

**Probabilities and Preferences:  
What Economics Can Teach Doctors and Patients  
Making Difficult Treatment Decisions**

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**Introduction**

Most clinicians and patients reading our title will probably raise their eyebrows, and then turn to another article. They might think, “What does economics have to do with patient care – aside from determining who pays the bills?” But the realm of economics that this article addresses is not financial in nature; rather, it focuses on how people do and should make difficult decisions when outcomes are uncertain. Economists study such problems in a broad variety of contexts, ranging from investments in a risky stock market to international nuclear diplomacy to life-and-death medical decisions.

Economists distill choices under uncertainty into two basic parts – the *probabilities* of every possible outcome being considered, and the individual's *preferences* with regard to those outcomes.<sup>(1)</sup> By examining these two components of decision-making – probabilities and preferences – economists hope to make sense of complicated and often agonizing processes. In the most formal approach, these principles can be used to perform a “decision analysis,” in which all of the preferences and probabilities are quantified as precisely as possible and then

analyzed to determine the best option. In the medical context, the patient's preferences should be applied, though often the doctor serves as the patient's agent. Formal decision analyses frequently appear in the medical literature as a guide to clinicians. But even a much less formal approach can be valuable, for the principles of economic decision analysis can be a useful way to organize one's thinking when approaching an important treatment decision.

In situations where consequences are great and probabilities are poorly defined – as in many life-and-death medical decisions – decision analysis is hardest to apply. But it is also in those situations where it is most useful. It is precisely when our thinking gets overwhelmed by the magnitude of a decision, and our probability judgments stymied in situations not well documented or even previously encountered, that it is most helpful to have a system for working through the options. This paper presents several key points to bear in mind when approaching such decisions, employing the economist's bedrock concepts of probabilities and preferences.

## **Probabilities**

In any treatment decision, there are numerous relevant probabilities to consider. Take, for example, the initial treatment decision for a newly identified cancer. Among the most important probabilities are the likelihood of full remission of the cancer after treatment, the risk of cancer recurrence after remission, and the risks of various side effects from treatment. For each competing treatment option, the probability of each of these distinct outcomes should be estimated for the patient in question. While this approach is familiar, at least in concept, to clinicians and presumably to many patients as well, such problems are rarely attacked systematically, which allows strong decision biases to creep into choices.(2) Below we present several potential stumbling blocks in thinking about these probabilities.

### *Partial vs. Integrated Probabilities*

Many clinical decisions are plagued by probabilities that are ambiguous, or at least are so treated. In our research on clinical decision-making, patients frequently tell us that when they ask about their prognosis, they are told, “Every patient is different – I couldn’t give you a reliable probability estimate.” This kind of response sometimes reflects the lack of any data in the clinical literature, but it often indicates that a patient’s disease has not been fully characterized by the physician.

For instance, think about a hypothetical patient considering surgery followed by chemotherapy for a solid tumor that may or may not be localized. Let’s say that if micrometastases have already occurred, untreatable metastatic disease will recur after treatment with 95% probability, meaning surgery plus chemotherapy would cure the disease only 5% of the time. But suppose that, if the tumor is truly localized, the treatment has an 85% cure rate. The clinician, who does not know which type of tumor the patient has, may say, “It depends – without knowing the tumor type, I can’t offer a specific probability.” Yet, there is still a probability that can be estimated, and it simply involves considering both parts of the uncertainty: first, which tumor type the patient has; and second, the probabilities of different outcomes for alternative treatments of each type. If our hypothetical patient has a 50% chance of each tumor type, then the overall treatment success rate for surgery + chemotherapy is simply the average of our two cases: half the time (micrometastatic disease) a 5% cure rate, and the other half (localized) an 85% cure rate, for an overall cure rate from treatment of 45% [ $50\% \times (0.05) + 50\% \times (0.85) = 45\%$ ].

The probabilities that patients and doctors should most care about are the overall outcome probabilities – in decision-analytic language called “integrated probabilities” – and not intermediate or partial ones, which consider only a piece of the overall picture. People often look to intermediate probabilities (such as the 85% cure rate of our hypothetical treatment for a localized tumor), perhaps focusing on the most likely or best outcome, and make decisions based

solely on these values. The temptation to this approach is great when there is more uncertainty about the initial state (*e.g.*, whether or not our hypothetical patient had micrometastatic disease).(3) But this approach can induce both doctor and patient to latch on to a probability that misrepresents reality by telling only part of the story. A patient inclined to optimism might focus on the 85% cure rate for a localized tumor and decide that surgery plus chemotherapy is highly desirable, whereas a more pessimistic patient might see the 95% failure rate for micrometastatic disease and decide to forego treatment. Neither approach is appropriate, because each essentially ignores half of the possibilities. In this case, a single treatment is being considered, with two overall outcomes: cure (45%) and future metastatic disease (55%).

