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Putting Knowledge into Practice:

Does Information on Adverse Drug Interactions Influence People's Dosing Behavior?

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Abstract

Objective: Adverse drug events relating to drug-drug interactions are a common cause of patient harm. Central to avoiding this harm is the patients' understanding that certain drug combinations present a synergistic risk. Two studies tested whether providing individuals with information about a drug combination that presents a synergistic (cf. additive) risk would elicit higher perceived risk and, therefore, would result in greater precaution in terms of dosing behavior. **Design**: Both studies employed an experimental design. **Methods:** Participants were presented with a scenario describing how two symptoms of an infection could each be treated by a different drug. In Experiment 1, information about the effects of combining the two drugs was varied: (i) no information, (ii) combination elicits an additive risk, or (iii) combination elicits a synergistic risk. In Experiment 2, the size of the risk (small or large) and the participant's role (patient or doctor) was also varied. **Results:** In both experiments, perceived risk and negative affect increased in response to information about the increased probability of side effects from the drug-drug interaction. Despite these increases, participants did not adjust their drug dosing behavior in either experiment: dosing was similar when these interactions were large or small, or when they were due to synergistic or additive effects. **Conclusions:** People may struggle to transfer their knowledge of drug-drug interaction risks into decision making behaviors. Care should be taken not to assume that holding accurate risk perceptions of a drugs side effect will result in decisions that help avoid adverse drug events.

Keywords: drug dosing; drug interactions; adverse drug events; risk perception; synergistic risk

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Recent studies indicate among the adult population in developed countries nearly 70% now use medicinal drugs, over 20% are prescribed five or more drugs, and approximately 12% are exposed to potentially serious drug-drug interactions (Fokter, Možina, & Brvar, 2010; Guthrie, Makubate, Hernandez-Santiago, & Dreischulte, 2015; Slovic, Peters, Grana, Berger, & Dieck, 2007). With the adverse effects of drug-drug interactions accounting for increased hospital admissions and higher levels of morbidity and mortality, avoiding and managing the risk of harmful drug-drug interactions is of growing importance (McDonnell & Jacobs, 2002; Pirmohamed et al., 2004). However, the day-to-day responsibility of safely using combinations of medicinal drugs often rest with lay individuals acting in non-clinical contexts without professional supervision (e.g., at home; Britten, 2009; Friedman, Geoghegan, Sowers, Kulkarni, & Formica, 2007). Hence, a sound appreciation of the health risks associated with combining certain drugs (e.g., combining a prescription drug with an over-the-counter drug) may be essential for many individuals if they are to avoid the adverse effects of harmful drug-drug interactions.

Central to avoiding the potential harm associated with certain drug-drug combinations is an understanding that the combination presents a *synergistic risk* (Bell, 1998; Sellers, Schoedel, & Romach, 2006). Specifically, the term 'synergistic risk' refers to the notion that the probability of a specific adverse outcome (e.g., internal bleeding) attributable to a combination of factors (e.g., taking both aspirin and warfarin) is greater than the sum of the probabilities attributable to each of those factors individually (Dawson & Dohle, 2016; Dawson, Johnson, & Luke, 2014; French, Marteau, Sutton, & Kinmonth, 2004). Hence, if a person understands that certain drug-drug combinations elicit this 'greater-than-additive'

magnitude of risk, then it would seem reasonable to assume that he/she should recognize the need to avoid using those particular drugs in combination or, at least, to appreciate that there is probably a need to reduce the dosage of one or both drugs. This assumption about risk perceptions influencing risk-related behaviors is supported by a wealth of research showing that a higher perceived risk for a specific adverse health outcome is often positively correlated with adopting behaviors that help to minimize that risk; e.g., individuals who perceive a higher probability of contracting a specific disease are more likely to obtain a vaccination for that disease (Brewer et al., 2007; Floyd, Prentice-Dunn, & Rogers, 2000; Weinstein, 1980).

