MAKING MEDICAL DECISIONS UNDER UNCERTAINTY

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In 20 years of medical practice, the one thing I know is that there is more uncertainty than surety in all I do.
—G.B. Alcorn, general practitioner

The practice of medicine has been called the art of making decisions without adequate information [1]. As has been observed by Australian general practioner G.B. Alcorn, even the most routine office visits entail medical decisions that must be made under uncertainty [2].

Nearly every aspect of the physician-patient encounter contributes elements of uncertainty to the decision-making process. During a typical patient encounter, for example, a physician takes a history and generates a differential diagnosis of diseases, each of which has some likelihood of causing the patient's complaint. Then, she orders diagnostic tests, each with different probabilities of accurately detecting disease. On the basis of the results of these tests, she prescribes a course of therapy that has some probability of improving the patient's symptoms. Finally, the physician schedules a follow-up appointment to evaluate the outcome of the treatment and faces further uncertainty even in determining whether the treatment was effective (eg, the results of the laboratory test improve, but the patient's symptoms persist). It can be difficult for both physicians and patients to appreciate the complexity of the uncertainties involved in medical practice, how poorly they are understood, and the ease with which reasonable people can arrive at different conclusions at each step in the decision-making process.

Unfortunately, many physicians lack adequate training in matters of uncertainty, and their responses to uncertainty can have negative effects on clinical performance and patient outcomes [3–5]. This article describes common problems in managing uncertainty in medical practice as well as strategies for reducing that uncertainty. The insights and approaches discussed are drawn from the disparate literatures of cognitive psychology, medical decision making, medical education, decision science, probability theory, and statistics.

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Common Cognitive Errors in Managing Uncertainty

Practicing physicians tend to believe that they are immune from common errors of clinical reasoning [6]. However, research has demonstrated that physicians' judgments are no less susceptible to errors in reasoning than are those of nonphysicians [7–14]. Furthermore, people in general often rely on simplifying principles that reduce the complex tasks of assessing probabilities and predicting values to simpler judgments [11,15]. These simplifying principles (also known as *heuristics*) can be quite useful, but they also may lead to significant, systematic errors. Understanding the circumstances in which heuristics are likely to produce faulty clinical reasoning may help to minimize errors in judgment.

The Availability Heuristic

The availability heuristic refers to the process of estimating the frequency of an event by the relative ease with which examples of that event come to mind [11]. For example, a young woman calls her physician from her honeymoon complaining of dysuria and crampy suprapubic pain. The physician thinks to herself, "It is likely that this patient has cystitis; I see cystitis frequently in my young female patients." She calls in a prescription for an antibiotic, and the patient recovers well.

However, the availability heuristic may lead to biased judgments by overemphasizing the importance of past experiences and underestimating the importance of considering the base rate of disease. Overreliance on the availability heuristic may occur when a diagnosis comes easily to mind—when a physician is familiar with a disease, had a recent patient with the same diagnosis, uses a mnemonic that allows her to easily remember some diagnoses but not others, or had a prior experience that made a lasting impression. For example, because a physician misdiagnosed a prior patient by not considering pheochromocytoma, she reasons that the next patient who presents with hypertension may well have a pheochromocytoma despite its low prevalence.

To avoid errors that arise from reliance on the availability heuristic, physicians should consistently develop complete differential diagnoses when patients present with even seemingly common complaints. Numerous print [16] and Internet aids are available to help physicians develop appropriate differential diagnoses from a list of patient characteristics and laboratory values (Table).

The Representative Heuristic

The representative heuristic refers to the practice of assessing the likelihood of an event on the basis of its close resemblance to other well-defined events (ie, "If it walks like a duck and talks like a duck, then it must be a duck") [1]. This heuristic can be helpful in making rapid diagnoses. For example, to diagnose a patient who presents with a ham-colored, macular rash on her palms and the soles of her feet, a physician may assess the extent to which the patient resembles other patients with secondary syphilis. The physician may decide that the resemblance is significant, order the appropriate serologic tests, and make the correct diagnosis. However, the representative heuristic is subject to several biases that can lead the clinician to make errors in judgment.

