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Pancreatic cancer treatment costs, including patient liability, by phase of care and treatment modality, 2000–2013

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Abstract

Objectives: Our study provides phase-specific cost estimates for pancreatic cancer based on stage and treatment. We compare treatment costs between the different phases and within the stage and treatment modality subgroups.

Methods: Our cohort included 20,917 pancreatic cancer patients from the Surveillance, Epidemiology, and End Results (SEER)-Medicare database diagnosed between 2000 and 2011. We allocated costs into four phases of care-staging (or surgery), initial, continuing, and terminal– and calculated the total, cancer-attributable, and patient-liability costs in 2018 US dollars. We fit linear regression models using log transformation to determine whether costs were predicted by age and calendar year.

Results: Monthly cost estimates were high during the staging and surgery phases, decreased over the initial and continuing phases, and increased during the three-month terminal phase. Overall, the linear regression models showed that cancer-attributable costs either remained stable or increased by year, and either were unaffected by age or decreased with older age; continuing phase costs for stage II patients increased with age.

Conclusions: Our estimates demonstrate that pancreatic cancer costs can vary widely by stage and treatment received. These cost estimates can serve as an important baseline foundation to guide resource allocation for cancer care and research in the future.

Abbreviations: AJCC = American Joint Committee on Cancer, CI = confidence interval, CMS = Centers for Medicare and Medicaid, CPT = Current Procedural Terminology, HCPCS = Healthcare Common Procedure Coding System, HMO = Health Maintenance Organization, ICD-9-CM = International Classification of Diseases, Ninth Revision, Clinical Modification, NS = Not Significant, SBRT = Stereotactic Body Radiation Therapy, SEER = Surveillance, Epidemiology, and End Results.

Keywords: healthcare costs, pancreatic cancer, phase of care, SEER-Medicare, treatment

1. Introduction

Approximately 56,770 new cases of pancreatic cancer and 45,570 deaths are expected in the United States in 2019.[1] Its average 5-year survival rate is 8.5%, the lowest of all cancers as reported by the Surveillance, Epidemiology, and End Results (SEER) Program.[2,3] Due to changing demographics and trends in incidence and death rates, pancreatic cancer is projected to become the second leading cause of cancer-related death by 2030.[4]

Of the current treatments for pancreatic cancer, only surgical resection is potentially curative. Because pancreatic cancer is initially asymptomatic and difficult to detect with existing screening methods, 75% to 80% of patients present with advanced disease at diagnosis and do not qualify for surgery. Furthermore, the post-surgery 5-year survival rate is a discouraging 15% to 20%.[5,6] Systemic therapies for metastatic disease have remained minimally effective over the last few decades,[4] and pancreatic cancer is considered resistant to new immunotherapy treatments.[6,7] Given the projected rise in disease burden through 2030, there is intense interest in developing novel treatment methods.

Combination chemotherapy regimens have improved progression-free and overall survival, both in the metastatic and adjuvant setting.[8–11] Targeted therapy, such as PARP inhibitors for BRCA2 germline mutations, are being actively investigated.[12,13] These regimens, however, have clear cost implications, due to the use of newer, more expensive agents and the longer duration of active therapy. In addition, opting for best supportive care – and thereby foregoing expensive treatments that can place economic pressure on health care systems while worsening a patient's quality of life – may be considered as a legitimate alternative to

Editor: Feng Yang.

NIH/NCI R01 CA226629, American Cancer Society – New England Division – Ellison Foundation Research Scholar Grant (RSG-15–129-01CPHPS).

The authors have no conflicts of interests to disclose.

Supplemental Digital Content is available for this article.

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How to cite this article: Tramontano AC, Chen Y, Watson TR, Eckel A, Sheehan DF, Peters MLB, Pandharipande PV, Hur C, Kong CY. Pancreatic cancer treatment costs, including patient liability, by phase of care and treatment modality, 2000–2013. Medicine 2019;98:49(e18082).

Received: 23 April 2019 / Received in final form: 9 September 2019 / Accepted: 23 October 2019

http://dx.doi.org/10.1097/MD.0000000000018082

later-line chemotherapy for metastatic patients.[14–16] Studies have shown that as recently as 5 years ago, almost 40% of newly diagnosed pancreatic cancer patients in the US opted solely for best supportive care without any cancer-directed therapy.[17] As more treatment options become available for pancreatic cancer patients, it will be necessary to assess the trade-off between costs and survival benefits associated with each available cancer intervention option. To better assess these trade-offs, improved understanding of the costs of current modalities is needed.

While costs of pancreatic cancer care have previously been estimated using medical claims data,[18,19] a comparison of the costs of different treatment modalities (surgery, chemo, chemoradiation) has not, to our knowledge, been published to date. In this study, we allocated total, patient-liable, and cancer-attributable costs for pancreatic cancer patients into 4 phases of care and compared costs within and between treatment modalities and stages at diagnosis. We compared treatment costs between the different phases and within the stage and treatment modality subgroups.

2. Materials and methods

2.1. Cancer patient inclusion/exclusion criteria

Our observational analysis included 20,917 Medicare beneficiaries aged 66 and older who were diagnosed with pancreatic cancer between 2000 and 2011, captured using the Surveillance, Epidemiology and End Results (SEER)-Medicare database. SEER, a resource of the National Cancer Institute, includes clinical, demographic, and cause-of-death information from 18 cancer registries across the US, representing about 28% of the US population.[20] Medicare provides health insurance coverage for approximately 97% of Americans aged 65 or older.[21] The SEER-Medicare database links these 2 databases for patients 65 and older, with approximately 95% of patients 65 and older in the SEER files linked to the Medicare enrollment file.[21] A detailed description of SEER-Medicare can be found at https://healthcaredelivery.cancer.gov/seermedicare/.

