Cost Considerations in the Management of Cancer in the Older Patient

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This paper provides an overview of several prominent articles and empirical studies on supportive care and cancer-related costs faced by older cancer patients. It focuses primarily on individuals 65 years of age and over and reviews several types of cancer.

The overall cost of cancer in 2005 was $209.9 billion: $74 billion for direct medical costs (prevention, screening, diagnosis, treatment, and palliation) and $118.4 billion for indirect mortality costs.[1-3] (Indirect mortality cost refers to the cost of lost productivity due to premature death, with "premature" indicating the difference in life expectancies at given ages of individuals with and without the disease.) Medicare or private health insurance programs cover approximately one-third of cancer-related costs. Non-reimbursed or "out-of-pocket" costs constitute the remaining two-thirds.

The most costly cancers for men are prostate, lung, and colorectal cancers, with the corollary in women being breast, colorectal, and lung cancers.[4] Seniors aged 65 years and over represent 12% of the population in the United States, but account for approximately 56% of cancer cases. This disparity is due, in part, to the increased prevalence of cancer as people age and the high rate of comorbid medical illnesses in older individuals. Care for older individuals may require complex protocols that are likely to be costly, and choice of therapy may also be restricted relative to toxicity of the agent and expected years of life remaining.[5,6] Insurance helps, but patients are bearing a growing portion of these expenditures and may face financial hardships as a result of nonreimbursed cancer costs.[7]

This paper provides an overview of several prominent articles and empirical studies on supportive care and cancer-related costs faced by older cancer patients. It focuses primarily on individuals 65 years of age and over (and where cost information was available, also considers those aged 50 to 64) and reviews several types of cancer. We consider direct, indirect and out-of-pocket expenditures in this discussion.

Background

Americans 65 years of age and older currently account for more than 13% of the US population. Based on current projections by the US Bureau of Census, by 2030, one in five Americans will be over 65 years of age, reflecting 20.1% of the total population (70.2 million persons).[8] The oldest old-Americans age 85 and older—represent the fastest-growing segment of the US population, with more than 50,000 Americans having reached 100 years of age or more. Attendant to this unprecedented aging explosion is the increased incidence of cancer. The cancer burden of the elderly is high in the United States and has increased over time, with 60% of all malignant tumors occurring among persons aged 65 years and older.

Access to Affordable Cancer Care

A recent study of various cancer types found that fewer than 4% of patients were uninsured at the time they were considered for initial treatment, 48% had private insurance or HMO coverage, 16.8% had Medicare but no supplemental insurance, and 7.5% of patients had Medicaid insurance.[9] Most but not all individuals with health insurance have at least some level of coverage for pharmaceuticals. Because of coverage gaps, deductible requirements, and copayments, out-of-pocket expenditures may be large for cancer patients.[10] Recent technologic developments have also affected costs. These include the advent of targeted drugs and other high-tech therapy (Table 1).[4,11-14] Furthermore, while Medicare Part D might reduce the costs faced by some Medicare beneficiaries, it does not necessarily do so for cancer patients who require costly chemotherapy.
Physiologic Changes of Aging
Aging patients present with comorbidities, such as hypertension, diabetes mellitus, osteoporosis, and osteoarthritis.[15] Certain physiologic changes of aging (decreased renal function, impaired hepatic Blood flow, and decreased cardiac reserve, among others) along with pathologic changes combine to effectuate a decrease in the functional status of the elderly cancer patient and to render cancer care in the elderly more expensive over time. Furthermore, elderly patients with cancer who are contemplating surgical treatment and/or chemotherapy will often require more preoperative studies and laboratory tests in an effort to minimize their risks from potentially toxic treatment, thus increasing costs of cancer care.

Many cancer drugs are metabolized by the liver and can fall prey to specific physiologic changes that are attendant to aging. Liver Blood flow decreases by 0.3% to 1.5% per year; liver size also decreases, and liver function sees a decrement of 25% to 30%. Decreases in hepatic Blood flow lead to increases in serum drug levels and drug half-lives for drugs in phase I hepatic metabolism. This can result in decreased clearance and increased toxicity with the administration of commonly used chemotherapy drugs. Despite the impact of physiologic changes in the elderly that might negatively impact cancer treatment, improvements in supportive care over the last 10 to 20 years have enabled physicians to offer more aggressive, and often costly, treatments to older patients.

