

AN APPLICATION OF DECISION THEORY TO A MEDICAL  
DIAGNOSIS-TREATMENT PROBLEM

Allen S. Ginsberg  
Fred L. Offensend

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ABSTRACT

The decision faced by a physician when confronted by a patient with an undetermined disease may be simply stated as: "What course of action, in the form of diagnostic tests and/or treatments, should be taken?" In most cases, this problem can be characterized as a sequential decision under uncertainty. Since this is a class of problems for which Decision Theory has proved a useful tool, it appears fruitful to attempt to apply it to the physician's problem. In the following paper we will explore this possibility by describing the application of decision theoretic techniques to a specific case. We first comment on why we feel the model we propose is more appropriate than other methods of treating the problem. Then, we briefly describe the proposed model in the abstract. The main body of the paper describes a specific problem and its solution by decision theoretic techniques. In the final section we point out some of the shortcomings of our particular analysis and some of the problems that might be encountered in a more general setting.



AN APPLICATION OF DECISION THEORY TO A MEDICAL

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Allen S. Ginsberg \*

The RAND Corporation, Santa Monica, California;  
Stanford University, Stanford, California

Fred L. Offensend

Stanford University, Stanford, California

Introduction

Our basic assumption in constructing the model is that the doctor wishes to choose the course of action which will maximize his and/or the patient's "satisfaction." We have chosen to define "satisfaction" as expected utility, both because of its intuitive appeal and the well-known arguments for the rationality of maximizing expected utility.<sup>[1]</sup> Given this objective, the physician often has many courses of action open to him, both now and in the future. He may elect to perform one or a series of diagnostic tests, or to apply one or more treatments for the suspected disease, or to use some combination of

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<sup>[1]</sup> Luce, R. D. and Raiffa, H., *Games and Decisions*, New York, John Wiley & Sons, 1967, Chap. 2.

the tests and treatments. It seems plausible that he would base his decisions on such factors as:

1. His judgment, based on the symptoms evidenced and preliminary tests, as to what are the likelihoods of the possible diseases.
2. His assessment of the amount of information which he is likely to gain from further testing.
3. The possibility of side effects from the tests and treatments.
4. The value or utility to him and/or the patient of the various outcomes which might accrue from any particular course of action.

In some manner the physician must process these considerations in order to make his decision. It is this processing which we have attempted to formalize by use of the concepts of Decision Theory. We are not proposing to completely replace the judgment and experience of the physician and/or the patient in determining the necessary data. We simply intend to illustrate a formal procedure for obtaining and processing the appropriate data for making this decision in the face of uncertainty. In our technique, the doctors play a very large role in determining the values of all input parameters. It is conceivable that with the development of appropriate medical data systems their part in this role will be diminished, but, we believe, never entirely eliminated.

It is in this sense of formalizing the data processing (a process at which humans are notoriously bad) that our methods may be preferable over current practice -- i.e., the decision made by the

physician without the aid of formal models. Though the above conjecture has not been tested, it seems likely that as the situation becomes more complex (e.g., more possible actions and outcomes) it becomes increasingly difficult for the human mind to process the relevant data in order to maximize the expected utility.

Given our objective of maximizing expected utility over all possible actions and outcomes, the work that has been done with formal models of differential diagnosis<sup>[2]</sup> is unsatisfactory. Simply stated, most of this work is directed at making probabilistic statements about the possible diseases which the patient might have. When the confidence level (or alternatively, conditional probability) of a particular disease reaches a prescribed level as testing progresses, then the appropriate treatment is applied. This method in no sense maximizes expected utility. Rather, it maximizes the probability of achieving a cure. Though in some rare situations this may be equivalent to the expected utility criterion, maximizing the probability of a cure completely ignores potentially relevant factors such as side effects and dollar costs of tests. Given that one possible side effect is death, it seems that these are fairly serious omissions. Furthermore, the differential diagnosis approach cannot take into account the fact that the state of the patient can change over time regardless of what actions are taken (i.e., he may spontaneously get better or worse or new symptoms may appear). In other words, considering the diagnosis and treatment as two separate decision problems

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[2] Jacquez, John A., editor, *The Diagnostic Process*, Ann Arbor, Proceedings, Conference at University of Michigan, May 1963, Malloy Lithographing, Inc., 1964.

and not taking into account the values of the possible outcomes, ignores what we feel are the realities of the problem and can achieve the maximum utility only in the simplest of circumstances or by luck.

### The General Model

We first illustrate the general approach to modelling the diagnosis-treatment decision problem by a simple hypothetical example. Figure 1 shows the general outline of the decision tree resulting from the model.

Let us assume that a patient comes to the physician exhibiting some set of non-normal symptoms. The doctor wishes to set a course of action which will maximize the expected utility of the outcomes resulting from this plan. The set of technologically feasible actions that might be taken at the first step consists of diagnostic tests, treatments, or simply doing nothing. The determination of exactly which elements make up this set of actions is dependent on many factors, such as: the symptoms exhibited; the patient's previous history; the current prevalence of various diseases; and others. This determination could be made by some formal set of rules, by the physician's judgment or some combination of these two selection modes. In our application we have chosen to use the physician's judgment as to what alternatives are technologically feasible at the first stage and at all succeeding stages. In our hypothetical example, let us assume that the set of feasible actions at the first stage are: (1) to perform diagnostic Test I, (2) to apply Treatment I, (3) to apply Treatment II or, (4) to wait and do nothing for some specified period