Patients were excluded from our study if they had previous or subsequent cancer diagnoses other than pancreatic cancer, if cancer stage at diagnosis was not recorded, if diagnosis was made at autopsy, or if the date of diagnosis was unknown. Patients were excluded if they were not continuously enrolled in both Medicare Part A and Part B coverage during the 15 months before cancer diagnosis through death or the end of 2013, if they received Medicare benefits because of disability or end-stage renal disease (as they may not be representative of the general population), or if they enrolled in a Health Maintenance Organization (HMO) at any time during the study period. We defined cancer stage using the SEER stage variable for the sixth edition of the American joint Committee on Cancer (AJCC) Cancer Staging Manual and mapped those diagnosed between 2000 and 2003 to the appropriate AJCC 6th edition stage using the SEER variables for extension of disease and lymph node involvement and excluded patients with unknown stage. Finally, we excluded patients with discrepancies of greater than three months between the date of death recorded in Medicare and the date of death recorded in SEER, those who had costs with unknown claims dates, and those with any post-death costs.

2.2. Matched control cohort

Control subjects were beneficiaries from the random sample of 5% of all Medicare enrollees who were aged 65 years and older, were not diagnosed with any cancer, and were continuously enrolled in Medicare Part A and B through the study period. Patients were excluded if they were also enrolled in an HMO. We matched these control patients to pancreatic cancer patients within each phase on an individual level (1:1) by sex, 5-year age group, and SEER registry region (Northeast, South, Midwest, West).[22] By taking each pancreatic cancer patient's costs and subtracting the costs of a comparable patient without cancer, we were able to create estimates of the average cancer-attributable costs of pancreatic cancer patients.

2.3. Treatment modalities

The identification of treatment modalities for patients diagnosed with stages I-III pancreatic cancer was based on treatment(s) received during the 2 months before cancer diagnosis through 6 months after diagnosis. We considered the 2 months before diagnosis to account for treatments given to symptomatic pancreatic cancer patients who had not yet been diagnosed with pancreatic cancer, as well as for possible errors in treatment dates recorded in the claims data. Treatment groups for stage IV patients were defined by treatment(s) ever received before death or the end of the study period. Patients who were not actively treated with surgery, radiation, or chemotherapy were defined as having received best supportive care. Patients remained in their stage and treatment group throughout the study. For example, a stage I patient who received chemoradiation but no surgery within the specified time defined above remained in the chemoradiation group. A full list of treatment codes can be found in Table, Supplemental Digital Content 1, http://links.lww.com/MD/D454, which includes all codes used.

2.4. Phases of care

We allocated costs into 4 phases of care–staging (or surgery), initial, continuing, and terminal (Fig. 1).[22–24] One month was defined as 30 days for all calculations. Each patient who received surgery had a 1-month surgery phase, beginning on the date of major surgery. In our data, over half of patients (56.4%) received surgery within 1 month of diagnosis; therefore, the varying amount of time between diagnosis and surgery dates was excluded. Patients who did not receive surgery had a 1-month staging phase beginning on the date of diagnosis; the stage of cancer was determined during this time. This 1-month staging phase was based on typical practice at our institution. Subsequently these patients had an initial, continuing, and terminal phase, defined in the same way as for surgery patients. The one-month staging, or surgery, phase was followed by a 6-month initial phase, a continuing phase varying in length between patients depending on how long each survived, and a 3-month terminal phase ending on the date of death. Patients who survived beyond the end of 2013 were not considered to have a terminal phase. For patients who died too early to have had all 4 phases of care, time and costs were first allocated to the terminal phase, followed by the surgery or staging phase, and, lastly, the initial phase. For example, a pancreatic cancer patient who died 9 months after diagnosis would contribute 3 months to the terminal phase, 1 month to the staging (or surgery) phase, and 5 months to the initial phase.

Previous studies allocating cancer treatment into phases of care in the US have used varying lengths of time to define the terminal phase. Some have, for example, defined this period as 6 or 12

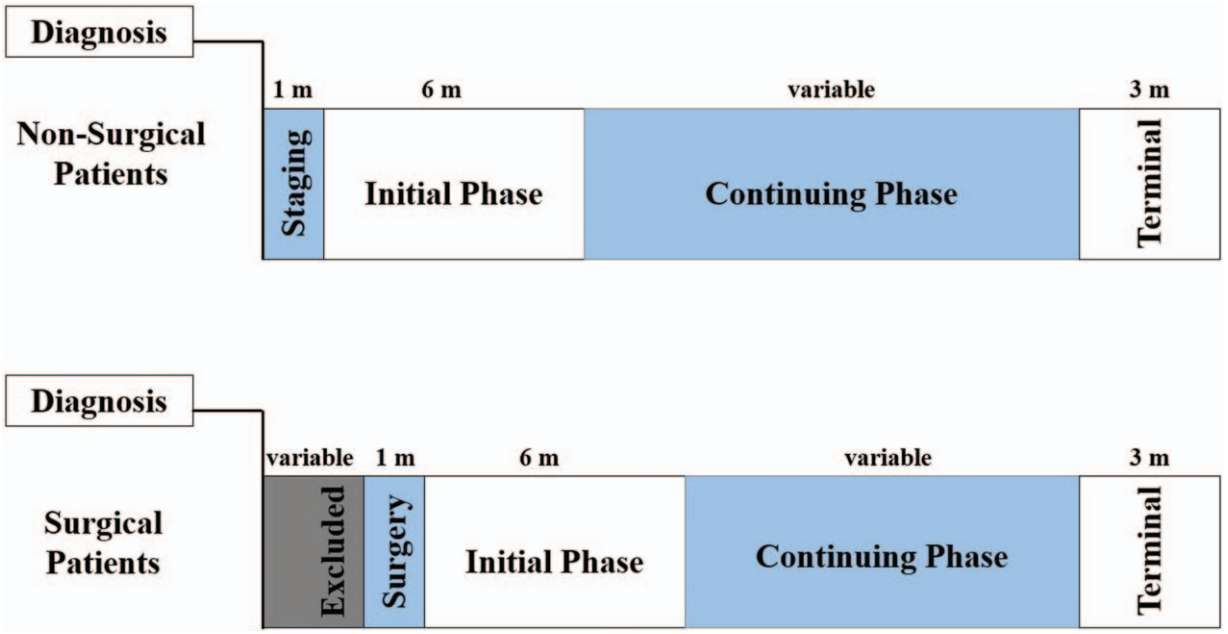

Figure 1. Phases of care timeline for non-surgical patients and for surgical patients.

months long.[22–24] Since pancreatic cancer has a high mortality rate, with few patients surviving beyond 12 months after diagnosis, we chose to use a 3-month terminal phase. For a full account of the reasoning behind our choice, see the Figure in Supplemental Digital Content 2, http://links.lww.com/MD/D455. The terminal phase is not the same as best supportive care; patients can be on active treatment during this phase.

