Use of Influence Diagrams to Structure Medical Decisions -

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Influence diagrams are compact representations of decision problems that are mathematically equivalent to decision trees. The authors present five important principles for structuring a decision as an influence diagram: 1) start at the value node and work back to the decision nodes; 2) draw the arcs in the direction that makes the probabilities easiest to assess; 3) use informational arcs to specify which events will have been observed at the time each decision is made; 4) ensure that missing arcs reflect intentional assertions about conditional independence and the timing of observations; and 5) **ensure that there** are no cycles in the influence diagram. They then build an influence diagram for the problem of staging non-small-cell lung cancer as an illustration. Influence diagrams offer several strengths for structuring medical decisions. They represent graphically and compactly the probabilistic relationships between parameters in the model. Influence diagrams also allow the model to be structured in a fashion that eases the necessary probability assessments, regardless of whether the assessments are based on available evidence or on expert judgment. Influence diagrams provide an important complement to decision trees, especially for representing probabilistic relationships among variables in a decision model. Key words: decision analysis; influence diagrams; decision tree; decision techniques; cost-effectiveness analysis.
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Influence diagrams are compact representations of decision problems that are mathematically equivalent to decision trees. They provide an alternate syntax for expressing the theorems and mathematics underlying probability and expected-utility theory.“’ In this paper, we demonstrate the process of creating influence diagrams for medical decisions. After providing a simple example, we discuss the important principles to use in structuring and representing a decision as an influence diagram. We then build an influence diagram for the problem of staging non-small-cell lung cancer as an illustration.

In this article, we assume that the reader is familiar with the elements of the influence diagram (decision nodes, chance nodes, deterministic nodes, value nodes, and arcs) and familiar with their meanings.[1-3]

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A Simple Influence Diagram

We first describe a simple influence diagram; this diagram is useful for demonstrating the principles that follow. Suppose that we wish to analyze the decision of whether to perform a bacterial culture for a 15-year-old male patient who presents with sore throat. Our concern is that the patient may have a streptococcal infection; failure to treat such an infection with antibiotics may lead to unnecessary morbidity, or even to mortality. If the patient’s sore throat is not due to streptococcal infection, however, antibiotics will be ineffective and will incur unnecessary financial costs and health risks. For this example, we ignore monetary costs and make our decision based on quality-adjusted life expectancy QALE). We assume that failure to treat a streptococcal infection imposes a small but nonzero chance of developing rheumatic heart disease. We also assume that early treatment of a streptococcal infection may reduce the number of days in which the patient has a sore throat (controversial, although useful for our example), but imposes a small chance of death from anaphylaxis.

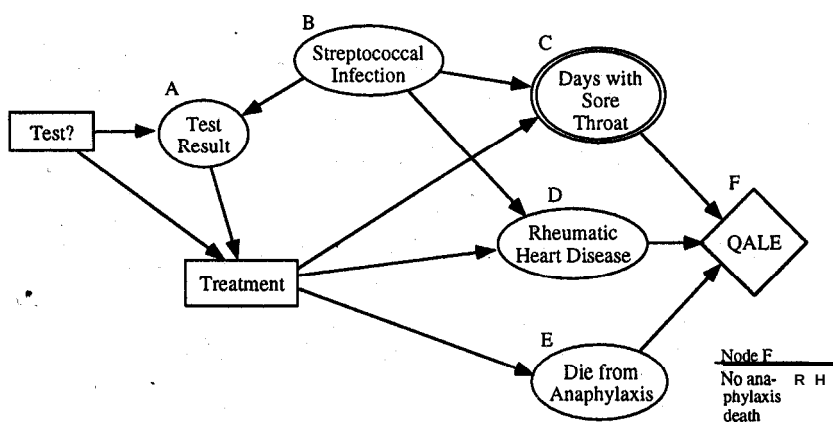
Figure 1 shows the complete influence diagram for our example. The tables on figure 1 provide the assessments required by the influence diagram and are based on a decision analysis reported by Dippel and colleagues.[4] Our convention for tables associated with chance nodes is to arrange the conditioning events in a column at the left of the table, and place the possible values for the chance variable across the top of the table. Each cell in the table is the probability of the event specified by that column, conditioned on the events specified by that row. Thus, as noted in the table associated with Node A, we have assumed that throat culture offers a sensitivity of 90% and a specificity of 70%.

The simple example of the test and treatment decision for a patient with sore throat demonstrates how influence diagrams provide an alternative syntax to decision trees. Although influence diagrams are mathematically equivalent to decision trees, the process of structuring a decision with an influence diagram differs somewhat from that of structuring a problem with a decision tree. We turn now to five important principles for structuring medical decisions as influence diagrams, referring to our example to highlight the important issues.

Principles for Structuring Influence Diagrams

As is true of any modeling project, the creation of influence diagrams requires judgment and experience.[5] Although there are many approaches, we believe five general principles are useful when building an influence diagram: 1) Start at the value node and work back to the decision nodes. 2) Draw the arcs in the direction that makes the probabilities easiest to assess. 3) Use informational arcs to specify which events will have been observed at the time each decision is made. 4) Ensure that missing arcs reflect intentional assertions about conditional independence and the timing of observations. 5) Ensure that there are no cycles in the influence diagram. Because each of these five issues can be applied thoughout the modeling process, they are best thought of as principles rather than steps. We review each of these principles in turn.

1. Start at the value node and work back to the decision nodes. Although there are other approaches to building influence diagrams, starting at the value node is useful for most decision prob-



Node A		Probability Test+	Test −	NA
Test	Strep present	0.90	0.10	0
	strep absent	0.30	0.70	0
No test	Strep present	0	0	1
	Strep absent	0	0	1

Node B	Probability Strep present	Strep absent
	0.60	0.40

Node C		Days with sore throat
Treat	Strep present	3
	Strep absent	4
Donot treat	Strep present	4
	Strep absent	4

Node D		Probability RHD	No RHD
Treat	Strep present	0.000013	0.999987
	Strep absent	0	0
Do not treat	Strep present	0.000063	0.999937
	Strep absent	0	0

Node E	Probability Die from ana-phylaxis	Do not die from ana-phylaxis
Treat	0.000003	0.999997
Do not treat	0	1

Node F			QALE
No ana-phylaxis death	RHD	3 sore throat days	24.996 yrs
		4 sore throat days	24.995 yrs
	No RHD	3 sore throat days	59.996 yrs
		4 sore throat days	59.99s yrs
Die from anaphylaxis			0 yrs

FIGURE 1. Influence diagrams for the sore-throat problem. Tables show the assessments required to specify fully the influence diagram, and are based on a decision analysis by Dippel et al.' QALE = quality-adjusted life expectancy; Strep = streptococcal infection; RHD = rheumatic heart disease; NA = test result not available.

