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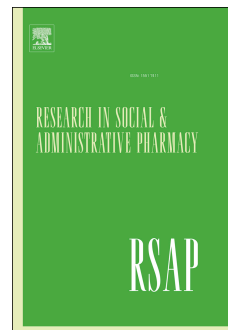
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Michael Bitonti, Payal Patel, Rebecca Dickinson, Peter Knapp, Susan J. Blalock



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The Effect of Counseling on Willingness to Use a Hypothetical Medication
and Perceptions of Medication Safety

Michael Bitonti^a

Payal Patel^a

Rebecca Dickinson^b

Peter Knapp^c

Susan J. Blalock^d

^aEshelman School of Pharmacy, University of North Carolina at Chapel Hill

^bSchool of Healthcare, University of Leeds, Leeds, UK

^cDepartment of Health Sciences and the Hull York Medical School, University of York, York,
UK

^dPharmaceutical Outcomes and Policy, Eshelman School of Pharmacy, University of North
Carolina at Chapel Hill

Corresponding Author: Michael Bitonti, 7611 Sumter Heights Ct, Apt 1311, Raleigh, North
Carolina, 27617. Phone: (336) 214-3212. Email: michael_bitonti@unc.edu.

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Abstract

Background: Poor medication adherence is an ongoing issue, and contributes to increased hospitalizations and healthcare costs. Although most adverse effects are rare, the perceived risk of adverse effects may contribute to low adherence rates.

Objectives: The objective of this study was to determine how adverse effect likelihood and pharmacist counseling on adverse effect prevention affects individuals': (1) willingness to use a hypothetical medication and (2) perceptions of medication safety.

Methods: This study used a 3x3 experimental design. Participants (n=601) viewed a hypothetical scenario asking them to imagine being prescribed an anti-asthma medication that could cause fungal infections of the throat. Participants were randomized to 1 of 9 scenarios that differed on: probability of developing an infection (5%, 20%, no probability mentioned) and whether they were told how to reduce the risk of infection (no prevention strategy discussed, prevention strategy discussed, prevention strategy discussed with explanation for how it works). Participants were recruited through Amazon Mechanical Turk.

Results: Participants were less willing to take the medication ($F=12.86$, $p<0.0001$) and considered it less safe ($F=13.11$, $p<0.0001$) when the probability of fungal infection was presented as 20% compared to 5% or when no probability information was given. Participants were more willing to take the medication ($F=11.78$, $p<0.0001$) and considered it safer ($F=11.17$, $p<0.0001$) when a prevention strategy was given. Finally, there was a non-statistically significant interaction between the probability and prevention strategy information such that provision of prevention information reduced the effect of variation in the probability of infection on both willingness to use the medication and perceived medication safety.

Conclusions: Optimal risk communication involves more than informing patients about possible adverse effects. Pharmacists could potentially improve patient acceptance of therapeutic recommendations, and allay medication safety concerns, by counseling about strategies patients can implement to reduce the perceived risk of adverse effects.

Keywords: Risk communication, pharmacist counseling, medications, adverse effects

Introduction

It is estimated that about 50% of the United States population has used at least one prescription medication within the previous month, and roughly 22% has used three or more.¹ However, adherence to medications continues to be a major issue. A recent study found that 18% of cardiac prescriptions were not filled by patients four months after a major coronary event.² Other research has found that only 37% of patients were adherent to statin therapy and only 66% to medications used in diabetes.^{3,4} High levels of medication adherence for long-term conditions can reduce rates of hospitalization and lower overall healthcare costs.^{3,5} A recent Cochrane Review on improving medication adherence found that the most beneficial strategies were highly complex and involved consistent follow-up, but provided only marginal benefit in adherence rates.⁶ Thus, the optimal strategy for increasing medication adherence remains unknown.

The World Health Organization identifies five categories of factors contributing to medication nonadherence: economic, health-system, patient-related, condition-related, and therapy-related. Among therapy-related factors, adverse effects of the medication are a major obstacle.⁷ The presence of adverse effects has been shown to decrease adherence to a wide variety of medications, including glucocorticoids and antidepressants.^{8,9} Nearly all medications carry the risk of unwanted adverse effects, with varying degrees of likelihood and severity; however, most adverse effects are relatively rare or can be mitigated with proper counseling and monitoring. For instance, medications that cause stomach upset are often recommended to be taken with food to prevent irritation to the GI tract and the resultant nausea.

