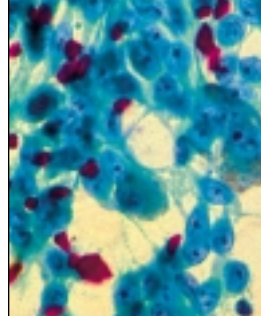


CANCER ECONOMICS: ON VARIATIONS IN THE COSTS OF TREATING CANCER

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Introduction

That cost concerns drive developments in health care management and policy is everywhere apparent. Managed care contracting and other recent changes in third-party reimbursement practices are constant reminders at the institutional level. At the public policy level, cost issues shape current Congressional deliberations on a "Patients' Bill of Rights" and reform of the Medicare program, among others. Given this pervasive concern, it is remarkable how little we actually know about the costs of delivering medical services. To be sure, we have an increasingly refined set of National Health Accounts, and there is a burgeoning literature on cost-benefit analysis (CBA), cost-effectiveness analysis (CEA), and cost-utility analysis (CUA) in health care. However, the National Health Accounts estimate broad expenditure aggregates, and CBA, CEA, and CUA studies focus mostly on cost *comparisons* of specific therapies used by only small fractions of given patient populations. Dealing with cost issues also requires good data on what some call *attributable* costs, the cumulative value of resources used to treat full episodes of a health condition from the time of initial diagnosis to death. Although the line between various types of health-related cost analyses often blurs, a key point is that attributable cost studies conceptually encompass the entire population of incident or prevalent cases of a given disease, and they generate patient-level cost estimates from the bottom up. Attrib-

utable cost studies of this sort provide significant benchmarks for managerial and policy deliberations about health care cost containment. Viewed from this perspective, the fact that they are in short supply at the moment is a serious matter.

The primary objective of this paper is to appraise how much we know currently about the attributable costs of cancer treatment. Cost containment issues are as vexing in cancer care as they are elsewhere, and gauging the attributable costs of lifetime episodes of specific malignancies is increasingly important in an era of rapid technological advance and improving survivorship. The next section sets out briefly what ideally we would like to know about cancer costs or, put differently, the desiderata of an applied research program on this topic. What we actually know about the costs of cancer treatment is then briefly reviewed, with special emphasis on crucial relationships such as cost variations across disease stages at diagnosis. The final section pulls together some general inferences from the review.

What Should We Know About Treatment Costs?

In principle, we would like to measure cumulatively the value of all resources allocated to treat a specific disease from the date of diagnosis onward. This means enumerating the units of each and every health care service used to treat the disease and then assigning dollar weights to those units to

Oncology practice and economic realities are inexorably linked today. Developments in cancer economics are explored in this regular feature.

reflect the “worth” or “scarcity value” of their resource inputs. Although only certain phases or elements of this cumulative record may be of interest to given payers or providers, the value of all resources devoted to the complete episode of the disease is needed to judge the overall allocation of resources from a societal perspective. A major reason is that many services can be substituted for one another, and these substitutions may occur in response to changing economic and technological conditions. When they do, partial pictures of the cost structure are likely to provide misleading advice. For instance, focusing only on the cost of inpatient services in the treatment mix may mislead when outpatient treatments are substituted for inpatient ones. Focusing on the costs of formal treatment when substitutions to home care occur is similarly misleading. In the latter case, purchases by households of, say, in-home nursing services must be tallied in the same way that nursing home utilization is tallied. Cost profiles must therefore systematically document the utilization of all attributable services as well as break down the value of those services according to care setting and the time course of the disease.

A number of technical issues must be resolved in order to gauge treatment costs in this way, beginning with access to data sets with sufficiently detailed records to track the services used by each individual in a defined population of persons with the disease over time. Data on unit costs, charges, or reimbursements must also be avail-

able to use as value weights in calculating the cumulative profile of treatment costs. Methodologically, investigators must also grapple with some special characteristics and problems of cost data. For instance, they have to deal with missing data and adjustments for patients who die or are lost to follow-up.¹ Since cost distributions typically have extremely long right-hand “tails,” investigators also have to deal with data transformations and other methods for normalizing the underlying distributions.² Assuming these technical issues are handled appropriately, central tendencies in the data can be examined and the factors that shape the distribution of costs across patients can be analyzed.

