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Dated:

The Effect of Risk Information Communicated in Plain Language Combined with Natural Frequencies on Individual Risk Perception of Medication Side Effects

By

Collin Beatty

A thesis submitted in partial fulfillment

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To the faculty of the University of Houston College of Pharmacy:

The members of the committee appointed to examine the thesis of Collin Beatty find it satisfactory and recommend that it be accepted on April 15th, 2013.

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To

My wife, Kara Keuthan Beatty,

My parents Sheryle Gordan and Coke Beatty,

and

My wonderful family and friends.

Abstract

The Effect of Risk Information Communicated in Plain Language Combined with Natural Frequencies on Individual Risk Perception of Medication Side Effects

Objectives: The primary objective of this study was to determine whether describing the probability of experiencing a particular medication side effect in plain language and natural frequencies would result in a difference in the perceived risk of the medication, perceived harm of the side effects and intent to remain adherent as compared to describing side effect risks in plain language only. The secondary objective was to determine the correlation with perceived risk and harm of side effects and intent to remain adherent.

Methods: The study design was an experimental two by three factorial survey. The effects of three independent variables (communication type [plain language vs. combined], severity of side effects [high vs. low], and frequency of side effects [high vs. low]) were measured across the dependent variables of perceived risk, perceived harm and intent to remain adherent. Four drug facts boxes were shown to participants, who were then asked to rate their perceived risk of experiencing the side effects, the perceived harm of the side effects and their intent to remain adherent to the medication on visual analog scales. Each drug facts box listed uses of the medication and one specific side effect. The probability of experiencing the side effect was described in either plain language or a combination of plain language and the natural frequency (i.e., 5 out of 100 people). Multiple analysis of variance (MANOVA) were conducted for the model and significant effects were analyzed with a poc-host Tukey test. Means were significant at $p < 0.05$.

Results: 100 students at the University of Houston College of Pharmacy completed the survey. MANOVA showed there were no significant effects for communication type (plain language or combination) alone ($F_{3,390} = 1.97$, $p = 0.118$). However, the model of communication type, severity and frequency was significant ($F_{3,390} = 4.33$, $p = 0.005$). The overall effects of communication type, severity and frequency had a significant effect on the dependent variable perceived risk ($F_{7,392} = 190$, $p < 0.0001$). The effect of communication type on perceived risk was significantly different ($F_{1,392} = 5.5$, $p = 0.0195$). There was also a difference between severity ($F_{1,392} = 17.87$, $p < 0.0001$) and frequency ($F_{1,392} = 1225$, $p < 0.0001$). Tukey post-hoc analysis indicated that the combination communication type group had significantly higher risk perception scores (M = 46.6, 95% CI [44.2, 49.1]), compared to the risk perception scores for the plain language group (M = 42.5, 95% CI [40.1, 44.9]), p = 0.019). The overall effect of communication type, severity and frequency on intent to adhere to therapy was significant ($F_{7,392} = 2.6$, $p = 0.01$). There was no significant difference between communication type on the intent to remain adherent ($F_{1,392} = 0.07$, $p = 0.786$). There was a significant difference on intent to remain adherent for severity ($F_{1,392} = 6.84$, $p = 0.009$) and frequency ($F_{1,392} = 8.2$, $p = 0.004$). Mean scores for intent to adhere in the combined communication type group were slightly higher (M = 85.5, 95% CI [82.9, 88.0]) compared to the plain language group (M = 84.9, 95% CI [82.4, 87.5]), but were not statistically significant (p = 0.786). Mean scores in the high severity group were significantly lower (M = 82.8, 95% CI [80.3, 85.4], $p < 0.009$) than mean scores for the low severity group (M = 87.6, 95% CI [85.1, 90.2]). The mean scores for the high frequency group were also significantly lower (M = 82.6, 95% CI [80.0, 85.2], p = 0.004) compared to means for the low frequency group (M = 87.9, 95% CI [85.3, 90.4]). The overall model of communication

type, severity and frequency and the effect on perceived harm was significant ($F_{7,392}$= 91.46, $p < 0.0001$). There was no significant effect of communication type on perceived harm ($F_{1,392}$ = 0.2, p = 0.659). There was a negative correlation between perceived risk and intent to remain adherent (r = -0.189, n = 400, p = < 0.001). A spearman product-moment correlation coefficient was computed to assess the relationship between the variables perceived harm and intent to remain adherent. There was a negative correlation between perceived harm and intent to remain adherent (r = -0.261, n = 400, p = < 0.001).

Conclusions: Results of this study suggest that communication style does play a role in risk perception of medication side effects. However, as side effects become more severe and occur more often, this effect seems to diminish. There was no effect of communication type on participants intent to remain adherent. The participants were all students at various stages in pharmacy education and so are educated on the importance of adherence. It is striking to see that the known importance of adherence is shared amongst students in pharmacy school. Further studies in the general population may be warranted to test the effects of communication style on adherence.

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CHAPTER ONE

Background and Statement of the Problem

This chapter will describe the background issues surrounding the study, medication adherence, costs associated with medication adherence and current recommendations for communicating information to improve adherence. This section will also state the current problems and describe the research question and objective of the study.

Medication Adherence

One of most common methods for treating many medical disorders are self-administered medications. Many chronic conditions require that patients take often several medications on a daily basis for many years. The effectiveness of such chronic medication therapy depends on adherence to the prescriber's instructions (Bosworth, 2010). The term medication adherence is now preferred over the term medication compliance (Osterberg & Blaschke, 2005). "Compliance" generally assumes that patients have taken a more passive role in their treatment and are simply following the orders of their physician without any engagement (Osterberg & Blaschke, 2005). In contrast, "adherence" is defined the extent to which patients follow instructions but involves more patient choice and is intended to be non-judgmental (Haynes et al., 2005).

Examples of medication non-adherence include delaying prescription refills, failing to fill a prescription, cutting/splitting dosages or reducing the frequency of administration (Bosworth, 2010). Patients are frequently non-adherent to their medications and this can have significant health consequences (World Health Organization, 2003). It is estimated that

approximately half of the 3.2 billion prescriptions annually dispensed in the United States are not taken as prescribed (Osterberg & Blaschke, 2005). Other studies have shown that patients with chronic conditions adhere to only about 50-60% of their prescribed medications (Avorn et al., 1998) despite proven evidence of their efficacy in reducing mortality and improving cardiovascular outcomes (Benner et al., 2002). In other developed countries these patterns of adherence are similar (Balkrishnan, 2005). Unfortunately, the true rates of non-adherence may be much higher, since traditionally patients with patterns of non-adherence are significantly underrepresented in medical research (Bosworth, 2010). Non-adherence has significant costs to the United States health system as well as the health of the world population.

