

Different Methods of Presenting Risk Information and Their Influence on Medication Compliance Intentions: Results of Three Studies

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ABSTRACT

Background: Pharmaceutical noncompliance is an increasingly important problem in the United States, leading to hundreds of thousands of deaths and billions of wasted dollars each year. Patients' fear of adverse events (AEs) is one possible reason for lack of compliance.

Objectives: The aims of the 3 studies described in this article were to investigate whether commonly used methods of conveying AE risk might influence subjects' perceptions of their risk of experiencing drug-related AEs and whether disclosing this information by other means might subsequently influence their intentions to comply with prescribed medication regimens.

Methods: In study 1, randomly selected participants were surveyed to estimate their percentage risk for medication AEs. In study 2, randomly selected participants were presented with a fictitious medical scenario, informed of their AE risk either in terms of specific percentages or in general semantic terms (eg, "some people may experience..."), and then asked to rate their fear of AEs and likelihood of compliance. Study 3 was a randomized, controlled experiment in which we duplicated the methods of study 2, with the addition of real-life stimuli (pharmaceutical advertisements).

Results: In study 1, 40 subjects were surveyed. Participants overestimated their risk of AEs when information was disclosed semantically. In study 2, people were more fearful of experiencing AEs and less likely to intend to comply with prescribed medication regimens (both, $P < 0.01$) when presented with AE risk information in the form of semantic risk frames rather than actual risk percentages. In study 3, 120 subjects participated. Again, participants expressed stronger intent to comply with medication regimens when they received AE risk information as percentages rather than in semantic terms ($P < 0.04$). In addition, intend-

ed likelihood to comply was negatively correlated with fear of experiencing AEs ($P < 0.01$).

Conclusions: In these studies, informing participants of actual percentage risk of AEs was associated with less fear about AEs and greater intent to comply with prescribed regimens. Using verbal descriptors to disclose AE risk information was associated with less intent to comply. (*Clin Ther.* 2006;28:129-139) Copyright © 2006 Excerpta Medica, Inc.

Key words: compliance, adherence, overestimation, adverse reaction, drug labeling, advertising, direct-to-consumer.

INTRODUCTION

Lack of patient compliance with prescribed medication regimens has become an increasingly important issue in the United States, resulting in rising health care costs and adverse clinical outcomes such as increased morbidity and mortality rates.¹ It is estimated that only ~50% of people take their medications as prescribed, and fear of adverse events (AEs) is one barrier to compliance.^{2,3} The costs of noncompliance are substantial. Research by the US Office of the Inspector General⁴ indicates that in the United States, 125,000 deaths per year, 10% of hospital admissions, and up to 23% of nursing home admissions each year could be avoided if people took their medications as prescribed. In fact, noncompliance is estimated to cost nearly \$100 billion a year in the United States.⁵

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There are certainly cases in which it is reasonable for people to worry about the risks associated with AEs. Older patients, those with multiple prescriptions, and patients with chronic disease states may be justified in their fears because these groups are especially susceptible to AEs.^{6,7} However, other people may be unreasonably overestimating their risk for AEs, which may subsequently reduce compliance.

It has long been established that people tend to lend too much weight to small probabilities and too little weight to larger probabilities.⁸ This leads people to believe that the likelihood of uncommon events is much higher than what is objectively true, which influences their behaviors in a wide array of domains.⁹ However, the extent of this bias toward overweighting small probabilities can be influenced by a variety of factors.