Since control noncancer subjects did not have cancer diagnoses, they were each randomly assigned a "pseudodiagnosis" date that matched the diagnosis date of one of the pancreatic cancer patients.[22]. Control patients were assigned to two phases of care—the continuing phase and the terminal phase. The terminal phase was defined as the last 3 months of life and the continuing phases was defined as all months between the "pseudodiagnosis date" and terminal phase. Cancer patients who died of cancer were matched to continuing control subjects, and cancer patients who died of other causes were matched to terminal control subjects to best reflect cancer-attributable costs.[22] Average monthly costs of care were calculated for each phase for control subjects in the same manner as for cancer patients.

2.5. Cost of cancer care

Total and patient-liability costs were allocated to each phase of care, for each patient. Costs were defined as the sum of Medicare reimbursements (payments from Medicare to the service provider), co-insurance reimbursements (payments from a co-insurer to the service provider), and deductibles and co-payments billed to patients. Patient-liability costs paid out-of-pocket at the time of service could not be differentiated from those paid by a purchased Medigap policy, insurance sold by private companies to help cover coinsurance, copayment, and deductible costs.[25]

Cancer-attributable costs for each patient were estimated for the initial, continuing, and terminal phases. These costs were determined by subtracting the matched noncancer patient's average monthly phase costs from the pancreatic cancer patient's average monthly phase costs. Cancer-attributable costs incorporate not only the direct cost of cancer treatment, but also other healthcare costs incurred during phases of treatment beyond the average patient's healthcare costs. As cancer-attributable costs are expected to account for most costs in the 1-month surgery and staging phases, only total and patient-liability costs are reported for these phases.

Costs were converted to constant 2018 US dollars by adjusting Part A claims using the Centers for Medicare and Medicaid (CMS) Prospective Payment System Hospital Price Index and Part B claims using the Medicare economic index.[26,27] All mean cost estimates reported are per month unless otherwise noted.

2.6. Statistical analysis

For each individual patient, total, patient-liability, and cancer-attributable costs were calculated. We report the mean monthly cost estimates and 95% confidence intervals (CI) for each phase of care; we stratified by AJCC 6th edition, the standard before 2010. (Cost estimates by historic stage are found along with those by AJCC stage in the Tables, Supplemental Digital Content 3–6, http://links.lww.com/MD/D456.) We do not report treatment modality costs where less than 10% of patients within a stage group received that treatment, except for best supportive care costs, which are shown for all groups. Multiple linear regression models using log transformation were fit to estimate population average costs for each phase, stage at diagnosis, and treatment modality. Scaled calendar year (calendar year-2000), age, and an interaction term for year and age were included as independent variables in the models and were dropped, using backwards stepwise selection, until all terms in the model were significant at the $\alpha = .05$ level. A full description of model parameters is found in Text, Supplemental Digital Content 7, http://links.lww.com/MD/D457: Description of Parameters and Tables, Supplemental Digital Content 8–11, http://links.lww.com/MD/D458: Linear

Regression Results. The cost estimates in initial and continuing phases were calculated using the selected linear regression model with age variable set to the median age at diagnosis (70 years) and the year variable set to 18 (calendar year 2018).[28] For cost estimates in the terminal phase, median age at death (72 years) was used.[28] All analyses were performed using SAS 9.4.

Our study was approved by the Institutional Review Board at Massachusetts General Hospital.

3. Results

3.1. Patient characteristics

Our cohort of 20,917 pancreatic cancer patients had a median (25th, 75th percentile) age of diagnosis of 76 (71, 81) and included 9580 (45.8%) males. Most patients (82.5%) were non-Hispanic White. Over one-half (53.7%) were diagnosed at stage IV, and only 7.8% were diagnosed at stage I. Among treatment modalities, the highest number of patients received best supportive care (32.6%), while only 17.2% of patients received surgery (either alone or with another form of treatment). A full list of descriptive characteristics is listed in Table 1.

The majority of patients (20,354; 97.3%) had died by the end of the study period. Of these, 17,508 (86.0%) had died of their pancreatic cancer, and an additional 228 (1.1%) had an operative death. The median (25th, 75th percentile) survival among patients who died of pancreatic cancer was 4.9 months (2.1, 10.3). Among all patients, 15,017 (71.8%) had survival times of 10 months or less; these patients had no designated continuing phase. 9229 (44.1%) patients lived 4 months or less after their diagnosis. These patients had no designated initial or continuing phases.

The mean (95% CI) phase length (in months) for each phase within each stage is reported in Table 2. Among stage I patients who contributed to the phase, the mean lengths were 4.80, 25.45, and 2.70 months for the initial, continuing, and terminal phases, respectively. For stage II, the mean lengths were 4.80, 17.11, and 2.73 months for the initial, continuing, and terminal phases, respectively. Stage III patients had mean lengths of 4.43, 10.84, and 2.69 months for the initial, continuing, and terminal phases, respectively. Stage IV patients had the lowest mean lengths-3.54, 7.77, and 2.30 months for the initial, continuing, and terminal phases, respectively.

3.2. Mean stage-specific costs

Mean (95% CI) monthly total cost estimates for each stage are shown in Figure 2. Total cost estimates were highest in the staging phase, decreased in the initial and continuing phases, and increased again in the terminal phase. This trend was seen in all stages. Total, cancer-attributable, and patient-liability cost estimates by stage and phase are reported in Table 2. For Stage I patients, mean monthly cancer-attributable costs were $5470 (95% CI: $5000-$5940) in the 6-month initial phase, $2821 ($2515-$3127) in the continuous phase, and $9899 ($8952-$10845) in the 3-month terminal phase. Mean monthly cancer-attributable costs for stage II patients were $6497 (95% CI: $6229-$6765) in the 6-month initial phase, $3574 ($3336-$3813) in the continuous phase, and $11,058 ($10,577-$11,539) in the 3-month terminal phase. Stage III patients had mean monthly cancer-attributable costs of $8484 (95% CI: $7978-$8989) in the 6-month initial phase, $5126 ($4449-$5803) in the continuous phase, and $11,222 ($10,551-$11,892) in the 3-month terminal phase. For Stage IV patients, mean monthly cancer-attributable costs were $7787 (95% CI: $7539-$8305) in the 6-month initial phase, $5515 ($5200-$5830) in the continuous phase, and $12,746 ($12,480-$13,011) in the 3-month terminal phase.

