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Costs and Trends in Pancreatic Cancer Treatment

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Abstract

BACKGROUND—Pancreatic cancer poses a substantial morbidity and mortality burden in the United States, and predominantly affects older adults. The objective of this study was to estimate the direct medical costs of pancreatic cancer treatment in a population-based cohort of Medicare beneficiaries, and the contribution of different treatment modalities and health care services to the total cost of care and trends in costs over time.

METHODS—In the linked Surveillance, Epidemiology, and End Results (SEER)-Medicare database, pancreatic cancer patients were identified who were aged 66 years or older and who were diagnosed from 2000 to 2007. Total direct medical costs were estimated from Medicare payments overall and within categories of care. Costs attributable to pancreatic cancer were estimated by subtracting the costs of medical care in a matched cohort of cancer-free beneficiaries.

RESULTS—A total of 15,037 patients were identified, of whom 97% were observed from diagnosis until death. Mean total direct medical costs were \$65,500. Mean total costs were greater for patients with resectable locoregional disease (\$134,700) than for those with unresectable locoregional or distant disease (\$65,300 and \$49,000, respectively). Hospitalizations and cancer-directed procedures collectively accounted for the largest fraction of health care costs. The total cost of care appeared to increase slightly over the study period ($P = .05$). The mean costs attributable to pancreatic cancer were \$61,700.

CONCLUSIONS—Despite poor prognosis and short survival, the economic burden of pancreatic cancer in the elderly is substantial. Demographic trends, greater use of targeted therapies, and possible implementation of screening strategies are likely to impact treatment patterns and costs in the future.

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CONFLICT OF INTEREST DISCLOSURE

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Keywords

pancreas cancer; adenocarcinoma; treatment; cost; Surveillance; Epidemiology; and End Results; Medicare; health care services

INTRODUCTION

Pancreatic cancer is the fourth leading cause of cancer-related mortality in the United States.¹ Surgery is the only potentially curative option, but fewer than 20% of patients are candidates for resection.^{1,2} Palliative chemotherapy and radiation therapy produce modest improvements in survival, but sustained response rates are low, and attempts to improve outcomes in unresectable patients have been only modestly successful.³⁻⁵

In addition to the morbidity and mortality burden, the costs of treating pancreatic cancer are high and increasing.⁶⁻¹¹ More than 70% of cases are diagnosed in patients aged 65 years and older.¹² Thus, in the United States, the Medicare program pays for a substantial fraction of associated costs. Prior estimates of the costs of treating pancreatic cancer in Medicare beneficiaries have not been reported at a patient level, and population level estimates are now outdated.⁶ Our objectives were to estimate the direct medical costs of pancreatic cancer treatment in older Americans; to evaluate the contribution of specific treatment modalities and health care services to the total cost of care; and to examine trends in costs over time.

MATERIALS AND METHODS

Data Source

This retrospective, population-based cohort study was conducted using the Surveillance, Epidemiology, and End Results registries linked to Medicare claims data set (SEER-Medicare). The SEER program, sponsored by the National Cancer Institute, is a consortium of cancer registries in selected states and geographic areas covering approximately 28% of the US population.¹³ The SEER registries collect information on demographic characteristics, site and extent of disease, clinical and pathological stage, and first course of cancer-directed therapy, with active follow-up for date and cause of death. Medicare is the primary health insurer for 97% of the US population aged 65 years and older, covering inpatient hospital care (Part A) and outpatient care and physician services (Part B). The SEER-Medicare files were used in accordance with a data-use agreement between National Cancer Institute and Centers for Medicare & Medicaid Services, and the study was approved by the institutional review board at Memorial Sloan-Kettering Cancer Center.

Study Cohort

We identified Medicare beneficiaries aged 66 years or older with a pathologically confirmed primary diagnosis of pancreatic adenocarcinoma (*International Classification of Diseases for Oncology, Third Edition* site codes C25.0–C25.3, C25.7–C25.9), from January 1, 2000, through December 31, 2007. Beneficiaries aged 66 and older were included to ensure a full year of Medicare claims prior to diagnosis for identifying comorbid conditions. We excluded patients with neuroendocrine tumors, tumors in situ, and those diagnosed only at the time of

death. We also excluded individuals who were enrolled in a Medicare managed care plan and those who did not have continuous coverage with both Parts A and B of Medicare from at least 1 year prior to diagnosis through death or end of follow-up, because these beneficiaries would not have complete claims for the estimation of comorbidity and identification of treatment.

