Primer: demystifying risk—understanding and communicating medical risks

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SUMMARY

Assessments of risk are a critical part of the practice of evidence-based medicine. Comprehension of various risk measures, such as absolute risk, relative risk, attributable risk, odds ratio, and hazard ratio, is essential to understand the medical literature, and to communicate health risks effectively. Complex risk measures, including number needed to treat and survival estimates that are adjusted for competing risks, are often misunderstood. Communication of these concepts to patients can be a challenge. The patient's perception of risk stems not only from the way risks are stated, but also from family history, personal experiences, cultural norms, and beliefs. A multifaceted approach to risk communication that uses both qualitative and quantitative assessments of risk, and addresses the timing and permanence of risks, is necessary to ensure the patient understands the potential risks. Successful communication involves interaction with the patient to understand the patient's perspective and to aid in personalized decision-making. In the face of uncertainty, making a provisional decision with a plan to review it later can be a good strategy. Verifying the patient's comprehension can help ensure that the decisions reached are informed and acceptable.

KEYWORDS absolute risk, competing risk, hazard ratio, relative risk, risk communication

REVIEW CRITERIA

Statistical articles cited in this Review are from the authors' collections. A search of PubMed was performed to elicit information on risk communication. Search terms included "risk communication", "risk", and "evidence-based medicine". Relevant references from retrieved articles were also examined.

CME

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INTRODUCTION

Even though risk information is abundant in medical and nonmedical settings (e.g. the chance of precipitation in the daily weather forecast) most people do not understand commonly used concepts of risk. Medical risk information contributes to the understanding, prevention and treatment of disease.[1] Comprehension of this information is critical for the physician and the patient, because decisions based on risk estimates can have long-lasting consequences. Among other things, the ability to appreciate risk might inspire patients to comply with treatment and to modify high-risk lifestyle choices. Clinicians must, therefore, not only understand risk, but also be able to communicate potential risks and benefits to their patients effectively. The goal of this article is to help physicians understand risk measures and the issues surrounding risk communication.

UNDERSTANDING RISK

Risk is reported in many different ways in the medical literature. Risk measures can pertain to the development of an outcome at a specific time point (fixed-time measures), or to the rate of development of an outcome over a period of time (rate-based measures). In addition, many complex risk measures have been derived from other risk measures.

Fixed-time measures

The most well-known measures of risk are coupled with 2×2 tables that tabulate the presence or absence of a risk factor (such as methotrexate initiation) against a yes or no outcome at a fixed time point (such as infection at 2 years after methotrexate initiation), as shown in Table 1. Other fixed-time measures include absolute risk, risk difference, relative risk (RR) and odds ratio (OR) (Table 2).

Table 1 Hypothetical study data for methotrexate initiation as a risk factor, and an outcome of infection at 2 years after initiation of methotrexate.

Risk factor	Number of patients with outcome		Total
	Infection	No infection	
Methotrexate	130 (A)	370 (B)	500 (A+B)
No methotrexate	90 (C)	410 (D)	500 (C+D)
Total	220 (A+C)	780 (B+D)	1,000

A is the number of individuals with the risk factor who experience the outcome. B is the number of individuals with the risk factor who do not experience the outcome. C is the number of patients without the risk factor who do experience the outcome. D is the number of patients with neither the risk factor nor the outcome.

Table 2 Summary of fixed-time risk measures.

Risk measure	Other names	Definition	Interpretation	Results[a]
Absolute risk	Prevalence of outcome	$\frac{A}{A+B}$	The percentage of patients with the risk factor who experienced the outcome	26%
Risk difference	Absolute risk reduction	$\frac{A}{A+B} - \frac{C}{C+D}$	Patients with the risk factor have this additional percentage risk of the outcome, compared to patients without the risk factor	8%
Relative risk	Risk ratio	$\frac{A/(A+B)}{C/(C+D)}$	Patients with the risk factor have this multiple of the risk of the outcome, compared to patients without the risk factor (relative risk can be misleading unless given in context with absolute risk)	1.44
Odds ratio	None	$\frac{A/B}{C/D} = \frac{AD}{BC}$	Patients with the risk factor have this multiple of the odds of having the outcome, compared to patients without the risk factor (odds ratio is equivalent to relative risk only if the outcome is rare)	1.60

Letters (A,B,C,D) have the same meanings as in Table 1 (A is the number of individuals with both the risk factor and the outcome; B is the number of individuals with the risk factor who do not experience the outcome; C is the number of patients without the risk factor who experience the outcome; D is the number of patients with neither the risk factor nor the outcome). [a]These results are calculated using data from the example in Table 1.

