Patients increasingly seek more active participation in health care decisions, and many groups have called for a shift toward more meaningful dialogue between patients and physicians.\textsuperscript{1–3} Informed or shared decision making requires that patients understand their medical condition, know what treatments are available, understand the expected outcomes of treatments, and assess these expected outcomes according to their personal values.\textsuperscript{4} One essential component of this process is knowledge of the scientific uncertainties that pervade and complicate every step of medical decision making. A recent summary of the state of medical knowledge reported that nearly half (47\%) of all treatments for clinical prevention or treatment were of unknown effectiveness and an additional 7\% involved an uncertain tradeoff between benefits and harms.\textsuperscript{5} Discussing the many uncertainties associated with a clinical decision is thought to be a critical element of an informed decision. Nonetheless, empirical evidence suggests that clinicians rarely communicate uncertainty about evidence to patients. Analysis of 1057 clinical encounters by primary care physicians and surgeons\textsuperscript{2} found that only 16\% to 18\% of discussions met the minimum criteria for an informed decision; discussion of uncertainty about risks and benefits of treatment was done only 1\% of the time for basic decisions.
6% for intermediate decisions, and 16.6% for complex decisions.

The rapid growth of medical knowledge has spurred interest in rating the quality of medical evidence. Sophisticated rating systems have been developed to stratify evidence according to its scientific credibility and level of uncertainty. Considerable progress has been made in developing such rating systems by initiatives such as the Cochrane Collaboration, Evidence-Based Practice Centers, US Preventive Services Task Force, and Consumer Reports on Health. In contrast, researchers have only begun to investigate ways to present scientific uncertainty to health care consumers.

With increasing attention paid to helping patients use research evidence to inform personal health decisions, this review was undertaken to address the following questions: How do we conceptualize uncertainty? How do we assess uncertainty? What are the best practices for communicating uncertainty about harms and benefits of treatment? How do patients and physicians respond to uncertainty? Where are the gaps in the literature?

CONCEPTUALIZING UNCERTAINTY AND ITS SOURCES

There are various definitions and interpretations of uncertainty. The Merriam-Webster dictionary defines uncertainty as “the state of being indefinite, indeterminate, unreliable, unknown beyond doubt, not clearly identified or defined, and/or not constant.” Another proposed definition of uncertainty is “a cognitive state created when an event cannot be adequately defined or categorized due to lack of information.” In the health domain, Mishel has broadly defined uncertainty in illness as “the inability to determine the meaning of illness related events,” which results from the ambiguity, complexity, and unpredictability of illness or deficiency of information about one’s illness and its consequences.

In measurement and science, uncertainty often has a slightly different and technical meaning related to imprecision in measurement. The National Institute of Standards and Technology defines the uncertainty of a measured result as the standard deviation of the collection of data samples approximating the measurand, the quantity being measured. Similarly, the International Vocabulary of Basic and General Terms in Metrology defines uncertainty as “a parameter associated with the result of a measurement, that characterizes the dispersion of the values that could reasonably be attributed to the measurand. The parameter may be a standard deviation or the width of a confidence interval.” Sources of this type of uncertainty include data acquisition, sampling, quantification, and interpolation. These groups distinguish between uncertainty and error, in which uncertainty represents the range of all determinations, whereas error refers to the difference between an individual result and the true value of the measurand. Error consists of a random component and a systematic component but is an idealized concept, and its magnitude cannot be known exactly.

The variety of ways in which uncertainty has been defined and conceptualized reflects its many potential sources. Because our primary interest is in informed decision making in the health care domain, we have chosen to focus specifically on uncertainties that relate to patients’ understanding of the outcomes of medical interventions. For our purposes, therefore, we differentiate between 5 main types or sources of uncertainty: 1) risk, or uncertainty about future outcomes; 2) ambiguity, or uncertainty about the strength or validity of evidence about risks; 3) uncertainty about the personal significance of particular risks (e.g., their severity, timing); 4) uncertainty arising from the complexity of risk information (e.g., the multiplicity of risks and benefits or the instability of risks and benefits over time); and 5) uncertainty resulting from ignorance. These different sources of uncertainty are not often distinguished in the risk communication literature but should be clarified when discussing uncertainty in medical decision making.

Fundamental uncertainty about the future occurrence or nonoccurrence of a given outcome lies at the core of the notion of risk. Risk estimates describe this uncertainty in probabilistic terms and are derived from empirical observations of an outcome’s occurrence within a given population. Yet risk estimates embody additional uncertainties as well. First, because risk estimates are not truly predictive but rather postdictive (i.e., they explain past patterns of occurrence in a reference population), their use for the purposes of informing decisions regarding an individual’s outcome requires a leap of faith that the future, and all of its deterministic elements, will be the same as the past.