Covariates

Demographic characteristics available in the SEER data set included age, race, sex, geographic location, and marital status. Census tract median income, categorized in quartiles, was used as a measure of socioeconomic status, in the absence of individual-level information. Clinical covariates included tumor location within the pancreas and SEER historic stage. Localized and regional disease were combined as locoregional, but then distinguished on the basis of the resectability of their disease. Patients with locoregional disease who had a claim for a surgical procedure with potentially curative intent were classified as resectable, and all others were classified as unresectable, consistent with prior studies.^{14,15} Comorbidity was estimated using the Charlson comorbidity index, based on Medicare claims in the year prior to pancreatic cancer diagnosis.^{16,17}

Direct Medical Costs

Costs were defined as the amount reimbursed by Medicare. These were actual payments derived from reimbursement formulas that are intended to reflect the average resource utilization for each good and service.^{13,18–20} Two separate endpoints were estimated: direct medical costs, expressed as total and monthly costs, and costs attributable to pancreatic cancer, a component of total direct medical costs.

Total direct medical costs were estimated from all Medicare claims between time of diagnosis and time of death or end of follow-up. Mean monthly costs were total direct medical costs divided by the number of months patients were alive. In addition to overall total and mean monthly costs, we also estimated total and monthly costs within mutually exclusive categories of care. Cancer-directed procedure costs included Medicare payments for pancreatic resections and biliary drainage procedures. Chemotherapy and radiotherapy costs included Medicare payments for chemotherapy administration, specific chemotherapeutic agents, radiation therapy planning, and administration. Inpatient and hospice care costs included Medicare payments for all hospitalizations and hospice care, respectively. "Other" costs were defined as any additional care reimbursed by Medicare and included Medicare payments for outpatient services unrelated to chemotherapy or radiation therapy, home health care, and durable medical equipment.

In order to estimate costs attributable to pancreatic cancer, costs in a matched group of cancer-free Medicare beneficiaries were subtracted from the costs in the cancer cohort. Cancer-free beneficiaries were matched 1:1 by sex, race, year of birth, and SEER registry to each pancreatic cancer case. The average monthly cost of medical care for each cancer-free beneficiary was calculated based on the 12 months of claims in the calendar year of their matched case's cancer diagnosis. This average monthly cost was then multiplied by the number of months the matched case was alive. Costs attributable to pancreatic cancer were

the total costs of care for each case minus his or her matched cancer-free beneficiary's medical care costs over the same survival duration. If more than one match was available, a single control was selected at random. Cancer-free matches faced the same exclusion criteria as cases with respect to Medicare enrollment and HMO (health maintenance organization) participation. In addition, eligible controls were required to live at least as long as their matched case.

All costs are reported in 2009 US dollars. We used the Hospital Wage Index²¹ and the Medicare Economic Index²² to adjust payments for inpatient and outpatient services, respectively, for inflation. We also adjusted for geographic price variability using the Acute Inpatient Prospective Payment System Wage Index^{23,24} for inpatient services and the Medicare Geographic Practice Cost Index²⁵ for outpatient services.

Statistical Analysis

Mean total direct medical costs and costs by category were estimated for the entire cohort by stage at diagnosis. All cost estimates are presented rounded to the nearest \$100. Survival was estimated using Kaplan-Meier methods.²⁶ Trends over time were evaluated using linear regression models with year of diagnosis as the independent variable and costs as the dependent variable.¹⁸ For patients whose treatment costs spanned more than 1 calendar year, all costs were assigned to the year of diagnosis.¹⁸ Statistical analyses were performed using SAS software (version 9.2; SAS Inc, Cary, NC).