The absolute risk is the probability of a patient (or patients) experiencing the outcome, which is estimated as a simple percentage. The absolute risk can be estimated for a population or for particular groups, such as those with and without a risk factor. For the methotrexate users in Table 1, the absolute risk is $A \div (A+B)$, or $130 \div 500 = 26\%$, compared to $C \div (C+D)$, or $90 \div 500 = 18\%$ for those without methotrexate exposure. The risk difference (or absolute risk reduction) is $26\% - 18\% = 8\%$. Methotrexate users are estimated to have a 26% chance of infection within 2 years, which represents an additional 8% risk over that of patients without methotrexate exposure.

The RR is also termed the risk ratio; RR is the ratio of the absolute risks for those with the risk factor compared to those without the risk factor. Since RR is a ratio, $RR = 1$ means the risk is equivalent in the two groups; $RR > 1$ indicates a higher risk, and $RR < 1$ indicates a lower risk, for those with the risk factor compared to those without the risk factor. In the example in Table 1, the RR is $[A \div (A+B)] \div [C \div (C+D)]$, or $0.26 \div 0.18 = 1.44$. Methotrexate users, therefore, have 1.44 times the risk (or a 44% higher chance) of experiencing infection, compared to patients without methotrexate exposure. For rare events, a large RR can sometimes be unduly alarming. For instance, the RR of death from lightning strike is threefold higher for residents of Kentucky than for Nevada residents, but the total fatalities for both states combined averages only one per year.[2] RR can be misleading on its own, and some knowledge of the absolute risk is needed in order to interpret an RR properly.

The odds of an outcome is the ratio of the probability that it will occur, to the probability that it will not. Returning to the example in Table 1, the odds of infection among methotrexate users

is 0.26 ÷ 0.74 = 0.35. ORs are used to compare the odds between two groups. The OR of infection for methotrexate users compared to non-users is estimated as (A ÷ B) ÷ (C÷D), or 0.35 ÷ 0.22 = 1.60. Methotrexate users, therefore, have 60% higher odds of experiencing infection than patients without methotrexate exposure.

The OR is commonly reported because it can be estimated using data obtained from several different study designs: these include subsets of an entire population; sample sizes that are balanced in relation to the assigned treatment (such as in Table 1, which includes 500 methotrexate users and 500 nonusers); or subgroups of patients who experienced specific outcomes (e.g. 500 patients with and 500 without infection). In contrast, the absolute risk, risk difference and RR cannot be properly estimated from a study in which samples are chosen on the basis of the outcome, such as a case–control study. In addition, logistic regression models, which are commonly used to analyze yes or no outcomes, naturally produce an OR.

Rate-based measures

The above measures implicitly assume that all patients are followed for a fixed time frame (e.g. RR of infection at 2 years). When patients have widely disparate amounts of follow-up, rate-based measures can be used.

One such measure, the risk rate, is estimated as the total number of patients who reach the outcome, divided by the total observation time. The total observation time, measured in person-years, is the sum of the observation times for all individuals in the study. For instance, a study with three patients who were observed for 12.3, 1.0 and 4.1 years, respectively, would have a total observation time of 17.4 person-years. In the example from Table 1, if the 500 methotrexate users were observed for 1,000 person-years (an average of 2 years per patient, rather than exactly 2 years each), the risk rate is 130 events ÷ 1,000 person-years, or 13% per year. If patients without methotrexate exposure also had 1,000 person-years of observation, then the rate ratio would match the RR, since (130 ÷ 1,000) ÷ (90÷1,000) = 1.44. Alternatively, if patients without methotrexate exposure had 1,050 person-years of observation, the rate ratio—more commonly called the hazard ratio (HR) or the standardized mortality ratio for the outcome of death—would be 1.52.