Several studies show that when information about the adverse side effects of a drug is effectively communicated, individuals can form relatively accurate perceptions of the related risks and, thereafter, utilize the information to make informed intentions about using the drug safely (Berry, Raynor, Knapp, & Bersellini, 2004; Knapp, Gardner, Carrigan, Raynor, & Woolf, 2009; Sinayev, Peters, Tusler, & Fraenkel, 2015). However, to the best of our knowledge, this body of research has not specifically examined the perceived risk of harmful synergies associated with certain drug-drug combinations and, more importantly, has not assessed the influence that these risk perceptions might have on related drug-drug dosing decisions. Clearly, a better understanding of the relationship between risk perceptions and risk behaviors for drug-drug combinations could provide important insights into the role of patient/lay behavior in adverse drug interactions and, therefore, illuminate possible approaches for reducing the prevalence of these adverse events.

In this paper, we present two studies that assessed how an awareness of the synergistic risk attributable to a drug-drug combination might influence decision making regarding the use of that combination. In both studies, we examined the possibility that the information about the risk magnitude (additive vs. synergistic) associated with the drug-drug

combination might influence perceived risk and subsequent dosing decisions. Based on extant evidence (Berry et al., 2004; Knapp et al., 2009; Sinayev et al., 2015), we anticipated that providing individuals with information about a drug combination that presents a synergistic (cf. additive) risk would elicit higher perceived risk and, therefore, would result in greater precautionary behavior in the form of reduced dosing of, or abstaining from, one or both drugs.

Method

Experiment 1

In the first experiment, we examined whether and under which conditions participants would adjust their drug dosing behavior if they received information about the side effects of two interacting drugs. Care was taken to present a realistic scenario in which drug interactions might occur. Two symptoms of an illness were described that differed in terms of severity; they were treatable with two different drugs that only had an influence on one symptom.

We hypothesized that, compared to participants who received no information on side effects or information on an additive drug interaction, participants who received information on a synergistic drug interaction would have higher risk perceptions and more negative affect with regard to combined drug use. Furthermore, participants would reduce the dosage for the two drugs (especially the drug dosage for the less severe, harmless symptom) if they received medical information stating that the likelihood of adverse side effects would be high due to a synergistic interaction between the two drugs.

Participants. We recruited an age- and gender-diverse convenience sample of 120 adults (40% male; age: $M = 29.52$, $SD = 10.16$). Participants were recruited through flyers and posters distributed at public places such as supermarkets in the city of Zurich,

Switzerland, as well as links on webpages. Participants were compensated CHF 20 for participating in the lab-based experiment. The majority of the participants (81.6%; $n = 98$) reported high educational attainment (had attended college or university, whether graduated or not).

Design and procedure. The experiment employed a between-subjects design. Participants were randomly assigned to 1 of 3 conditions (side effects: none, additive, synergistic). The dependent variables were drug dosage, perceived risk, and negative affect.

Upon arriving at the laboratory, participants were seated in cubicles, where the entire experimental procedure took place. All participants were first asked to imagine themselves in a medical scenario in which they were suffering from a serious, life-threatening infection that had two symptoms: a high thrombosis risk and a strong, painful headache. To treat the symptoms two liquid drugs were available: drug A (a prescription only antithrombotic/coagulation-inhibitor) would minimize the risk of thrombosis but have no influence on the headache, whereas drug B (an over-the-counter painkiller) would eliminate the headache but have no influence on the thrombosis[a]. Participants were further informed that according to the package insert, the recommended adult dose for drug A was 5-15 mL one to three times daily, and for drug B, 10-15 mL up to three times daily. Drug dosage recommendations were vaguely formulated to allow some leeway to adjust or reduce the dosage.

The scenarios only differed in terms of the described side effects of the two drugs. In the control condition, no side effects were mentioned. In the additive scenario, participants were presented with three statements that were allegedly taken from the drugs' package

[a] The medical scenarios were a representation of the empirical evidence showing that a synergistic risk of internal bleeding can be attributable to the combined use of aspirin and warfarin. Note, however, that aspirin is not only a painkiller but often used as a coagulation-inhibitor. In contrast, in the scenarios it was stated that the drugs only had an influence on one of the symptoms, in order to emphasize that the painkiller had no effect on the life-threatening thrombosis. Therefore, no drug or illness names were given to prevent that participants' knowledge of the drugs or illness had an influence on their decisions.

inserts. The first statement described the relative frequency of an adverse side effect of drug A ("1 in 100 people who take the antithrombotic/coagulation-inhibitor experience internal bleeding"). The second statement described the relative frequency of the same adverse side effect for drug B ("1 in 100 people who take the painkiller experience internal bleeding"). The third statement described the relative frequency for the same adverse side effect given exposure to a combination of both drugs and presented an additive interaction ("2 in 100 people who take both the antithrombotic/coagulation-inhibitor and the painkiller experience internal bleeding"). The synergistic side effect scenario was identical to the additive side effects scenario; however, the third statement was altered to describe a synergistic interaction ("20 in 100 people who take both the antithrombotic/coagulation-inhibitor and the painkiller experience internal bleeding").