RESULTS

Cohort Characteristics

The study cohort included 15,037 patients diagnosed with pancreatic adenocarcinoma between 2000 and 2007. Most patients (58%) were diagnosed with distant disease. Patients diagnosed with locoregional disease were somewhat more likely to be female and to have cancers in the head of the pancreas. Patients with resectable locoregional disease were younger and healthier than those with unresectable locoregional or distant disease. They were also more likely to be married, white, and reside in urban areas and in census tracts with greater median income (Table 1).

For the entire cohort, median overall survival was 4.1 months (95% CI = 4.0, 4.2 months). Median survival was 15.2 months (95% CI = 14.6, 16.0 months) for resectable locoregional disease, 5.8 months (95% CI = 5.6, 6.0 months) for unresectable locoregional disease, and 2.6 months (95% CI = 2.5, 2.7 months) for distant disease (Fig. 1). The proportions of patients alive at 1 and 5 years were 20% and 2.3%, respectively, and less than 3% of patients were alive at the end of study period.

Direct Medical Costs

Mean total direct medical costs for the cohort were \$65,500 (standard deviation [SD], \$65,400). Total costs were highest for resectable locoregional disease (\$134,700; SD, \$90,300) and lowest for distant disease (\$49,000; SD, \$48,800). Costs for unresectable locoregional disease were \$65,300 (SD, \$58,100). Mean monthly costs were \$22,300 (SD,

\$56,100). Patients diagnosed with distant disease incurred the greatest monthly costs (\$25,300; SD, \$57,900), followed by resectable (\$19,200; SD, \$62,800) and unresectable locoregional disease (\$17,500; SD, \$48,000).

The relative contribution of each health care service category is presented in Table 2. Hospitalizations accounted for the largest fraction of health care costs overall and for patients with unresectable locoregional and distant disease. For patients with resectable locoregional disease, cancer-directed procedures accounted for the largest percentage of costs. Hospice care accounted for the smallest percentage of total costs and was lowest for resectable locoregional patients. The proportion of costs attributable to chemotherapy and radiation therapy was also lowest for resectable locoregional disease, whereas the proportion of costs attributable to “other” health care services was consistent across stages.

Over the study period, the cost of treating pancreatic cancer appeared to increase, but this trend was only marginally significant (parameter estimate of \$692, 95% CI = $-\$0.42$ to $\$1384$; $P = .05$) (Fig. 2). The costs of “other” health care services increased (parameter estimate of $\$1090$, 95% CI = $\$843$ to $\$1337$, $P < .001$) (Fig. 3), primarily due to a rise in costs associated with outpatient care and physician services. Costs of cancer-directed procedures decreased during the study period (parameter estimate of $-\$616$, 95% CI = $-\$854$ to $-\$379$, $P < .001$). Costs associated with chemotherapy and radiation therapy, hospitalizations unrelated to pancreatic cancer surgery, and hospice care did not change significantly.

Mean incremental medical costs (costs attributable to pancreatic cancer) were $\$61,700$ (SD, $\$65,100$) (Fig. 4). The lowest incremental costs were incurred by those with distant disease ($\$46,600$; SD, $\$48,200$), and the highest incremental costs were incurred by those with resectable locoregional disease ($\$126,200$; SD, $\$94,900$). For unresectable locoregional disease, incremental costs were $\$61,300$ (SD, $\$58,000$). Costs of care not attributable to pancreatic cancer accounted for approximately 6% of total costs, and this proportion was fairly consistent across stages.

DISCUSSION

More than a decade ago, investigators noted a paucity of literature on the economics of pancreatic cancer, concluding that future studies should take advantage of the administrative data from large populations.¹⁰ Since then, few subsequent studies have been published, and most research in this area remains focused on the cost or cost-effectiveness of specific interventions, such as surgical procedures,^{27–35} chemotherapy, and radiation therapy.^{36–40} Using a large, population-based data set, we estimated total direct medical costs of more than $\$65,000$ per pancreatic cancer patient, and we observed a marginal increase in costs over time.

Our estimate of the total direct medical cost of care for pancreatic cancer patients ranks at the lower end of the range of cost estimates reported for other cancers in the Medicare population.¹⁹ However, survival for other cancers, such as breast, prostate, colorectal,

bladder, and even lung, is typically much longer.¹⁹ Considering their limited life expectancy, pancreatic cancer patients incur substantial costs in a very short time period.