The HR estimate above can be biased if baseline rates change over time, such as complication rates after surgery. A common approach that adjusts for this variation is to estimate the HR with a Cox proportional hazards model. An HR = 2 means that, on a given day, an individual with the risk factor is twice as likely to experience the outcome in question compared to an individual without the risk factor, independent of the absolute underlying rate at which the outcome occurs. Over a long period of time, the chance that a patient with the risk factor will experience the outcome before a patient without the risk factor is HR ÷ (HR + 1), which is 67% for HR = 2. The HR, however, does not provide information about how rapidly an end point is reached, nor how many patients will actually reach it.[3]

Although RR, HR, and OR are used interchangeably, they are not quite equivalent. For rare outcomes, the discrepancy between these three measures is small. The OR always overestimates the RR (because the RR < HR < OR when the RR > 1). This exaggeration of the RR is only sizable for risk factors with large effects, so this bias does not change the qualitative conclusion.[4,5]

Complex risk measures

Several risk measures stem from those described above: these include the number needed to treat (NNT), relative risk reduction (RRR), attributable risk, and cumulative incidence. The NNT estimates the number of patients who must be treated to prevent a particular outcome in one patient. NNT is computed as the reciprocal of the risk difference. If the risk factor causes (rather than prevents) an outcome, this same measure is called the number needed to harm. In the example in Table 1, the risk difference is 0.08, so the number needed to harm is 1 ÷ 0.08 = 12.5. On average, one additional infection will occur within 2 years for every 12.5 patients treated with methotrexate.

The RRR is the risk difference divided by the absolute risk in those exposed to the risk factor. In the example, RRR = (0.26 – 0.18) ÷ 0.26 = 31%, so elimination of methotrexate use would reduce the number of infections in these patients by 31%. The RRR is also referred to as the attributable risk, or the etiologic fraction.

Population attributable risk (PAR) refers to the proportion of an outcome in the population that could be prevented by the elimination of a causal risk factor.[6] Estimation of the PAR in the example would require estimates of the prevalence of methotrexate use in the population and the RR of infection with methotrexate use. The PAR helps to determine which risk factors have

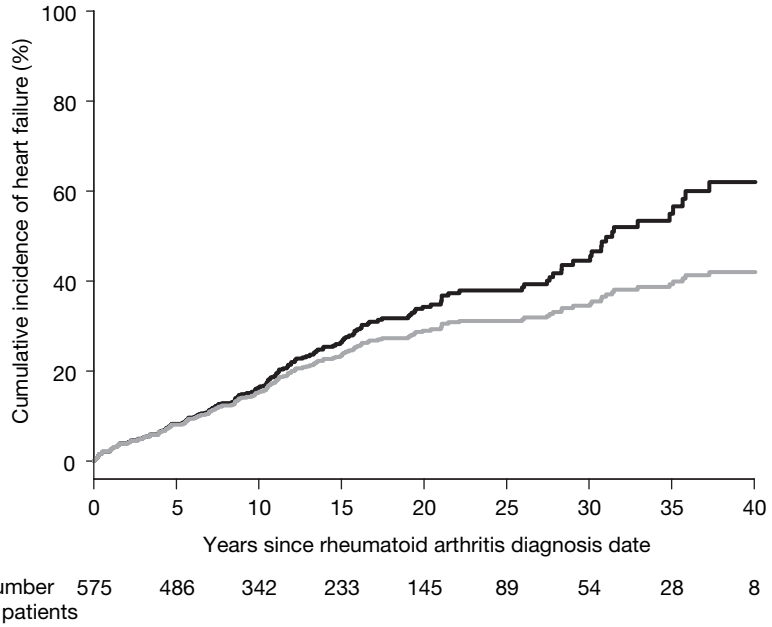

Figure 1 The cumulative incidence of heart failure in 575 patients with time after a diagnosis of rheumatoid arthritis. The upper curve is estimated using Kaplan–Meier methods (black line), and the lower curve represents the cumulative incidence adjusted for the competing risk of death (gray line).

the greatest impact on the health of a community, but this measure has little meaning in the context of an individual's health.

For long-term studies, the relationship between a risk factor and an outcome could be presented in a series of tables like Table 1, each of which represents a different time point. This notion is the basis for survival analysis, a technique that is applicable to a wide variety of yes or no outcomes, not just death. In addition, survival analysis makes optimal use of incomplete information; for example, a patient followed for 3 years without experiencing the outcome can be included in an estimation of the probability of experiencing the outcome at 4 years. Such individuals, those who are 'lost to follow-up' or 'censored', can contribute to risk estimates for the time that they are observed, but are excluded from the analysis at the time when the relevant information is no longer available.

