

# Cost-effectiveness of Treatment Strategies for Pancreatic Head Adenocarcinoma and Potential Opportunities for Improvement

Daniel E. Abbott, MD<sup>1</sup>, Ryan P. Merkow, MD<sup>2,7</sup>, Scott B. Cantor, PhD<sup>3</sup>, Jason B. Fleming, MD<sup>4</sup>, Gauri R. Varadhachary, MD, MBBS<sup>5</sup>, Christopher Crane, MD<sup>6</sup>, David J. Bentrem, MD<sup>2</sup>, and Karl Y. Bilimoria, MD, MS<sup>2,7</sup>

<sup>1</sup>Department of Surgery, University of Cincinnati, Cincinnati, OH; <sup>2</sup>Surgical Outcomes and Quality Improvement Center, Department of Surgery, and Northwestern Institute for Comparative Effectiveness Research in Oncology, Robert H. Lurie Comprehensive Cancer Center, Feinberg School of Medicine, Northwestern University, Chicago, IL; <sup>3</sup>Department of Biostatistics, The University of Texas MD Anderson Cancer Center, Houston, TX; <sup>4</sup>Department of Surgical Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX; <sup>5</sup>Department of Gastrointestinal Medical Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX; <sup>6</sup>Department of Radiation Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX; <sup>7</sup>Division of Research and Optimal Patient Care, American College of Surgeons, Chicago, IL

## ABSTRACT

**Background.** Generally dismal outcomes have led to a nihilistic attitude toward treating pancreatic cancer, while fiscal constraints have increased scrutiny of treatments costs. Our objective was to compare the cost-effectiveness of various treatment strategies for resectable pancreatic head adenocarcinoma, and to identify opportunities for improved cost effectiveness.

**Methods.** A decision model compared 6 strategies: no treatment, radiotherapy only, chemotherapy only, chemotherapy plus radiotherapy, surgery alone, and surgery plus adjuvant therapy. Outcomes and probabilities were identified using the National Cancer Data Base, the American Cancer Society National Surgical Quality Improvement Program, and the literature. Costs were estimated using Medicare payment. Incremental cost-effectiveness ratios (ICERs) were calculated, and sensitivity analyses were performed by varying potentially modifiable parameters of the model. Survival was reported in quality-adjusted life-months (QALMs).

**Results.** Surgery plus adjuvant therapy, chemotherapy alone, and no treatment were the only viable strategies in terms of cost effectiveness. Surgery plus adjuvant therapy versus no treatment demonstrated an incremental cost-effectiveness ratio (ICER) of \$7,663/QALM.

Theoretically increasing survival in node-negative, margin-negative patients from 14 to 22 QALMs produced the largest reduction in the ICER for surgery plus adjuvant therapy compared to no treatment (\$6,386/QALM), whereas reducing the perioperative mortality from 3 to 1 % had only a marginal effect. The ICER was significantly lower for high-performing centers (\$5,991/QALM) than for low-performing centers (\$9,144/QALM).

**Conclusions.** Surgery plus adjuvant therapy for resectable pancreatic head adenocarcinoma extends survival, but at considerable expense. Significant cost reductions could be realized by improving treatment outcomes to levels of high-performing centers and development of increasingly effective adjuvant therapies.

Pancreatic cancer often presents at an advanced stage, and survival is generally poor even when resectable at diagnosis. Surgery for pancreatic cancer has historically been associated with considerable morbidity and mortality, while effective adjuvant systemic therapies for pancreatic adenocarcinoma have been elusive. These factors have led to an often pessimistic and nihilistic approach to treating pancreatic cancer.<sup>1,2</sup>

Currently, it is generally thought that multimodality therapy for resectable pancreas cancer offers the best hope for meaningful long-term survival.<sup>3–6</sup> Surgical resection is the only potentially curative intervention, though adjuvant (or neoadjuvant) chemotherapy and/or radiotherapy may extend survival.<sup>7–9</sup> However, even with appropriate use of these treatment strategies, the improvement in survival can

be marginal, often measured in months. Furthermore, poor quality of life (QOL) resulting from disease- and treatment-related factors may mitigate the perceived benefits associated with any form of treatment. Additionally, the financial costs associated with treating pancreas cancer are significant, particularly with a multimodality approach. As health care expenses in the United States continue to rise, there is increased scrutiny of how health care is delivered.<sup>10–12</sup>

Although some investigators have attempted to quantify the financial and QOL ramifications of treating pancreatic cancer, to our knowledge no studies have compared the costs and outcomes associated with various treatment strategies for pancreas cancer.<sup>13–16</sup> Because practice patterns vary considerably between, and even within, institutions that treat pancreas cancer, an excellent opportunity exists to identify the cost-effectiveness of different treatment regimens. Furthermore, the effect of high-performing and low-performing centers on cost of care is an important and potentially modifiable factor that should be incorporated into medical decision making. The aims of this study were to (1) examine the cost effectiveness of treating pancreatic cancer with a multimodality approach versus other treatment strategies and (2) determine how potentially modifiable factors could impact the cost effectiveness of treating pancreatic cancer.

