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TREATMENT DECISION-MAKING IN CATASTROPHIC ILLNESS

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It is well established that the social and economic environment of medical care distinguishes its provision from that of other goods and services.[1,7,11] While scholars have studied the influences of this idiosyncratic environment, there is relatively little empirical knowledge about how it affects decision-making in specific medical contexts. Through general conceptual discussion and consideration of a case study of leukemia chemotherapy, this paper examines the medical decision-making process in one specific context: the response of physicians to the availability of an innovative treatment for a catastrophic illness. The manner in which the medical profession deals with serious illness is relevant to concerns as diverse as the promotion of economic efficiency and the preservation of human dignity.

Decision-Making with Respect to Innovation

A decision-making problem may be modeled as follows: the decision-maker has an objective function which specifies how quantities of identified inputs interact to produce quantities of the objective. The decision-maker chooses the quantities and mix of inputs to achieve as much of the objective as possible, subject to existing constraints.

In an environment of readily available information and complete knowledge (of relevant production technologies, etc.), decision-making may be reduced to to a mechanistic process. The human element enters when there is risk or uncertainty, as in the decision whether or not to use an innovation. In this case, the decision-maker must make imperfect judgments on relationships and outcomes (uncertainty) or must weigh and value the risk associated with the possibility of a variety of outcomes. Even if they possess similar information and knowledge, different decision-makers will vary in their assessments of the

likelihood of alternative outcomes; in addition they will differentially value anticipated risk. Consequently, they may arrive at different decisions, or they may arrive at similar decisions but following varying periods of deliberation. These differences will be accentuated by variations in the timing and quantity of information acquisition.

The literature on response to innovation offers several insights into the factors influencing decision-makers' responses to innovation.[5,6,8,9,10,16] Central among these are the following:

- Decision-makers tend to adopt innovations more rapidly the greater the innovation's perceived relative advantages, the smaller the investment it requires (in terms of physical capital, learning of new skills, etc.), the greater its testability, the less its technical complexity, and so on.[8,10,16]

- Decision-makers tend to be risk averse. Caution dictates the wisdom of adopting a "wait-and-see" attitude in order to avoid the hazards of risk and uncertainty. The late adopter of an innovation may reap some of the benefits of early users' costly experimentation. "[P]otential users...have an incentive to let others try [innovations] first and identify the defects," as well as establish the potential profitability. Even in the highly competitive arena of economic activity, firms demonstrate considerable risk aversion and conservatism in their approach to innovations.[9]

- Partly as a consequence of this risk aversion, it appears that the probability that nonusers will adopt an innovation is an increasing function of the proportion of their peers (colleagues or competitors) who are already using the innovation.[8] This imitation phenomenon reflects both the prima facie positive evidence implicit in the fact of growing usage by peers and the increasing availability of objective evidence about the innovation's relative

advantages and deficiencies. Such evidence increases knowledge of how to best use the innovation and decreases uncertainty about the results of using it. Risk aversion and imitation are responsible for the frequently documented S-shaped innovation diffusion pattern wherein diffusion is initially gradual and then accelerates.[15]

In short, an innovation will be used if it contributes cost-effectively to the realization of the decision-maker's objective. The risk and uncertainty inherent in most innovations generally act as deterrents to rapid adoption in a population of risk averse potential users. One possible exception merits attention here because of its relevance to medical treatment decision-making. An organization which finds itself in a dismal situation (e.g., a firm verging on bankruptcy) may be highly reponsive to an innovation. The organization's fiscal (or other) condition triggers a search for a new means of assuring survival, existing techniques having failed. To a successful (profitable) organization, use of an innovation implies the risk of damaging the status quo, in addition to the possibility of enhancing success. To the organization whose survival is in jeopardy, an innovation offers the hope of improvement, while downside risk is low by definition.

The Environment of Catastrophic Illness Care

The physician with a seriously ill patient often faces a decision-making problem analytically similar to that of the entrepreneur or manager of a near-bankrupt firm: confronted with imminent demise -- of the patient or the firm -- the decision-maker has a strong inducement to use an innovation which might alter the status quo, assuming that the innovation does not impose substantial costs which the decision-maker will have to bear. (An entrepreneur might rationally

choose to accept existing losses rather than risk incurring additional liabilities.)

An entrepreneur confronts the serious possibility of the demise of a firm infrequently and rarely repeatedly; repeated confrontations would generally lead to the firm's bankruptcy. In contrast, physicians routinely deal with dire medical situations in which remissions or cures are impossible or highly improbable, given existing therapies. For a number of reasons, physicians are permitted and encouraged to use innovative therapies even before the therapies' efficacy has been demonstrated and largely irrespective of their cost. A physician's decision to use a poorly understood innovation may well be individually rational in the face of a likely death or serious impairment. At the same time, the social desirability of widespread adoption may remain open to question.