Survival risk is often estimated using the Kaplan–Meier method.[7] The Kaplan–Meier curve starts at a value of 1 and decreases, which estimates the fraction of patients who have not yet had the outcome. Sometimes it is preferable to plot the complement of this curve, which estimates the fraction of patients who have experienced the outcome.[8]

When multiple outcomes are possible, it is important to distinguish between the Kaplan–Meier estimate and the cumulative incidence of an outcome adjusted for competing risks. For instance, the Kaplan–Meier estimate of heart failure in patients with rheumatoid arthritis (RA) at 40 years of follow-up is 0.62 (Figure 1). This estimate means that 62% of patients with RA will develop heart failure by 40 years after diagnosis, but assumes that no other outcome (e.g. death) will precede, and thus preclude, heart failure. Since the average age of patients with RA at diagnosis is 58 years, many patients will experience other outcomes before heart failure can occur, and this 62% heart failure rate will not actually be observed. The Kaplan–Meier estimate is of interest from a biological point of view. It estimates the heart failure rate that would be observed if all other competing outcomes were removed and, therefore, addresses the evolution of that single process.

The cumulative incidence adjusted for competing risks estimates the fraction of patients in whom heart failure will actually be observed, which may be more relevant from a clinical and/or patient perspective.[9] The adjusted cumulative incidence of heart failure is 42% at 40 years, which is much lower than the Kaplan–Meier estimate (Figure 1).[10] Adjusted cumulative incidence estimates are becoming more prevalent in the literature, often under the label of 'lifetime risk', and are particularly important in elderly patients or those at increased risk for comorbidities.

COMMUNICATION OF RISKS

Decision-making for an individual patient is a complex task that combines knowledge of risk with uncertainty and risk perception.[11] For the clinician, effective communication involves relating and explaining relevant risk information to the patient, individualizing the message, seeking the patient's perspectives, and confirming that they understand what has been explained (Box 1).

Relate relevant evidence

Evaluation of relevant literature can be time-consuming: literature can be scarce for some diseases, or it might be abundant but present conflicting results.[12] Before consultation with a patient, the clinician should critically examine the evidence by comparing results across studies, assessing each study's strengths and

weaknesses, and identifying misleading claims.[13] For instance, clinical trials in RA often report radiographic outcomes in terms of the mean response, which summarizes the response of the group, but not that of an individual.[14] A mean response can be misleading, because a seemingly meaningful value could result from a few patients with spectacular responses and numerous patients with no response.

Uncertainty stems from a lack of relevant or clear evidence, as well as from the translation of risk assessments derived from populations or groups into risk assessments for individuals. Physicians should acknowledge the variability inherent in all measures of risk (i.e. those described above, plus others such as median survival).[15,16] These measures summarize average risks and, therefore, cannot definitively determine the prognosis for a particular patient. Understanding the strengths and limitations of risk measures can help physicians provide their patients with accurate information.[17] Physicians could also relate their own opinions of risk, which should be stated as such, because expert opinion is a valuable decision aid. Provisional decision-making, based on current information and perceptions with a planned review of the decision at a later date, is a reasonable approach in the face of uncertainty because it allows for inclusion of newly available information.

The physician must also decide which risks are relevant, and must balance how much the patient needs to know with how much the patient wants to know. Consideration of what information medical peers would generally disclose, or what a reasonable person would want to know could help, but both these paradigms are imprecise.[11] The physician should discuss health risks with a patient on the basis not only of the patient's concerns, but also on the relevance and importance of these risks in the context of the patient's health status, even if the patient might be less informed or less concerned about certain risks.

Box 1 summary of RISK communication.

- R—Relate relevant evidence
- I—Individualize the message, using a flexible approach
- S—Seek the patient's perspectives and share the decision-making
- K—Check the patient's understanding, monitor, and review decisions

Individualize the message

Effective communication of risk is complex, because none of the various quantitative risk measures (e.g. absolute risk or RR) is generally understood by patients. Studies report that patients prefer statements that involve RRR, but this measure can be misleading if not discussed in the context of absolute risks.[18,19] Some experts believe NNT is the best risk measure, despite evidence that it is difficult to understand.[20] Furthermore, qualitative statements about risk (e.g. 'rare' or 'low-risk') are vague and may elicit false reassurance. Graphical displays of risk, such as bar or pie graphs and partitioned depictions of 100 people, can improve patient comprehension.[21] In addition, comparison of medical risks to common nonmedical risks (e.g. the risk of an automobile accident) can aid interpretation.[22] A list of the risk of various accidental deaths is available from the National Safety Council.[23]

Risk framing—that is, whether a risk is described as 'affecting 1 in 100 people' or as 'not affecting 99% of people'—can also mislead patients. The latter phrase is overwhelmingly preferred by patients, even though both statements attempt to convey the same information.[24] This problem can be avoided if both phrases are used simultaneously to describe risk (e.g. 'among 100 people, 1 will be affected and 99 will not').