Cost of Non-adherence

A 2003 report from the World Health Organization states that improving the staggering rates of non-adherence to medical therapy would result in more improved health outcomes overall than any new medical treatments (World Health Organization, 2003). Non-adherence to medication puts great costs into the U.S. health system and is detrimental to patient health. Non-adherence to medication is estimated to lead to 89,000 avoidable hospitalizations and add $100 billion in avoidable costs annually (Cutler & Everett, 2010). An estimated 33-69% of medication-related hospital admissions in the United States are due to medication non-adherence (Osterberg & Blaschke, 2005). Additionally, poor adherence leads to poor medical outcomes. A report by the New England Healthcare Institute (NEHI) indicated that the annual cost of healthcare for diabetics is nearly doubled in those patients who are non-adherent (NEHI, 2009). Reports also show that mortality is significantly higher

for non-adherent patients with diabetes and hypertension (NEHI, 2009). Medication adherence can significantly improve medical costs (Sabate, 2003). For example, it is estimated that in 2003, for every additional dollar spent on adhering to a prescribed medication, medical costs would be reduced by $7 for people with diabetes, $5.10 for people with high cholesterol, and by $3.98 for people with high blood pressure (Sabate, 2003).

Factors Affecting Adherence

Factors affecting medication adherence are related to patient factors, clinician factors and the patient-provider relationship, health-care factors, and environmental factors (Bosworth, 2010). Health-care and environmental factors include issues such as high medication copayments and tiered prescription plans, lack of access to providers, social support systems, poverty and even the weather (Bosworth, 2010). However, patient beliefs are found to impact medication adherence much more than clinical or socio-demographic factors (Horne and Weinman, 1998).

Patient factors that may affect rates of adherence to medication include tolerability of adverse side effects of medication (Osterberg & Blascke, 2005), poor communication between provider and patient (Osterberg & Blascke, 2005), and lack of information about side effects (NEHI, 2009). Other patient factors include poor memory, low literacy, polypharmacy and complex regimens (Bosworth, 2010).

The relationship between provider and patient plays an important role in medication adherence, particularly in areas of trust between provide-patient, and communication of medication information (Bosworth, 2010). It has been observed that patients feel empowered when they receive information about side effects (Grime et al., 2007). Patients prefer to

receive complete information about side effects (Ziegler et al., 2001) but also prefer simpler, easier to read instructions for medication use than are often provided in pharmacies today (Morrow et al 2004). However, the information exchange between physicians or pharmacists and patients is often incomplete (Svarstad et al., 2004) (Tarn et al., 2006). The gap in communication about medication cost and medication side effects plays a significant role in medication adherence (Haynes, McKibbon and Kanani, 1996).

Recommendations for the Communication of Side Effects

Given the importance of good information about side effects and the impact it has on adherence, it is vital to know the optimal methods for communicating such information. The likelihood of experiencing a side effect from a certain medication is a probability event. Patients must weigh the risks of taking the medication versus the benefit. Hence, a patient's ability to assess risk is important. Risk information can be presented in a variety of formats including verbal (plain language), numerical and graphical (Visschers et al., 2009). The European Union (EU) and Medicines and Healthcare Products Regulatory Agency (MHRA) issued a report stating that the risk of side effects should be communicated in both verbal and numerical descriptors (European Commission, 1998).

Figure 1: EU/MHRA Verbal Descriptors

EU Verbal Descriptor	EU Probability of Side Effect Occurrence
Very common	>10%
Common	>1% and <10%
Uncommon	0.1% to 1%
Rare	0.01% to 0.1%
Very rare	<0.01%

Unfortunately, these descriptors have some serious flaws. The descriptors were implemented without any evidence-based research. And the verbal language recommended by the EU/MHRA is not correlated well with what the public thinks of as risk terms. In fact patients, doctors and the general public tend to overestimate risk based on the MHRA recommendations (Berry, Holden & Bersellini, 2004), (Knapp, Raynor & Berry, 2004). It is unclear that the combination of verbal and numerical frequency is superior to either format alone (Knapp et al., 2009). Numerous studies on the formats of risk information have been conducted but no overall picture exists to explain the optimum method of combining various formats of risk information (Visschers et al., 2009).

Research Question

The MHRA descriptors show that patients process information in different ways than caregivers. The question this raises is:

- Does describing frequency of side effects in plain language and numerical terms make the side effects seem less risky than describing side effects in plain language only?

Research Objective

The objective of this study is to determine the optimal method for communicating risk information about side effects to individuals. By appropriately presenting risk information about side effects, patients should perceive the side effects as appropriate risk and thus be more inclined to remain adherent.

CHAPTER TWO

Review of the Literature and Theory

This chapter will focus on the importance of communicating side effect risks to patients, methods of such communication (graphical, verbal and numerical) as well as current recommendations for communication of side effects. The chapter will also describe the Health Belief Model (HMB) as the theoretical basis for the current study and discuss the conceptual framework based on the HBM. Finally, the hypotheses for the current study are listed.

Communication of Side Effect Risk

Any information about the probable outcome of engaging in a certain behavior requires that the individual make a risk assessment. In the case of medicines, an expert caregiver is available to explain the risks of the medications. Studies show that patients and caregivers prefer different methods of either receiving or delivering information about probabilities. People in general tend to focus more on qualitative (plain language) aspects of risk information compared to the quantitative (numerical) aspects (Visschers et al., 2009).

It is imperative that providers communicate the risks and benefits of medication therpapy with patients. The patients of physicians who interactively communicate have better glycemic control of their diabetes (Schillinger et al., 2003) than patient's whose physicians do not communicate well with. When communicating information about probable outcomes, caregivers generally prefer to express the outcome as a verbal probability (i.e., likely, possibly, rarely) (Erev and Cohen, 1990). Providers are often ambivalent about written

information despite the fact that many patients value such written information (Grime et al., 2007). In fact, written information leads to greater patient-physician interaction and can improve health outcomes such as vaccination rates (Jacobson et al., 1999). In general, verbal information leads to better understanding (Spandorfer et al., 1995). But there is wide variability in the interpretation of plain language statements. For example, Shaw and Dear (1990) asked parents of babies to interpret risk statements such as "likely" and "rarely". Patients reported wide ranges of statistical probabilities amongst each plain language risk statement. Also, Brun and Teigen (1988) found that when people were asked to assign risk probabilities to verbal statements either in context of influenza vaccines or no context at all, there was again great variability of the risk statements. The table below shows the wide distribution that can be seen amongst common verbal statements.

Table 1: Variability of commonly used probability statements

Probability Expression	**Associated Numerical Probability: Mean (SD)**			
	Shaw & Dear (1990)	***Brun & Teigen (1988)***	***Kong et al. (1986)***	***O'Brien (1989)***
Very Likely	86% (15%)	-	85% (NS)	72% (NS)
Likely	66% (17%)	70% (15%)	63% (NS)	69% (NS)
Possibly	62% (17%)	52% (17%)	27% (NS)	30% (NS)
Rarely	20% (19%)	-	14% (NS)	19% (NS)

The European Union (EU) and Medicines and Healthcare Products Regulatory Agency (MHRA) issued a report stating that the risk of side effects should be communicated in both verbal and numerical descriptors (European Commission, 1998). Table [#] shows the verbal descriptors and the corresponding probability outcome. Unfortunately, these descriptors have some serious flaws.

Berry, Knapp and Raynor (2002) surveyed participants to determine how they interpreted the EU assigned verbal probabilities. The mean perceived numerical probabilities that the participants associated with each EU verbal probability were described by Berry (2002). All participants generally overestimated the risk that was suggested by the EU probabilities. This is consistent with research that shows individuals tend to have difficulty comprehending small probabilities (Cook and Bellis, 2001).