Use of expensive new therapies of unknown efficacy is permitted by the unorthodox economic environment in which catastrophic illness care is delivered. In the present context, the most important of the market imperfections and idiosyncrasies which pervade medical care[1,7,11] is the severance of the conventional bond between consumption of a good or service and financial liability. Widespread insurance coverage imposes the liability for most catastrophic illness care on third parties, private and public insurers. When the patient's insurance coverage and other resources are inadequate, individual or institutional price discrimination may pass costs on to other patients. In short, the financial constraint on consumption is effectively removed from the delivery of catastrophic illness care. Patients' demand for care is economically unconstrained and, of greater importance, physicians acting as demand agents for their patients (discussed below) need not be concerned about the financial implications of

their demand decisions.

Use of new therapies is encouraged by a variety of factors. One is the tendency of the physician-patient trust relationship to foster "Cadillac care":

> Delegation and trust are the social institutions designed to obviate the problem of informational inequality...[T]he patient must delegate to the physician much of his freedom of choice. He does not have the knowledge to make decisions of treatment, referral, or hospitalization. To justify this delegation, the physician finds himself somewhat limited... The safest course to take to avoid not being a true agent is to give the socially prescribed 'best' treatment of the day. Compromise in quality, even for the purpose of saving the patient money, is to risk an imputation of failure to live up to the social bond.[1]

In the case of catastrophic illness, "best" treatment usually implies the physician's taking some positive therapeutic action, often irrespective of its efficacy. Medicine's general pro-therapy bias[4] is strongly reinforced by reactions to a desperate situation: patients feel comforted by medical attention, however technically ineffective it may be; and beyond their agency role, physicians apparently deal with their own sense of frustration or impotence by "taking action." "[P]hysicians...get nervous about <u>not</u> treating...It is difficult to do nothing; [they] are neither trained nor conditioned for it... How should one behave when <u>nil desperandum</u> collides with <u>primum non nocere</u>?" [3]

Physicians <u>are</u> trained to follow therapeutic leads set either by top experts or by their immediate colleagues. The medical research/education establishment fosters imitative behavior -- and innovative behavior -- at the earliest stages in the training of physicians. Governmentally and privately subsidized research is housed, in the main, in and around educational centers; hence medical students are exposed to, and often participate in, work on the frontiers of clinical medicine. The students' role models are innovators.

Modernity may become a goal in itself; at a minimum, it is viewed as producing professional respect. The innovative propensity is passed on to each generation of medical students, which attempts to establish its superiority over preceding generations by becoming more technically sophisticated. This creates a demand for medical research and its products. Through the professional literature and seminars and meetings, practitioners who have completed their formal training are supplied with information on, and encouraged to keep up with, recent developments.

Imitative behavior may or may not be accompanied by a thorough understanding of the medical problem, or of the therapy. For specific decision-making purposes, imitative behavior tends to be substituted for comprehensive personal understanding most commonly when the costs of waiting for such understanding are perceived as too high. If the prognosis for an illness is a few days of mild fever and nausea, there is no compelling reason for a physician to prescribe a drug about which very little is known; in fact, the danger of toxicities is a compelling reason not to prescribe the drug. If, however, the prognosis is imminent death, the relative risks of trying a novel and promising therapy are small. In other words, the worse the prognosis, the less is the risk differential between trying and not trying the therapy. The former may introduce uncertainty and variance in the outcome, but a not unreasonable assumption is that both the uncertainty and the variance are desirable relative to the near-certainty outcome of not trying the therapy. From the physician's perspective, the only "cost" of using a technique which proves to be a failure is that things are not better. There is no counterpart in medicine to the financial risk accepted by the business entrepreneur who decides to use an innovation.

In short, in dealing with catastrophic illness, physicians have powerful incentives to try any therapy which is available and few financial deterrents

to doing so. In a fundamental sense, the major constraint is the technology itself, the "state of the art."

A Model of Treatment Decision-Making in Leukemia

Leukemia and Its Therapy

The leukemias are cancers of the blood. Acute leukemia is the leading childhood cancer, though leukemias kill many more adults than children. Prior to the late 1940s, these diseases had not responded to any therapy. With the development of the early anti-cancer drugs, physicians had a relatively easy method of treating leukemias, a method whose initial successes in inducing remissions in leukemic children provided reason for optimism. Since the 1940s, physicians have experimented with an arsenal of drugs -- individually, in combination, with varying dosages and timing of dosages -- and they have achieved mixed results. Only one of the four leukemias considered in the study reported below -- the acute leukemia of childhood -- yielded significant ground to drug therapy during the two decades following its first use. Yet large percentages of each of these four closely related diseases have long received chemotherapy. (Many of the victims of chronic leukemia are treated only for symptomatic relief. Chemotherapy of the acute leukemias is virtually always administered with the goal of remission or cure.) Table 1 presents distinguishing characteristics of these leukemias.