In particular, the way we communicate risk information plays an important role in how people understand risk,^{10,11} accept or deny risk, and deal (or refrain from dealing) with risk information.^{10,12} Some ways of describing uncertainty tend to distort people's perceptions of risk, whereas other methods tend to lead to relatively more accurate risk assessment.¹² Applied studies of risk communication have been used to improve people's comprehension of risk in a variety of domains, including law,^{13,14} medical diagnosis,¹⁵ weather reports,¹⁶ and AIDS counseling.¹⁷

In this article, we propose that the principles of risk communication could similarly improve patients' understanding of AE risks and, in doing so, increase both patients' knowledge and their intent to comply with prescribed medication regimens. Framing information more effectively might increase patients' confidence in the medication and increase rates of compliance, if that is warranted. Typically, AE information is disclosed using ambiguous semantic descriptions, such as "some people may experience," "side effects may include," or "commonly reported side effects are." These semantic descriptors do not express the exact percentage of risk and are subject to personal interpretation. People's percentage interpretations of risk could, therefore, conceivably be quite inflated.¹⁸ Disclosing the actual percentages associated with AEs may improve the accuracy of people's risk estimates.

In the United States, there has been little or no research on the effects of different methods of disclosing AE risk information.¹⁹ The US Food and Drug

Administration (FDA) has issued guidelines on the type of information to be disclosed.²⁰⁻²⁴ In these guidelines, the FDA has requested that advertisements for prescription drugs for humans include a brief summary conveying information on AEs, contraindications, and efficacy. A drug is considered *misbranded* if it fails to bear these warnings.²⁰ However, there has been little, if any, instruction on how to best communicate that information.¹⁹ Alternatively, the European Union (EU) has issued verbal descriptor guidelines²⁵ for medication AEs, ranging from *very rare* (occurring in <0.01% of participants in clinical trials) to *very common* (occurring in >10% of participants in clinical trials). This announcement has led European²⁶ and Canadian²⁷ researchers to test different methods of disclosing AE risk information. In one study, researchers informed participants of their risk for AEs using either the current verbal descriptors issued by the EU or the assigned equivalent risk percentages.¹⁸ They found that people who were verbally informed about the AE risk overestimated their risk and rated themselves as less likely to take the medication than those who were given the actual percentage likelihood of experiencing specific AEs.

However, studies on conveying AE risk information have used the EU-assigned verbal descriptors. It is unknown whether this overestimation would occur in the United States, where verbal descriptor guidelines do not exist.²⁰ Because the United States lacks guidelines on how to present information, pharmaceutical companies appear to use their own terminology to convey AE risk. Very little is known about how people interpret and understand the previously described semantic terminology. This article reports the results of a series of studies designed to investigate whether the currently used semantic framing of AE risk might influence subjects' perceptions of their risk of experiencing drug-related AEs and whether disclosing this information by other means might subsequently influence their intentions to comply with prescribed medication regimens.

PARTICIPANTS AND METHODS

The following studies, which were conducted between April 2003 and February 2005, were approved by the Stanford University internal review board for human subjects. There was no outside source of funding provided for any of these studies. Each participant provided written informed consent.

Study 1

In study 1, we predicted that the methods of conveying AE risk that are currently used in the United States (ie, semantic presentation of risk information) might lead people to overestimate their risk of AEs.

Twenty pharmaceutical advertisements were randomly sampled from various waiting room magazines from a local health clinic. The advertisements were selected by research assistants blinded to the purpose of the experiment and were analyzed to assess how they presented AE risk information.

Potential participants were approached randomly at various locations in Stanford, California, by research assistants who were blinded to the purpose of the experiment. Participants were presented with a written vignette that conveyed AE information about a fictitious "drug X" in the same format (semantically—eg, "some people may experience side effects from drug X") as was used in the selected advertisements. They were not shown the actual advertisements. Participants were asked to imagine that their physician had prescribed drug X for them. They were then given a survey questionnaire and asked to estimate the percentage risk of AEs resulting from the use of drug X.

Objective rates for the most frequent AEs were determined, based on the clinical trial information from the selected advertisements.

Study 2

Study 2 was a randomized, controlled experiment. We predicted that framing risk information using actual percentage likelihood of AEs (according to clinical trial data), rather than the semantic framing that is most commonly used in American pharmaceutical advertisements, would reduce fear of AEs and increase intentions to adhere to treatment regimens.