### Table 1

**Estimated Annual Costs of Approved Targeted Drugs for Cancer**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Indication</th>
<th>Estimated Annual Cost of Drug</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bevacizumab</td>
<td>Colorectal cancer</td>
<td>$100,000</td>
</tr>
<tr>
<td>Cetuximab</td>
<td>EGFR-positive colorectal cancer, pancreatic, head/neck, NSCLC</td>
<td>$100,000</td>
</tr>
<tr>
<td>Panitumab</td>
<td>Metastatic colorectal carcinoma</td>
<td>$100,000</td>
</tr>
<tr>
<td>Alemtuzumab</td>
<td>B-cell CLL</td>
<td>$64,000</td>
</tr>
<tr>
<td>Dasatinib</td>
<td>Chronic, accelerated, or myeloid or lymphoid blast phase CML and Philadelphia chromosome–positive ALL</td>
<td>$47,000</td>
</tr>
<tr>
<td>Imatinib</td>
<td>CML, gastrointestinal stromal tumors</td>
<td>$45,952</td>
</tr>
<tr>
<td>Bortezomib</td>
<td>Multiple myeloma</td>
<td>$45,000</td>
</tr>
<tr>
<td>Erlotinib</td>
<td>NSCLC, malignant mesothelioma</td>
<td>$31,000</td>
</tr>
<tr>
<td>Trastuzumab</td>
<td>Breast cancer</td>
<td>$30,000</td>
</tr>
<tr>
<td>Gefitinib</td>
<td>NSCLC</td>
<td>$21,963</td>
</tr>
<tr>
<td>Rituximab</td>
<td>Low-grade and follicular B-cell non-Hodgkin’s lymphoma, CLL, multiple myeloma, Waldenström’s macroglobulinemia, hairy-cell leukemia</td>
<td>$20,000</td>
</tr>
<tr>
<td>Gemtuzumab</td>
<td>CD33-positive acute myeloid leukemia</td>
<td>$13,279</td>
</tr>
</tbody>
</table>

*ALL = acute lymphocytic leukemia; CLL = chronic lymphocytic leukemia; CML = chronic myelogenous leukemia; EGFR = epidermal growth factor receptor; NSCLC = non-small-cell lung cancer.*

Adapted from Tighe et al.[14]
Particularly, improvements in antiemetic therapy and mucositis prevention have facilitated the administration of cytotoxic therapies to older patients. Older patients are also at higher risk for bone marrow suppression during chemotherapy, and the aggressive use of granulocyte and erythrocyte growth factors in the course of chemotherapy has lessened the risk of severe neutropenia or anemia in the older patient during therapy.[15,16] New mucositis prevention protocols, intensive care unit monitoring, and the introduction of lower-intensity chemotherapy preparation regimens have made allogeneic transplant a possibility in some patients as old as 80 years.[17]

Medical Costs
Medical costs are categorized as (1) direct medical costs; (2) direct nonmedical costs, ie, amounts spent for caregivers and travel; (3) indirect costs, ie, the economic value of lost productivity due to illness, disability, and death (mortality); and (4) intangible costs, ie, costs associated with pain, suffering, and grief. Pilot studies indicate that direct nonmedical, indirect, and intangible costs may account for 75% of the total cost of cancer care.[18]

"Time costs," defined as time invested by the patient in the hospital, emergency room, doctor's office, or outpatient surgical facility getting chemotherapy or radiation (and in transit), is another important cost consideration. For patients 65 years and older in all phases of care, time costs were found to vary by tumor site and phase of care (Table 2).[2,19,20] Total patient time costs in the initial phase of care were $2.3 billion. Per-patient time costs were as low as $270 for those diagnosed with prostate cancer; for individuals with lung cancer, costs grew by phase to as much as $7,390 in the last year of life.[20]

