Communicating Information Concerning Potential Medication Harms and Benefits:

What gist do numbers convey?

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**Abstract**

**Objectives:** Fuzzy trace theory was used to examine the effect of information concerning medication benefits and side-effects on willingness to use a hypothetical medication.

**Methods:** Participants (N=999) were recruited via Amazon Mechanical Turk. Using 3 x 5 experimental research design, each participant viewed information about medication side effects in 1 of 3 formats and information about medication benefits in 1 of 5 formats. For both side-effects and benefits, one format presented only non-numeric information and the remaining formats presented numeric information. **Results:** Individuals in the non-numeric side-effect condition were less likely to take the medication than those in the numeric conditions (p < 0.0001). In contrast, individuals in the non-numeric benefit condition were more likely to take the medication than those in the numeric conditions (p < 0.0001). **Conclusions:** Our findings suggest that non-numeric side-effect information conveys the gist that the medication can cause harm, decreasing willingness to use the medication; whereas non-numeric benefit information has the opposite effect. **Practice Implications:** Presenting side-effect and benefit information in non-numeric format appears to bias decision-making in opposite directions. Providing numeric information for both benefits and side-effects may enhance decision-making. However, providing numeric benefit information may decrease adherence, creating ethical dilemmas for providers.

**1. Introduction**

Medications play an important role in the management of many acute and chronic health conditions. Global spending for medications was estimated at $989 Billion (US$) in 2013 and is projected to reach $1.3 Trillion in 2018 [1]. Used appropriately, medications can reduce morbidity and mortality rates. However, all medications also have the potential to cause harm (e.g., unpleasant side effects, allergic reactions) and most carry some risk of serious adverse effects. Principles of informed consent, informed and shared decision-making, and professional ethics all emphasize the importance of patients’ understanding the potential harms and benefits of recommended therapies [2-5]. To help achieve this goal, many countries require that patients be given written medication information (WMI), usually in leaflet form, when they obtain a licensed medication [6-8]. However, patients often have difficulty understanding and using this information [9-12].

In the US and across the European Union, most WMI provided to patients with prescription medications contains limited information on the probability of harms and benefits. For example, information available for atorvastatin in the USA, a medication used to treat hypercholesterolemia, contains the statement: *“This drug may cause muscle pain, tenderness, or weakness. Sometimes, a very bad muscle problem may happen that may lead to kidney problems. Rarely, deaths have happened in people who get these problems when taking drugs like this one.”*[13] However, the probability of these events is not provided. Similarly, limited numeric information is typically provided on the probability of benefit. For example, the same WMI for atorvastatin contains the header “*What is this drug used for*?” followed by a list of bullet points that include “It is used to prevent heart attacks” and “It is used to prevent strokes.” However, no information is provided about the extent to which the risk of heart attacks and strokes is reduced by using this medication. In countries of the European Union, most WMI contain some numeric information for medication harms, but still lack numeric benefit information [14, 15].

Efforts are ongoing in many countries to improve the usability of WMI [16-19]. Considerable research has examined the effect that different message formats have on comprehension of harms and benefits; on risk perceptions; and on behavioral intentions [20, 21]. People are more likely to overestimate medication harms when presented using a non-numeric format rather than a numeric one [22-27]. Another study demonstrated that provision of numeric information increases willingness to use a hypothetical medication compared to non-numeric formats [28]. However, there is no consensus concerning the best numeric format to use [21, 29]. Much less research has focused on how to best convey information about medication benefits, although there is evidence that patients tend to overestimate the likelihood of benefit [30, 31]. Another study found that providing numeric information on medication benefits corrected overestimates and reduced willingness to use the medication [32].