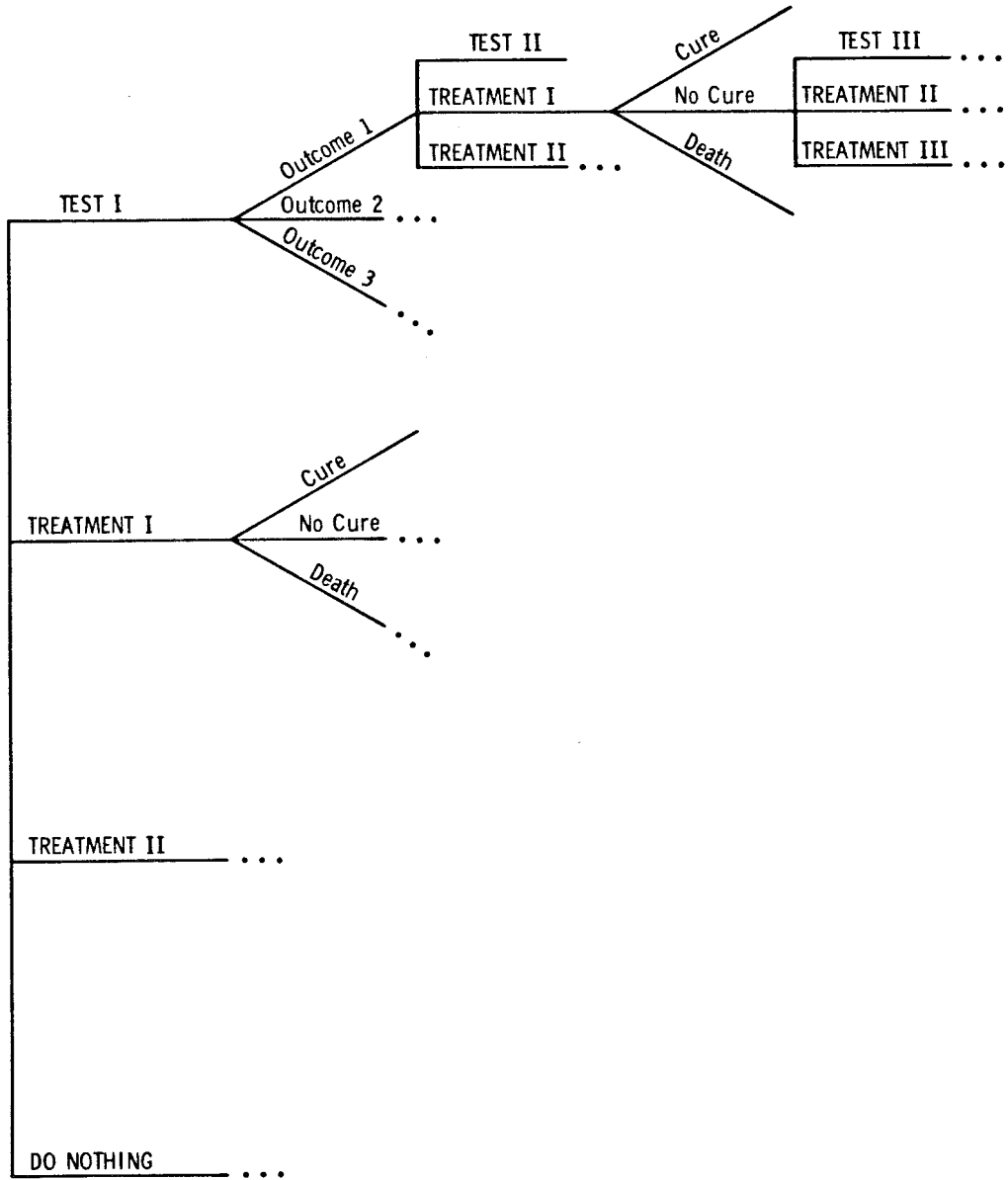


Fig. 1 -- Hypothetical Decision Tree

of time. These actions are shown as the set of horizontal branches on the decision tree in Fig. 1.

The model then assumes that one of a finite set of outcomes will result from each of the actions. The description of these outcomes is extremely crucial since it has a major effect on the validity of the model and also determines what data, in the form of probabilities and utilities, must be provided to the model for its solution. There are several ways of defining an outcome of either a test or a treatment action. For instance, in the case of a test, an outcome might be "the detection of a new symptom" (e.g., an abnormally low white blood cell count), or "a quantitative statement of a medical parameter" (e.g., the white blood cell count is x%), or "the test results indicate that with probability  $p$ , the patient has disease  $i$ ." The relative merits of the different formulations are not at all clear, but because of the relative simplicity of obtaining the probabilities and of structuring the model, we have chosen a modification of the last definition. In our model a test outcome is a statement by the interpreter of the test results that (1) he thinks the patient has one of a set of possible diseases given the test results (we call this a positive outcome), or (2) no new information has been gained (a negative outcome). The probability distribution on these outcomes, given the use of a particular test, is determined by application of conditional probability rules to the physician's prior probabilities of each of the diseases and the conditional probabilities that the test will indicate a particular disease given that the patient does in fact have that disease. At the present, we cannot say any more

in favor of this method of defining outcomes over the other possibilities, other than that it seems reasonable and leads to a workable solution.