Table 1

Description of 20,917 pancreatic cancer patients.

Characteristic	N (%)
Sex	
Male	9580 (45.8)
Female	11,337 (54.2)
Race/ethnicity	
White	17,247 (82.5)
Black	2084 (10.0)
Hispanic	475 (2.3)
Asian	1001 (4.8)
Native American/Alaska Native	89 (0.4)
Unknown	21 (0.1)
Year of diagnosis	
2000	1390 (6.7)
2001	1502 (7.2)
2002	1575 (7.5)
2003	1687 (8.1)
2004	1743 (8.3)
2005	1742 (8.3)
2006	1813 (8.7)
2007	1796 (8.6)
2008	1903 (9.1)
2009	1876 (9.0)
2010	1935 (9.3)
2011	1955 (9.4)
Age at diagnosis	
65–69 yr	3884 (18.6)
70–74 yr	5399 (25.8)
75–79 yr	5317 (25.4)
80–84 yr	3873 (18.5)
85+ yr	2444 (11.7)
Stage at diagnosis	
AJCC Stage	
Stage I	1626 (7.8)
Stage II	6333 (30.3)
Stage III	1728 (8.3)
Stage IV	11,230 (53.7)
Historic Stage	
Local	1626 (7.8)
Regional	7146 (34.2)
Distant	12,145 (58.1)
Treatment modality	
Best supportive care	6826 (32.6)
Surgery	1245 (6.0)
Surgery and chemotherapy	568 (2.7)
Surgery and radiation	435 (2.1)
Surgery, chemotherapy, and radiation	1361 (6.5)
Chemotherapy	3599 (17.2)
Radiation	2728 (13.0)
Chemotherapy and Radiation	4155 (19.9)
Cause of death*	
Pancreatic cancer	17,508 (86.0)
Operative†	228 (1.1)
All other causes	2618 (12.9)

* Percentages represent proportions among the 20,354 (97.3%) total deaths during the study period.

† Operative death is defined as death within 30 days of surgery to remove pancreatic cancer.

Table 2

Mean monthly cost estimates for each phase by stage at diagnosis.

	Mean phase length* (95% CI)	Total monthly cost (95% CI)	Monthly patient-liability cost (95% CI)	Monthly cancer-attributable cost (95% CI)
Stage I				
Surgery	0.99 (0.98–0.99)	$57,003 ($53,407–$60,601)	$2462 ($2308–$2616)	NA
Staging	0.95 (0.93–0.96)	$16,039 ($14,837–$17,241)	$1660 ($1569–$1752)	NA
Initial	4.80 (4.69–4.91)	$6700 ($6258–$7143)	$933 ($880–$986)	$5470 ($5000–$5940)
Continuing	25.45 (23.34–27.56)	$3857 ($3569–$4146)	$501 ($464–$537)	$2821 ($2515–$3127)
Terminal	2.70 (2.67–2.74)	$12,753 ($11,891–$13,615)	$983 ($930–$1037)	$9899 ($8952–$10,845)
Stage II				
Surgery	0.98 (0.98–0.99)	$61,806 ($60,057–$63,555)	$2541 ($2448–$2635)	NA
Staging	0.94 (0.93–0.95)	$17,652 ($16,985–$18,409)	$1770 ($1718–$1823)	NA
Initial	4.80 (4.75–4.86)	$7750 ($7542–$7958)	$1116 ($1086–$1147)	$6497 ($6229–$6765)
Continuing	17.11 (16.32–17.90)	$4707 ($4494–$4920)	$641 ($612–$671)	$3574 ($3336–$3813)
Terminal	2.73 (2.71–2.75)	$13,421 ($12,966–$13,877)	$1028 ($1001–$1054)	$11,058 ($10,577–$11,539)
Stage III				
Surgery	0.95 (0.92–0.98)	$58,780 ($52,851–$64,707)	$2814 ($2393–$3234)	NA
Staging	0.94 (0.93–0.95)	$14,999 ($14,001–$15,997)	$1617 ($1547–$1687)	NA
Initial	4.43 (4.31–4.54)	$9594 ($9099–$10,090)	$1329 ($1267–$1391)	$8484 ($7978–$8989)
Continuing	10.84 (9.71–11.97)	$6338 ($5695–$6981)	$837 ($772–$902)	$5126 ($4449–$5803)
Terminal	2.69 (2.66–2.72)	$13,361 ($12,724–$13,998)	$1040 (4995–$1085)	$11,222 ($10,551–$11,892)
Stage IV				
Surgery	0.95 (0.93–0.98)	$55,538 ($49,545–$61,532)	$2483 ($2173–$2793)	NA
Staging	0.89 (0.88–0.90)	$15,045 ($14,520–$15,569)	$1614 ($1580–$1648)	NA
Initial	3.54 (3.48–3.61)	$9000 ($8765–$9235)	$1242 ($1214–$1271)	$7787 ($7539–$8305)
Continuing	7.77 (7.20–8.36)	$6767 ($6476–$7058)	$848 ($805–$891)	$5515 ($5200–$5830)
Terminal	2.30 (2.29–2.32)	$15,009 ($14,766–$15,250)	$1261 ($1241–$1279)	$12,746 ($12,480–$13,011)

* Among patients who contributed to the phase.
CI = Confidence Interval.

