (4.5)
Breast HR–	16,779	6694 (39.9)	6609 (39.4)	2472 (14.7)	1004 (6.0)
Cervix	3389	1294 (38.2)	651 (19.2)	879 (25.9)	565 (16.7)
Colon and rectum	71,047	19,614 (27.6)	20,922 (29.4)	19,351 (27.2)	11,160 (15.7)
Esophagus	5667	1336 (23.6)	1451 (25.6)	1255 (22.1)	1625 (28.7)
Head and neck	23,756	6672 (28.1)	3584 (15.1)	3987 (16.8)	9513 (40.0)
Kidney	28,463	18,655 (65.5)	2134 (7.5)	4293 (15.1)	3381 (11.9)
Liver	11,671	5393 (46.2)	2392 (20.5)	2215 (19.0)	1671 (14.3)
Lung and bronchus	92,472	30,539 (33.0)	4883 (5.3)	22,692 (24.5)	34,358 (37.2)
Lymphoid	37,697	11,243 (29.8)	6041 (16.0)	6873 (18.2)	13,540 (35.9)
Ovary	9052	1697 (18.7)	810 (8.9)	3781 (41.8)	2764 (30.5)
Pancreas	15,446	1864 (12.1)	4929 (31.9)	1419 (9.2)	7234 (46.8)
Prostate	124,058	626 (0.5)	104,010 (83.8)	9726 (7.8)	9696 (7.8)
Stomach	8801	3702 (42.1)	1355 (15.4)	961 (10.9)	2783 (31.6)
Uterus	23,865	16,937 (71.0)	1946 (8.2)	3562 (14.9)	1420 (6.0)

**Table 2.** Patient characteristics by cancer type and stage on diagnosis date.

Cancer Type	All Stages	Stage I	Stage II	Stage III	Stage IV
<b>Anus</b>					
Age, mean (SD)	66.1 (12.0)	65.6 (12.4)	66.8 (11.8)	65.3 (12.0)	66.9 (11.5)
Female, n (%)	1793 (63.3)	391 (60.2)	692 (62.1)	585 (68.7)	125 (57.9)
<b>Bladder</b>					
Age, mean (SD)	74.8 (9.7)	74.9 (9.4)	75.7 (10.0)	73.3 (9.5)	73.2 (9.9)
Female, n (%)	5302 (27.3)	2722 (24.7)	1447 (30.0)	427 (29.5)	706 (33.6)
<b>Breast HR+</b>					
Age, mean (SD)	70.4 (9.9)	71.0 (8.9)	70.3 (10.4)	68.1 (11.9)	68.0 (12.4)
Female, n (%)	102,391 (99.0)	56,816 (99.5)	31,645 (98.6)	9371 (98.1)	4559 (98.6)
<b>Breast HR-</b>					
Age, mean (SD)	68.0 (11.0)	69.1 (9.2)	67.6 (11.5)	66.2 (12.9)	67.1 (12.5)
Female, n (%)	16,765 (99.9)	6692 (100.0)	6604 (99.9)	2469 (99.9)	1000 (99.6)
<b>Cervix</b>					
Age, mean (SD)	63.9 (13.7)	62.9 (13.8)	65.5 (12.7)	62.7 (14.2)	66.1 (13.5)
Female, n (%)	3389 (100.0)	1294 (100.0)	651 (100.0)	879 (100.0)	565 (100.0)
<b>Colon and rectum</b>					
Age, mean (SD)	72.4 (10.8)	73.0 (9.9)	73.8 (10.5)	71.4 (11.0)	70.8 (12.0)
Female, n (%)	37,111 (52.2)	10,206 (52.0)	11,250 (53.8)	10,073 (52.1)	5582 (50.0)
<b>Esophagus</b>					
Age, mean (SD)	70.7 (9.7)	72.0 (9.9)	70.4 (9.5)	69.8 (9.6)	70.6 (9.6)
Female, n (%)	1372 (24.2)	348 (26.0)	382 (26.3)	301 (24.0)	341 (21.0)
<b>Head and neck</b>					
Age, mean (SD)	68.5 (10.7)	70.6 (10.1)	69.8 (11.0)	68.0 (10.8)	66.8 (10.7)
Female, n (%)	7233 (30.4)	2326 (34.9)	1241 (34.6)	1207 (30.3)	2459 (25.8)
<b>Kidney</b>					
Age, mean (SD)	68.9 (10.4)	68.2 (10.5)	68.1 (10.1)	70.1 (9.5)	71.7 (10.6)
Female, n (%)	11,597 (40.7)	7911 (42.4)	820 (38.4)	1556 (36.2)	1310 (38.7)
<b>Liver</b>					
Age, mean (SD)	67.8 (10.1)	67.6 (10.3)	65.3 (9.4)	69.2 (9.8)	70.1 (10.1)
Female, n (%)	3649 (31.3)	1766 (32.7)	656 (27.4)	641 (28.9)	586 (35.1)
<b>Lung and bronchus</b>					
Age, mean (SD)	72.2 (9.1)	72.4 (8.7)	70.7 (8.8)	71.8 (9.5)	72.4 (9.3)
Female, n (%)	48,902 (52.9)	17,294 (56.6)	2441 (50.0)	11,737 (51.7)	17,430 (50.7)
<b>Lymphoid</b>					
Age, mean (SD)	70.8 (11.7)	71.7 (10.8)	70.1 (12.9)	70.4 (11.6)	70.6 (11.7)
Female, n (%)	18,777 (49.8)	5835 (51.9)	3082 (51.0)	3387 (49.3)	6473 (47.8)
<b>Ovary</b>					
Age, mean (SD)	69.2 (11.2)	67.0 (11.6)	68.7 (10.9)	68.7 (10.9)	71.4 (11.2)
Female, n (%)	9052 (100.0)	1697 (100.0)	810 (100.0)	3781 (100.0)	2764 (100.0)
<b>Pancreas</b>					
Age, mean (SD)	73.5 (9.5)	74.8 (10.6)	72.5 (9.1)	72.6 (9.4)	74.0 (9.4)
Female, n (%)	8243 (53.4)	1034 (55.5)	2647 (53.7)	786 (55.4)	3776 (52.2)
<b>Prostate</b>					
Age, mean (SD)	69.6 (7.2)	73.1 (7.6)	69.6 (7.0)	67.5 (6.0)	71.9 (9.4)
Female, n (%)	N/A	N/A	N/A	N/A	N/A
<b>Stomach</b>					
Age, mean (SD)	72.8 (10.4)	73.8 (10.3)	71.4 (10.2)	70.9 (10.6)	72.7 (10.4)
Female, n (%)	3319 (37.7)	1508 (40.7)	450 (33.2)	336 (35.0)	1025 (36.8)
<b>Uterus</b>					
Age, mean (SD)	68.6 (9.2)	68.3 (9.0)	69.6 (9.4)	68.8 (9.7)	70.4 (9.4)
Female, n (%)	23,865 (100.0)	16,937 (100.0)	1946 (100.0)	3562 (100.0)	1420 (100.0)

