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Health system costs for cancer medications and radiation treatment in the four most common cancers.

Journal:	*CMAJ Open*
Manuscript ID	CMAJOpen-2019-0114
Manuscript Type:	Cohort (retrospective)
Date Submitted by the Author:	25-Jul-2019
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More Detailed Keywords:	
Keywords:	Health economics, Health services research, Oncology
Abstract:	Background: Previous costing and resource estimates for cancer have not been robust due to lack of comprehensive data on cancer-related medication and radiation treatment. We calculated mean overall costs per patient per cancer medication and radiation, as well as, by disease and stage in the first year (365 days) after diagnosis for the most prevalent cancers. Methods: A retrospective cohort study design was used to identify population health system resources and costs ($CAN) for patients diagnosed with breast, colorectal, lung and prostate cancers between January 1, 2010 and December 31, 2015. The overall average cost per patient in 365 days after diagnosis was determined for cancer-related medications and radiation treatment using two novel costing algorithms. The cost by disease, disease subtype and stage were determined. Results: There were 168,316 Ontarians diagnosed with breast

	(N=50,141), colorectal (CRC, N=38,108), lung (N=34,809) and prostate (N=45,258) cancer. Cancer-related medications overall mean costs were $8,167 (95% CI: 8,023-8,311); $6,568 (6,446-6,691); $2,900 (2,816-2,984); and $1,211 (1,175-1,247) for breast, CRC, lung and prostate, respectively. Mean overall radiation treatment costs were $18,529 (18,415-18,643); $15,177 (14,899-15,456); $10,818 (10,669-10,966); and $16,887 (16,648-17,125). Interpretation: In general, Stage III and IV were the most expensive disease stages across all four cancers for cancer-related medications and radiation treatment. Our work updates previous costing estimates to help understand resources and costs critical to health system planning in a single payer system.

STROBE Statement—Checklist of items that should be included in reports of ***cohort studies***

	Item No	Recommendation	Location in study
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	Page 1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	Page 4
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	Page 6
Objectives	3	State specific objectives, including any prespecified hypotheses	Page 6
Methods			
Study design	4	Present key elements of study design early in the paper	Pages 7-8
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	Page 7
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	N/A
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	N/A
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	Pages 7-9
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	Pages 7-8
Bias	9	Describe any efforts to address potential sources of bias	N/A
Study size	10	Explain how the study size was arrived at	N/A
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	N/A
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	N/A
		(*b*) Describe any methods used to examine subgroups and interactions	N/A
		(*c*) Explain how missing data were addressed	N/A
		(*d*) If applicable, explain how loss to follow-up was addressed	N/A
		(*e*) Describe any sensitivity analyses	N/A
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	Pages 10-11
		(b) Give reasons for non-participation at each stage	N/A
		(c) Consider use of a flow diagram	N/A
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic,	Pages 10-11

		clinical, social) and information on exposures and potential confounders	
		(b) Indicate number of participants with missing data for each variable of interest	N/A
		(c) Summarise follow-up time (eg, average and total amount)	Pages 10-11
Outcome data	15*	Report numbers of outcome events or summary measures over time	Pages 10-11
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Pages 10-11
		(*b*) Report category boundaries when continuous variables were categorized	N/A
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N/A
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	N/A
Discussion			
Key results	18	Summarise key results with reference to study objectives	Page 12
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	Pages 13-14
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	Pages 12-14
Generalisability	21	Discuss the generalisability (external validity) of the study results	Pages 14-15
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	Page 2

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.

Health system costs for cancer medications and radiation treatment in the four most common cancers

Running Title: Cost of drugs and radiation in the four most common cancers

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Funding

This project was funded by a Health Services Network grant from the Ontario Institute for Cancer Research.

Contributor's Statement

As authors of the study, Nicole Mittmann, Ning Liu, Stephanie Cheng, Soo Jin Seung and Farah Saxena contributed to the design of the study, interpretation of the data, the writing and editing of the manuscript, as well as, the selection of journal publication. Nicole Look Hong, Craig Earle, Matthew Cheung, Natasha Leighl, Natalie Coburn, Carlo DeAngelis and William Evans contributed to the interpretation of the data, the writing and editing of the manuscript.

Acknowledgement

This study was supported by ICES, which is funded by an annual grant from the Ontario Ministry of Health and Long-Term Care (MOHLTC). The opinions, results and conclusions reported in this paper are those of the authors and are independent from the funding sources. No endorsement by ICES or the Ontario MOHLTC is intended or should be inferred.

Parts of this material are based on data and/or information compiled and provided by the Canadian Institute for Health Information (CIHI). However, the analyses, conclusions, opinions and statements expressed in the material are those of the author(s), and not necessarily those of CIHI.

Parts of this material are based on data and information provided by Cancer Care Ontario (CCO). The opinions, results, views and conclusions reported in this paper are those of the authors and do not necessarily reflect those of CCO. No endorsement by CCO is intended or should be inferred.

We thank IMS Brogen Inc. for use of their Drug Information database.

Conflict of Interest:

There are no conflicts to declare. NGC receives salary support from Cancer Care Ontario, as well as the Sherif and MaryLou Hanna Chair in Surgical Oncology.

ABSTRACT

Background: Previous costing and resource estimates for cancer have not been robust due to lack of comprehensive data on cancer-related medication and radiation treatment. We calculated mean overall costs per patient per cancer medication and radiation, as well as, by disease and stage in the first year (365 days) after diagnosis for the most prevalent cancers.

Methods: A retrospective cohort study design was used to identify population health system resources and costs ($CAN) for patients diagnosed with breast, colorectal, lung and prostate cancers between January 1, 2010 and December 31, 2015. The overall average cost per patient in 365 days after diagnosis was determined for cancer-related medications and radiation treatment using two novel costing algorithms. The cost by disease, disease subtype and stage were determined.

Results: There were 168,316 Ontarians diagnosed with breast (N=50,141), colorectal (CRC, N=38,108), lung (N=34,809) and prostate (N=45,258) cancer. Cancer-related medications overall mean costs were $8,167 (95% CI: 8,023-8,311); $6,568 (6,446-6,691); $2,900 (2,816-2,984); and $1,211 (1,175-1,247) for breast, CRC, lung and prostate, respectively. Mean overall radiation treatment costs were $18,529 (18,415-18,643); $15,177 (14,899-15,456); $10,818 (10,669-10,966); and $16,887 (16,648-17,125).

Interpretation: In general, Stage III and IV were the most expensive disease stages across all four cancers for cancer-related medications and radiation treatment. Our work updates previous costing estimates to help understand resources and costs critical to health system planning in a single payer system.

INTRODUCTION

Cancer is clinically burdensome to patients and becoming increasingly burdensome economically. Treatment is associated with substantial financial toxicity (1). When planning system health services, it is important to understand both the resources and costs associated with cancer treatment. Although many publications outlining treatment costs exist, namely through disease cohort studies and modelling, the majority are unable to capture direct costs with a population level approach.

In this study, we used previously-constructed costing algorithms to examine cancer-related medication and radiation resources and costing across the four most common cancers, namely breast, colorectal (CRC), lung, and prostate in the province of Ontario, Canada. The overarching objective was to examine the costs for radiation treatment and cancer-related medications in the first year after diagnosis for breast, lung, CRC, and prostate cancer patients. Secondary objectives were to examine the costs for radiation treatment and cancer-related medications between patients of different stage at the time diagnosis, within the same type of cancer and by cancer subtype; and to examine the costs for radiation treatment and cancer-related medications among patients diagnosed with different type of cancer, across different stages and by cancer subtype.