## METHODS

### *Decision Analytic Model*

We constructed a decision tree (TreeAge Pro2011, TreeAge Software, Williamstown, MA) to compare 6 treatment strategies for radiographically resectable pancreatic head adenocarcinoma: no treatment ( $n = 15,429$ ), radiotherapy alone ( $n = 1,187$ ), chemotherapy alone ( $n = 2,234$ ), chemotherapy plus radiotherapy ( $n = 6,249$ ), surgery alone, and surgery plus adjuvant therapy ( $n = 2,127$  for patients undergoing resection) (Fig. 1). Neoadjuvant chemoradiation followed by surgery as a seventh strategy is currently under investigation and not included. Patients with locally advanced or metastatic pancreas cancer were not considered in the analysis. The 6 treatment strategies incorporated treatment probabilities, perioperative outcomes and cost. Within the surgical strategies, patients were either found to have unresectable tumors in the operating room, completed resection and survived, or died in the perioperative period. Patients who underwent a resection successfully and survived could experience: no complication, a minor complication or a major complication. Rates of adjuvant chemotherapy or radiotherapy populated the probabilities of terminal nodes of the surgery plus adjuvant therapy cohort.

Effectiveness was defined in terms of quality-adjusted life-months (QALMs). Cost-effectiveness analysis was used

to report cost per unit of survival in terms of incremental cost-effectiveness ratios (ICERs), calculated as the difference in costs divided by the difference in effectiveness between a given strategy and the next most cost-effective alternative. QOL adjustments were made according to the following published QOL indices: 0.66, 0.68, and 0.65 for surgery, chemotherapy/radiotherapy, and no treatment (same as preoperative QOL), respectively.<sup>13,16</sup>

### *Clinical Interventions and Treatment Outcomes*

Perioperative outcome probabilities and survival for the 6 strategies were based on the most recent data available from the American College of Surgeons National Cancer Data Base (NCDB, survival data from 1990 to 1999, utilization and outcome data from 2003–2005), the American College of Surgeons National Surgical Quality Improvement Program (2005–2009), and published literature (Table 1).<sup>1,17–22</sup>

Complications were defined as “minor” if no invasive intervention was required and “major” if an invasive intervention and/or a significantly extended hospital stay was required. Minor complications included wound infection, deep-venous thrombosis/pulmonary embolism, pneumonia, grade A and B pancreatic fistulas, and delayed gastric emptying. Major complications included reoperation, drainage of an intra-abdominal abscess and grade C pancreatic fistula.

Probabilities of chemotherapy and/or radiotherapy administration for patients discovered at operation to have unresectable tumors were defined as the same as the probabilities for patients who did not undergo surgery at all. On the basis of data from the literature and unpublished data from The University of Texas MD Anderson Cancer Center, rates of biliary stenting for operative patients and nonoperative patients were defined as 67 and 89 %, respectively.

Chemotherapy was included in the analysis as adjuvant therapy in the surgical cohort and as single-modality treatment in the nonsurgical cohort. Adjuvant chemotherapy was defined as gemcitabine 1,000 mg/m<sup>2</sup> 3 infusions per month for 6 months.<sup>4</sup> Two alternate adjuvant chemotherapy regimens, included in the sensitivity analysis in the surgery plus adjuvant therapy cohort, were: (1) gemcitabine 1,000 mg/m<sup>2</sup> 3 times per month for 1 month, followed by capecitabine 800 mg/m<sup>2</sup> b.i.d. for 28 days (with concurrent radiotherapy) followed by gemcitabine 1,000 mg/m<sup>2</sup> 3 times per month for 4 months, and (2) gemcitabine 1,000 mg/m<sup>2</sup> 3 times per month concurrent with erlotinib 100 mg daily for 6 months.<sup>23,24</sup> Although the gemcitabine/erlotinib regimen has been studied in the treatment of metastatic pancreas cancer, not as adjuvant therapy, this was included as an accepted regimen that is substantially more costly. Chemotherapy in the nonsurgical cohort was defined as gemcitabine 600 mg/m<sup>2</sup> concurrent with