Abbreviations. N/A, not available; SD, standard deviation.

between Stages IV and II). Between-stage cost differences were larger in Year 1 than in Year 5 for almost every cancer.

### Cost by time since diagnosis

Costs were highest in the first year after diagnosis in every cancer, regardless of stage at diagnosis. Year 5 costs were lowest in almost every cancer, regardless of stage at diagnosis (Figure 1).

Costs in Months 1–6 were uniformly higher than in Months 7–12. The mean (SD) costs during Months 1–6 for beneficiaries diagnosed at Stage I ranged from \$5280 (\$10,198) (prostate) to \$56,807 (\$77,502) (lymphoid), while

for Months 7–12 it ranged from \$1871 (\$7508) (prostate) to \$25,446 (\$52,128) (pancreas). For beneficiaries diagnosed at Stage IV, costs in Months 1–6 ranged from \$32,050 (\$47,257) (prostate) to \$89,338 (\$103,577) (lymphoid) and in Months 7–12 ranged from \$21,502 (\$43,307) (prostate) to \$51,322 (\$75,203) (esophagus).

### Relative contribution of cost components by stage

Combining all cancer types at all stages, inpatient costs were 56.6% of total costs in the first 6 months after diagnosis and 58.6% of total costs in Year 1. This share declines to 37.2% in Year 5 (results not displayed). In most cases (13 of 17 cancers), inpatient costs in Year 1 were a higher proportion of