Disregarding the prevalence of disease. To determine physicians' aptitude for accurately assessing disease prevalence, researchers asked physicians at 4 Harvard Medical School teaching hospitals the following question: "If a test to detect a disease whose prevalence is 1 in 1000 has a sensitivity of 100% and a specificity of 95%, what is the chance that a person found to have a positive test has the disease, assuming you know nothing about the person's history, symptoms, or signs?" [17]. (*Sensitivity* and *specificity* refer to a test's ability to detect a diseased patient in the presence of disease and to detect a nondiseased person in the absence of disease, respectively [18].) Of the 60 physicians surveyed, only 11 (18%) answered correctly that a person with a positive test result has a 1 in 51 (less than 2%) chance of having the disease. The correct answer may be found by calculating the *predictive value* of the test result using a 2×2 table (Figure 1).

In the study example [17], the low prevalence of disease will result in more false-positive than true-positive results. For a disease with a prevalence of 1 in 1000, a test that is 100% sensitive will yield a *true-positive result* only for the single diseased person. However, because the test is only 95% specific, it will also yield a *false-positive result* 5% of the time. In this hypothetical situation, 5% of 999 test results (approximately 50 test results) will be false-positives. Therefore, the chance that a person who tests positive has the disease is 1 in 51.

This simple example demonstrates the importance of carefully considering the underlying prevalence of disease when relying on the representative heuristic. The features of a case history that make it representative of a disease are not the only characteristics that affect the probability that the disease is present. Even if a patient's features correspond closely with the characteristic findings of a disease, the disease is not likely present if it occurs only rarely in a given population.

Information about the prevalence of common diseases is increasingly available from large epidemiologic studies. The National Center for Health Statistics (NCHS) provides data from a number of large surveys that collect detailed information about a variety of illnesses and disabilities in the United States (*see* Table). NCHS information is organized by state so that physicians can readily determine the local prevalence of common diseases.

Choosing poor clinical cues. The representative heuristic enables a physician to decide whether a patient with certain clinical cues belongs to a class of patients with a given disease. However, a poor choice of clinical cues in managing uncertainty can lead to 2 common errors.

First, all the cues used to decide whether a patient's findings are representative of a disease are not necessarily strongly predictive of the disease. In addition, the cues most representative of a disease may be absent in diseased persons and present in persons without the disease [1]. Physicians often are taught the predictive value of classic features of a disease, but rarely are they taught about, nor is it easy to find data regarding, the frequency of those symptoms in persons without the disease.

Second, the representative heuristic is prone to error when the clinical cues provide redundant or highly correlated information about a patient's condition. For example, when classic symptoms of a disease occur together (eg, cough and sputum production in pneumonia), the presence of one predictor is as valuable as the presence of both predictors. Therefore, physicians should not overvalue the information from such redundant clinical cues but should seek additional cues that provide noncorrelated corroboration of the diagnosis. Information about which clinical cues are independent predictors of disease are increasingly available in the form of clinical prediction rules for the diagnosis and management of various diseases [19–34]. The creators of these rules typically identify the least number of distinguishing historical, physical, and laboratory features