Much of the research on medication harm and benefit communication has been atheoretical [29]. Consequently, it is hard to explain why people appear to overestimate medication harms and benefits in the absence of numeric information. In this paper, we report the results of a study designed to test predictions derived from *fuzzy trace theory* (FTT) concerning the differential effects of numeric and non-numeric information about medication harms and benefits on willingness to use a medication and perceptions of safety and effectiveness [33-35]. Briefly, FTT is a dual-process model of memory, reasoning, judgment and decision-making that has been used to study how people make decisions involving uncertainty. FTT posits that, when an individual is exposed to any meaningful stimulus (e.g., WMI), two types of representations are encoded in memory, a verbatim representation and one or more gist representations. Verbatim representations capture the exact words, numbers, or images included in the stimulus, whereas gist representations capture the essential, bottom-line meaning of the stimulus to the person, including its emotional meaning [33]. Multiple gist representations may be encoded in response to the same stimulus, including relatively crude categorical gist representations (e.g., that the medication may cause serious side effects) and somewhat more precise ordinal gist representations (e.g., the risk of the medication causing serious side effects is low). A central tenet of FTT is that gist representations are retained in memory longer than verbatim representations and are more easily accessed when needed to make decisions. Therefore, when making judgments and decisions, people tend to rely on gist representations, unless the task requires recall of more precise information.

Within the context of the current study, FTT predicts that when individuals are presented with non-numeric side effect information, they are likely to form the categorical gist representation that taking the medication can cause harm, leading to risk avoidance (i.e., reduced willingness to use the medication). In contrast, when individuals are presented with non-numeric benefit information, FTT predicts that they are likely to form the categorical gist representation that taking the medication can help, leading to greater willingness to use the medication. Addition of numbers to the format allows individuals to extract somewhat more precise gist representations (e.g., not everyone who takes the medication is harmed or benefits from treatment). In the case of side-effect information, this more precise gist representation would promote greater willingness to use the medication; but, numeric benefit information would have the opposite effect. To test these predictions, we presented individuals with written information concerning the potential harms and benefits associated with a hypothetical medication used to treat high cholesterol. The format of the information was varied systematically across experimental groups. Participants received information either in a numeric or a non-numeric format. In addition, the numeric formats varied the probability of medication harms and benefits. Based on FTT, we predicted that individuals would be less willing to use the medication when (1) harms were presented in non-numeric format and (2) benefits were presented in numeric format. We also predicted that willingness to take the medication would not vary as a function of the probability of either medication harms or benefits. Thus, we are suggesting the difference in how people respond to numeric versus non-numeric harm and benefit information is a function of the *presence* of numbers in the numeric format rather than their precise value..

**2. Materials and Methods**

To recruit participants, we posted a link to the survey on Amazon Mechanical Turk (www.mturk.com) [36]. The title of the survey link was “Answer a survey about prescription medication information.” A total of 1,070 individuals accessed the link to the survey, which was administered via Qualtrics® software, and agreed to participate in the study. However, 71 of these individuals failed an attention check question that appeared as the second question in the survey – and we removed these participants from the sample. Thus a total of 999 individuals completed the survey. All participants were paid fifty US cents for completing the survey, undertaken on May 13, 2015.

**2.1 Experimental Materials**

The study used a 3 x 5 experimental research design with participants randomized to condition. The experimental materials used were adapted from Peters and colleagues [28]. All participants were told: *“Imagine that you have been diagnosed with high cholesterol, a major cause of heart disease and stroke. Your doctor has prescribed you a new medication to lower your cholesterol. It can reduce your risk of having a heart attack or stroke, but it has possible side effects. The table below shows how the medication can help and the possible side effects the medication can cause.”* Each participant viewed information about medication side effects (SE) in 1 of 3 probability-format conditions and medication benefits in 1 of 5 probability-format conditions. The 3 side-effect conditions were:

1. Low SE Probability, Numeric Format;
2. High SE Probability, Numeric Format; and
3. Non-numeric Format.

The 5 benefit conditions were:

1. Low Benefit Probability, Risk With and Without Treatment Numeric Format;
2. High Benefit Probability, Risk With and Without Treatment Numeric Format;
3. Low Benefit Probability, Risk Difference Numeric Format;
4. High Benefit Probability, Risk Difference Numeric Format; and
5. Non-numeric Benefit Format.