Cancer Type	Stage I		Stage II		Stage III		Stage IV	
	Mean	(SD)	Mean	(SD)	Mean	(SD)	Mean	(SD)
<b>Anus</b>								
Year 1	\$42,493	(94,142)	\$58,334	(69,024)	\$72,012	(89,891)	\$96,306	(86,096)
Year 2	\$6,321	(18,151)	\$16,351	(52,822)	\$23,456	(61,780)	\$50,455	(80,195)
Year 3	\$5,894	(19,016)	\$9,368	(26,948)	\$24,206	(107,200)	\$40,318	(61,871)
Year 4	\$4,904	(14,314)	\$9,430	(43,633)	\$12,272	(48,994)	\$46,389	(134,580)
Year 5	\$6,025	(27,590)	\$6,604	(30,887)	\$6,784	(22,789)	\$23,511	(46,651)
<b>Bladder</b>								
Year 1	\$32,151	(70,978)	\$74,227	(125,088)	\$86,885	(97,518)	\$134,909	(166,015)
Year 2	\$15,010	(43,106)	\$28,933	(75,456)	\$30,524	(63,524)	\$62,323	(104,162)
Year 3	\$10,959	(35,738)	\$18,605	(50,892)	\$27,341	(70,763)	\$46,934	(144,038)
Year 4	\$9,113	(30,933)	\$12,981	(42,661)	\$13,804	(58,541)	\$27,733	(65,457)
Year 5	\$8,074	(51,851)	\$10,687	(40,917)	\$7,526	(31,516)	\$17,059	(56,242)
<b>Breast HR+</b>								
Year 1	\$23,556	(26,984)	\$35,727	(41,392)	\$55,767	(49,630)	\$83,047	(91,225)
Year 2	\$4,694	(17,377)	\$8,246	(23,333)	\$17,006	(39,015)	\$62,122	(75,375)
Year 3	\$3,614	(17,853)	\$6,335	(28,241)	\$14,529	(38,466)	\$65,432	(77,016)
Year 4	\$3,564	(19,290)	\$6,867	(29,917)	\$17,611	(49,569)	\$73,378	(115,001)
Year 5	\$3,298	(15,453)	\$6,805	(31,474)	\$18,025	(82,839)	\$64,715	(74,905)
<b>Breast HR-</b>								
Year 1	\$39,408	(37,721)	\$56,095	(55,073)	\$74,141	(56,406)	\$110,163	(95,770)
Year 2	\$8,200	(23,498)	\$16,396	(49,304)	\$32,623	(57,160)	\$82,118	(87,130)
Year 3	\$6,002	(42,091)	\$11,004	(38,755)	\$25,798	(67,789)	\$76,691	(79,918)
Year 4	\$4,687	(22,758)	\$9,682	(35,583)	\$29,765	(186,386)	\$72,283	(87,050)
Year 5	\$4,655	(23,968)	\$8,281	(37,943)	\$16,951	(45,578)	\$59,572	(76,532)
<b>Cervix</b>								
Year 1	\$36,751	(68,126)	\$52,969	(56,235)	\$76,750	(87,691)	\$116,473	(137,059)
Year 2	\$7,990	(31,247)	\$17,315	(49,038)	\$31,550	(76,987)	\$55,740	(79,922)
Year 3	\$7,043	(32,801)	\$9,332	(35,329)	\$28,006	(76,686)	\$34,074	(62,126)
Year 4	\$6,088	(26,206)	\$7,263	(28,567)	\$16,203	(41,606)	\$33,824	(77,918)
Year 5	\$5,187	(23,025)	\$8,534	(31,174)	\$10,230	(30,335)	\$21,568	(50,677)
<b>Colon and rectum</b>								
Year 1	\$45,907	(101,961)	\$67,332	(138,345)	\$87,411	(135,097)	\$146,370	(166,367)
Year 2	\$6,974	(32,315)	\$11,639	(48,587)	\$20,744	(56,984)	\$76,579	(92,688)
Year 3	\$5,952	(27,962)	\$10,167	(39,577)	\$18,640	(48,092)	\$73,912	(103,439)
Year 4	\$5,760	(28,316)	\$8,437	(34,100)	\$17,375	(50,612)	\$61,875	(88,631)
Year 5	\$5,312	(29,642)	\$8,043	(33,773)	\$14,395	(51,748)	\$48,178	(71,172)
<b>Esophagus</b>								
Year 1	\$73,595	(111,977)	\$100,089	(111,244)	\$124,041	(158,227)	\$144,019	(158,949)
Year 2	\$22,297	(73,413)	\$37,910	(78,817)	\$53,896	(118,301)	\$92,868	(145,763)
Year 3	\$15,617	(55,601)	\$28,523	(87,105)	\$34,427	(83,191)	\$65,185	(99,566)
Year 4	\$10,476	(34,487)	\$17,992	(52,145)	\$37,076	(99,604)	\$49,404	(111,596)
Year 5	\$8,757	(40,632)	\$11,959	(35,029)	\$13,500	(32,215)	\$29,052	(49,015)
<b>Head and neck</b>								
Year 1	\$32,311	(80,388)	\$62,913	(262,147)	\$85,369	(133,630)	\$103,472	(143,331)
Year 2	\$12,374	(48,810)	\$18,594	(72,113)	\$23,454	(66,348)	\$32,473	(96,712)
Year 3	\$7,970	(32,443)	\$13,901	(50,280)	\$14,485	(54,111)	\$19,962	(74,347)
Year 4	\$6,512	(31,473)	\$8,742	(39,318)	\$10,939	(38,897)	\$13,668	(45,947)
Year 5	\$5,163	(22,970)	\$6,737	(30,324)	\$8,392	(39,946)	\$11,057	(51,134)

Figure 1. Total cancer-related healthcare costs by cancer type, stage at diagnosis, time period, and cost quintile<sup>a,b</sup>.