Two medicine bottles labelled "A" and "B" that contained 200mL of the alleged drugs (which was in fact coloured water), two transparent cups labelled "A" and "B", and a tablespoon with a volume of 15mL were placed in front of the participants. All participants were asked to use the spoon and the two cups to indicate the entire amount of drug A and drug B that they would take during 5 days. The instructions also emphasized that they could omit the dosing of either or both drugs.

Following the dosing, participants answered a short questionnaire. Perceived risk was measured with the question '"How probable is it to experience internal bleeding because of taking drug A and drug B during the same period?"; participants could answer on a scale ranging from 1 (*not at all probable*) to 9 (*very probable*). Negative affect was measured with the question "How scared are you to experience internal bleeding because of taking drug A and drug B during the same period?"; participants could answer on a scale ranging from 1 (*not at all scared*) to 9 (*very scared*). These two questions were not asked in the control condition because no information on side effects was given in this scenario. A manipulation

check asked about the perceived severity of the two symptoms; participants were asked to indicate on a scale from 1 (*not at all serious*) to 9 (*very serious*) how serious they felt the thrombosis and the headache were. After participants left the room, the volume of medicine (in mL) participants had poured into each of the two cups was recorded.

Statistical analyses. Because it was possible for participants to reduce the overall dosage by reducing the dosage of only drug A or drug B, or, alternatively, by reducing the dosage of both drugs, we added the dosage of drugs A and B to create a measure of combined dosage. We used an analysis of variance (ANOVA) to detect differences in the continuous variables (drug A dosage, drug B dosage, combined dosage, subjectively perceived risk, negative affect) across the scenarios. Significant univariate effects were followed up using pairwise comparisons with Bonferroni adjustments. Simple *t* tests were used for the manipulation check. The alpha error was set at 0.05. We performed all analyses by using SPSS statistical software, version 22.0.

Results

Manipulation check. As expected, the symptoms of the infection were perceived differently in terms of severity. The headache (M = 5.17, SD = 1.83) was perceived as significantly less severe, $t(118) = 13.78$, $p < 0.001$, than the thrombosis (M = 7.71, SD = 1.37).

Drug Dosage. Table 1 shows the means and standard deviations for the dosages of drug A, drug B, and the combination of drug A and B. Results of an ANOVA with dosage of drug A as the dependent variable demonstrated that the three conditions were significantly different from each other, $F(2, 117) = 4.24$, $p = 0.017$, $\eta_p^2 = .07$. Post hoc tests revealed that the dosage of drug A was significantly higher in the control condition than the synergistic condition, but not higher than the additive condition. Moreover, there was no difference in dosage between the synergistic condition and the additive condition (for post-hoc tests, see

also Table 1). An ANOVA with dosage of drug B as the dependent variable was also significant, $F(2, 117) = 7.02$, $p = 0.001$, $\eta_p^2 = .11$. As indicated by post hoc tests, the dosage in the control condition was significantly higher than in the two other conditions but, again, no differences between dosages emerged between the synergistic and the additive condition. The ANOVA for the combined drug dosage of drugs A and B revealed a similar pattern of results. There was a significant difference between the three conditions, $F(2, 117) = 8.44$, $p < 0.001$, $\eta_p^2 = .13$, which was due to differences between the control condition and the other two conditions. The dosage in the synergistic and the additive condition, however, was not significant.

[Insert Table 1 about here]

Perceived risk and negative affect. An ANOVA with perceived risk of side effects as the dependent variable was significant, $F(1, 78) = 11.21$, $p = 0.001$, $\eta_p^2 = .13$. As illustrated in Table 1, perceived risk was higher in the synergistic condition. Similarly, an ANOVA with negative affect as the dependent variable was significant, $F(1, 78) = 5.19$, $p = 0.026$, $\eta_p^2 = .06$, with negative affect being higher in the synergistic (cf. additive) condition.