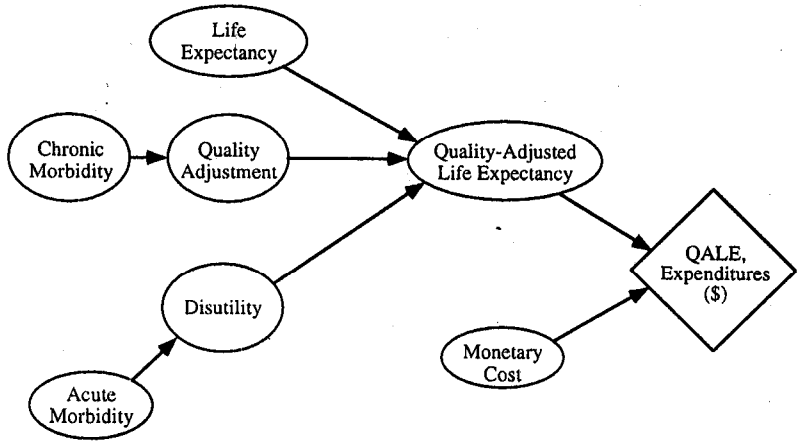


FIGURE 2. Predecessors of the value node for medical decisions. Overall value depends on quality-adjusted life expectancy (QALE) and cost. QALE depends on life expectancy, quality adjustment for chronic morbidity, and disutility of acute morbidity.

1ems.[6,7] This process provides a mechanism for linking the outcomes of interest to the interventions under consideration, based on the available evidence.'

Because every influence diagram includes a value node, the first step in applying the first principle is to determine what factors affect the decision maker's preferences. The value node reflects the outcomes of interest to the decision maker. Its parents (i.e., the nodes that have arcs pointing into the value node) are those events that affect directly how the decision maker values the outcome.[1-3] The parents of the value node, therefore, reflect the attributes of the utility function to be used in the analysis. In the sore-throat example described above, the overall value of the decision depends on the patient's length and quality of life, so the parents of the value node correspond to the factors that affect directly each of these attributes.

As part of modeling a decision problem, the analyst must decide which attributes of the possible outcomes to include in the analysis. In general, medical decisions result in outcomes that affect the attributes of length of life, quality of life, and monetary costs; the utility function to be used in the analysis is an assertion by the analyst of the relevant components of utility in the decision. The analyst represents these factors in an influence diagram as the parents of the value node. Events that alter quality of life may be short-term (e.g., a five-day hospital stay) or long-term (e.g., permanent blindness), and several methods have been proposed for quantifying preferences for such outcomes.[9-11] In a cost-effectiveness analysis, for example, effectiveness might be measured by QALE. Figure 2 illustrates this arrangement. The overall value of the decision depends on QALE and costs. QALE depends on life expectancy, on the quality adjustment for long-term morbidity, and on the short-term quality adjustment (or disutility) for short-term morbidity. As detailed in the appendix, specific assumptions about the utility function (i.e., constant proportional tradeoff and risk neutrality1 have implications for the structure of the influence diagram.

After we have determined the parents of the value node, we can expand the influence diagram iteratively by considering what decisions or chance events affect directly each of those parents. In a surgical decision, for example, length of life will be affected directly by whether perioperative mortality occurs. As we demonstrate in the example of lung-cancer staging below, we link the interventions under consideration to the outcomes of interest by working our way back from the value node.

2. ***Draw the arcs in the direction that makes the probabilities easiest to assess.*** This principle is a reminder to take advantage of the added flexibility for representing probabilistic conditioning that the influence diagram provides.[1,2,12,13] Figure 3a, for example, shows two chance nodes with the arc pointing from Test Result to Disease. The required probability assessments for this diagram are the probability of each test result, the probability of disease among those patients with a positive test, and the probability of disease among those patients with a negative test. In contrast, figure 3b shows the same two nodes with the arc pointing in the opposite direction, from Disease to Test Result. The required probability assessments for figure 3b are the probability of disease, the probability of a positive test among those patients with the disease (the sensitivity of the test), and the probability of a negative test among those patients without the disease (the specificity of the test). Typically, the available evidence (e.g., disease prevalence, test sensitivity and specificity) will make one set of assessments preferable to the other, so the arc should be drawn in the direction consistent with the easiest assessment (e.g., from Disease to Test Result). In the sore-throat influence diagram shown in figure ***1,*** for example, we have drawn the arc from Streptococcal Infection to Test Result, implying that the available assessments

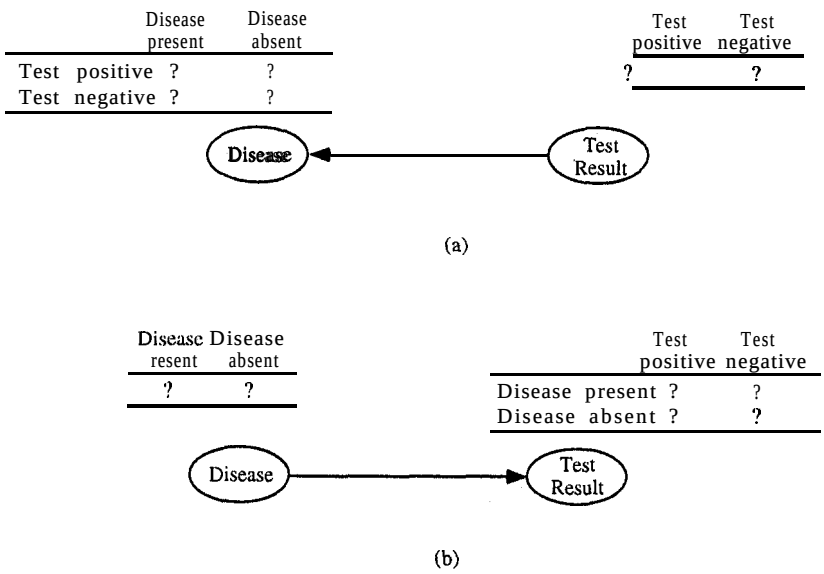


FIGURE 3. Two influence diagrams and their implications for probability assessment. (a) Influence diagram drawn in observation ordering, with arc from Test Result to Disease. (b) With arc from Disease to Test Result.

are the prior probability of streptococcal infection **(0.6,** table for node B) and test sensitivity and specificity (0.9 and **0.7,** respectively; table for node A). When data are unavailable, one set of assessments may best reflect how experts view the probabilistic relationships.[10]

3. Use informational arcs to specify, which events will have been observed at the time each decision is made. The third principle highlights the fact that influence diagrams require the analyst to indicate the timing of observable events in reference to each decision being modeled. For example, in figure 1 the informational arc from the Test Result node to the Treatment node 'is an assertion that the results of the throat culture will be known prior to the treatment decision. Failing to include this arc is equivalent to asserting that the treatment decision will be made before the test result is known. It is therefore important to include informational arcs that make apparent the events known at the time of each decision.