METHODS

Clinical and health administrative databases were linked using unique encoded identifiers and analyzed at ICES. ICES is an independent, non-profit research institute whose legal status under Ontario's health information privacy law allows it to collect and analyze health care and demographic data, without consent, for health system evaluation and improvement. These administrative databases allow researchers to identify and quantify the health system resources, after which, they can be valued with unit costs. Wodchis and colleagues developed a costing algorithm based on these database that allows the calculation of person-level health care costs (referred hereinafter as the Person-Level Case Costing Methodology or PLCCM) (2). In this algorithm, the cost of services that are episodic in nature are estimated using a cost per weighted case (CPWC) methodology, whereas the cost of services that are reported by visits or claims can be more directly obtained. A number of studies have used the PLCCM to estimate the costs of different diseases across the continuum of care (3-7). In order to enhance the PLCCM with comprehensive costing for cancer treatments, we recently created two additional oncology-specific costing methodologies: one for cancer-related medications (Cancer Medication Costing Algorithm, CMCA) and one for radiation treatment (Cancer Radiation Costing Algorithm, CRCA). The algorithms and their validation, are described elsewhere (8).

Study Design

A retrospective cohort study design was used to identify population health system resources and costs for patients diagnosed with incident breast (ICD-O-3 C500 –

C509), lung (ICD-O-3 C340-C343,C348-C349), CRC (ICD-O-3 C18.X (excluding C181 – appendix), C199, C209), and prostate cancer (ICD-O-3 C61) cases diagnosed from January 1 2010 to December 31 2014. ICES, a Prescribed Entity under the provincial Personal Health Information and Protection of Privacy Act, encodes a personal identifier, which allows linkage of data from different care providers and across sectors in health administrative databases. Individuals without valid health insurance or ineligible for health insurance were excluded from the analysis. The first index cancer was used if a patient was diagnosed with more than one of those four cancers during the accrual period. Demographic variables included those available from the administrative databases including age, gender, location of residence, comorbidity, income and exposure to health system resources. End of follow-up was defined as the earliest of death date, one year after cancer diagnosis, or 1 day before the diagnosis of a second cancer and were censored and adjusted for 365 days.

Algorithm Development

We applied two provincial costing algorithms to these cohorts to identify direct health system, total and disaggregated, undiscounted costs based on a single-payer government perspective (Ontario, Canada). A comprehensive description of both algorithms are found in a previous publication (8). In short, we created and used two oncology-specific costing methodologies: one for cancer-related medications (Cancer Medication Costing Algorithm, CMCA) and one for radiation treatment (Cancer Radiation Costing Algorithm, CRCA) for more specific, comprehensive cancer costing evaluations. We used a bottom-up approach to determine cost of treatment at the

individual patient encounter level. Where individual patient health sector costs were not available (e.g., system or institutional costs), then a top-down approach was used to allocate aggregated costs to each patient encounter. Direct treatment costs were calculated from the perspective of the Ontario public healthcare payer; costs incurred by the individual patient or private insurers were not addressed. The CMCA estimated the per person costs for patients who received cancer-related medications, both treatment and supportive. The CRCA estimates the per person costs for patients undergoing radiation therapy. Costs were disaggregated into planning and treatment costs. Costs (mean, median, SD, IQR) for all patients in the cohort (intent to treat analysis) and cost for those individuals who used the resource (clinically evaluable) were determined.

Analysis

The primary analysis calculated the mean overall cost per patient per cancer-related medication and radiation by disease and stage in the first year (365 days) after diagnosis. A secondary analysis examined cost by disease subtype. For breast cancer, subtypes included (i) hormone receptor (estrogen and/or progesterone) positive + HER2 overexpressed; (ii) hormone receptor positive + HER2 negative; (iii) hormone receptor negative + HER2 overexpressed; and (iv) hormone receptor negative + HER2 negative. For lung cancer, we stratified costs into i) Non Small Cell Lung Cancer (NSCLC) and ii) Small Cell Lung Cancer (SCLC). CRC was stratified into i) colon and ii) rectal. The cost by stage in prostate cancer was calculated. Finally, costs for those individuals who survived for two or more years were also calculated.

RESULTS

There were 168,316 Ontarians diagnosed with one of breast, colorectal, lung and prostate cancer between January 1, 2010 and December 31, 2015. The mean age of all cancer patients at diagnosis was 66.1 (SD: 12.4) years, with the mean age being the highest in lung cancer [68.8 (10.4) years] and lowest for breast cancer [61.3 years (13.7)] and overall equally divided by gender for CRC and lung cancer. The average follow-up time for all four disease sites was 10 months (Table 1).

Breast Cancer

The majority of women with a diagnosis of breast cancer (N=50,141) were diagnosed in the early stages (Stages I/II). 93% had an entire year of follow-up and 67% were not hospitalized (Table 1). The majority of women at all stages used cancer-related medications (63.2%) and the mean cost was $8,167 (95%CI: $8,023-$8,311) over the one-year period (Table 2). Eighty-one percent of individuals used radiation services within one year after diagnosis and for those who did, the mean cost was $18,529 (95%CI: $18,415-$18, 643) (Table 3). Overall cancer-related drug costs and radiation costs increased by stage (Figure 1A, Figure 2A). Women who were HER2+ had 6 to 10-fold higher overall cancer related drug costs (Appendix Table 1).

Colorectal Cancer

38,109 had a diagnosis of colorectal cancer at a mean age of 68 years and there were slightly more males (54.5%). Of those staged, half were diagnosed in Stage III/IV (Table 1). Sixteen percent of individuals died in the year following their diagnosis. The mean overall costs for cancer related medications [$9,637 (95%CI: $9,431-$9,843)] and

radiation treatment [$15,188 (95%CI: $14,899-$15,456)] and was highest in those with a Stage III diagnosis (Table 2 and 3). The cost of cancer-related treatment medications was highest in those individuals with a Stage IV diagnosis. When stratified into colon and rectal diseases, overall costs for medications were similar for both disease sites but higher in the rectal disease group for radiation costs (Appendix Table 1 and 2).

Lung Cancer

The majority of lung cancer cases (N=34,809) were diagnosed in Stage IV. There was an equal split between genders and the mean age was 69 years. More than half of patients died within one of diagnosis and more than two thirds died within two years of a diagnosis (Table 1). Eighty percent of individuals with a diagnosis of lung cancer used cancer-related medications and 67% of individuals received radiation treatment. The mean overall cost for cancer-related drugs was $2,900 (95%CI: $2,816-$2,984) and increased by stage of disease. The mean overall cost for radiation treatment was $10,818 (95%: $10,669-$10,966) where costs in Stage II and III were highest (Table 2 and 3). Treatment drugs were more costly than supportive drugs (Figure 1C) and radiation treatment was more costly than planning and operational costs (Figure 2C). When stratified into NSCLC and SCLC cases, Stage III costs were still highest for cancer-related medication and radiation treatment (Appendix, Table 1).

Prostate Cancer

The mean age of prostate cancer patients (N=45,258) at diagnosis was 68 years. Most patients were not hospitalized and thus did not have a Charlson score. Less than 5%

died during the one year follow up period (Table 1). Half of men received cancer-related medications and radiation treatment, with the proportion increasing by stage for cancer medications related cohort and increased radiation utilization being highest in State II and III (Table 2 and 3). The overall cost per stage increased as the stage of prostate cancer increased in severity (Figure 1D, Figure 2D).

INTERPRETATION

This study examined disease-specific and stage specific costs associated with important cancer-related medications and radiation treatment using two novel costing algorithms leveraging population level administrative databases. The costs presented also provide more granularity by disease subtype. Previous published costing studies using the PLCCM algorithm underestimated the critical costs related to cancer treatment around medications and radiation as one cannot easily identify cancer-specific drugs and supportive drugs or identify treatment and planning radiation costs. With respect to radiation treatment, a recent summary of studies examining radiation costs showed that there is a wide range of costs (9), with some based on US estimates (10-13) or older data (14). Our results show that Stage III and IV cancers are generally the most expensive stages for both medications and radiation across all four disease sites. More specifically, certain subtypes within each cancer type showed greater costs in the first year after diagnosis. Although not described here, each individual resource utilized by a cohort of individuals can be identified and explored using this bottom-up costing algorithm approach.