Pharmacists can play a significant role in preventing adverse effects from occurring in their patients. Including a pharmacist on inter-disciplinary teams conducting patient rounds in an Intensive Care Unit has been shown to significantly reduce adverse effects, and discharge

counseling with a pharmacist has been shown to lower the rate of preventable adverse medication-related events following hospital admission.^{10,11} In addition, pharmacists can play a leading role in increasing medication adherence. A recent study found medication reviews and follow-up telephone calls with a pharmacist increased adherence to lipid-lowering therapies.¹² Another study found that implementation of a pharmacist-led asthma management service in community pharmacies led to improvements in the use of preventative asthma medications.¹³ Other research has shown implementation of a pharmacist-driven medication therapy management program to increase cardiovascular medication use, while also improving cardiovascular risk factors such as systolic and diastolic blood pressure.¹⁴ However, little research has examined the effect of patient-pharmacist counseling concerning medication risks specifically.

The concept of “risk” is multidimensional.¹⁵ With respect to medication risk communication, two types of information are especially important for pharmacists to provide: (1) the probability of experiencing specific adverse effects and (2) strategies patients can implement to reduce the risk of experiencing these effects. Past research has demonstrated that numerical adverse effect information is easier for patients to accurately comprehend compared to non-numerical information.^{16,17} Patients tend to overestimate the likelihood of adverse effects when non-numeric, qualitative descriptors (e.g., common, rare) are used to communicate risk likelihood instead of, or in addition to, numerical information (e.g., 10% of patients; 1 in 10 patients) alone.^{18,19} Overestimates of risk likelihood can make patients less willing to take a medication.^{16,20}

In a previous study by this research team that was guided by *fuzzy trace theory* (FTT),²¹⁻²³ it was demonstrated that simply informing individuals that a specific adverse effect may occur

without providing any indication of the probability of occurrence can reduce willingness to use the medication and that this effect can be mitigated by providing numeric probability information.²⁴ Briefly, FTT is a dual process model of memory reasoning and development. It suggests that when individuals are exposed to a meaningful stimulus, they encode two types of representations in memory: a specific verbatim representation that captures the exact words/numbers conveyed and one or more gist representations that capture the essential bottom line meaning of the information. Moreover, past research has found that when people are making judgments and decisions, they tend to rely on the gist representations that have been stored in memory in response to previously presented information, rather than the verbatim representations.²³ Thus, the findings from the research team's previous study suggested that when individuals are told that a medication can cause a particular adverse effect without being given any probability information, they tend to form a categorical gist representation (e.g., the medication can cause harm), leading to risk avoidance (e.g., reduced willingness to use the medication); whereas, providing numerical probability information allows individuals to form somewhat more precise, ordinal gist representations (e.g., the risk of the medication causing harm is small).

In the study reported in this paper, findings from the research team's previous study were followed up by examining the possibility that unconditional estimates of risk probability (5% versus 20%) may be less meaningful and, consequently, have less impact on judgment and decision making, when patients are counseled about precautions they can take to reduce risk. It was hypothesized that:

- (1) Individuals will be less willing to use a hypothetical asthma medication (and consider the medication less safe) when told that the medication can cause an adverse effect (i.e., fungal

infection of the throat) without being given any information concerning risk probability versus being informed that the likelihood of the adverse effect is 5% or 20%;

- (2) Individuals will be most willing to use the medication and consider it most safe when counseling on how to prevent the adverse effect is provided; and
- (3) There will be an interaction between the probability and prevention information such that, among individuals counseled on how to prevent the adverse effect, willingness to use the medication and perceptions of medication safety will not be affected by the probability of the adverse effect.

Materials and Methods

To recruit participants, a link was posted to an Internet-based survey on Amazon Mechanical Turk (AMT) (www.mturk.com).²⁵ AMT is an internet crowdsourcing marketplace where registered users sign up and are able to complete various tasks requiring human intelligence for payment. The title of the survey link was “Answer a survey about prescription medication information.” The first screen of the survey informed individuals that they were being asked to participate in a research study. To obtain informed consent, individuals were required to click a button indicating they agreed to participate in the study. The study was approved by the Institutional Review Board at the University of North Carolina at Chapel Hill.

Participants were adults aged 18 years or older and living in the United States. There were no other study inclusion or exclusion criteria. A total of 633 Mechanical Turk workers accessed the link to the survey, which was administered via Qualtrics[®] software, and agreed to participate in the study. However, 32 of these individuals failed an attention check question that appeared as the second question in the survey and these participants were removed from the sample, leaving 601 study participants. The attention check question instructed participants to

select “Somewhat likely” as the response to the question. Selecting any other response invoked a skip pattern within Qualtrics that prevented the individual from completing the remainder of the survey. This was done to prevent robots from completing the survey. The survey required approximately five minutes to complete. All participants were paid fifty US cents for completing the survey. All data was collected on June 1, 2015.

Experimental Materials

The study used a 3 x 3 experimental research design. An experimental research design was used to enhance the internal validity of the study. All participants read a brief, hypothetical scenario that began as follows:

“Imagine you have recently been experiencing episodes of wheezing and shortness of breath. You visit your family doctor and he tells you that you have asthma. He assures you that asthma is treatable and writes you a prescription for an inhaler called Cradulox. The directions say ‘inhale one puff twice daily.’ Your doctor refers you to your local pharmacy. The pharmacist fills your prescription, explains how to use the inhaler, and states that it can cause fungal infections in the throat.”