The definition of outcomes of treatments is more straightforward. We have assumed for convenience that if the treatment associated with a particular disease is applied and the patient does in fact have that disease, the disease will be arrested with certainty. If the wrong treatment is applied, the outcome will be the result of what happens during the time period required to administer the treatment plus any side effects of the treatment (e.g., nothing happens; the disease progresses to a new, specified level; the patient dies, etc.). Again we have chosen to use the physician to specify these possibilities and their associated probabilities. The probabilities of the outcomes occurring are computed by a straightforward application of Bayes' Theorem to the prior probabilities of the diseases and the relevant likelihoods.

Returning to our hypothetical example we see that if outcome 1 results from the use of Test I, the doctor has listed the next set of possible actions as: (1) apply Test II, (2) Treatment I, and (3) Treatment II. The dashed lines indicate places where the tree in fact continues on, but have been left out for reasons of clarity. Then, for example, if he chooses to apply Treatment I, the possible outcomes are: (1) the disease is arrested, (2) the condition is unchanged, or (3) the patient dies. The first and last outcomes are terminal outcomes and require that utilities or values be assigned to them. In the case of no cure, a new set of actions is possible and so the tree continues until only terminal outcomes remain. The method of obtaining the utilities will be discussed in detail in the description of the case study.

Once the decision tree has been structured, the relevant probabilities obtained and computed, and the appropriate values assigned, the decisions

which maximize expected utility at each stage are determined by the standard rollback technique (i.e., starting at last stage compute the expected utility of all outcomes associated with each action, choose the action with the largest expected utility, assign that utility to the outcome preceding this set of actions and continue backward through the tree).

In order to illustrate the general concepts outlined above and to demonstrate the feasibility of applying them to the real world, we present a case study which was recently completed. This case was an actual decision problem faced by doctors during the spring of 1967 at the Stanford Children's Convalescent Home in Palo Alto, California.

### The Case Study

#### A. Case History

A five-year-old boy was admitted to the hospital complaining of back pain. Preliminary X-rays revealed that two, and possibly three, vertebrae had collapsed. Numerous routine laboratory tests were conducted, but none of the results were positive. Two needle biopsies and an open-back biopsy (see Table II for description) were tried, but the results were negative (the open-back biopsy was terminated at the beginning of the operation because the patient suffered a temporary cardiac arrest). Subsequent X-rays, taken four months after the initial ones, indicated that a third vertebra had collapsed and that a fourth was beginning to deteriorate, thereby increasing the chances of severing the spinal cord and causing paralysis. Thus, it was very important that a decision be made as to what action the physicians should take.

B. The Decision Stated

The decision facing the physicians can be stated as: "Should the physicians attempt some more diagnostic tests (and if so, which ones); wait for new symptoms to appear; or should they start treating the patient for one of the diseases he might possibly have?"

C. Structuring the Decision

The physicians felt that the patient had one of four diseases. They are listed along with their treatments in Table I. The probability of his having a fifth disease was felt to be negligible. Aside from routine laboratory tests, the doctors indicated that there were four diagnostic tests which they could try. Table II presents a brief description of these tests. Since the doctors stated that they would be reluctant to use X-ray therapy unless they were quite certain that the boy had cancer or histio-cytosis, it was assumed that Treat Infection was the only immediate treatment alternative open to them (even though X-ray therapy was a technologically feasible alternative, subsequent calculations verified this assumption). Thus, there were five immediate alternatives to choose among: the four diagnostic tests and the choice of treating a possible infection with antibiotics. Depending upon which disease the boy actually had and which diagnostic tests the doctors employed, one of several possible terminal outcomes would occur. The various principal outcomes are listed in Table III. It should be noted that there are several variations to the outcome "Cure" (see, for example, Table V). Due to the damage caused by the continuing progression of the disease, there is a difference between

Table I - Possible Diseases

<u>Disease</u>	<u>Description</u>	<u>Treatment</u>
<i>Infection</i>	One of a general class of infections such as <i>Tuberculosis</i> or <i>Staphylococcus</i>	Antibiotics
<i>Bone cancer</i>	A malignant bone growth	Massive X-ray therapy
<i>Histio-Cytosis</i>	A non-malignant bone growth	Limited X-ray therapy
<i>Rheumatoid Nodule</i>	A destructive bone growth	No effective treatment known

Table II - Possible Diagnostic Tests

<u>Test</u>	<u>Description</u>
Wait N Days	Wait for a set period of time (N = 1, 2, ... days) hoping that a new symptom will manifest itself or that a spontaneous cure will appear
Needle Biopsy	A hollow needle is used to obtain a very small section of bone; low probability of obtaining a diseased sample
Open-Back Biopsy	Portions of two or three ribs are removed and the adjacent vertebrae can be sampled
Open-Chest Biopsy	By opening the chest, the surgeon can get samples of up to eight or nine vertebrae; very high probability of obtaining a diseased portion of bone

Table III - Possible Terminal Outcomes

<u>Outcome</u>	<u>Description</u>
Cure	Pathologic condition is arrested
Kyphosis	A severe degree of spinal deformity
Paralysis	Paralyzed from the lower back down
Death	Death