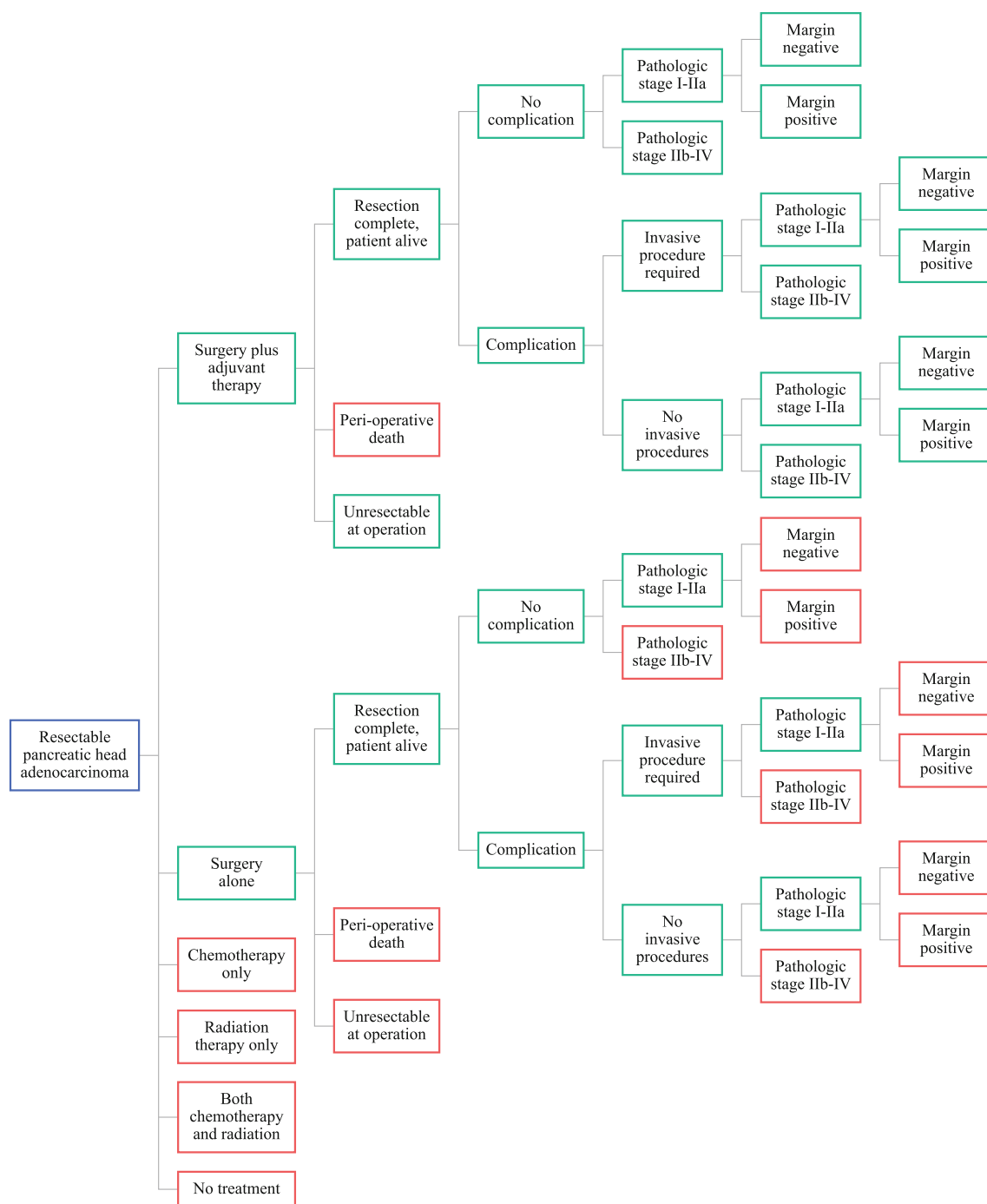


**FIG. 1** Decision analytic tree for 6-strategy model; terminal nodes in surgery plus adjuvant therapy strategy representing adjuvant radiotherapy, adjuvant chemotherapy, and both adjuvant chemotherapy and radiotherapy not shown due to size

cisplatin 30 mg/m<sup>2</sup>, both 3 times per month for 4 months. This was chosen on the basis of National Comprehensive Cancer Network guidelines outlining the use of gemcitabine and cisplatin for treatment of locally advanced pancreas cancer (analogous to unresected disease).<sup>25</sup> The regimens were based on a body surface area of 1.8 m<sup>2</sup>.

Radiotherapy was defined as the administration of 50.4 Gy of external-beam radiotherapy in 28 fractions.

This regimen was applied both for adjuvant therapy and for patients who did not undergo surgery.