Figure 2: Mean probability estimates of EU verbal descriptors

EU Verbal Descriptor	Mean (SD) Probability Estimate (Berry 2002)	EU Probability of Side Effect Occurrence
Very common	65% (24.5%)	>10%
Common	45% (22.2%)	>1% and <10%
Uncommon	18% (13%)	0.1% to 1%
Rare	8% (7.5%)	0.01% to 0.1%
Very rare	4% (6.7%)	<0.01%

Role of Context in Perception of Verbal Probability

Context of risk also seems to play a role in assessment of verbal risk probabilities (Visschers et al., 2009). People interpret risks differently whether drugs are advertised in a magazine or television format (Morris et al., 1986). A study by Weber and Hilton found that participants would assign similar numerical probabilities to the verbal statements "possible" and "slight chance" depending on the combination of perceived personal base rate and severity of the event (Weber and Hilton, 1990). Patients also take in to account the associated benefits of drug therapy when interpreting risk information. A study by Cohen & Neumann (2007) showed that while the annual fatality risk for the multiple-sclerosis drug, natalizumab

is 65 per 100,000 person-years, about 1 in 6 patients taking the drug would accept the risk, given the benefit they perceive (Cohen and Neumann, 2007). This is in contrast to the great concern about motor vehicle fatalities which in context, occur at a rate of 10.6 per 100,000 person-years. When risk is communicated in terms of overall life expectancy, rather than in terms of the risk for disease people are able to recall the information much better (Galesic and Garcia-Retamero, 2011).

Patients however, seem to prefer different methods of communication and are inconsistent in how they make decisions based on that information. Patients actually prefer to receive such information as a numerical probability (i.e., 25%, 1 in 4) rather than as a verbal probability (Erev and Cohen, 1990). However, patients only seem to make decisions based on numbers about half the time (Holmes-Rovner et al., 2005). Not surprisingly, physicians have a difficult time determining their patient's preferred method for receiving information (Freeman and Bass, 1992). When reading prescriptions labels, the majority of patients prefer to see side effects integrated into the main section of text and prefer to have incidence levels of side effect occurrence listed (Davis, 2007). Tables can be useful for displaying side effects and benefits of medication, as most people (even those with relatively low formal education) can interpret such information (Schwartz, Woloshin and Welch, 2007).

Graphical Expression of Risk Information

Expressing risk information in graphical formats can be another useful way of communicating risks to patients. Although not the subject of this paper, this section will briefly review the use of graphs and illustrations in communicating risk information and discuss some of the concerns regarding their use.

In some cases, patients prefer information about medications to be presented graphically (Goodyear-Smith et al., 2008). Emergency center discharge instructions have been shown to be more effective in improving patient comprehension in patients who are nonwhite or have less than a high-school education (Austin et al., 1994). Patients receiving illustrated discharge instructions about wound care were more likely to answer 100% of questions about proper wound care correctly, although only 46% of patients were able to do so (Delp and Jones, 1996). Illustrations also improved compliance to 79% (Delp and Jones, 1996). When looking are risk information, people tend to focus more on the number of people who have died or experienced the adverse event as opposed to the overall number treated, a phenomenon described as denominator neglect (Garcia-Retamero and Dhami, 2011) and leads to inaccurate risk assessment. Using graphs can alleviate denominator neglect and lead to better risk assessment (Garcia-Retamero and Dhami, 2011), as well as better knowledge (Hawley et al., 2008). Also, pie charts and vertical or horizontal bars are effective in removing the effects of framing bias, especially in people with low-numeracy (Garcia-Retamero and Galesic, 2010). When using pictograph bar charts, horizontal pictographs seem to be easier to read, undertand and are more preferred (Price, Cameron and Butow, 2007).

While graphs may be useful, communicators should not assume that graphs are more intuitive than text (Ancker et al., 2006). Interpretation of pictographs is influenced by education, age and socioeconomic differences and may vary significantly from how medical professionals interpret the same pictographs (Chuang et al., 2010). Excess information displayed as thermometers, crowd figures/smiley faces, etc., may be unhelpful and lead to information overload for patients (Edwards et al., 2005). Complex pictographs have no

advance over text and patients may require training before pictographs are very useful in helping them understand medication use, which may be a significant barrier to adoption (Katz, Kripalani and Weiss, 2006).

Verbal Risk Information

Delivery of risk information matters a great deal in compliance. Verbal risk statements are advantageous in that they are easy and natural to use and may better capture a person's emotional interest (Lipkus, 2007). As discussed earlier, verbal information naturally leads to greater variability in interpretation of the risk statement. Research is developing in the area of using common "stems" for using verbal predictors (e.g., likely, unlikely, very likely) but no consensus has yet been reached (Lipkus, 2007). Information delivered verbally was shown to reduce compliance, whereas information delivered numerical was shown to increase compliance (Young and Oppenheimer, 2006). Introduction of qualifying statements such as "may" or "if . . . may" lead to more positive attitudes about the appeal of a medication or the willingness to experience side effects (Davis, 2007) but this does not necessarily translate to risk comprehension. Research shows that when information is presented in plain language – 8th grade reading level or lower – that patients comprehend the information better (Clement et al., 2009) (Jolly, Scott and Sanford, 1995) and it is recommended that verbal information be presented in plain language (Fagerlin, Zikmund-Fisher, and Ubel, 2011).

Because of the inherent variability in interpreting verbal risk information, developers of education material are encouraged to avoid the use of verbal descriptors alone in describing risks (Fagerlin et al., 2007)

Numerical Risk Information

The numerical skills of people play a strong role in how they interpret numerical risk information (Keller and Siegrist, 2009). When asked to determine the absolute risk of treatment by interpreting different formats of numerical risk information, only about 2/3rd of all participants were able to achieve "passing" comprehension scores (Woloshin and Schwartz, 2011). Generally treatments are regarded as more efficacious when benefits are presented as relative risk information as opposed to absolute risk or number needed to treat (Covey, 2007), (Sheridan, Pignone and Lewis, 2003). Presenting numerical benefit as relative risk reduction also increases the likelihood of patients accepting treatment compared to absolute summary information (number needed to treat, absolute risk reduction, etc.) (Carling et al., 2009). However, it is important to realize that many people have poor numeracy as demonstrated by tests that measure an individual's ability to perform on numeracy tests (Gigerenzer et al., 2007). In the case of low numeracy, primers may help people interpret and understand medical risk information (Woloshin, Schwartz and Welch, 2007). Research consistently shows that presenting information in frequencies (i.e., 1 out of 100) rather than percentages (i.e., 1%) leads to better understanding of risk information on the part of both physicians and patients (Hoffrage and Gigerenzer, 1998), (Gigerenzer and Edwards, 2003). People also have difficulty when denominators contain very large numbers and consistently overestimate risk of large denominators vs small denominators (1,200 out of 10,000 vs 12 out of 100) (Garcia-Retamero and Galesic, 2010).