Calculating mean costs over a given study population and classifying them by type of service setting are obvious beginning points for cumulative cost analysis. Whether mean costs of different cohorts are changing and/or whether cost elements are increasing or decreasing over time are also results of considerable interest to clinicians, managers and policy makers. However, cost analyses should not necessarily be limited to just such descriptive accounts of cost profiles. More extensive analytic efforts are needed to understand the factors that account for the dispersion observed about mean costs. To begin with, the shapes (skewness and kurtosis) of cost distributions are critical to judging the success or failure of cost containment efforts.³ Knowledge of the factors that systematically influence cost differentials is also crucial. The

expectation that costs will vary directly with stage at diagnosis is a case in point. If more complex therapies are generally required to treat more advanced disease, we should detect a systematic relationship between cost profiles and stage, and we can use the measured differentials in appraising, among others, the potential cost-effectiveness of screening efforts that result in downstaging. Yet, even within stage strata, variations in cost profiles are still likely, perhaps even large ones. One reason is the continuing uncertainty about the efficacy of various cancer therapies and the corresponding variation in patient treatment regimens, each with its own cost structure.⁴ Other reasons stem from practice style differences relating to both the characteristics of patients and the providers treating them.⁵ For instance, older patients may be treated less aggressively than their younger counterparts, or patients with significant comorbidities may be treated less aggressively than those with only cancer. Other socioeconomic characteristics of patients and providers such as insurance coverage, available social support, implementation of clinical practice guidelines, and/or provider profiling may also influence costs. Practice styles and thereby treatment costs also differ dramatically across geographical areas.⁶ Suitably structured statistical analyses should be able to identify and gauge the impact of these systematic effects on cost profiles. Although there may still be residual or “unexplained” variance, it should be purely random, ie, statistical noise. In general terms, this point

Selected Characteristics of Recent Studies on the Attributable Costs of Cancer

Studies	Cancer Sites	Study Population (Dx Dates)	Cancer Cases	Cost Measure (Observation Period)	Cost Estimate(s): Cumulative Period (Reference Year)
DESCRIPTIVE					
Riley et al ⁹	Colorectal Prostate Breast Lung Bladder	Medicare/SEER (1973-1989)	287,013	Medicare payments (1984-1990)	≤35 years post Dx by phase (1990)
Taplin et al ¹⁰	Breast Prostate Colon	HMO panel/ SEER region (1973-1994)	6,107	HMO incurred costs (1990-1991)	Initial, continuing terminal phases (1992)
Logorreta et al ¹¹	Breast	HMO panel (1989)	200	HMO expenditures (1989-1992)	≤4 years post Dx (1993)
Polednak et al ¹²	Breast	State registry/ discharge data (1991)	377	Inpatient charges (1991-1993)	≤2 years post Dx (1993)
Etzioni et al ¹³	Ovarian	Medicare/SEER (1973-1989)	5,012	Medicare payments (1984-1990)	≤15 years post Dx by phase (1990)
Fireman et al ¹⁴	Breast Prostate Lung Colon Rectum Lymphoma Ovarian	HMO panel/ SEER region (1973-1991)	21,997	HMO incurred costs/ non-HMO charges (1987-1991)	≤15 years post Dx by phase (1992)
Brown et al ¹⁵	Colorectal	Medicare/SEER (1983-1993)	64,507	Medicare payments/ copayments (1990-1994)	25 years post Dx by phase (1994)
Penson et al ¹⁶	Prostate	Disease-specific CaPSURE database (1990-1997)	235	Service use (times) Medicare values (1994-1996)	≤1 year post Dx (1996)
MULTIVARIATE					
Hillner et al ¹⁷	Lung	Private insurance/ State registry/age <65 (1989-1991)	336	Blue Cross/Blue Shield payments and copayments (1989-1993)	≤2 years post Dx (1992)
Penberthy et al ¹⁸	Lung Prostate Colorectal Breast	Medicare/ State registry (1985-1988)	11,025	Medicare payments (1985-1988)	≤1 year post Dx (1997)
Du et al ¹⁹	Pancreas	Hospital series (1992-1995)	103	Hospital expenditures (1992-1998)	6 & 12 months and lifetime post Dx (1998)
Chirikos et al ²⁰	Breast Lung Ovarian Lymphoma	Hospital series (1995-1998)	1,860	Hospital charges (1995-1999)	≤4 years post Dx (1997)
Dx = diagnosis CaPSURE = Cancer of the Prostate Strategic Urologic Research Endeavor					

suggests that cost variations should be investigated in a multivariate statistical framework.

What Do We Currently Know About Cancer Treatment Costs?