A prior payer-based study of the economic impact of pancreatic cancer in working-age adults found incremental monthly and lifetime costs of \$7279 and \$40,233, respectively.⁷ An analysis conducted from a hospital perspective reported 6-month and lifetime costs of \$37,327 and \$48,803 in patients with a median survival of 7 months.⁸ It is not surprising that our estimates were higher, because we included all costs reimbursed by Medicare and studied exclusively an older population.⁹

Within specific categories of care, hospitalizations were a substantial driver of costs. These results are consistent with previous studies of pancreatic cancer^{7-9,41,42} and other cancers.^{18,19,43} The proportion of costs attributable to inpatient care unrelated to cancer-directed procedures was highest for those diagnosed with distant disease, possibly due to extensive hospitalization over a limited time period.^{8,41,44} In addition, inpatient costs were relatively stable over time, although we did observe an increase in costs of outpatient care and physician services. In recent years, across a range of cancer types and stages of disease, treatment costs have shifted away from the inpatient setting toward outpatient care.⁴⁵

Not surprisingly, cancer-directed procedure costs were highest for patients with resectable locoregional disease and accounted for the largest proportion of costs among this group. Prior reports of the underutilization of surgery in potentially resectable patients, accompanied by our finding that white patients and those residing in urban and more affluent areas were more likely to have a resection, suggest potentially higher costs if all eligible candidates received a resection.^{46,47} Our estimate of costs associated with cancer-directed procedures also included the costs of endoscopically placed biliary and enteral stents. In recent years, these interventions have emerged as less expensive alternatives to palliative surgery for malignant biliary and intestinal obstruction, respectively, but a lack of randomization and variations in research methods have impaired cost comparisons.^{31,34,48,49} It is possible that, because we did not note any significant change in the cost of resectable locoregional disease over the study period, a trend toward the performance of less costly stenting may be contributing to lower costs for cancer-directed procedures.

The proportion of costs attributable to hospice use was lower for patients with resectable locoregional disease than for those with unresectable locoregional or distant disease. A recent study evaluating end-of-life care in Medicare beneficiaries dying of pancreatic cancer found that patients with locoregional disease who had a surgical resection were less likely to enroll in hospice before death and had a lower odds of hospice use.⁴⁴ This study also reported that hospice use increased over time, but early enrollment decreased, which may explain the consistency in hospice costs we observed over the study period.⁴⁴ Given the low proportion of overall costs attributable to hospice care, our findings suggest an underutilization of this service among the pancreatic cancer population. A previous study reported that 43% of patients do not use these services,⁴⁴ even though patients who receive early palliative care have been shown to live longer than those who delay treatment.⁵⁰

Chemotherapy and radiation therapy accounted for a greater proportion of costs in patients with unresectable locoregional and distant disease compared with those who had resectable locoregional disease. Recent evidence suggests that patients presenting with distant or unresectable locoregional pancreatic cancer are more likely to receive chemotherapy within the last month of life.⁴⁴ Average chemotherapy costs were highest in patients with resectable locoregional disease, who may receive chemotherapy in the adjuvant setting and later with palliative intent at the time of disease progression. Although there has been a steady increase in adjuvant chemotherapy use and a growing interest in neoadjuvant therapy for the resected population, we did not observe any significant increase in the cost of chemotherapy and radiation therapy over the study period.^{51,52}

Several limitations should be noted. First, we defined pancreatic cancer-related costs as the difference between total costs among pancreatic cancer patients and a cohort of patients who were cancer-free. This approach provides an estimate of the costs attributable to pancreatic cancer, but it does not assess which health services were specifically related to the disease. Thus, if patients with pancreatic cancer are using general, non-cancer specific medical care to a greater extent than patients without cancer, costs of pancreatic cancer care may be overestimated.

Second, the costs of orally administered prescription drugs such as erlotinib were not captured in our analysis, because these costs were not covered by Medicare prior to 2007. Erlotinib was approved by the US Food and Drug Administration in November 2005 for the treatment, in combination with gemcitabine, of patients with locally advanced, unresectable, or metastatic pancreatic carcinoma. The average incremental cost of adding erlotinib to gemcitabine is estimated at \$15,194 per patient.³⁸ Thus, our findings likely underestimate the total direct medical costs of care in the most contemporary cohorts of patients with newly diagnosed pancreatic cancer.