An equally important problem is that risk estimates necessarily have limited applicability at the individual level. Many argue that risk indeed loses precise meaning with respect to individual persons and events because individuals either will or will not be affected. Although risk estimates might
accurately predict the aggregate number of outcomes in a population, they cannot specify their exact distribution\textsuperscript{15} nor what is most critical for decision making at the individual level: the future outcome of any given person. No matter how much any given person resembles other individuals statistically identified as falling into one risk category or another, any one person’s outcome is unknowable and may diverge from the categorical norm. The irreducible nature of this uncertainty poses a fundamental limit to the value of risk estimates in individual decision making. In addition, there are some types of events that are beyond the realm of prediction.\textsuperscript{16}

The 2nd type of uncertainty in our schema relates not to the occurrence of future outcomes but to the quality of the risk information at hand. Decision theorists have used the terms ambiguity and vagueness to describe this type of uncertainty, which relates to the “reliability, credibility, or adequacy” of risk information.\textsuperscript{17,18} Ambiguity or vagueness is high when risk information is unreliable, conflicting, incomplete, unknown, unknowable, or when expert knowledge is contested. This type of uncertainty, which relates to the strength of scientific evidence, has several sources, including missing or inconsistent empirical data or conflicting expert opinions and recommendations.

The strength of scientific evidence is affected by many factors. These include, but are not limited to, study design (randomized controlled trial v. observational), blinding, duration of treatment and follow-up, appropriateness of the outcome measures used, controlling of confounders in design and analysis, sample size, and sample population. Inadequacies in any of these factors can affect the validity (i.e., increase uncertainty) of the study’s findings, making it more prone to bias or chance events. Extrapolating risks derived from studies examining one duration of treatment to another, from one formulation to another, from a composite end point to its components, or from one population to another also introduce ambiguity, as do differences in how the same studies are interpreted. For example, a study examining congruence among different meta-analyses\textsuperscript{19} found differences among reported findings to be relatively small in comparison to substantial disagreement in the authors’ interpretations with regard to clinical applications of the findings.

Uncertainty regarding a risk estimate is often expressed statistically through the use of a confidence interval (CI) around a point estimate of risk. CIs express the dispersion around a point estimate arising from sampling issues and sample size. The appropriate interpretation of a CI requires an understanding of the difference between accuracy, or how close an estimate is to the actual or true value, and precision, or the reproducibility of the estimate. CIs reflect the precision of an estimate but not its accuracy. As such, CIs capture some—but not all—of the ambiguity pertaining to a risk estimate.

The 3rd and 4th types of uncertainty in our schema relate to the personal significance of risks and to uncertainty arising from the complexity of risk information, respectively. In the health care domain, the clinical significance of risks for various outcomes is often unclear. For example, clinicians and patients may be uncertain about the severity of these outcomes, their tolerability, scope, timing, or temporal impact. At the same time, uncertainties may arise from the sheer complexity of risk information. For example, decision makers often need to process and interpret multiple risks simultaneously and to make sense of risks that change over time and as a consequence of different actions.\textsuperscript{20} The optimal way of processing risk information in these circumstances is not clear even for expert decision makers or complex computerized decision support systems, and it depends on various assumptions that are difficult to make explicit. Additional uncertainties about the correct diagnosis and about the natural history of a disease may further magnify any uncertainty about the outcomes of treatment because the likelihood of benefit (but not risk) is predicated on the patient’s having the condition in question.

Uncertainty may also arise from ignorance of relevant information. Evaluating risks, making clinical diagnoses, and making treatment decisions within the confines of a brief clinical encounter require that many facts be left unknown, unspoken, or crudely summarized. This can lead to uncertainty about the current state of a patient. Many doctors fail to review\textsuperscript{21} or document family history,\textsuperscript{22} and patients have been shown to inaccurately recall important risk factors that are used to calculate risks.\textsuperscript{22} This type of uncertainty is common in many clinical circumstances yet is difficult to assess.

PROBLEMS IN ASSESSING UNCERTAINTY

Aside from the conceptual problems involved in defining uncertainty and its sources, assessing uncertainty presents an additional challenge. To promote informed decision making in health care, one would like to be able to specify or quantify the
uncertainty pertaining to information about the risks and benefits of a given intervention. Yet this task is made problematic not only by the variety of types of uncertainty (some of which may not lend themselves to quantification at all) but also by methodological difficulties.

For example, even if one focuses only on uncertainty pertaining to the statistical precision of a risk estimate (a type of ambiguity), the assessment and calculation of uncertainty through the use of confidence intervals (or $P$ values) can be challenging. One problem is that it may be possible to apply more than one CI when expressing ambiguity, and the choice of CI is itself ambiguous. A data set can be examined in its entirety (larger $N$, smaller CI) or in subgroups (smaller $N$, larger CI), and risk estimates from these alternative analyses can differ substantially in magnitude and dispersion. Although the overall risk may appear to be more precise than the risks associated with subgroups because of tighter CIs, a subgroup analysis may more accurately reflect the risk pertinent to members of that subgroup (but with less precision). For example, the National Surgical Adjuvant Breast and Bowel Project P-1 trial found that tamoxifen increased the risk of endometrial cancer 2.5-fold (relative risk [RR] = 2.53, CI = 1.35–4.97) among all women. However, age was an effect modifier: The RR was 1.21 (0.41–3.6) among women younger than 51 years but 4.01 (1.7–10.9) among women 51 years or older. In such cases, it is not clear which CI best reflects the point estimate and associated uncertainty pertaining to an individual woman: the more accurate estimate that factors in her age, or the more precise estimate that does not.