Fortunately, the medical literature often provides integrated probabilities in the form of 5-year and 10-year survival rates. These values tell a clinician and patient, taking all the various intermediate outcomes into account, the ultimate probability of mortality vs. survival in a given time period. Of course, it is desirable to refine these probabilities further, based on clinical and pathological characteristics in each case, when such data are available. When such refinements can be made – for instance, determining that the tumor in our previous example is 80% likely to be localized, based on biopsy results – integrated probabilities remain the right decision guideline. In this case, the probability of cure given treatment would be 69% [ $80\% \times (0.85) + 20\% \times (0.05) = 69\%$ ].

### *Relative Risk vs. Absolute Risk*

In medical journals, as well as the lay press, the effects of interventions or risk factors are frequently stated in terms of relative risk (RR). This has more to do with statistical considerations and getting articles published than in how clinicians and patients should make decisions. In fact, the relevant measurement of risk for clinical decision-making is *absolute* risk (AR).

For instance, consider the choice between external beam radiation and radical prostatectomy for clinically localized prostate cancer. Focusing solely on the side effects of each treatment, data from one recent study could be provided to patients in the following form: “Two years following treatment, surgery leads to nearly five times as much urinary incontinence as radiation (RR 4.87); radiation leads to a 2.5-fold increase in fecal urgency, frequency, or pain compared to surgery (RR = 2.55); and surgery slightly increases the risk of erectile dysfunction (RR = 1.29).”<sup>(4)</sup> From these data, the patient might infer that the decision is basically a trade-off between urinary incontinence and GI discomfort – with minimal differences in sexual function.

However, these relative risk numbers can readily lead us astray, because a relationship between two small risks (say, a 6% to 7% ratio) can be the same as a relationship between two large ones (a 60% to 70% ratio). The importance of relative risks can only be gauged if we know the original risk of each procedure, which when multiplied by the RR tells us the change in the absolute probability. Absolute risks tell the full story, as shown in Table 1. Note that, even though its RR is low, the biggest difference in side effects between the two treatments is in erectile dysfunction. It is by far the most common side effect. If each of the side effects were judged equally unpleasant, then erectile dysfunction would be the most important because it occurs most frequently.

Of course, another critical consideration is the probability that the cancer recurs after treatment. Presumably, surgery is contemplated because it is often thought to promote survival. The question then is whether it should be chosen despite its more frequent serious side effects. Our next section discusses mechanisms for evaluating the tradeoff between quality and quantity of life.

## **Preferences**

Once the relevant probabilities have been estimated, the economist's approach to decision-making assesses a person's preferences regarding the possible outcomes. The term "preference" can be applied at multiple levels. At its most basic, a preference simply ranks the outcomes: Do I prefer outcome A or outcome B? Such a ranking is all that is needed if each alternative leads to a certain outcome. But for medical decision-making, where each treatment may lead probabilistically to a number of different outcomes, more than a qualitative rank-ordering is required to make meaningful comparisons.

To evaluate trade-offs of different possibilities, economists use quantitative methods to evaluate preferences – which in the jargon of economics are called "utilities." One common metric in health economics is the Quality-Adjusted Life Year, or QALY.<sup>(5)</sup> The QALY in effect combines a patient's attitude about length of life and quality of life into one number. For instance, how does a particular patient feel about a year with erectile dysfunction as compared to the two extremes of death or perfect health?

The procedure works as follows: We assign a QALY score of 1 to a year with full health, and a score of 0 to death. We then ask, "Imagine you have one year to live but suffer from erectile dysfunction (ED). If a potentially fatal treatment for ED were available, what chance would you take of immediate death to be restored to perfect health?" If a particular patient says that he would take a 20% chance of death, then his QALY equivalent for a year with erectile dysfunction is 0.8, as seen in the calculation:

Utility of a year with erectile dysfunction =  $0.2(\text{death}) + 0.8(\text{perfect health})$ . Plugging in the utility values for death and full health, this gives:  $0.2 \times (0) + 0.8 \times (1) = 0.8$ .

Once we have the absolute risk probabilities, as illustrated in Table 1, and the patient's preferences in terms of QALYs, as just calculated, we are prepared to conduct a full decision

analysis. Such an analysis computes the expected number of QALYs the patient will receive for each of the possible treatments. The treatment offering the highest expected QALY total is the preferred treatment that should be selected. Quite simply, it gives the patient the highest output based on his/her own preferences and probabilities. As a simple example, imagine that Treatment X for cancer yields a 10-year life-expectancy but always causes erectile dysfunction, and Treatment Y yields a 9-year life-expectancy without causing any erectile problems. Using the QALY of 0.8 for erectile dysfunction, Treatment X yields a QALY total (often called a “quality-adjusted life expectancy”) of  $10 \times 0.8$  QALYs = 8 QALYs. Treatment Y produces a quality-adjusted life expectancy of  $9 \times 1.0$  QALYs = 9 QALYs. Thus, for this particular patient, Treatment Y is the preferred decision.