As a way of answering this question, a MEDLINE search of the recent cancer literature was conducted to identify attributable cost studies. Because costs can be influenced by the way health care is financed, the search was restricted to the United States. It was further restricted to studies that appeared on an initial reading to encompass full patient populations, not just subsets undergoing particular therapies or procedures as would nominally be the case in comparative cost studies. To illustrate, more narrowly focused cost studies of alternative cancer drugs⁷ or biopsy techniques,⁸ to name just two, were excluded from consideration in this review. This winnowing ultimately yielded 15 studies⁹⁻²³ published between 1995 and early 2001 that generally met the inclusion criteria, 12 unambiguously so.⁹⁻²⁰

The Table summarizes selected characteristics of these 12 analyses relating to their study populations and costing methodologies. The Table also divides these studies somewhat arbitrarily into two categories: (1) descriptive accounts of attributable treatment costs for common site-specific cancers and (2) studies using multivariate modeling techniques to account for cost variations in such cancer populations. Although a detailed descrip-

tion of the methods and findings of each of these papers is beyond the scope of this essay, the following subsections review the main features and highlights of each of the two categories of studies.

Descriptive Analyses

The studies set out in chronological order in the top panel of the Table are quite diverse, but they do share several common features. To begin with, each examines the costs of one or more site-specific malignancies. This fact suggests that investigators share the tacit assumption that costs vary across sites and, correspondingly, that cost analysis must begin at the level of site-specific strata. This group of studies also generally shares a common methodological approach. They link registry information on a defined population of incident cancer cases to longitudinal administrative records that provide a basis for tracking patients and thereby estimating treatment costs.^{24,25} A number of the studies draw on the National Cancer Institute's (NCI) Surveillance, Epidemiology and End Results (SEER) Cancer Registry data, either for the entire set of nine tumor registries based on geographical area and population that comprise the full SEER program or to just a single geographical area within the overall program, to identify site-specific incident cases. In turn, SEER cases are linked either to claims files of Medicare beneficiaries (≥ 65 years of age) or to the cost/administrative data bases of specific health maintenance organizations (HMOs) in order to track the utilization of services over time.

These data linkages are both a major strength and potential weakness of attributable cost studies. A major strength is that fairly large numbers of site-specific cancer cases can be identified and then followed from the point of initial diagnosis onward in time. For example, Riley et al⁹ identified more than 287,000 cases diagnosed with any one of five different types of cancer and then matched these incident cases at the person-level to Medicare files to track medical care use and costs. A potential weakness is that SEER registrants are not necessarily representative of the overall population of cancer cases in the United States. Moreover, the characteristics of Medicare and HMO enrollees differ from those of the general population, and the service/benefit packages of each kind of plan are not altogether representative of those around the country. A more serious weakness is that these linked sets have gaps arising from death and/or insurance plan disenrollment, and they encompass not only relatively short periods of time, but often periods that do not correspond fully to the survival experiences of the incident cohort. Riley et al⁹ match cases diagnosed in the period 1973-1989 ("Dx Date" in the Table) to Medicare files covering just the period 1984-1990 ("Observation Period" in the Table). The matched set is thus a combination of incident and prevalent cases diagnosed and treated at various times under different technologic regimes.

The absence of complete or lengthy follow-up data on a single incident population in these stud-

ies has given rise to the convention of delineating “phases” of care, typically subdivided into “initial,” “continuing” and “terminal” care. The first and last of these phases generally encompass time blocks of 6-18 months, the initial period being the first 6-18 months following diagnosis and the final period being the 6-18 months prior to death. Thus, patients who die within the first year of diagnosis typically only have a terminal phase, whereas those who survive 3 years or less typically have just initial and terminal year values. Several studies restrict their focus to just the initial or terminal phases, in some instances because of the lack of data. As might be expected, studies encompassing all three phases do not necessarily have the same number of sample observations in each phase. The classification scheme permits mixed data on incident and prevalent cases to be exploited as fully as possible. This is especially true for data on “continuing cost,” which are adjusted to a “person-year” basis and then linked to conditional survival probabilities for each year in the period between the end of the initial phase and the beginning of the terminal phase. Thus, investigators such as Riley et al⁹ are able to estimate the cumulative costs of cancer cases for upwards of 35 years postdiagnosis by summing the costs in each of the three phases, suitably adjusted for the probabilities that cases survive each year of the hypothetical 35-year follow-up period. It is worth noting that these cumulative sums are typically adjusted to constant dollars corresponding to a given calendar year

(labeled “Reference Year” in the Table); in some studies, moreover, these cost streams are discounted back to present value sums in the reference year.