Kidney								
Year 1	\$30,139	(96,384)	\$42,172	(104,003)	\$50,296	(128,496)	\$134,166	(168,073)
Year 2	\$6,584	(27,036)	\$13,569	(50,378)	\$20,918	(59,204)	\$79,784	(108,784)
Year 3	\$6,523	(37,405)	\$12,848	(43,224)	\$19,729	(59,340)	\$67,521	(86,871)
Year 4	\$5,561	(26,861)	\$12,983	(48,690)	\$17,823	(47,586)	\$62,662	(94,314)
Year 5	\$5,202	(25,806)	\$11,286	(45,530)	\$14,899	(43,781)	\$49,846	(68,429)
Liver								
Year 1	\$73,816	(123,787)	\$79,630	(122,356)	\$123,003	(143,956)	\$155,515	(169,517)
Year 2	\$45,320	(113,132)	\$50,064	(96,965)	\$70,240	(149,450)	\$75,347	(92,550)
Year 3	\$33,117	(90,267)	\$40,324	(94,170)	\$50,573	(96,075)	\$65,133	(77,279)
Year 4	\$24,053	(62,104)	\$28,272	(63,310)	\$47,094	(85,608)	\$67,138	(133,565)
Year 5	\$19,835	(61,850)	\$20,696	(52,226)	\$37,157	(62,307)	\$54,590	(122,354)
Lung and bronchus								
Year 1	\$54,606	(116,903)	\$85,118	(125,923)	\$110,815	(144,585)	\$148,426	(162,632)
Year 2	\$19,759	(60,444)	\$33,188	(71,159)	\$53,520	(93,565)	\$81,584	(112,886)
Year 3	\$16,039	(50,659)	\$28,785	(74,887)	\$41,553	(104,707)	\$68,446	(104,565)
Year 4	\$14,120	(53,306)	\$21,241	(55,876)	\$34,052	(68,844)	\$57,445	(103,267)
Year 5	\$12,027	(43,897)	\$20,497	(61,217)	\$27,585	(79,764)	\$46,219	(83,845)
Lymphoid								
Year 1	\$81,796	(138,922)	\$109,177	(142,123)	\$119,439	(153,988)	\$140,565	(195,866)
Year 2	\$20,997	(67,621)	\$33,434	(87,075)	\$40,655	(103,767)	\$39,912	(84,718)
Year 3	\$15,740	(53,248)	\$23,462	(72,436)	\$28,536	(64,929)	\$29,945	(93,887)
Year 4	\$12,945	(40,883)	\$19,471	(79,251)	\$22,333	(63,510)	\$25,501	(128,486)
Year 5	\$12,684	(42,948)	\$15,203	(48,326)	\$20,157	(57,059)	\$21,128	(59,366)
Ovary								
Year 1	\$46,992	(72,700)	\$66,326	(105,927)	\$95,256	(128,841)	\$122,529	(143,390)
Year 2	\$8,384	(36,160)	\$16,602	(40,345)	\$43,027	(68,721)	\$55,906	(76,446)
Year 3	\$7,311	(26,048)	\$20,059	(49,417)	\$45,831	(73,621)	\$59,121	(87,657)
Year 4	\$7,978	(39,352)	\$20,318	(54,564)	\$45,896	(71,940)	\$53,413	(81,343)
Year 5	\$6,875	(35,639)	\$18,235	(66,640)	\$42,306	(78,540)	\$54,233	(77,999)
Pancreas								
Year 1	\$94,636	(117,636)	\$129,640	(170,910)	\$121,089	(137,740)	\$149,455	(182,814)
Year 2	\$32,365	(62,877)	\$55,166	(84,432)	\$74,392	(142,017)	\$92,832	(190,264)
Year 3	\$24,069	(63,988)	\$45,372	(87,738)	\$72,378	(94,561)	\$80,589	(107,321)
Year 4	\$13,479	(34,092)	\$38,719	(76,087)	\$65,601	(103,467)	\$65,819	(96,787)
Year 5	\$11,242	(43,296)	\$29,078	(68,676)	\$46,366	(62,072)	\$64,252	(87,013)
Prostate								
Year 1	\$7,640	(17,378)	\$21,988	(35,907)	\$25,296	(27,817)	\$58,783	(92,344)
Year 2	\$2,361	(8,767)	\$5,591	(21,792)	\$7,063	(20,282)	\$46,559	(79,839)
Year 3	\$2,809	(11,941)	\$4,401	(19,509)	\$6,176	(24,029)	\$47,108	(81,495)
Year 4	\$1,075	(3,118)	\$4,169	(21,504)	\$6,388	(25,272)	\$45,159	(96,642)
Year 5	\$2,536	(10,111)	\$3,899	(21,494)	\$6,245	(26,337)	\$36,276	(75,146)
Stomach								
Year 1	\$81,661	(125,873)	\$101,824	(107,679)	\$136,484	(168,505)	\$156,982	(175,009)
Year 2	\$18,352	(53,441)	\$38,227	(84,321)	\$41,994	(69,322)	\$88,111	(140,747)
Year 3	\$11,589	(38,544)	\$26,365	(68,767)	\$40,737	(93,738)	\$64,751	(95,699)
Year 4	\$8,856	(35,367)	\$18,954	(68,833)	\$27,996	(84,264)	\$50,693	(87,225)
Year 5	\$5,886	(33,233)	\$13,213	(37,706)	\$20,940	(71,058)	\$33,560	(73,621)

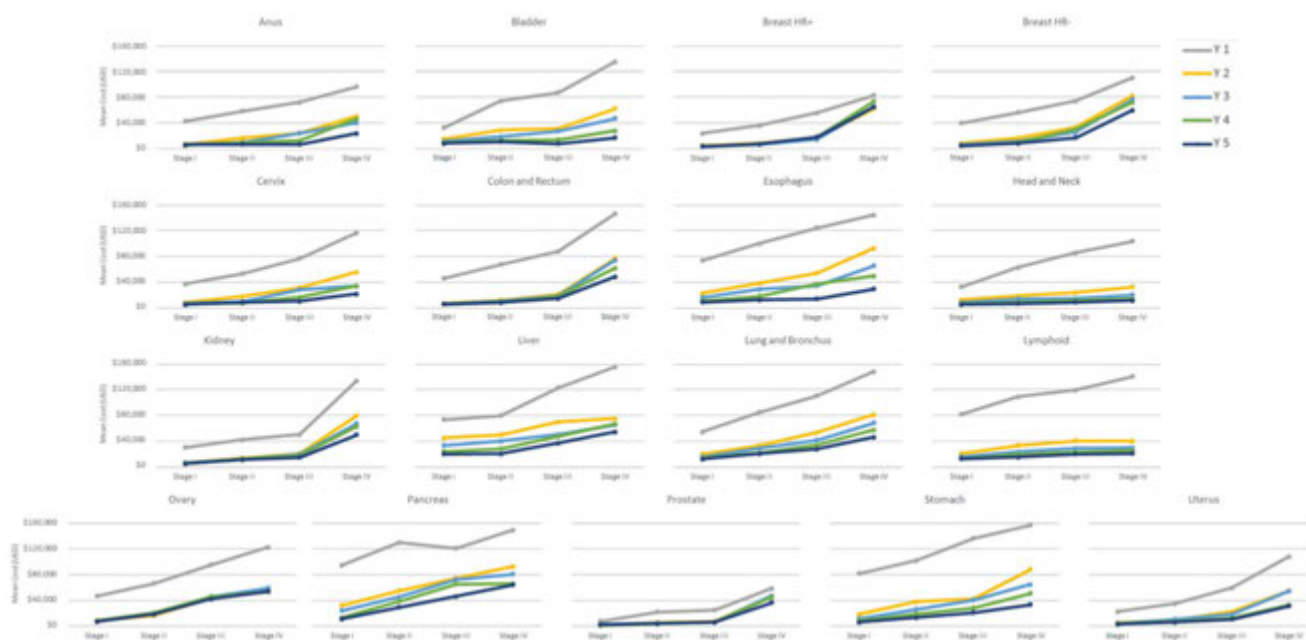
Uterus								
Year 1	\$22,687	(39,338)	\$34,737	(40,548)	\$59,583	(109,722)	\$108,196	(129,370)
Year 2	\$5,202	(26,246)	\$9,260	(34,056)	\$22,422	(61,093)	\$54,903	(104,569)
Year 3	\$4,601	(26,258)	\$10,472	(53,637)	\$18,491	(68,151)	\$54,332	(120,474)
Year 4	\$4,387	(60,275)	\$7,310	(29,193)	\$12,081	(36,732)	\$32,796	(73,628)
Year 5	\$3,057	(19,119)	\$5,796	(22,635)	\$10,807	(36,856)	\$31,200	(89,781)