Although a strictly quantitative approach of this sort may not always be feasible – or even desirable – in the context of a patient-doctor encounter, explicitly asking patients to think carefully about such tradeoffs when approaching a treatment decision does gather critical information for decision-making and helps to organize thinking. (With experience, simpler surrogate procedures for eliciting QALY values may be developed, in the spirit of the 1 to 10 ranking scales used to gauge patients’ pain assessments.) Ducking the issue of calibrating outcomes, or merely acknowledging that some outcomes are “very bad,” misses important information. Below we discuss some of the salient points to bear in mind when discussing preferences about treatments.

### *Patient Preferences Should Usually (But Not Always) Determine the Treatment Decision*

Some clinical decisions are straightforward because one option is essentially preferable for any reasonable person. In clinical language, this often takes the form of a “consensus guideline.” In the language of economics, this concept is called “stochastic dominance.”

Consider a situation where all patients have the same ranking of outcomes, *e.g.*, full health, minimal side effects, significant side effects, death. We may have two treatments, with neither superior in every case, but one yields a more favorable distribution of outcomes than the other. That is, it has at least an equal and sometimes a higher probability of all groups of more favored outcomes, as shown in Table 2. Treatment B is preferable to A for anyone whose ranking of outcomes goes from left to right, as would be normal. That is because the best outcome is more likely for B, as is the probability of one of the first two outcomes (52% versus 50%), or for one of the first three outcomes (91% versus 90%). Nevertheless, Treatment A *will* sometimes yield full health when Treatment B would produce death or significant side effects. But when the probabilities are cumulated across all outcomes, B is definitely preferred, or as economists would phrase it: “B is stochastically dominant.”

Following this prescription would seem obvious, but often it is violated, at least as judged from the standpoint of the patient. For example, if physicians feel that adverse health outcomes resulting from treatment toxicity are somehow philosophically (or legally) worse than adverse outcomes resulting from a failure to treat, they may choose not to offer a treatment with 4% mortality even though other sources of mortality without it will be 8%. Were doctors to act in this manner, they would be violating the dictum to follow the patient’s preferences for decisions that affect them. Economists refer to this as the agency problem, where the more knowledgeable agent makes choices that in part reflect his own interests, at the expense of the supposed beneficiary, in this instance the patient.

Turning to real-world examples, stochastic dominance includes trivial cases – such as where a treatment is available that cures a cancer with minimal side effects (*e.g.*, removal of a localized melanoma) – but also slightly more subtle examples, such as the following case. With surgery only, invasive bladder cancer has a roughly 70% five-year disease-free survival.<sup>(6)</sup> To date, there is no definitive evidence of a survival benefit of adjuvant chemotherapy as an

accompaniment to surgery, but imagine that future studies reveal that surgery plus cisplatin-based chemotherapy increases five-year bladder cancer-free survival by 15%. This benefit would have to be balanced against a documented increased mortality risk of slightly under 1% from cisplatin-related leukemia.(7) Even though a patient receiving treatment may die of leukemia, which wouldn't have occurred without chemotherapy, the initial decision based on these hypothetical data is still clear-cut: surgery without chemotherapy gives 70% five-year cancer-free survival; surgery plus chemotherapy boosts survival to 84%. The patient's preferences would not affect this treatment decision, so long as he or she prefers cancer-free survival to disease recurrence or death and does not care whether nature or treatment caused the outcome, or whether possible future disease and death is caused by bladder cancer or leukemia.

But in many other cases there would be no "consensus guideline" as to the single best treatment, even if all probabilities were known. In these cases the optimal treatment will vary, even for patients with identical clinical situations and prognoses. For instance, returning to the example of clinically localized prostate cancer, two patients of similar age, similar overall health, and similar prostate disease (*e.g.*, PSA levels and velocity, Gleason scores, and clinical tumor staging) may desire very different treatments based on variation in their preferences. A patient whose sole concern is avoiding metastatic disease and early death may choose surgery to minimize the risk of recurrence, while another patient with the same clinical features but who strongly values sexual functioning and urinary continence may choose watchful waiting. Patient preferences become salient when there is no consensus – and the lack of consensus may be due, not simply to a lack of data, but more profoundly to patient-specific subjective tradeoffs between length of life and quality of life, as well as which *elements* of quality of life the patient finds most important. Thus, even if future randomized controlled trials of prostate cancer treatments indicate a clear survival benefit for external beam radiation and/or radical prostatectomy but at the expense of significant side effects, some patients may still reasonably choose less aggressive

therapy (such as seed radiation or watchful waiting) due to a strong preference for living without sexual, urinary, or rectal side effects.