3.3. Total cost during the staging phase by treatment

Among patients who received active treatment other than surgery, total monthly costs during the 1-month staging phase ranged from $6001 (95% CI: $4882-$7375) for stage IV patients who received chemoradiation to $20,279 (95% CI: $17,188-$23,371) for stage II patients who received radiation alone (Table, Supplemental Digital Content Table 3, http://links.lww.com/MD/D456). These costs remained stable or decreased over the study period and were not affected by age in the linear regression models. Patient liability costs ranged from $716 (95%

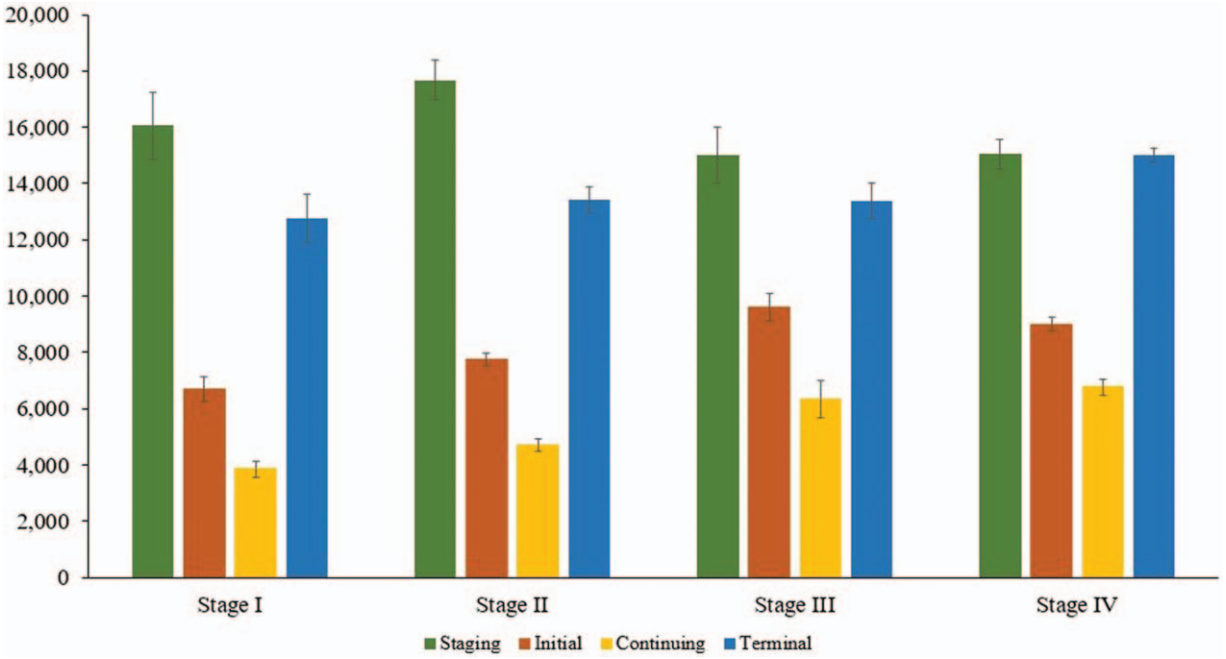

Figure 2. Mean total monthly cost estimates by phase and AJCC stage.

CI: $487-$1052) to $2688 (95% CI: $1694-$4263) (Table, Supplemental Digital Content Table 3, http://links.lww.com/MD/D456). Differences in staging costs may be partially attributed to treatment regimens received within this month.

3.4. Total cost during the surgery phase

Costs estimates for the 1-month surgery phase for AJCC stage are reported in Table 2 and historic stage are reported in Table, Supplemental Digital Content 4, http://links.lww.com/MD/D456. The mean total cost for patients during the one-month surgery phase ranged from $55,538 95% CI: ($49,545-$61,532) for stage IV to $61,806 ($60,057-$63,555) for stage II. The mean patient liability cost was $2658 (95% CI: $2492-$2824) and ranged from $2462 ($2308-$2616) for stage I to $2814 ($2393-$3234) for stage III. The 228 patients with an operative death had a mean total cost of $271,304 (95% CI: $227,836-$314,772); the mean patient liability cost was $11,351 (95% CI: $9487-$13,215).

3.5. Cancer-attributable costs of treatment during the initial phase

Costs estimates, including those attributable to cancer, during the 6-month initial phase for stage and treatment subgroups are shown in Table 3. Among patients who received active treatment, the mean cancer-attributable monthly costs ranged from $2232 (95% CI: $1278-$3185) for stage I patients who received surgery to $10,046 (95% CI: $9328-$10,766) for stage III patients who received chemoradiation. Within each stage, costs were highest for patients treated with chemoradiation, ranging from $7819 (95% CI: $7460-$8194) to $10,046 (95% CI: $9328-$10,766) per month. Notably, the mean cancer-attributable cost among stage I patients who received chemoradiation was 341% higher than those who received surgery ($9860, (95% CI: $8554-$11,167) and $2232, (95% CI: $1278-$3185), respectively). The mean cost among stage II patients who received chemoradiation was 134% higher than those who received surgery ($9560, (95% CI: $9058-$10,063) and $4085, (95% CI: $3293-$4877), respectively). Patient liability costs among patients receiving active treatment ranged from $466 (95% CI: $328-$604) to $1695 ($1623-$1768), with the highest costs seen among patients who received chemoradiation. Similar results were seen when this cohort was stratified by historic stage (local, regional, distant; see Table, Supplemental Digital Content 5, http://links.lww.com/MD/D456).

Results from the linear regression models showed that mean cancer-attributable costs either were unaffected by year or increased over the study period. These costs were largely unaffected by age. Exceptions were stage II patients who received either chemoradiation or all 3 treatments, and stage III patients who received radiation, where costs decreased with increasing age, and stage I patients who received best supportive care, in which cost estimates increased with age. Tables of parameter estimates are found in the Tables, Supplemental Digital Content 8-11, http://links.lww.com/MD/D458.

3.6. Cost by treatment modality during the continuing phase

Monthly treatment cost estimates during the continuing phase are shown in Table 3 for AJCC stage and Table, Supplemental Digital Content 5, http://links.lww.com/MD/D456 for historic stage. Only 25% of patients had a continuing phase of at least 1 month. Among these patients, the median (25th, 75th percentile) phase length was 8.8 months (4.0, 20.0). Overall, monthly costs were lower during the continuing phase than the initial phase. Average monthly cancer-attributable costs among patients who received active treatment ranged from $1503 (95% CI: $1079-$1926) for stage I patients who received surgery to $6630 (95% CI: $3868-$9393) for stage II patients who received radiation; stage II radiation patients had a 340% higher mean cost than those who received surgery. As with the initial phase, monthly cancer-attributable costs were primarily highest among patients receiving chemoradiation, with the exception of patients diagnosed with stage II disease, who had the highest costs if they received radiation. Patient liability costs ranged from $361 (95% CI: $300-$423) to $1179 (95% CI: $1124-$1235).