Our efforts in designing more comprehensive costing algorithms have face validity when compared to methods and studies conducted by other Canadian and international investigators (15-20). We expect costs from other administrative databases studies not using the costing algorithms to have lower overall costs and we expect difference in costs when compared to international studies. For example, our overall mean oneyear medication costs of $1,211 (95%CI: $1,175 - $1,247) for prostate cancer were higher from those reported one year after diagnosis ($514 CAN 2007) as calculated by Krahn et al because of the inclusion of additional medication databases (15). Additionally, radiation costs in that study were reported as negligible because the databases for planning, treatment and operational costs were not included. Moreover, stage-specific costs calculated in our study could not be compared to those in Krahn's study because stage based costing was not assessed (21). Internationally, our one-year mean post index radiation costs of $16,442 (95%CI: $16,293-$16,591) for women with stage I and $19,973 (95%CI: $19,781-$20,165) for stage II breast cancer were in line with those from insurance claims for radiation ($14,910 US$) in women with stage I/II breast cancer (16). Mean medication costs were different based on our cohort of women with early stage disease [(Stage I: $5,409 (95%CI: $5,207-$5,611); Stage II: $8,519 (95%CI: 8,314, 8,724)] compared to $13,373 US in that US cohort. These variances are mostly likely reflective of differences in health system frameworks and funding, but highlight opportunities for improving costs for healthcare systems.

Strengths of this work include the comprehensiveness of the data for the entire provincial population of 35 million residents, but there are also some limitations. Our

analysis provides costs only for initial care in the first year after a cancer diagnosis and does not consider the cost of maintenance, survivorship and end of life phases of care. We used this time horizon as it was in line with other phase-based costing approaches (21-23). We did, however, establish that even in one year, that there are survival differences across the 4 most common cancers with one year survival for breast being highest after diagnosis compared to one year survival in lung cancer.

Finally, it is important to highlight that this study reported only on the publicly funded health system costs. We did not have access to costs incurred by the individual patient or private insurers and as such, they are not addressed in this analysis. Understanding this type of utilization and cost information would be important in cohorts where the mean age at diagnosis was younger than 65 years as oral drugs costs are unknown.

This works sets the stage for establishing the health system costs for cancer-related medications and radiation therapy which can be used as baseline utilization and costs for future innovations and incremental analyses. Although, all cohorts were anchored at 2015, the algorithms created can examine the cost by any disease site, stage or phase of care, including updated time horizons, based on the defined cohorts because it uses a resource based bottom-up calculation. A number of studies have already leveraged the two cancer specific costing algorithms (24, 25); ongoing analyses include examining costs in melanoma, pancreatic, gastric, esophageal and lung cancer. Future work will examine other phases of care in the care continuum and will generate costs across other disease sites and subtypes. Understanding the resources and cost of publicly

funded medications and radiation therapy are critical to health system planning and sustainability in a single payer system. Previous costing and resource estimates have not been robust due to the lack of comprehensive data on cancer-related medication and radiation treatment. Our work updates previous costing estimates. More refined costing estimates are useful as inputs to allow for more robust health economic modelling and health system planning.

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Table 1. Characteristics of cancer patients diagnosed between 2010-2015, by primary cancer site

Characteristics	Measure	Breast Cancer (N=50,141)	Colorectal Cancer (N=38,108)	Lung Cancer (N=34,809)	Prostate Cancer (N=45,258)	TOTAL (N=168,316)
Female		50,141 (100.0%)	17,327 (45.5%)	17,001 (48.8%)	0 (0.0%)	84,469 (50.2%)
Age at cancer diagnosis, years	Mean ± SD	61.3 ± 13.7	68.4 ± 13.3	68.8 ± 10.4	67.5 ± 9.5	66.1 ± 12.4
	Median (IQR)	61 (51-71)	69 (59-79)	69 (62-76)	67 (61-74)	66 (58-75)
Rural residents		6,176 (12.3%)	5,642 (14.8%)	5,523 (15.9%)	6,513 (14.4%)	23,854 (14.2%)
Neighbourhood Income	Lowest	8,497 (16.9%)	7,217 (18.9%)	8,232 (23.6%)	6,934 (15.3%)	30,880 (18.3%)
	Second lowest	9,608 (19.2%)	7,754 (20.3%)	7,538 (21.7%)	8,442 (18.7%)	33,342 (19.8%)
	Middle	9,918 (19.8%)	7,705 (20.2%)	6,772 (19.5%)	8,910 (19.7%)	33,305 (19.8%)
	Second highest	10,873 (21.7%)	7,804 (20.5%)	6,479 (18.6%)	9,804 (21.7%)	34,960 (20.8%)
	Highest	11,048 (22.0%)	7,461 (19.6%)	5,635 (16.2%)	10,986 (24.3%)	35,130 (20.9%)
	Missing	197 (0.4%)	167 (0.4%)	153 (0.4%)	182 (0.4%)	699 (0.4%)
Cancer stage at diagnosis	I	20,759 (41.4%)	8,269 (21.7%)	6,104 (17.5%)	10,154 (22.4%)	45,286 (26.9%)
	II	18,607 (37.1%)	9,124 (23.9%)	2,855 (8.2%)	22,103 (48.8%)	52,689 (31.3%)
	III	6,786 (13.5%)	10,755 (28.2%)	6,989 (20.1%)	5,664 (12.5%)	30,194 (17.9%)
	IV	2,433 (4.9%)	6,848 (18.0%)	17,714 (50.9%)	4,058 (9.0%)	31,053 (18.4%)

Characteristics	Measure	Breast Cancer (N=50,141)	Colorectal Cancer (N=38,108)	Lung Cancer (N=34,809)	Prostate Cancer (N=45,258)	TOTAL (N=168,316)
	Unknown	1,556 (3.1%)	3,112 (8.2%)	1,147 (3.3%)	3,279 (7.2%)	9,094 (5.4%)
Charlson score *	0	13,232 (26.4%)	20,017 (52.5%)	13,051 (37.5%)	17,244 (38.1%)	63,544 (37.8%)
	1	1,896 (3.8%)	4,017 (10.5%)	3,543 (10.2%)	2,529 (5.6%)	11,985 (7.1%)
	≥2	1,215 (2.4%)	2,723 (7.1%)	3,123 (9.0%)	1,832 (4.0%)	8,893 (5.3%)
	Not hospitalized	33,798 (67.4%)	11,351 (29.8%)	15,092 (43.4%)	23,653 (52.3%)	83,894 (49.8%)
Days of follow-up†	Mean ± SD	347.7 ± 68.9	307.2 ± 117.3	233.0 ± 139.7	353.7 ± 54.1	316.4 ± 107.1
	Median (IQR)	365 (365-365)	365 (365-365)	287 (84-365)	365 (365-365)	365 (365-365)
Months of follow-up†	Mean ± SD	11.4 ± 2.3	10.1 ± 3.9	7.7 ± 4.6	11.6 ± 1.8	10.4 ± 3.5
	Median (IQR)	12 (12-12)	12 (12-12)	9 (3-12)	12 (12-12)	12 (12-12)
Died during follow-up†		1,782 (3.6%)	6,369 (16.7%)	17,745 (51.0%)	1,535 (3.4%)	27,431 (16.3%)
Died within 2 years after diagnosis		3,557 (7.1%)	9,971 (26.2%)	23,506 (67.5%)	3,256 (7.2%)	40,290 (23.9%)
Had an entire year of follow-up†		46,574 (92.9%)	29,434 (77.2%)	15,482 (44.5%)	42,865 (94.7%)	134,355 (79.8%)
Reason for end of follow-up†	Died during follow-up	1,782 (3.6%)	6,369 (16.7%)	17,745 (51.0%)	1,535 (3.4%)	27,431 (16.3%)
	Had a 2nd cancer	1,787 (3.6%)	2,314 (6.1%)	1,598 (4.6%)	865 (1.9%)	6,564 (3.9%)
	End of 1-year follow-up	46,572 (92.9%)	29,425 (77.2%)	15,466 (44.4%)	42,858 (94.7%)	134,321 (79.8%)

*: Charlson score calculated using hospitalization data in the 2 years before cancer diagnosis

† End of follow-up was defined as the earliest of death date, 1 year after cancer diagnosis, or 1 day before the diagnosis of a second cancer.