Another problem in assessing uncertainty is posed by the use of composite end points, which combine more than one clinical end point into a single measure of impact. Composite end points typically combine more frequent but less clinically important events (e.g., laboratory abnormalities) with less frequent but more clinically important events (e.g., death, stroke) to increase statistical power (by increasing the event rate). However, these events may differ substantially in terms of their effects, the uncertainty surrounding their effects, and their clinical significance. These differences among the events that are integrated within composite end points make the specification of uncertainty very difficult and may lead to biased estimates. Composite end points that are largely based on less important clinical end points may overestimate the impact and underestimate the uncertainty of treatment on more important end points.

A further difficulty in assessing uncertainty is introduced by the different types of summary statistics used to express risk. For example, there is general concurrence that the risks of treatment should be communicated as absolute risks (ARs), not RRs. Communicating the benefits and risks of treatment in relative rather than absolute terms can influence a patient’s perception of a therapy’s effectiveness, making the benefits of a treatment appear more favorable or conversely, emphasizing its risks. These framing effects concerning the point estimates of risks have been well studied and have been shown to affect treatment decisions. However, relatively little is known about how to estimate or communicate the associated CI of absolute risks. Converting an RR into an AR is relatively simple, but computing the CI associated with the calculated AR is not. When ARs are not reported, or when the patient differs from the cohort on which the reported ARs are based, ARs and their associated CIs must be calculated. To translate RRs into ARs, the individual’s baseline (pretreatment) risk for a condition is combined with the RR of the treatment on that condition using simple multiplication. For example, a person with a 10% baseline risk who takes a treatment that has an RR of 2.5 for that condition will experience an AR of 25% ($0.10 \times 2.5$) with treatment.

Estimating the CI for the AR, however, is more challenging. Simply finding the CI associated with an individual’s baseline risk estimates can be difficult because these often appear in monographs or older journals that may be difficult to access. Once the publication is found, identifying the appropriate CI for a risk estimate typically involves tedious multistep table look-ups, graphical interpretations, and cross-comparisons. Finally, these published tables and graphs require many simplifications from the exact calculations, thus introducing further uncertainty. For example, a 40-year-old woman whose 30-year breast cancer risk is calculated exactly as being 7.3% (CI = 7–8) is estimated from the tables and graphs as having a risk of 7.5% (6–10). The developers of key risk prediction models have emphasized the uncertainty associated with their models and the importance of conveying this uncertainty to patients: “All of the estimates discussed here are associated with error; this fact should be transmitted to the patient should any estimates be given in a clinical setting.” Nonetheless, when such risk models

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are promulgated, their associated CIs are typically not reported.

To estimate the CI of a calculated AR, one needs to combine the CI surrounding the patient’s baseline risk with the CI of the RR. Although these calculations are intended to measure the uncertainty of the AR, they also introduce a substantial amount of uncertainty. This uncertainty stems from differences between the study population used to develop the risk model and the individual to whom it is being applied, as well as the extent to which the model may be misspecified. Misspecification may result from omission of important but as yet unidentified risk factors associated with the disease of interest or failure to include specific study design elements such as matching schemes. Combining the CI of the 2 distributions assumes that the 2 are independent, an assumption that is unlikely to be true. The CI of risk prediction models are tightest in the middle of their prediction range (i.e., for those at average risk) and widen the further the deviation from the average. On the other hand, because most clinical trials are conducted on high-risk populations, their tightest CIs are typically among those at higher risk.

These and other methodological uncertainties confound the quantification of uncertainty regarding risk estimates and pose challenges for the task of communicating uncertainty to individual decision makers.

**POTENTIAL APPROACHES TO COMMUNICATING UNCERTAINTY**

Problems in both the conceptualization and assessment of uncertainty have important implications for the task of communicating uncertainty. There are multiple types of uncertainty that clinicians may want and need to communicate to patients, and the assessment of these uncertainties is not straightforward. Furthermore, the communication of uncertainty to patients may serve different purposes and goals, for example, to convey doubt or to increase the level of confidence in a finding, to inform patients about their estimated disease risk and the limitations of these estimates, or to help patients understand the general complexity or unpredictability of illness and its management. Moreover, these goals are not always consistent with one another and may require focusing on particular types, assessments, or approaches to communicating uncertainty. Yet we know very little about the optimal approaches and outcomes of communicating different types of uncertainty. Although there is a growing literature on approaches to communicating risks (i.e., probabilities or likelihoods), little attention has been given to communicating uncertainty.

In this section, we review possible approaches for communicating uncertainty and the limited evidence for the effectiveness of these approaches. For the most part, the discussion will relate to the communication of statistical uncertainty, or ambiguity, given the existing literature. However, much of what is written on this topic concerns communication of risk, not uncertainty.

Uncertainty and ambiguity may be communicated in a variety of ways, including verbally, numerically, or visually. Verbal methods using subjective descriptive words such as *highly uncertain* have the advantage that people think they understand what is being said; however, interpretation of such terms has been shown to be highly variable. The use of numbers to depict uncertainty and ambiguity potentially allows for more precision and avoids variable interpretation. However, there are many different ways in which information about risks may be communicated quantitatively. They can be described using RRs, ARs, frequencies, or number needed to treat; the measure used can affect how the information is understood and answered. Ambiguity might be communicated in terms of any or all of these summary statistics; however, these possibilities have not been evaluated.