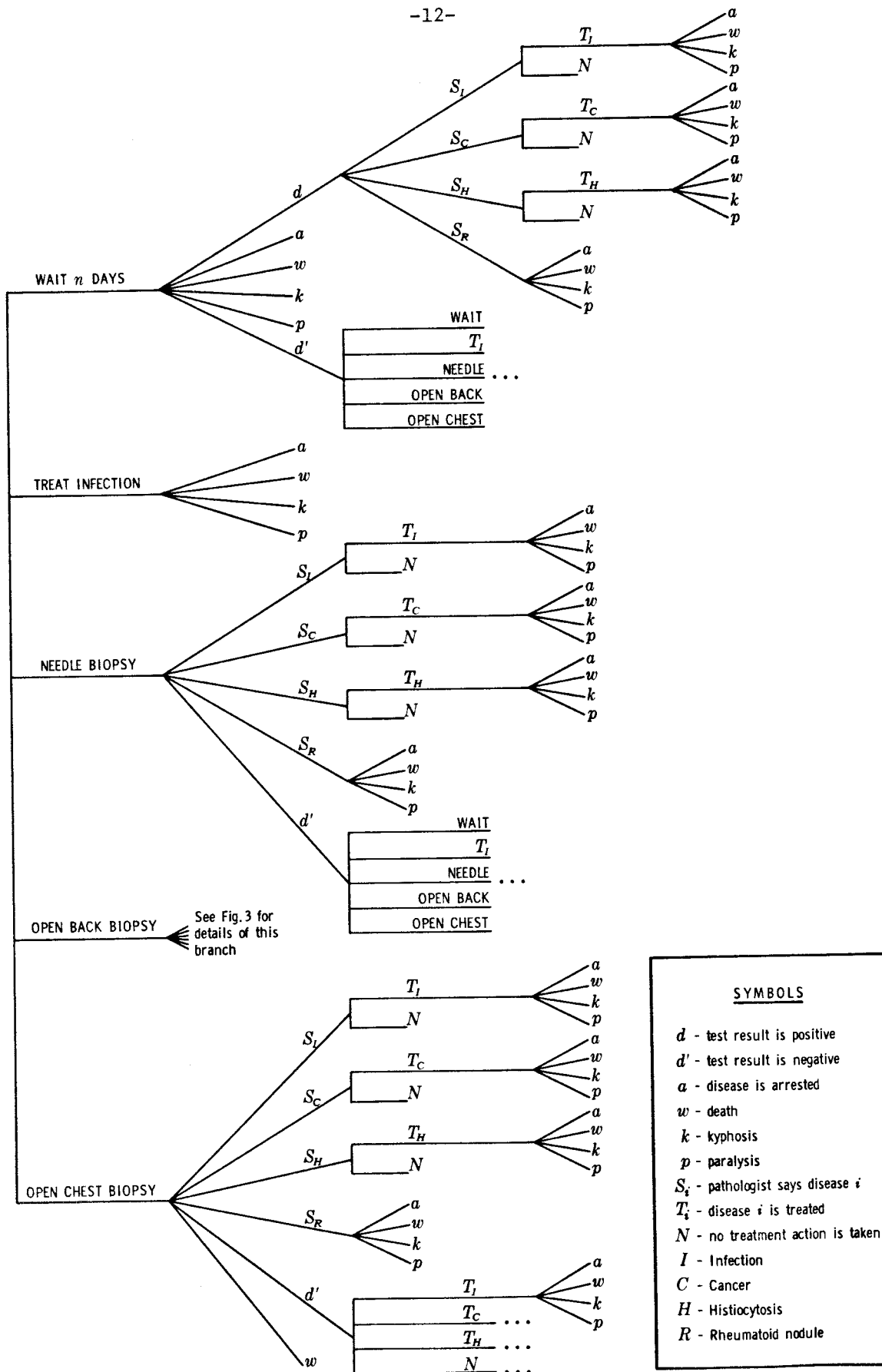
Cure Now and, say, Cure Two Months From Now. Cure Cancer is assumed to mean "arrest the disease as is best possible, thereby increasing the boy's life by two or three years."

It was assumed that no more tests would be attempted if the antibiotics were used, because it would be at least six weeks before the doctors knew whether or not the antibiotic treatment had worked. Similarly, because of the drastic nature of the two surgical biopsies, it was assumed that no more tests would be tried if a surgical biopsy were undertaken. Thus, the Treat Infection, Open-Back Biopsy, and Open-Chest Biopsy were considered to be terminal actions in the sense that no future tests could be tried if these tests were undertaken. On the other hand, the Wait N Days and Needle Biopsy alternatives are sequential in nature. That is, if they tried one of these tests, then depending upon the results of the test, they could elect to try another of the same test or a different diagnostic procedure. This process could theoretically continue indefinitely. The decision tree in Fig. 2 is greatly simplified, but it shows the basic relationships between all the alternatives and outcomes. Figure 3 shows the Open-Back Biopsy branch of this tree in detail.

#### D. Determination of Probabilities

This section will describe how the probabilities were determined for only one of the alternatives. The other probabilities were determined in an exactly analogous manner, but they are not included for reasons of brevity.