Third, our findings only apply to older pancreatic cancer patients covered by Medicare. Costs may differ in a younger population, who comprise approximately 30% of all pancreatic cancer patients, due to differences in their age and insurance coverage. Finally, although Medicare payment amounts were used to reflect the true resource costs of care, our analysis excluded out-of-pocket costs borne directly by patients.

Conclusions

Our analysis of this older, population-based cohort suggests that, given the short survival time, the economic burden of pancreatic cancer is substantial. Hospital services, including cancer-directed procedures and other inpatient care, accounted for the largest proportion of costs per patient. Average total costs increased marginally between 2000 and 2007, perhaps reflecting the minimal progress that has been made in treating this disease. Changes in treatment patterns and increasing costs are likely to be more substantial in the future as a greater understanding of the biology of pancreatic cancer leads to the dissemination of novel therapies and screening techniques.^{53,54} Any therapeutic advances that can meaningfully extend survival or improve quality of life will be hailed as major achievements in this disease. However, as the total economic burden for the treatment of pancreatic cancer

increases with the aging of the population, it will be essential to evaluate the value of expensive new therapies in relation to their expected health benefit.

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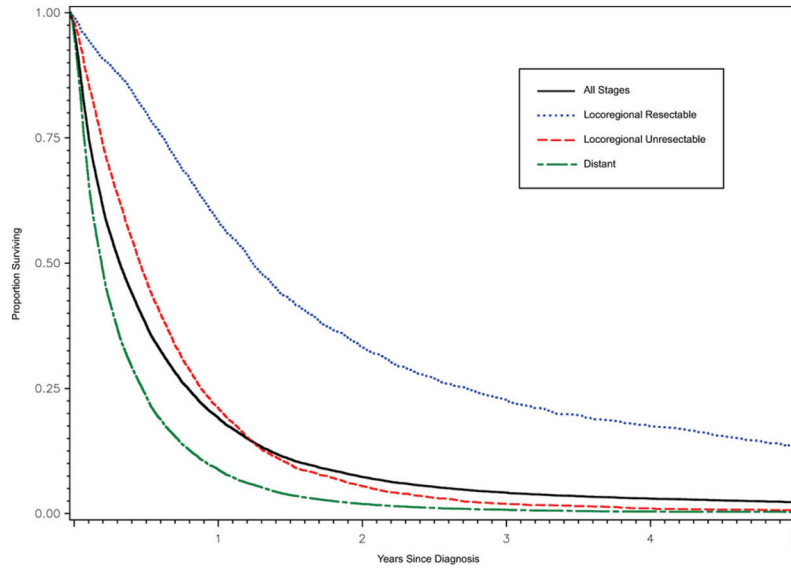


Figure 1.
Overall survival is shown by stage at diagnosis.

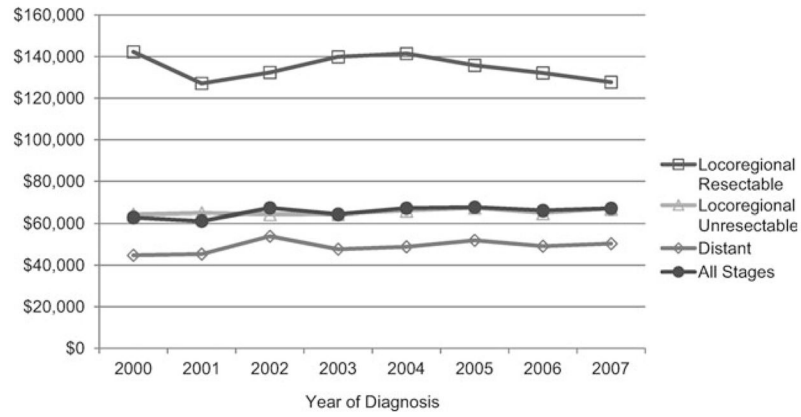


Figure 2. Trends in mean total costs are shown by stage at diagnosis. Costs were estimated from Medicare reimbursement for all health services, adjusted for inflation and geographic variability. There appeared to be a marginal increase in mean total costs for the overall cohort between 2000 and 2007 ($P = .05$).