The next portion of the scenario differed across experimental groups. The two experimental factors manipulated were (1) probability of developing a fungal infection (i.e., low probability, high probability, no probability mentioned) and (2) strategy for preventing fungal infections (i.e., no prevention strategy discussed, prevention strategy discussed, prevention strategy discussed including an explanation of how the prevention strategy reduces the risk of experiencing a fungal infection) (Table 1). Participants in the low probability group were told fungal infections occur in 5% of patients who use the inhaler; whereas, participants in the high probability group were told fungal infections occur in 20% of inhaler users. Participants in the no probability group were

simply told the inhaler can cause fungal infections. With respect to prevention information, participants in the group that received a prevention strategy were told that rinsing their mouth out with water after inhaler use can reduce the risk of getting a fungal infection. Participants in the group receiving an additional explanation were told that the medication can get stuck in the back of the throat and allow fungi to grow, but water helps to wash the medication away (Table 1). In all groups, the scenario ended with the following statement: “The pharmacist tells you that there are five refills available on the prescription, and to call the pharmacy if you have any questions.” After reading the scenario, participants answered seven questions concerning their perception of the safety and effectiveness of the hypothetical medication. Participants were able to refer to the scenario while answering the questions.

The medication described in the scenario, Cradulox, is completely fictional. This was done to avoid potential biases amongst participants who may have used other medications in the past or know others who have. Asthma was chosen as the disease state for the study because it is a common disorder, affecting about 40 million people in the United States, including children and young adults as well as older individuals.²⁶ Fungal infection was the adverse effect chosen for the scenario to ensure clinical relevance because it is an actual adverse effect common to many asthma inhalers.

Measures

Two primary and four secondary outcome variables were assessed. Measures used to assess these variables were used in a previous study.²⁴ Results from that study support the construct validity of the measures.

Primary Outcome Variables.

The primary outcome variables were: (1) willingness to take the medication and (2) perceived medication safety. Willingness to take the medication was assessed by asking: “If you had asthma and your doctor prescribed this medication for you, how likely is it that you would take it?” Participants answered on a 7-point scale ranging from *Very Unlikely* to *Very Likely*. Participants were also asked: “What is the most important reason for how likely or unlikely you would be to take this medication?” The following options were provided: (a) *the adverse events are not very serious*, (b) *any serious adverse events are very unlikely*, (c) *prefer to avoid taking medications and will do something else*, (d) *a lot of people will get fungal infections and I don’t want to be one of them*, (e) *I would like to get rid of the wheezing and shortness of breath*, and (f) *none of the above*. This measure was modeled after a question developed by Peters et al.¹⁶ Perceived medication safety was assessed by asking: “How safe or dangerous is this medication?” Participants answered on a 7-point scale ranging from *Very Safe* to *Very Dangerous*.

Secondary Outcome Variables.

Four secondary outcome variables were assessed. First, participants were asked to respond to the following statement: “The potential benefits of taking this medication outweigh the potential risks.” Responses were recorded on a 7-point scale ranging from *Strongly Agree* to *Strongly Disagree*. Next, participants were asked, “If you had asthma and took this medication, how likely is the medication to help you?” Responses were recorded on a 7-point scale ranging from *Very Likely* to *Very Unlikely*. The final two variables used the same response scale, and were as follows: “If you had asthma and took this medication, how likely is the medication to cause side effects?” and “How likely are you to recommend this medication to somebody else with asthma?” The latter variable was included because people taking medications often make

recommendations to friends and family members regarding their own experience with different medications, especially concerning effectiveness and adverse effects.

Demographics.

The following demographic information was assessed: age, gender, race, education, and status as a healthcare provider. Healthcare provider status was assessed to ensure that these individuals were not overrepresented in the sample, as they likely have greater knowledge of both asthma and anti-asthma medications compared to the general public, which could bias study findings. In addition, participants were asked to rate their own overall health, with the options being *poor*, *fair*, *good*, *very good*, or *excellent*. They were also asked whether they were currently taking a prescription medication regularly and whether they had ever had a serious side effect from a medication.

Manipulation Check Questions.

The final three items in the survey were designed as manipulation checks. Participants were not able to view the scenario when answering these questions. First, participants were asked: “If 100 people used Cradulox, how many do you think would develop a fungal infection of the throat.” Second, participants were asked to respond to the following statement: “There are things that people can do to reduce the risk of developing a fungal infection when using Cradulox.” Responses were recorded on a 7-point scale ranging from *Strongly Agree* to *Strongly Disagree*. Finally, participants were asked, “Which of the following is most likely to reduce the risk of developing a fungal infection when using Cradulox?” The available choices were (a) *taking the medication with food*, (b) *rinsing your mouth out with cool water following use*, (c) *using the medication at night prior to bedtime*, and (d) *none of the above*.