The frequency of potential harms shown in the high SE probability condition were the same as those used by Peters and colleagues except that the risk of the rare serious side-effect (i.e., rhabdomyolysis) was doubled (i.e., 2 rather than 1) to avoid the need for fractions in the low SE probability condition. The benefit information described the effect of the medication in reducing the risk of heart attack or stroke and we used a relevant meta-analysis of trials, to estimate the values in the low benefit probability conditions [37]. The estimated benefit was doubled in the high benefit conditions. As an example, Figure 1 shows the information presented in the *High* *SE Probability, Numeric Format─High Benefit Probability, Risk Difference Numeric Format* condition. Table 1 provides a description of the information corresponding to each experimental condition.

**2.2 Measures**

**2.2.1 Outcome variables.** Willingness to take the medication was the primary outcome variable, assessed by asking: *“If you had high cholesterol and your doctor prescribed this medication for you, how likely is it that you would take it?”* Responses were recorded on a 7-point scale ranging from 0=*Very unlikely* to 6=*Very likely*. Participants were also asked to indicate the most important reason for their response using an established measure [XX]. Options provided were: a) most of 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) there are too many possible adverse events; e) a lot of people will experience at least one of the adverse events, and I don't want to be one of them; f) the very serious muscle damage; g) other; and h) none of the above.

Five secondary outcome variables were assessed. First, participants were asked to agree or disagree with the statement, *“The potential benefits of taking this medication outweigh the potential risks”,* responding on a 7-point scale (0=*Strongly disagree* to 6=*Strongly agree)*. Second, participants were asked *“How safe or dangerous is this medication?”* (0=*Very dangerous* to 6=*Very safe)*. Third, participants were asked *“If you had high cholesterol and took this medication, how likely is the medication to help you?”* Fourth, participants were asked *“If you had high cholesterol and took this medication, how likely is the medication to cause side effects?”* Finally, *“How likely are you to recommend this medication to somebody else with high cholesterol?”* These last three questions were all answered on scales, 0=*Very unlikely* to 6=*Very likely*.

**2.2.2 Health and Medication Use.** Perceived health status was assessed on a 5-point scale (1=*Poor* to 5=*Excellent)*. Participants were also asked if they were currently taking prescription medications (Yes/No) and whether they had ever experienced a serious medication side effect (Yes/No).

**2.2.3 Demographic characteristics.** The following socio-demographic characteristics were assessed: age (in years), gender, race (dichotomized as White/Nonwhite), education (dichotomized as University Graduate/ Not University Graduate), and self-identified as a health care provider (Yes/No).

**2.3 Statistical Analysis**

All analyses were performed using PC-SAS version 9.4[38]. Descriptive statistics were used to summarize participant characteristics. Linear regression was used to assess the effect of numeric versus non-numeric side-effect and benefit information on the outcome variables. A separate model was used for each outcome variable. Each regression model controlled for age, gender, race, education, health status, current medication use, and experience of serious medication side-effects. We also tested for an interaction between the risk and benefit information conditions by adding a multiplicative interaction term to each model. Pairwise comparisons examined mean differences on the outcome variables among the three risk and five benefit conditions. Statistical significance was set at alpha error = 0.05.

**3. Results**

The mean age of participants (N=999) was 33.9 (SD=11.1). Most participants were male (56.4%), white (73.3%), and had graduated from university (56.2%). The percentage of participants reporting being in excellent, very good, good, fair, and poor health were 11.6, 39.5, 35.0, 11.4, and 2.4, respectively. About one-third (31.3%) of participants were currently using a prescription medication and 19.7% reported ever experiencing a serious medication side-effect. None of these variables differed significantly across the experimental conditions.

**3.1 Differences between Numeric versus Non-Numeric Conditions**

In regression analyses, the interaction between the side-effect and benefit format conditions was not statistically significant for any of the outcome variables examined. Therefore, only main effects of the conditions were examined. As predicted, individuals in both numeric side-effect conditions reported being more likely to take the medication, compared to those in the non-numeric side-effect condition (Table 2 and Figure 2). This pattern was replicated for all five secondary outcomes, with individuals in both numeric side-effect conditions reporting more favorable beliefs toward medication use compared to individuals in the non-numeric side-effect condition.