Discussion

The results of Experiment 1 show that, contrary to our expectations, participants did not adjust the dosage of one or both drugs when they learned that the two drugs' side effects interact synergistically (cf. additively). This is noteworthy because one of the symptoms was markedly less severe than the other symptom; thus, a reduction of the dosage of drug B would have been possible without compromising one's fundamental health. However, participants realized that the synergistic interaction scenario implied a higher risk of side effects, and also showed more negative affect regarding side effects. Therefore, it remains unclear why participants did not adjust or omit the dosing of one of the two drugs.

One possibility could be that the sample size was too small to detect any difference in dosing. Another possibility is that participants visualized themselves strongly in the role of a patient suffering from a displeasing headache and, therefore, were reluctant to negate the opportunity to address this problem by reducing the dosage of drug B. We conducted Experiment 2 to address these issues. Specifically, a larger sample size was employed to increase the test power, and we also manipulated the participants' role as being either patient or doctor. By putting participants in the role of a doctor deciding on a patient's treatment, we believed participants might be less influenced by the envisaged pain of the headache and would feel less pressure to recommend a less essential drug.

We also recognized that it was unclear whether the higher risk perceptions and increased negative affect in the synergistic scenario in Experiment 1 occurred because (i) the drugs interacted synergistically or (ii) the absolute risk of side effects was much higher relative to the additive scenario. To disentangle these two possibilities, we varied the risk magnitude of the drug interaction in Experiment 2 so that, as a between-subjects factor, small or large risk magnitudes were described in both the additive and synergistic scenarios.

Experiment 2

For Experiment 2, we recruited a demographically diverse sample large enough to detect an effect of medium size for dosing behavior. The dosing task was also adjusted in order to make it possible to conduct the study online. The same scenario as in Experiment 1 was used in Experiment 2, but we added two additional side effect conditions and a new factor that manipulated the participants' role. Moreover, we also took into account that participants' dosing decisions, risk perception, and affect might be influenced by their numeracy skills, i.e. their ability to understand and process statistical and mathematical concepts (Fagerlin et al., 2007). This construct was therefore included as a control variable.

Method

Participants. A priori, we calculated the required sample size using G*Power 3 (Faul, Erdfelder, Lang, & Buchner, 2007). Assuming an effect size of $f = 0.25$, an α level of 0.05, and a power of $(1 - \beta) = 0.80$, the minimum sample size was $N = 196$. More participants were recruited to ensure that an appropriate sample was obtained even if some participants had to be excluded (see below). Participants were recruited via Amazon's Mechanical Turk and had to be US residents and at least 18 years old. They were compensated $1.00 upon completion.

A total of 445 participants completed the study. To make sure that participants paid sufficient attention to the instructions, we included a modified Instructional Manipulation Check (IMC; Goodman, Cryder, & Cheema, 2013; Oppenheimer, Meyvis, & Davidenko, 2009). Participants were excluded from further analyses when they failed the IMC ($n = 13$), resulting in a final sample size of $N = 432$ (46.3% females; the demographic analysis is shown in Table 2). The average age was 35.1 years ($SD = 11.3$).

[Insert Table 2 about here]

Design and procedure. The experiment employed a 5 (side effects: none, small additive, small synergistic, large additive, large synergistic) x 2 (role: patient, doctor) between-subjects design. Participants were randomly assigned to the experimental conditions. Drug dosage, perceived risk, and negative affect served as dependent variables.

Participants were asked to imagine the same medical scenario as described in Experiment 1. The only difference was the dosage form and recommendation for the two drugs: both drugs were tablets, and the recommended adult dose for drug A was 1 or 2 tablets every 3 to 4 hours, and for drug B, 1 or 2 tablets every 3 to 4 hours as required. Participants were presented with one of five side effect conditions. In the control condition, no side effects were mentioned. All other scenarios comprised three statements (see Table 3). The first and second statement described the relative frequency of an adverse side effect of drug A

and drug B, respectively. The third statement described the relative frequency for the same adverse side effect given exposure to a combination of the two drugs. The frequency specified in the third statement was either small or large, and presented either an additive or a synergistic combination of the frequencies described in the first two statements. In addition, half of the participants decided on their own course of treatment for the infection ('patient' role) and the other half imagined being a physician recommending a treatment to a patient who was suffering from the infection ('doctor' role).