Statistical Analysis

All analyses were completed using PC-SAS version 9.4 (SAS Institute Inc., 2013). Descriptive statistics were used to summarize the participant characteristics. Student t-tests and chi-square tests were conducted to determine if the experimental groups differed with respect to any of the demographic characteristics assessed. To determine the effectiveness of the experimental manipulations, the percentage of participants in the low and high probability conditions who responded correctly to the question asking, “If 100 people used Cradulox, how many do you think would develop a fungal infection of the throat?” were calculated (Note: Because this analysis assessed participant recollection of the probability information included in the experimental manipulation, participants who received no probability information were not included in this analysis). The “correct” answer corresponded to participants’ group assignment and differed for those in the low and high probability conditions (i.e. 5 out of 100 people or 20 out of 100 people were considered correct answers, respectively). The percentage of participants in each group who correctly responded that the risk of fungal infections could be reduced by rinsing one’s mouth out with cool water following use was also calculated. Linear regression was used to assess the effect of the two experimental conditions (i.e. probability of fungal infections and prevention information to reduce risk) on the primary and secondary outcome variables. A separate regression model was run for each outcome variable. Each model included a term indexing the multiplicative interaction between the two experimental conditions. If the interaction term was not statistically significant, the model was rerun with the interaction term deleted. Significant main effects were followed up using the Newman-Keuls method to evaluate between group differences while controlling for the inflation of Type I error when making multiple comparisons.²⁷ Power analyses indicated that a sample size of 601 provides over 80% power to detect a small sized effect (SD=0.2) with alpha (2-tailed) set at 0.05.²⁸

Results

Demographics

The mean age of participants ($n = 601$) was 33 years ($SD = 10.9$) and most identified as white (78.2%), male (60.1%), and 52.1% had a bachelor's degree or higher. Participants reported their health as poor (1.8%), fair (9.3%), good (29.6%), very good (41.8%), or excellent (17.5%). Only 22 participants (3.7%) identified themselves as a healthcare professional. About a quarter (26.8%) of participants reported using a regular prescription medication, and 16% reported having experienced a serious side effect from a medication. None of the participant characteristics differed significantly across the experimental conditions.

Manipulation Checks

A total of 169 (87.6%) participants in the high probability group correctly answered that 20 out of 100 people would develop a fungal infection when using Cradulox. Likewise, 179 (86.9%) participants in the low probability group correctly answered that 5 out of 100 people would develop an infection. Among participants who were not given any probability information, the median probability estimate was 5.0 (Mean = 12.4, $SD = 15.3$, $IQR=3.0-15.0$).

Participants given prevention information or prevention information plus an explanation were more likely to agree that there are things people can do to reduce the risk of developing a fungal infection when using Cradulox, with means of 5.3 and 5.4, respectively, compared to 2.9 in the no prevention information group ($F(2,598)=322.38$, $p < 0.0001$). Almost all participants who were given either prevention information (96.7%) or prevention information plus an explanation (97.5%) correctly indicated that the risk of developing a fungal infection while using Cradulox could be reduced by rinsing one's mouth with cool water following use. Of the participants given no prevention information, 38.7% answered correctly.

Assessment of Interactions

The interaction between the two experimental conditions (probability of fungal infection and prevention information) was not statistically significant for any of the primary or secondary outcome variables. However the interaction terms approached statistical significance for both of the primary outcome variables: willingness to take the medication ($F(4,592)=1.83$, $p=0.12$) and perceived medication safety ($F(4,592)=1.68$, $p=0.15$). Therefore, to explore the nature of these possible interactions, the sample was stratified by the type of prevention information provided (i.e., none, prevention information only, prevention information plus explanation). As shown in Figure 1, among individuals who were given no prevention information, participants who were told that the risk of fungal infection was 20% reported being less willing to take the medication and perceived the medication as less safe compared to those who were told that the risk of fungal infection was 5% (Willingness to Take: Means \pm SE = 3.61 ± 0.20 versus 4.79 ± 0.19 , $p < 0.0001$, respectively; Medication Safety: Means \pm SE= 3.45 ± 0.15 versus 4.32 ± 0.13 , $p < 0.0001$). Similarly, among individuals who were given prevention information combined with an explanation, participants who were told that the risk of fungal infection was 20% reported being less willing to take the medication and perceived the medication as less safe compared to those who were told that the risk of fungal infection was 5% (Willingness to Take: Means \pm SE = 4.40 ± 0.20 versus 5.08 ± 0.17 , $p = 0.01$, respectively; Medication Safety: Means \pm SE= 3.90 ± 0.15 versus 4.47 ± 0.14 , $p = .01$). However, among individuals who were given prevention information only, there was little difference between participants who were told that the risk of fungal infection was 20% versus 5% on either of these variables (Willingness to Take: Means \pm SE = 4.66 ± 0.17 versus 4.98 ± 0.14 , $p= 0.15$, respectively; Medication Safety: Means \pm SE= 4.17 ± 0.13 versus 4.46 ± 0.11 , $p =0.10$).