#### Cost Data

This study was performed from a societal/payer perspective, such that cost is synonymous with payment or reimbursement, not hospital charges. Costs were based on

**TABLE 1** Perioperative outcomes and their probabilities used to populate surgical strategies (surgery alone and surgery plus adjuvant therapy)

| Characteristic                                                   | Probability | Source |
|------------------------------------------------------------------|-------------|--------|
| Outcome                                                          |             |        |
| Taken to surgery, resection complete, patient lives              | 0.80        | 17,18  |
| Tumor found to be unresectable at operation                      | 0.17        | 17     |
| Perioperative death                                              | 0.03        | 18     |
| Preoperative biliary stent placement                             |             | 19     |
| No                                                               | 0.33        |        |
| Yes                                                              | 0.67        |        |
| Complication after surgery                                       |             | 18,19  |
| No                                                               | 0.49        |        |
| Yes                                                              | 0.51        |        |
| Complication type if complication present                        |             | 18,19  |
| Minor                                                            | 0.74        |        |
| Major                                                            | 0.26        |        |
| Final pathologic stage                                           |             | 17     |
| I–IIa                                                            | 0.35        |        |
| IIb–IV                                                           | 0.65        |        |
| Margin status for pathologic stage I–IIa                         |             | 17     |
| Negative                                                         | 0.84        |        |
| Positive                                                         | 0.16        |        |
| Major complication precludes adjuvant therapy                    |             | 17     |
| No                                                               | 0.59        |        |
| Yes                                                              | 0.41        |        |
| Treatment after tumor found to be unresectable at operation      |             | 17     |
| Chemotherapy only                                                | 0.36        |        |
| Radiotherapy only                                                | 0.1         |        |
| Both chemotherapy and radiotherapy                               | 0.54        |        |
| Treatment after surgery, pathologic stage I–IIa, margin negative |             | 17     |
| Chemotherapy only                                                | 0.19        |        |
| Radiotherapy only                                                | 0.06        |        |
| Both chemotherapy and radiotherapy                               | 0.75        |        |
| Treatment after surgery, pathologic stage I–IIa, margin positive |             | 17     |
| Chemotherapy only                                                | 0.15        |        |
| Radiotherapy only                                                | 0.09        |        |
| Both chemotherapy and radiotherapy                               | 0.76        |        |
| Treatment after surgery, pathologic stage IIb–IV                 |             | 17     |
| Chemotherapy only                                                | 0.24        |        |
| Radiation only                                                   | 0.05        |        |
| Both chemotherapy and radiotherapy                               | 0.71        |        |

NCDB National Cancer Data Base, NSQIP National Surgical Quality Improvement Program

**TABLE 2** Estimates for professional and hospital reimbursement based on Medicare reimbursement

| Intervention (CPT code)                                                                                                                                                                                                                                                   | Cost, 2011 U.S. dollars |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------|
| Intervention components                                                                                                                                                                                                                                                   |                         |
| Endoscopic biliary stent placement                                                                                                                                                                                                                                        |                         |
| Procedure (43268)                                                                                                                                                                                                                                                         | 484                     |
| Interpretation (74330)                                                                                                                                                                                                                                                    | 50                      |
| Chemotherapy                                                                                                                                                                                                                                                              |                         |
| Consultation (99245)                                                                                                                                                                                                                                                      | 216                     |
| Peripherally inserted central catheter (36569)                                                                                                                                                                                                                            | 259                     |
| Professional/infusion fees (96413/96415)                                                                                                                                                                                                                                  | 146/32                  |
| Gemcitabine per 200 mg (J9201)                                                                                                                                                                                                                                            | 95                      |
| Cisplatin per 10 mg (J9060)                                                                                                                                                                                                                                               | 2                       |
| Capecitabine per 500 mg (J8521)                                                                                                                                                                                                                                           | 22                      |
| Erlotinib per 100 mg                                                                                                                                                                                                                                                      | 86                      |
| Surgical intervention                                                                                                                                                                                                                                                     |                         |
| Consultation (99245)                                                                                                                                                                                                                                                      | 216                     |
| Exploratory laparotomy (49000)                                                                                                                                                                                                                                            | 759                     |
| Pancreaticoduodenectomy (48150)                                                                                                                                                                                                                                           | 3057                    |
| Anesthesia—unresectable tumor (00794—2 hours)                                                                                                                                                                                                                             | 336                     |
| Anesthesia—pancreaticoduodenectomy (00794—6 hours)                                                                                                                                                                                                                        | 673                     |
| Epidural anesthesia (64483)                                                                                                                                                                                                                                               | 240                     |
| Frozen section analysis (88331)                                                                                                                                                                                                                                           | 91                      |
| Pathology review of permanent sections (88309)                                                                                                                                                                                                                            | 342                     |
| Radiotherapy (50.4 Gy, 28 fractions)                                                                                                                                                                                                                                      |                         |
| Initial office visit (99243)                                                                                                                                                                                                                                              | 94                      |
| Treatment planning (77290, 77014, 77263, 77300 × 5, 77295)                                                                                                                                                                                                                | 3,198                   |
| Treatment (77414 × 28, 77417 × 5, 77336 × 5, 77427 × 5)                                                                                                                                                                                                                   | 8,582                   |
| Hospital reimbursement for                                                                                                                                                                                                                                                |                         |
| Unresectable tumor found in operating room (DRG 437)                                                                                                                                                                                                                      | 7,804                   |
| Uncomplicated resection (DRG 407)                                                                                                                                                                                                                                         | 23,430                  |
| Minor complication after resection (DRG 406)                                                                                                                                                                                                                              | 31,302                  |
| Major complication after resection (DRG 405)                                                                                                                                                                                                                              | 54,460                  |
| Interventions                                                                                                                                                                                                                                                             |                         |
| Adjuvant chemotherapy: gemcitabine 1000 mg/m <sup>2</sup> 3 times per month for 6 months                                                                                                                                                                                  | 19,068                  |
| Chemotherapy-alone cohort: gemcitabine 600 mg/m <sup>2</sup> concurrent with cisplatin 30 mg/m <sup>2</sup> , both 3 times per month for 4 months                                                                                                                         | 9,885                   |
| First alternate chemotherapy for sensitivity analysis: gemcitabine 1000 mg/m <sup>2</sup> 3 times per month for 1 month, followed by capecitabine 800 mg/m <sup>2</sup> b.i.d. for 28 days, followed by gemcitabine 1000 mg/m <sup>2</sup> 3 times per month for 4 months | 19,511                  |