Table. Resources for Managing Medical Uncertainty

Resource	Reference No./ Internet Address	Comment
General references		
Against the Gods: The Remarkable Story of Risk	39	Discussion of risk, the history of probabilistic reasoning, and its influence on a range of subjects, from medicine to wine making to the stock market
Judgment Under Uncertainty: Heuristics and Biases	10	Comprehensive discussion of heuristics and common cognitive errors
Medical Decision Making	1	General description of the influences of uncertainty on medicine; useful primer for understanding Bayes' theorem
Differential diagnostic tools		
Common Diagnostic Tests: Use and Interpretation	18	Review of characteristics (eg, sensitivity, specificity) of commonly used diagnostic tests
Differential Diagnosis of Common Complaints	16	Symptom-oriented approach to developing a differential diagnosis for 36 common complaints
D_x*plain*	dxplain.mgh.harvard.edu/dxp	Online tool that allows health care professionals to enter a set of clinical findings (ie, signs, symptoms, laboratory data) and retrieve a ranked list of diagnoses that may explain the patient's clinical manifestations
Med*Swift*	www.saol.com/medswift	Commercial software that allows users to enter symptoms and retrieve differential diagnoses derived from data provided by the manufacturers
Conferences		
Society for General Internal Medicine	www.sgim.org	Short courses and workshops that emphasize creating and implementing practice guidelines and measuring and improving quality of care
Society for Medical Decision Making	polaris.nemc.org/smdm/old/welcome.html	Short courses and workshops that emphasize decision and cost-effectiveness analysis, cognitive aspects of decision making, and judgment and decision psychology
Data sources		
National Center for Health Statistics	www.cdc.gov/nchs	Ongoing survey to provide current statistical data on the prevalence, distribution, and effects of illness and disability in the United States
National Health and Nutrition Examination Survey	www.cdc.gov/nchs/nhanes.htm	Survey of information regarding the health and diet of the United States' population; data are collected using both home interview and mobile health testing
National Nursing Home Survey	www.cdc.gov/nchs/about/major/nnhsd/nnhsd.htm	Survey of data regarding nursing home patients (eg, demographics, living arrangements, functional status)
Guidelines		
ALCHEMIST	37, 38 alchemist.stanford.edu	Online tool for generating evidence-based clinical practice guidelines that are specific and relevant to a particular patient population and that can be automatically modified over time
National Guidelines Clearinghouse	www.guidelines.gov	Compendium of guidelines produced in the United States and Canada
Primary Care Clinical Practice Guidelines	medicine.ucsf.edu/resources/guidelines	Compendium of clinical practice guidelines on a range of clinical topics
Clinical prediction rules		
Various articles from the medical literature	19–34	Algorithms and prediction rules for various conditions and diseases

that are highly associated with a particular diagnosis (eg, patients likely to benefit from hospitalization for community-acquired pneumonia versus those likely to fare well with outpatient treatment).

Using small sample sizes. When physicians compare the features of a particular patient with those of previous patients, it can be difficult for them to account for the relatively small sample sizes of personal experience. For example, a patient presents with headaches that occur most often in the morning, and his physician has 2 patients in her practice with sleep apnea, each of whom presented only with morning headaches. Therefore, the physician concludes that this patient has sleep apnea, even though he did not complain of the sleep abnormalities that typify the diagnosis. Drawing conclusions based on small sample sizes can result in incorrect diagnoses.

Regression to the mean. Physicians often perform therapeutic trials. If a patient's condition improves following treatment for a particular disease, the perceived likelihood increases that the patient suffers from the hypothesized disease. The positive change in the patient's condition is thought to be representative of a cause-and-effect relationship [1]. However, the patient's condition may have improved as a result of chance variation rather than as a true treatment effect, a process known as *regression to the mean*. Regression to the mean occurs because many biologic processes can be described by a bell-shaped curve (ie, they are normally distributed). In any population, an extreme value (ie, an outlier) is likely to be followed by a value that is closer to the mean.

For example, the sons of exceptionally tall mothers are likely to be both taller than their peers and shorter than their mothers. The same is true of apparent treatment effects, because the natural course of many common medical problems is self-limited such that most patients are likely to improve. Therefore, what may be understood as a treatment effect that confirms a physician's suspicion that her patient has the disease for which the treatment was prescribed may actually be a result of the underlying disease process (ie, a tendency toward improvement).

The Anchoring Heuristic

Physicians tend to make decisions about a diagnosis based on an initial consideration of a patient's condition that is adjusted through the addition of clinical information to yield a final answer. When physicians correctly estimate the probability of disease before obtaining diagnostic tests—when they correctly *set the anchor*—and then use test results to appropriately adjust that probability, this heuristic is useful to the diagnostic process. However, the anchoring heuristic may result in poor judgments because accurately setting the anchor probability and making adequate adjustments are difficult tasks. Initial information and positive and confirmatory evidence (especially from redundant or correlated cues) often are overvalued.

To avoid the pitfalls of the anchoring heuristic, physicians can use Bayes' theorem to appropriately adjust an initial probability estimate based on new data. A comprehensive discussion of Bayes' is beyond the scope of this paper, although excellent discussions of its clinical use are available elsewhere [1,35,36].