The Model

As noted earlier, a decision to use or not to use an innovation is generally based on the contribution that that innovation is expected to make toward realizing the decision-maker's objective, compared with the cost of

TABLE 1. Characteristics of the Four Leukemias

Type of Leukemia	Blood Cell Type Affected	Most Frequent Victims	Prognosis without Therapy	Nature of Therapy	Prognosis with Therapy
Acute Lymphocytic (ALL)	Lymphocyte	Children	A few months	Originally 1 or 2 drugs. Currently multiple drug therapy with CNS irradiation and much supportive therapy.	Complete remissions expected. Median survival 3-5 years; some cures.
Acute Myelocytic (AML)	Granulocyte	Adults	1-2 months	1- or 2-drug therapy through period studied.	Partial remissions possible, though not common until most recent years. No appreciable extension of median survival through period studied (through 1968).
Chronic Lymphocytic (CLL)	Lymphocyte	Adults, generally middle-aged to elderly	A few years	1- or 2-drug therapy.	Unchanged. Chemotherapy treats symptoms only.
Chronic Myelocytic (CML)	Granulocyte	Adults	A few years (shorter on average than for CLL)	1- or 2-drug therapy.	Unchanged. Chemotherapy treats symptoms only.

use. A mechanistic view of the physician-qua-demand-agent for the patient would suggest that the physician's objective is to improve the health or comfort of the patient.* Thus, the decision of whether or not to use a therapy would rest on a comparison of the expected health improvement with the anticipated costs of the therapy, both economic and medical (e.g., risk of suffering due to toxicities).

Of course, as observed above, other factors may complicate the decision-making: in a medically desperate situation, physicians may not have sufficient information to predict the costs and benefits of using a treatment, yet they may still choose to administer the therapy for reasons that are both rational and emotional. The rational component is recognition that risk and uncertainty may be desirable when the certainty outcome of not using the treatment is near-term death, severe morbidity, or incapacitating disability. The emotional component is the compelling need felt by many physicians to "do something, anything" when confronted with a dire medical situation, even if that something has virtually no chance of improving the situation and may even cause suffering.[3,4]

Physicians cannot know precisely how a given therapy will affect a given patient. What they can do is observe certain variables and then estimate an

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*The decisions of whether or not to treat a seriously ill patient, and if so how, are generally made by the physician in charge of the case. This is not to suggest a lack of consultation with the patient, but rather recognizes the critical importance of the trust relationship in the situation: not only must the patient rely on physicians for reasons of technical knowledge, but in addition many patients and their families are relieved to have someone else take responsibility for such serious, potentially emotional decisions. Thus, the decision-making process focuses on the physician. The patient's role is mostly passive, though there are exceptions: for religious or other non-economic reasons, the patient may overrule a physician's decision or recommendation, an occurrence not considered in the analysis which follows; or conventional economic demand factors may come into play. Acknowledging these exceptions, and recognizing that the patient is the ultimate consumer of the therapy, this is primarily an analysis of physician decision-making.

outcome for a patient, both with and without use of the treatment in question. To the extent that physicians accurately perceive the roles of these variables in influencing health improvement, and to the extent that the improvement of their patient's health is their sole objective, one would expect variables significant in influencing positive treatment decisions to be correlated with improved health status. If the variables which influence treatment decisions did not play significant roles in affecting the patient's health, this would suggest either that the physicians did not understand the effects of certain variables on health improvement, and hence relied on other considerations, or else that health improvement was not the sole objective motivating use/rejection decisions.

In comparing the medical treatment decision-making process with conventional decision-making, it is useful to think of classes of relevant variables which play the roles identified in the general discussion of decision-making. Thus we need to identify a variable indicative of the decision-maker's objective, and a set of factors involved in the production or realization of the objective, including both technical inputs and constraints. Each of these categories is discussed briefly below. The specific variables employed in the empirical analysis are enumerated and defined in Table 2.

The objective. For many not-for-profit activities, the objective function is either multi-dimensional or ill-defined. In the treatment of catastrophic illness, the primary objective is "improved health." This may mean objective physical improvement -- for example, disease remission or increased survival time -- or it may refer to the easing of suffering, both physical and psychological. With respect to the latter, it is important to