<sup>a</sup> Due to variable follow-up length, sample sizes vary for each point estimate.

<sup>b</sup> All costs adjusted to 2016 USD.

Shading illustrates costs by quintile within each cancer:

4 most expensive time-stage periods
4 least expensive time-stage periods



**Figure 2.** Total cancer-related healthcare costs by cancer type, stage at diagnosis, and time period.

total costs for beneficiaries diagnosed in Stage IV compared to those diagnosed at Stage I (Figure 3 and Supplemental Tables). In Years 2–5, inpatient costs across cancer types and stages were substantially lower than in Year 1 (Figure 3 and Supplemental Tables).

### Relative contribution of cost components by stage

Results of the sensitivity analyses are reported in Supplemental Tables. Annualized costs were higher than non-annualized costs because of loss to follow-up (presumably death). This difference was larger for the lung and bronchus cohort (Stage I: \$54,606 versus \$33,953; Stage II: \$85,118 versus \$49,650; Stage III: \$110,815 versus \$49,142; Stage IV: \$148,426 versus \$50,398) than for the prostate cohort (Stage I: \$7640 versus \$6258; Stage II: \$21,988 versus \$18,241; Stage III: \$25,296 versus \$21,514; Stage IV: \$58,783 versus \$33,515), likely a result of higher mortality in these groups. In the comparison for annualized versus combined semi-annualized costs, differences between annualized and

semi-annualized costs are small across all cancers in Stage I, with inconsistent bias (range –\$2974 to \$13,861), but annualized costs are consistently higher across cancers in Stage IV (range \$3983–\$30,698), supporting that loss of follow-up associated with higher mortality leads to bias when annualizing costs.

### Discussion

In this study of more than half a million Medicare beneficiaries with 17 different cancer types, we found that diagnosis at a later stage was consistently more expensive than earlier-stage diagnosis. Increased cancer-related cost associated with later-stage diagnosis can be seen as early as 6 months from diagnosis and persists for at least 5 years after diagnosis. Across the cancer cohorts, first-year costs for beneficiaries with Stage IV cancer were 1.6 to 7.7 times that of beneficiaries with Stage I cancer. While the difference in cancer-related costs was greatest between beneficiaries diagnosed in Stage IV and Stage I, it remained statistically significantly higher for nearly all cancers