Combining Verbal and Numerical Information

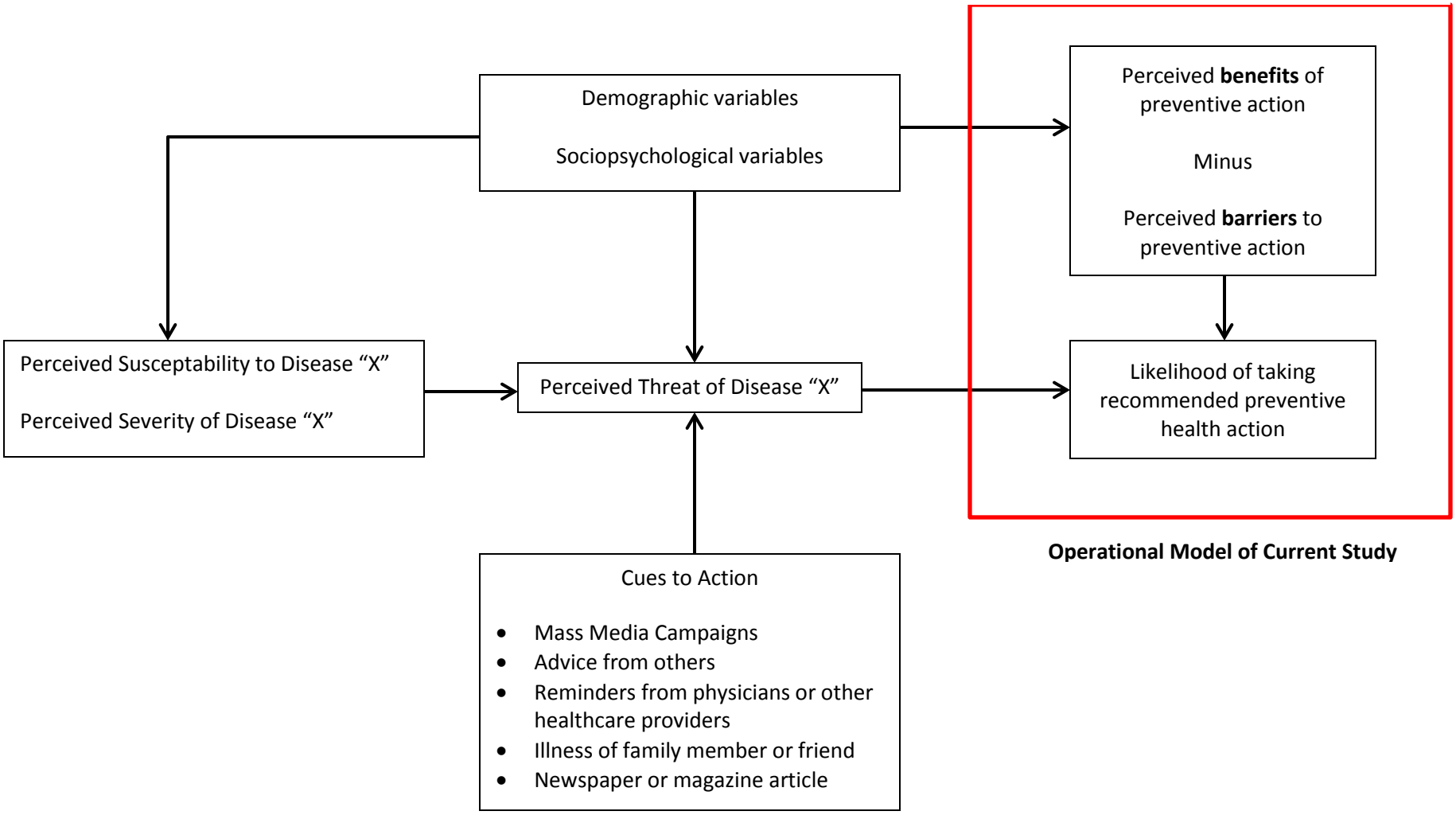
When drug facts boxes are used to give both numerical and verbal risk information, people have greater understanding and knowledge of the actual risks and benefits of medications (Schwartz, Woloshin and Welch, 2009). Combining numerical information can lower perceived risks to more accurate levels in women who are assessing their risk for breast cancer (Quillin et al., 2004).

Theory

Health Belief Model

The Health Belief Model (HBM) originated in the 1950s as a means of determining factors that predicted whether an individual would choose to take preventive health measures (Janz and Becker, 1984). As shown in Figure 2, the likelihood of an individual taking a recommended preventive health action is influenced by a number of factors including 1) perceived susceptibility to a specific disease, 2) perceived severity of the disease, 3) perceived threat of the disease, 4) perceived benefits of the preventive action minus the perceived barriers to the preventive action, 5) demographic and psychosocial variable and finally, 6) cues to action such as advice from friends or authority figures.

Figure 3: Health Belief Model



Of the factors that influence preventive health behaviors, perceived barriers consistently show the highest levels of significance in studies assessing the HBM (Janz and Becker, 1984). In a review of HBM studies, it was shown in 21 of 23 studies that barriers played a significant role in health behavior (Janz and Becker, 1984).

Risk Perception of Side Effects and Medication Adherence

Perceived medication side effects are common barriers to medication adherence and have been shown to negatively correlate with adherence (Kelly, 1987). That is, if an individual perceives the side effects of a medication to be more risky or severe, they are less likely to remain compliant. In patients taking statin drugs, patients who felt the drug could potential harm them were two and a half times more likely to be non-adherent (Mann et al, 2007). When risks are perceived as high this tends to lead to poorer health outcomes (Sivell et al., 2008). Other studies have shown that individuals with a better understanding of risks associated with certain behaviors are more likely to be higher risk-takers than those with lower understanding (Cook and Bellis, 2001). Also, as risk perception increases, so do stress levels - but stress will decrease when risk is accurately assessed (Hopwood et al., 1998). This suggests that providing more precise risk information should lead to improved adherence. Risk perception was positively correlated with the intention to seek information or take a medication in women who were prescribed the breast cancer prophylaxis drug Tamoxifen (Dillard et al., 2011). To be sure, other barriers to care can arise as the same study showed that three months later, there was no correlation with risk perception and actual behavior, suggesting a temporal effect of risk perception (Dillard et al., 2011).