<table>
<thead>
<tr>
<th>Cancers That Are Common in the Older Individual</th>
<th>Average Medicare Payments per Individual in First Year Following Diagnosis (2004$)</th>
<th>Average Time Cost Estimates, Initial Phase of Care</th>
<th>Direct Medical Costs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lung</td>
<td>$24,700</td>
<td>$4,730</td>
<td>4.68</td>
</tr>
<tr>
<td>Breast</td>
<td>$11,000</td>
<td>$1,135</td>
<td>5.98</td>
</tr>
<tr>
<td>Colorectal</td>
<td>$24,200</td>
<td>$4,382</td>
<td>5.71</td>
</tr>
<tr>
<td>Prostate</td>
<td>$11,000</td>
<td>$881</td>
<td>4.61</td>
</tr>
<tr>
<td>Head/neck</td>
<td>$18,000</td>
<td>$2,579</td>
<td>—</td>
</tr>
<tr>
<td>Leukemia</td>
<td>$18,000</td>
<td>Not available</td>
<td>—</td>
</tr>
</tbody>
</table>

*Cancer Costs
Breast Cancer
In 2006, breast cancer was the most costly cancer for women.[4] Rao et al assessed the cost of treating Medicare beneficiaries with metastatic breast cancer from 1997 to 1999. Mean total direct medical cost was $35,164 per patient as compared to $4,176 per person for the control group, primarily explained by a difference in admission rates (the metastatic breast cancer group averaged 1.7 inpatient admissions per patient, whereas the controls averaged 0.3 inpatient admissions per patient) and length of stay per admission (14.4 days for metastatic breast cancer vs 1.6 days for controls). Metastatic breast cancer patients who were older had lower direct costs than did those who were younger. Since older metastatic breast cancer patients received less combination therapy, the cost of their illness was inversely proportional to their age.

Prostate Cancer
This sex-specific cancer is diagnosed in more than 200,000 men annually, most of whom are over 50
years of age. A longitudinal study of prostate cancer treatments for individuals of all ages and risk levels considered all health-care costs associated with the treatment of prostate cancer, including those associated with side effects and relapse.[21] Prostate-related costs varied according to the patient's age, risk factors, and type of treatment provided. More costly therapies (eg, external-beam irradiation and androgen deprivation) are more commonly used for high-risk older patients; lower cost treatments are used more frequently for younger patients with relatively lower risks. Over 5.5 years, average cumulative costs of prostate cancer were $42,570, ranging from $32,135 for watchful waiting to $69,244 for androgen deprivation therapy.[21] Costs for the 6 months following treatment were $11,495; watchful waiting was the least costly option at $2,568, while external-beam irradiation was the most costly at $24,204.[21]

Colorectal Cancer
Colorectal cancer is the third most common cancer in the United States, accounting for 10.7% of all new cancers (Table 2). Total annual US spending for this disease is approximately $8.4 billion, accounting for 12% of all cancer treatment expenditures.[19] It disproportionately affects older patients, with median age at diagnosis being 71 years. The advent of new pharmaceuticals is one of the primary drivers of colorectal cancer cost. The cost of drug treatment for colorectal cancer rose 340-fold between 1994 and 2004, but only doubled the median survival.[22]

Hematologic Malignancies
Leukemia represents 2.4% of all new cancers for all age groups, accounting for 3.7% of all cancer treatment expenditures. The United States spends about $2.6 billion per year on medical treatment for people of all ages who are being treated for Leukemia.[23] Another important hematologic malignancy, multiple myeloma disproportionately affects older African-American males. It is incurable but requires costly lifelong drugs and expensive stem cell therapy. Chronic lymphocytic Leukemia (CLL) is most common in the elderly, with a median age of diagnosis of about 64 to 70 years.[24] Cost drivers identified for CLL included costs associated with chemotherapy, intravenous immunoglobulins, transplantation, and the differential staining cytotoxicity assay.[24] According to the US Healthcare Cost and Utilization Project (HCUP), CLL accounted for 6% of total Leukemia charges in 2001.[24]

Acute myelogenous Leukemia (AML) accounts for about half of Leukemia cases, and annual incidence is about 11,900. The prevalence increases with age (median age of onset is 67 years) and is greater in men than in women.[1,4] Fewer than 10% of older persons survive long term with this diagnosis. Mortality rates of 10% to 40% are associated with AML following induction chemotherapy and are commonly attributable to sepsis and pneumonia.

