Risk Communication in Rheumatoid Arthritis

LIANA FRAENKEL, SIDNEY BOGARDUS, JOHN CONCATO, and DAVID FELSON

ABSTRACT. ***Objective.*** Some people believe that certain issues should be protected from all trade-offs. These issues are referred to as "protected values." We investigated whether some patients with rheumatoid arthritis (RA) treat the risk of adverse effects (AE) as "protected values," i.e., as unacceptable regardless of how small the risk.

Methods. Patients with RA rated willingness to risk 17 different AE on a visual analog scale, where 0 = not willing under any circumstances and 100 = definitely willing. Participants then rated willingness to take medication as the risk of each AE was progressively decreased by 2 levels from its actual risk, using a 5 level scale ranging from 10 in 100 to 1 in 100,000.

Results. Between 32% and 39% of participants were not more willing to accept a risk of AE causing reversible cosmetic changes (e.g., acne), between 35% and 47% were not more willing to accept a risk of AE causing reversible discomfort (e.g., rash), and between 41% and 45% were not more willing to accept a risk of AE causing potential irreversible damage (e.g., pneumonitis) as the probability of each of these AE was substantially decreased. Unwillingness to accept risk of toxicity was especially evident for cancer, where 66% of patients refused to accept a risk of cancer occurring in 1 in 100,000 persons.

Conclusion. Among patients particularly concerned with the risk of drug toxicity, many remain unwilling to accept the risk of AE even when their probability is decreased to levels far below their actual risk. These results suggest that patients may treat particularly worrisome AE as protected values, which may lead to poor decision-making in clinical practice. (J Rheumatol 2003;30:443–8)

Key Indexing Terms:
RISK COMMUNICATION NUMERACY DRUG TOXICITY RHEUMATOID ARTHRITIS

Effectively communicating the risk and benefits of available treatment alternatives is an essential component of medical care. This is particularly true regarding the treatment of rheumatoid arthritis (RA), where there are now multiple treatment options available, each with distinct risk profiles.

Effective communication of risk is difficult, however, in part because of limitations associated with both the provision and interpretation of probabilistic information[1-8]. At the most basic level, there is little agreement on how to present risk information in clinical practice, with some investigators arguing for the use of verbal phrases such as "rare" or "frequent" and others advocating the use of quantitative estimates (e.g., proportions or percentages). Use of words is limited by the wide range of values that patients and physicians assign to verbal expressions of probability[2,6,9-11], whereas the use of numbers is limited by the difficulties many patients have understanding and applying quantitative information[1,7].

In a previous study we found that patients were unwilling to accept many of the adverse effects (AE) commonly associated with medications used to treat arthritis. Based on these results we hypothesized that some patients may treat specific AE as "protected values"[12]. People with protected values believe that certain objects should be protected from any and all trade-offs with other values no matter how small the risk. For example, people with protected values for forest conservation believe that forests should be protected from loggers no matter how small the threat to the forest. Studies have shown that protected values often result from incorrect assumptions and may therefore lead to poor decision-making.

To test our hypothesis, we examined whether using several strategies to facilitate risk-communication, patients alter their willingness to take medications as the risk of toxicity is substantially decreased, and whether increased willingness to accept the risk of toxicity varies depending on the specific AE.

MATERIALS AND METHODS

Patients. Consecutive patients with RA belonging to a community rheumatology practice serving New Haven, Connnecticut, and surrounding areas were asked to participate in a study examining the importance patients attach

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to specific side effects. Interviews were scheduled in patients' homes or their doctor's office according to patients' choice. All interviews took place at least 2 weeks after seeing a rheumatologist, orthopedist, or primary care doctor. Patients were recruited and interviewed by a trained research assistant.

Data collection. Participants were told that the objective of the study was to examine the importance that patients with arthritis assign to different side effects. Participants were presented with descriptions of 17 AE commonly associated with nonsteroidal antiinflammatory agents (NSAID), low dose (≤ 10 mg/day) prednisone, and disease modifying agents (DMARD) of comparable efficacy. AE were chosen based on those reported in clinical trials and longterm followup studies[13-16]. We excluded laboratory abnormalities because Fries, *et al*[17] found that patients had difficulty judging the importance of abnormal blood tests. AE were presented in random order, without reference to specific medications, in order to minimize bias due to personal knowledge or experience with medications.