Eleven advertisements for heart-disease drugs were randomly selected from magazines available for reading in the reception area of the Department of Psychology at Stanford University by research assistants who were blinded to the purpose of the experiment. Only advertisements that contained clinical trial information were selected. As in study 1, objective rates for the most frequently occurring AEs were calculated using the clinical trial information from these advertisements. The risk of AEs for the randomly selected medications was pooled, and the mean of the pooled values was used as the mean rate of drug-related AEs for a typical heart dis-

ease medication, a control value against which participants' perceived risk for AEs was compared.

Participants were recruited from psychology courses on the Stanford University campus by research assistants who were blinded to the purpose of the experiment. Participants were randomly assigned to 1 of 2 risk-framing groups (percentage or semantic). They were presented with a written vignette asking them to imagine that they were experiencing symptoms of heart disease and had been advised by their physician to take "drug X" to help them. Depending on participants' risk-framing group, AE information about drug X was presented in either semantic or percentage form. Participants assigned to the semantic group were told, "some people may experience side effects from the drug." Those assigned to the percentage group were told that they had a "0.051 greater than placebo risk of experiencing side effects" from the drug.

Participants in both groups were then asked to fill out a questionnaire assessing their perceived risk of experiencing side effects with drug X. They were asked to indicate their likelihood of taking the drug (9-point scale; 1 = very unlikely, 9 = very likely) and fear of AEs (9-point scale; 1 = not fearful, 9 = very fearful). They also were asked to state which AEs they were thinking of when assessing their risk.

Study 3

Study 3 was a randomized, controlled experiment in which we sought to replicate the results of study 2 and test their validity in a more realistic setting by giving people actual pharmaceutical advertisements to measure their intended rates of compliance.

Potential participants were randomly selected by research assistants at various locations in Stanford, California. Subjects were assigned to 1 of 2 risk groups (percentage or semantic) and asked to fill out a questionnaire assessing their perceived risk for AEs. All subjects were shown the print advertisements for 2 randomly selected drugs (the order was counterbalanced, and each subject was shown advertisements for both drugs) and given a vignette in which they were asked to imagine that they had the condition described in the advertisement and that their doctor had prescribed the medication for them. Participants were not asked whether they actually had either of the conditions described in the advertisements.

The vignette given to the semantic group stated, "some people may experience side effects from the

drug." The vignette given to the percentage group stated that there was a "0.051 greater than placebo risk of experiencing side effects from the drug." Participants in both groups were then asked to indicate their likelihood of taking the drug (9-point scale; 1 = very unlikely, 9 = very likely) and fear of AEs (9-point scale; 1 = not fearful, 9 = very fearful), and to state which AEs they were thinking of when assessing their risk.

Finally, participants in both groups were asked to state whether they would consider their risk percentage to be high or low (binomial) and to indicate quantitatively whether this percentage was high or low risk (9-point scale; 1 = very low, 9 = very high). In addition, they were asked to quantify their perceived risk relative to the average person (9-point scale; 1 = very low risk, 9 = very high risk). Those presented with the semantic risk information were also asked to quantify, as a percentage, their perceived risk of drug-related AEs.

Statistical Analysis

The present studies were designed to test whether semantic presentation of information would lead participants to overestimate their risk for AEs (study 1) and decrease their intended compliance compared with disclosing the actual percentage risk for AEs (studies 2 and 3). SPSS software (SPSS Inc., Chicago, Illinois) was used to perform *t* tests of the mean differences between groups. In study 1, participants' mean perceived risk for AEs was compared with their actual (calculated) risk for AEs according to the clinical trial information. In studies 2 and 3, participants' mean perceived risk for AEs was compared in the semantic and percentage risk groups. Mann-Whitney *U* tests were used to confirm the results using a nonparametric method. In study 3, we also calculated the power of our statistical results, which was high (>99%).