Main Effect of Probability Information

Linear regression analysis showed that probability of occurrence was a significant predictor of willingness to take the medication ($F(2,596) = 12.86, p < 0.0001$) and perceived medication safety ($F(2,596) = 13.11, p < 0.0001$) (see Table 2). Consistent with study hypotheses, participants were significantly less willing to take the medication when a high adverse effect probability was given compared to a low probability or no probability. Participants were significantly more likely to perceive the medication as safe in the low probability condition compared to the high probability and no probability condition. Linear regression analyses showed that probability was also a significant predictor of the belief that medication benefits outweigh risks ($F(2,596) = 9.55, p < 0.0001$), likelihood of the medication helping ($F(2,596) = 3.63, p < 0.05$), likelihood of the medication causing side effects ($F(2,596) = 45.2, p < 0.0001$), and likelihood of recommending the medication to others ($F(2,596) = 9.2, p = 0.0001$). Participants in the high probability condition were less likely than those in the other two groups to agree that benefits outweigh the risks and that the medication was less likely to help. Participants in the low probability condition thought the medication was less likely to cause side effects and were more likely to recommend it to others compared to participants in the other two groups (see Table 2).

Main Effect of Prevention Strategy Information

Linear regression analysis showed that prevention strategy information was a significant predictor of willingness to take the medication ($F(2,596) = 11.78, p < 0.0001$) and perceived medication safety ($F(2,596) = 11.17, p < 0.0001$) (Table 3). Consistent with study hypotheses, participants were significantly less willing to take the medication when no prevention strategy was given compared to prevention information with or without an explanation. Participants

perceived the medication as least safe when no prevention strategy was given and safest when prevention strategy information was given. Participants who received a prevention strategy plus an explanation perceived the medication as safer than those who received no information but less safe than those who received prevention information only. Linear regression analyses also showed that prevention strategy information was a significant predictor for the belief that medication benefits outweigh risks ($F(2,596) = 12.03, p < 0.0001$) and the likelihood of recommending the medication to others ($F(2,596) = 7.61, p = 0.0005$). Participants not given any prevention information were less likely to consider that the benefits of the medication outweigh the risks compared to participants in the other two groups. Participants not given any prevention information were also significantly less likely to recommend the medication to others compared to participants in the other two groups. There were no significant differences among the three groups for perceived likelihood of the medication helping or the likelihood of experiencing medication side-effects (see Table 3).

Reasons for Willingness to Take the Medication

Table 4 shows the reasons participants gave for being likely or unlikely to use the medication. Only three of the six reasons revealed significant differences between groups. Participants in the low probability condition were more likely to select *any serious adverse events are very unlikely* as their reason ($\chi^2(2) = 12.39, p = 0.002$) compared to participants in the other two probability groups. Participants in the high probability condition were more likely than either of the other conditions to select *a lot of people will get fungal infections and I don't want to be one of them* ($\chi^2(2) = 16.96, p = 0.0002$). Participants given prevention information plus an explanation were most likely to choose *the adverse events are not very serious* as their reasoning for how likely or unlikely they would be to take the medication, followed by participants given

only prevention information ($\chi^2(2) = 18.08, p < 0.0001$). Participants not given any prevention information were more likely to choose *a lot of people will get fungal infections and I don't want to be one of them* as their reasoning ($\chi^2(2) = 18.97, p < 0.0001$). There were no significant between group differences among participants selecting *prefer to avoid taking medications and will do something else, I would like to get rid of the wheezing and shortness of breath*, and *none of the above*.

Discussion

The vast majority of past research on medication risk communication has focused on how probabilistic information is best conveyed. Much less attention has been given to other risk dimensions that may be equally or more important such as severity and controllability.^{15,29,30} The study reported in this paper was designed to address this knowledge gap by examining how information concerning precautions patients can take to reduce the risk of adverse effects may influence willingness to use a medication and perceptions of medication safety. This focus was based on two factors. First, if patients adopt recommended precautions while using a prescribed medication, their objective risk of experiencing adverse effects should be reduced and this may be reflected in perceived risk as well. Second, educating patients about safety precautions is likely to enhance perceptions of the extent to which the risk is controllable. This is important because past research has demonstrated an inverse association between perceived controllability and perceived risk.³¹

Most study hypotheses were at least partially supported. First, it was predicted that individuals who were told that a hypothetical medication can cause fungal infections of the throat without being given any probability information would be less willing to take the medication and perceive it as less safe compared to individuals who were told that the risk was either 5% or

20%. However, it was found that the mean for all of the outcome variables in the group that was given no probability information fell between the means observed in the high and low probability groups. Further, although individuals who received no probability information reported being as likely to take the medication as individuals in the low probability group, they perceived the medication as less safe. These findings suggest that, while patients may agree to take a medication even if they are not told the probability of adverse effects, they might have residual concerns about medication safety that, in real-life situations, could manifest as premature medication discontinuation or lower adherence rates.³²⁻³⁸ Research suggests that health care providers rarely provide quantitative probability information when counseling patients.²⁹ In addition, most of the written information provided to patients in the United States simply lists possible adverse effects, without providing any probability information. However, written medication information provided to patients in the European Union does include this type of information.³⁹ Research is needed to determine if these different types of information formats have differential effects on real-life judgment and decision-making.