Furthermore, many people, including experts, have difficulty understanding and combining statistical information effectively. Numeracy—the ability to comprehend quantitative information—is manifest in the way in which people process statistical information. One study found that individuals with high numeracy were less biased by framing effects and more influenced by affective meaning than were those with low numeracy. Another study found that individuals with low numeracy tend to better comprehend information about the comparative quality of 2 choices when it is simplified (e.g., by highlighting relevant or meaningful information). It is also possible that numeracy is reflected in people’s ability to understand and process information about statistical uncertainty or ambiguity, but this possibility has not been explored.

Visual depictions of data may facilitate rapid understanding of numerical expressions of uncertainty, particularly if large amounts of numerical information must be presented. However, little is known about how ambiguity might be depicted visually. Limited work suggests that the visual depiction of statistical uncertainty may exploit the
ability of the eye to quickly detect discontinuities in an image and to interpret these discontinuities as areas with distinct data characteristics. Techniques that have been used to depict uncertainty have incorporated discontinuities such as surface roughness, blurring, and oscillations, depth-shaded holes, noise, and texture, and the translation, scaling, rotation, warping, and distortion of geometry. Animation effects have been used to simplify the visualization of statistical uncertainty by not displaying all of the information at once and by mapping uncertainty to animation parameters (speed, motion blur, duration, and range of motions) and sound effects (pitch, duration, timbre, and volume). Most visualizations rely on the box plot or variants thereof, which divides the data into 4 quartiles, draws a box around the central 50% of the data, and includes lines (whiskers) encompassing the range. Most visual depictions of ambiguity attempt to portray confidence intervals around a risk estimate, but uncertainty around other measures, such as the number needed to treat, has also been illustrated.

Few of these approaches for visualizing ambiguity appear to have been tested for their effect on comprehension and choices, and existing studies have been inconclusive. One study compared 9 graphics depicting ambiguity about a weather forecast. They found that participants were most familiar with the pie chart and histogram, but familiarity did not correspond to improved understanding. The pie chart and cumulative density function were best at communicating whether a value fell within a specified range. However, no single graph consistently dominated the others in terms of improving the understanding of uncertain data; the authors suggested using a combination of graphics to communicate statistical uncertainty.

A 2nd study elicited reactions to visual depictions of uncertainty about risk estimates. In one of the depictions, participants were shown a line graph displaying a point estimate and subsequently one displaying both a point estimate and CIs associated with the risk reduction of breast cancer mortality. Less educated women perceived the point estimate with CI as making the information seem “vague” or “wishy-washy,” and it decreased trust in the information presented. More educated women, however, were more accepting of ambiguity, and most women in this group felt that the CI should be presented. Thus, patient characteristics may influence understanding of, and response to, uncertainty about risks.

### Table 1 Categories of Effectiveness Used by the BMJ Clinical Evidence Series

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Icon</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beneficial</td>
<td>📈</td>
<td>for which effectiveness has been demonstrated by clear evidence from RCTs or the best alternative source of information, and for which expectation of harmfulness is small compared with the benefits.</td>
</tr>
<tr>
<td>Likely to be beneficial</td>
<td>📈</td>
<td>for which effectiveness is less well established than for those listed under “beneficial.”</td>
</tr>
<tr>
<td>Tradeoff between benefits and harms</td>
<td>📈</td>
<td>for which clinicians and patients should weigh up the beneficial and harmful effects according to individual circumstances and priorities.</td>
</tr>
<tr>
<td>Unknown effectiveness</td>
<td>📈</td>
<td>for which there are currently insufficient data or data of inadequate quality.</td>
</tr>
<tr>
<td>Unlikely to be beneficial</td>
<td>📈</td>
<td>for which lack of effectiveness is less well established than for those listed under “likely to be ineffective or harmful.”</td>
</tr>
<tr>
<td>Likely to be ineffective or harmful</td>
<td>📈</td>
<td>for which ineffectiveness or harmfulness has been demonstrated by clear evidence.</td>
</tr>
</tbody>
</table>

**PAST APPROACHES TO COMMUNICATING UNCERTAINTY**

There are many recommendations for and examples of communicating uncertainty in the literature, although few are supported by evidence. Most have been limited to efforts at verbally summarizing the quality of scientific evidence pertaining to a given health intervention. Several widely used rating systems use simple descriptive terms to describe uncertainty, typically combining the strength of the evidence with the magnitude of the benefit. For example, the BMJ Publishing Group’s *Clinical Evidence* reports categorize the effectiveness of interventions as being either beneficial, likely to be beneficial, a tradeoff between benefits and harms, unknown effectiveness, unlikely to be beneficial, or likely to be ineffective or harmful (Table 1). Similarly, the US Preventive Services Task Force combines verbal ratings of the strength of the evidence of effectiveness with an estimate of net benefit (benefits minus harms;
Table 2  How the US Preventive Services Task Force Grades Its Recommendations

<table>
<thead>
<tr>
<th>Strength of Overall Evidence of Effectiveness</th>
<th>Estimate of Net Benefit (Benefits Minus Harms)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Substantial</td>
<td>Moderate</td>
</tr>
<tr>
<td>Good</td>
<td>A</td>
</tr>
<tr>
<td>Fair</td>
<td>B</td>
</tr>
<tr>
<td>Poor</td>
<td>I—Insufficient Evidence</td>
</tr>
</tbody>
</table>

The US Preventive Services Task Force (USPSTF) grades its recommendations based on the strength of evidence and magnitude of net benefit (benefits minus harms).