RESULTS

Study 1

The selected advertisements in study 1 were for atorvastatin calcium (Lipitor, Parke-Davis, New York, New York), celecoxib (Celebrex, G.D. Searle & Company, New York, New York), cholestyramine (Questran, Par Pharmaceutical Inc., Spring Valley, New York), diclofenac (Voltaren, Novartis Pharmaceuticals Corporation, East Hanover, New Jersey), donepezil hydrochloride (Aricept, Eisai Inc., Teaneck, New Jersey), eletriptan hydrobromide (Relpax, Pfizer Inc., New York, New York), fluoxe-

tine hydrochloride (Sarafem, Warner Chilcott, Inc., Rockaway, New Jersey), fluticasone (Flonase, GlaxoSmithKline, Research Triangle Park, North Carolina), fluticasone propionate and salmeterol (Advair Diskus, GlaxoSmithKline), ibuprofen (Advil, Wyeth Pharmaceuticals, Madison, New Jersey), lansoprazole (Prevacid, TAP Pharmaceuticals Inc., Lake Forest, Illinois), naproxen (Naprosyn, Roche Pharmaceuticals, Nutley, New Jersey), rosiglitazone maleate (Avandia, GlaxoSmithKline), rosuvastatin calcium (Crestor, AstraZeneca Pharmaceuticals LP, Wilmington, Delaware), salmeterol (Serevent Diskus, GlaxoSmithKline), sertraline hydrochloride (Zoloft, Pfizer Inc.), sildenafil citrate (Viagra, Pfizer Inc.), simvastatin (Zocor, Merck & Company, Whitehouse Station, New Jersey), terbinafine hydrochloride (Lamisil, Novartis Pharmaceuticals Corporation, East Hanover, New Jersey), and vardenafil hydrochloride (Levitra, Bayer Pharmaceuticals Corporation, West Haven, Connecticut). These advertisements most commonly (13/20 advertisements) conveyed risk by stating, "some people may experience," but statements such as "side effects may include," "the most common side effects are," and "in rare cases, x, y, and z can occur" were also used.

Based on the clinical trial information for the 20 randomly chosen advertisements, the most commonly occurring AEs were diarrhea (reported in 18 of 20 advertisements), headache (17 of 20), and nausea (17 of 20). When the mean occurrence of these AEs was calculated, the mean risk for experiencing diarrhea was 0.025, headache 0.011, and nausea 0.025. The pooled risk for the 3 most common AEs was 0.020.

Forty subjects were randomly selected to participate in the survey. Respondents perceived the statement "some people may experience" to indicate a greater risk of AEs (mean perceived risk, 0.213) than the actual rate of 0.020 calculated from the clinical trial data. It is possible that these participants were thinking of their risk of experiencing any AEs, rather than just the 3 most common drug-related AEs. In this case, the upper bound would be more closely approximated by the sum of the risk of individual AEs, rather than by the mean of the risks of individual AEs. However, it should be noted that the risk of any AE was still <0.10, based on our calculations; even with this more conservative measure, the subjects' estimate of their risk could still be considered an overestimation.

Study 2

The selected advertisements in study 2 were for the β -blockers acebutolol (Sectral, ESP Pharma, Edison, New Jersey) and atenolol (Tenormin, AstraZeneca Pharmaceuticals LP); the angiotensin-converting enzyme inhibitors enalapril (Vasotec, Merck & Company) and lisinopril (Prinivil, Merck & Company); the statins lovastatin (Mevacor, Merck & Company) and simvastatin (Zocor, Merck & Company); the nitrate isosorbide mononitrate (Imdur, AstraZeneca Pharmaceuticals LP); the calcium-channel blockers amlodipine (Norvasc, Pfizer Inc.) and felodipine (Plendil, AstraZeneca Pharmaceuticals LP); and the antiplatelet agents aspirin (Bayer Pharmaceuticals Corporation) and ticlopidine (Ticlid, Roche Pharmaceuticals).