Target Disorder

Diagnostic Test Result	Present	Absent	Total
Positive	1 (a)	50 (b)	51
Negative	0 (c)	950 (d)	950
Total	1	1000	

Sensitivity = a ÷ (a + c) = 1/1 = 100%
Specificity = d ÷ (b + d) = 950/1000 = 95%
Predictive value of a positive test = a ÷ (a + b) = 1/51 = 2%

Figure 1. Example of a 2 × 2 table. (Data from Casscells W, Schoenberger A, Graboys TB. Interpretation by physicians of clinical laboratory results. N Engl J Med 1978;299:999–1001.)

Simplifying Heuristics

Given the enormous complexity of medical decisions and the increasingly short amount of time in which they are made, physicians may be tempted to oversimplify not only the generation of differential diagnoses, but also the evaluation of information from diagnostic tests and the range of therapeutic interventions they consider using. For example, physicians may wish to describe the accuracy of a screening test in a single number, but relying on the test's sensitivity while ignoring its specificity will result in diagnostic errors.

Alternatively, physicians who are uncomfortable assessing disease probability may choose to perform a given procedure if there is *any* chance the disease is present—an especially tempting heuristic for diseases associated with considerable morbidity or mortality [3].

Other physicians may feel uneasy when assessing the probability that a treatment will be efficacious and may reason, "If but one patient is saved, the effort is worthwhile" [3]. Unfortunately, these simplifications may lead physicians to overutilize resources and to provide more—rather than more efficient—medical care.

Uncertainty Due to Inadequate Knowledge of Relevant Data

Relevant data regarding diagnostic accuracy, prognosis, and treatment effects are unavailable to physicians in many clinical situations. The data may not exist or may be published in journals unavailable to physicians, or physicians may not possess the skills necessary to retrieve them. Alternatively, information regarding the diagnostic test or treatment in question may be available, but the data may have been generated in a different clinical situation. In these situations, it is difficult for a physician to know how best to apply the published conclusions to the patient at hand. Similarly, the variance associated with the estimate of risk provided in the literature may be so wide that it may not be of practical use for patient care.

Given the uncertainty inherent in caring for patients and the demonstrated errors in judgment to which all people, including physicians, are prone, the medical community should develop strategies to recognize and minimize uncertainty whenever possible. Clinicians should insist upon knowing and understanding the data upon which their medical practices are built. Such an evidence-based approach could be the guiding principle for selecting continuing medical education (CME) programs and professional development activities: to learn and use the best available data pertaining to the greatest proportion of patients (*see* Table). Even when following a clinical guideline or pathway, physicians should examine the underlying evidence, use that information to guide therapy, and share their knowledge with patients. For example, a recently developed Web-based tool automatically creates clinical practice guidelines from existing decision models [37,38]. Using this tool, clinicians can enter local prevalence and cost data into an established model to generate an evidence-based clinical practice guideline that is customized for their specific patient population and that can be modified automatically over time as the underlying decision model or evidence evolves.

Understanding the Language of Uncertainty

Most modern physicians are trained in the language of signs and symptoms of disease but not in mathematics and probability, although it was Girolamo Cardano—a physician—who in 1525 wrote *Liber de Ludo Aleæ* (*Book on Games of Chance*) and introduced the world to the notion of probability [39]. A lack of familiarity with the language of uncertainty is a fundamental source of difficulty for physicians when faced with managing uncertainty in clinical practice. Physicians often use phrases such as *chances are*, *rule out*, and *it is likely that*. The imprecision of this language not only may confuse patients; it also may reflect a general discomfort with the probabilistic nature of medical decision making. However, characterizing medical uncertainties as probabilities may alleviate some of this confusion.

