Effect of Counseling on Patient's Perception of Medication Risk

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Introduction

It is estimated that about 50% of the United States population has used at least one prescription drug within the previous month, and roughly 22% has used three or more (CDC website, 2015). 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 (Jackevicius, 2008). Other research has found that only 37% of patients are adherent to statin therapy (Wu, 2011) and only 66% to antidiabetic medications (Yeaw, 2009). High levels of medication adherence for long-term conditions can reduce rates of hospitalization and lower overall healthcare costs (Wu, 2011; Sokol, 2005). However, the question of how to increase medication adherence remains unanswered.

The World Health Organization identifies five factors contributing to medication nonadherence: economic, health-system, patient-related, condition-related, and therapy-related. Among therapy-related factors, adverse effects of the drug are a major obstacle (Sabate, 2003). The presence of adverse effects has been shown to decrease adherence to a wide variety of drugs, including glucocorticoids (Arena, 2010) and antidepressants (Weissman, 2012). Nearly all drugs carry the risk of unwanted side 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, or at least providing strategies to minimize or treat the adverse effects. Direct pharmacist counseling has been shown to lower the rate of preventable adverse drug events following hospital discharge (Schnipper, 2006). In addition, recent studies have shown pharmacist interventions and

counseling to yield improvements in adherence to lipid-lowering therapies (Hedegaard, 2015) and asthma inhalers (Naik-Panvelkar, 2015).

Along with proper counseling, it is critical that patients understand the relationship between the actual likelihood of an adverse effect occurring and the possibility of themselves experiencing the adverse effect after taking the drug. Knowing the risks associated with a drug are important for the patient to make an informed decision on whether or not they want to take a medication. Prior research has shown numerical adverse effect information to be easier for patients to accurately comprehend compared to non-numerical information (Peters, 2014; West, 2013). Patients tend to overestimate the likelihood of an adverse effect when given non-numerical information, such as "common" or "rare," compared to a percentage or ratio, such as "10% of patients" or "1 in 10 patients" (Knapp, 2005) and when given combined non-numerical and numerical information rather than numerical information alone (Knapp, 2015).

The objective of this study is to assess how two factors (the likelihood of the adverse effect occurring, and pharmacist counseling on prevention of an adverse effect) affect patients' perceptions of the safety of a newly prescribed medication and the likelihood that patients will take the medication. The study hypotheses were as follows: (1) individuals will be most willing to use the medication and will consider it safest when the probability of a side-effect is low, (2) individuals will be most willing to use the medication and consider it safest when counseling on how to prevent the side-effect is provided, and (3) there will be an interaction between the provision of probability and prevention information such that, among individuals given prevention information, perceptions of medication safety and willingness to use the medication will not be affected by the probability of experiencing the side-effect.

Materials and Methods

The study used a 3 x 3 experimental research design. 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., 5%, 20%, 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) (see 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 survey was created using Qualtrics software and study participants were recruited through Amazon Mechanical Turk. A total of 633 Mechanical Turk workers agreed to participate and accessed the survey. However, 32 individuals failed an attention check within the survey and were therefore excluded. 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. Study participants were adults aged 18 years or older and living in the United States. All data was collected on June 1, 2015.

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. (2014). 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?"

Demographics. The following demographic information was assessed: age, gender, race, education, and status as a healthcare provider. 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, we calculated 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?" The "correct" answer corresponded to participants' group assignment and differed for those in the low and high probability conditions. We also calculated 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. 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 via independent group t-tests to evaluate between group differences.

Results

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 (1.83%), fair (9.32%), 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 ($p < 0.0001$). 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.

Effect of Probability Information

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. Therefore, this section and the next section focus on the main effects of each condition.

Linear regression analysis showed that probability of occurrence was a significant predictor of willingness to take the medication ($F = 12.86$, $p < 0.0001$) and perceived medication safety ($F = 13.11$, $p < 0.0001$) (see Table 2). Consistent with study hypotheses, participants were significantly less willing to take the medication when a high side-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 ($F = 9.55$, $p < 0.0001$), likelihood of the medication helping ($F = 3.63$, $p < 0.05$), likelihood of the medication causing side effects ($F = 45.2$, $p < 0.0001$), and likelihood of recommending the medication to others ($F = 9.2$, $p = 0.0001$). 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).

Effect of Prevention Strategy Information

Linear regression analysis showed that prevention strategy information was a significant predictor of willingness to take the medication ($F = 11.78$, $p < 0.0001$) and perceived medication safety ($F = 11.17$, $p < 0.0001$) (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 just received prevention information. Linear regression analyses also showed that prevention strategy information was a significant predictor for the belief that medication benefits outweigh risks ($F = 12.03$, $p < 0.0001$) and the likelihood of recommending

the medication to others (F = 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 between group differences. Participants in the low probability condition were more likely to select *any serious adverse events are very unlikely* as their reason ($x^2(2)$ = 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* ($x^2(2)$ = 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 just prevention information ($x^2(2)$ = 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 ($x^2(2)$ = 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