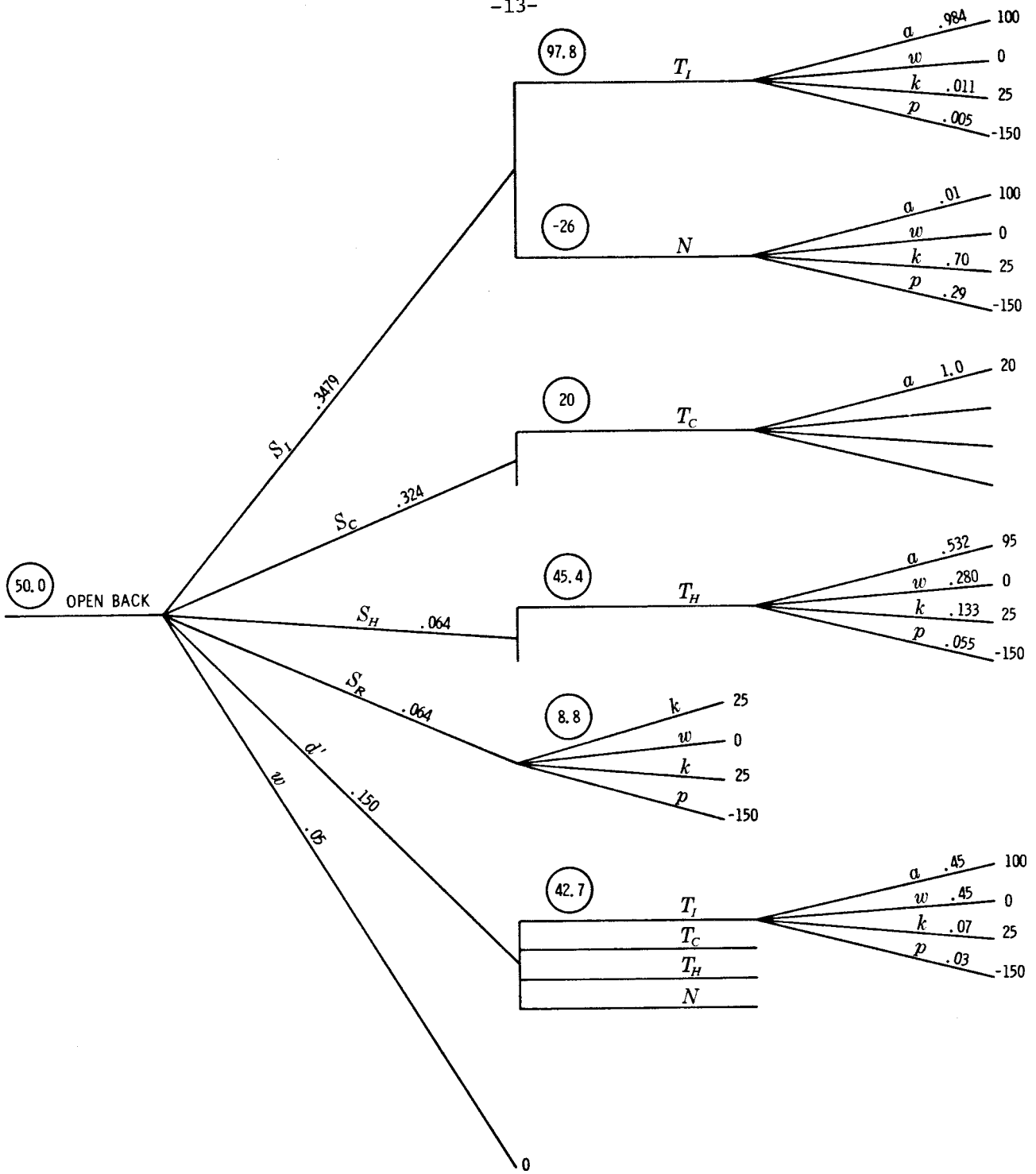
Examining Fig. 2, we see that two types of probabilities make up



SYMBOLS	
$d$	- test result is positive
$d'$	- test result is negative
$a$	- disease is arrested
$w$	- death
$k$	- kyphosis
$p$	- paralysis
$S_i$	- pathologist says disease $i$
$T_i$	- disease $i$ is treated
$N$	- no treatment action is taken
$I$	- Infection
$C$	- Cancer
$H$	- Histiocytosis
$R$	- Rheumatoid nodule

Fig. 2 -- Case Study Decision Tree





SYMBOLS

$d'$  - test result is negative  
 $a$  - disease is arrested  
 $w$  - death  
 $k$  - kyphosis  
 $p$  - paralysis

$S_j$  - pathologist says disease  $j$   
 $T_j$  - disease  $j$  is treated  
 $N$  - no treatment action is taken

$I$  - Infection  
 $C$  - Cancer  
 $H$  - Histiocytosis  
 $R$  - Rheumatoid nodule

(XX.X) ≡ expected utility of alternatives

Fig. 3 -- Open-Back Biopsy Branch  
 (Doctor A's Data)

the general decision tree. There is, first of all, the test outcome probability that the test is positive and that the pathologist says the sample is of disease  $i$ . There is also the "treatment outcome" probability, the probability that the patient has disease  $i$  given that test  $j$  was performed and that the pathologist said that he had disease  $i$ . For our case, the "treatment outcome" probabilities are actually the same as the conditional probabilities of identifying the correct disease given a particular test, since we assumed that the disease would be arrested with probability one if it were diagnosed correctly and treated accordingly.

It is difficult to elicit the test outcome and treatment outcome probabilities directly, since they depend not only upon the characteristics of the test, but also upon the patient's history. It is more expedient to ask the physician to estimate simpler probabilities and then use Bayes' Theorem to evaluate the desired probabilities. The simpler probabilities can be classified into two types: the prior and the identification probabilities. The priors (listed in Table IV) are the probabilities which the doctor assigns to each of the four diseases before any new tests are performed. The identification probabilities are the probabilities that the pathologist says disease  $j$ , given that the boy has disease  $i$  (in our case  $i, j = 1, 2, 3, 4$ ). The boy's two physicians gave quite consistent identification probabilities; reference will be made later as to how discrepancies in their priors were handled.