Second, participants who received information concerning the prevention of fungal infections, with or without an explanation of how the prevention strategy worked, reported being more willing to use the medication than participants who were not given this type of information. However, participants who received an explanation of how the prevention strategy worked rated the medication as less safe compared to those who were given prevention information alone. This may be because the explanation made the possibility of experiencing a fungal infection more salient to participants as they completed the questionnaire. Nonetheless, participants who received the explanation were more likely than those in the other two groups to indicate that their primary reason for being willing to take the medication was that the adverse effects were not

very serious. These findings highlight the complexity of the risk communication process, and there is no previous research that has examined the impact of precaution information on medication risk perception. Thus, more research is needed to better understand how patients interpret information concerning the prevention of adverse events and how they utilize this information when making judgments and decisions concerning medication use.

Third, although not statistically significant, the findings suggested the possibility of an interaction between information concerning the probability of experiencing an adverse effect and provision of information on how to reduce the risk of experiencing the effect. Consistent with study hypotheses, provision of risk prevention information reduced the effect of variation in the probability of the adverse effect (i.e., 5% versus 20%) on both willingness to use the medication and perceived medication safety. These findings must be interpreted cautiously. However, they underscore the need for research that attempts to better understand how communication about different risk dimensions (e.g., probability, severity, controllability) interact with one another. It is also important to examine the effect of preexisting beliefs on risk information processing. In the same way that individuals have mental representations of illnesses,⁴⁰ they also have mental representations of treatment options, including medications.³²⁻³⁵ Research suggests that judgment and decision making is influenced most by those memory representations that are activated by characteristics of the decision-making context (e.g., environmental cues).²¹ Thus, it seems likely that the impact of medication risk communications depends on a combination of (1) the information explicitly provided and (2) individuals' preexisting mental representations, rather than either of these factors in isolation.

Finally, individuals who were told that the risk of fungal infection was 20% rated the medication as less likely to help than individuals in the other two groups. Although unexpected,

this finding is consistent with previous research that has demonstrated an inverse association between perceived risk and perceived benefits.³¹

Limitations

This study has several limitations that should be noted. First, real patients were not studied. Participants were recruited through a crowdsourcing internet marketplace and most were fairly young, relatively healthy, and well-educated. Thus, the generalizability of the study findings to a more typical patient population remains open to question. Second, participants read a hypothetical scenario that provided a limited amount of information. In an actual counseling session, pharmacists have the opportunity to tailor information on the basis of patient characteristics and patients have the chance to ask questions if information the pharmacist provides is unclear. In addition, non-verbal communication can facilitate patient understanding, and the study methods did not allow for this type of effect. Finally, there may be differences among participant characteristics that influence risk perception and associated behaviors, such as tendency towards risk aversion, numeracy, and literacy skills. These were not assessed in this study.

Conclusion

Despite these limitations, the findings suggest that optimal risk communication involves far more than simply informing patients about possible adverse effects. Providing patients with a numerical estimate of the probability of experiencing specific adverse effects may reduce overestimation of risk probability and lead to greater acceptance of therapy and long-term adherence. But, counseling patients about strategies they can implement to reduce the risk of adverse effects may be equally or more important. Further research is needed to examine the effect of adverse effect counseling on medication adherence, ideally within the context of real

life clinical encounters. Ultimately, helping patients understand how to minimize medication risks may increase patient acceptance of therapeutic recommendations and lead to improved health outcomes.

ACCEPTED MANUSCRIPT

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Table 1. *Additional Information Presented to Participants in Scenario Depending on Experimental Condition*

Probability	Prevention Strategy		
	No Information	Prevention Strategy Only	Prevention Strategy Plus Explanation
No Information	—	He says that these infections can be prevented by rinsing your mouth out with cool water after you use it.	He says when the medication is inhaled, some of it gets stuck in the back of your throat and allows fungi to grow. Rinsing with water removes any of the medication stuck in your throat.
Low	He says that these infections occur in about 5% of people who use Cradulox.	He says that these infections occur in about 5% of people who use Cradulox, but they can be prevented by rinsing your mouth out with cool water after you use it.	He says that these infections occur in about 5% of people who use Cradulox, but they can be prevented by rinsing your mouth out with cool water after you use it. He says when the medication is inhaled, some of it gets stuck in the back of your throat and allows fungi to grow. Rinsing with water removes any of the medication stuck in your throat.
High	He says that these infections occur in about 20% of people who use Cradulox.	He says that these infections occur in about 20% of people who use Cradulox, but they can be prevented by rinsing your mouth out with cool water after you use it.	He says that these infections occur in about 20% of people who use Cradulox, but they can be prevented by rinsing your mouth out with cool water after you use it. He says when the medication is inhaled, some of it gets stuck in the back of your throat and allows fungi to grow. Rinsing with water removes any of the medication stuck in your throat.