Bennett and Schumock conducted a review of clinical and economic findings for the use of hematopoietic growth factors in older adults with AML.[25] Their review included an Eastern Cooperative Oncology Group (ECOG) study of AML patients who had been randomized to receive granulocyte-macrophage colony-stimulating factor (GM-CSF [Leukine]) or placebo. Cost savings were estimated at $2,310 with GM-CSF (1997 costs); savings were likely due to the decreased number of days with a low neutrophil count (13 vs 17, P < .05) and the corresponding reduction in the number of severe infections (9.6% vs 36.2%, P = .002) in the treatment vs placebo groups.

Head and Neck Squamous Cell Cancer
Together, small cell and squamous cell carcinomas of the head and neck (SCCHN) comprise 5% of all cancers in men and 2% in women. SCCHN carries a poor prognosis and a 5-year survival rate of less than 50%. Recent data are lacking, but a retrospective cohort analysis of Surveillance, Epidemiology, and End Results (SEER) data (1991-1993) concluded that the health economic burden of SCCHN is substantial, with costs that are comparable to or higher than those of other solid tumors.[26] Health-care costs were significantly higher for those with SCCHN than for those without the diagnosis. Average Medicare payment (in 1998 US dollars) for SCCHN patients was $25,542 higher than that of matched comparison patients, with monthly payments 3 times as high ($1,428 vs $446, respectively).[26] For patients with advanced disease, the costs were even greater. Resource utilization, particularly among patients with advanced-stage disease, accounts for a significant percentage of the costs, largely due to longer hospital stay and utilization of home health care and hospice services.

Lung Cancer
Lung cancer is one of the most costly cancers—annual total costs were estimated at $9.6 billion in 2004.[22] Lung cancer ranks as second most common among noncutaneous malignancies, and non-small-cell lung cancer (NSCLC) accounts for most cases. Lung cancer primarily afflicts older adults, the median age at diagnosis being 68 years, with 40% of patients older than 70 years of age at the time of diagnosis.
Ramsey et al examined community chemotherapy treatment patterns for patients (mean age, 75 years) with advanced NSCLC, diagnosed between 1994 and 1999 (n = 14,875). Patients with locally advanced stage III/IV disease at diagnosis were stratified based on chemotherapy agents received during the first 3 months postdiagnosis. Approximately 31% received chemotherapy, 8% received surgery, and 53% received radiation therapy. Medical care costs were substantially higher for those receiving chemotherapy than for those who did not; costs were highest for those receiving both radiation and chemotherapy. Lifetime costs were more than $10,000 higher for those receiving platinum/taxane combinations than for other regimens, although survival was similar.

Emerging Cancer Drugs
Cost may prohibit access to newly approved targeted cancer drugs that offer promising vehicles for treatments associated with marked improvements in clinical outcomes (Table 1). These new drugs, available for difficult-to-cure cancers, selectively target malignant cells and result in fewer side effects than standard chemotherapeutic agents. The drugs comprise two classes of novel targeted cancer agents: (1) monoclonal antibodies that bind to surface antigens present only on tumor cells, not the surrounding cells, and (2) kinase inhibitors that regulate tumor and tumor vessel growth. A recent study found that the annual cost per patient of targeted drugs for cancer typically ranges from $20,000 to $50,000, but may be as low as $13,279 and as high as $100,000.