A common error in structuring influence diagrams is to place 'arcs from chance nodes to decision nodes in an attempt to represent that the decision should depend on the uncertainties in some events (e.g., the decision to treat should depend on how uncertain the decision maker is about the presence or absence of disease). It is important to remember that arcs into decision nodes represent information that is known or revealed at the time of the decision; putting an arc from Streptococcal Infection to the Treatment decision node in Figure **1** would assert that the presence or absence of streptococcal infection is known with certainty at the time that the treatment decision is made. Placing such an arc in an influence diagram is analogous to building a decision -tree with the Disease chance node to the left of the Treatment decision, which is usually inappropriate. We make a similar error if we place an arc from the value node to a decision node to represent that the decision should be influenced by how we value the outcome. Such an arc is an assertion that the utility of the decision (not the expected utility, but rather the exact utilily) will be known prior to making the decision, and that assertion is also incorrect. The algorithm used to analyze the influence diagram will account for the effects of uncertainty and utility on the preferred alternative for each decision in the model.'

4. ***Ensure that missing arcs reflect intentional assertions about conditional independence and the timing ofobservations.*** The fourth principle is to review the influence diagram to ensure that the absence of an arc between any two nodes is an intended assertion about the relationship of those nodes. The precise meaning of the absence of an arc depends primarily on the node into which the arc would point. The absence of an arc from a chance node to a decision node is an assertion that the chance event will not be observed by the time the decision is made. Thus, in figure 1 the absence of an arc from Streptococcal Infection to Treatment reflects the fact that the true state of infection will not be known at the time the treatment decision is made. Informational arcs reflect timing of observations relative to decisions, and thus their presence or absence should have been reviewed as part of the third principle.

The absence of an arc between two chance nodes indicates an assertion of independence or conditional independence. For example, the lack of an arc from Test Result to Rheumatic Heart Disease in figure 1 is an assertion that, conditioned on Streptococcal Infection and Treatment, the chance of rheu-

matic heart disease is independent of the test result. This assertion means that if we knew the true infection state of the patient and which treatment decision had been made, the chance of rheumatic heart disease would not depend on the results of the throat culture.

The issue of conditional independence often arises in testing decisions. In a decision involving the use of two tests, for example, we might assume that the results of the first test and those of the second test are independent, conditioned on whether the patient is truly diseased or not (i.e., the sensitivity and specificity of the second test are not affected by the results of the first test, conditioned on the true disease state of the patient). To simplify the assessments, an analyst may assume that conditional independence holds, even if such an assumption is not true. The decision to assume conditional independence involves a tradeoff between the effort required for the additional probability assessments and the effect of the assumption of conditional independence on the results of the analysis.[14]

5. Ensure that there are no cycles in the influence diagram. Cycles among nodes are not allowed in influence diagrams. A cycle is present whenever there are arcs that form a path from a node back to itself. Figure 4a, for example, illustrates a cycle among three chance nodes. Such a structure is not allowed because it represents an infeasible expansion ordering of the joint probability distribution.[1-3] (This type of cycle is unrelated to cycles used in Markov and simulation modeling. Such cycles represent increments of time during which transitions can occur from one health state to another. The cycles that are not allowed in an influence diagram represent circular reasoning rather than changes in health states over time.)

Cycles involving decision nodes also are not allowed. Consider the cycle in figure 4b. The arc from the Test Result node to the treatment decision indicates that the test result is known prior to the treatment decision being made. The arc from the Disease? node to the Test Result node indicates that the test result depends on whether the patient is diseased (e.g., a positive test is more likely among patients with the disease). Finally, the arc from the Treatment decision node to the Disease? node is an assertion that the probability of disease depends on the treatment alternative selected (this assertion, as we shall see, does not usually make sense, and usually reflects a failure to distinguish the event of disease before the treatment decision is made from the event of disease after the treatment decision is made).

To understand why a cycle such as the one shown in figure 4b is not allowed, we consider the case of a perfect test, a completely effective treatment, and a patient who is known to have the disease. Because the patient has the disease, and the test is perfect, the test result is positive. We observe this result prior to making the decision; based on it, we decide to treat the patient. Because the treatment is completely effective, the patient will no longer have the disease: the test result becomes negative, and we must decide not to treat. In this situation, the cycle requires that the disease be both present and absent, the test both positive and negative, and the patient both treated and untreated.

The creation of cycles such as the one depicted in figures 4a and b is a common error. Such cycles usually indicate that event definitions need to be made more clear, especially with regard to the timing of events. If, for example, we distinguish between disease at the time that the treatment decision is made and disease after treatment, the cycle disappears, as shown in figure 4c.

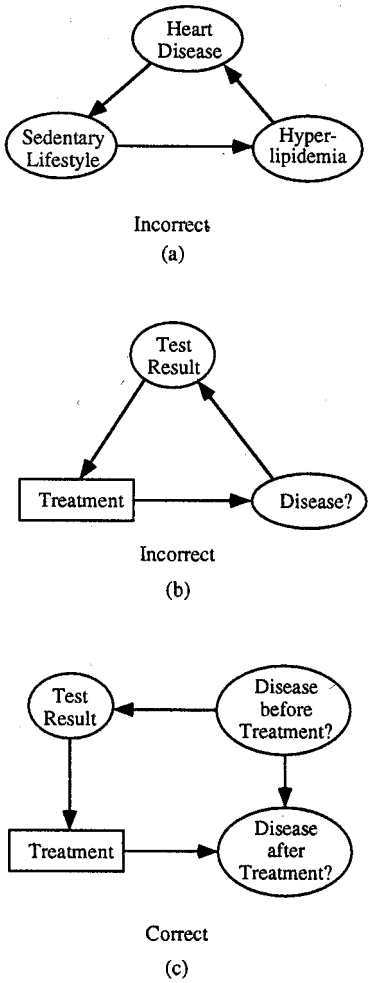


FIGURE 4. Examples of cycles in influence diagrams. (a) A cycle involving three chance nodes. (b) A cycle involving a decision node. (c) Improved definition of events, which often resolves cycles.