Table 2. *Means (SE) for Outcome Variables by Type of Probability Information Received.*

Outcome Variable	No Probability	Low Probability	High Probability
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Likely to Take Medication	4.77 (1.46) ^a	4.95 (1.36) ^a	4.21 (1.59) ^b
Medication Safety	4.19 (1.16) ^a	4.42 (1.04) ^b	3.82 (1.19) ^c
Medication Benefits Outweigh Risks	4.56 (1.37) ^a	4.79 (1.33) ^a	4.19 (1.39) ^b
Medication Likely to Help	5.05 (0.90) ^a	5.11 (0.88) ^a	4.87 (0.95) ^b
Medication Likely to Cause Side Effects	2.69 (1.36) ^a	1.73 (1.38) ^b	2.95 (1.32) ^a
Likely to Recommend Medication	3.52 (1.51) ^a	3.89 (1.39) ^b	3.25 (1.59) ^a

Note: For each outcome variable, superscripts (a, b, c) are used to indicate which groups (i.e., No Probability, Low Probability, High Probability) differed from one another at $p \leq 0.05$. For each outcome variable, the means for groups that share a common superscript are not statistically different (i.e., $p > 0.05$). In contrast, the means for groups that have different superscripts are statistically different (i.e., $p \leq 0.05$).

Table 3. Means (SE) for Outcome Variables by Type of Prevention Information Received.

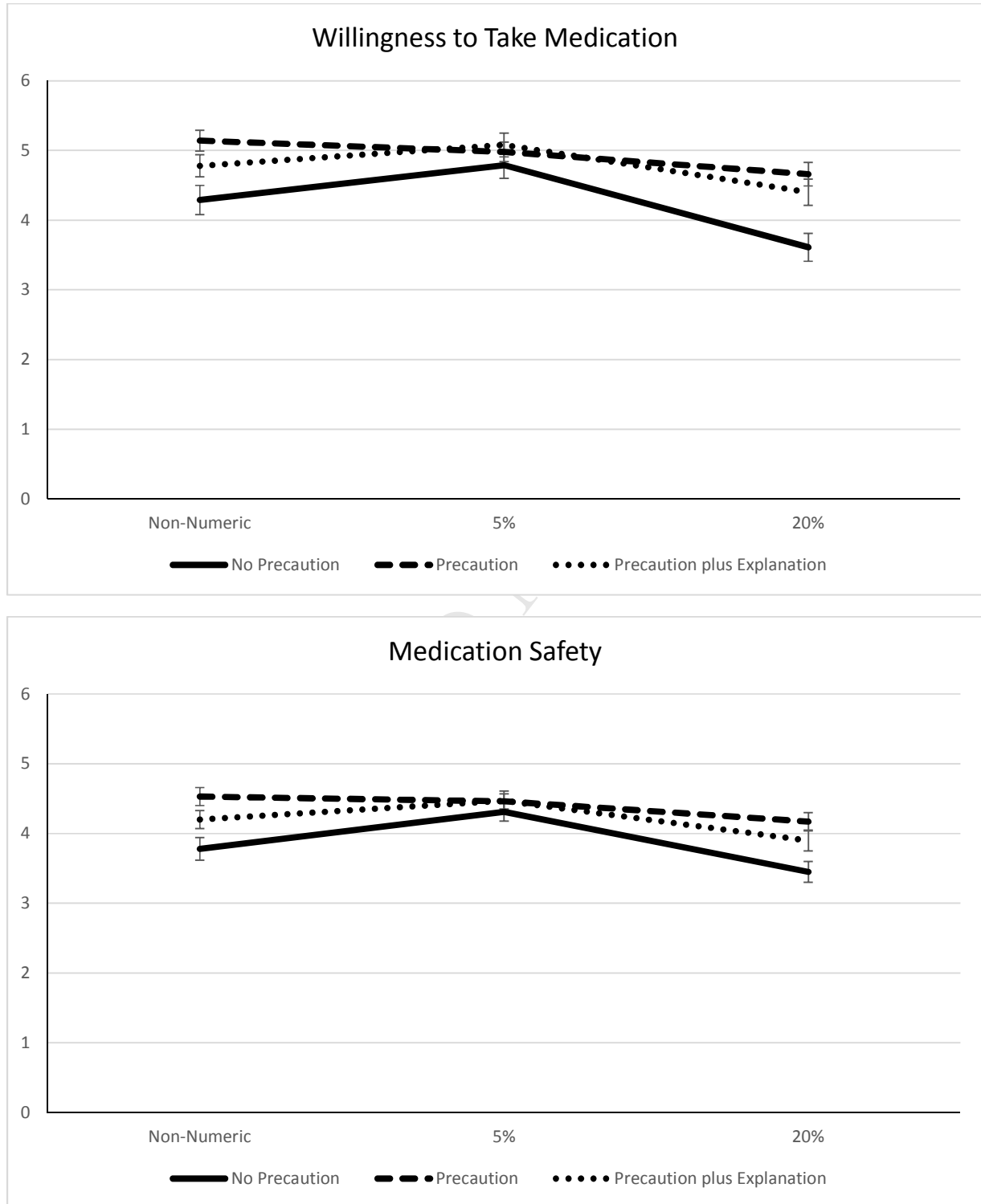
Outcome Variable	No Prevention Information	Prevention Information	Prevention Information and Rationale
Likely to Take Medication	4.23 (1.67) ^a	4.94 (1.27) ^b	4.75 (1.47) ^b
Medication Safety	3.85 (1.19) ^a	4.40 (1.05) ^b	4.17 (1.16) ^c
Medication Benefits Outweigh Risks	4.11 (1.46) ^a	4.71 (1.24) ^b	4.70 (1.38) ^b
Medication Likely to Help	4.90 (0.93) ^a	5.06 (0.86) ^a	5.06 (0.94) ^a
Medication Likely to Cause Side Effects	2.48 (1.42) ^a	2.39 (1.48) ^a	2.48 (1.45) ^a
Likely to Recommend Medication	3.21 (1.59) ^a	3.72 (1.47) ^b	3.74 (1.44) ^b