Also as predicted, individuals in all the numeric benefit conditions reported being less likely to take the medication compared to those in the non-numeric benefit condition (Table 2 and Figure 3). However, the difference between the *High Benefit, Risk With and Without Treatment* condition and the non-numeric benefit condition was not statistically significant. In addition, compared to individuals in each of the numeric benefit conditions, individuals in the non-numeric condition reported that the medication was more likely to help, were more likely to agree that medication benefits outweigh the risks, and were more likely to say they would recommend the medication to others. This pattern was not replicated for two of the secondary outcome variables: medication safety and likelihood of causing side-effects. However, one would expect these variables to be less affected by the format of medication benefit information.

**3.2 Differences among the Numeric Side-Effect/Benefit Conditions**

No differences were found between the low and high numeric side-effect conditions for any of the outcome variables (Figure 2). However, some differences were observed among the numeric benefit conditions (Figure 3). First, individuals in the *High Benefit, Risk With and Without Treatment* condition reported that the medication was more likely to help, compared to individuals in the other numeric benefit conditions. Second, compared to individuals in both *Low Benefit* conditions, individuals in the *High Benefit, Risk With and Without Treatment* condition reported being more likely to take the medication and to recommend the medication to others, and were more likely to agree that medication benefits outweigh the risks. In contrast, no differences on any of the outcome variables were observed between the *High* versus *Low Benefit, Risk Difference* conditions.

**3.3 Relationship between Socio-Demographic Characteristics and Outcome Variables**

As shown in Table 2, several socio-demographic characteristics were significant predictors of the outcome variables. The strongest associations involved race and current medication use. Compared to non-white participants, white participants reported being more likely to take the medication, perceived the medication as safer, and were less likely to believe that the medication would cause side-effects. Compared to participants who were not currently using any medications, current medication users reported being more likely to use the medication, perceived the medication as safer, were more likely to recommend the medication to others, and were more likely to agree that medication benefits outweigh the risks.

**3.4 Reasons for Willingness to Take the Medication**

Among individuals who reported being unlikely to take the medication (n=247), the most common reasons given were: prefer to avoid taking medications and will do something else (30.0%, n=74), there are too many possible adverse events (23.9%, n=59), and the potential for very serious muscle damage (23.9%, n=59). Among individuals who reported being likely to take the medication (n=682), the most common reasons given were: most of the adverse events are not very serious (41.8%, n=285) and any serious adverse events are very unlikely (34.2%, n=233). Finally, among individuals who reported being neither likely nor unlikely to take the medication (n=70), the most common reasons given were: prefer to avoid taking medications and will do something else (35.7%, n=25), there are too many possible adverse events (24.3%, n=17), and the very serious muscle damage (14.3%, n=10).

**4.** **Discussion and Conclusion**

**4.1 Discussion**

Most of our predictions, derived from FTT, were supported. As predicted, participants were most willing to use the medication when they viewed information about: (1) medication harms in a numeric format and (2) medication benefits in the non-numeric format. These effects of message format were also reflected in the secondary outcomes. Moreover, willingness to use the medication did not vary between the two levels of harm examined, despite the probability of side-effects in the high probability condition being twice that of the low probability condition. Thus, at least with respect to the harm information, it was the addition of numbers to the information provided that changed the gist conveyed, rather than the precise numbers themselves. Similarly, varying the probability of benefit did not affect participant judgments when the *Risk Difference* format was used. Participants who were told that 2,250 strokes/heart attacks could be prevented by treating 100,000 people with the medication were no more willing to use the medication or rate it as more likely to help than participants who were told that only 1,125 strokes/heart attacks could be prevented in 100,000 people. However, when benefit information was presented in the *Risk With and Without Treatment* format, the probability of benefit did make a difference. Here, participants who saw the high probability of benefit message were more willing to use the medication than people who saw the low probability of benefit message.