[Insert Table 3 about here]

Following the presentation of the scenario, participants in the patient role were asked to indicate how many tablets of drug A and drug B they would take during one entire week (i.e., 7 days) at the maximum; participants in the doctor role were asked to indicate how many tablets of drug A and drug B the patient should take during one entire week at the maximum. In both conditions, it was emphasized that the dosing of either or both drugs could be omitted.

Perceived risk, negative affect, and perceived severity of the two symptoms were measured with the same questions as in Experiment 1. Only the question on negative affect had to be adjusted in the doctor role condition (i.e., "How scared are you that the patient may experience internal bleeding because of taking drug A and drug B during the same period?"). We used 6-point, instead of 9-point, Likert scales for all questions as this was deemed more manageable in an online study. As control variables, we measured subjective numeracy, which was assessed using the 8 items of the numeracy scale developed by Fagerlin and colleagues (2007) (α = .84).

Statistical analyses. We added the dosage of drugs A and B to attain a combined measure of drug dosage. The dosages of drug A, drug B, and drugs A and B when combined

were highly skewed and therefore log transformed.[b] All other analyses were identical to Experiment 1.

Results

Manipulation check. As expected, the headache (M = 3.39, SD = 1.39) was perceived as significantly less severe than the thrombosis (M = 5.46, SD = 0.91; $t(431) = 26.36$, $p < 0.001$).

Drug Dosage. Means and standard deviations for the dosages of drug A, drug B, and drugs A and B when combined are shown in Table 4. Results of an ANOVA with dosage of drug A as the dependent variable showed that the main effect for role was significant, $F(1, 422) = 6.01$, $p = 0.015$, $\eta_p^2 = .01$, indicating that dosage of drug A was higher when participants were in the doctor (cf. patient) role. Neither a main effect for side effects nor an interaction between role and side effects was found, both $p > .185$. Concerning dosage of drug B, the ANOVA showed no main effect for role or an interaction between role and side effects (both $p > .086$), but a main effect for side effects was revealed, $F(4, 422) = 7.23$, $p < 0.001$, $\eta_p^2 = .06$. Post hoc tests demonstrated that the control group's dosage was higher compared to the other four side effect scenarios, but that the four side effect scenarios were not statistically different from each other. An ANOVA with the combined dosage of drug A and B as dependent variable showed a main effect for role, $F(1, 422) = 8.79$, $p = 0.003$, $\eta_p^2 = .02$, indicating that participants in the doctor role administered a higher dosage compared to participants in the patient role. In addition, a main effect for side effects was found, $F(4, 422) = 2.52$, $p = 0.041$, $\eta_p^2 = .02$. As indicated by post hoc test, only the 'large synergistic' condition was significantly different from the control group, whereas all other side effect conditions did not differ from the control group. In addition, the four side effect scenarios

[b] The difference in terms of skewness between the two experiments was probably due to the fact that the 200ml bottles in Experiment 1 implied an upper limit for the dosing.

were not different from each other. No indication for an interaction between role and side effects was found, $p > .156$. All effects remained stable when controlling for subjective numeracy.

[Insert Table 4 about here]

Perceived risk and negative affect. Means and standard deviations for perceived risk and negative affect are shown in Table 4 as well. Results of an ANOVA with perceived risk as the dependent variable showed a significant main effect for side effects, $F(3, 339) = 13.42$, $p < 0.001$, $\eta_p^2 = .11$. Post hoc tests showed participants believed that side effects were more probable in the two large risk scenarios (both additive and synergistic) compared to the two small risk scenarios. Neither a main effect for role nor an interaction between role and side effects was found, both $p > .592$. The ANOVA results for perceived risks were similar when controlling for subjective numeracy.

As for negative affect, the ANOVA showed no main effect for role or an interaction between role and side effects (both $p > .075$), but a main effect for side effects, $F(3, 339) = 22.44$, $p < 0.001$, $\eta_p^2 = .17$. Post hoc tests demonstrated that two large risk scenarios (both additive and synergistic) triggered the highest negative affect, whereas the small additive scenario triggered the lowest negative affect. The results remained stable when subjective numeracy was entered as a covariate.