Conceptual Framework of Study

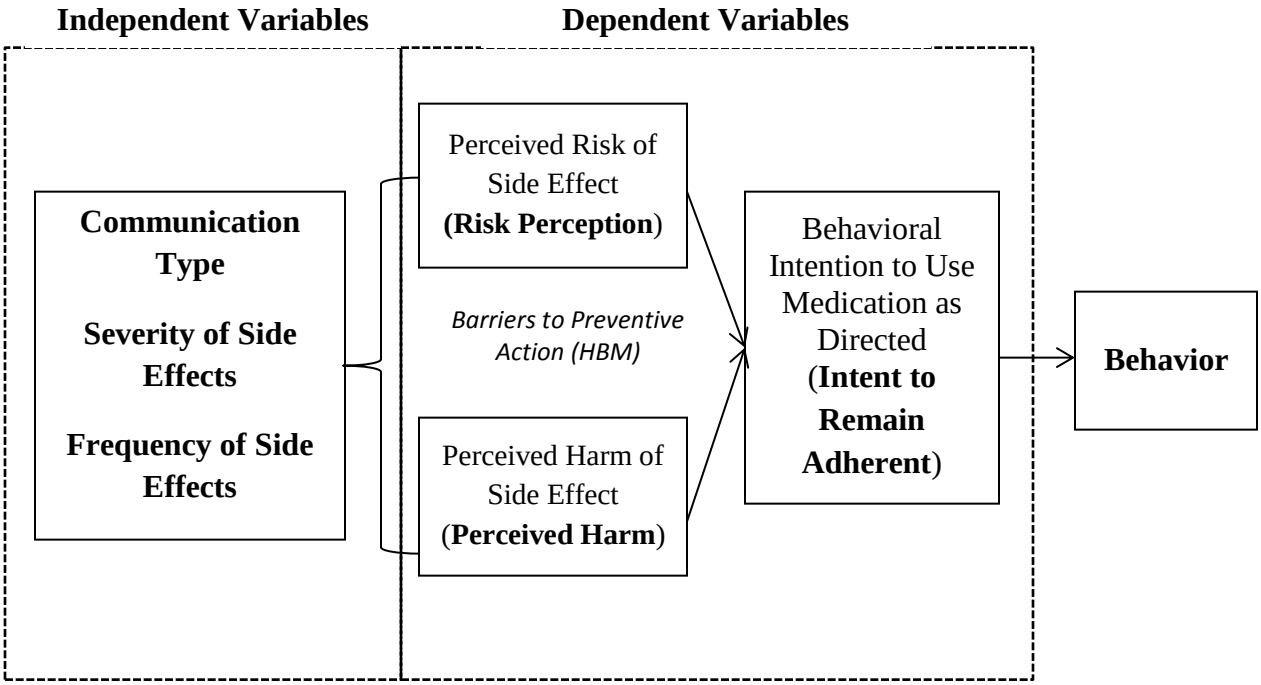
As the Health Belief Model states, lowering barriers to preventive action can lead to the desired preventive action. Based on the review of literature above, this study postulates to use the following dependent variables as barriers to preventive action:

1. Perceived risk of side effect (risk perception)
2. Perceived harm of side effect (perceived harm)

According to the HBM, modulating these variables should lead to an effect on the behavior of taking medications. Due to constraints of the resources available to the researcher, adherence to medication is not able to be measured directly. However, a reasonable substitute will be used – the intent to remain adherent as indicated by participants.

The effects of the independent variables of communication type, severity of side effects and frequency of side effects will be assessed for effects on risk perception, perceived harm and intent to remain adherent.

Figure 4: Conceptual Framework of the Study based on the Health Belief Model (Janz and Becker, 1984)



Hypotheses

- Describing the frequency of side effects in plain language and numerical language (combined) will make side effects seem less risky than only describing side effects in plain language.

- Describing the frequency of side effects in plain language and numerical language (combined) will make side effects seem less harmful than only describing side effects in plain language.

- Describing the frequency of side effects in plain language and numerical language (combined) will increase the intent to remain adherent than only describing side effects in plain language.

Assumptions

The study makes the following assumptions:

1. Mean scores for perceived risk, perceived harm and intent are normally distributed.
2. Participants provided accurate responses to the risk perception and demographic questions and that the instruments adequately captured their perceptions.
3. Participants behaved rationally and made use of all the information provided in the questionnaire. They considered the implications of their responses before they decided to select a particular response.

CHAPTER THREE

Methodology

This chapter will describe the methodology used in this study, including study design, design of survey, descriptions of the independent and dependent variables as well as the statistical hypotheses being tested. Data collection methods, questionnaire design are also described.

Study Design

The study design used to evaluate risk perception of side effects and intent to remain adherent was an experimental 2 x 3 factorial design. Three independent variables were evaluated (communication type, severity of side effect and frequency of side effect), each with two levels (plain language or combination, high or low, high or low). Students at the University of Houston College of Pharmacy were invited to participate in an on-line survey administered through Qualtrics. The study was designed to measure subjects' perceived risk of experiencing side effects of medications and their intent to take the medication as directed by their physician. Data was collected from November 4, 2012 to November 18, 2012.

An initial risk evaluation was completed by each subject. Subjects were then shown four drug facts boxes randomized to either the plain language (PL) group or combined language (Combo) group. The order in which subjects were shown each drug facts box was randomized. Immediately after reading the drug facts presented for each drug, subjects were asked to rate the perceived risk of experiencing the side effect, perceived harm of the side

effect and their intent to adhere to therapy on a visual analog scale (0-100, 100 being absolute risk/harm/intent to adhere).

Independent Variables

Three independent variables are assessed, each with two levels. Communication type has levels of plain language only and combined (plain language plus natural frequency). The plain language level consists of a risk statement written in plain language (e.g., "rarely causes. . ."). The combined level consists of the same plain language risk statement but with an added statement of the natural frequency of the side effect (e.g., 10 people out of 100). Severity of side effects and frequency of side effects have two levels each (high or low).

Table 2: Levels of Independent Variables

Variable	**Level**
Communication Type	Plain language
	Combined (plain language *plus* natural frequency)
Severity of Side Effect	High
	Low
Frequency of Side Effect	High
	Low

Design of the Drug Facts Box

Evidence suggests that specific choices about the format and layout of prescription drug labels facilitate communication with and understanding by patients (Shrank et al., 2007). Drugs were designated as A, B, C and D to remove any potential bias of

previous knowledge about currently available medications. Benefits of each medication were explained in order to control for effects of framing. Benefits were explained as "current uses" of the drug. One side effect was selected from the literature for each medication. Side effects were selected based on the frequency of occurrence and potential severity. Package inserts and other literature was consulted in the selection of appropriate frequencies for each side effect for all study medications except for Drug C. The side effect frequency for Drug C was described as 85%, which is higher than literature reports. The frequency was adjusted to be similar to the other high frequency side effect for Drug B to give comparable information. All information was written at an 8th grade reading level so as to be in plain language per recommendations (Fagerlin, Zikmund-Fisher, and Ubel, 2011).

Table 3: Description of Study Drugs Side Effects and Frequencies from Literature

Study Name	**Medication**	**Side Effect**	**Experiencing Side Effect (%)**	**Literature Source**
Drug A	Aspirin	Stomach bleeding	2%	Kaufman et al., 1993
Drug B	Niacin	Facial flushing	88%	Niaspan [package insert]
Drug C	Rituximab	Loss of immune function	85%	*See comments in text
Drug D	Cetirizine	Headache	5%	Zyrtec [package insert]

Severity and Frequency of Side Effects

Severity and frequency of side effect were manipulated by creating four "Drug Facts" boxes. Each drug had side effect information that was classified into two levels based on severity of the side effect and frequency of the side effect.

Table 4: Classification of Study Drugs by Severity and Frequency of Side Effects

Variable	Level	Drug	Content
Severity of Side Effect	High	A	Stomach bleeding
		C	Loss of immune function
	Low	B	Flushing of the face
		D	Headache
Frequency of Side Effect	High	B	88 out of 100
		C	85 out of 100
	Low	A	2 out of 100
		D	5 out of 100

Prior to distribution of the survey, a pilot check was administered to various people to determine that side effects were perceived to be severe in a consistent manner. A formal manipulation check to verify that participants perceived stomach bleeding and loss of immune function as "high" severity side effects and flushing of the face and headache as "low" severity side effects was conducted as part of the survey. At the end of the survey, participants were asked to rank each side effect in order from most to least severity. Side effects ranked "1" were perceived as highest severity, where "4" were perceived as lowest severity.