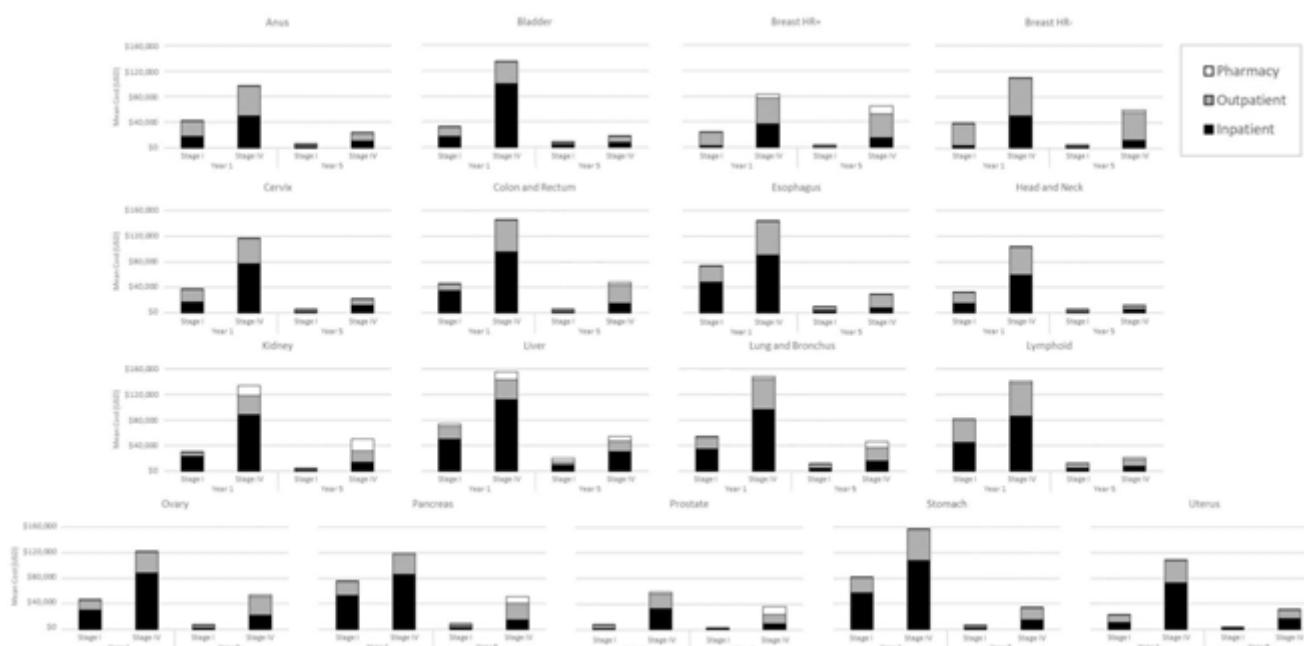


**Table 3.** Differential total cancer-related healthcare costs by cancer type, stage IV vs other stages.

Time Period	Cancer Type	Stage IV – Stage I Difference (95% CI)	Stage IV – Stage II Difference (95% CI)	Stage IV – Stage III Difference (95% CI)	
Months 1–6 <sup>a</sup>	Anus	\$25,862 (16,381–35,343)	\$15,478 (6622–24,334)	\$7607 (–1493 to 16,707)	
	Bladder	\$53,304 (50,192–56,415)	\$27,700 (24,297–31,103)	\$17,963 (13,351–22,575)	
	Breast HR+	\$27,126 (26,133–28,119)	\$21,141 (20,115–22,166)	\$13,425 (12,219–14,631)	
	Breast HR–	\$29,814 (26,944–32,684)	\$22,643 (19,771–25,515)	\$16,566 (13,285–19,848)	
	Cervix	\$37,064 (29,827–44,302)	\$23,420 (15,020–31,820)	\$14,178 (6574–21,781)	
	Colon and rectum	\$45,837 (43,551–48,123)	\$31,417 (29,180–33,654)	\$19,397 (17,125–21,670)	
	Esophagus	\$26,685 (19,726–33,645)	\$4491 (–2175 to 11,157)	–\$5885 (–12,720 to 951)	
	Head and neck	\$47,838 (44,104–51,572)	\$26,279 (21,749–30,809)	\$9501 (5163–13,839)	
	Kidney	\$46,792 (43,995–49,589)	\$39,562 (34,841–44,282)	\$35,279 (31,646–38,912)	
	Liver	\$37,582 (33,155–42,008)	\$36,350 (31,028–41,672)	\$13,881 (8856–18,906)	
	Lung and bronchus	\$39,802 (38,389–41,215)	\$21,404 (18,499–24,309)	\$15,233 (13,772–16,694)	
	Lymphoid	\$32,530 (29,373–35,688)	\$15,134 (11,298–18,970)	\$12,065 (8464–15,666)	
	Ovary	\$33,837 (27,826–39,849)	\$21,366 (13,561–29,172)	\$7426 (2943–11,910)	
	Pancreas	\$21,839 (16,735–26,942)	–\$1068 (–4648 to 2511)	\$11,875 (6366–17,385)	
	Prostate	\$26,771 (24,231–29,311)	\$13,313 (12,512–14,114)	\$12,290 (11,102–13,478)	
	Stomach	\$27,226 (22,272–32,180)	\$11,663 (4798–18,529)	–\$4127 (–11,816 to 3562)	
	Uterus	\$42,625 (40,090–45,160)	\$32,716 (29,283–36,149)	\$22,149 (19,158–25,141)	
	Months 7–12 <sup>b</sup>	Anus	\$24,147 (17,379–30,915)	\$17,277 (10,905–23,650)	\$13,408 (6864–19,951)
		Bladder	\$31,726 (28,228–35,224)	\$18,167 (14,372–21,961)	\$14,937 (9985–19,889)
		Breast HR+	\$24,520 (23,706–25,335)	\$18,524 (17,686–19,362)	\$6754 (5787–7722)
Breast HR–		\$33,984 (30,500–37,468)	\$24,821 (21,334–28,307)	\$13,874 (9989–17,758)	
Cervix		\$19,596 (14,360–24,831)	\$17,734 (11,840–23,628)	\$10,738 (5200–16,277)	
Colon and rectum		\$37,930 (36,742–39,118)	\$34,439 (33,269–35,609)	\$24,958 (23,771–26,145)	
Esophagus		\$34,840 (28,185–41,496)	\$25,531 (19,215–31,848)	\$14,739 (8212–21,265)	
Head and neck		\$18,968 (13,066–24,871)	\$14,369 (7158–21,579)	\$9300 (2281–16,318)	
Kidney		\$38,574 (36,937–40,212)	\$37,262 (34,800–39,724)	\$32,740 (30,760–34,719)	
Liver		\$21,274 (16,080–26,468)	\$15,104 (9392–20,815)	\$1704 (–4181 to 7589)	
Lung and bronchus		\$33,495 (32,397–34,594)	\$24,342 (22,274–26,410)	\$12,629 (11,419–13,839)	
Lymphoid		\$14,627 (12,607–16,646)	\$8282 (5778–10,787)	\$3389 (1032–5746)	
Ovary		\$24,009 (20,763–27,255)	\$18,810 (14,644–22,976)	\$9065 (6474–11,655)	
Pancreas		\$20,334 (16,029–24,639)	\$10,028 (6884–13,172)	\$3,522 (–1058 to 8102)	
Prostate		\$19,632 (17,782–21,482)	\$15,788 (15,215–16,362)	\$13,637 (12,816–14,458)	