Discussion

Experiment 2 replicates the findings of Experiment 1. Again, participants' risk perception and negative affect was influenced by the different side effect conditions. When confronted with a high interaction (either additive or synergistic) participants expressed a higher perceived risk of side effects and felt more negative affect. However, participants dosing behavior was similar when these interactions were large or small or due to synergistic or additive effects. Moreover, participants in the patient role were more cautious in terms of

dosing behavior, which replicates similar findings that have shown that choosing for others differs from choosing for oneself in making treatment decisions (Zikmund-Fisher, Sarr, Fagerlin, & Ubel, 2006).

General Discussion

Both of our studies show that risk perceptions and affect are influenced by information about the increased risk of side effects from drug-drug interactions. More specifically, the results show that both risk perceptions and negative affect increase, irrespective of whether the risk results from a synergistic or additive interaction, when the resultant risk magnitudes are relatively large. While it may seem unremarkable that subjective concern about side effects increases in response to higher magnitudes of risk, it is particularly surprising that, despite these increases, individuals' do not adjust their drug dosing behavior accordingly. That is, we found that dosing behavior is unaffected by whether a drug interaction is additive or synergistic and, more notably, whether the interaction presents a small or large risk of adverse side effects. This indicates that people may struggle to transfer their knowledge of drug-related risks into behavioral decisions (i.e., to reduce or omit certain drugs) in a way that could help them to avoid severe health consequences. Hence, while many extant studies have focused on the importance of helping individuals to develop accurate perceptions of the risk associated with certain medicinal drugs, the evidence presented here points towards a greater need to focus on understanding whether individuals effectively utilize accurate risk perceptions to make decisions that lead to the avoidance or minimization of drug-related risks.

Given the surprising nature of our findings, it is important to consider possible explanations. One consideration is that the experimental design may have elicited a 'demand effect' in which participants simply maintained certain drug dosage levels across all conditions because they felt this was expected of them when treating the symptoms. However,

this seems unlikely because the 'doctor condition' in Experiment 2 provided participants with the opportunity to objectively evaluate how the more serious matter of internal bleeding might be minimized/avoided by reducing or omitting the dosage of the drug used to treat the less serious headache. Relatedly, our measures of perceived risk and affect show that the participants *did* appreciate the increased risk of internal bleeding when using both drugs, so they were aware of the need to take action to mitigate this risk and they had been made aware that they could omit either drug altogether.

An alternative explanation for our findings is that, while there is extensive evidence showing a positive correlation between higher risk perceptions and the adoption of precautionary behaviors (see Introduction), there is also some evidence showing that heightened risk perceptions and/or negative affect do not always determine whether individuals instigate precautionary actions (Liberman & Chaiken, 1992; Schwarzer, 1994; Weinstein, Sandman, & Roberts, 1991). For example, Bowen et al. (2004) found that perceived risk, worry and anxiety were not related to an individual's participation in cancer screening or prevention actions such as physical exercise or eating fruit and vegetables (Bowen, Alfano, McGregor, & Andersen, 2004). In the context of our studies, there are a number of potential reasons why such a disassociation between risk perceptions and precautionary behaviors may have occurred. First, our participants may have processed the personal relevance of the risk information in a defensive manner and, therefore, neglect to adjust their dosing behavior accordingly (Good & Abraham, 2007). Second, it may be that our participants experienced some degree of 'unrealistic optimism' about whether the side effects would specifically affect them (Weinstein, 1980). Finally, it may have been that our participants perceived their own actions as a relatively weak mechanism for reducing the risk of the side effects; research by Slovic et al. (2007) shows that individuals often perceive themselves (cf. drug manufacturers and regulators) as the least able to reduce the risks

associated with prescription drugs. While each of these possible explanations may seem plausible, their credibility is questionable when one considers why these effects (i.e., defensive processing, unrealistic optimism, low self-efficacy) would have persisted in the 'doctor condition' of Experiment 2, where the participants made decisions for another person.