Nature's Tree<sup>[3]</sup> provides a good means of organizing the above data

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[3] Howard, R. A., "Bayesian Decision Models for System Engineering," *IEEE Transactions on Systems Science and Cybernetics*, Vol. SSC-1, pp. 36-40, November 1965.

Table IV - Prior Probabilities

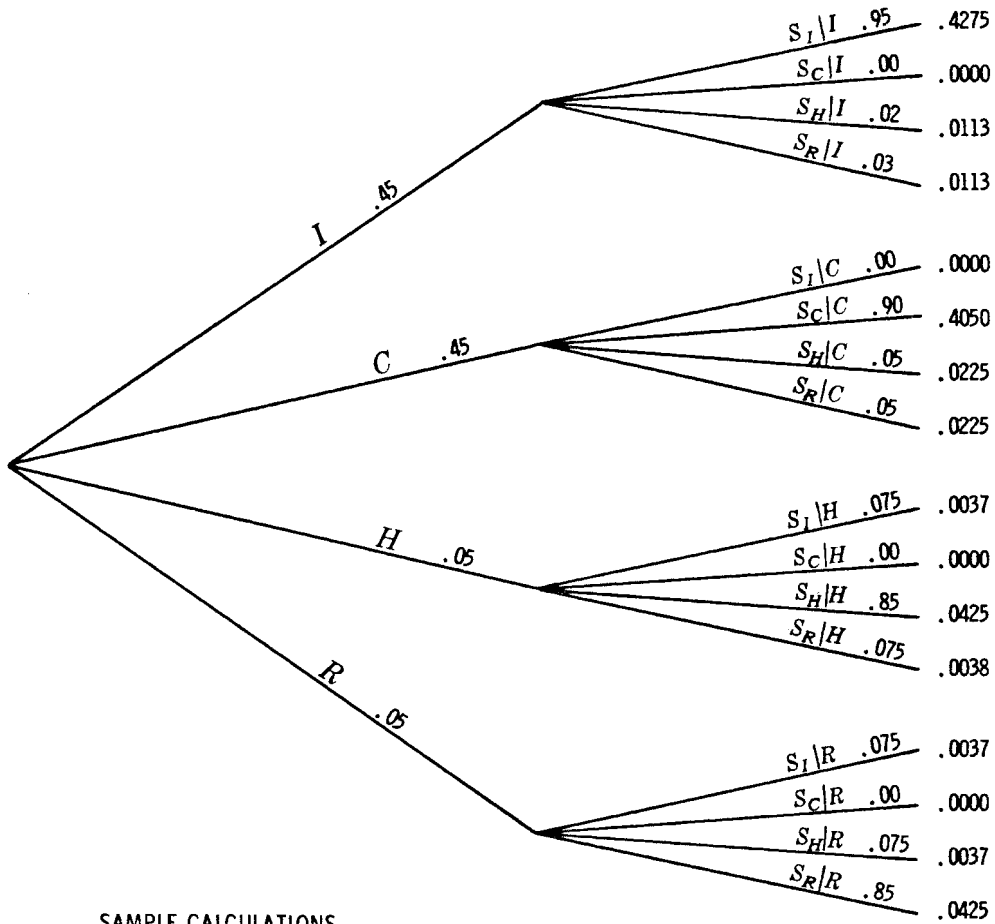
<u>Disease</u>	<u>Doctor A</u>	<u>Doctor B</u>
<i>Infection</i>	0.45	0.15
<i>Bone cancer</i>	0.45	0.25
<i>Histio-Cytosis</i>	0.05	0.50
<i>Rheumatoid Nodule</i>	0.05	0.10

and calculating the two types of outcome probabilities. Such a tree must be constructed for each test alternative, since the outcome probabilities are dependent upon the test performed. Nature's Tree and sample calculations for the Open-Back Biopsy are presented in Fig. 4.

E. Value Analysis

Normally, one does not speak of the value of death or paralysis in quantitative terms, and so it was not immediately obvious how the values of the outcomes pertinent to this study would be measured. As discussed below, the theorems of utility theory are used to produce a meaningful set of values. The values determined were those of the two primary physicians, since they were assumed to be the decision makers in this case.

The expected value theorem of utility theory states that, if an individual is indifferent between receiving a guaranteed prize or participating in a lottery, then the utility of the guaranteed prize is equal to the expected utility of the lottery. This theorem can be used to determine the values of the outcomes in this study. One can arbitrarily set the utilities of the two outcomes at 0 and 100



SAMPLE CALCULATIONS

$$\begin{aligned}
 P(S_I) &= .4275 + .0037 + .0037 = .4349 \\
 P(S_C) &= .4050 \\
 P(S_H) &= .0800 \\
 P(S_R) &= .0801 \\
 \\ 
 P(I|S_I) &= .4275 / .4349 = .984 \\
 P(C|S_C) &= 1.000 \\
 P(H|S_H) &= .532 \\
 P(R|S_R) &= .532
 \end{aligned}$$

SYMBOLS

- $I$  - Infection
- $C$  - Cancer
- $H$  - Histiocytosis
- $R$  - Rheumatoid nodule
- $S_i$  - Test interpreter says disease  $i$

Fig. 4 -- Nature's Tree for Open-Back Biopsy (Dr. A)

and then ask the decision maker what the probabilities of winning two outcomes must be, such that he is indifferent to receiving a guaranteed prize or participating in the lottery. The utility of the certain outcome is the expected value of the lottery, using the probabilities which the decision maker gave. The value of a fourth outcome can be determined by constructing new lotteries and eliciting new indifference data from the decision maker, and so on.