Other aspects of risk, such as timing, permanence and severity, must also be addressed. Even a high risk for a severe outcome might be acceptable if the outcome has a short duration (e.g. temporary disability following surgery). In addition, it can be difficult for patients to accept present risk for future gain. For instance, the costs and risks associated with early aggressive treatment of RA must be explained in the context of prevention of long-term disability and morbidity. In contrast, balancing present gains against future risk, or quality of life against quantity of life, is a complex issue for patients. For example, glucocorticoid treatment might improve short-term outcomes for patients with RA, but could result in serious complications later. Physicians should engage in a thorough discussion of risk, which addresses the timing, permanence and severity of risk, and uses a variety of risk measures, to ensure that patients understand the potential risks.

Seek the patient's perspective

The patient's perception of risk stems not only from the way that risks are stated, but also from family history, personal experiences, cultural norms, and beliefs. Patients tend to underestimate large risks and overestimate small risks, especially if these risks receive significant media coverage. A phrase meant to reassure a patient, such as a statement that the risk of a serious outcome is only 1 in 100, might instead cause the patient to worry about being that one person. The patient's risk perception might be affected by the words used to describe the risks, as well as the physician's tone of voice and body language.[11]

Misunderstanding of risk can result from low literacy and age, as well as cultural and language barriers. At least a sixth-grade reading level is needed to comprehend RRR and other risk measures.[25] Older patients (i.e. those aged >75 years) might also have difficulty comprehending numeric expressions of risks, such as percentages.[26]

In addition, many factors can influence patient decision-making: these include the costs and availability of alternative treatments, transportation needs, the cultural meanings attached to care processes, and the implications for family relationships. Understanding these issues is an important aspect of communication between patients and physicians.

Verify the patient's understanding

Following any communication of risk, the patient's understanding of the stated risks and the planned course of action should be verified,[27] because health-related decision-making can be agonizing and decisions can have long-lasting consequences. Decision aids are being developed to assist patients to make difficult health decisions, but their implementation is problematic.[28] Once a decision is reached, a plan to monitor the patient for potential risks and adverse events that result from the decision must be devised, which should include periodic re-examination of possible alternatives.

CONCLUSIONS

Risk is described using a variety of risk measures, each of which has a different use and interpretation. Complex risk measures are often misunderstood. A clear understanding of risk concepts is necessary for clinicians to evaluate the evidence and to facilitate their discussions of risk with the patient.

Effective risk communication requires a flexible approach that utilizes a variety of communication strategies. Ensuring that patients understand risk might be time-consuming, but such discussions should not be rushed. Failure to discuss a patient's perception of risk might result in unsatisfactory decisions being made.

In this age of personalized medicine, patients are better informed than ever before. Patients have preferences about the amount and type of risk information they want, and how much they wish to participate in the decision-making process. Knowledge of the patient's preferences in this regard is needed in order to tailor the message to the patient. Increasingly, patients seek information on risk outside the context of the office visit, through media such as medical publications and the internet, which physicians must be able to interpret and place into context for the individual patient. Monitoring the patient's progress and reviewing medical decisions when circumstances change is essential to good patient care.

KEY POINTS

- The absolute risk, risk difference, relative risk and odds ratio are risk measures that pertain to the development of an outcome at a specific time point (fixed-time measures)
- The risk ratio and hazard ratio are risk measures that pertain to the rate of development of an outcome over a period of time (rate-based measures)
- Many complex risk measures, such as the number needed to treat, relative risk reduction, and survival estimates adjusted for competing risks, are derived from other risk measures
- The patient's perception of risk stems from many sources, such as family history, personal experiences, cultural norms, and beliefs
- Physicians should engage in a thorough discussion, which addresses the timing, permanence and severity of risks, and uses a variety of risk measures, to ensure that patients understand the potential risks
- Making a provisional decision based on current information and perceptions with a planned review at a later date is a reasonable approach in the face of uncertainty, because it allows for inclusion of new information

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Competing interests
The authors declared that they have no competing interests.