Table 2. Use of cancer-related medication and mean (95% CI in parentheses) medication costs in 1 year after diagnosis among cancer patients diagnosed between January 1, 2010 and December 31, 2015, by cancer stage at the time of diagnosis

Cancer site	Measures	Overall	Stage I	Stage II	Stage III	Stage IV	Unknown Stage
Breast	**No. of patients**	50,141	20,759	18,607	6,786	2,433	1,556
	No. (%) used medication	38,484 (76.8%)	13,111 (63.2%)	16,061 (86.3%)	6,451 (95.1%)	2,009 (82.6%)	852 (54.8%)
	Mean (95% CI) of medication cost*	8,167 (8,023, 8,311)	5,409 (5,207, 5,611)	8,519 (8,314, 8,724)	12,046 (11,657, 12,434)	12,460 (11,328, 13,592)	4,454 (3,656, 5,252)
Colorectal	**No. of patients**	38,108	8,269	9,124	10,755	6,848	3,112
	No. (%) used medication	27,749 (72.8%)	4,675 (56.5%)	6,421 (70.4%)	9,482 (88.2%)	5,634 (82.3%)	1,537 (49.4%)
	Mean (95% CI) of medication cost*	6,568 (6,446, 6,691)	785 (683, 887)	2,778 (2,624, 2,933)	9,637 (9,431, 9,843)	11,442 (11,075, 11,809)	3,196 (2,782, 3,610)
Lung	**No. of patients**	34,809	6,104	2,855	6,989	17,714	1,147
	No. (%) used medication	27,673 (79.5%)	4,470 (73.2%)	2,469 (86.5%)	6,050 (86.6%)	13,910 (78.5%)	774 (67.5%)
	Mean (95% CI) of medication cost*	2,900 (2,816, 2,984)	612 (546, 679)	1,415 (1,278, 1,552)	2,291 (2,155, 2,428)	4,207 (4,060, 4,354)	2,129 (1,673, 2,585)
Prostate	**No. of patients**	45,258	10,154	22,103	5,664	4,058	3,279

	No. (%) used medication	22,599 (49.9%)	3,231 (31.8%)	11,763 (53.2%)	2,798 (49.4%)	3,276 (80.7%)	1,531 (46.7%)
	Mean (95% CI) of medication cost*	1,211 (1,175, 1,247)	268 (239, 296)	966 (932, 1,000)	825 (763, 888)	3,236 (3,060, 3,413)	1,461 (1,303, 1,620)

*: Among those who had used cancer-related medication.

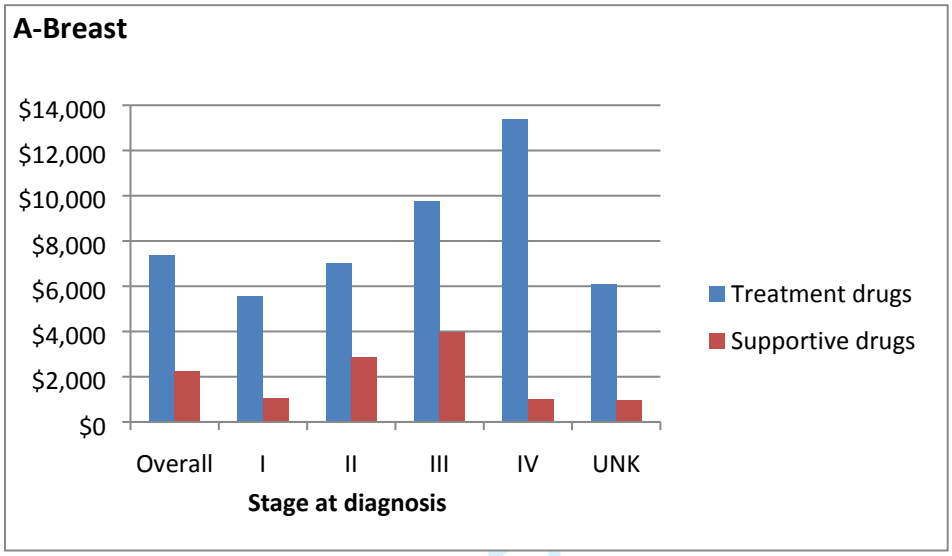
Table 3. Use of radiation treatment and mean (95% CI in parentheses) radiation treatment costs in 1 year after diagnosis among cancer patients diagnosed between January 1, 2010 and December 31, 2015, by cancer stage at the time of diagnosis

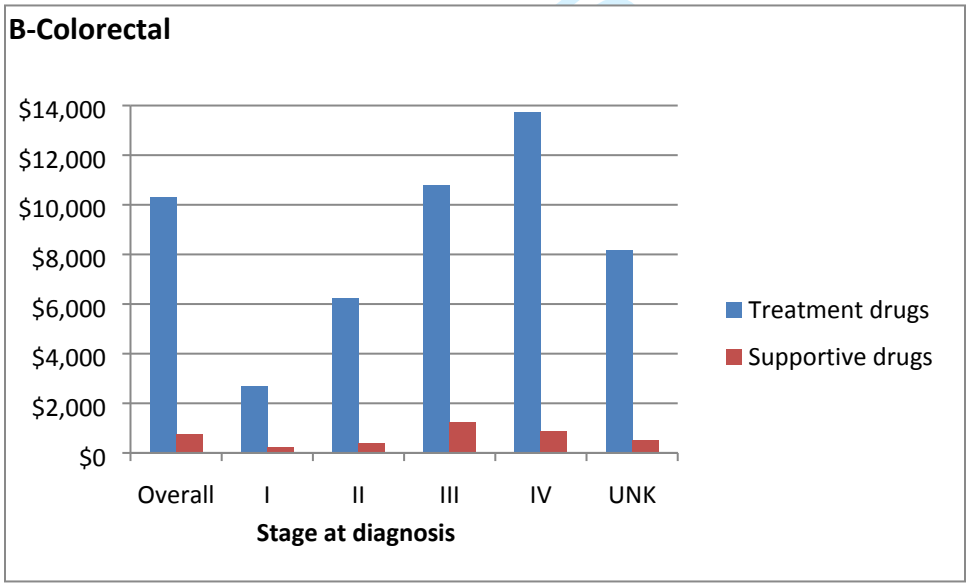
Cancer site	Measures	Overall	Stage I	Stage II	Stage III	Stage IV	Unknown Stage
Breast	**No. of patients**	50,141	20,759	18,607	6,786	2,433	1,556
	No. (%) used radiation	40,659 (81.1%)	17,206 (82.9%)	15,306 (82.3%)	6,054 (89.2%)	1,487 (61.1%)	606 (38.9%)
	Mean (95% CI) of radiation cost*	18,529 (18,415, 18,643)	16,442 (16,293, 16,591)	19,973 (19,781, 20,165)	23,821 (23,512, 24,131)	8,476 (7,894, 9,057)	13,141 (12,220, 14,063)
Colorectal	**No. of patients**	38,108	8,269	9,124	10,755	6,848	3,112
	No. (%) used radiation	8,979 (23.6%)	1,052 (12.7%)	1,979 (21.7%)	3,803 (35.4%)	1,877 (27.4%)	268 (8.6%)
	Mean (95% CI) of radiation cost*	15,177 (14,899, 15,456)	10,613 (9,809, 11,416)	17,400 (16,807, 17,992)	18,853 (18,439, 19,266)	8,444 (7,957, 8,932)	11,689 (10,077, 13,301)
Lung	**No. of patients**	34,809	6,104	2,855	6,989	17,714	1,147
	No. (%) used radiation	23,158 (66.5%)	2,330 (38.2%)	1,527 (53.5%)	5,864 (83.9%)	13,005 (73.4%)	432 (37.7%)
	Mean (95% CI) of radiation cost*	10,818 (10,669, 10,966)	7,982 (7,610, 8,353)	13,002 (12,321, 13,682)	17,790 (17,416, 18,165)	8,019 (7,877, 8,160)	8,009 (7,093, 8,925)
Prostate	**No. of patients**	45,258	10,154	22,103	5,664	4,058	3,279