TABLE 2. Variables*

Variable Name	Definition	Role in Analysis	Mean Value** For ALL	AML	CLL	CML
SUR_i	Survival time of patient i, in months	Objective	15.01	3.83	37.41	24.08
$TREAT_i$	Whether (1) or not (0) patient i received chemotherapy	Decision variable	0.81	0.66	0.35	0.50
AGE_i	Age of patient i at time of diagnosis, in years	Independent influence on SUR_i. May also influence physician's sense of desperation	5.67	58.50	68.41	61.77
HOS_i	Hospital in which patient i hospitalized; high quality (1) or low quality (0) for chemotherapy	Measure of quality of hospital facilities and personnel for delivery of chemotherapy	0.46	0.38	0.30	0.31
$PVTPT_i$	Private (1) or ward (0) patient	Indicator of patient i's socioeconomic status	0.75	0.84	0.80	0.79
ART_t	Number of articles in leading medical journals in year t (the year of patient i's diagnosis) on the chemotherapy of this leukemia	Indicator of professional scientific interest and dissemination of knowledge	7.99	3.78	1.66	2.45
PCT_{t-1}	Percentage of Connecticut patients diagnosed in year t-1 to whom drug therapy was administered	Measure of colleagues' experience. An indicator both of learning about this therapy and simply of a state-wide trend in therapy	0.79	0.64	0.31	0.46

TABLE 2 (cont'd)

Variable Name	Definition	Role in Analysis	Mean Value** For ALL	AML	CLL	CML
MST_{t-2}	Median survival time, in months, of Connecticut patients treated in year t-2 (period necessary for such information to be ascertained)	Indicator of degree of success with this chemotherapy realized by physicians in Connecticut. Measure of average state-wide technological capabilities and learning	10.35	1.39	25.87	22.16
$TECH_t$	Median survival time, in months, for patients treated in year t by members of a leading clinical research group (Acute Leukemia Group B)	State of the art. Indicator of therapy trend and maximum (average) potential at time t	15.06	--Not applicable-- (For other than ALL, state-of-the art therapies did not change significantly during period studied, 1947-68, inclusive.)		
$ALART_t$	Values of ART_t for ALL	Included in treatment decision-making equations for AML, CLL, and CML as indicators of experience and success with similar therapy for a related disease (ALL) which has yielded ground to drug therapy	--		7.99	
$ALPCT_{t-1}$	PCT_{t-1}		--		0.79	
$ALMST_{t-2}$	MST_{t-2}		--		10.35	
$ALTECH_t$	$TECH_t$		--		15.06	

*Derivation and meaning and limitations of variables are discussed in detail in reference 14.

**Data are discussed in the next section of this paper and in reference 14.

recognize that one objective of the physician decision-maker may be to reduce his or her own psychological discomfort; administering therapy may partially achieve this objective, irrespective of its effects on the patient's health status.[3]

In the case of the acute leukemias, the principal goal of chemotherapy is to increase the patient's survival time. This is the only objective explicitly quantified. However, other objectives can be ascertained from the analysis. They are discussed in the next section of the paper.

Inputs and constraints. The production or attainment of increased survival time is a function of the knowledge of the medical personnel delivering care, the technology available to them, and the condition of the patient. Knowledge can be obtained both from personal experience and from non-experiential sources (the professional literature, seminars, etc.). The technology consists both of facilities and equipment specific to the therapy and of general facilities for supportive therapy.

Production of increased survival time is fundamentally constrained by the state of the art, the capability of the best therapy administered under optimal conditions. In a given case, the ability of therapy to enhance survival time depends on the individual patient's condition: the older the patient, the more advanced the disease, the less effective will be the therapy. Finally, economic factors can act as a constraint either on the fact of therapy or on its quality, by affecting the demand of either the patient or the physician.

The conceptual model is as follows:

$$(1) \qquad SUR_i = f(X_1, \ldots, X_n)$$

$$(2) \qquad TREAT_i = 1 \quad \text{if} \quad E(SUR_i) \geq SUR_i^* \qquad = 0 \quad \text{if} \quad E(SUR_i) < SUR_i^*$$

Equation (1) says that the objective, survival time (SUR_i), is a function of a series of variables (identified in Table 2). Equation (2) says that a physician will choose to administer chemotherapy to patient i if the expected value of patient i's survival time ($E(SUR_i)$) equals or exceeds some threshold value (SUR_i^*).

SUR_i^* may vary from physician to physician and even among patients for a given physician. In addition, for individual patients, physicians can only guess at $E(SUR_i)$, and the variance is so large that the expected value is not only very difficult to determine but also not necessarily very meaningful. It seems more likely that physicians' treatment decisions are influenced by individual observable variables which they believe to be associated with health improvement. For this reason, and in order to explore other influences on the treatment decision besides objective health improvement, both the survival time and the treatment decision-making equations are specified independently as functions of a similar set of variables. (The variables are identical except that the decision-making equation includes the variables with the "AL" prefix in order to allow for the possibility of "cue-borrowing," a phenomenon discussed in the next section.)* This approach permits comparison of the roles of individual

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*Theoretically the survival time equation should include measurement of the fact and nature of treatment as independent variables. This study's only relevant variable, $TREAT_i$, was excluded for the following reasons:

During the period studied, the medical evidence demonstrates that chemotherapy for other than childhood ALL did not increase survival time. The use of drugs for symptomatic relief in the sicker chronic leukemia patients, who died earlier, would lead to a spurious negative correlation between $TREAT_i$ and SUR_i.