A more plausible explanation may be that our participants underutilized the risk magnitude information (and its influence on their perceptions and affective state) when making their dosage decisions. In support of this possibility, research evidence suggests that for many individuals to execute precautionary health behaviors, it is often necessary for them to understanding more than just risk magnitudes (Ajzen, 1977; Rothman & Kiviniemi, 1999; Tversky & Kahneman, 1977). For instance, unlike numerical probabilities, information about the antecedent mechanism underlying a specific health risk can help people to form a salient mental image of the conditions that elicit a particular health issue and, therefore, provides the individual with a clearer understanding of how that issue might be minimized or avoided (Dawson, Johnson, & Luke, 2012; Kreuter & Strecher, 1995; Rothman, Kelly, Weinstein, & O'Leary, 1999). In the specific context of risk and decision making concerning prescription drugs, Jungermann and colleagues have illustrated how people may better understand the risks associated with particular medicinal drugs if they develop or "run" a mental model of how the drug works inside the body and how the mechanisms of contraindications can manifest (Jungermann, Schutz, & Thuring, 1988). This literature showing that probabilistic information can be neglected in medical decision making seems to provide the most plausible explanation for the absence of a relationship between our participant's responses to the different risk magnitudes and their dosing decisions.

There are some limitations to our studies that could be addressed in future research. Firstly, in both studies we used a non-patient sample and a hypothetical scenario that was presented via a vignette-based methodology. This approach allowed us to study how

information on drug-drug interaction risks may affect dosing behavior, while also providing us with a degree of experimental control over the risk information presentation; this is something that is not typically feasible or ethical using real patients. However, we cannot rule out the possibility that the hypothetical behavior in our experiment may differ from people's actual behavior in real life. Second, we used single-item measures for risk perception and negative affect, which may have jeopardized the reliability and sensitivity of these measures. Hence, we may have underestimated the effect of information of drug-drug interactions on risk perception and negative affect. Third, we used a frequency format to present the risk information to our participants because studies have shown that this format can facilitate an accurate understanding of risk magnitudes (Cosmides, 1996; Knapp et al., 2009). However, it is possible that using other formats and processes to communicate risk information may have different effects on dosing decisions. Therefore, we recommend that future studies examine the influence of different formats on behavioral decisions and, in particular, assess messages that encourage individuals to develop/run mental models of the antecedent mechanisms underlying harmful drug-drug interactions.

Conclusion

Several studies show that what people most want to know about drugs, and what they believe will most influence their decision to take a drugs, is the risk of side-effects (Berry, Gillie, & Banbury, 1995; Berry, Michas, Gillie, & Forster, 1997; Ziegler, Mosier, Buenaver, & Okuyemi, 2001). However, our studies show that, while information about the harmful side effects of drug-drug interactions can be processed to the degree that it increases perceived risk and elicits negative affect, it does not necessarily influence the final decision about whether to use the drugs and in what quantities. Hence, academics and health professionals must take care not to assume that accurate comprehension of information about

drug-related risks will translate into the desired precautionary behaviors. Our findings point towards a pressing need to better understand how drug risk information can be improved to ensure that it facilitates decisions that minimizes adverse drug incidents. This might be achieved by warning people more directly about the risks of drug-drug interactions (e.g., warning labels), using techniques that stimulate relevant mental models of the antecedent mechanisms, or simply helping medicinal drug users to develop a greater appreciation of the important role that they play in negating harmful drug-drug interactions. Future research should assess these and other approaches to identify how lay individuals can help avoid the adverse effect of harmful drug-drug interactions.

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Tables

Table 1.

Study 1: Means (Standard Deviations) of Drug Dosages, Perceived Risk and Negative Affect Regarding Combined Drug Use

	Side Effects		
	None	**Additive**	**Synergistic**
Dosage Drug A	94.53^{a} (40.77)	$73.87^{a,b}$ (36.89)	71.30^{b} (39.58)
Dosage Drug B	73.90^{a} (52.90)	40.28^{b} (40.56)	41.32^{b} (42.48)
Dosage Drug A + Drug B	168.43^{a} (81.48)	114.15^{b} (64.84)	112.62^{b} (59.35)
Perceived Risk	-	3.58^{a} (1.66)	4.97^{b} (2.06)
Negative Affect	-	4.80^{a} (2.23)	5.98^{b} (2.38)

Note. Means with differing superscripted letters within rows are significantly different ($p < .05$).

Table 2.