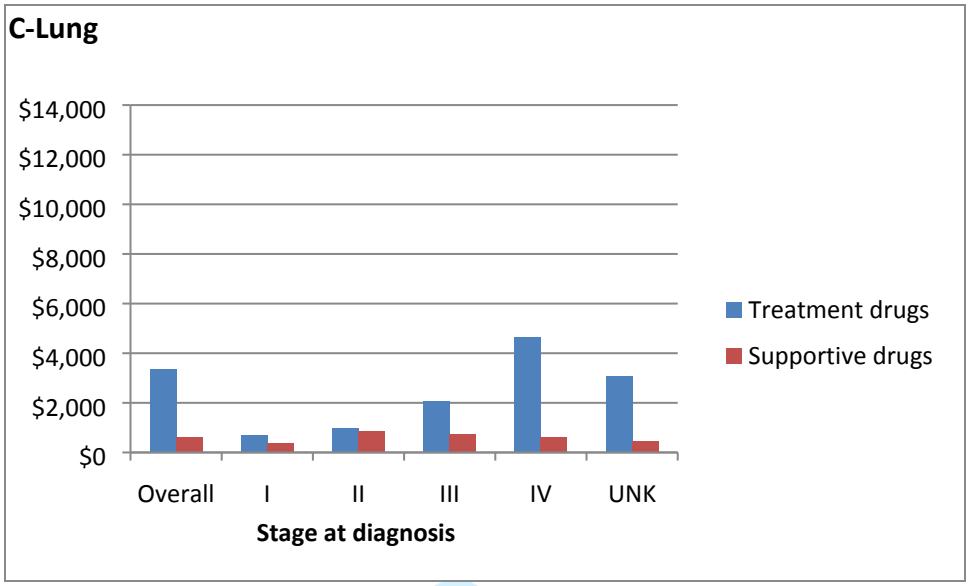
	No. (%) used radiation	23,207 (51.3%)	3,228 (31.8%)	13,433 (60.8%)	3,701 (65.3%)	2,478 (61.1%)	367 (11.2%)
	Mean (95% CI) of radiation cost*	16,887 (16,648, 17,125)	6,467 (6,006, 6,928)	20,543 (20,219, 20,867)	17,765 (17,168, 18,362)	10,264 (9,717, 10,812)	10,564 (8,985, 12,142)

*: Among those who had a non $0 radiation cost.

Figure 1: Disaggregated mean cancer-related medication costs (treatment and supportive) for different primary cancer sites by cancer stage at diagnosis. Among those who had a non-zero cost. A-breast cancer; B-colorectal cancer; C-lung cancer; D-prostate cancer.






C-Lung
$14,000
$12,000
$10,000
$8,000
$6,000
$4,000
$2,000
$0
Overall
I
II
III
IV
UNK
Stage at diagnosis
Treatment drugs
Supportive drugs