Several important findings emerged from this study. First, the mean for all of the outcome variables in the group that was given no information regarding the probability of experiencing a fungal infection fell between the means observed in the high and low probability groups. Compared to participants in the low probability group, participants who received no probability information were less likely to: consider the medication safe, recommend the medication to others, and indicate that the low likelihood of serious adverse events was their primary reason for being willing to take the medication. They were also more likely than those in the low probability group to think the medication would cause side effects; however, they were not less willing to take the medication. These inconsistent findings may reflect uncertainty regarding the likelihood of adverse effects among those who received no probability information in this study, and it also shows that other factors are likely involved in patient decision-making regarding medication use. It is important to note that in real life practice, patients are rarely given numerical information regarding the likelihood of adverse effects. Therefore, the information given to participants in the non-numeric group most closely resembles that given to actual patients. Our 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. In real life, this concern could manifest as premature medication discontinuation or lower adherence rates. This suggests that more specific counseling may be helpful for patients to correctly self-assess their own risk of experiencing adverse effects when taking a medication. This may be especially beneficial to those with adequate health literacy. Future research should examine whether providing patients with information concerning the probability of medication side-effects prior to the initiation of therapy leads to greater long-term adherence.

Second, providing participants with information concerning the prevention of fungal infections resulted in participants: being more willing to use the medication, perceiving that the medication was safer, indicating that medication benefits outweighed the risks, and being more likely to recommend the medication to others. As expected, prevention information had no effect on how likely the medication was perceived to help, as these two factors are unrelated. Providing prevention information also did not change the perceived likelihood of the medication causing side effects. Most likely this is because all participants except those in the non-numeric condition were given explicit information regarding the probability of the side-effect occurring. Although it is impossible for physicians and pharmacists to discuss every potential side-effect with patients, discussing prevention strategies for the more common side effects may be beneficial.

Third, addition of an explanation for how the prevention strategy works affected only one of the outcome variables and this effect was in the opposite direction of that expected. That is, participants rated the medication as safer when an explanation was not given and only prevention information was provided. 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. It is possible this additional information may in fact be beneficial to patients with higher health literacy, and detrimental to those with lower health literacy. 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.

Prior research comparing non-numerical information on adverse effect likelihood to numerical information showed that subjects given non-numerical information tend to be less willing to use a medication and more likely to overestimate the likelihood of the adverse effect (Blalock, 2016; Peters, 2014; Berry, 2004). Other research has assessed the combination of numerical and non-numerical information and found an overestimation of risk (Knapp, 2015). The present study took a different approach to previous research designs and compared the provision of numerical information to simply mentioning an adverse effect as being possible, which is consistent with most written medication information given to patients in the United States. We found that most participants in the non-numeric group estimated the likelihood of experiencing a fungal infection as between 3% and 15%. Additional research is needed to determine if, in the absence of numerical information, perceived probability estimates vary as a function of medication, adverse effect of interest, and patient characteristics.

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 our study methods did not allow us to capture these types of effects.

Despite these limitations, our findings suggest that providing patients with information regarding the probability of adverse effects and strategies to minimize potential risks may have a

significant, beneficial impact on patient perceptions of medication safety and their willingness to use a medication. It is already known that pharmacists are well-suited to help improve medication adherence and health outcomes. Prior research has shown that pharmacist-driven interventions can improve cardiovascular medication use, reduce cardiovascular-related medical expenses, and improve cardiovascular risk factors such as systolic and diastolic blood pressure (Bunting, 2008). Similar beneficial outcomes have been demonstrated with diabetes (Cranor, 2003) and asthma (Bunting, 2006), as well. Further research is needed to specifically address 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 enhance long-term adherence, leading to improved health outcomes.

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 Probability Condition.*

Outcome Variable	No Probability	Low Probability	High Probability
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: conditions with different superscripts ('a', 'b', 'c') are significantly different from one another ($p < 0.05$).

Table 3. *Means (SE) for Outcome Variables by Prevention Information Condition.*

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)	5.06 (0.86)	5.06 (0.94)
Medication Likely to Cause Side Effects	2.48 (1.42)	2.39 (1.48)	2.48 (1.45)
Likely to Recommend Medication	3.21 (1.59)[a]	3.72 (1.47)[b]	3.74 (1.44)[b]

Note: conditions with different superscripts ('a', 'b', 'c') are significantly different from one another ($p < 0.05$).

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

Reason	Probability Condition			Prevention Information Condition		
	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	13.37	7.77	8.29	3.14[a]	10.05[b]	15.92[c]
Any serious adverse events are unlikely	21.78[a]	33.01[b]	18.65[a]	22.51	29.19	21.89
Prefer to avoid taking medications	9.41	8.25	9.84	7.33	8.13	11.94
A lot of people will get fungal infections	9.90[a]	6.80[a]	19.69[b]	20.42[a]	7.66[b]	8.46[b]
Would like to get rid of wheezing and shortness of breath	43.56	42.72	42.49	44.02	43.98	40.80
None of the above	1.98	1.46	1.04	2.62	0.96	1.00

Note: conditions with different superscripts ('a', 'b', 'c') are significantly different from one another ($p < 0.05$).

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