Notice that, in large influence diagrams, the application of the final two principles-examining missing arcs to ensure that they reflect intended assertions of conditional independence and avoiding the creation of cycles-can involve substantial work. Indeed, as the number of nodes in the diagram grows, the search for cycles and missing arcs may lead to a combinatorial explosion. The problem of cycles is related to the flexibility that influence diagrams afford in terms of assessment ordering. As such, the search for cycles is a step not usually required with the decision-tree representation. In contrast, examination of missing arcs to ensure that the assertions of conditional independence are intended is common to both influence diagrams and decision trees. In fact, the influence diagram eases the examination of conditional independence by making such assertions apparent graphically; in the decision tree, the analyst must examine the numerical values of variables to evaluate assumptions of conditional independence.

These five principles assist the analyst in structuring medical decisions as influence diagrams. We now turn to structuring the problem of lung-cancer staging as an influence diagram.

Example: Lung-cancer Staging

Consider the case of a patient with a known non-small-cell carcinoma of the lung. The primary tumor is 1 cm in diameter; a chest x-ray examination suggests that the tumor does not abut the chest wall or mediastinum. Additional workup reveals no evidence of distance metastases. The preferred treatment in such a situation is thoracotomy, followed by lobectomy or pneumonectomy, depending on whether the primary tumor has metastasized to the hilar lymph nodes.

Of fundamental importance in the decision to perform thoracotomy is the likelihood of mediastinal metastases. If mediastinal metastases are known to be present, most clinicians would deem thoracotomy to be contraindicated: thoracotomy subjects the patient 'to a risk of death but confers no health benefit. (Some surgeons attempt to resect mediastinal metastases that are ipsilateral to the primary tumor, but this approach remains controversial.) If mediastinal metastases are known to be absent, thoracotomy offers a substantial survival advantage, so long as the primary tumor has not metastasized to distant organs. There are several diagnostic tests available to assess any involvement of the mediastinum. For this example, we shall focus on computed tomography (CT) of the chest and mediastinoscopy. Our problem involves three decisions. First, should the patient undergo a CT scan? Second, given our decision about CT and any CT results obtained, should the patient undergo mediastinoscopy? Third, given the results of any tests that we have decided to perform, should the patient undergo thoracotomy?

We assume that CT offers an overall sensitivity and specificity of about 80% for detecting mediastinal metastases,[15] and we initially ignore any mortality associated with CT. Mediastinoscopy is an invasive test in which most (but not all) of the mediastinal lymph nodes can be sampled, Pathologists analyze the tissue obtained by mediastinoscopy to determine whether tumor has spread to the sampled nodes. The specificity of mediastinoscopy approaches lOO%-roughly equal to the specificity of the histologic samples it produces. The sensitivity of mediastinoscopy is about S0%, reflecting the possibilities of failing to sample involved nodes or of failing to obtain metastatic tumor from nodes that were sampled.[16] The mortality rate for mediastinoscopy depends on the characteristics of the individual patient, but in general is less than l%.[17,18]

We make the following simplifying assumptions to present the structuring process most clearly:

1. We evaluate the alternatives on the basis of life expectancy (i.e., we ignore any effects of testing and treatment on quality of life, and also ignore issues of cost).

2. We fix the order of the diagnostic tests (CT first, then mediastinoscopyl. This assumption seems reasonable clinically, and it simplifies the resulting influence diagram; it is not, however, required for the problem to be structured as an influence diagram. Later we discuss the effect on the influence diagram of removing this assumption.

3. We assume that the presence or absence of hilar metastases does not affect the decision to perform thoracotomy or survival, and we thus ignore the information that CT provides about hilar metastases. In practice, the presence or absence of hilar metastases affects whether the surgeon will perform a lobectomy or a pneumonectomy.

4. We assume that prior evaluation has not identified distant metastases.

STRUCTURE OF THE INFLUENCE DIAGRAM

We first focus on the value node, Life Expectancy. Life expectancy (after adjustment for age, sex and comorbidities) will depend on the stage of the tumor, mortality from diagnostic or therapeutic procedures, and the treatment decision. Using the TNM

staging system, the stage of the tumor depends on the size and location of the primary tumor, the presence or absence of mediastinal and hilar metastases, and the presence or absence of distant metastases.[19] Based on our assumptions, the tumor is known to be of stage T = 1 (l-cm tumor with no involvement of chest wall or mediastinum), M = 0 (no distant metastases), and either N = 0 (no local metastases), N = 1 (hilar metastases only), or N = 2 (mediastinal metastases). In our simplified example, we assume that the presence of hilar metastases does not affect the treatment decision or survival. The Life Expectancy node therefore should be influenced by the Mediastinal Metastases, Treatment, Treatment Death, and Mediastinoscopy Death nodes as shown by bold arcs and nodes in figure 5a.

The occurrence of death from thoracotomy or radiation therapy (Treatment Death) depends on the treatment chosen (Treatment), and the occurrence of death from mediastinoscopy (Mediastinoscopy Death) depends on whether a mediastinoscopy is performed (Mediastinoscopy?). These influences are depicted in figure 5b.

At the time of the treatment decision, the results of CT and mediastinoscopy (if these tests are performed) will be known, as will whether the patient died from the mediastinoscopy. Figure 5c includes two nodes representing the results of the tests (CT Result and Mediastinoscopy Result), and an additional decision node representing the decision to perform the CT (CT?). The arc from the CT? decision to the CT Result node reflects that no test result will be available if the CT is not performed. Similarly, an arc from the Mediastinoscopy? node to the Mediastinoscopy Result node represents the unavailability of a result if that test is not performed. The arc from Mediastinoscopy Death to Treatment indicates that the patient's vital status will be known at the time of the treatment decision (i.e., no treatment can be considered if the patient dies from the mediastinoscopy). The informational arcs from Mediastinoscopy Result and CT Result to Treatment shows that these results will be known at the time the treatment decision is made.

In figure 5d two of the 'new arcs indicate that mediastinoscopy result and the CT result depend on whether mediastinal metastases are present. The third new arc shows that the results of the CT will be observed before the mediastinoscopy decision is made.

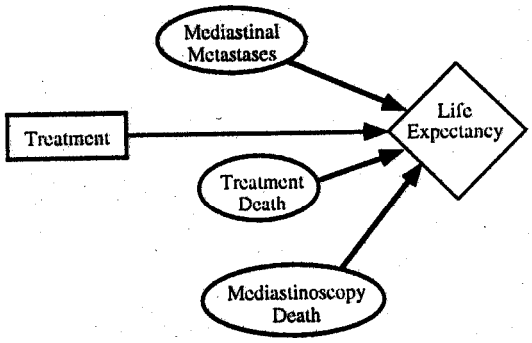
Figure 5e shows three new no-forgetting arcs. Specifically, the decision to perform CT will be known at the time that the mediastinoscopy and treatment decisions are reached, and the decision to perform mediastinoscopy will be known at the time that the treatment decision is made.