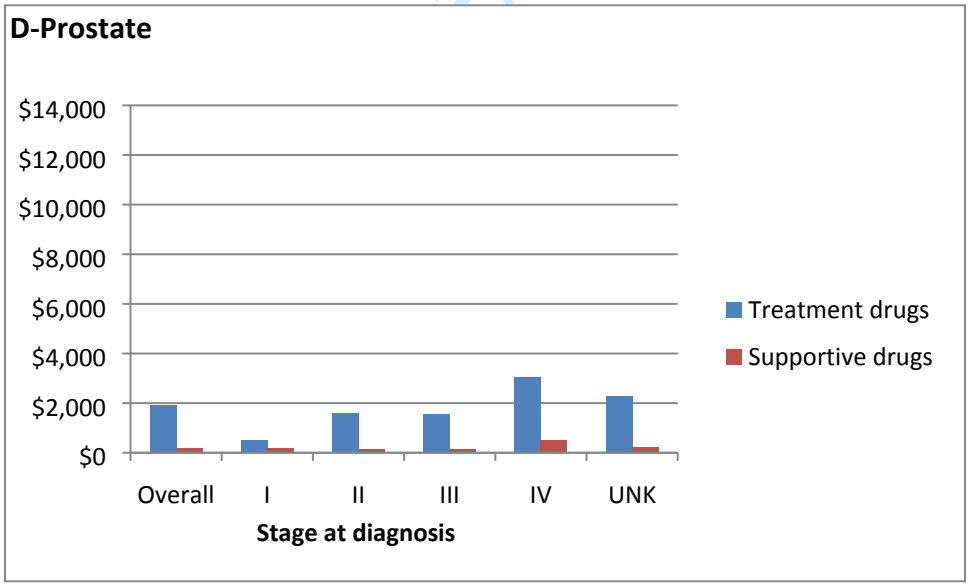
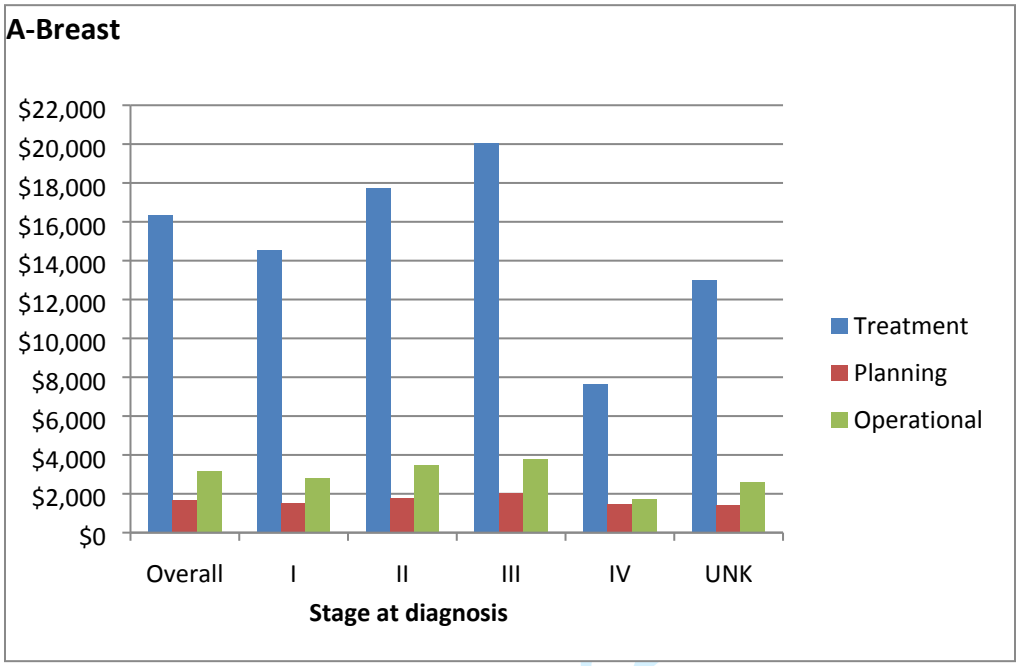
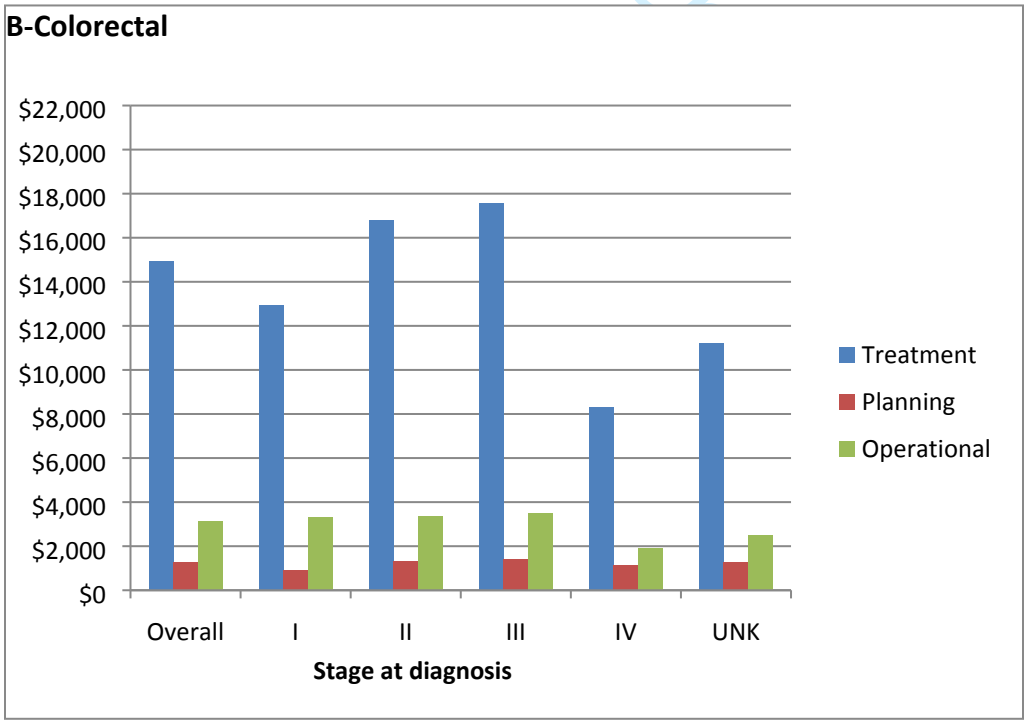
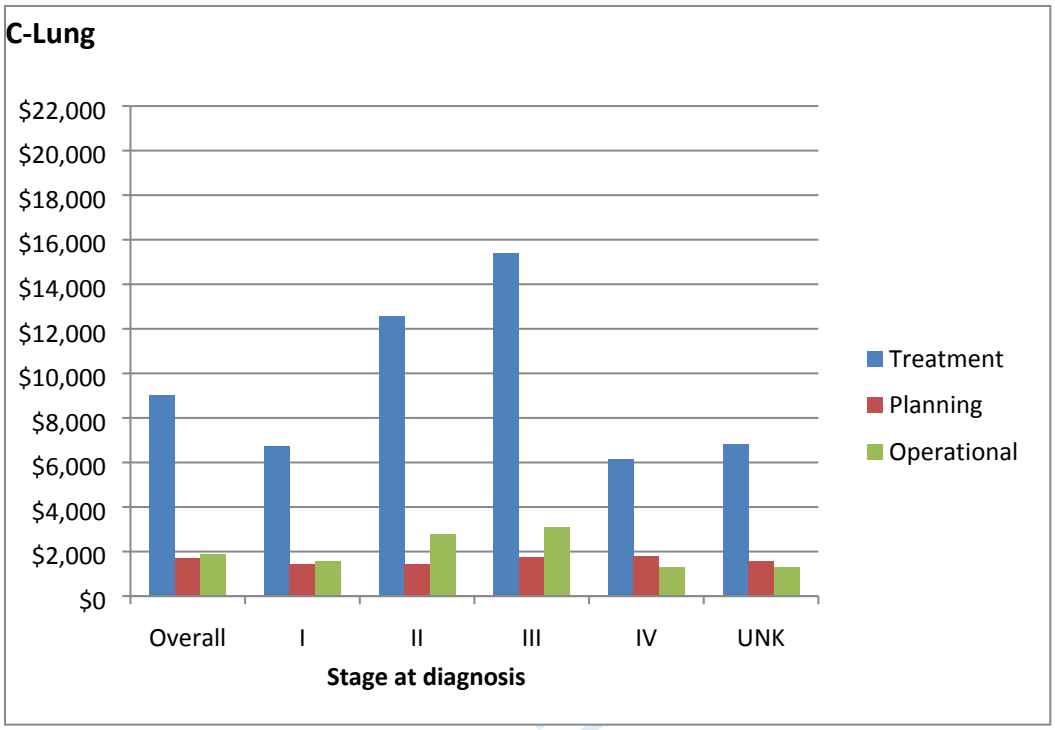
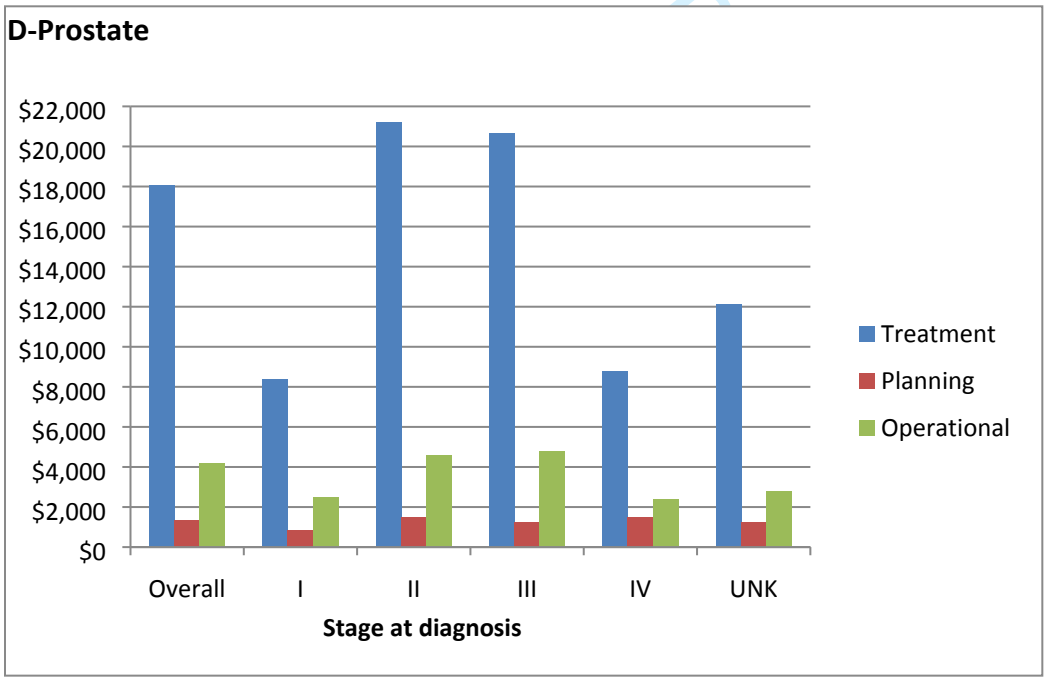

D-Prostate
$14,000
$12,000
$10,000
$8,000
$6,000
$4,000
$2,000
$0
Overall
I
II
III
IV
UNK
Stage at diagnosis
Treatment drugs
Supportive drugs

Figure 2: Disaggregated mean radiation treatment costs (planning, treatment and operational) for different primary cancer sites by cancer stage at diagnosis.
Among those who had a non-zero cost. A-breast cancer; B-colorectal cancer; C-lung cancer; D-prostate cancer.