The common methods used to discuss medical uncertainty serve 2 primary functions: 1) to describe the relationship between risk factors and their associated diseases and 2) to describe the probability that treatments will produce their intended outcomes. For example, a patient who is newly diagnosed with essential hypertension must decide whether to begin long-term antihypertensive therapy. The patient's physician wants to counsel him about the risks of cardiovascular (CV) death in patients with untreated hypertension but recognizes that many patients do not consider hypertension to be a real disease because it does not cause overt symptoms or disability. However, she wants to inform her patient about his risk for developing another illness or condition (eg, stroke) that would cause increased morbidity or mortality. In order to counsel her patient, the physician must consider the probability of CV death in patients without hypertension, in those with untreated hypertension, and those with treated hypertension. She can chose to discuss the use of antihypertensive treatment for reducing the risk of CV death in terms of relative risk reduction or absolute risk reduction.

Measures of Relative Risk

The term *relative risk* (RR) refers to the ratio of the risk of an outcome (eg, CV death) in persons with the factor of interest (eg, untreated hypertension) to those without the factor [40]. RR is calculated by dividing the rate of the outcome in exposed subjects by the rate in unexposed subjects. The physician in this example can calculate her patient's RR by creating a 2×2 table using data from the Framingham study [41] (Figure 2). The Framingham researchers found that 13 per 100 treated hypertensive patients followed for 10 years died of CV causes, compared with 28 per 100 untreated hypertensive patients followed for the same period of time. Based on calculation of the RR, the physician might tell the patient that his risk of dying from CV death with antihypertensive treatment is nearly half (46%) what it would be without therapy.

	Cardiovascular Death: Present	Cardiovascular Death: Absent	Total
Treated Hypertensive Patients	13 (a)	87 (b)	100
Untreated Hypertensive Patients	28 (c)	72 (d)	100
Total	41	159	

$$RR = \frac{\text{Rate of outcome in treated persons}}{\text{Rate of outcome in untreated persons}} = \frac{a \div (a + b)}{c \div (c + d)} = \frac{0.13}{0.28} = 46\%$$

$$RRR^* = \frac{\text{Rate of outcome in untreated persons} - \text{Rate of outcome in treated persons}}{\text{Rate of outcome in untreated persons}} = \frac{0.28 - 0.13}{0.28} = 54\%$$

$$OR = \frac{\text{Odds of outcome in treated persons}}{\text{Odds of outcome in untreated persons}} = \frac{a \div b}{c \div d} = 0.15/0.39 = 38\%$$

$$ARR = \text{Rate of outcome in treated persons} - \text{Rate of outcome in untreated persons} = [c \div (c + d)] - [a \div (a + b)] = 0.28 - 0.13 = 15\%$$

$$NNT = 1/ARR = 6.7$$

*RRR may also be calculated as follows: 1 – RR = RRR.

Figure 2. Example of a 2 × 2 table used to estimate relative and absolute risk. RR = relative risk; RRR = relative risk reduction; OR = odds ratio; ARR = absolute risk reduction; NNT = number needed to treat. (Data from Sytkowski PA, D'Agostino RB, Belanger AJ, Kannel WB. Secular trends in long-term sustained hypertension, long-term treatment, and cardiovascular mortality. The Framingham Heart Study 1950 to 1990. Circulation 1996;93:697–703.)

Alternatively, the physician may calculate her patient's *relative risk reduction* (RRR), which describes the degree to which an intervention reduces a patient's risk for a particular outcome. RRR is sometimes also referred to as *percent risk reduction*. Therefore, the physician may tell her patient that antihypertensive treatment will reduce his relative risk of CV death by 54%.

Another relative measure of disease occurrence—the *odds ratio* (OR)—is used to estimate RR when data are obtained from case-controlled studies; OR is a useful estimate when the disease of interest is rare and the sampling error is small. The OR is defined as the odds in favor of an outcome in an exposed group divided by the odds in favor of an outcome in an unexposed group. According to the OR, the patient in question is 38% as likely to suffer CV death with antihypertensive treatment versus without such treatment. In this example, the OR (38%) is somewhat lower than the RR (46%), because the rate of CV death is much higher in the untreated group compared with the treated group. Therefore, in this case, the OR is a relatively less reliable estimator of the RR.