**TABLE 2** continued

| Intervention (CPT code)                                                                                                                                            | Cost, 2011 U.S. dollars |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------|
| Second alternative chemotherapy for sensitivity analysis: Erlotinib 100 mg daily concurrent with gemcitabine 1000 mg/m <sup>2</sup> 3 times per month for 6 months | 34,571                  |
| Radiotherapy—50.4 Gy, 28 fractions                                                                                                                                 | 11,875                  |
| Surgery for unresectability determined in operating room—all professional and technical components                                                                 | 1,644                   |
| Completed resection—all professional and technical components                                                                                                      | 4,621                   |

CPT Current Procedural Terminology, DRG diagnosis-related group

Medicare payment in 2011 U.S. dollars. Technical and professional fees were based on Current Procedural Terminology codes and obtained from the Center for Medicare and Medicaid Services (Table 2).<sup>26</sup> Hospital payment was based on International Classification of Disease, 9th edition (ICD-9), procedural and diagnosis-related group (DRG) codes. A cost-to-charge ratio of 0.202 was calculated from costs and charges for DRG code 407 (uncomplicated resection) and applied to ICD-9 code 527 (radical pancreaticoduodenectomy), and this value was used for payment for uncomplicated cases. Hospital payment for cases with “minor” and “major” complications was based on the severity-refined DRGs complicating condition (CC) and major complicating condition (MCC) modifiers. Payment for codes with CC and MCC modifiers were determined by multiplying the payment for the uncomplicated ICD-9-based code by a coefficient determined by charges for CC and MCC DRGs (406 and 405, respectively). ICD-9 and DRG code payment data were obtained from the Nationwide Inpatient Sample from the Healthcare Cost and Utilization Project of the Agency for Healthcare Research and Quality.<sup>27</sup> Costs, if referenced before 2011, were adjusted for inflation by the consumer price index.

Surgical expenses for pancreaticoduodenectomy included reimbursement for an initial office visit, pancreaticoduodenectomy, anesthesia with epidural placement, and pathologic evaluation. If resection was not performed, payment for pancreaticoduodenectomy was exchanged for payment for an exploratory laparotomy. The cost of reoperation included the surgeon’s fee for an exploratory laparotomy. Chemotherapy costs were determined by payment for specific J codes and professional and infusional services. Radiotherapy costs were based on payment for the initial office visit, subsequent treatment planning and definitive treatment. Not included in the analysis were readmission after surgery, admission for complications of chemotherapy or radiotherapy, and

end-of-life care costs, such as hospice care. No discounting was required because all patients had quality-adjusted life expectancy of less than 12 months.

### Sensitivity Analyses

Sensitivity analyses were performed on the basis of variations in intervention, outcome, and reimbursement patterns. One-way sensitivity analyses included alternatives for the following surgery-associated parameters: perioperative mortality rate, complication rate, rate of tumors deemed unresectable at operation, cost of adjuvant chemotherapy, reimbursement for minor and major complications, and survival rate of patients with node-negative, margin negative resections. These results were reported with a tornado diagram, a graphical representation of the relative influence of these variables on the ICER of surgery plus adjuvant therapy versus no treatment.