For childhood acute leukemia (ALL), treatment definitely did increase survival time. However, problems in the data set recommended against including $TREAT_i$. Specifically, $TREAT_i$ is collinear with other important variables. Its inclusion in regressions masks the effects of variables like $TECH_t$ whose influences need to be observed to compare the determinants of the treatment decision with these variables' roles in the production of survival time.

Secondly, survival time in ALL is highly dependent on the specifics of the chemotherapy administered. By the early 1960s, virtually every child with ALL received chemotherapy, yet there were great disparities in the types and qualities of therapies. $TREAT_i$ misses these subtleties completely.

independent variables in influencing survival time and the physician's decision to administer or to withhold chemotherapy.

$$(1') \quad SUR_i = \alpha_0 + \alpha_1 AGE_i + \alpha_2 HOS_i + \alpha_3 PVTPT_i + \alpha_4 ART_t + \alpha_5 PCT_{t-1} + \alpha_6 MST_{t-2} + \alpha_7 TECH_t + \varepsilon_1$$

$$(2')^* \quad TREAT_i = \beta_0 + \beta_1 AGE_i + \beta_2 HOS_i + \beta_3 PVTPT_i + \beta_4 ART_t + \beta_5 PCT_{t-1} + \beta_6 MST_{t-2} + \beta_7 TECH_t + \beta_8 ALART_t + \beta_9 ALPCT_{t-1} + \beta_{10} ALMST_{t-2} + \beta_{11} ALTECH_t + \varepsilon_2$$

Results and Discussion

The primary source of data for the empirical study was the Connecticut Tumor Registry of the Connecticut State Department of Health. This Registry is a unique resource, containing data on all reported cases of cancer among the residents of the entire state dating from 1935. The present study examined all cases of the four leukemias diagnosed from 1947 through 1968, excluding some incomplete records and cases falling outside of prespecified age categories.**

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*$TECH_t$ is included only for ALL, while the variables with the prefix "AL" are included only for AML, CLL, and CML.

**For details on these and the other data -- their nature, problems, and deficiencies -- and on the diseases and their therapies, see reference 14.

Table 3 presents regression results fitting the data to the survival time equation (1'), using a limited dependent variable regression package. Tables 4 and 5 present Probit analysis fits to the treatment decision equation (2'). Table 4 excludes the ALL variables from the regressions for the other leukemias, thus yielding a set of variables identical to those of the survival time equation. Table 5 includes the ALL variables. The limitations imposed by data availability and quality are substantial, yet these results permit several generalizations.

From Table 3, we see that the only clear determinants of survival time are the patient's condition (represented here by the single variable, AGE_i) and the technical capability of the therapy (represented by the state of the art median survival, $TECH_t$, measured only for childhood acute leukemia; recall that the state of the art -- in terms of increasing survival time -- did not change significantly for the other leukemias throughout the period studied). The near-significant coefficients of PCT_{t-1} suggest that some learning-by-doing may have been occurring, but this effect is not pronounced. (The coefficients imply small elasticities at the means, ranging from -0.17 for CLL to 0.55 for AML.) The nonsignificance and suggested negative tendency of the study's sole indicator of the quality of facilities and personnel for administering chemotherapy (HOS_i) probably reflect the fact that many patients were treated first at "lower quality" hospitals and then, after therapeutic failure, were transferred to one of the "higher quality" hospitals. Patients were reported as having been in one of the high quality hospitals if during the course of the disease they were <u>ever</u> in one of them. Hence the average physical condition of patients

TABLE 3. Determinants of Survival Time

(Numbers in parentheses are asymptotic t statistics)

Variable	Disease			
	ALL	AML	CLL	CML
CONSTANT	2.828 (0.81)	5.351 (2.89)	104.513 (8.73)	41.314 (4.99)
AGE_i	-.461 (-2.71)	-.095 (-5.00)	-.977 (-6.50)	-.483 (-6.67)
HOS_i	-1.851 (-1.13)	-.513 (-0.65)	-2.098 (-0.67)	-1.656 (-0.64)
$PVTPT_i$	-.117 (-0.07)	-.178 (-0.17)	8.328 (2.28)	3.480 (1.13)
ART_t	-.136 (-0.61)	.087 (0.69)	.629 (0.59)	.508 (0.88)
PCT_{t-1}	7.667 (1.48)	3.281 (1.58)	-20.769 (-1.75)	12.151 (1.96)
MST_{t-2}	-.201 (-0.55)	.012 (0.01)	-.026 (-0.17)	.075 (0.33)
$TECH_t$	.819 (3.53)			
Ages (in years)	0-19	20-98	40-98	20-98
N	268	752	693	419
df	7	6	6	6
$-2 \ln \lambda$	91.37	20.90	62.38	39.53

(λ is the likelihood ratio. $-2 \ln \lambda$ is distributed chi-square with degrees of freedom equal to the number of variables, including the constant term, minus 1.)