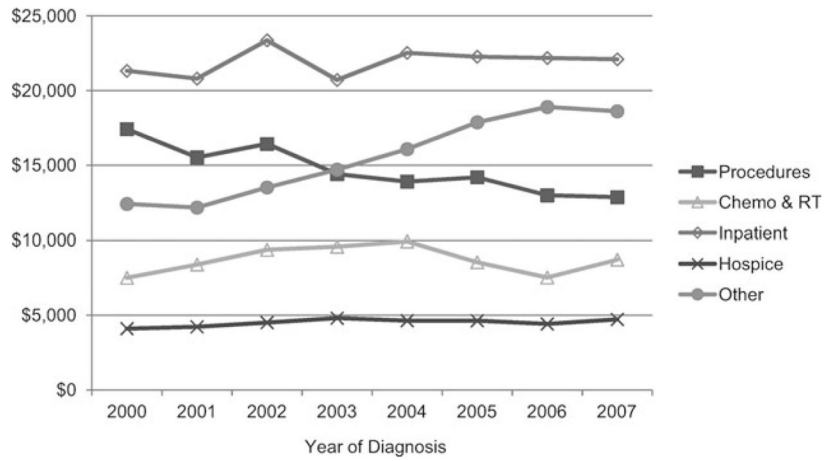


Figure 3. Trends in mean costs are shown by category. Costs were estimated from Medicare reimbursement for health services within each category, adjusted for inflation and geographic variability. “Other” costs increased between 2000 and 2007 ($P < .001$). Procedure costs decreased ($P < .001$). Chemo indicates chemotherapy; RT, radiation therapy.

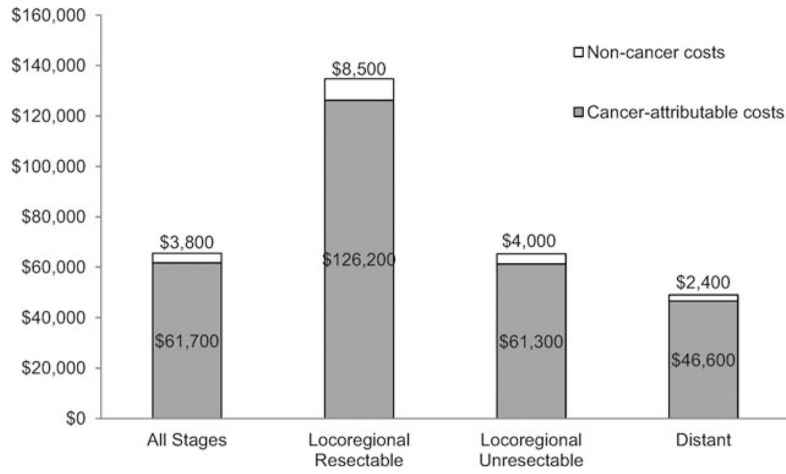


Figure 4. Mean total and incremental costs are shown by stage at diagnosis. Costs were estimated from Medicare reimbursement for health services within each category, adjusted for inflation and geographic variability. Non-cancer costs were estimated from cancer-free Medicare beneficiaries matched 1:1 by sex, race, year of birth, and Surveillance, Epidemiology, and End Results (SEER) registry to each pancreatic cancer case. The mean monthly costs of medical care for each cancer-free beneficiary was based on the 12 months of claims in the year of diagnosis of their matched case. This average monthly cost was then multiplied by the number of months the matched case was alive. Cancer-attributable costs were the total costs in pancreatic cancer cases minus total costs in the matched cancer-free cohort over the same survival duration.