To address outcomes associated with low-performing or high-performing centers, the model was populated with clinical outcomes from low-performing and high-performing centers with data obtained from the literature. The variables used for this analysis included perioperative mortality rate (0.15 for low-performing and 0.01 for high-performing), overall complication rate (0.61 for low-performing and 0.41 for high-performing), “unresectable at operation” rate (0.31 for low performing and 0.09 for high-performing), margin positivity rate in patients with pathologic stage I–IIa disease (0.36 for low-performing and 0.14 for high-performing), and median survival in patients with node-negative, margin-negative resections (14 months for low-performing and 22 months for high-performing; QOL adjusted).<sup>18,19,21,28,29</sup>

## RESULTS

### Base Case

The 6 treatment strategies with their associated costs, effectiveness and ICERs are shown in Table 3 and Fig. 2. The least costly strategy was no treatment, at a total cost of \$692. This reflected the cost of medical oncology consultation and endoscopic biliary stent placement, if applicable, and was associated with a median survival of 2.7 QALMs. When all possible permutations of additional treatment modalities were considered, both cost and effectiveness of treatment increased, as expected. As incremental cost and effectiveness were considered, radiotherapy alone, chemotherapy plus radiotherapy, and surgery alone were dominated (more costly and/or less effective than at least 1 other strategy). The ICER for chemotherapy alone compared to no treatment was \$3,022 per QALM. The ICER

**TABLE 3** Cost-effectiveness of treatment strategies for resectable pancreatic head adenocarcinoma

| Strategy                          | Cost, 2011<br>U.S. dollars | Effectiveness<br>QALMs | ICER               |
|-----------------------------------|----------------------------|------------------------|--------------------|
| No treatment                      | 692                        | 2.7                    | –                  |
| Radiotherapy alone                | 12,351                     | 4.8                    | Dominated          |
| Chemotherapy alone                | 10,361                     | 5.9                    | 3,022 <sup>a</sup> |
| Chemotherapy plus<br>radiotherapy | 22,236                     | 6.7                    | Dominated          |
| Surgery alone                     | 33,539                     | 6.8                    | Dominated          |
| Surgery plus adjuvant<br>therapy  | 58,166                     | 10.2                   | 7,663 <sup>a</sup> |

*QALM* quality-adjusted life-month, *ICER* incremental cost-effectiveness ratio

“Dominated” defines a strategy that is either more costly and/or less effective than at least one other strategy

<sup>a</sup> Cost per additional QALM compared with no treatment

for surgery plus adjuvant therapy compared to no treatment was \$7,663 per QALM, while the ICER for surgical resection plus adjuvant therapy compared to chemotherapy alone was \$11,117 per QALM, or \$133,404 per additional quality-adjusted life-year.

#### *Impact of Low- Versus High-performing Centers*

When the model was populated with data reflective of low-performing centers, the ICER for surgery plus adjuvant therapy versus no treatment increased to \$9,144 per QALM (Table 4). Conversely, when the model was populated with data reflective of high-performing centers, the ICER for surgery plus adjuvant therapy versus no treatment decreased to \$5,991 per QALM.

#### *Sensitivity Analyses*

Further sensitivity analyses were performed for a variety of clinically important variables. When the perioperative mortality rate was theoretically lowered to 1 % (compared to 3 % in the base case), the ICER for surgery plus adjuvant therapy versus no treatment decreased only marginally, to \$7,504 per QALM from \$7,663/QALM in the base case. However, when the perioperative mortality rate was increased to 15 %, the ICER for surgery plus adjuvant therapy versus no treatment increased to \$8,247/QALM.<sup>28</sup> A similar pattern was seen for alterations in the “unresectable at operation” rate: lowering the rate to 9 % compared to 17 % in the base case decreased the ICER for surgery plus adjuvant therapy versus chemotherapy alone only marginally (\$7,363/QALM) whereas increasing the rate to 31 % increased this ICER to \$8,084/QALM.<sup>29</sup> Similarly, altering the surgical complication rate between

41 and 61 % had only a marginal effect on the ICER for surgery plus adjuvant therapy versus chemotherapy alone (Fig. 3).

However, there was one factor that significantly decreased the ICER for surgery plus adjuvant therapy versus chemotherapy alone: survival of patients with node-negative, margin-negative resections. When the median survival of such patients was increased to 22 QALMs (compared to 14 QALMs in the base case), the resultant ICER was \$6,386 per QALM, compared to \$7,663/QALM in the base case (Fig. 3).

Because coding and billing variability could alter our results, alternate payment patterns were also tested. If minor complications were reimbursed within a range defined by “no CC” and “CC” DRG designations, the ICER for surgery plus adjuvant therapy versus chemotherapy alone decreased by less than \$400/QALM, compared to the base case. This was also true when hospital payments for major complications were applied on the basis of a range defined by “CC” and “MCC” modifiers. Of all the cost-related variables, the one with the largest effect on cost-effectiveness was the cost of adjuvant chemotherapy: with the most expensive regimen (\$34,571; gemcitabine plus erlotinib), the ICER for surgery plus adjuvant therapy increased to \$9,226/QALM, whereas with the least expensive regimen (\$9,885), this ICER decreased to \$6,737/QALM (Fig. 3).