Stomach		\$33,064 (29,151–36,978)	\$17,070 (12,134–22,007)	\$13,965 (8332–19,598)	
Uterus		\$24,738 (23,206–26,269)	\$20,381 (18,451–22,311)	\$9902 (8164–11,641)	
Year 1 <sup>c</sup>		Anus	\$53,813 (37,844–69,782)	\$37,972 (23,098–52,846)	\$24,294 (9026–39,563)
		Bladder	\$102,758 (97,091–108,424)	\$60,682 (54,487–66,876)	\$48,024 (39,668–56,381)
		Breast HR+	\$59,491 (57,898–61,085)	\$47,321 (45,674–48,967)	\$27,280 (25,348–29,212)
	Breast HR–	\$70,755 (66,154–75,355)	\$54,068 (49,469–58,666)	\$36,022 (30,791–41,252)	
	Cervix	\$79,722 (67,557–91,888)	\$63,504 (49,465–77,542)	\$39,723 (26,878–52,569)	
	Colon and rectum	\$100,463 (96,445–104,481)	\$79,038 (75,103–82,973)	\$58,959 (54,968–62,950)	
	Esophagus	\$70,424 (58,546–82,302)	\$43,929 (32,565–55,294)	\$19,977 (8310–31,645)	
	Head and neck	\$71,161 (64,717–77,605)	\$40,559 (32,739–48,379)	\$18,104 (10,606–25,601)	
	Kidney	\$104,027 (99,018–109,036)	\$91,994 (83,662–100,326)	\$83,870 (77,410–90,329)	
	Liver	\$81,699 (73,559–89,838)	\$75,885 (66,190–85,580)	\$32,511 (23,233–41,789)	
	Lung and bronchus	\$93,820 (91,196–96,444)	\$63,308 (57,975–68,642)	\$37,611 (34,884–40,338)	
	Lymphoid	\$58,769 (53,242–64,296)	\$31,388 (24,638–38,137)	\$21,126 (14,779–27,472)	
	Ovary	\$75,537 (64,981–86,093)	\$56,203 (42,495–69,911)	\$27,273 (19,333–35,212)	
	Pancreas	\$54,818 (45,211–64,425)	\$19,814 (13,110–26,519)	\$28,365 (18,058–38,673)	
	Prostate	\$51,143 (47,016–55,270)	\$36,795 (35,564–38,026)	\$33,487 (31,678–35,297)	
	Stomach	\$75,322 (66,792–83,851)	\$55,158 (43,559–66,757)	\$20,498 (7463–33,533)	
	Uterus	\$85,509 (81,157–89,860)	\$73,459 (67,650–79,267)	\$48,613 (43,529–53,697)	
	Year 5 <sup>d</sup>	Anus	\$17,486 (7960–27,012)	\$16,907 (7589–26,224)	\$16,727 (7209–26,246)
		Bladder	\$8986 (2578–15,394)	\$6372 (–444 to 13,188)	\$9533 (1606–17,460)
		Breast HR+	\$61,416 (59,498–63,335)	\$57,910 (55,957–59,862)	\$46,690 (44,568–48,811)
Breast HR–		\$54,917 (49,939–59,896)	\$51,291 (46,291–56,291)	\$42,621 (37,324–47,918)	
Cervix		\$16,381 (10,157–22,604)	\$13,034 (6354–19,713)	\$11,338 (4663–18,012)	
Colon and rectum		\$42,866 (40,703–45,028)	\$40,134 (37,969–42,300)	\$33,782 (31,584–35,981)	
Esophagus		\$20,295 (11,259–29,330)	\$17,093 (7857–26,328)	\$15,552 (5771–25,333)	
Head and neck		\$5894 (3939–7849)	\$4320 (1852–6787)	\$2665 (224–5105)	
Kidney		\$44,645 (41,384–47,905)	\$38,560 (34,779–42,341)	\$34,947 (31,406–38,488)	
Liver		\$34,755 (16,658–52,852)	\$33,894 (15,386–52,402)	\$17,433 (–2334 to 37,200)	
Lung and bronchus		\$34,192 (31,282–37,102)	\$25,722 (21,521–29,922)	\$18,633 (15,337–21,929)	
Lymphoid		\$8,444 (6437–10,450)	\$5925 (3480–8369)	\$971 (–1443 to 3386)	
Ovary		\$47,359 (40,252–54,465)	\$35,998 (26,995–45,001)	\$11,927 (5228–18,627)	
Pancreas		\$53,010 (41,064–64,956)	\$35,174 (23,952–46,396)	\$17,885 (–2483 to 38,253)	
Prostate		\$33,740 (28,392–39,088)	\$32,377 (31,396–33,359)	\$30,031 (28,858–31,204)	
Stomach		\$27,674 (20,158–35,189)	\$20,347 (11,999–28,695)	\$12,620 (3411–21,828)	
Uterus		\$28,143 (24,802–31,484)	\$25,404 (21,713–29,094)	\$20,393 (16,838–23,947)	

Abbreviation. CI, confidence interval.