**4.1.1 Effects of Information Concerning Potential Medication Harms**

The prediction that people would be least willing to use the medication when harm information was presented using a non-numeric format was based on the notion that when people are presented with non-numeric side effect information, they are likely to form the categorical gist representation that taking the medication can cause harm and that the provision of numeric side effect information allows them to form more precise gist representations (e.g., only some people who take the medication are harmed). However, the reasons participants gave for being likely or unlikely to use the medication suggest a slightly different explanation. Over 60% of participants identified reasons that mentioned the severity of medication side effects (e.g., the potential for very serious muscle damage, that most serious side effects are unlikely, most side effects are not serious). This suggests that concerns about the one side effect described as very serious (i.e., rhabdomyolysis) was the main influence on participant judgments. Thus, in the non-numeric condition the salient gist to many participants seemed to be that the medication could cause *serious* harm (a categorical gist representation), but the numeric information supported formation of the more precise ordinal gist representation, *The risk of the medication causing serious harm is low*. Although the precise risk of the serious side effect did not affect participant judgments, both probability levels were consistent with a very low risk of serious harm (i.e., 1 or 2 out of 100,000 people treated). If the probability of this side effect had been higher, a difference between the low and high probability groups might have been observed.

**4.1.2 Effects of Information Concerning Potential Medication Benefits**

Our prediction that the mere presence of numbers quantifying the probability of benefit would reduce willingness to use the medication was supported. This prediction was based on the notion that when people are exposed to benefit information in non-numeric format they tend to form the categorical gist representation, *Taking* *the medication can help*, increasing willingness to use the medication. Addition of numbers to the format supports the formation of more precise gist representations (e.g., *Only some people who take the medication are helped*). When numeric benefit information was presented using the *Risk Difference* format, participant judgments did not vary as a function of the probability of benefit, suggesting that the high and low benefit materials conveyed the same gist. However, participant judgments did vary as a function of the probability of benefit when numeric benefit information was presented using the *Risk With and Without Treatment* format. In the low benefit condition, where individuals saw the rate of heart attack or stroke with treatment as 3.9% and the rate without treatment as 5.0% (values dervied from clinical trials), participants were more likely to form the gist representation, *Using the medication only helps a little*. In contrast, in the high benefit condition, where individuals saw the rate with treatment as 1.95% and the rate without treatment as 5.0%, participants were more likely to form the gist representation, *Using the medication helps a lot*. Thus, it appears that the *Risk With and Without Treatment* format is superior to the *Risk Difference* format in conveying meaningful information concerning the probability of benefiting from treatment.

**4.1.3 Limitations**

The study used a convenience sample and collected data using the Internet. Most respondents were healthy young adults and were not currently using any prescription medications. Thus, the generalizability of our findings to more representative patient populations is unknown. Moreover, the experimental scenarios described a hypothetical medication. The extent to which participant responses reflect the actual choices they would make in real life is also unknown.

**4.2 Conclusion**

Despite these limitations, our findings demonstrate the potential value of FTT for understanding how people extract meaning from information concerning medication harms and benefits. As predicted by FTT, providing numeric information on the probability of side effects increased willingness to use the medication; whereas providing numeric information on the probability of benefitting from medication use had the opposite effect. Our findings suggest that numbers matter because of the gist they convey and that the absence of numbers also conveys gist. Our findings also highlight the complexity of the medication harm/benefit communication process. Additional research, testing theoretically informed predictions, is needed to better understand how individuals extract meaningful gist from information concerning potential medication harms and benefits and to identify message formats most likely to result in enhanced comprehension and decision making.

**4.3 Practice Implications**

Most current WMI provides little numeric information on the probability of potential harms or benefits. Peters and colleagues [28] have called for the inclusion of numeric information on side effects in WMI. However, our findings suggest that including side effect information in numeric format and benefit information in non-numeric format is likely to result in a substantial bias favoring medication use. Alternatively, both types of information could be presented in numeric format, as is done in drug facts boxes [32]. Our findings also support using the *Risk With and Without Treatment* format to convey benefit information. This format is used in drug facts boxes [32]. However, inclusion of numeric benefit information in WMI is likely to increase patient reluctance to initiate and continue therapy, potentially creating ethical dilemmas for health care providers.

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