Using lay terminology adapted from patient information sheets published by the Arthritis Foundation, each AE was described in terms of severity and reversibility of symptoms, likelihood of occurrence, and sequelae[18]. In view of the literature documenting significant variability in patients' ability to interpret probabilities and patient preferences for the presentation of probabilistic information[4], we used both verbal phrases (e.g., "high," "low," or "very low," chance) and proportions (e.g., "10 in 100," "1 in 100," or "1 in 1000") to describe the likelihood of AE[19]. The likelihood of each AE was chosen based on those reported in the textbook *Rheumatology*[20-22]. For each AE we chose the lowest estimate of risk reported in the literature. In addition, we provided participants with familiar examples to facilitate understanding of less common events[1,23]:

The risk of a side effect happening in:		Is the same as the risk of:
1 person in 100 (one in a hundred)	→	Being audited by the IRS over the next year
1 person in 1000 (one in a thousand)	→	A frequent motorcycle rider being killed in an accident in the next year
1 person in 10,000 (one in ten thousand)	→	Dying in a car accident in the next year if you drive 100 miles per week
1 person in 100,000 (one in a hundred thousand)	→	Dying in a car accident in the next year if you drive 10 miles per week

Participants rated willingness to take a medication associated with the actual risk of each AE, using a visual analog scale (VAS), where 0 = "not willing under any circumstances" and 100 = "definitely willing." This score is referred to here as the baseline score. Participants with baseline scores < 100 on the VAS were then asked to rate their willingness to take medication, using the same VAS, as the risk of each AE was progressively decreased by 2 levels from its actual risk (Appendix).

Levels of risk were based on a previously published 5 level scale: "high" (10 in 100), "low" (1 in 100), "very low" (1 in 1000), "extremely low" (1 in 10,000), "almost no risk" (1 in 100,000)[19]. Patients were considered more willing to take medication in response to a decreased risk of toxicity if their baseline VAS scores increased by any amount as the probability of each AE was lowered by 2 levels.

Participants were asked to assume the same medication benefit while rating each AE. Medication benefit was described in terms of symptom relief and improvement in physical and emotional function. Patients were also asked to assume the medication was given as a pill taken once daily, and that while taking the medication they needed to have blood tests once every 2 months.

We collected sociodemographic data, information regarding medication use, personal experience with AE, and self-rated arthritis related health status[24]. Preference for disclosure of information regarding potential drug toxicity was determined as previously described[25] using 4 questions from a validated questionnaire[26]: "Even if the news is bad I should be well informed," "It is important for me to know all the side effects of my medications," "When there is more than one way to treat a problem, I should be told about each one," and "I should be given information only when I ask for it."

All data were collected during face-to-face interviews administered by a trained research assistant. The research assistant read aloud the descriptions of AE, familiar examples, and rating exercises.

Analysis. We first report the percentage of patients with a baseline VAS score < 100 for each AE, and of these, the percentage of patients more willing to take medication as the risk of each AE was decreased by 2 levels. Analyses were restricted to patients with a VAS score < 100 for each AE in order to eliminate misclassification of subjects due to ceiling effects of the scale.

We created a summary toxicity variable to examine the association of patient characteristics and increased willingness to take medication in response to lowering the risk of AE. Patients whose ratings on the VAS (where 0 = "not willing under any circumstances" and 100 = "definitely willing") did not increase after the risk was decreased by 2 levels for any of the AE were classified as unwilling to respond to a decreasing risk of toxicity. Associations between patient demographic and clinical characteristics with willingness to respond to a decreasing risk of AE were ascertained using t test and chi-square statistics for continuous and categorical variables, respectively. All analyses were performed using SAS software, version 6.12 (SAS Institute, Cary, NC, USA).

Table 1. Patient characteristics.