Based on the clinical trial data for the 11 randomly chosen advertisements, the most frequently occurring AEs were dizziness (reported in 10 of 11 advertisements), diarrhea (11 of 11), and nausea (11 of 11). The mean risk for experiencing these AEs was calculated and found to be 0.02 more than placebo for dizziness, 0.013 more than placebo for diarrhea, and 0.018 more than placebo for nausea. The pooled risk for these 3 AEs was 0.017. To create a conservative measure against our hypothesis, we used a more conservative estimate of 0.051 (3 times the objective AE rate).

Thirty-one subjects participated in the survey. As predicted, respondents expressed a stronger intention to comply with the prescribed treatment regimen when they were given percentage information about their risk of AEs (mean [SD] intention score, 7.44 [1.5]) than those who were given the semantic framing (mean [SD] intention score, 3.1 [2.3]). This difference was statistically significant with a test that did not assume equal variances ($t_{29} = 6.30$; $P < 0.01$). We confirmed this with a Mann-Whitney nonparametric test ($U = 14.5$; $P < 0.01$). Those in the percentage group also expressed less fear of experiencing drug-related AEs (mean [SD] fear score, 3.1 [1.6]) than those in the semantic group (mean [SD] fear score, 5.3 [2.6]; $t_{29} = -2.86$, not assuming equal variances [$P < 0.01$]; Mann-Whitney $U = 59$, with a nonparametric test [$P < 0.02$]). There was a significant negative relationship between fear of AEs and compliance intentions ($r_{29} = 0.45$; $P = 0.01$), suggesting that participants who expressed the most fear of AEs were also the least likely to express intent to comply with the medication regimen.

We recorded participants' perceptions of AEs associated with the drug to make sure they reflected the nature of the actual AEs. Indeed, people's responses conformed to common AEs associated with these medications. The most popular responses were nausea, headache, rash, and diarrhea.

Study 3

The advertisements used in study 3 were for fluticasone propionate (Flonase, GlaxoSmithKline) and atorvastatin calcium (Lipitor, Pfizer Inc.). The advertisement for fluticasone propionate stated that some people may experience headache, nosebleed, and sore throat. The clinical trial information for AEs with the highest reported dosage of fluticasone propionate indicated that headache occurred at a mean rate of 0.015 more than placebo, nosebleed occurred at a mean rate of 0.015 more than placebo, and sore throat occurred at a mean rate of 0.006 more than placebo. The advertisement for atorvastatin calcium stated that the most common AEs were gas, constipation, stomach pain, and heartburn. The clinical trial information for AEs for the largest reported dosage of atorvastatin calcium indicated that gas occurred at a mean rate of 0.021 less than placebo, constipation occurred at a mean rate of 0.007 less than placebo, stomach pain occurred at a mean rate of 0.014 more than placebo, and heartburn occurred at a rate of 0.02 less than placebo. All of these estimates were $<5\%$ greater than those for the placebo group. Therefore, we kept our conservative estimate of AEs occurring at a rate of 0.051 greater than placebo when we communicated risk to the percentage group.

The participant sample included 120 participants, 66 male and 54 female. Participants indicated a greater intention to comply when presented with an advertisement for fluticasone propionate (mean [SD] intention score, 6.9 [2.0]) than for atorvastatin calcium (mean [SD] intention score, 4.6 [2.5]). This difference was statistically significant ($t_{118} = 5.5$; $P < 0.01$). Participants to whom AE information was disclosed in percentages indicated greater intent to take medication as prescribed (mean [SD] intent score, 6.2 [2.5]) than those who received a semantic descriptor (mean [SD] intent score, 5.3 [2.5]) (Table I). These differences were statistically significant, not assuming equal variances ($t_{118} = -2.1$; $P < 0.04$). This result was confirmed with a nonparametric test (Mann-Whitney $U = 1400$; $P < 0.04$). Participants in the semantic group

Table I. Assessments of adverse event (AE) risk, fear of AEs, and intention to comply with prescribed medication regimen among 120 people in Stanford, California, who were presented with a fictitious medical scenario, shown 2 drug advertisements, and given AE risk information in semantic terms (eg, "some people may experience...") or as specific percentages for particular AEs.