A. The USPSTF strongly recommends that clinicians provide [the service] to eligible patients. The USPSTF found good evidence that [the service] improves important health outcomes and concludes that benefits substantially outweigh harms.

B. The USPSTF recommends that clinicians provide [the service] to eligible patients. The USPSTF found at least fair evidence that [the service] improves important health outcomes and concludes that benefits outweigh harms.

C. The USPSTF makes no recommendation for or against routine provision of [the service]. The USPSTF found at least fair evidence that [the service] can improve health outcomes but concludes that the balance of benefits and harms is too close to justify a general recommendation.

D. The USPSTF recommends against routinely providing [the service] to asymptomatic patients. The USPSTF found at least fair evidence that [the service] is ineffective or that harms outweigh benefits.

I. The USPSTF concludes that the evidence is insufficient to recommend for or against routinely providing [the service]. Evidence that [the service] is effective is lacking, of poor quality, or conflicting, and the balance of benefits and harms cannot be determined.

The USPSTF grades the quality of the overall evidence for a service on a 3-point scale (good, fair, poor).

Good: Evidence includes consistent results from well-designed, well-conducted studies in representative populations that directly assess effects on health outcomes.

Fair: Evidence is sufficient to determine effects on health outcomes, but the strength of the evidence is limited by the number, quality, or consistency of the individual studies; generalizability to routine practice; or indirect nature of the evidence on health outcomes.

Poor: Evidence is insufficient to assess the effects on health outcomes because of limited number or power of studies, important flaws in their design or conduct, gaps in the chain of evidence, or lack of information on important health outcomes.

The popular lay publication Consumer Reports Best Buy Drugs explains the benefits and risks of treatments to consumers by using subjective terms (“about 30%,” “up to 7%”) and by reporting ranges that imply a CI but that are not explicitly defined (“between 17% and 25% are pain-free”). Uncertainty about individual variation is communicated by stating.

It’s very important for you to know that people respond differently to the various treatments. You may get little or no relief from one and respond much better to another. . . . But it’s possible that you would not be helped by one of the three treatments. In that case,
you should try one of the others. Doctors are very used to trying another [treatment] if the first one they prescribe for you does not seem to be working.

Data are lacking regarding outcomes of these approaches to communicating uncertainty for either physicians or patients involved in treatment decision making. According to the recent Cochrane review of decision aids, for instance, few of the 131 decision aids reviewed included a description of the level of uncertainty about the evidence.39

POTENTIAL OUTCOMES OF COMMUNICATING UNCERTAINTY

To identify appropriate ways to communicate uncertainty to patients, it is important to understand the potential outcomes of this endeavor. Although empirical evidence in the health domain is lacking, there is a substantial literature on the psychological and behavioral effects of uncertainty in other decision-making domains.

COGNITIVE AND BEHAVIORAL OUTCOMES OF COMMUNICATING UNCERTAINTY

One concern about communicating uncertainty is that doing so may have deleterious as well as beneficial effects. To the extent that communicating uncertainty entails the transfer of additional, complex information, it has the potential to overwhelm and confuse patients and to impair their ability to make truly informed decisions. Ample research in decision psychology has shown that a surfeit of information does not necessarily facilitate informed decision making and may in fact hinder it.39 Full disclosure of all the benefits and risks associated with a medical treatment may exceed patients’ capacity to process and use this information effectively.52 The provision of added information about medical uncertainty may have similar outcomes with respect to patient understanding and decision making.

A potentially effective way of mitigating these negative outcomes of complex health information may be to tailor the information to individual patients, altering the specific type or amount of information presented according to various characteristics (e.g., gender, culture, education, psychological factors, or behaviors of interest) that relate to patients’ capacity to use or respond to such information. Presumably, such tailoring enhances behavior change in response to information.56–58 Health information might also be tailored according to patients’ individual disease risks or risk factors. For example, the provision of individualized disease risk estimates has been found to increase patients’ uptake of screening tests, particularly in patients at high risk for disease.59 Tailoring the communication of health information according to patients’ individual disease risks, however, is problematic given the substantial uncertainties implicit in individual risk estimates.14 Furthermore, the tailoring of any type of health information according to individual patient characteristics still raises a larger question about the optimal amount and type of information to be conveyed to patients from an ethical, as well as a psychological, standpoint. Until these issues are resolved, a critical issue is to better understand the potential outcomes of communicating uncertainty to patients in general.

Empirical and theoretical work on judgment and decision making provides insights on the potentially negative effects of communicating uncertainty about risk information and the mechanisms for these effects. A large body of past research has shown that both laypersons and experts trained in statistics tend to simplify and use mental shortcuts, or heuristics, when interpreting risk information.60 Patients often simplify probabilistic information into 2 broad categories (e.g., “I will get the disease” or “I will not get the disease”). People’s reliance on heuristics and other simplifying strategies points to inherent limitations in human cognitive processing.62 These limitations have been described extensively and raise the possibility that people may not always respond in adaptive ways to the provision of complex probabilistic information. For example, some have argued that decision makers have a fundamental preference and need to rely on mental representations of the bottom-line meaning or gist of a choice option, rather than the detailed or verbatim representation that includes the accompanying details.63, 64 For these reasons, decision makers may find details about the uncertainty pertaining to risk information of limited relevance or overly difficult to process or understand.