## **DISCUSSION**

A variety of treatment strategies are employed to treat pancreatic cancer. Most studies show that the combination of surgical resection, chemotherapy and radiotherapy is associated with the best clinical outcomes. However, to our knowledge, there has been no study that compares the cost-effectiveness of these strategies. On the basis of cost data estimated using Medicare payment, we report that surgery plus adjuvant therapy costs \$7,663 per QALM of survival when compared to no treatment.

As an individual modality, surgical resection is clearly more expensive than chemotherapy or radiotherapy. Not only are highly skilled and costly registered nurses, surgeons and anesthesiologists required for optimal intraoperative and postoperative care, but the physical resources required for a pancreaticoduodenectomy are significant. These include operating room time, space, and equipment and use of an inpatient hospital bed for 7 days or more.

We are not, of course, advocating that surgical resection be eliminated as a treatment modality for pancreas cancer. From a policy perspective, we would argue that society should have a higher willingness to pay threshold for

**FIG. 2** Plot of cost versus effectiveness for 6 treatment strategies; slopes of diagonal lines represent incremental cost-effectiveness ratios (ICERs). *QALM* quality-adjusted life-month

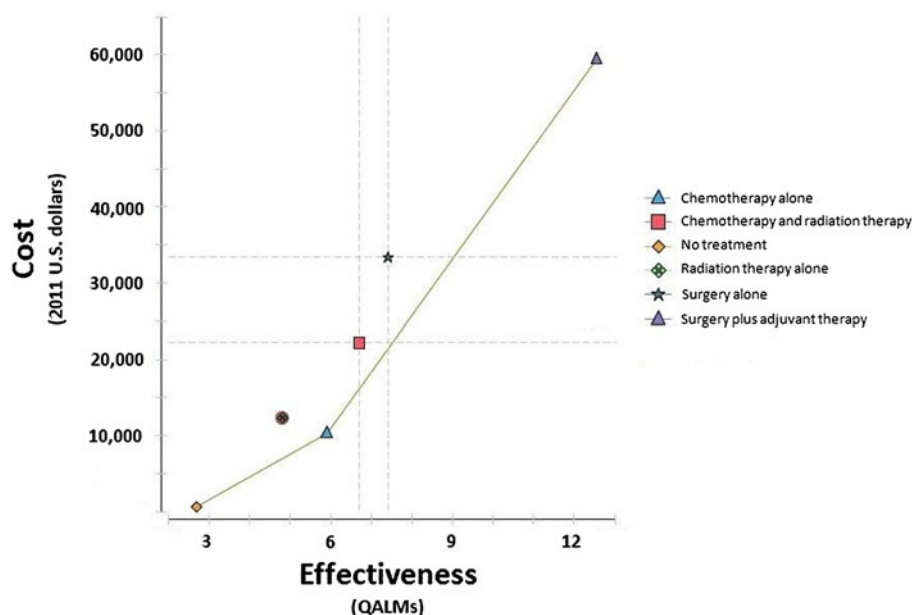


**TABLE 4** Comparison of intervention-specific ICERs for variables reflecting low-performing and high-performing centers

| Treatment strategy                                   | ICER for variables reflecting low-performing centers (cost per additional QALM, 2011 U.S. dollars) | ICER for variables reflecting high-performing centers (cost per additional QALM, 2011, U.S. dollars) |
|------------------------------------------------------|----------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------|
| Chemotherapy alone vs. no treatment                  | 3,022                                                                                              | 3,022                                                                                                |
| Surgery plus adjuvant therapy vs. no treatment       | 9,144                                                                                              | 5,991                                                                                                |
| Surgery plus adjuvant therapy vs. chemotherapy alone | 18,050                                                                                             | 7,377                                                                                                |

ICER incremental cost-effectiveness ratio, *QALM* quality-adjusted life-month

potentially curative interventions than for interventions that are not curative, as it is clear that for pancreatic head adenocarcinoma surgical resection is the only modality that offers long-term (greater than 2 years) survival. Although the expense of surgical intervention is clearly substantial, our data demonstrate that optimizing certain modifiable perioperative variables can significantly decrease costs. Decreases in perioperative mortality rates, rates of finding unresectable disease in the operating room, and complication rates can all decrease the overall cost of care for patients undergoing pancreaticoduodenectomy. Thus, practitioners should be particularly focused on vigilant postoperative care and use of high-quality imaging to