Measures of Absolute Risk

Physicians alternatively may choose to discuss the risk of CV death in patients with sustained hypertension in terms of *absolute risk reduction* (ARR). ARR is defined as the incidence of an outcome in an exposed group (eg, treated hypertensive patients) minus the incidence of an outcome in an unexposed group (eg, untreated hypertensive patients) [42]. Therefore, the ARR for antihypertensive therapy is 15 deaths per 100 patients treated for 10 years (ie, 0.28 – 0.13 = 0.15). Based on this calculation, the physician might tell her patient that antihypertensive

therapy can prevent 15 CV deaths for every 100 hypertensive patients (or 15% of patients) treated for 10 years.

The ARR can then be used to calculate the *number needed to treat* (NNT), which is defined as the number of patients who need to be treated to prevent 1 bad outcome of interest. The NNT is the inverse of the ARR (1 / ARR). In this example, the average NNT would be 6.6 hypertensive patients (1 / 0.15) in order to avoid a single CV death. The most formal statement of this result would be that "the expected number of patients who need to be treated for 10 years to prevent 1 additional CV death relative to no treatment is 6.6" [43].

Practical Considerations for Using Risk Ratios

These closely related measures of risk are potential sources of confusion for physicians. It is no small task to convert information from the medical literature into these ratios to express the relevant risks to patients. Such difficulty should be expected because statisticians and physician researchers continue to debate the relative merits of describing trial results in terms of relative versus absolute risk. A comprehensive discussion of the advantages and disadvantages of these approaches can be found elsewhere [43]. However, practicing physicians seeking to use knowledge gained from the medical literature to inform clinical decisions and discussions with patients should consider the data used to calculate reported ratios. Specifically, physicians should consider the following: What values comprise the denominator (eg, 28 among 100 hypertensive patients or 28 among 100,000 patients from the general population)? Over what interval is the risk being evaluated (eg, 1 year or 10 years)? Are the risks cumulative over time?

In addition, a measure of variance is associated with each measure of risk and may be reported as a *standard deviation*, *standard error*, or *confidence interval*. The variance associated with each measure of risk (eg, RR versus ARR) is calculated differently, so the certainty of each estimate differs accordingly. Significant differences in variances of a given risk ratio also may result from differences in the sample size used to calculate the ratio. For example, there may be a 10% risk of disease given exposure to a particular risk factor. However, this 10% risk may have been calculated from a ratio of 1 / 10 or 100 / 1000, each of which conveys a different degree of uncertainty. Adding 1 subject to each ratio would thus alter the ratios very differently—1 / 10 would become 2 / 11 (18%) and 100 / 1000 would become 101 / 1001 (10.1%). Therefore, a ratio calculated using a smaller denominator is far less stable—and has a greater variance—compared with a ratio derived from a larger population.

Notwithstanding these considerations, understanding the language of uncertainty and probability can help physicians use the medical literature more precisely both to make clinical decisions and to communicate with patients.

Conclusion

Despite the mammoth gains in biomedical knowledge that have occurred since Sir William Osler commented that medicine is a science of uncertainty and an art of probability, the management of patients continues to require making decisions without certain knowledge of the patient's condition, without a language for communicating or assessing likelihood of disease, without appropriate training in manipulating probabilities, and with a dependence on heuristics that can lead to severe errors in reasoning.

However, physicians can do more to recognize, understand, and manage uncertainty in their practices. Medical schools and residency programs can strive to integrate probability theory (for understanding uncertainty), mathematics (for synthesizing evidence and estimating outcomes), and health economics and decision theory (for making probability-based decisions) into their curricula. Research has demonstrated that traditional teaching methods do not provide students with skills for estimating disease probability; however, innovative teaching methods can improve students' understanding of uncertainty, use of diagnostic test results, and application of clinical decision tools (eg, Bayes' theorem) [44–47]. Physicians in practice can also choose evidence-based CME and self-directed learning programs to accomplish the same goals.

This article presents an approach to managing uncertainty in medical practice based on knowing the evidence upon which medical practices are based, recognizing the sources of uncertainty in those practices, and making a commitment to acquire more skills to manage the uncertainty affecting patients. Such a strategy cannot prevent bad outcomes, but it may reduce the number of bad decisions.

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