Variable	No. of Subjects	Mean (SD) Value	SE	P*
AE risk				
Own risk compared with average person†				<0.02
Semantic	61	4.0 (1.9)	0.2	
Percentage	59	3.2 (1.4)	0.2	
Percent estimate				
Semantic	59	14.7 (14.6)	1.9	
Percentage	-	-	-	
Quantitative risk estimate†				<0.01
Semantic	61	4.2 (2.1)	0.3	
Percentage	59	3.1 (1.4)	0.2	
Compliance intention‡				
Semantic	61	5.3 (2.5)	0.3	<0.04
Percentage	59	6.2 (2.5)	0.3	
Fear§				
Semantic	61	4.5 (2.4)	0.3	<0.01
Percentage	59	3.0 (1.7)	0.2	

*Based on 2-tailed Student *t* test.

†Rated on a 9-point scale (1 = very low risk; 9 = very high risk).

‡Rated on a 9-point scale (1 = very unlikely; 9 = very likely).

§Rated on a 9-point scale (1 = not fearful; 9 = very fearful).

also expressed more fear of AEs (mean [SD] fear score, 4.5 [2.4]) than did participants in the percentage group (mean [SD] fear score, 3.0 [1.7]). This difference was statistically significant, not assuming equal variances ($t_{118} = 4.0$; $P < 0.01$). We confirmed this difference with a nonparametric test (Mann-Whitney $U = 1118$; $P < 0.01$). Participants in the semantic group also perceived themselves to be at greater risk of experiencing AEs (mean [SD] risk assessment, 4.0 [1.9]) than those in the percentage group (mean [SD] risk assessment, 3.2 [1.4]; $t_{118} = 2.5$ [$P < 0.02$]).

Participants' binomial ratings of risk also varied by the method of framing. Participants in the percentage group (those perceiving themselves to be at low risk [$n = 50$] vs those perceiving themselves to be at high risk [$n = 8$]) were more likely to describe themselves as being at low risk than those in the semantic group (low risk [$n = 40$] vs high risk [$n = 20$]; $\chi^2 = 6.2$ [$P < 0.02$]). Participants in the percentage condition also assessed their quantitative risk as being lower than that

in the semantic group (mean [SD] values, 3.1 [1.4] vs 4.2 [2.1]; $t_{118} = 3.21$ [$P < 0.01$]) (Table I). We confirmed this result with a nonparametric test (Mann-Whitney $U = 1303$; $P < 0.01$). Those in the semantic group reported their perceived risk percentage as being high (mean assessment, 0.147) compared with the actual (conservative) likelihood of AEs as presented in the advertisements (mean, 0.051; $P < 0.01$).

A person's intended likelihood of taking the medication was negatively correlated with fear of experiencing AEs ($r = -0.581$; $P < 0.01$), likelihood of experiencing AEs compared with the average person ($r = -0.264$; $P < 0.01$), and binomial ($r = -0.257$; $P < 0.01$) and quantitative ($r = -0.401$; $P < 0.01$) perception of whether he or she was at low or high risk for AEs (Table II). There was a positive relationship between expressed fear of experiencing AEs and perceived likelihood of experiencing AEs compared with the average person ($r = 0.566$; $P < 0.01$), as well as a correlation between fear of experiencing AEs and

Table II. Correlations between assessments of adverse event (AE) risk, fear of AEs, and intention to comply with prescribed medication regimen among 120 people in Stanford, California, who were presented with a fictitious medical scenario, shown 2 drug advertisements, and given AE risk information in semantic terms (eg, "some people may experience...") or as specific percentages for particular AEs.