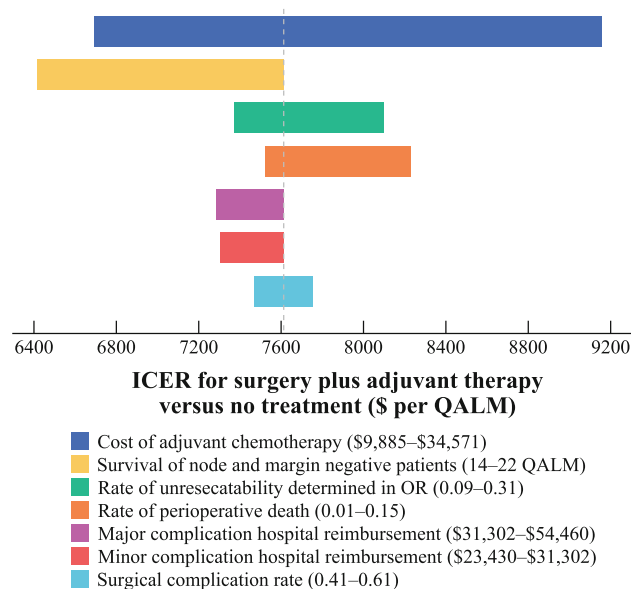


**FIG. 3** Tornado diagram demonstrating change in ICERs for surgery plus adjuvant therapy versus no treatment based on 1-way sensitivity analyses

appropriately select candidates for surgery. When all of these variables are optimized, as can be achieved at high-performing centers, significant savings can be realized.

This association between lower health care costs and high performance health care delivery is being increasingly recognized. Using Medicare outcome and cost data, Birkmeyer et al. recently demonstrated that for selected surgical procedures, payments to hospitals in the highest complication quintile (as opposed to the lowest) were between \$2,719 and \$5,353 higher per patient.<sup>30</sup> These data add to previous studies revealing similar results: high volume

(essentially high performance) centers performing a complex surgical procedure—pancreatic resection—have improved outcomes at lower costs.<sup>31,32</sup>

Interestingly, increased survival of patients undergoing pancreaticoduodenectomy had the greatest impact on the cost-effectiveness of surgical intervention. This is an important observation for 2 reasons. First, increasingly effective chemotherapy that extends survival should enhance the cost-effectiveness of multimodality therapy; significant resources should be devoted to finding breakthroughs in systemic therapy. Second, tumors with more favorable tumor biology than adenocarcinoma but that require the same anatomic resection (e.g., neuroendocrine tumors of the pancreas) should be associated with increased cost-effectiveness of surgical resection.

There are limitations to this study. First, certain outcomes and costs associated with all 6 strategies, such as readmission after surgery or chemotherapy, were not included in the model. Although this was considered using the best available data from the literature, we felt that straying from the precise data afforded us from the NCDB could lead to increased error, and the scope of this study needed to be curtailed at a reasonable stopping point. Because the dataset could not reliably inform us on rates of readmission or transfer to skilled nursing facilities, inclusion of this endpoint would have been speculative. Second, our perioperative outcome data were culled from a national cancer registry. Critics may argue that such data, reported in a heterogeneous manner from participating hospitals, may not be accurate. This criticism may have some merit, but we would suggest that these data reflect actual practices nationwide rather than what is reported in the literature by, for the most part, high-volume centers. And, by incorporating data from registries and expert centers, our sensitivity analyses were able to determine how such variance could influence our conclusions. Third, cost data were based on Medicare payment. Although these payment amounts are based on actual figures, not all patients undergoing treatment for pancreatic adenocarcinoma are covered by public payers, and so such payment data may not be generalizable to all patients. However, the Medicare payment data are representative of societal cost, and have been used widely for cost effectiveness research.<sup>10,33,34</sup>

The ICERs reported here can be measured against other interventions in cancer care. A commonly accepted willingness to pay is \$50,000 per QALY (or \$4,166/QALM), though this amount is debated in the literature.<sup>13,35</sup> The cost of some cancer therapies approximate this willingness to pay, while others greatly exceed this threshold. For example, a study evaluating the cost-effectiveness of adding cisplatin to gemcitabine in advanced biliary cancers demonstrated that combination therapy had an ICER of \$59,480 per QALY compared to gemcitabine alone.<sup>36</sup> In

contrast, the addition of one well known antiangiogenic agent, bevacizumab, to a standard treatment regimen in advanced ovarian cancer has been shown to have an ICER of \$479,712 per progression-free life year of survival.<sup>37</sup> Here, we report that surgery plus adjuvant therapy has an ICER of \$133,404 per QALY compared to chemotherapy alone—a cost between these two examples. Again, we believe that surgical intervention is worthy of a much larger willingness to pay, as the possibility of curative therapy must be given special consideration.

In conclusion, treatment for pancreatic adenocarcinoma is expensive relative to the survival benefit that treatment affords to patients afflicted with this aggressive disease. This is largely due to the poor outcomes associated with even the best treatment available. The addition of surgical resection to chemotherapy and radiotherapy is costly, but it is associated with increased survival. This study has demonstrated that by treating patients at centers that perform optimally, these costs can be mitigated. Furthermore, breakthroughs in early detection or systemic therapy that significantly improve survival will clearly improve the cost-effectiveness of all treatment regimens for pancreas cancer.

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