C-Lung
$22,000
$20,000
$18,000
$16,000
$14,000
$12,000
$10,000
$8,000
$6,000
$4,000
$2,000
$0
Overall
I
II
III
IV
UNK
Stage at diagnosis
Treatment
Planning
Operational


D-Prostate
$22,000
$20,000
$18,000
$16,000
$14,000
$12,000
$10,000
$8,000
$6,000
$4,000
$2,000
$0
Overall
I
II
III
IV
UNK
Stage at diagnosis
Treatment
Planning
Operational

Appendix 1. Use of cancer-related medication and mean (95% CI in parentheses) cancer-related medication costs in 1 year after diagnosis among cancer patients diagnosed between January 1, 2010 and December 31, 2015, by cancer subtype and cancer stage at the time of diagnosis

Cancer site	Cancer subtype	Measures	Overall	Stage I	Stage II	Stage III	Stage IV	Unknown Stage
Breast †	Hormone Receptor + HER 2 +	No. of patients	4,010	1,219	1,708	838	232	13
		No. (%) used chemotherapy	3,751 (93.5%)	1,089 (89.3%)	1,630 (95.4%)	813 (97.0%)	207 (89.2%)	12 (92.3%)
		Mean (95% CI) of chemotherapy cost*	30,453 (29,828, 31,077)	28,075 (27,036, 29,114)	29,485 (28,677, 30,293)	32,399 (31,177, 33,620)	43,801 (38,327, 49,274)	15,601 (5,305, 25,896)
	Hormone Receptor + HER 2 -	No. of patients	29,241	13,920	10,876	3,441	921	83
		No. (%) used chemotherapy	21,541 (73.7%)	8,324 (59.8%)	9,103 (83.7%)	3,271 (95.1%)	779 (84.6%)	64 (77.1%)
		Mean (95% CI) of chemotherapy cost*	2,971 (2,899, 3,044)	1,464 (1,381, 1,548)	3,568 (3,452, 3,683)	5,267 (5,042, 5,492)	2,633 (2,151, 3,115)	928 (655, 1,201)
	Hormone Receptor - HER 2 +	No. of patients	1,954	498	815	483	151	7
		No. (%) used chemotherapy	1,807 (92.5%)	417 (83.7%)	779 (95.6%)	465 (96.3%)	139 (92.1%)	7 (100.0%)
		Mean (95% CI) of chemotherapy cost*	32,383 (31,463, 33,303)	27,848 (26,276, 29,421)	31,484 (30,345, 32,624)	33,476 (31,768, 35,185)	47,987 (41,800, 54,175)	19,928 (3,604, 36,251)
	Hormone Receptor - HER 2 -	No. of patients	4,249	1,229	2,117	716	180	7
		No. (%) used chemotherapy	3,872 (91.1%)	1,045 (85.0%)	1,979 (93.5%)	688 (96.1%)	154 (85.6%)	6 (85.7%)
		Mean (95% CI) of chemotherapy cost*	5,329 (5,122, 5,536)	4,532 (4,174, 4,890)	5,496 (5,211, 5,781)	6,550 (5,968, 7,133)	3,230 (2,456, 4,003)	2,915 (463, 5,367)
Colorectal	Colon	No. of patients	25,312	5,140	6,754	6,635	4,734	2,049
		No. (%) used chemotherapy	18,367 (72.6%)	2,970 (57.8%)	4,619 (68.4%)	5,838 (88.0%)	3,854 (81.4%)	1,086 (53.0%)
		Mean (95% CI) of chemotherapy cost*	6,505 (6,348, 6,662)	531 (422, 640)	2,170 (2,000, 2,341)	10,326 (10,043, 10,609)	11,342 (10,887, 11,796)	3,566 (3,037, 4,095)
	Rectal	No. of patients	12,796	3,129	2,370	4,120	2,114	1,063
		No. (%) used chemotherapy	9,382 (73.3%)	1,705 (54.5%)	1,802 (76.0%)	3,644 (88.4%)	1,780 (84.2%)	451 (42.4%)
		Mean (95% CI) of chemotherapy cost*	6,693 (6,500, 6,886)	1,226 (1,021, 1,431)	4,337 (4,014, 4,660)	8,534 (8,251, 8,816)	11,659 (11,040, 12,277)	2,305 (1,705, 2,906)
Lung	Non-small	No. of patients	30,091	5,959	2,715	5,858	14,531	1,028

Cancer site	Cancer subtype	Measures	Overall	Stage I	Stage II	Stage III	Stage IV	Unknown Stage
	cell	No. (%) used chemotherapy	23,831 (79.2%)	4,346 (72.9%)	2,340 (86.2%)	5,061 (86.4%)	11,392 (78.4%)	692 (67.3%)
		Mean (95% CI) of chemotherapy cost*	3,051 (2,955, 3,148)	579 (512, 647)	1,364 (1,222, 1,506)	2,325 (2,165, 2,486)	4,712 (4,535, 4,889)	2,241 (1,734, 2,749)
	Small cell	No. of patients	4,718	145	140	1,131	3,183	119
		No. (%) used chemotherapy	3,842 (81.4%)	124 (85.5%)	129 (92.1%)	989 (87.4%)	2,518 (79.1%)	82 (68.9%)
		Mean (95% CI) of chemotherapy cost*	1,965 (1,882, 2,048)	1,769 (1,404, 2,134)	2,334 (1,855, 2,813)	2,117 (1,960, 2,275)	1,921 (1,816, 2,027)	1,181 (835, 1,528)
Prostate		No. of patients	45,258	10,154	22,103	5,664	4,058	3,279
		No. (%) used chemotherapy	22,599 (49.9%)	3,231 (31.8%)	11,763 (53.2%)	2,798 (49.4%)	3,276 (80.7%)	1,531 (46.7%)
		Mean (95% CI) of chemotherapy cost*	1,211 (1,175, 1,247)	268 (239, 296)	966 (932, 1,000)	825 (763, 888)	3,236 (3,060, 3,413)	1,461 (1,303, 1,620)

*: Among those who had a non $0 chemotherapy medication cost.

†: Results for those with missing Hormone Receptor information or missing HER 2 information were not included.

Appendix 2. Use of radiation treatment and mean (95% CI in parentheses) radiation treatment costs in 1 year after diagnosis among cancer patients diagnosed between January 1, 2010 and December 31, 2015, by cancer subtype and cancer stage at the time of diagnosis

Cancer site	Cancer subtype	Measures	Overall	Stage I	Stage II	Stage III	Stage IV	Unknown Stage
Breast†	Hormone Receptor + HER 2 +	No. of patients	4,010	1,219	1,708	838	232	13
		No. (%) used radiation	3,430 (85.5%)	1,027 (84.2%)	1,470 (86.1%)	780 (93.1%)	147 (63.4%)	6 (46.2%)
		Mean (95% CI) of radiation cost*	19,600 (19,198, 20,002)	16,618 (15,978, 17,259)	20,464 (19,856, 21,072)	23,866 (23,024, 24,708)	9,303 (7,333, 11,274)	16,132 (9,049, 23,216)
	Hormone Receptor + HER 2 -	No. of patients	29,241	13,920	10,876	3,441	921	83
		No. (%) used radiation	24,532 (83.9%)	11,751 (84.4%)	9,049 (83.2%)	3,095 (89.9%)	615 (66.8%)	22 (26.5%)
		Mean (95% CI) of radiation cost*	18,343 (18,200, 18,485)	16,438 (16,262, 16,615)	19,724 (19,476, 19,972)	23,744 (23,310, 24,178)	7,548 (6,702, 8,394)	9,088 (4,630, 13,546)
	Hormone Receptor - HER 2 +	No. of patients	1,954	498	815	483	151	7
		No. (%) used radiation	1,666 (85.3%)	397 (79.7%)	718 (88.1%)	452 (93.6%)	96 (63.6%)	3 (42.9%)
		Mean (95% CI) of radiation cost*	19,872 (19,272, 20,473)	15,689 (14,560, 16,818)	20,697 (19,823, 21,571)	24,149 (23,007, 25,291)	11,089 (8,727, 13,451)	12,751 (284, 25,219)
	Hormone Receptor - HER 2 -	No. of patients	4,249	1,229	2,117	716	180	7
		No. (%) used radiation	3,691 (86.9%)	1,067 (86.8%)	1,844 (87.1%)	649 (90.6%)	125 (69.4%)	6 (85.7%)
		Mean (95% CI) of radiation cost*	19,616 (19,228, 20,004)	17,375 (16,759, 17,992)	20,013 (19,463, 20,562)	23,692 (22,739, 24,646)	11,771 (9,107, 14,436)	18,563 (7,004, 30,122)
Colorectal	Colon	No. of patients	25,312	5,140	6,754	6,635	4,734	2,049
		No. (%) used radiation	1,722 (6.8%)	90 (1.8%)	343 (5.1%)	530 (8.0%)	642 (13.6%)	117 (5.7%)
		Mean (95% CI) of radiation cost*	6,508 (6,022, 6,994)	6,145 (3,825, 8,465)	8,527 (7,284, 9,770)	7,799 (6,781, 8,818)	4,068 (3,554, 4,583)	8,401 (6,460, 10,343)
	Rectal	No. of patients	12,796	3,129	2,370	4,120	2,114	1,063
		No. (%) used radiation	7,257 (56.7%)	962 (30.7%)	1,636 (69.0%)	3,273 (79.4%)	1,235 (58.4%)	151 (14.2%)
		Mean (95% CI) of radiation cost*	17,235 (16,929, 17,540)	11,030 (10,183, 11,878)	19,260 (18,629, 19,891)	20,643 (20,222, 21,063)	10,719 (10,063, 11,375)	14,236 (11,876, 16,596)
Lung	Non-small cell	No. of patients	30,091	5,959	2,715	5,858	14,531	1,028
		No. (%) used radiation	19,603 (65.1%)	2,208 (37.1%)	1,403 (51.7%)	4,876 (83.2%)	10,750 (74.0%)	366 (35.6%)