Also relevant to the discussion of potential outcomes of communicating uncertainty in health care is the literature on decision psychology. A number of studies have shown that people generally prefer to avoid ambiguity; when confronted by ambiguous information about risks, people tend to appraise these risks pessimistically and avoid making decisions.17, 65, 66 This phenomenon has been termed...
Ambiguity aversion and has been demonstrated in a number of decision-making settings. Ambiguity aversion has been shown to persist even when odds favor the ambiguous option, although the level of risk appears to affect people’s reactions to ambiguity. At very low probabilities of the unambiguous option, decision makers become indifferent to ambiguity and may even become ambiguity seeking. Ambiguity aversion may also depend on whether gains or losses are at stake. With potential gains (e.g., winning money), people are ambiguity averse, whereas with potential losses (e.g., losing money), people are ambiguity seeking. However, this finding has not been consistently obtained, and ambiguity aversion itself varies considerably among individuals and across different decision-making circumstances. Ambiguity aversion may also vary according to how information on ambiguity is framed, for example, in terms of gains versus losses or verbally versus quantitatively.

Ambiguity aversion may have various psychological and behavioral manifestations. For example, ambiguity regarding estimates of risks of an adverse outcome may lead people to perceive themselves at higher risk and to have greater distrust in the information at hand. However, relatively little research has directly explored how ambiguity aversion may be manifest in the domain of health-related decisions and outcomes. Using hypothetical scenarios, Ritov and Baron and Meszaros and colleagues showed that increasing people’s awareness of ambiguity about a vaccine’s safety made them reluctant to receive it. Other studies have shown that perceptions of ambiguity regarding health risks and disease prevention recommendations are associated with ambiguity-averse perceptions and emotions and lower uptake of screening and preventive interventions. Intervention studies have demonstrated that informing people about uncertainties surrounding cancer screening measures decreases their interest in screening, also implying that people are ambiguity averse. For instance, there is conflicting evidence about the effectiveness of breast self-examinations (BSEs) for early detection of breast cancer. Following the disclosure of the uncertainty about evidence, some patients may ignore the positive evidence about BSEs and decide not to perform BSEs.

Communicating uncertainty may also prompt different information-seeking behaviors. Some patients may respond to uncertainty by actively seeking information. The attempt to resolve uncertainty may help them to cope with it; knowledge about uncertainty can motivate patients to seek discussions with their health care providers, which may comfort patients who prefer to take an active decision-making role in their medical care. However, uncertainty may also lead to information avoidance and confusion if patients lack the proper resources to interpret available information and manage uncertainty. In one study, for example, 13% of people who were tested for HIV never received their results, even though in a separate study, those who initially avoided learning their HIV status showed an improvement in mood upon receiving their test results (regardless of their HIV status). Information avoidance may be used as a coping strategy by people who have difficulty tolerating potential but uncertain negative health consequences. A similar example is those who receive or fill prescriptions but do not take medications because of their fear of side effects.

### Emotional Outcomes of Communicating Uncertainty

Most of the literature about emotional responses to uncertainty pertains to uncertainty in a broad sense that includes, but is not limited to, the specific types of uncertainty outlined in this article. Lazarus and Folkman’s stress and coping theory posits that the cognitive appraisal of a stressor such as uncertainty occurs in 2 steps. First, a person interprets the meaning of a stressor and its relationship to his or her experiences and values. Next, a person assesses his or her resources and capacity for coping with a given stressor.

This theory maintains that patients who negatively appraise uncertainty might correspondingly experience subsequent fear, anxiety, panic, and a desire to reduce uncertainty. These negative emotional responses may lead to heightened vigilance about illness, which may further exacerbate worry about illness. However, uncertainty might not always have negative emotional effects; when confronted by uncertainty about an illness or treatment, some people are able to maintain hope and optimism. Optimism can encourage patients to accept treatments and maintain an active response to their illness if they perceive great potential benefits. However, false hopes about treatments can lead some patients to ignore real risks of other lifestyle behaviors. For instance, diabetic patients who believe that insulin alone can control blood sugar levels might not additionally alter their dietary habits.
In addition to influencing emotions during decision making, communicating uncertainty may influence patients’ emotional responses following a decision. Past research has shown that patients can experience 3 types of regret following treatment decisions: outcome regret, which is regret about a negative health outcome following a decision; option regret, which is regret about the choice one made; or process regret, which is regret about the quality of the decision-making process (e.g., it was too hasty). It is possible that communicating uncertainty can lead to increased satisfaction in the quality of the decision-making process, thereby reducing option or process regret following a decision. However, it is also possible that communicating uncertainty can cause patients to blame themselves in the case of bad outcomes, leading to more regret.

Although these findings relate to emotional responses to uncertainty in a very general sense, they may also be applicable to understanding the effects of particular types of uncertainty, such as ambiguity, as they additionally apply to the particular domain of health care decisions. These outcomes need to be examined further.