Coverage and Reimbursement
Out-of-Pocket Expenditures
Cancer treatment in individuals over 70 years of age results in significant out-of-pocket expenditures (OOPE). Langa examined OOPE, including prescription medications and home care services. Cancer-related medications accounted for $1,120 per year in spending and home care services for $250 per year. Low-income individuals spent about 27% of their annual income in these areas, compared with only a 5% annual income expenditure for high-income individuals without cancer. A prior history of Cancer Resulted in an additional $240 OOPE per year. Current cancer treatment was associated with an additional $670 per year, even after controlling for sociodemographics, living situation, functional limitations, comorbid chronic conditions, and insurance coverage. Costs were driven, in part, by inpatient care; those undergoing active cancer treatment were more likely to be hospitalized at least once in the prior 2 years (56% vs 31% for those with no cancer history). OOPE for insured women with breast cancer who were covered by private, Medicare, or Medicaid health insurance included lost income costs of $1,455 per month, on average. The financial burden of breast cancer was greatest for those with an annual household income < $30,000 and lowest for those with an annual income > $60,000, accounting for a mean of 98% of monthly income in the lowest income group, but only 26% in the highest. The OOPE was $1,687 for women under 65 years old and $627 for older women. The difference in expenditures was mostly attributed to a decrement in income (due to reduced work ability and early retirement) in younger women, accounting for approximately $727 per month.

For a cohort of insured breast, colorectal, prostate, lung, and head and neck cancer patients, McKoy et al estimated costs incurred by those aged less than 65 years as compared to those 65 years and older. Cancer burden was found to be considerable when measured in dollar expenditures per month, with the total cost ranging from $0 to $28,291.67. Mean total OOPE ranged from $0 to $28,291.67 per month. The investigators found no significant differences in actual or adjusted costs relating to hospital bills, medications and herbs/supplements/vitamins across breast cancer or other cancer groups by age.

Reimbursement by Third-Party Payers
Insurance coverage and reimbursement policies for cancer care and related prescription drug coverage vary by type of payer and coverage policy. Working-age individuals may receive insurance through employment-based health insurance, through the purchase of private health insurance, or by seeking assistance from states, local governments, and charities. These types of insurance generally extend coverage for inpatient and outpatient care and may include other benefits/services such as pharmaceuticals, home health care, and rehabilitation. Insurance policies typically require copayments (usually approximately 20% of the approved amount) and annual deductibles.

Coverage and reimbursement policies, whether for medical care or pharmaceuticals, differ by type of drug and whether it is administered in the inpatient hospital setting, the outpatient clinic setting, or the patient's home. Many private insurers and HMO formularies include some of the targeted cancer drugs and will pay for the drugs, provided prior authorization and medical necessity requirements are met. In addition, many pharmaceutical manufacturers provide their own reimbursement programs to make targeted drug therapies affordable for patients.
Cancer Insurance
Cancer insurance, known as a specified disease policy, provides limited benefits, is activated only when the insured is diagnosed with cancer, and may impose increased premium rates with aging. There are three types of cancer insurance policies: (1) an expense incurred policy, which pays a percentage for expenses listed up to the benefit or policy's maximum dollar limit; (2) an indemnity policy, which pays for all listed benefits up to a set limit; and (3) a first-diagnosis or first-occurrence cancer policy, which pays a lump sum upon the diagnosis of cancer. Preexisting exclusions and waiting periods apply to those purchasing these products.[31] The majority of companies selling cancer policies do so directly to large businesses for payroll deductions and through associations. A few cancer insurance products are offered through direct marketing to individuals, but they are rarely available to Medicare beneficiaries.

Medicare
Total medical care expenditures for oncology account for 10% of all Medicare expenditures.[32] Medicare Part A covers inpatient cancer care, whereas Part B covers cancer screening services, breast cancer, and many types of chemotherapy and related treatment modalities. Medicare will not pay for certain cancer-related expenses, such as those that are considered experimental or some oral medicines commonly used to treat cancers of the breast and prostate.[22] Medicare supplemental insurance is available privately to help pay for some but not all expenses that are not covered by Medicare. For patients with Medicare Plus Choice, pharmaceutical coverage is provided. Medicare Part D also provides a drug benefit that covers both cancer pharmaceuticals and noncancer drugs. Most patients are responsible for an annual deductible ($250), and those with prescription expenses more than $2,250 are subject to a coverage gap.[33] When the coverage gap or "donut hole" is reached, the patient is fully responsible for payment for the nondiscounted cost of prescribed drugs. In 2007, this "donut hole" in coverage will end once the patient spends $3,850 in OOPE for covered drugs, deductibles, and copayments. Expenditures for nonformulary and noncovered drugs are excluded from the calculation. After spending $3,850, the patient becomes eligible for catastrophic drug coverage for the remainder of the year.