TABLE 4. Determinants of the Treatment Decision, Excluding the ALL Variables From the AML, CLL, and CML Equations (Numbers in parentheses are asymptotic t statistics)

Variable	Disease			
	ALL	AML	CLL	CML
CONSTANT	-1.252 (-2.93)	-.223 (-0.92)	.041 (0.10)	-.298 (-0.67)
AGE_i	.001 (0.03)	-.014 (-4.54)	-.012 (-2.51)	-.012 (-2.62)
HOS_i	.616 (2.54)	.374 (3.50)	.333 (3.05)	.565 (3.91)
$PVTPT_i$	-.039 (-0.17)	.153 (1.12)	-.226 (-1.74)	.443 (2.59)
ART_t	.016 (0.50)	.011 (0.64)	.023 (0.60)	.039 (1.24)
PCT_{t-1}	1.142 (1.17)	1.849 (6.67)	2.243 (5.14)	1.839 (5.28)
MST_{t-2}	.058 (0.61)	.022 (0.22)	-.012 (-1.41)	-.019 (-1.58)
$TECH_t$	.048 (1.38)			
Ages (in years)	0-19	20-98	40-98	20-98
N	268	752	693	419
df	7	6	6	6
$-2 \ln \lambda$	73.35	118.08	52.99	78.79

(λ is the likelihood ratio. $-2 \ln \lambda$ is distributed chi-square with degrees of freedom equal to the number of variables, including the constant term, minus 1.)

TABLE 5. Determinants of the Treatment Decision, Including the ALL Variables

(Numbers in parentheses are asymptotic t statistics)

Variable	Disease		
	AML	CLL	CML
CONSTANT	-.695 (-2.17)	-.685 (-1.32)	.191 (0.38)
AGE_i	-.016 (-4.92)	-.012 (-2.54)	-.013 (-2.85)
HOS_i	.356 (3.25)	.357 (3.18)	.561 (3.77)
$PVTPT_i$	.124 (0.88)	-.239 (-1.80)	.386 (2.21)
ART_t	-.001 (-0.03)	.038 (0.88)	.005 (0.15)
PCT_{t-1}	.138 (0.31)	-.100 (-0.13)	.005 (0.01)
MST_{t-2}	.020 (0.17)	.003 (0.34)	-.031 (-2.32)
$ALART_t$	-.037 (-2.22)	-.050 (-2.78)	-.032 (-1.07)
$ALPCT_{t-1}$	2.497 (4.88)	1.672 (3.28)	1.121 (1.71)
$ALMST_{t-2}$	-.045 (-1.67)	-.054 (-1.96)	.019 (0.49)
$ALTECH_t$	.035 (2.05)	.045 (2.16)	.026 (0.94)
Ages (in years)	20-98	40-98	20-98
N	752	693	419
df	10	10	10
$-2 \ln \lambda$	147.91	69.97	84.22

(λ is the likelihood ratio. $-2 \ln \lambda$ is distributed chi-square with degrees of freedom equal to the number of variables, including the constant term, minus 1.)

in the higher quality hospitals was probably much poorer than that of the average patient in the state. Unfortunately, the data did not permit separation of these influences.

The economic factor ($PVTPT_i$) is not important in the determination of survival time. This fact is of most interest in the case of childhood acute leukemia, the one leukemia for which chemotherapy significantly increases longevity. The tentative implication of this analysis is that ability to pay for an expensive therapy does not influence outcome for a child seriously ill with leukemia. Implicitly, this suggests that the economic factor is not important in the determination of receipt of therapy, nor in the quality of therapy administered as measured by outcome. This is corroborated by the analysis of treatment decision-making, discussed below. The one instance in which socio-economic status is associated with greater longevity -- chronic lymphocytic leukemia in middle-aged and elderly adults -- probably reflects the fact that more affluent patients are generally healthier (for reasons of diet, habits, etc.). This interpretation is also supported by analysis of the treatment decision-making findings.

Comparison with the above of the results presented in Tables 4 and 5 sheds considerable light on the determinants of the decision to administer drug therapy to or to withhold it from the victims of leukemia.

While the technical capability of ALL therapy ($TECH_t$) had an obvious impact on survival outcomes, its influence on actual treatment decisions is not of comparable importance. Combined with the nonsignificance of the measures of recent state-wide achievement (MST_{t-2}) and of professional scientific

interest (as reflected in number of journal publications, ART_t),* this suggests that the effectiveness of therapy was of less direct consequence in childhood leukemia treatment decisions than other considerations. This finding is consistent with the conventional wisdom[4] and is supported by other results discussed below.