Note: For each outcome variable, superscripts (a, b, c) are used to indicate which groups (i.e., No Prevention Information, Prevention Information, Prevention Information and Rationale) differed from one another at $p \leq 0.05$. For each outcome variable, the means for groups that share a common superscript are not statistically different (i.e., $p > 0.05$). In contrast, the means for groups that have different superscripts are statistically different (i.e., $p \leq 0.05$).

Table 4. Most Important Reasons (%) for Willingness to Take Medication

Reason	Type of Probability Information Received			Type of Prevention Information Received		
	No Probability (N = 202)	Low Probability (N = 206)	High Probability (N = 193)	No Prevention Information (N = 191)	Prevention Information (N = 209)	Prevention Information and Explanation (N = 201)
The adverse events are not very serious	13.4 ^a	7.8 ^a	8.3 ^a	3.1 ^a	10.1 ^b	15.9 ^c
Any serious adverse events are unlikely	21.8 ^a	33.0 ^b	18.6 ^a	22.5 ^a	29.2 ^a	21.9 ^a
Prefer to avoid taking medications	9.4 ^a	8.2 ^a	9.8 ^a	7.3 ^a	8.1 ^a	11.9 ^a
A lot of people will get fungal infections	9.9 ^a	6.8 ^a	19.7 ^b	20.4 ^a	7.7 ^b	8.5 ^b
Would like to get rid of wheezing and shortness of breath	43.6 ^a	42.7 ^a	42.5 ^a	44.0 ^a	44.0 ^a	40.8 ^a
None of the above	2.0 ^a	1.5 ^a	1.0 ^a	2.6 ^a	1.0 ^a	1.0 ^a

Note: This table presents the percentage of participants who endorsed different reasons for either taking or not taking the hypothetical medication stratified by the two experimental conditions: *Type of Probability Information Received* and *Type of Prevention Information Received*. Within each condition, superscripts (a, b, c) are used to indicate which specific groups (e.g., No Probability versus Low Probability, No Probability versus High Probability, Low versus High Probability) differed from one another at $p \leq 0.05$. For each reason, differences between groups that share a common superscript are not statistically significant (i.e., $p > 0.05$); whereas, differences between groups that have different superscripts are statistically significant (i.e., $p \leq 0.05$).

Figure 1. *Interaction of Probability and Prevention Strategy Information*

- Participants were less willing to take the medication when the probability of an adverse effect occurring as high than if the probability was low or not given
- Participants perceived the medication as less safe when the probability of an adverse effect occurring as high than if the probability was low or not given
- Participants were more willing to take the medication when a prevention strategy was given than when no prevention strategy was given
- Participants perceived the medication as more safe when a prevention strategy was given than when no prevention strategy was given
- There was a non-statistically significant interaction between the probability and prevention strategy information such that giving the prevention information reduced the effect of variation in the probability on both willingness to use the medication and perceived medication safety