Variable	Compliance	Fear of AEs	Risk Compared with Average Person	Percent Estimate of AE Risk	Quantitative Estimate of AE Risk	Binomial Assessment of Risk Level
Compliance						
Pearson correlation	1	-0.581*	-0.264*	0.231	-0.401*	-0.257*
2-tailed <i>P</i>	-	<0.001	0.004	0.078	<0.001	0.005
No. of subjects	120	120	120	59	120	118
Fear of AEs						
Pearson correlation	-0.581*	1	0.566*	0.127	0.743*	0.548*
2-tailed <i>P</i>	<0.001	-	<0.001	0.336	<0.001	<0.001
No. of subjects	120	120	120	59	120	118
Risk compared with average person*						
Pearson correlation	-0.264*	0.566*	1	0.393*	0.627*	0.402*
2-tailed <i>P</i>	0.004	<0.001	-	0.002	<0.001	<0.001
No. of subjects	120	120	120	59	120	118
Percent estimate of AE risk*						
Pearson correlation	0.231	0.127	0.393*	1	0.167	0.031
2-tailed <i>P</i>	0.078	0.336	0.002	-	0.205	0.817
No. of subjects	59	59	59	59	59	58
Quantitative estimate of AE risk*						
Pearson correlation	-0.401*	0.743*	0.627*	0.167	1	0.632*
2-tailed <i>P</i>	<0.001	<0.001	<0.001	0.205	-	<0.001
No. of subjects	120	120	120	59	120	118
Binomial assessment of risk level*						
Pearson correlation	-0.257*	0.548*	0.402*	0.031	0.632*	1
2-tailed <i>P</i>	0.005	<0.001	<0.001	0.817	<0.001	-
No. of subjects	118	118	118	58	118	118

*As assessed by participant.

quantitative ($r = 0.743$; $P < 0.01$) and binomial ($r = 0.548$; $P < 0.001$) estimates of being at low or high risk for AEs. This suggests that individuals who believed that AEs were more likely to occur were also more fearful of those AEs and less likely to intend to comply with the treatment regimen.

As in study 2, we recorded participants' responses to make sure that they were similar to the types of AEs that the drugs were actually known to produce. Participants appeared to be accurate; the most popular responses were the actual AEs stated in the advertisements that they read.

DISCUSSION

The results of these 3 studies support and extend the findings of earlier studies that the semantic methods of framing AE information used in the United States lead to overestimation of AE risk and reduced intent of compliance with prescribed medication. Because pharmaceutical companies and pharmacists frequently present risk information semantically,^{19,27} patients might perceive their risk to be much greater than clinical trial results would suggest. This overestimation of side-effect risk may contribute to reduced rates of compliance. We propose that framing AE information using actual percentage likelihood may help to decrease this overestimation and may, in turn, lead to increased prescription compliance.

In study 1, we found that the semantic methods of disclosure do indeed inform consumers that they may experience AEs but do not provide any indication of who will experience AEs, or how likely the AEs are to occur. Perhaps as a result, people appeared to believe that AEs were quite likely to occur; in fact, the risk information is only included in advertisements because pharmaceutical manufacturers are required to report any AEs experienced by participants during clinical trials.³

It is interesting to note that, in study 1, participants thought that there was >20% chance of AEs when, in fact, <5% of people appear to experience AEs. Believing that >2 of 10 people who take a medication will experience AEs could make patients reluctant to comply with prescribed medication regimens. Such discrepancies could be partly responsible for noncompliance with treatment regimens. People's interpretations of the semantic descriptors may lead them to overestimate the risk of AEs, which may produce a perception that the risk of taking the medicine out-

weighs its benefits. To be better informed about the medication, a consumer could review clinical trials information, but studies in the United Kingdom have found that most patients do not read information in the medication labeling.^{28,29} Presenting AE information in a more accessible format might affect patients' desire and ability to read label information.