Individual Differences in Patient Responses to Uncertainty

Patients’ cognitive, emotional, and behavioral responses to uncertainty are themselves uncertain and may depend on several individual patient characteristics. For example, the patient’s desired role in his or her medical care may be important. Some hypothesize that patients who consider themselves knowledgeable and competent prefer to make their own health decisions under uncertainty, and those who consider physicians the absolute experts prefer to defer decisions to physicians. Others have suggested that “patients most want to introduce their own extra-medical values when medical factors alone do not seem to be decisive.” Deber and colleagues found that the type of decision-making task can affect patients’ desired role in the process; patients may desire involvement in tasks such as determining the acceptability of risks but may prefer their physicians to identify treatment options, risks and benefits of treatments, and probabilities of risks and benefits occurring. When faced with a mismatch in decision-making preference and physician behavior, some patients might distrust their physician or become less satisfied with their care.

Patients’ values and preferences for medical care may also affect how they perceive and respond to uncertainty about health-related risks. For example, those who are averse to medications might perceive uncertainty about medication risks more negatively than those who are comfortable with prescription medications. As a result, they might decide not to take the medication because of risk uncertainty.

Individual personality traits may affect patients’ responses to uncertainty. For example, social psychologists have identified 2 personality types that may influence information-seeking behavior under uncertainty: uncertainty-oriented individuals, who tend to process uncertainty and seek out relevant information to allow for resolution of it, and certainty-oriented individuals, who tend to gravitate toward familiar situations that are less ambiguous and who tend to rely on respected others to make decisions. Similarly, cognitive processing styles such as monitoring (vigilantly seeking and attending to information) or blunting (distracting oneself from information, blunting its impact) can affect the manner in which patients perceive risks and uncertainties surrounding their health condition.

Finally, uncertainty may affect physicians as well as patients, inducing anxiety and excessive concern about bad outcomes. Physicians and medical trainees tend to fear that patients will perceive them as inadequate or ineffective, which may influence their willingness to disclose uncertainty to patients as well as their use of health care resources.

Patients’ responses to uncertainty may also be influenced by physicians’ reactions to it. Physicians are often concerned that acknowledging uncertainty to patients may undermine patient trust and satisfaction. However, some research has shown that patient satisfaction is affected by the manner in which the physician handles uncertainty, not whether or not he or she presents uncertainty, consistent with previous theories. When physicians are comfortable with uncertainty and collaborate with their patients in their medical care, patient trust and satisfaction are actually high.

HELPING PATIENTS COPE WITH UNCERTAINTY

Because of patients’ complex cognitive, emotional, and behavioral responses to uncertainty, many argue that the focus of risk communication should be on helping patients tolerate and cope with uncertainty rather than simply helping them understand it. Uncertainty can be stressful and anxiety provoking...
for patients throughout the illness experience. Some have suggested practical ways for physicians to help their patients cope with uncertainty: assure patients that they will answer all questions about their health, refer patients to other sources such as reputable Web sites, remain open and sympathetic to patients, inform patients of physicians' own biases and values, and inform patients of alternative treatments. Others propose that physicians should clarify the type of uncertainty that is the most distressing to patients (e.g., uncertainty about probabilities, uncertainty about sources of information, uncertainty about evidence) and be available to explain the complexities of each. Although these tasks make sense and are ethically justifiable, it remains unclear whether they are truly beneficial and feasible for physicians to perform.

RECOMMENDATIONS BY EXPERT GROUPS

Some organizations have made explicit recommendations concerning the need for and possible approaches to communicating uncertainty. The International Patient Decision Aids Standards collaboration recommends communicating uncertainty and providing concrete examples to help explain it:

It’s very important to acknowledge uncertainty in probability estimates. Often the uncertainty is large, especially if evidence is scarce or events are rare. It’s probably wise to do simple things such as rounding off numbers (to avoid false illusions of precision), using phrases like “our best guess is . . .,” give ranges, or provide 95% confidence intervals.

Even with the best evidence from large studies, the issue of stochastic uncertainty remains. Essentially, we never quite know who are the patients who are going to be affected, and who the treatment is going to be most useful for. One way to deal with this uncertainty might be to say: “If 100 patients like you are given no treatment for five years, 92 will live and eight will die. Whether you are one of the 92 or one of the eight, I do not know. Then, if 100 patients like you take a certain drug every day for five years, 95 will live and five will die. Again, I do not know whether you are one of the 95 or one of the five . . . .”

Despite these limitations from uncertainty, practitioners generally feel that we can still try to make decisions about what the best treatment plan is for an individual person, based on what happens to these groups of patients in the studies. Hence the value, it is thought, of presenting the information about benefits and harms to aid the decision making process. Both sources of uncertainty should be acknowledged in comprehensive discussions of risks in patient decision aids.

In addition, there have been numerous articles in the medical literature advocating that physicians discuss uncertainty. One states,

While often difficult, a discussion of uncertainties is crucial for a patient’s comprehensive understanding of the options. Thoughtful discussion can promote trust and encourage adherence. Examples: “The chance that this will help is excellent.” “Most patients with this condition respond well to this medication, but not all.”