Variable	(Total = 100)
Age, mean ± SD yrs	68 ± 12
Women	73
Race	
Caucasian	84
African-American	7
Other	9
Arthritis related health status	
Very well	30
Well	45
Fair	21
Poor	4
Very poor	0
Marital status	
Single	12
Married	58
Widowed	26
Separated/divorced	4
Level of education	
Some high school	13
High school graduate	30
Some college	29
College graduate	28
Employment status	
Employed	18
Retired	64
Disabled/unemployed	18
Current medication use	
DMARD	81
Low dose prednisone	68
NSAID	39

RESULTS

One hundred of 170 patients (59%) who were approached agreed to participate. The most common reasons for refusal were "too busy" or "not interested." Nonparticipants were

younger (66 ± 14 vs 68 ± 12 yrs, mean ± SD), and a greater proportion were female (81% vs 73%), married (96% vs 58%), and currently employed (54% vs 18%) compared to participants. Current DMARD use did not differ between participants and nonparticipants.

Patient characteristics are described in Table 1. Eighty-one were currently using one or more DMARD and 29 had previously experienced AE related to DMARD. Seventy-five stated that they were doing very well or well with respect to their arthritis compared to other people their age. The score for preference for information disclosure was 86 ± 13 mean ± SD (median 88, range 44–100), reflecting a strong preference for full disclosure of risks and information regarding treatment alternatives.

Effect of decreasing the probability of toxicity on patient willingness to accept risk. The percentage of patients who were not more willing to take medication as the risk of toxicity was significantly decreased for each AE is presented in Figure 1. Despite being repeatedly reminded of the significance of less frequent and rare events using the familiar examples, between 32% and 39% were not more willing to accept a risk of reversible cosmetic AE including hirsutism, alopecia, acne, and weight gain as the risk of each of these AE was progressively decreased. Between 35% and 47% were not more willing to accept a risk of AE causing reversible discomfort including rash, stomatitis, nausea and vomiting, and diarrhea as the risk of each of these AE was significantly decreased. Between 41% and 45% were not more willing to accept a risk of more serious AE causing potential irreversible damage such as pneumonitis, major infection, and liver damage as the risk of each of these AE was significantly decreased. Unwillingness to accept risk, however, was especially evident for cancer, in which 66% of patients refused to alter their willingness to take a medication as the probability of this AE was progressively decreased from 1 in 1000 to 1 in 100,000 persons.

Associations between patient characteristics and willingness to accept risk. Twenty percent of the patients surveyed were not more willing to take medications after the risk was decreased by 2 levels for any of the AE studied. These patients