Table 5: Mean Rank Order of Side Effect Severity

Severity Level	Side Effect	Mean Rank (1-4)
High	Loss of immune function	1.3
	Stomach bleeding	1.8
Low	Headache	3.4
	Flushing of the face	3.6

Communication Type

Risk information for each drug is expressed as plain language or a combination of plain language and natural frequencies. The plain language risk statement was based on the established frequency of the side effect. Plain language and natural frequency statements were inserted into the sentence describing side effects and always followed the corresponding structure:

Plain language: Drug [X] can [Y] cause [Z].

Combined: Drug [X] can [Y] cause [Z]. Out of 100 people taking Drug [X], [W] will experience [Z].

Where,
X = drug letter (A-D)
Y = plain language risk statement
Z = side effect for drug
W = natural frequency for side effect

Natural frequency information was based on frequency of side effects reported in scientific literature for the analog drugs.

Table 6: Communication Terms by Side Effect Frequency

Side Effect	**Frequency (%)**	**Plain Language Statement**	**Natural Frequency**
Stomach bleeding	2%	Rarely	2 out of 100
Headache	5%	Rarely	5 out of 100
Loss of immune function	85%	Very likely	85 out of 100
Flushing of the face	88%	Very likely	88 out of 100

Probability of Drug Side Effects: Plain Language and Combined Language

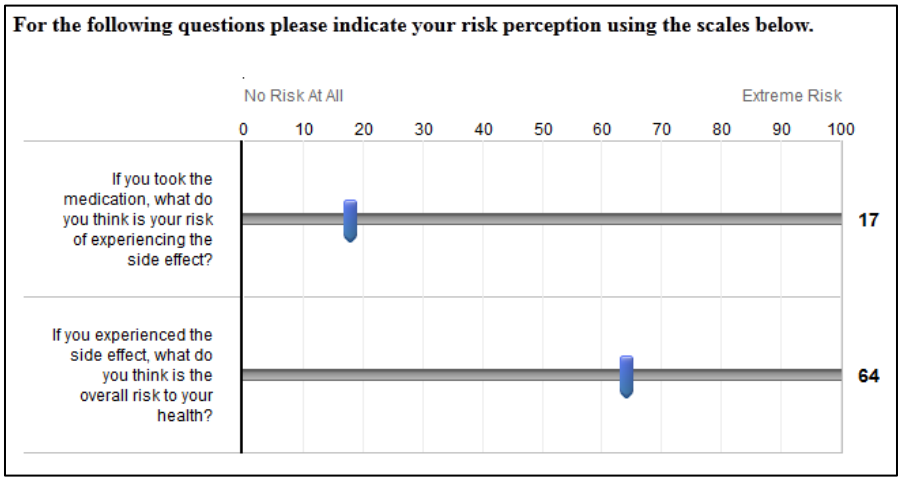
To test the hypothesis, the probability of each side effect was described in one of two ways. The plain language group explained the side effect in plain language only. The combined group explained the probability of experiencing the side effect in plain language and numerical frequency (natural frequency).

Each subject responded to a series of questions to assess their general level of risk perception about medications. Subjects were then shown a series of four drug facts boxes containing information about four different drugs. The side effect of each drug was accompanied by a risk statement for the probability of experiencing the side effect randomly expressed in plain language only or plain language plus numerical information.

Dependent Variables: Risk, Harm and Intent

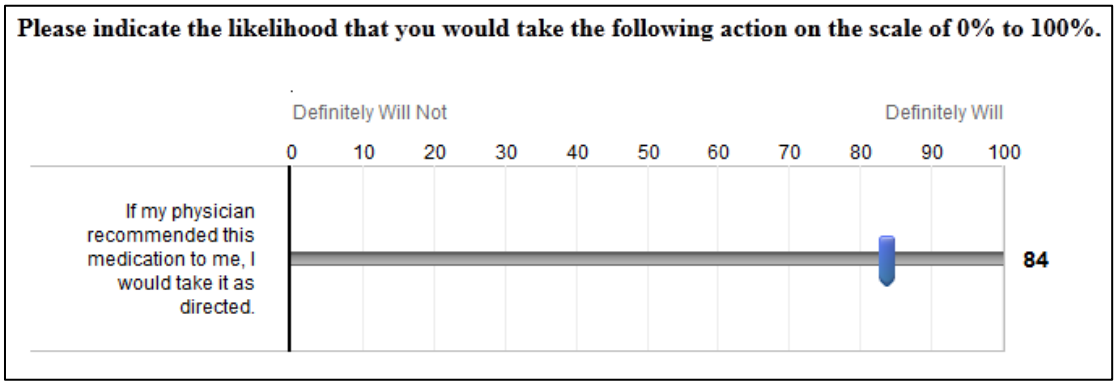
The primary objectives of this study were to evaluate the perceived riskiness of side effects (Risk), perceived harm from experiencing the side effect (Harm) and the participants' intent to adhere to therapy (Intent). Risk, harm and intent were measured on a 100-point visual analog scale. Higher scores indicated greater perceived riskiness, harm or intent. To measure Risk, participants were asked to rate their perceptions on a Visual Analog Scale ranging from zero to 100, with zero meaning "no risk" and 100 meaning "absolute risk."

Figure 5: Measuring Risk Perception and Perceived Harm (Visual Analog Scales)



Intent was measured by a single question: "if my physician recommended this medication to me, I would take it as directed." Participants rated the likelihood they would follow the direction on a Visual Analog Scale ranging from zero to 100, with zero meaning "definitely will not" to 100 meaning "definitely will." A single Intent Score was obtained for each participant. Lower scores indicate less likelihood of adherence, higher scores indicated greater likelihood of adherence.

Figure 6: Measuring Intent to Remain Adherent (Visual Analog Scale)



Questionnaire Design

The questionnaire was designed using Qualtrics© software. Sections included:

1. Consent Form
2. General Risk Assessment
3. Drug Facts Box (A-D)
4. Overall Harm/Benefit
5. Demographics

The general risk assessment included eight questions about the participants' general perception of the risk for medications. Participants were asked to rate the first seven questions on a 7-point Likert scale (1 – strongly disagree, 7 – strongly agree). Participants were asked to rate the final risk assessment question on a Visual Analog Scale from 0-100. Participants were able to drag a sliding bar on the scale to indicate their risk perception. Below are the risk assessment questions:

1. I believe that in general medications approved by the FDA are safe.
2. I believe that medications prescribed by my physicians are less risky.
3. In general medications do not have many side effects.
4. I believe that there is no risk if medications are taken appropriately.
5. I believe that in general I am vulnerable to side effects from the use of medications.
6. I believe that in general taking medications to treat any disorder is very risky.
7. I believe that in general I can avoid risk associated with the use of medications.
8. How risky do you believe it is in general to take medications for any condition?