On the other hand, some argue that the dispersion around a point estimate is irrelevant when a choice needs to be made between 2 uncertain options and that the decision in such cases should be based on which option has the highest expected net benefit. The costs of failing to adopt a new treatment simply because the difference in net benefit is not statistically significant can be substantial. This approach does not imply that treatment decisions should be based on poor-quality evidence but rather that the amount of information that should be acquired is an empirical rather than ideological question, differing across different clinical decisions.

CONCLUSIONS: CRITICAL KNOWLEDGE GAPS AND FUTURE RESEARCH NEEDS

Although the ideal of informed or shared decision making implies a need for communicating uncertainty to patients, this task is problematic for many reasons. From a conceptual standpoint, it is unclear which of the many types and sources of uncertainty clinicians should communicate to their patients. Exactly what is meant by the term uncertainty and the ethical justification for communicating different types of uncertainty are themselves uncertain. More work is needed to define the circumstances in which uncertainty ought to be communicated. Should this be a function of the magnitude of uncertainty surrounding these options and/or the magnitude of the consequences of these choices? Should it depend on the number of choices available, the novelty of the treatments being considered, or whether there is a clear dominant option? What aspects of uncertainty should be communicated, given the task? Are there patient characteristics that may influence when we should or should not
include uncertainty in risk communication or how the subject should be approached?

Many of these questions are conceptual and ethical in nature, rather than empirical, and raise the larger question of whether there is any level of acceptable uncertainty. Deciding between various treatment options is inherently situation specific, and there is no universally acceptable absolute level of acceptable risk; one’s acceptance of risk is contingent on many factors.\textsuperscript{106,107} Acceptable risk refers to the risk associated with the most acceptable option in a particular decision.\textsuperscript{107} Is there an analogous concept of acceptable uncertainty? If so, how might different ways of judging thresholds of acceptable uncertainty be defined, and from whose perspective?

From an empirical standpoint, we know little about how to measure and quantify uncertainty and the various factors contributing to it. What types of uncertainty do commonly used measures of uncertainty (such as confidence intervals) actually capture? Can measures of specific contributors to uncertainty be combined to estimate the total or composite uncertainty in a finding? Exploration of the use of different characterizations of risk and uncertainty (i.e., uncertainty about the time to event, a continuous variable, rather than the likelihood of the event, a dichotomous variable at the individual level) may help move the field forward given the irreducible uncertainty surrounding individual predictions when using the likelihood of an event as the outcome measure. Research is needed to develop these measures of component and composite uncertainty and to validate them; they then need to be disseminated to decision makers and researchers.

A further empirical problem is that the optimal methods and outcomes of communicating different types of uncertainty are not known. There is suggestive, but not definitive, evidence about how various types of uncertainty are differentially interpreted by patients, clinicians, and researchers and how these interpretations affect clinical decision making as well as other patient-centered outcomes such as perceptions and well-being. The manner in which uncertainty is communicated can affect how it is perceived and responded to, but little is known about the mechanisms of these framing effects. It is unclear whether uncertainty is best presented verbally, numerically, graphically, or using multiple formats. Studies exploring how perceptions of and responses to uncertainty are potentially affected by its framing (i.e., certainty v. uncertainty, gain v. loss), choice of specific terms, measurement units and scale, and graphics would help to clarify this critical issue.

More research is needed on potential tradeoffs in communicating uncertainty. Tailoring information to the individual’s risks has the advantages of making information more relevant and reducing the volume of information, but the more tailored the information, the greater the uncertainty associated with risk prediction. Thus, there may be an inherent tradeoff between the degree of personalization of risk information and its uncertainty. There may also be a tradeoff between the completeness of information given and the efficacy of this information in terms of how it is processed and responded to. In addition, there may be a tradeoff between the precision of a risk estimate and its accuracy. Further exploration of these potential tradeoffs could help inform discussion of when and how to communicate uncertainty.

The increasing focus on personalized medicine\textsuperscript{108} mandates a more sophisticated understanding of the limitations and errors in applying and communicating population-based, epidemiologic findings to the individual. Because of the poor positive predictive value of most of the risk factors (including genetic markers) for common noninfectious diseases, most people who will eventually get a disease will not be designated as high risk by population-based risk prediction tools.\textsuperscript{14,109} Furthermore, how patients respond to personalized risk estimates is poorly understood. Fischoff writes, “Asking people about the risks to others like themselves is not the same as asking them about their personal risk. Nor need reports about others’ risk levels be taken personally.”\textsuperscript{109} Exactly how to use risk estimates and risk prediction tools to improve and inform individual treatment decisions, while acknowledging and communicating their limited power to predict individual futures, is a critical challenge that will become even more important as new disease biomarkers are discovered.

More work is also needed to differentiate the construct of uncertainty from risk in various conceptual models and theories of health behavior. Divergent conceptual models exist for understanding how people perceive and respond to uncertainty; further exploration of new models and attempts to reconcile differences across models could help advance these fields of inquiry.

RECOMMENDATIONS

At this time, there are no clear best practices for presenting uncertainty. The best method of presenting uncertainty depends on the task required of the
More conceptual, qualitative, and quantitative studies are needed to explore fundamental questions about how people process, interpret, and respond to various types of uncertainty inherent in clinical decisions. Much more research is also needed to broaden the scope of inquiry beyond the problems of communicating statistical uncertainty around a point estimate to the many other types of uncertainty relevant to the numerous decisions that patients and clinicians face.

REFERENCES