So far, our influence diagram adheres to at least two of the five principles presented in the previous section: *1) we* built it by working back from the value node, and 2) we structured it so as to simplify the probability assessments (e.g., the diagram requires the prior probability of mediastinal metastases and the sensitivity and specificity of CT, rather than the probability of a positive CT and CT's positive and negative predictive value for mediastinal metastases). The remaining principles to be applied concern the appropriate modeling of the timing of information relative to the decisions and assertions of conditional independence (i.e., principles 3 and 4), and checking the diagram to be sure no cycles exist (principle 5).

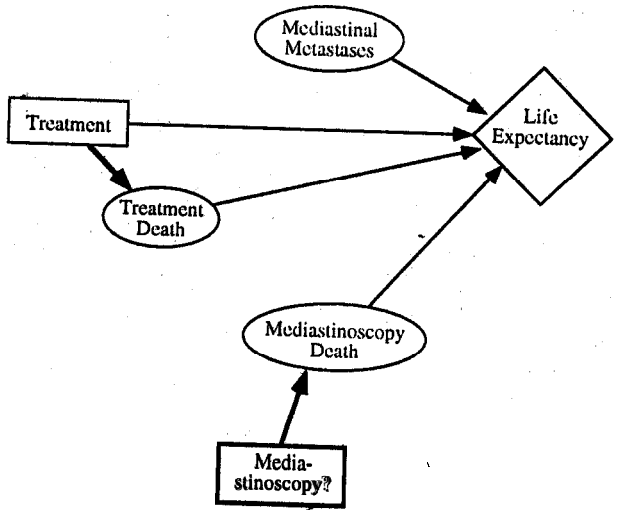
The third principle is to use informational arcs to specify which events will have been observed at the time each decision is made. The influence diagram in figure 5e makes the following assertions about the timing of information relative to decisions:

1. CT, if performed, occurs before mediastinoscopy (arc 1); thus, the result of the CT is known at the time that the mediastinoscopy decision is made (arc 2).
2. Mediastinoscopy, if performed, occurs before treatment (arc 31, and the results of both the CT and mediastinoscopy are known before the treatment decision is made (arcs 4 and 5).
3. The decision to perform CT is made before the treatment decision is made (arc 6).
4. If the patient dies as a result of the mediastinoscopy, that outcome will be known at the time that the treatment decision would have been made (arc 7).
5. Although the results of the tests (if performed) are known prior to the treatment decision, the true presence or absence of mediastinal metastases is not observed fully prior to any of the CT, mediastinoscopy, or treatment decisions. [The presence of enlarged nodes on CT increases the probability of mediastinal metastases, but does not necessarily indicate the true state of the patient. Although a positive mediastinoscopy does indicate the true state of the patient (if we assume specificity equal to 11, a negative mediastinoscopy does not.1

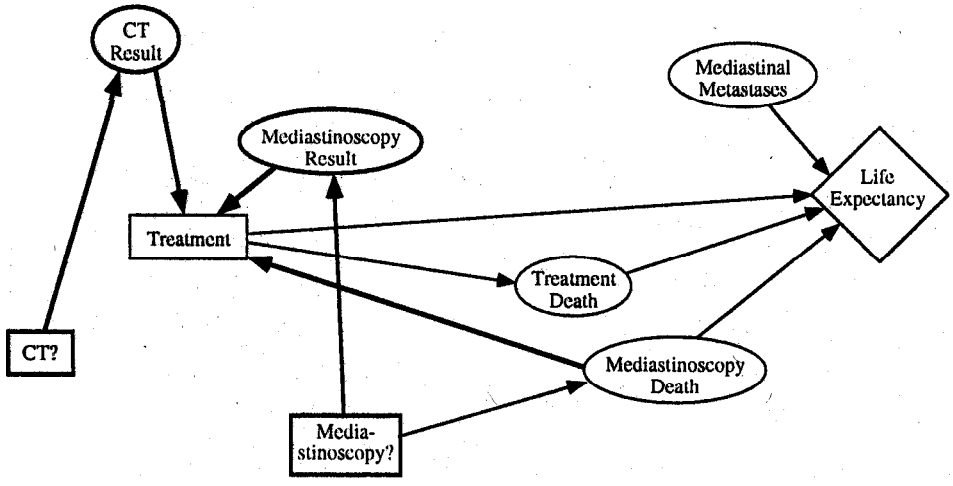
In accordance with the fourth principle, we review the diagram for conditional independencies involving chance nodes. These conditional independencies are represented graphically in the influence diagram by the *absence* of arcs.[1-3] Three of the conditional independencies revealed by the diagram in figure 5e follow:


Mediastinal Metastases
Treatment
Life Expectancy
Treatment Death
Mediastinoscopy Death

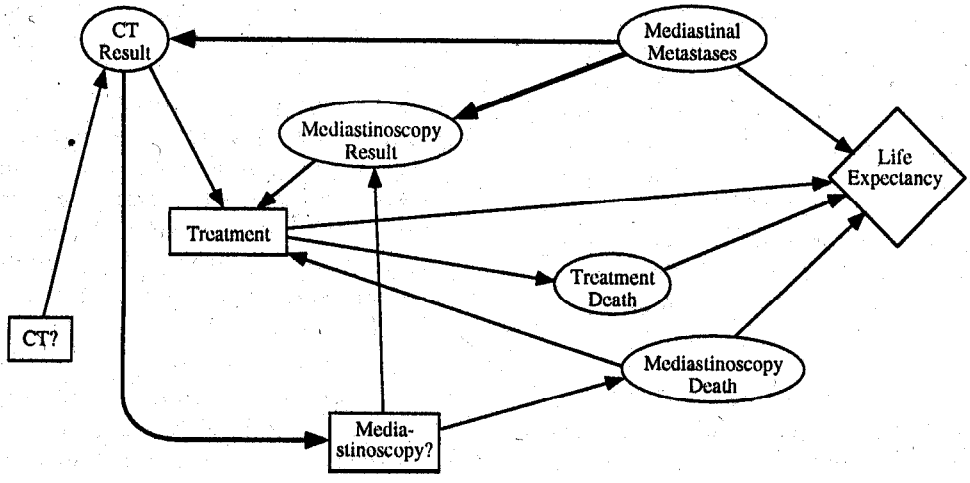
a.