Table 1

Characteristics of the Cohort by Pancreatic Cancer Stage at Diagnosis

Characteristic	All Patients		Locoregional Resectable		Locoregional Unresectable		Distant		P
	No.	%	No.	%	No.	%	No.	%	
Total	15,037	-	2,078	14%	4,234	28%	8,725	58%	<.0001
Age at diagnosis, y									
66-69	2,576	17%	464	22%	566	13%	1,546	18%	
70-74	3,807	25%	629	30%	933	22%	2,245	26%	
75-79	4,087	27%	594	29%	1,137	27%	2,356	27%	
80-84	2,926	19%	309	15%	914	22%	1,703	20%	
85+	1,641	11%	82	4%	684	16%	875	10%	
Sex									
Male	6,820	45%	889	43%	1,804	43%	4,127	47%	<.0001
Female	8,217	55%	1,189	57%	2,430	57%	4,598	53%	
Race									
White	12,838	85%	1,875	90%	3,550	84%	7,413	85%	
Black	1,437	10%	114	5%	438	10%	885	10%	
Other	762	5%	89	4%	246	6%	427	5%	<.0001
Census tract median income									
1st quartile	3,760	25%	403	19%	1,140	27%	2,217	25%	<.0001
2nd quartile	3,769	25%	499	24%	1,074	25%	2,196	25%	
3rd quartile	3,758	25%	541	26%	1,049	25%	2,168	25%	
4th quartile	3,750	25%	635	31%	971	23%	2,144	25%	
Urban-rural residence									
Metro	12,990	86%	1,830	88%	3,625	86%	7,535	86%	<.05
Non-metro	2,047	14%	248	12%	609	14%	1,190	14%	
Region									
Northeast	3,963	26%	614	30%	1,019	24%	2,330	27%	<.0001
South	2,605	17%	379	18%	745	18%	1,481	17%	
Midwest	2,195	15%	259	12%	620	15%	1,316	15%	
West	6,274	42%	826	40%	1,850	44%	3,598	41%	<.0001
Married									

Characteristic	All Patients		Locoregional Resectable		Locoregional Unresectable		Distant		P
	No.	%	No.	%	No.	%	No.	%	
Yes	8,137	54%	1,277	61%	2,143	51%	4,717	54%	
No	6,421	43%	741	36%	1,945	46%	3,735	43%	
Unknown	479	3%	60	3%	146	3%	273	3%	
Charlson comorbidity score									
0	7,928	53%	1,184	57%	2,177	51%	4,567	52%	<.0001
1	4,209	28%	597	29%	1,175	28%	2,437	28%	
2+	2,900	19%	297	14%	882	21%	1,721	20%	
Site									
Head	7,779	52%	1,558	75%	2,919	69%	3,302	38%	<.0001
Body/tail	3,278	22%	280	13%	525	12%	2,473	28%	
Duct/other	3,980	26%	240	12%	790	19%	2,950	34%	

Direct Medical Costs of Care by Category and Pancreatic Cancer Stage at Diagnosis

Table 2

Cost	All Stages (N = 15,037)		Locoregional Resectable (N = 2078)		Locoregional Unresectable (N = 4234)		Distant (N = 8725)	
	Mean	% Cost	Mean	% Cost	Mean	% Cost	Mean	% Cost
Total direct cost	\$65,500	100%	\$134,700	100%	\$65,300	100%	\$49,000	100%
Procedures	\$14,700	22%	\$51,000	38%	\$12,600	19%	\$7,000	14%
Chemo/radiotherapy	\$8,700	13%	\$13,600	10%	\$9,200	14%	\$7,300	15%
Inpatient	\$21,900	33%	\$34,100	25%	\$21,600	33%	\$19,200	39%
Hospice	\$4,500	7%	\$4,000	3%	\$6,300	10%	\$3,800	8%
Other	\$15,700	24%	\$32,000	24%	\$15,600	24%	\$11,700	24%
Average monthly cost	\$22,300	100%	\$19,200	100%	\$17,500	100%	\$25,300	100%
Procedures	\$5,100	23%	\$12,300	64%	\$4,800	27%	\$3,600	14%
Chemo/radiotherapy	\$1,400	6%	\$700	4%	\$1,100	6%	\$1,800	7%
Inpatient	\$10,300	46%	\$3,000	16%	\$7,000	40%	\$13,500	53%
Hospice	\$1,300	6%	\$300	2%	\$1,300	7%	\$1,500	6%
Other	\$4,200	19%	\$2,900	15%	\$3,300	19%	\$4,900	19%