Cancer-attributable costs for stage I patients were not affected by age or year in the linear regressions. In contrast, cancer-attributable costs for stage II patients overall increased during study period and for older patients.

3.7. Terminal phase costs

Most patients had terminal phase costs, with approximately 44% having costs only in this phase and the staging (or surgery) phase. Monthly treatment cost estimates for the 3-month terminal phase are shown in Table 4. Overall, costs in the terminal phase were higher than both the initial and continuing phases. The average cancer-attributable costs for patients who received active treatment ranged from $9133 (95% CI: $8100-$10,165) for stage III patients who received chemotherapy to $16,206 (95% CI: $13,469-$18,943) for stage II patients who received surgery. Cancer-attributable costs for stage IV patients were above $11,000 for all treatment groups. Patients liability costs ranged from $696 (95% CI: $581-$835) to $1137 (95% CI: $869-$1489). In the linear regression models, the cancer-attributable costs were unaffected by age or decreased for older patients and remained stable or increased during the study period (with the exception of a decrease among stage I chemoradiation patients). Similar results are reported for historic stage in Table, Supplemental Digital Content 6, http://links.lww.com/MD/D456.

3.8. Cost of best supportive care

Among patients who elected to not actively treat their pancreatic cancer (6826; 32.6%) and instead receive best supportive care, mean total costs during the month of staging ranged from $16,301 (95% CI: $14,819-$17,782) to $17,951 ($16,604-$19,298) (Table, Supplemental Digital Content Table 3, http://links.lww.com/MD/D456).

Although these patients did not incur costs of actively treating cancer, to enable comparison across modalities of cancer care we allocated costs of best supportive care into the same treatment phases. Average monthly cancer-attributable costs during the initial phase ranged from $3544 (95% CI: $2634-$5851) to $6503 (95% CI: $4834-$8172) and those during the continuing phase ranged from $1811 (95% CI: $971-$2652) to $3675 ($1478-$5870) (Table 2). Average monthly cancer-attributable costs during the terminal phase for patients receiving best supportive care ranged from $8830 (95% CI: $7568-$10,091) for stage I to $13,178 (95% CI: $12,685-$13,670) for stage IV (Table 3). Cancer-attributable costs for best supportive care patients were largely unaffected by year and age in the linear

Table 3

Mean monthly cost estimates by stage at diagnosis by treatment modality, and significant predictors of cancer-attributable costs during the initial and continuing phases*.

					Cancer-attributable cost predictors		
	N (%)	Total monthly cost (95% CI)	Monthly patient-liability cost (95% CI)	Monthly cancer-attributable cost (95% CI)	Year	Age	Year_Age
Initial Phase							
Stage I							
Best supportive care	229 (20.5)	$5020 ($4189–$5850)	$407 ($325–$489)	$3544 ($2634–$5851)		+	
Surgery	212 (19.0)	$3452 ($2562–$4343)	$466 ($328–$604)	$2232 ($1278–$3185)			
Chemoradiation	218 (19.5)	$10,987 ($9717–$12,257)	$1598 ($1492–$1704)	$9860 ($8554–$11,167)	+		
Surgery, chemo, and radiation	133 (11.9)	$7240 ($5898–$8583)	$1228 ($1127–$1329)	$6171 ($4751–$7591)	+		
Stage II							
Best supportive care	662 (14.8)	$5662 ($5128–$6195)	$431 ($378–$483)	$4265 ($3670–$4861)			
Surgery	546 (12.2)	$5305 ($4543–$6066)	$687 ($538–$836)	$4085 ($3293–$4877)			
Chemoradiation	851 (19.0)	$10,618 ($10,132–$11,104)	$1583 ($1535–$1630)	$9560 ($9058–$10,063)	+	–	
Surgery, chemo, and radiation	1031 (23.0)	$7450 ($7169–$7731)	$1337 ($1280–$1394)	$6342 ($6017–$6666)	+	–	
Stage III							
Best supportive care	159 (14.8)	$7552 ($5919–$9186)	$517 ($368–$666)	$6503 ($4834–$8172)			
Radiation	130 (12.1)	$9054 ($7701–$10,407)	$1154 ($973–$1335)	$8155 ($6790–$9519)		–	
Chemotherapy	234 (21.8)	$8884 ($7923–$9843)	$1294 ($1171–$1416)	$7645 ($6702–$8588)			
Chemoradiation	445 (41.5)	$11,183 ($10,495–$11,872)	$1695 ($1623–$1768)	$10,046 ($9328–$10,766)	+		
Stage IV							
Best supportive care	515 (14.2)	$6182 ($5526–$6837)	$513 ($438–$587)	$4840 ($4169–$5511)			
Chemotherapy	1282 (35.3)	$9070 ($8712–$9429)	$1377 ($1336–$1419)	$7766 ($7369–$8163)	+		
Chemoradiation	1455 (40.1)	$8760 ($8434–$9098)	$1695 ($1623–$1768)	$7819 ($7460–$8194)			
Continuing Phase							
Stage I							
Best supportive care	160 (15.9)	$4204 ($3284–$5123)	$398 ($314–$483)	$3075 ($2110–$4041)			
Surgery	281 (27.9)	$2549 ($2177–$2921)	$361 ($300–$423)	$1503 ($1079–$1926)			
Chemoradiation	135 (13.4)	$7007 ($5945–$8069)	$878 ($762–$993)	$6053 ($4958–$7149)			
Surgery, chemo, and radiation	169 (16.8)	$3181 ($2669–$3693)	$475 ($392–$557)	$2187 ($1602–$2773)			
Stage II							
Best supportive care	308 (8.8)	$4178 ($3280–$5074)	$364 ($304–$423)	$2803 ($1820–$3786)			
Surgery	500 (14.3)	$3226 ($2810–$3641)	$416 ($368–$464)	$1659 ($1106–$2212)	+	+	–
Surgery and chemotherapy	421 (12.0)	$4222 ($3804–$4641)	$644 ($588–$701)	$3141 ($2437–$3845)	+	+	–
Chemoradiation	515 (14.7)	$6946 ($6141–$7750)	$980 ($874–$1086)	$5806 ($4980–$6632)	+		
Surgery, chemo, and radiation	1107 (31.6)	$3898 ($3632–$4163)	$578 ($411–$610)	$2990 ($2708–$3273)	+	+	–
Stage III							
Best supportive care	60 (9.5)	$5026 ($2939–$7112)	$620 ($321–$919)	$3675 ($1478–$5870)		+	
Radiation	74 (11.7)	$7454 ($4772–$10,135)	$702 ($471–$933)	$6630 ($3868–$9393)			
Chemotherapy	124 (19.7)	$6612 ($5730–$7493)	$954 ($835–$1073)	$5340 ($4269–$6411)			
Chemoradiation	290 (46.1)	$6672 ($5642–$7703)	$918 ($824–$1011)	$5494 ($4430–$6561)		–	
Stage IV							
Best supportive care	111 (8.1)	$3186 ($2349–$4023)	$352 ($254–$450)	$1811 ($971–$2652)			
Chemotherapy	464 (33.9)	$7019 ($6544–$7493)	$1087 ($1025–$1150)	$5651 ($5112–$6189)	+	+	–
Chemoradiation	627 (45.8)	$7657 ($7224–$8091)	$1179 ($1124–$1235)	$6500 ($6048–$6951)		–	