After the general risk assessment, participants took part in the Drug Facts section. Participants were shown drug facts boxes for each of the four drugs (A-D) presented in random order. Each drug facts box was randomized to either plain language or combined language. Participants rated their perceived risk and intent after reading information for each drug.

After rating risk perception and intent for each drug, participants were asked to rank the side effects of the drugs in order from most harmful to least harmful. Then, participants were asked to rank the indications for each drug in order from most beneficial to least beneficial.

Finally, demographic information was collected on sex, race, age, educational level and employment in healthcare.

Data Collection

Survey invitations were emailed to students at the University of Houston College of Pharmacy. Invitations were sent to an email listserv for the following classes:

1. Class of 2013
2. Class of 2014
3. Class of 2015
4. Class of 2016

A link to the survey in each email allowed participants to anonymously participate in the study. No identifying information was collected. Survey responses were recorded by Qualtrics© into the survey database. Data was downloaded into Excel for coding.

Data Preparation

Survey data was downloaded from Qualtrics© into a Microsoft Excel™ data file. Collected data was coded and a code book was created. Missing data was imputed using a cold-deck imputation method (group mean for continuous variables and medians for Likert-scale type items). All coding was performed by the primary investigator.

Statistical Analysis

Descriptive statistics were performed on the variables. Means of continous and Likert-scale type items were calculated. Frequencies were calculated for ordinal and categorical response items. A multivariate analysis of variance test was performed to assess the differences in risk of experiencing side effect (Risk) and intent to remain adherent (Intent) between plain language and combined language groups, levels of severity (high or low) and levels of frequency (high or low).

Statistical Hypotheses

H_1: There is no difference in risk perception, perceived harm of side effects and intent to adhere to therapy between plain language and combined language groups.

The first hypothesis is further subdivided into three hypotheses:

H_{1a}: There is no difference in risk perception between plain language and combined language groups.

$$\mu_{rp1} = \mu_{rp2}$$

Where,

μ_{rp1} = mean risk perception score for plain language group

μ_{rp2} = mean risk perception score for combined language group

H_{1b}: There is no difference in perceived harm of side effects between plain language and combined language groups.

$$\mu_{hp1} = \mu_{hp2}$$

Where,

μ_{hp1} = mean risk perception score for plain language group

μ_{hp2} = mean risk perception score for combined language group

H_{1c}: There is no difference in intent to adhere to therapy between plain language and combined language groups.

$$\mu_{i1} = \mu_{i2}$$

Where,

μ_{i1} = mean risk perception score for plain language group

μ_{i2} = mean risk perception score for combined language group

H_2: There is no association between perceived risk of side effects and the intent to remain adherent.

$$H_2: \rho = 0$$

Where,

ρ = Spearman correlation coefficient

Human Subject Protection

The survey protocol was submitted to the Institutional Review Board at the University of Houston for approval. Data collection was started once approval was granted.

CHAPTER FOUR

Results

This chapter will discuss the results of the study including methods for coding and analysis of the survey data, sample characteristics, statistical results for dependent variables across all independent variables and significant differences and testing of the statistical hypotheses.

Survey Coding, Collection and Analysis

No identifying information was collected. The following schedule was followed in the data collected process:

1. Invitation 1: 11/4/2012
2. Invitation 2 (reminder): 11/8/2012

Survey collection was discontinued on 11/18/2012. A total of 100 surveys were completed. All data was automatically recorded by Qualtrics™. The survey data was downloaded into a Microsoft Excel™ spreadsheet for coding. Participants were assigned an ID number based on the order in which they began the survey.

Response Rate

400 invitations to participate in the survey were emailed via University of Houston College of Pharmacy listserv groups. 168 individuals responded. Of those, 100 completed the survey for an overall response rate of 25%.

Statistical Analysis

All statistical analyses were performed at the set priori alpha level of 0.05 using SAS© statistical software (version 9.3, SAS© Institute Inc., Cary, NC).

Sample Characteristics

Age: The mean age for participants was 24.65 (SD 2.89) years. Age of the participants ranged from 20 to 39 years.

Table 7: Age distribution of the study sample

Variable	Mean (SD)	Median	Range
Age	24.65 (2.89)	24	20 - 39

Gender: The study sample consisted of a majority of females.

Table 8: Distribution of gender in the study sample

Gender	Frequency (%)
Male	27 (27.0%)
Female	73 (73.0%)

Ethnicity: The majority of the participants were white (53%) or Asian (38%).

Table 9: Distribution of ethnicity in the study sample

Ethnicity	Frequency (%)
White	53 (53%)
African American	1 (1%)
Hispanic	4 (4%)
Asian	38 (38%)

Other	5 (5%)

Education Level: Majority of the participants reported at least some college (26%) or a bachelor's degree (62%). None of the sample had less than a high school education.

Table 10: Distribution of education level in the study sample

Education	**Frequency (%)**
Some College	26 (26%)
Bachelor's Degree	62 (62%)
Master's Degree	2 (2%)
Doctoral Degree	4 (4%)
Professional Degree	6 (6%)

Least Squares Means of Perceived Risk & Harm and Intention to Adhere

A multivariate analysis of variance (MANOVA) was conducted to measure the differences in least squares (LS) means across all three independent variables (severity, frequency and communication type) for the dependent variables of perceived risk, perceived harm and intent to adhere to therapy. Tukey-Kramer test was conducted to adjust for multiple comparisons and adjusted p-values are reported. Effects of the interactions between all three variables were measured as well.

Multivariate Effects

Multivariate effects of the independent variables communication type, severity of side effect and frequency of side effect were measured across the dependent variables of perceived risk, perceived harm and intent to remain adherent. There were no significant effects for the variable of communication type (plain language or combination) alone ($F_{3,390} = 1.97$, $p = 0.118$). When combined with severity, frequency, and severity*frequency, significant effects were found for communication type. The rest of the effects of the independent variables were found to be significant at $p < 0.05$.

Table 11: Multivariate Effects (MANOVA)

Independent Variable	**Wilk's Lambda**	**F (3,390)**	**p-value**
Communication Type	0.985	1.97	0.118
Severity	0.397	197.21	<0.001
Frequency	0.241	408.93	<0.001
Severity*Frequency	0.956	6.05	<0.001
Communication Type*Severity	0.943	7.91	<0.001
Communication Type*Frequency	0.943	7.86	<0.001
Communication Type*Severity*Frequency	0.968	4.33	0.005

Dependent Variable: Perceived Risk

Analysis of the dependent variable perceived risk was conducted. The overall effects of communication type, severity and frequency had a significant effect on the dependent variable perceived risk ($F_{7,392} = 190$, $p < 0.0001$).

The effect of communication type on perceived risk was significantly different ($F_{1,392}$ =5.5, p = 0.0195). There was also a difference between severity ($F_{1,392}$ = 17.87, p < 0.0001) and frequency ($F_{1,392}$ = 1225, p < 0.0001).