Research has suggested that consumers' attitudes about drugs are influenced by the way information is presented.^{30,31} Although the findings of the present 3 studies suggest that presenting actual percentages of the likelihood of experiencing AEs is associated with reduced fears of AEs and increased patient intention to comply with medication regimens, other methods of framing have also been proposed, including framing using frequencies,^{13,15,32} risk ladders,³³ community risk scales,³⁴ and magnifier scales.³⁵ It is beyond the scope of the present report to discern which technique might prove most valuable for increasing compliance. Rather, this article suggests only that framing affects the public's estimates of risk and intended rates of compliance, and that current methods of disclosing information about AE risk are not optimal.

Although this article has proposed that informing a person of actual percentage risk may reduce fear and increase intentions for compliance, there are other interventions that merit empirical investigation. For example, it may be beneficial to disclose which risk groups are most susceptible to AEs. Reports of AEs in clinical trials may come from groups with a greater likelihood of experiencing AEs with any medication. For example, an individual who takes several drugs has a greatly increased risk of experiencing AEs because of drug interactions.³ Conversely, it stands to reason that a person who does not take other medications may be less likely to experience AEs. It may be helpful to put labels on medication containers to warn high-risk populations of the increased danger of AEs, as well as to provide more accurate and helpful information to people at lower risk. Framing methods such as black-box warnings are now being used to illuminate these differences.³⁶ Yet, until we can provide a more accurate representation of who is at risk and what his or her risk is, people might continue to be overly fearful of AEs and have suboptimal rates of compliance.

One limitation of our studies is that behavioral measures of compliance were not gathered. However, research has suggested that measuring behavioral intentions is an accurate and strong predictor of actual

behavior.³⁷⁻⁴⁰ For example, in a meta-analysis on condom use, Sheeran et al⁴¹ found that the expressed intention to use condoms was one of the strongest predictors of actual condom use. Expressed intentions have been shown to predict a wide range of health-related behaviors,⁴² including breast cancer screenings,⁴³ cervical cancer screenings,⁴⁴ and genetic testing.⁴⁵ Although the present studies deal with medication compliance, intentions may indeed predict behavior as long as the behavior is in the same domain as the intention.⁴⁶ Therefore, we consider the present findings a compelling indication that people may be less likely to comply with a physician's prescription when AE information is presented using the currently employed semantic methods.

Another limitation is that all of the participants in the 3 studies were located in Stanford, California. It is possible that these participants were younger and more educated than the general US population, given that they were selected on or near a university campus, and that they may therefore have processed information in a different manner than older or less educated members of the public. For example, the participants might have been more familiar with dealing with percentages than people outside of this sample. In fact, given that some of the participants may have been physicians or medical students, they may have been more knowledgeable about the actual likelihood of experiencing drug-related AEs. However, this limitation makes the results all the more interesting, if even those expected to be best equipped to accurately understand risk information had trouble with current semantic framing. One might expect the observed association between semantic framing and fear of AEs to be even stronger outside of a presumably highly educated population.

Although the present studies attempted to investigate a barrier to medication compliance, the behavior pattern illustrated here should not be used to manipulate people into taking medications. Drugs should be used to maximize benefits and minimize harm.⁴⁷ However, the present studies suggest that the current methods of disclosing AE risks are not as effective as they could be. By changing the methods by which such information is conveyed to the public, it may be possible to increase both patient awareness and rates of compliance so that patients receive the treatment they need.¹⁸ It is important that methods of disclosing AE risk information consider how people understand and process that information. Changing

the ways in which AE risk information is framed for the general public may improve the evidence available for individual decisions and help to reduce both adverse clinical outcomes and wasted resources resulting from noncompliance.

CONCLUSIONS

In these studies, informing participants of actual percentage risk of AEs was associated with less fear about AEs and greater intent to comply with prescribed regimens. Using verbal descriptors to disclose AE risk information was associated with less intent to comply.

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