### *Preferences Incorporate More than Just the Outcomes Themselves*

Up to this point, we have been discussing patients' preferences about different outcome states: disease-free survival, erectile dysfunction, incontinence, etc. Preferences also include other factors, and we will consider three: 1) time preference, or impatience; 2) risk aversion; and 3) anxiety.

People generally do not value the present and the future equally. Economists and decision analysts assume (and evidence strongly supports the notion) that people value the present more highly than the future – that is, people are impatient.<sup>(8)</sup> In clinical settings, this may take the form of a patient who is looking forward to his daughter's wedding next year and therefore will not consider any treatment with a significant short-term mortality risk. Another example would be a patient who says, "I'd rather be feeling healthy and fit now while I'm younger, and I'm willing to accept the resulting illness when I'm older." Such a patient might prefer watchful waiting in the short-term, with more aggressive therapy down the road, if necessary – even though he may revise such a decision when the future *becomes* the present.

Another consideration is a patient's attitude towards risk. In a variety of settings, related to finances, educational choices, and health, many people prefer a sure thing – even if it is worth less on average – than a risky opportunity offering a better average outcome. For instance, a highly risk-averse patient may say, "I'm not willing to try an experimental treatment that could kill me immediately, even though it has a good chance to cure my disease and significantly extend my life; I'd rather take the more certain outcome – conservative therapy that rarely cures

but can manage my symptoms for several years.” A less risk-averse person would gladly accept the up-front risk for a significant gain in life expectancy.

A final consideration is that of anxiety – distress caused along the way by uncertainty about the outcomes. Some patients can live easily with uncertainty. Others may find the prospect of “not knowing” to be so upsetting that it drives their treatment decision toward alternatives promising earlier resolution. A 20-year-old woman with a BRCA-1 mutation may decide to have an immediate prophylactic bilateral mastectomy rather than waiting 5 years to do so, not because the risk of cancer during those intervening years is very high, but because she dreads the prospect of living for several years with the anxiety of a high cancer risk. Anxiety and risk-aversion are closely entwined, but they are not the same phenomenon. In the previous example regarding conservative vs. experimental therapy, risk aversion played a role but anxiety did not – the patient opting for experimental therapy did not experience any long-term anxiety, because the mortality risk was immediate. Anxiety requires not only risk, but time to worry about the risk before the uncertainty is resolved.

## **Conclusion**

When approaching a difficult treatment decision, clinicians and patients will benefit from examining the options along two basic dimensions: the probabilities of the various outcomes of each treatment, and the individual patient’s preferences regarding the treatment outcomes. The relevant probabilities for these decisions are the overall outcome probabilities, not intermediate or partial results, and absolute risks rather than relative risks should be the basis for decision. Patient preferences, on the other hand, differ from individual to individual. Specific information about them will be required to guide a treatment decision except when a single treatment is preferable for any reasonable set of preferences. Patient preferences will relate not only to the

ultimate outcomes in question but also the time-course, the riskiness, and the anxiety associated with each treatment choice.

While both probabilities and preferences play leading roles in the economist's approach to decision-making, the clinician's approach to these two dimensions must reflect the distinctive context of medical decision-making. Probabilities can often be distilled from objective evidence. The clinician's role is to provide the relevant statistics on the patient's disease and possible treatments, using his or her best judgment to adjust values to the patient's particular condition. But preferences are inherently subjective – in a mentally competent individual, they cannot be right or wrong – and the clinician's role in this realm is to help the patient discuss and explore his or her own preferences. It is by combining physicians' best estimates of probabilities with patients' best estimates of their own preferences that clinicians can help patients make the treatment decisions that are best for them.

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**Table 1: Percent of Patients Suffering Side Effects from External Beam Radiation and**

**Radical Prostatectomy**

	<u>Urinary Incontinence</u>	<u>GI Symptoms</u>	<u>Erectile Dysfunction</u>
Prostatectomy	11.2%	3.3%	79.6%
Radiation	2.3%	8.4%	61.5%
Prostatectomy vs. Radiation	+8.9%	-5.1%	+18.1%

**Table 2: Stochastic Dominance**

	<u>Full Health</u>	<u>Minimal Side Effects</u>	<u>Significant Side Effects</u>	<u>Death</u>
Treatment A	30%	20%	40%	10%
Treatment B	40%	12%	39%	9%