* A positive (+) symbol indicates that the covariate in the regression model has a parameter estimate greater than 0, while a negative (–) symbol indicates that the parameter estimate is less than 0. Except for best supportive care costs, treatment modality costs are not shown if less than 10% of patients within a stage received that treatment.
CI = Confidence Interval.

regression models, with the exceptions of stages I and III patients during the initial phase, where costs increased with age, and stage I patients during the terminal phase, where costs decreased with age.

4. Discussion

In this study, we derived phase-specific cost estimates for pancreatic cancer patients using SEER-Medicare data. Overall, costs were high during the 1-month staging and surgery phases, decreased over the initial and continuing phases, and increased during the patients' three-month terminal phase. This pattern was observed in all stage and treatment subgroups. The high costs in the 3-month terminal phase is consistent with studies that show high rates of aggressive care, such as intensive care admissions and ongoing chemotherapy treatment, in the final months of life among pancreatic and other cancer patients.[16,29–32] Average

Table 4

Mean monthly costs estimates by stage at diagnosis by treatment modality, and significant predictors of cancer-attributable costs during the terminal phase[*].

					Cancer-attributable cost predictors		
	N (%)	Total monthly cost (95% CI)	Monthly patient-liability cost (95% CI)	Monthly cancer-attributable cost (95% CI)	Year	Age	Year_Age
Terminal Phase							
Stage I							
Best supportive care	465 (33.1)	$11,426 ($10,302–$12,551)	$828 ($745–$912)	$8830 ($7568–$10,091)		–	
Surgery	196 (14.0)	$18,626 ($14,174–$23,077)	$1065 ($887–$1243)	$14,076 ($9266–$18,887)			
Radiation	174 (12.4)	$11,470 ($10,029–$12,590)	$960 ($795–$1125)	$9464 ($7911–$11,018)		–	
Chemoradiation	263 (18.7)	$12,260 ($10,700–$13,820)	$1122 ($1006–$1,238)	$10,448 ($8817–$12,079)	–	–	+
Stage II							
Best supportive care	1458 (25.6)	$12,236 ($11,514–$12,959)	$826 ($782–$871)	$10,166 ($9398–$10,935)			
Surgery	684 (12.0)	$19,141 ($16,469–$21,812)	$1066 ($966–$1166)	$16,206 ($13,469–$18,943)			
Chemoradiation	993 (17.4)	$12,273 ($11,674–$12,871)	$1185 ($1120–$1251)	$9828 ($9084–$10,573)	+	–	
Surgery, chemo, and radiation	929 (16.3)	$12,126 ($11,473–$12,778)	$1081 ($1026–$1136)	$9463 ($8703–$10,223)	+	–	
Stage III							
Best supportive care	432 (26.4)	$14,188 ($12,852–$15,524)	$902 ($824–$979)	$11,979 ($10,665–$13,292)			
Radiation	234 (14.3)	$15,738 ($13,641–$17,836)	$1163 ($1016–$1310)	$13,376 ($11,124–$15,628)		–	
Chemotherapy	311 (19.0)	$10,916 ($9947–$11,884)	$1023 ($916–$1130)	$9133 ($8100–$10,165)			
Chemoradiation	531 (32.4)	$12,416 ($11,517–$13,313)	$907 (823–$1179)	$10,398 ($9360–$11,436)			
Stage IV							
Best supportive care	3460 (34.4)	$15,615 ($15,164–$16,066)	$1157 ($1120–$1194)	$13,178 ($12,685–$13,670)			
Radiation	1579 (15.7)	$17,081 ($16,406–$17,756)	$1282 ($1239–$1345)	$14,410 ($13,657–$15,165)		–	
Chemotherapy	2545 (25.3)	$13,623 ($13,200–$14,045)	$1312 ($1279–$1345)	$11,641 ($11,187–$12,093)	+	–	
Chemoradiation	2298 (22.9)	$14,079 ($13,676–$14,481)	$1359 ($1323–$1394)	$12,007 ($11,537–$12,477)			

[*] A positive (+) symbol indicates that the covariate in the regression model has a parameter estimate greater than 0, while a negative (–) symbol indicates that the parameter estimate is less than 0. Treatment modality costs are not shown if less than 10% of patients within a stage received that treatment.
CI = Confidence Interval.

monthly patient-liability costs were typically highest for patients who received chemoradiation or radiation, possibly due to the higher number of visits associated with these treatments.

Mean cancer-attributable initial phase costs among stage I patients ranged from $2232 for those who received surgery to $9860 for those who received chemoradiation. Costs during the continuing phase range from $1503 for those who received surgery to $6053 for those who received radiation. This is unsurprising since many surgery patients received their treatment within the first month after diagnosis (surgery phase), while chemoradiation patients typically receive their treatment over several months. A similar trend was seen for stage II patients. Nearly half of stage III patients received chemoradiation, and these patients had the highest mean cancer-attributable costs in the initial and continuing phases. The majority of stage IV patients received chemotherapy, either alone or with radiation. Their monthly cancer-attributable costs where higher than those of stage IV patients on best supportive care in both the initial and continuing phases. Mean terminal phase cancer-attributable costs for stage IV patients were high in all treatment subgroups, ranging from $11,641 to $14,410 for chemotherapy and radiation patients, respectively.