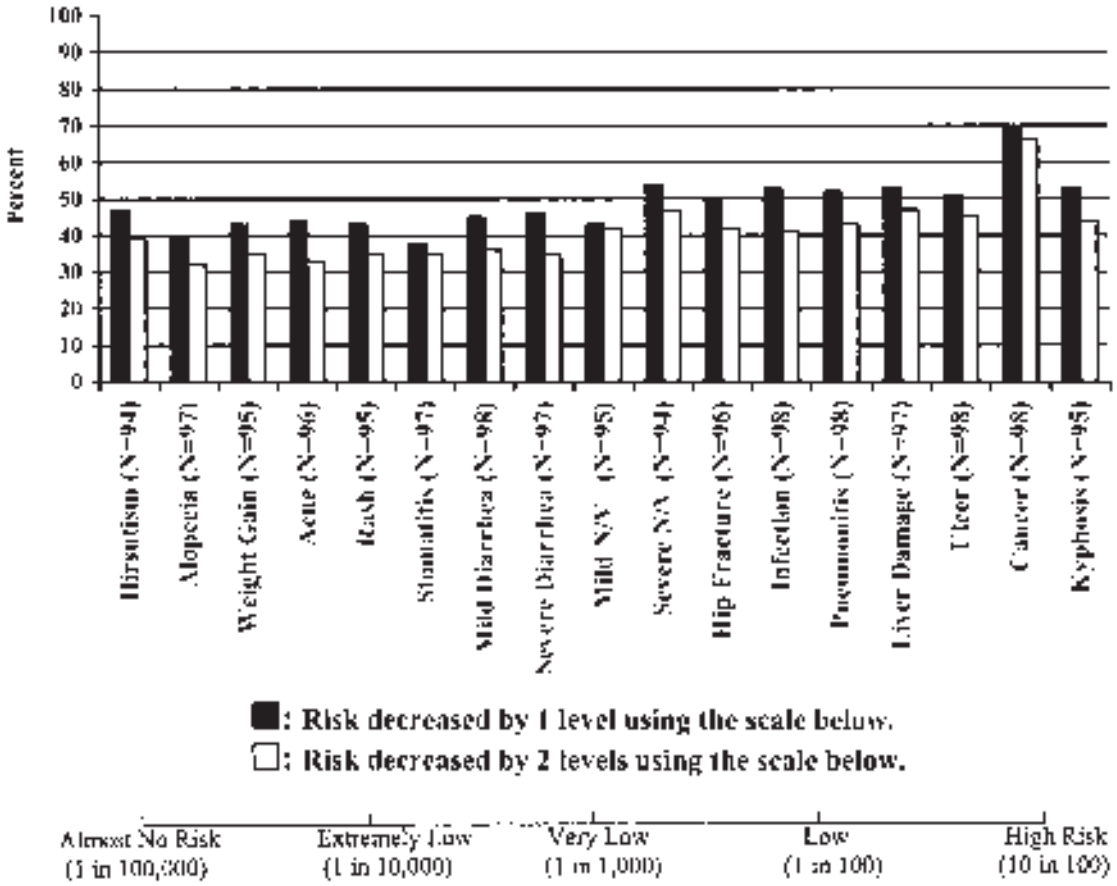

Figure 1. Number of patients with baseline score < 100 for each adverse event in parentheses. NV: nausea and vomiting.

had significantly lower mean baseline scores (i.e., VAS score for actual risk) for all 17 AE studied compared to their counterparts ($p < 0.0001$), indicating that they were generally more reluctant to take medications because of concerns regarding potential drug toxicity. We found no associations between patient demographic characteristics (including age, sex, education level, and marital and employment status) or preference for disclosure of information and increased willingness to take medications in response to lowering the risk of toxicity. However, patients who had previously experienced AE were more willing to take medications as the risk of toxicity was decreased compared to their counterparts (93% vs 74%; $p = 0.03$). Subjects reporting a poorer arthritis related health status were also more willing to take medications as the risk of toxicity was decreased (88% vs 77%; $p = 0.2$); however, this association did not reach statistical significance.

DISCUSSION

Our findings suggest that although many patients are more willing to take medications as the probability of toxicity is decreased, a significant number remain unwilling to accept the risk of AE, regardless of how small the risk. This was particularly true for cancer, where even a remote risk was regarded as unacceptable for most patients. These results are in keeping with those of Pullar, *et al*[27] and Ho, *et al*[28], who also found that patients' level of acceptable risk was far lower than the actual risk of drug toxicity. Taken together, these studies suggest that some patients treat certain AE as protected values, that is, they are unwilling to accept the risk of specific AE no matter how remote the risk of toxicity.

Participants who were not more willing to take medications as the risk of toxicity was lowered may have had difficulties understanding probabilistic information. However, we found no association between educational attainment and response to decreasing the risk of toxicity. It might have been expected that those with a higher education level would be more willing to take medication in response to decreasing the risk of AE, if numeracy was the main reason underlying patients' reluctance to accept toxicity. Further, willingness to respond to a lowered risk of AE varied with the perceived severity of toxicity, with respondents being more willing to take medications as the risk of minor AE was lowered compared to major AE. This finding also indicates that respondents understood the implications of decreased probabilities.

It is more likely that the unwillingness to accept risk we observed was due to patients' misperceptions related to the effects of toxicity. Psychologists have shown that lay people perceive risks based on their expected consequences, whereas experts' perception of risk is based more closely on probability estimates. For example, in a study in which respondents were asked to rate 30 activities and technologies in terms of risk, students rated nuclear power as the single greatest risk, whereas experts rated nuclear power twentieth, well below the risk of riding a bicycle[29]. Similarly, many women refuse hormonal replacement therapy because of the perceived risk of breast cancer, no matter how remote their individual risk[30,31]. These studies suggest that certain patients may perceive risk based primarily on the anticipated effects of AE as opposed to their actual likelihood.