We presented the lotteries to the doctors as a game, called "A Game with the Witch Doctor." Its rules are very simple. We told the physicians to forget their medical knowledge; the witch doctor is all-powerful. They were told that they had to play the game and that they could only play it once. All they had to do to play the game was make a choice between:

1. Being given a guaranteed outcome, and
2. Being allowed to draw one pill from an opaque bottle; if the pill is white they are guaranteed outcome I, and if it is black they are guaranteed outcome II.

We then asked them: How many white pills had to be in the bottle out of a total of 100 pills, such that they were indifferent to taking the guaranteed outcome or reaching into the bottle. For example, assuming that the guaranteed outcome was paralysis and that the physician preferred paralysis to death, then he would always take paralysis if there were 100 black pills (death) in the bottle. On the other hand, if there were all white pills (which would guarantee cure) in

the bottle, he would elect to play the lottery. At some intermediate mixture, the doctor would be indifferent to the two choices. This point of indifference gives the probabilities which equate the two lotteries, and the appropriate utility calculations can be made.

Some sample lotteries are presented in Fig. 5. We asked about thirty different sets of lotteries, some of them being rearrangements of the ones below. By rearranging the utilities, we were able to get cross-checks on consistency and make refinements on values which were not quite consistent. Sample calculations are also shown. The utilities of death and cure were arbitrarily set to be 0 and 100. A complete listing of the values for the two doctors is given in Table V.

Table V - Summary of Utilities

<u>Outcome</u>	<u>Doctor A</u>	<u>Doctor B</u>
U(cure/now)	100	100
U(cure/1 week)	95	100
U(kyphosis)	95	90
U(cure/histio-cytosis)	95	90
U(cure/1 month)	80	100
U(cure/6 months)	25	90
U(cure/cancer)	20	20
U(death)	0	0
U(paralysis)	-150	40

The game is quite difficult to play. The main problem is that the implications of the lotteries are hard to grasp. One easily forgets that the game can only be played once and that it must be played; thus, the element of risk is not as real as we would like it to be. Also, it is difficult for the physicians to visualize our somewhat