Mediastinal Metastases
Treatment
Life Expectancy
Treatment Death
Mediastinoscopy Death
Media-stinoscopy?

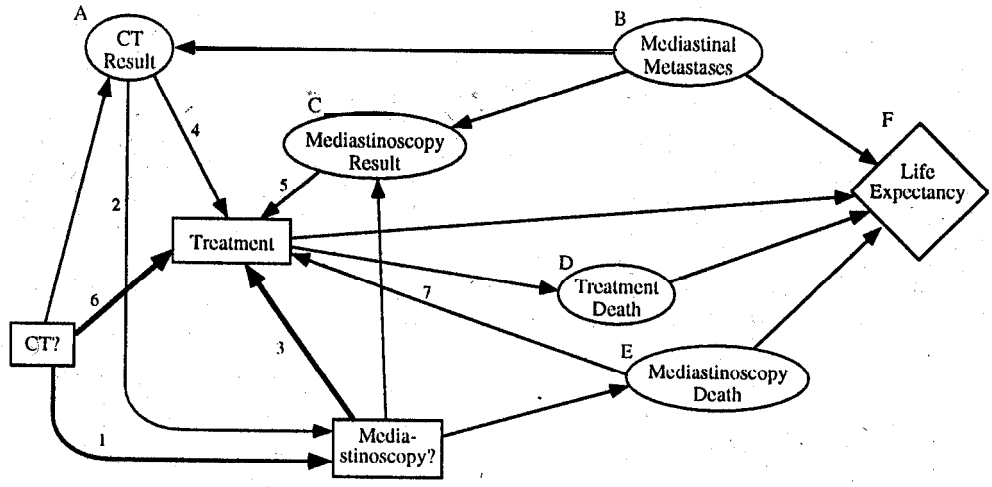
b.


CT Result
Mediastinal Metastases
Mediastinoscopy Result
Life Expectancy
Treatment
Treatment Death
CT?
Mediastinoscopy Death
Media-stinoscopy?

c.


CT Result
Mediastinal Metastases
Mediastinoscopy Result
Life Expectancy
Treatment
Treatment Death
CT?
Mediastinoscopy Death
Media-stinoscopy?

d.



e.

Node A		Probability		
CI	Med mets	0.82	0.18	0
	No med mets	0.19	0.81	0
No CT	Med mets	0	0	1
	No med mets	0	0	1

CT+: CT positive, CT−: CT negative, N/A: test result not available, med mets: mediastinal metastases

Node B	Probability	
	e me s	No med mets
	0.46	0.54

med mets = mediastinal metastases

Node C		Probability		
		M-scope+	M-scope−	N/A
M-scope	Med mets	0.82	0.18	0
	No med mets	0.005	0.995	0
Nom-scope	Med mets	0	0	1
	No med mets	0	0	1

mod mets: mediastinal metastases, M-scope: medistinoscopy

Node D	Probability	
	Die	Survive
Thoracotomy	0.037	0.963
Radiation therapy	0.002	0.998

Node E	Probability	
	Die	Survive
Mediastinoscopy	0.005	0.995
No mediastinoscopy	0	1

c ?				LE (yrs)
No m-scope death	No tx death	Thor	Med mets	1.80
			No med mets	4.45
		UT	Med mets	1.80
			No med mets	2.64
M-scope death or tx death				0

Tx = treament, m-scope = mediastinoscopy, Thor = thoracotomy, RT = Radiation therapy, med mets = mediastinal metastases

FIGURE 5 *(facing page and above).* Constructing the influence diagram for the lung-cancer-staging decision.'(a) The value node for the lung-cancer-staging decision.' Changes from one diagram to another are highlighted with bold arcs and nodes. (b) Inclusion of influences on the Treatment Death and Mediastinoscopy Death nodes. (c) Inclusion of test results and knowledge of mediaetinoscopy mortality prlor to the treatment decision. (d) Inclusion of the influence of medllstinal metastases on test results, and knowledge of CT results at the time of mediastinoscopy. (e) The completed influence diagram for the lung-cancer-staging decision. Tables show the assessments required to specify fully the'influenoe diagram, and are based on a decision analysis reported by Malenka and colleagues." Numbered arcs show the timing of events and decisions (see text).

1. The result of mediastinoscopy for mediastinal metastases, when conditioned on whether or not the patient has mediastinal metastases, is independent of the result of CT for mediastinal metastases (e.g., the probability of a false-negative mediastinoscopy does not depend on the CT result). This conditional independency is denoted in the influence diagram by the absence of an arc between the CT Result and Mediastinoscopy Result nodes.

2. The mortality of mediastinoscopy does not depend on whether the patient has mediastinal metastases (i.e., there is no arc from the Mediastinal Metastases node to the Mediastinoscopy Death node).

3. The mortality of treatment does not depend on whether the patient has mediastinal metastases (i.e., there is no arc from the Mediastinal Metastases node to the Treatment Death node).

If we believed that any of these assumptions about conditional independence were incorrect, we would add the appropriate arcs, which would increase the number of conditional probabilities that we would have to assess. The analyst's decision to include or omit an arc in an influence diagram depends on his or her understanding of the clinical problem and on the explicit assumptions he or she is willing to make. Our examples are illustrative, and a more comprehensive analysis of the problem might include additional arcs. If, for example, we believed that the sensitivity and specificity of mediastinoscopy are not independent of the CT result conditioned on whether mediastinal metastases are truly present or absent, we would add an arc from CT Result to Mediastinoscopy Result. This additional arc would triple the number of assessments required for the Mediastinoscopy Result node: we would need the sensitivity and specificity of mediastinoscopy for mediastinal metastases conditioned on a CT positive for mediastinal metastases, on a CT negative for mediastinal metastases, and on no CT result being available.

The fifth principle is to ensure that the influence diagram contains no cycles. A review of figure 5e shows that there are no cycles in our influence diagram. Although larger diagrams make it difficult to determine whether cycles exist, not every possible path needs to be examined. Specifically, nodes with arcs that only point directly into the value node cannot be part of a cycle because the value node has no children (i.e., no arcs going out from it). Similarly, nodes that "point only to predecessors of the value node cannot be part of a cycle. This rationale applies to any node whose arcs lead (either directly or indirectly1 to the value node. Thus, in figure 5e, the Treatment and Treatment Death nodes cannot be part of a cycle: their arcs lead directly only to the value node. Inspection of the remaining nodes shows that no cycles exist.