Overall, pancreatic cancer care costs did not decrease over time for this population. Our linear regression models found that cancer-attributable costs either remained stable or increased over the study period. Cancer-attributable costs were generally either unaffected by patient age or observed as decreasing with advancing age. One notable exception was seen in the continuing phase for stage II patients, whose cancer-attributable costs generally increased with age. It is possible that this is due to the relative paucity of new treatments available during the study timeframe, which included patients diagnosed from 2000 to 2011. Since that time, there have been substantial changes in the chemotherapy and radiation therapy options available to patients, including *nab*-paclitaxel, gemcitabine combination therapy, and FOLFIRINOX. In addition, radiation treatment options have changed, with stereotactic body radiation therapy (SBRT) becoming increasingly popular. These treatments are often more expensive than older regimens; the monthly cost of FOLFIRINOX, for example, is greater than that of gemcitabine monotherapy (Medicare average sales price of $8142 versus $1534 adjusted to 2018 dollars).[33]

While pancreatic cancer treatments may have changed, stage-specific survival has not varied greatly over time. Pancreatic cancer remains one of the most fatal cancers, with a current 5-year survival rate of 8.5% among all stages. Overall 5-year survival rates for patients diagnosed between 2010 and 2014 are 28.9%, 12.7%. 3.1%, and 2.0% for stages I, II, III, and IV, respectively.[34,35] This is only a modest improvement from rates for patients diagnosed between 2005 and 2009 (24.6%, 10.6%, 3.4%, and 1.7% for stages I, II, III, and IV, respectively).[34,35] Even if overall survival does change by stage, the phase-specific monthly costs can be used for comparisons.

Previous studies have calculated pancreatic cancer care costs by phase of care or care utilization.[18,19] Our estimates for the total cost of terminal care, which range from $32,748 to $57,432 over 3 months, appear higher than those estimated by Kaye 2018, which reported a $17,141 annual cost for terminal care. This difference can likely be attributed to the definition of the terminal phase employed by Kaye. The study considered 10 different

cancers and defined the terminal phase equally for each: as the last 12 months of life. We define the period length as three months based on data showing increasingly higher costs during the three months before death (Figure, Supplemental Digital Content 2, http://links.lww.com/MD/D455). We believe our definition allows us to more accurately determine costs of this financially distinct phase of pancreatic cancer care. Our estimates showed decreasing costs with increasing age for many of our treatment and stage subgroups, a finding that is consistent with the Kaye study.

High cost estimates are observed in the surgery phase, as is consistent with O'Neill 2012, which reported high costs for patients with resectable disease. While the O'Neill study provides important information on costs of health care services, it does not provide detailed costs based on AJCC stage or phase of care. These data are particularly important to cancer control policy decision makers and as cost-effectiveness modeling inputs. The O'Neill costs were also reported in 2009 dollars; our study provides cost estimates in 2018 dollars.

As pancreatic cancer is projected to become the second-leading cause of cancer-related death by 2030, the burden of treatment will continue to grow. As a result, targeted screening based on specific patient risk factors to improve rates of early diagnosis and survival have been a topic of much discussion and scientific investigation among clinicians and population scientists.[36,37] A possible shift in stage distribution at diagnosis will, in turn, affect treatment patterns, as patients diagnosed earlier in their disease course will generally have more treatment options and greater life expectancies than those diagnosed later. As a result, the rates at which patients undergo cancer-directed treatment is expected to rise. A comprehensive and detailed understanding of costs associated with treatments, such as those provided by our analysis, will allow for accurate estimates of current and future costs.

A strength of our study is that it provides comprehensive cost estimates for pancreatic cancer patients that are phase-specific and at the stage and treatment level. Our study is, however, subject to certain limitations inherent in the use of observational SEER-Medicare claims data, such as the exclusion of patients younger than 65. The regression models we developed from our SEER-Medicare analysis are based only on patients over age 65. Although one could extrapolate these results in predicting treatment costs for younger pancreatic cancer patients, these models have not been validated using a younger population. However, only 33% of pancreatic cancer patients are diagnosed prior to age 65.[28] As SEER does not collect data from all state cancer registries, our results may not be generalizable to a specific state or the entire US population.

Additionally, we do not have information on patients who received care through their HMO; therefore, our costs may not be representative of the HMO population. We do not have information on whether patient-liability costs were paid out-of-pocket or covered by Medigap. It is possible that misclassification of costs by phase of care may have occurred, resulting in less accurate estimates. For example, a patient who died in January 2014 will not have any costs in the terminal phase because our study end date was December 31, 2013. SEER-Medicare files do not contain information on confirmation of payment; however, total reimbursement amounts are set by CMS and health care providers are required by law to collect the entire amount. Our regressions are intended to compare time trends and therefore do not contain additional clinical covariates that may explain the variability in costs. Lastly, our study lacks information on newer pancreatic treatment regimens, such as FOLFIRINOX, because we do not have access to claims for patients diagnosed after December 2011.

In conclusion, our study provides greater detail about the economic burden of pancreatic cancer than has been previously published, highlighting the differences in monthly cost by stage of disease, treatment modality, and treatment phase. Perhaps most notably, pancreatic cancer care costs were estimated to increase during the last 3 months of life. These cost estimates can serve as important foundational data for healthcare systems and cancer control policy leaders amid efforts to guide resource allocation for cancer care and research in the future. They can be used in cost-effectiveness analyses to compare current and newer treatment modalities, which can inform practicing clinicians and health policy makers on which treatments are most cost-effective options for the health care system.

Acknowledgments

This study used the linked SEER-Medicare database. The interpretation and reporting of these data are the sole responsibility of the authors. The authors acknowledge the efforts of the National Cancer Institute; the Office of Research, Development, and Information, at the Centers for Medicare and Medicaid Services; Information Management Services (IMS), Inc.; and the Surveillance, Epidemiology, and End Results (SEER) Program tumor registries in the creation of the SEER-Medicare database.

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