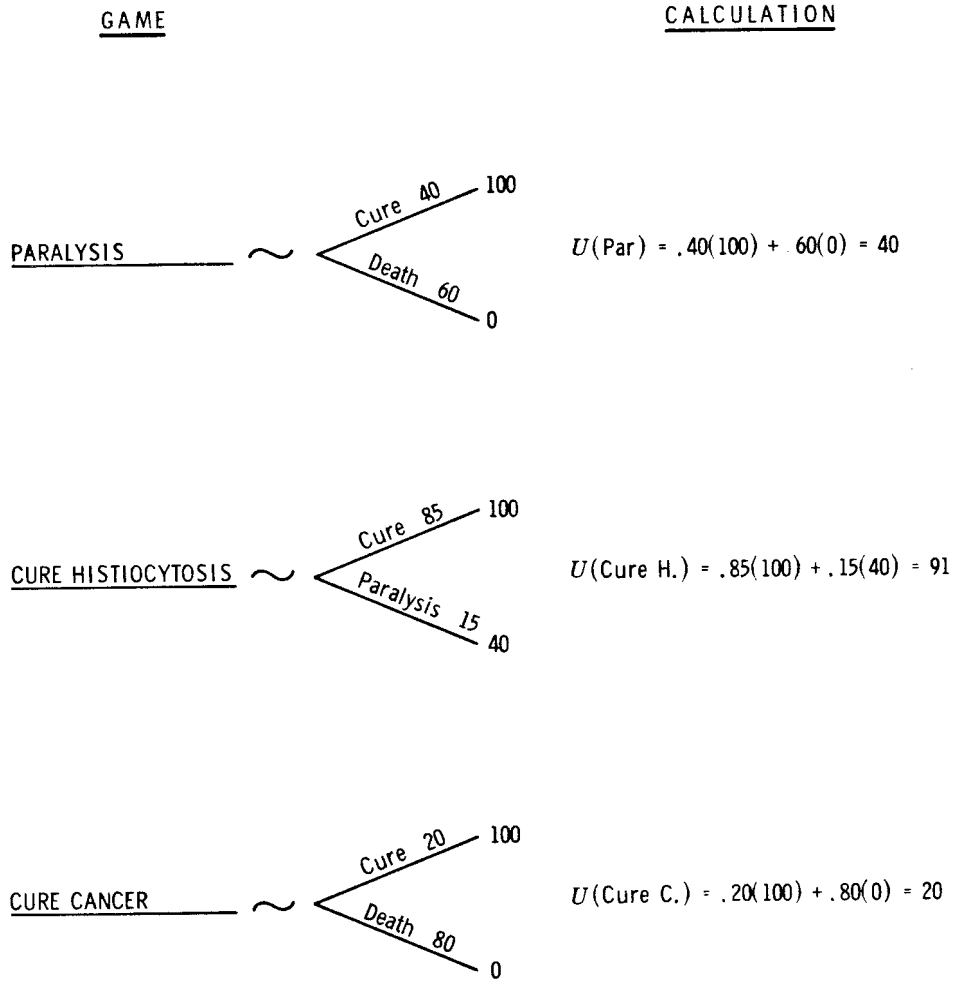


Fig. 5 -- Sample Lotteries

simplified outcomes. They are accustomed to considering, for example, specific degrees of kyphosis -- not one general impression of that state. In addition to understanding the game, another problem with the utility assignments is that they are likely to be dependent upon the mood of the doctor at the time of interview. For example, if the physician had just seen a depressed paraplegic, then he might assign a lower value to paralysis than may be normally given. These are perhaps the major problems in playing "A Game with the Witch Doctor." The game does not pretend to be a solution to these or all of the other problems associated with quantifying one's subjective feelings, but it is felt that this is a start in the direction of measuring the value of non-quantitative outcomes.

#### F. Results

The computational phase of the decision analyses is readily completed, once the problem is structured and the data are obtained. Using the rollback technique, the expected utility of each of the alternatives is calculated (see Fig. 5 for an illustration). The most desirable alternative is the one with the highest expected utility. The analysis was conducted separately for each of the two primary physicians, since they had such different value structures and prior probability assignments. Doctor A's highest expected utility alternative is the Open-Chest Biopsy (value 53). He may be indifferent between that and a few sequential needle biopsies whose value is about 53, but the indifference would last less than one month due to the decrease in value of cure with time. Doctor B is



indifferent to the alternatives of Wait One Month, Needle Biopsy, or Open-Chest Biopsy, mainly because of the constancy of his utility of cure for the first month. However, after about two months, he shows a definite preference for Open-Chest Biopsy. The results of our calculations are summarized in Table VI.

Table VI - Summary of Results

<u>Alternative</u>	<u>Doctor A</u>	<u>Doctor B</u>
Wait One Month	41	67
Wait Six Months	35	60
Treat Infection	43	54
Needle Biopsy	53	67
Open-Chest Biopsy	53	67
Open-Back Biopsy	50	64

The utility of the Needle Biopsy alternative is somewhat more difficult to determine than the other alternatives. This is because the actual Needle Biopsy branch has a limb which is indefinitely long, corresponding to the case in which the doctors elect to perform more needle biopsies, even though all of the previous ones were negative. However, because of the decreasing value of cure with time, it was possible to show that the Needle Biopsy branch had an upper-bounded value, corresponding to performing only one or two needle biopsies. It should be noted also that the utility of the Wait alternative is composed not only of the expected value of the five alternatives N days from now, but also the expected value of a spontaneous cure occurring during these N days. The other final values were calculated in a very straightforward fashion from the tree.

Though in general one should not attempt to make other than ordinal comparisons among utilities, the expected utilities of the first stage alternatives for both physicians appear, in some sense, to be quite close together. It is our conjecture that this is not a general effect, but rather a happenstance of the particular problem studied. If one is willing to say that distance between utilities is in some sense a measure of how much better one utility is than the other, then the results in our example do indicate that the doctors in this case were understandably hardpressed to choose a course of action, since the differences between courses of action were relatively small.

For the curious or practical-minded reader, we note that subsequent to, and independent of, our analysis, the physicians decided to perform the open-chest biopsy. Based on extensive examination of the samples of bone from the biopsy, the doctors felt that, with some small probability, the boy had a rheumatoid-type disease, but that the most likely "disease" was one unknown to medical science. Though this result is somewhat disappointing, it by no means detracts from our proposals. It does point out rather strongly that the results of the analysis are no better than the data that is input to it (i.e., in this case, inadequate prior probabilities).

#### Discussion

Because of the time pressures attendant upon this study, a number of simplifying and possibly unrealistic assumptions were made, such as:

1. Once an open-back or open-chest biopsy is performed, no further diagnostic testing is possible.
2. Once a particular treatment is applied, no further testing or treating can take place.
3. The possibilities of diseases other than the four considered are ruled out.
4. The time periods for the Wait alternative are chosen on a somewhat ad hoc basis.

In addition, some short cuts in the data gathering were taken which, given more time, we might have liked to revise. For example:

1. In some cases we elicited posterior probabilities from the doctors rather than attempting to get their prior and using the subsequent evidence to update these priors. One example is the probability of death occurring during the open-back or open-chest biopsies.
2. In some cases the outcomes were stated so that the probabilities and values were not independent. For example, the outcome "cure in one month" required the physician to implicitly estimate the possible consequences and their probabilities, that might be attendant upon waiting one month.

Additionally, it seems clear that a number of general problems need to be resolved before the general concept we advocate here can be made easily applicable across a wide range of diagnosis treatment problems. Specifically, we feel that further development is needed in the following areas:

1. Methods for simplifying the process of structuring the decision tree, particularly in the areas of defining test outcomes and treating time dependencies.

2. Better methods and rationales for establishing the utilities of outcomes, including the problem of dollar cost considerations when relevant.
3. Methods for limiting the length and breadth of the decision tree in order to keep the amount of computation to a reasonable level.

We would like to emphasize that in presenting this model and its application to this case study, we do not make any claims for its uniqueness or merit relative to other possible decision-theoretic models for solving the diagnosis-treatment problem. Clearly, further research is required before any such claims can be made. However, we feel that this work strongly supports the contention that many of the complex diagnostic-treatment problems facing physicians today can be effectively treated by decision theoretic techniques.