Study 2: Socio-demographic Characteristics of the Sample (N = 432)

Socio-demographic characteristic	**% of total**
Gender	
Male	53.7
Female	46.3
Health Insurance	
Yes	84.0
No	16.0
Age group	
18–24 years	16.2
25–34 years	41.2
35–44 years	23.6
45–54 years	12.3
55–64 years	4.9
65 years or older	1.9
Educational level	
High School/GED[a]	11.1
Some college	32.9
2-Year College Degree	10.0
4-Year College Degree	37.0
Master's Degree	7.4
Doctoral Degree	0.7
Professional Degree (MD, JD)	0.9
Combined annual household income	
not specified	1.9
under $20,000	15.3
$20,000 - $39,999	25.7
$40,000 - $59,999	21.8
$60,000 - $79,999	16.2
$80,000 - $99,999	8.1
over $100,000	11.1

Note. [a] Individuals who do not have a high school degree may take the General Educational Development tests (GED) to certify as having American high school-level academic skills.

Table 3.

Study 2: Summary of the Relative Frequency of Possible Side Effects Described in the Scenarios

Side Effects	Relative Frequency (Drug A)	Relative Frequency (Drug B)	Relative Frequency (Drug A and Drug B)
Control	-	-	-
Small Additive	1/100	2/100	3/100
Small Synergistic	1/100	1/100	3/100
Large Additive	10/100	10/100	20/100
Large Synergistic	1/100	1/100	20/100

Table 4.

Study 2: Means (Standard Deviations) of Drug Dosage, Perceived Risk and Negative Affect Regarding Combined Drug Use

	Side Effects				
	None	**Small Additive**	**Small Synergistic**	**Large Additive**	**Large Synergistic**
Dosage Drug A					
Patient	1.34[a] (0.51)	1.25[a] (0.44)	1.30[a] (0.54)	1.22[a] (0.62)	1.14[a] (0.44)
Doctor	1.46[a] (0.50)	1.30[a] (0.46)	1.24[a] (0.43)	1.46[a] (0.43)	1.39[a] (0.49)
Sum	1.40[a] (0.51)	1.27[a] (0.45)	1.27[a] (0.49)	1.34[a] (0.54)	1.25[a] (0.48)
Dosage Drug B					
Patient	1.27[a] (0.53)	1.00[a,b] (0.63)	0.99[a,b] (0.60)	0.80[b] (0.68)	0.80[b] (0.66)
Doctor	1.40[a] (0.54)	1.08[a,b] (0.55)	0.97[b] (0.63)	0.99[b] (0.74)	0.95[b] (0.76)
Sum	1.33[a] (0.53)	1.04[b] (0.59)	0.98[b] (0.61)	0.89[b] (0.71)	0.86[b] (0.71)
Dosage Drug A + Drug B					
Patient	1.62[a] (0.50)	1.46[a] (0.49)	1.53[a] (0.50)	1.49[a] (0.51)	1.33[a] (0.49)
Doctor	1.76[a] (0.47)	1.55[a] (0.43)	1.49[a] (0.39)	1.65[a] (0.47)	1.65[a] (0.38)
Sum	1.68[a] (0.49)	1.50[a,b] (0.46)	1.51[a,b] (0.45)	1.57[a,b] (0.49)	1.47[b] (0.47)
Perceived Risk					
Patient	-	3.16[a] (1.15)	3.35[a] (1.27)	4.04[b] (1.05)	4.31[b] (1.28)
Doctor	-	3.15[a] (1.22)	3.50[a.b] (1.47)	3.82[a.b] (1.03)	4.11[b] (1.12)
Sum	-	3.15[a] (1.17)	3.42[a] (1.36)	3.93[b] (1.04)	4.22[b] (1.20)
Negative Affect					
Patient		3.29[a] (1.56)	3.92[a] (1.57)	4.70[b] (1.26)	4.73[b] (1.25)
Doctor		3.07[a] (1.37)	3.60[a,b] (1.52)	4.11[b,c] (1.07)	4.81[c] (1.17)
Sum		3.19[a] (1.47)	3.78[b] (1.54)	4.41[c] (1.20)	4.77[c] (1.21)

Note. Drug dosage was log-transformed. Means with differing superscripted letters within rows are significantly different ($p < .05$).