We found that patients who had previously experienced AE were more willing to take medication as the risk of toxicity was decreased compared to those who had not previously experienced toxicity, suggesting that patients with personal experience related to drug toxicity might have a more accurate perception of the impact of AE on their quality of life[32] and less "fear of the unknown." This finding is consistent with studies of cancer patients, in which experience with chemotherapy was positively related to preference for more aggressive treatment[33,34].

Our results must be interpreted in view of the limitations of the study design. The participants were recruited from a single community practice and most were employed, thereby limiting the generalizability of the results to persons with similar demographic characteristics. In addition, our sample contained a relatively small number of men. Our results suggest that many patients are currently taking medications with risks they rated as unacceptable, which might indicate that some patients are not fully informed of all the possible AE associated with their medications. Our questionnaire, however, did not specifically address this concern.

In view of the known difficulties associated with communicating probabilistic information, we tried to maximize understanding of risk magnitude using several strategies. All AE were described using lay terminology and sequelae were specified. We provided numerical estimates (proportions) as well as commonly used verbal descriptions. We also repeatedly referred to a chart of familiar examples throughout the interview to increase understanding of rare events[1,23]. Lastly, we decreased probabilities by orders of magnitude, and defined increased willingness to take medication if baseline willingness increased by *any* amount as the probability of AE was substantially lowered. Despite these efforts, it is possible that a further decrease in risk or an alternative mode of presentation might have altered patient willingness to accept risk. However, given that our results revealed a reluctance to accept AE at levels far below their actual probability, it is unlikely that further decreasing the probability of AE would have changed the clinical significance of our results.

In summary, we found that among patients particularly concerned with the risk of drug toxicity, many treat certain adverse events as protected values; that is, they remain unwilling to accept the risk of these adverse events even when their probability is decreased to levels far below their actual risk. This is especially true for particularly dreaded adverse events such as cancer, suggesting that patients' perceptions of risk appear to be more closely related to the antic-

ipated effects of specific adverse events rather than their actual likelihood.

These findings may help physicians better understand patients' reluctance to accept the risk of certain drug toxicities, and help guide future interventions aimed at improving risk-communication in clinical practice. For example, for certain patients, methods aimed at improving understanding of the consequences of toxicity by providing audio or videotapes of patient testimonials might be a more effective way of communicating risk information than efforts to improve understanding of low probabilities.

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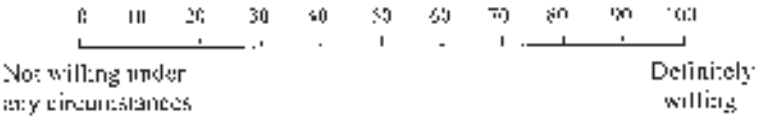
APPENDIX

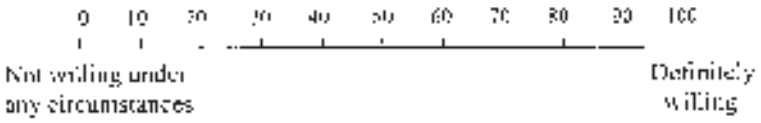
"The arthritis medication can cause severe diarrhea (you have stomach cramps and need to run to the bathroom every 2-3 hours during the day and night). The diarrhea goes away if the arthritis medication is stopped."

How willing are you to take this medication if there is a:

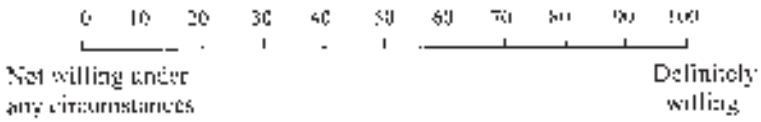
a. Low chance (approximately 1 person in a 100) of getting this side effect.



b. Very low chance (approximately 1 person in a 1000) of getting this side-effect.



c. Extremely low chance (approximately 1 person in a 10,000) of getting this side-effect.



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