Cancer site	Cancer subtype	Measures	Overall	Stage I	Stage II	Stage III	Stage IV	Unknown Stage
		Mean (95% CI) of radiation cost*	10,470 (10,311, 10,629)	7,602 (7,237, 7,967)	12,418 (11,715, 13,122)	17,314 (16,903, 17,724)	7,812 (7,660, 7,964)	7,202 (6,258, 8,145)
	Small cell	**No. of patients**	4,718	145	140	1,131	3,183	119
		No. (%) used radiation	3,555 (75.3%)	122 (84.1%)	124 (88.6%)	988 (87.4%)	2,255 (70.8%)	66 (55.5%)
		Mean (95% CI) of radiation cost*	12,733 (12,329, 13,138)	14,855 (12,574, 17,135)	19,603 (17,283, 21,923)	20,143 (19,244, 21,043)	9,002 (8,622, 9,381)	12,485 (9,789, 15,181)
Prostate		**No. of patients**	45,258	10,154	22,103	5,664	4,058	3,279
		No. (%) used radiation	23,207 (51.3%)	3,228 (31.8%)	13,433 (60.8%)	3,701 (65.3%)	2,478 (61.1%)	367 (11.2%)
		Mean (95% CI) of radiation cost*	16,887 (16,648, 17,125)	6,467 (6,006, 6,928)	20,543 (20,219, 20,867)	17,765 (17,168, 18,362)	10,264 (9,717, 10,812)	10,564 (8,985, 12,142)

*: Among those who had a non $0 radiation treatment cost.

†: Results for those with missing Hormone Receptor information or missing HER 2 information were not included.

Appendix 3. Use of cancer-related medication and mean (95% CI in parentheses) cancer-related medication costs in 1 year after diagnosis among cancer patients diagnosed between January 1, 2010 and December 31, 2015 *and who survived for 2 years or more*, by cancer stage at the time of diagnosis. This analysis was performed to exclude possible end-of-life chemotherapy costs.

Cancer site	Measures	Overall	Stage I	Stage II	Stage III	Stage IV	Unknown Stage
Breast	**No. of patients**	46,584	20,373	17,765	5,979	1,328	1,139
	No. (%) used medication	35,560 (76.3%)	12,793 (62.8%)	15,316 (86.2%)	5,700 (95.3%)	1,149 (86.5%)	602 (52.9%)
	Mean (95% CI) of medication cost*	8,454 (8,303, 8,606)	5,505 (5,299, 5,711)	8,731 (8,519, 8,943)	12,773 (12,353, 13,194)	17,557 (15,773, 19,342)	5,807 (4,706, 6,907)
Colorectal	**No. of patients**	28,137	7,581	7,848	8,725	2,184	1,799
	No. (%) used medication	20,456 (72.7%)	4,198 (55.4%)	5,575 (71.0%)	7,869 (90.2%)	1,992 (91.2%)	822 (45.7%)
	Mean (95% CI) of medication cost*	6,917 (6,777, 7,057)	779 (675, 883)	2,961 (2,791, 3,131)	10,557 (10,333, 10,782)	17,551 (16,940, 18,162)	4,474 (3,811, 5,137)
Lung	**No. of patients**	11,303	4,905	1,733	2,453	1,889	323
	No. (%) used medication	8,893 (78.7%)	3,477 (70.9%)	1,505 (86.8%)	2,146 (87.5%)	1,561 (82.6%)	204 (63.2%)
	Mean (95% CI) of	3,117 (2,942, 3,292)	518 (448, 588)	1,394 (1,237, 1,552)	2,740 (2,451, 3,029)	11,151 (10,398, 11,903)	2,592 (1,473, 3,712)

	medication cost*						
Prostate	**No. of patients**	42,002	9,919	21,235	5,525	2,546	2,777
	No. (%) used medication	20,012 (47.6%)	3,075 (31.0%)	11,090 (52.2%)	2,691 (48.7%)	1,946 (76.4%)	1,210 (43.6%)
	Mean (95% CI) of medication cost*	1,031 (996, 1,065)	260 (231, 288)	926 (892, 960)	782 (720, 844)	2,986 (2,750, 3,222)	1,355 (1,186, 1,524)

*: Among those who had used chemotherapy medication.

Appendix 4. Use of radiation treatment and mean (95% CI in parentheses) radiation treatment costs in 1 year after diagnosis among cancer patients diagnosed between January 1, 2010 and December 31, 2015 *and who survived for 2 years or more*, by cancer stage at the time of diagnosis

Cancer site	Measures	Overall	Stage I	Stage II	Stage III	Stage IV	Unknown Stage
Breast	No. of patients	46,584	20,373	17,765	5,979	1,328	1,139
	No. (%) used radiation	38,721 (83.1%)	17,001 (83.4%)	14,836 (83.5%)	5,485 (91.7%)	870 (65.5%)	529 (46.4%)
	Mean (95% CI) of radiation cost*	18,857 (18,742, 18,973)	16,504 (16,355, 16,654)	20,172 (19,978, 20,365)	24,618 (24,309, 24,927)	9,155 (8,346, 9,965)	13,851 (12,856, 14,846)
Colorectal	No. of patients	28,137	7,581	7,848	8,725	2,184	1,799
	No. (%) used radiation	6,673 (23.7%)	947 (12.5%)	1,672 (21.3%)	3,199 (36.7%)	708 (32.4%)	147 (8.2%)
	Mean (95% CI) of radiation cost*	17,229 (16,904, 17,554)	10,761 (9,902, 11,620)	18,227 (17,585, 18,869)	19,857 (19,415, 20,298)	11,866 (10,918, 12,814)	16,204 (13,811, 18,597)
Lung	No. of patients	11,303	4,905	1,733	2,453	1,889	323
	No. (%) used radiation	5,866 (51.9%)	1,554 (31.7%)	748 (43.2%)	2,063 (84.1%)	1,418 (75.1%)	83 (25.7%)
	Mean (95% CI) of radiation cost*	14,297 (13,947, 14,647)	7,715 (7,262, 8,167)	12,983 (11,957, 14,008)	22,227 (21,609, 22,844)	10,881 (10,318, 11,444)	10,662 (8,136, 13,188)
Prostate	No. of patients	42,002	9,919	21,235	5,525	2,546	2,777

	No. (%) used radiation	21,768 (51.8%)	3,184 (32.1%)	13,056 (61.5%)	3,625 (65.6%)	1,613 (63.4%)	290 (10.4%)
	Mean (95% CI) of radiation cost*	17,397 (17,148, 17,646)	6,466 (6,001, 6,930)	20,651 (20,322, 20,979)	17,836 (17,233, 18,439)	12,596 (11,822, 13,371)	12,123 (10,237, 14,008)

*: Among those who had a non $0 radiation cost.