Reimbursement for Older Patients in Clinical Trials
Older patients are underrepresented in cancer treatment trials.[34] Even though individuals age 65 and older account for 63% of the US population of cancer patients, they account for only 25% of subjects enrolled in clinical trials.[35,36] Bugeja found that 35% of original clinical research papers in the BMJ, Lancet, Thorax, and Gut excluded elderly persons (over age 75), unjustifiably citing family pressure, time constraints, and increased risks as reasons for exclusion.[37] Cost has been another barrier to older patients' participation in trials. Until recently, most insurers did not cover care provided in a clinical trial and Medicare excluded coverage of any costs associated with clinical trial participation, citing such treatment as experimental or investigational. Since patients often receive routine patient care services (eg, physician visits, hospital stays, clinical laboratory tests, x-rays, etc) whether or not they are participants in clinical trials, Medicare began reimbursing doctors for the routine care costs of clinical trials in 2002. The Centers for Medicare and Medicaid Services (CMS) subsequently revised its National Coverage Determination (NCD) for off-label use in cancer clinical trials in early 2005. Medicare now pays for both routine and nonroutine costs associated with the patient's care, as well as the off-label use of some anticancer drugs.[38,39] Following Medicare's lead, nearly half of all US states and several private insurers now cover the costs of patient care in "qualifying" clinical trials.

Cost vs Charges
Cost is the value that must be released in order to acquire a good or service. It may be total, fixed, or variable. Total cost refers to what is needed to operate at some particular rate of output. Fixed and variable costs are subsets of total cost, where fixed cost never changes, no matter how much service is used by the patient, and variable cost fluctuates depending on service utilization. Charges (patient bills) are often used as a proxy for cost. Charges may bear little resemblance to economic cost, and use of charges as a proxy for economic cost may be misleading relative to economic efficiency. Charges are based on actual prices for services provided and are sometimes aggregated into routine charges (room rates) and ancillary charges (the price of a tablet).

Summary
The total economic burden of cancer (all age groups) is more than $209 billion, with older populations accounting for a disproportionate amount of this expenditure. As the population in the United States continues to age, both the incidence and prevalence of cancer will increase, exerting an increased societal financial burden. Currently, 60% of all malignant tumors and 69% of all cancer deaths occur in persons 65 years and older. Furthermore, the leading types of cancers associated
with mortality in the elderly (lung, colon, prostate, and breast) levy a significant financial burden on this population.

While older patients may benefit from longer disease-free survival and potential cure because of aggressive cancer therapy, the increased cost associated with concomitant supportive care, extended length of hospital stay, home health assistance following discharge from the hospital, and adjuvant prescription medications impose a significant financial burden on this group of patients.[40,41] Direct medical expenditures covered by third-party insurers represent the largest, but not the only, component of the total economic burden of cancer. OOPM paid by the patient and the family is estimated to account for as much as 10% of direct medical expenditures. Lost time and economic productivity associated with cancer-related illness and death are undoubtedly important, but are as yet undetermined for older individuals.[22]

Conclusions
The cost of cancer care in the older individual remains both a clinical and policy concern, particularly for those currently undergoing treatment or who have a prior history of cancer. A concerted effort is needed to provide appropriate treatment modalities against a cost-effective backdrop to this population. Clinical trials that now recruit older patients in their evaluation of potential anticancer drugs are poised to make significant contributions to the body of knowledge. Although some encouraging changes have been effected in clinical trials relative to recruitment of older subjects, more sweeping measures need to be implemented. Undoubtedly, more research is needed to understand all the costs incurred for cancer in older individuals, in an effort to effectuate reforms of private and federal reimbursement schemes aimed at achieving equity, quality, and access to affordable cancer care for older individuals.

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