The patient's condition and personal characteristics, represented by AGE_i, play a role in the determination of both outcome and the treatment decision, though not necessarily for identical reasons. The patient's condition does have an objective impact on survival expectations and response to therapy. Physicians might be responding to this objective consideration in making therapy decisions, but in addition they may be responding to the subjective impact of having to deal with seriously ill patients. The desire to treat -- to intervene in a situation with a dire prognosis -- may be greater the more desperate the physician feels the situation to be. Quite naturally, a terminal illness in a child would generally be considered more tragic than terminal illness in an elderly person; similarly for a middle-aged adult as contrasted with a very old one. Indeed, while relative youth is associated with longer survival in all the leukemias, it is medically well-established that therapy per se did not increase survival expectations in other than childhood leukemia through the period studied. Thus the tendency for physicians to treat their younger AML, CLL, and CML patients would seem to indicate reaction to a sense of desperation.[13]

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*The nonsignificance of ART_t may reflect the way in which this variable was measured, rather than the phenomenon it was intended to measure. However, there is substantial evidence in the literature that the scientific and popular press may provide information about an innovation, but more personal contacts, e.g., colleagues' experiences with the treatment, have more significant influence in actual adoption decisions.[2]

The nonsignificance of AGE_i in the childhood ALL treatment decision regression may reflect either of two considerations and probably reflects both: first, while younger children fare better with therapy than do teenagers, nearly all children realize additional survival time as the result of therapy; even the relatively small increment in survival time realized by the older children may be enough to justify treatment in the minds of most physicians. Second, physicians view terminal illness in a child of any age as being a tragic event. The treatment of afflicted children of all ages may represent an attempt by physicians to alleviate their sense of impotence or desperation.

For all four leukemias it is clear that chemotherapy was administered more often in hospitals equipped and staffed to deliver high quality therapy. This is not surprising. Physicians at the better hospitals tend to believe in and be experienced with cancer chemotherapy; they tend to keep up with new developments in therapy; hence, ceteris paribus, patients who consult them are more likely to receive therapy than are individuals who consult physicians in or affiliated with other hospitals. In addition, especially in the case of acute leukemia, general practitioners or internists are often reluctant to treat; instead they will refer the patient to a specialist, who usually practices in one of the better hospitals.

The treatment decision equations permit some intriguing though highly tentative conjectures about the role of ability to pay in the receipt of therapy. For victims of the acute leukemias it appears that treatment decisions were independent of the patient's economic status ($PVTPT_i$). Note that the bulk of the period studied predates Medicare and Medicaid, so many of the poorer patients were uninsured or very inadequately insured. While some

leukemia therapy was funded by research grants, many of the poorer patients must have been the beneficiaries of individual or institutional price discrimination (redistribution). The important point is that the economic factor did not bar seriously ill people from receiving potentially beneficial therapy. The nonsignificance of economic status in the survival of children with acute leukemia further suggests that the quality of therapy was not significantly different.

The results for the chronic leukemias are somewhat more ambiguous but admit to plausible interpretations. The negative coefficient estimate for $PVTPT_i$ in the CLL regression probably reflects physicians administering the CLL chemotherapy only to their sickest patients, who tend to come from lower socio-economic groups. This interpretation is consistent with the significant positive coefficient estimate for $PVTPT_i$ in the CLL survival time regression. It is medically established that drug therapy did not significantly influence survival time in CLL patients; hence the significance of the economic variable must represent other, exogenous, factors. In the case of CML, a plausible conclusion is that ability to pay <u>did</u> influence the decision to administer drugs. As in CLL, CML drug therapy did not enhance survival expectations; rather it could palliate, and with fewer significant deleterious or discomfiting side effects than in CLL. Hence it appears that affluent CLL patients may have demanded and bought therapy which was not administered as frequently to poorer CML patients. Combined with the nonsignificance of economic status in the acute leukemia treatment decisions, this suggests the possibility that an approximation to conventional market behavior may characterize the demand for and provision of medical goods and services which either are not highly effective or which relate to a medical condition which is not

considered serious (i.e. threatening to life or limb, involving prolonged morbidity, etc.). By contrast, for reasonably effective therapies addressing serious medical problems (e.g., acute leukemia therapy), conventional market forces may often be inoperative.

The results involving the direct measure of quantity of recent experience with chemotherapy within the state (PCT_{t-1}) provide insight into the development of medical therapy trends. According to the survival equations (Table 3), experience per se did not necessarily convey useful learning to practitioners (defining "useful" as an improvement in outcomes). However, when the dichotomous treatment decision variable was regressed on the same set of variables (Table 4), PCT_{t-1} was invariably strongly statistically significant for other than ALL; in addition, its quantitative importance (coefficients relative to the magnitudes of the dependent variables) is considerably greater for the treatment decision. The inference is that there was a distinct trend phenomenon in which physicians followed their colleagues' therapeutic leads despite the lack of resultant improvement in their patients' survival expectations. For innovations in most settings, a comparable pattern of imitative behavior, with its consequent substantial diffusion, generally would require effective demonstration of the innovation's relative advantage (technical superiority, profitability, etc.).