Finally, many cost analyses net out attributable costs of the site-specific cancer by matching the case with a “control” subject without cancer. (Note that the sample sizes presented in the Table do not count these control subjects.) Cost histories for data pairs are then constructed, and the control amounts are subtracted from the case amounts to compute net costs attributable to the cancer. Studies using Medicare payment data, for instance, identify age/sex-matched beneficiaries and tally monthly payment amounts over the time period corresponding to the use of services by the case. The net difference between the case and control cost profiles is attributed to the cancer in question. These net cumulative cost amounts are then the primary focus of the empirical analyses carried out in these studies. In descriptive studies, the empirical work is limited to cross-classifications and simple univariate tests of differences in costs by age and stage at diagnosis.

The study of long-term attributable costs of colorectal cancer conducted by a team of investigators at the NCI’s Applied Research Branch¹⁵ illustrates such findings. Using SEER-Medicare linked data, these investigators gauge costs by Medicare payments (allowed charges plus patient cost-sharing amounts) for covered services, adjusted for inflationary trends and

geographical SEER area resource price differentials, among others. They find that cost streams extend over substantial periods of time and that most costs are incurred after the initial phase of treatment has been completed. They estimate, for example, that the average cost of the initial (6-month) phase of all colorectal cases is \$18,100 (in 1994 constant dollars), \$1,500 per year for each year of the continuing phase, and \$15,200 for the terminal phase of treatment. Coupled to survival data, total costs are estimated at a 3% discount rate to be \$31,300 on average for colon cancer and \$36,500 for cancer of the rectum. As anticipated, these costs vary by stage at diagnosis. Phase-specific costs generally increase from below-average amounts for in situ and stage I disease to significantly higher amounts for more advanced disease. However, the stage distribution of total costs is “∩” shaped, with stage I and stage II costs below or just equal to the overall average, stage III costs significantly above that average, but stage IV costs not only below mean costs but less than stage I costs.

Even though costs differ by stage, a noteworthy aspect of the data in the colorectal study (and other studies in the descriptive category of studies) is that dispersion of cost values about the mean is great and persists even after stage is taken into account. More particularly, coefficients of variation (CV), standard deviations as a percentage of their respective means, calculated from data presented in the colorectal analysis tend to be high and about the same for phase-specific

costs at all stages, even though costs differ by stage. Continuing monthly costs, for example, average \$363, \$443, and \$692 for stage II, stage III, and stage IV subjects, respectively; the corresponding CVs were 220%, 256%, and 179%. This may be interpreted as suggesting that stage-stratified cost distributions have long (right-hand) tails and that the distributional tails over all stages are quite “thick.” Much more than stage, in other words, must account for the variance over these distributions. The colorectal analysis shows that costs vary over age strata as well, but they do not examine other factors that might shape the cost distributions, especially type of therapy. Despite the close association between stage at diagnosis and choice of therapy, it is likely that treatment differences within stage strata will account for some additional amount of the observed variance of costs across the study population.

Findings in some other studies in this group hint at the possibility of substantially more complex relationships bearing on observed variations in costs. For instance, Taplin and colleagues¹⁰ fail to find statistically significant stage effects for the cumulative costs of prostate cancer cases. In contrast, Penson and colleagues¹⁶ in an analysis of covariance of the effects of stage and initial choice of therapy in a cohort of early stage (T1c and T2c) prostate carcinoma find significant stage effects when the data are stratified by type of treatment. Similarly, Legorreta and colleagues¹¹ as well as Taplin et al¹⁰ find “ \cap ” shaped profiles of costs with respect to stage

in their studies of the cumulative costs of breast cancer. Neither study assesses the effect of treatment on costs. While not necessarily disputing these findings, a more focused cost study by Barlow and colleagues²³ find treatment-related cost differences *within* early stage breast cancer strata (stage I, IIA and IIB), especially at the 5-year benchmark postdiagnosis. Interestingly, women undergoing breast-conserving surgery are less costly than counterparts undergoing mastectomy, controlling for age, stage, time since diagnosis, and several interaction terms. This result is attributed partially to differences between groups in the extent of adjuvant therapy, which in turn is influenced by age. These finding, in other words, strongly suggest the need to model cost streams in more explicit multivariate terms in order to appraise the independent or net effects of a variety of factors (in addition to disease stage) that bear on cumulative costs.