<sup>a</sup>All *p* values < .05 in Months 1–6, except Stage III anus (*p* = .196), Stage II esophagus (*p* = .43), Stage III esophagus (*p* = .23), Stage II pancreas (*p* = .91), and Stage III stomach (*p* = .63).<sup>b</sup>All *p* values < .05 in Months 7–12, except Stage III liver (*p* = .85), and Stage III pancreas (*p* = .32).<sup>c</sup>All *p* values < .01 in Year 1.<sup>d</sup>All *p* values < .05 in Year 5, except Stage II bladder (*p* = .13), Stage III head and neck (*p* = .09), Stage III liver (*p* = .14), Stage III lymphoid (*p* = .79), and Stage III pancreas (*p* = .20).



**Figure 3.** Contributors to costs by cancer types (Stage I vs. Stage IV, Years 1 and 5).

when comparing beneficiaries diagnosed in Stage IV to those diagnosed at Stages II and III (Table 3).

These findings may have important health policy implications. Detecting cancer at earlier stages encompasses two distinct ideas: early diagnosis (the earlier identification of symptomatic cancers) and screening (the identification of cancers before they become symptomatic). This study provides new evidence consistent with a large potential economic benefit of early diagnosis of cancer in the Medicare population. Our study demonstrates that a cancer diagnosis at an earlier stage is associated with significantly lower cancer-related costs and that, in most cases, this is true whether that earlier stage is Stage I, II, or III (Table 3). We also found that cost is highest in the immediate post-diagnosis period, either Months 1–6 or Year 1, and this is true regardless of cancer type or stage at diagnosis. Finally, for nearly all cancers, inpatient costs accounted for most observed costs in the first year after diagnosis, and this proportion was typically higher among beneficiaries diagnosed at later stages. Furthermore, the observed annual cost differential extends at least 5 years beyond diagnosis. Our findings may also be useful in estimating the impact on cancer care costs of the pandemic-induced reduction in cancer detection and screening<sup>18</sup>.

The results of this study are consistent with previous economic work on the cost of cancer by stage. In a 2020 SEER-Medicare study of annualized cancer-attributable costs for several cancers between 2013 and 2017, the authors found that costs generally increased by stage (local, regional, or distant) within each phase of care after diagnosis<sup>8</sup>. Similar to our analysis, the study showed that cost differences between higher and lower stages were greatest in the first year (initial phase) and substantially lower in subsequent years (continuing phase). Our estimates were higher than in Mariotto et al.<sup>8</sup>, likely because that study separated out end-of-life estimates, which we incorporated into our main estimates.

In consideration of the study findings, a few limitations are worth noting. First, we calculated costs using an annualization method, which extrapolated costs for all beneficiaries who lacked a full period of follow-up. Annualizing when most missing data result from death (as is in Medicare) overestimates costs. We address this limitation in two ways, both of which produce results consistent with the main findings. First, we reported first-year costs *via* two 6-month periods, with costs semi-annualized. Fewer people die or disenroll in the first 6 months after diagnosis, making these estimates less of an overestimate. Second, we compared the total of the two semi-annual periods to the first-year cost. We found the use of the 6-month estimates versus 1-year estimates does not materially change our findings.

Second, our cost comparisons between stages were not adjusted for differences in beneficiary characteristics. We chose to compare unadjusted costs for this study to focus on actual differences in costs. Some beneficiary characteristics may affect cancer stage at diagnosis through a direct mechanism; controlling for these differences would produce biased estimates. For example, in our study, a larger proportion of Black beneficiaries were diagnosed at later stages than White beneficiaries for most cancers (data not shown). Adjusting for this diagnosis stage difference would hide important cost differences.

Third, each measurement period comprised a different sample, which limits the comparability of beneficiaries over time. We used this cross-sectional approach to leverage as much data as possible and to capture costs for all beneficiaries who contribute data. Had we followed a single cohort over the full 5-year period, we would have had substantially smaller samples due to loss to follow-up and more importantly, we would have selected a healthier group of surviving beneficiaries, likely leading to an underestimation of costs at earlier time periods.

Finally, our cancer-related cost estimates were based on cost data from 2012 to 2016, which we would expect to have increased over time due to increased costs for newer, more current treatments such as immunotherapies or targeted therapies. Nonetheless, we believe that the observed cost patterns by stage would persist even with the introduction of new cancer treatments and their associated costs during a more recent time period.

## Conclusion

This large study of the cost of cancer-related care in the Medicare population showed beneficiaries whose cancers are diagnosed at later stages incur much higher cancer-related healthcare costs than those diagnosed at earlier stages. This pattern persists across different cancers and for at least 5 years after diagnosis. Early cancer detection may lead to more efficient treatment, lower disease management costs, and better health outcomes.

## Transparency

### Declaration of funding

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### Declaration of financial/other relationships

Dr. Reddy is an employee of PHAR, LLC, which was paid by GRAIL, LLC to conduct this research. Dr. Broder is an employee of PHAR, LLC, which was paid by GRAIL, LLC to conduct this research. Dr. Chang is an employee of PHAR, LLC, which was paid by GRAIL, LLC to conduct this research. Mr. Paydar is an employee of PHAR, LLC, which was paid by GRAIL, LLC to conduct this research. Dr. Chung is an employee of GRAIL, LLC with equity in the company. Dr. Kansal is an employee of GRAIL, LLC with equity in the company. Peer reviewers on this manuscript have no relevant financial or other relationships to disclose.

### Author contributions

All authors fulfilled the ICMJE authorship requirements.

### Data availability statement

Data are available from National Cancer Institute, Healthcare Delivery Research Program.

### Previous presentations

Figures and tables in this manuscript have been included in posters presented at the 2021 Hematology/Oncology Pharmacy Association (HOPA) virtual conference.

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