To specify fully the influence diagram, we must make the appropriate probability and value estimates for each node. The tables in figure 5e show these assessments, and are based on a similar analysis reported by Malenka and colleagues.[15] We assume that CT has a sensitivity of 82% and a specificity of 81% (node A), that mediastinoscopy has a sensitivity of 82% and a specificity of 99.5% (node Cl, and that the prior probability of mediastinal metastases is 46% (node B). We assume mortality rates of 0.2% for radiation therapy and of 3.7% for thoracotomy (node D), and a mortality rate of 0.5% for mediastinoscopy (node E). As shown in **the** table for the Life Expectancy node (node F), we assume that the life expectancy of a patient with mediastinal metastases is 1.80 years, regardless of the treatment. For 'patients with no mediastinal metastases, thoracotomy offers greater life expectancy than does radiation therapy (4.45 years versus 2.64 years).

We evaluated the folly specified influence diagram. Given our assumptions, strategies for lung cancer staging offer very similar life expectancies. The optimal strategy is to perform CT. If the CT is negative for mediastinal metastases, the model recommends performing a thoracotomy without mediastinoscopy. If the CT is positive for mediastinal metastases, the model recommends performing mediastinoscopy. If the mediastinoscopy is negative for mediastinal metastases, the patient should undergo thoracotomy; if mediastinoscopy detects mediastinal metastases, the patient should undergo radiation therapy. This strategy offers a life expectancy of 3.124 years. Using mediastinoscopy without CT offers a life expectancy of 3.115 years; thoractomy without CT or mediastinoscopy offers a life expectancy of 3.114 years.

ARBITRARY SEQLJENCING OF CT AND MEDIASTINOSCOPY

For the influence diagram shown in figure 5e, we assumed that CT, if performed, would precede mediastinoscopy. This sequence seems reasonable clinically, but we can restructure the influence diagram to allow arbitrary sequencing of the two tests. Such an analysis would be useful when the preferred order of the tests is unknown, for example, when two non-invasive tests are available. The alteration involves modeling two test decisions explicitly; the alternatives for either decision are CT, mediastinoscopy, or neither (i.e., do not test). Each of these test decisions leads to a test result, with the result of the first test known at the time that the second test decision is made. Because mediastinoscopy can be performed as either the first or the second test, there is a possibility of death from either of the two tests (this addition to the model also allows us to incorporate the low, but finite, risk of death from CT). In addition, because one possible (although not clinically reasonable) combination is CT followed by CT, or mediastinoscopy followed by mediastinoscopy, the first and second test results should ***not*** be independent conditioned on the presence or ab-

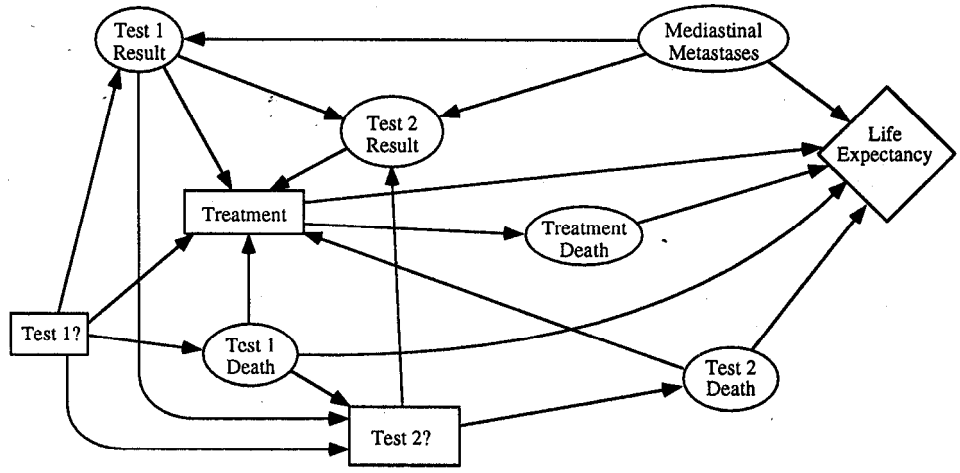


FIGURE 6. Influence diagram that allows arbitrary sequencing of CT and mediastinoscopy.

sence of **mediastinal metastases. It is the strong de**pendence between sequential CTs or mediastinoscopies in this setting that makes such a combination of little clinical value.

Figure 6 shows an influence diagram that allows for arbitrary sequencing of CT and mediastinoscopy. The first decision (Test l?) that is made is which test to do first, if any; the alternatives are CT, mediastinoscopy, or neither. The arc from the Test l? decision node to the Test 1 Result node indicates that the result of the first test depends in part on the alternative selected first (e.g., if neither test is performed, no test result will be available). The arc from the Test l? decision node to the Test 1 Death node reflects that the likelihood of dying from the first test depends on which testing alternative is selected. The second decision is which test (if any) to do next; as they were with the first testing decision, the alternatives are CT, mediastinoscopy, or neither. The arcs into the Test 2? node assert the information known at the time of that decision: what the first test is (if any), what the result of the first test is (if any), and whether the patient died as a result of the first test. The arcs into the Test 2 Result node implythat the result of the second test is influenced by the alternative selected for that test (e.g., if neither test is performed, no test result will be available), by the result of the first test (e.g., a repeat CT is likely to give the same results as the initial CT), and by the presence or absence of mediastinal metastases. The likelihood of dying as a result of the second test depends on which testing alternative is selected (e.g., deciding not to do a second test reduces to zero the chance of dying from the second test); this influence is depicted by the arc from the Test 2? node to the Test 2 Death node.

Notice that the influence diagram hides a substantial increase in the number of assessments that are necessary for an analysis of arbitrary test sequencing. The Test 2 Result node, for example, is conditioned on Test 2? (three alternatives: CT, mediastinoscopy, or neither), Test 1 Result (three outcomes: positive for mediastinal metastases, negative for mediastinal metastases,. or results not available), and Mediastinal Metastases (two outcomes: present or absent). Thus the probability table for Test 2 Result would have 18 rows (3 X 3 X 21, one for each conditioning combination. Although the diagram for arbitrary test sequencing remains graphically compact, the sizes of the tables associated with the diagram increase substantially.

Software for Constructing and Evaluating Influence Diagrams

Software programs for analyzing influence diagrams have lagged behind those developed for decision trees. Nonetheless, several software packages offer the opportunity to use influence diagrams, at least in a limited manner. These programs include **Analytica,**[16] **DATA** 3.0," DPL,[18] and Precision Tree,[19] among others. Influence diagram software is evolving rapidly, and a review of existing and emerging programs is beyond the scope of this paper.

Summary and Conclusions

Influence diagrams provide a new syntax for structuring medical decision problems. Although in-, fluence diagrams are mathematically equivalent to decision trees, using them to structure decision problems is substantially different from using trees. Specifically, influence diagrams are typically constructed with a focus on what affects utility and highlight graphically probabilistic relationships and influences. In contrast, decision trees are usually constructed with a focus on the temporal order of decisions and emphasize structural asymmetry.