Multivariate Modeling

The studies in the lower panel of the Table use explicit multivariate modeling to sort out cost drivers.¹⁷⁻²⁰ The study by Penberthy and colleagues¹⁸ is representative. They attempt to predict Medicare costs for beneficiaries with breast, colorectal, lung, and prostate cancer. The study links Medicare claims data to the Virginia Cancer Registry to account for observed variations in cancer costs over the initial year of treatment. They specify a more complex regression model (instrumental variables) to estimate the effects of various “demand-related”

and “supply-related” factors on costs. In their specification, costs are the dependent variable, and the set of independent or regressor variables includes age, race, gender, marital status, income, education, predicted number of oncology-related medical specialists in the local market, stage, comorbidity index, type of treatment, length of stay (LOS), and LOS * comorbidity interaction terms. Not unexpectedly, the analysts find substantial inter- and intra-cancer variation in cancer costs, with mixed results on age and stage. In the latter case, they detect significant treatment effects that may confound the stage predictors. They also find that comorbidities and socioeconomic characteristics of patients, especially income class, are significant predictors. The analysis, in other words, suggests some part of the variation in costs must be attributable to practice patterns and provider/patient preferences, matters that might be targeted by cost containment efforts and stricter adherence to clinical pathways, among others. Nonetheless, the study examined only initial treatment in the first year following diagnosis and, despite the large number of regressors, it had rather poor data fits as evidenced by coefficients of determination (R-squares) of only between 0.4 and 0.5. The authors make a strong case for future work that will account for more of the unexplained variance in their models.

Similar results were obtained in other studies in this category. On the one hand, treatment effects controlling for stage as well as socioeconomic characteristics of

patients and providers tend to be strong predictors of cost variations. A study of costs of treating non-small-cell lung cancer cases,¹⁷ for example, finds highly significant regression coefficients on treatment variables, controlling for stage differences, which are not themselves statistically significant. A study of pancreatic cancer costs¹⁹ finds, among other things, that type of insurance coverage, particularly Medicare plus private “wrap-around” coverage, significantly raises the costs of care. On the other hand, most of these studies fail to explain much of the variance in costs across patients. Coefficients of determination are generally less than 0.5, ie, the analyses explained less than half of the variance in the cumulative costs of the patient populations being studied.

Discussion

Three general inferences may be drawn from this brief review.

First, we still do not know a great deal about the levels and distributions of costs of treating various cancers, though the knowledge base has grown in recent years. Not surprisingly, we know most about the four or five most common cancers, but these diseases account for only approximately 50%-60% of the cases, deaths, and total direct costs of the top 15 malignancies at present.²⁶ Consequently, we must learn more about the cost consequences of the other major cancer sites. Similarly, available studies focused on selected patient populations, par-

ticularly SEER registrants linked to Medicare and large HMO claims files. Since age is an important covariate and HMO enrollees and providers are highly selected, this focus results in data gaps. These gaps are further exacerbated by the fact that Medicare and HMO costs do not encompass all relevant services, especially the costs of nursing home care and the non-medical expenses of the household attributable to cancer.²⁷ For these reasons, new patient populations as well as new arrangements for accessing cancer data must be accorded high priority on the applied research agenda.²⁸

Second, the research completed thus far confirms the general suppositions that cancer treatment costs vary substantially over patient populations and that commonplace covariates do not account for much of this variation. Indeed, even such obvious cost determinants as stage at diagnosis are not always detected statistically and, even when they are, they account for only a small percentage of the variance in statistical terms. Thus, analytic studies designed to account for factors that explain more of the variance in statistical terms are needed. Statistical modeling should explore in more detail covariates in each cancer that raise the proportion of “explained variance,” giving due consideration to statistical issues that arise in empirical cost investigations. It is worth noting in this regard that there is a large econometric literature on the cost structure of health care organizations, particularly hospitals, that can pro-

vide a template for methodological guidance in this work.²⁹ This means that the research agenda can move forward quickly if, and when, suitable priority is accorded work on patient-level variations in cancer treatment costs.

Finally, outcome measures must be built more explicitly into attributable cost analyses. A major reason for wide variations in cost profiles in the first place is the continuing uncertainty about the value of cancer treatment itself. In many cases, there is no single, dominant therapy of proven efficacy, so patients are treated by a variety of alternative means, each with its own cost structure. Costs should be scaled by outcomes to assess whether marginal differences in cost effectiveness can be detected and thus provide a basis for judging the relative costs of various therapeutic strategies. The claims and Registry data linkages exploited in recent research permit survivorship to be used as an outcome measure, though few studies have done so in explicit fashion. Were attributable cost studies extended along these lines, they would complement current CBA-, CEA-, CUA-related research and thereby pave the way for identifying truly cost-efficient cancer care.

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