The trend phenomenon takes on a new dimension when one compares Tables 4 and 5. In Table 5 -- the regressions which include the ALL variables in the decision equations of the other leukemias -- PCT_{t-1} is clearly nonsignificant, in striking contrast to Table 4. However, in Table 5 the corresponding ALL variable ($ALPCT_{t-1}$) is significantly correlated with $TREAT_i$, as is the measure of the ALL state of the art ($ALTECH_t$). In other words,

in cases of leukemia other than the childhood variant, the decision to administer drug therapy appears to have been significantly affected by the recent trend (both quantity of experience and degree of success) in administering chemotherapy to the victims of the childhood disease. Indeed, the amount of ALL experience clearly dominated the influence of the disease's own trend (PCT_{t-1}). In a sense, the trend in the treatment of the childhood disease -- the one successful leukemia chemotherapy -- diffused to the handling of the other leukemias. This effect was notably stronger for AML and CLL than it was for CML,a predictable result as AML and CLL are more closely related to ALL (by disease severity and by cell type, respectively) than is CML. This provides support for the concept of "cue-borrowing" in treatment decision-making: following the more successful treatment trends for similar therapies in closely related diseases. Apparently indirect success influenced physicians' leukemia treatment decisions more than did direct failure. This is consistent with the apparent need felt by physicians to take positive therapeutic action in caaes of serious illness.

Conclusion

Conclusions drawn on the basis of this empirical study must be accompanied by several caveats: this is a case study, one whose generalizability remains to be established; and the data are imperfect, as is the modeling. Still, the findings provide strong suggestive evidence for several tentative conclusions.

The principal general observation is that, at least in the case of catastrophic illness, the medical decision-making process with respect to the

use or nonuse of an innovation does differ from the process which occurs in other settings which have been studied. This is a function of the compelling nature of many medical situations and of the unorthodox, relatively unconstrained economic environment in which individual use/nonuse decisions are made. Manifestations of the difference in decision-making processes include the following:

- In the dire medical situation, decision-makers are less cautious or conservative in deciding to use an innovation than would be more conventional market decision-makers. The former seem to require less proof of efficacy (relative advantage) than the latter. Indeed, the usual market usage decision is predicated almost exclusively on the expected contribution of the innovation to the firm's profitability, while in the medical setting both the inherent merits of the therapy (the analog to profitability) and the medical situation itself influence usage decisions. That is, as illustrated by the case study, a desperate medical situation may promote use of a therapy irrespective of its efficacy. Thus, other things being equal, diffusion of an innovation may be more rapid or extensive in the desperate medical context than in the conventional market.[13]

- Even in the instance of the firm verging on bankruptcy -- perhaps the closest market analog to the catastrophic illness situation -- innovation adoption is not costless. While such a firm might be more receptive to innovation than a more stable firm, its entrepreneur must weigh the potentially significant costs of using the innovation against its anticipated benefits. A decision not to use an innovation, and thus to accept near-certain dissolution, might well be rational. In an important respect, the costs to both physicians

and patients of therapeutic failure with the medical innovation are very limited, given the near certainty of death, severe disability, etc. without using the innovation and the absence of direct financial implications attached to use. This would seem to account in part for physicians' preference for an active therapy, and their apparent inability to consider "doing nothing" as a viable option in cases of serious illness.

- Physicians may place more emphasis on indirect encouraging evidence about a therapy than on direct discouraging information. This was suggested by the "cue-borrowing" phenomenon in leukemia chemotherapy in which physicians appear to have based therapy decisions for AML, CLL, and CML more on the successful trends in ALL treatment than on the disappointing results of these diseases' own therapies. Such "cue-borrowing" may be an important determinant of the development of many treatment trends in medicine.

In sum, in a conventional market environment an innovation must demonstrate its superiority to alternatives, including using nothing, in order to be accepted by a large segment of the population it is designed to benefit. In a dire medical situation, the innovation's preferredness may be assumed until demonstrated otherwise. I am not arguing that this is irrational or undesirable; in a desperate situation, use of an unknown quantity may indeed by logically preferable to the dismal outcome associated with other approaches. Rather, I wish to emphasize the existence of differences in decision environments and hence in decision outcomes, and the concomitant implications for the allocation of resources both within medicine and among sectors.

In an important sense, much of medical decision-making, and hence behavior, is constrained by technology and by the state of knowledge rather

than by conventional economic considerations. We live in an era in which medical knowledge is changing rapidly and new understanding is frequently accompanied by a profusion of new technology and technique. Not all of these technical changes are necessarily worth their cost,[12] yet they are not forced to survive orthodox market tests. As both existing and proposed legislation promise to remove the delivery of medical care even further from the conventional marketplace, we must develop an understanding of decision-making within the medical marketplace so that we may determine the rules and regulations by which it should governed.

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