In structuring medical decisions as influence diagrams, it is useful to employ five principles: 1) Start at the value node and work back to the decision nodes; 2) draw the arcs in the direction that makes the probabilities easiest to assess; 3) use informational arcs to specify which events will have been observed at the time each decision is made; 4) ensure that missing arcs reflect intentional assertions about conditional independence and the timing of observations; and 5) ensure that there are no cycles in the influence diagram. As we have demonstrated with the lung-cancer-staging example, influence diagrams can represent compactly complex decisions and highlight probabilistic relationships.

Influence diagrams offer several strengths for structuring medical decisions. Most of these advantages attain because influence diagrams represent graphically the relationships between parameters in the model; in the influence diagram, probabilistic modeling assumptions do not require examination of the model at the level of numerical assessments. Assertions of conditional independence are evident at the level of structure in influence diagrams (i.e., by the absence of arcs), but at the level of number in decision trees (i.e., by the probability assessments). This attribute of influence diagrams provides advantages for problems with complex probabilistic relationships. Asymmetry in decision alternatives or structure of a decision problem is not represented graphically in the influence diagram, however. Such problems may be easier to represent as decision trees. The influence diagram streamlines the early modeling process by allowing the analyst to focus temporarily on the level of structure without concern about assessing the probabilities that will be required eventually by the model. The ability to focus on model structure with a compact representation makes influence diagrams exceptionally useful for the early stages of modeling, especially in a group setting. Influence diagrams thus provide a powerful complement to decision trees for representing and analyzing medical decisions.

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APPENDIX

In many situations, the analyst assumes a constant proportional tradeoff between length of life and quality of life.[17] Under this assumption, the time tradeoff associated with being in a particular health state is independent of the time spent in that state. For example, if the assumption of a constant proportional tradeoff holds, then a person who is willing to give up one year of life to avoid five years of blindness would also be willing to give up four years of life to avoid 20 years of blindness (a time-tradeoff quality adjustment of 0.8). This assumption is depicted graphically in the influence diagram (figure 2) by the absence of an arc from the Life Expectancy node to the Quality Adjustment node (the absence of the arc indicates conditional independence).

The validity of the assumption of constant proportional tradeoff has been questioned.[21,22] Adding an arc from Life Expectancy to Quality Adjustment would allow us to represent the quality adjustment as a function of life expectancy, but would require that we assess a quality adjustment for each possible life expectancy in the model (figure A). Similarly, monetary costs may be ongoing for the remainder of the patient's life (e.g., the costs of dialysis) or may vary according to the patient's chronic morbidity (e.g., income lost from days of work missed due to back pain). Acute morbidity can also incur monetary costs. The analyst can represent such situations in the influence diagram by adding arcs from the Life Expectancy, Chronic Morbidity, and Acute Morbidity nodes to the Monetary Cost node (figure A).

Most medical decision analyses use either life expectancy or quality-adjusted life expectancy (QALE) as the measure of utility. The use of either life expectancy or QALE is appropriate for only those decision makers who are risk-neutral. A risk-neutral decision maker is indifferent between an outcome with certainty (e.g., 12 years of life) and a lottery with the same expectation (e.g., a 0.5 probability of 24 years of life and a 0.5 probability of immediate death). Thus, for a risk-neutral decision maker, we can substitute the expectation of a distribution (say, on years of life after a given treatment) for the distribution. Although such a substitution is convenient analytically, the assumption of risk neutrality has been shown to be incorrect for some decision makers.[23,24] Decision makers may be risk-averse, or risk-seeking, rather than risk-neutral. For decision makers who are risk-averse or risk-seeking, we cannot simply substitute the expectation of a distribution for the distribution, because the decision maker is not indifferent between a certain number of quality-adjusted years of life and a gamble whose expectation is the same number of quality-adjusted years of life.

Incorporation of nonneutral attitudes toward risk in an influence diagram requires two steps. First, we must include the probability distribution on quality-adjusted years of life rather than just noting quality-adjusted life expectancy [which is the mean (or expectation) of that distribution].[25] Second, we must assess a utility function on quality-adjusted years of life. This utility function assesses whether the decision maker is risk-averse or risk-seeking for gambles that involve length and quality of life. A full discussion of risk-preference measures is beyond our present scope, but, in terms of the influence diagram of figure A, incorporating risk attitude would require changing the Life Expectancy node to Length of Life, changing Quality-Adjusted Life Expectancy to Quality-Adjusted Years of Life, and modifying the value node to include a utility function on quality-adjusted years of life. (Such a utility function embodies risk attitude on gambles involving years of life; that risk attitude could be modeled as an additional node.) Although changing the name of a node seems trivial, the implication in terms of the assessment task is substantial: The full probability distribution on years of life for each set of parents of the Length of Life node must be assessed. This additional assessment requirement, coupled with the computational advantages that we obtain by assuming risk neutrality, typically leads to the exclusion of risk attitude from medical decision analyses. Although decision trees and influence diagrams can incorporate risk preference equally well, the influence diagram's focus on the value node may highlight an analyst's assumptions about the utility function.

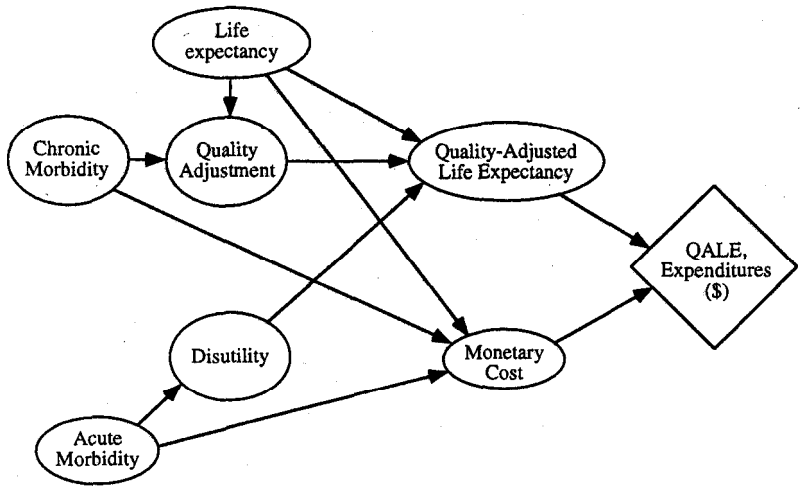

FIGURE A. A general version of a value node that accounts for QALE and monetary expenditures.