Table 12: Sum of Squares for Dependent Variable: Perceived Risk

Variable	**DF**	**Type III SS**	**Mean Square**	**F Value**	**Pr > F**
Communication Type	1	1669.3	1669.3	5.5	0.0195
Severity	1	5419.5	5419.5	17.87	<.0001
Frequency	1	371695	371695	1225.73	<.0001
Severity*Frequency	1	2122.3	2122.3	7	0.0085
Communication Type*Severity	1	6229.6	6229.6	20.54	<.0001
Communication Type*Frequency	1	6947.6	6947.6	22.91	<.0001
Communication Type*Severity*Frequency	1	2239.3	2239.3	7.38	0.0069
Model	7	404443	57778	190.53	<.0001
Error	392	118872	303.25		
Corrected Total	399	523315			

Mean Risk Perception Scores

The effects of communication type, severity of side effect and frequency of side effect were statistically significant for perceived risk of experiencing side effect. Scores were measured on a visual analog scale from 0 to 100. Higher scores indicate higher perceived

risk. Tukey post-hoc analysis indicated that the combination communication type group had significantly higher risk perception scores (M = 46.6, 95% CI [44.2, 49.1]), compared to the risk perception scores for the plain language group (M = 42.5, 95% CI [40.1, 44.9]), p = 0.019). Risk perception scores were significantly higher in the "high severity" group (M = 48.3, 95% CI [45.8, 50.7]) compared to the "low severity" group (M = 40.9, 95% CI [38.5, 43.3]), p < 0.001. Risk perception scores were significantly higher in the "high frequency" group (M = 75.1, 95% CI [72.7, 77.6]) as compared to the "low frequency" group (M = 14, 95% CI [11.6, 16.4]), p < 0.001).

Table 13: Means of Perceived Risk of Experiencing Side Effect

Variable	Level	Mean (95% CL)	Difference (95% CL)	%	p-Value
Communication Type	Plain Language	42.5 (40.1, 44.9)			
	Combination	46.6 (44.2, 49.1)	4.1 (0.67, 7.5)	9.6%	0.019
Severity of Side Effect	Low	40.9 (38.5, 43.3)			
	High	48.3 (45.8, 50.7)	7.4 (3.9, 10.8)	18.1%	<0.001
Frequency of Side Effect	Low	14.0 (11.6, 16.4)			
	High	75.1 (72.7, 77.6)	61.4 (57.7, 64.6)	438%	<0.001

Effects of Severity*Communication Type on Risk Perception

The effect of severity of side effects on communication type was measured. Mean risk perception scores for the combination of plain language communication and low severity side effects was significantly lower than all other combinations of communication type and severity (M = 34.9, 95% CI [31.4, 38.4]), p<0.001. Differences in least squares means for all

other combinations were not statistically significant. See Appendix [#] for complete tables of comparisons between groups and p-values.

Table 14: Mean Risk Perception Scores for Communication Type*Severity

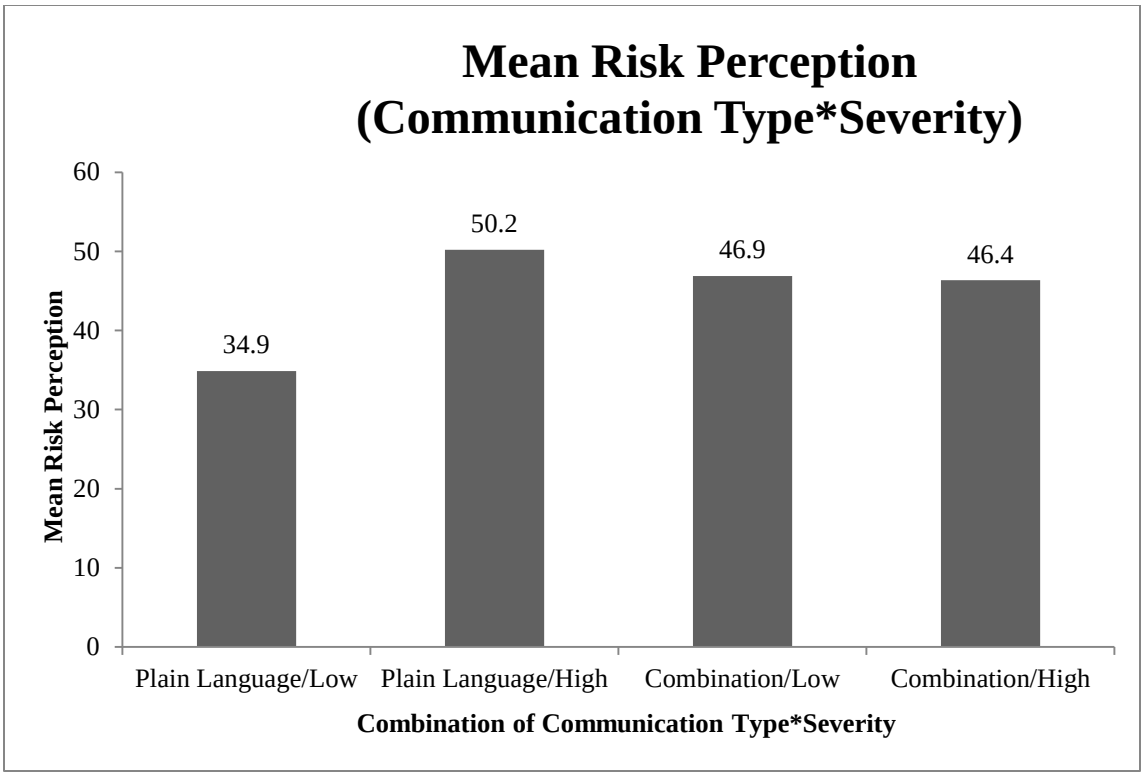
Communication Type	**Severity**	**Mean Risk Perception**	**95% CI**	
Plain Language	Low	34.9	31.4	38.4
Plain Language	High	50.2	46.8	53.5
Combination	Low	46.9	43.5	50.3
Combination	High	46.4	42.9	49.9

Significant effects for the combination of plain language & low severity were found between the other three combinations. Differences in means between groups are described in Table [#] and were statistically significant ($p < 0.001$).

Table 15: Significant Effects of Communication Type*Severity on Risk Perception

Communication Type/Severity	**Communication Type/Severity**	**Difference**	**p value**
Plain Language/Low	Plain Language/High	-15.3	<0.001
	Combination/High	-11.5	<0.001
	Combination/Low	-12.0	<0.001

Figure 7: Mean Risk Perception (Communication Type*Severity)



Effects of Frequency*Communication Type on Risk Perception

The combined effect of communication type and frequency of side effects was measured and Tukey post-hoc analysis completed. Frequency of side effect had a stronger effect than communication type on risk perception of side effects. Mean risk perception scores for the high frequency, combination communication type group were significantly higher than scores for all other combinations ($M = 81.4$, 95% CI [77.9, 84.6]), $p < 0.001$. Similarly, risk perception scores for the high frequency, plain language group ($M = 68.9$, 95% CI [65.5, 72.3]) were significantly higher than the low frequency, plain language group ($M = 16.1$, 95% CI [12.7, 19.6]) or the low frequency, combination group ($M = 11.9$, 95% CI [8.5, 15.3]), $p < 0.001$. When the frequency was high, the combination communication type group had significantly higher risk scores ($M = 81.4$, 95% CI [77.9, 84.6]), than the plain language group ($M = 68.9$, 95% CI [65.5, 72.3]), $p < 0.001$.

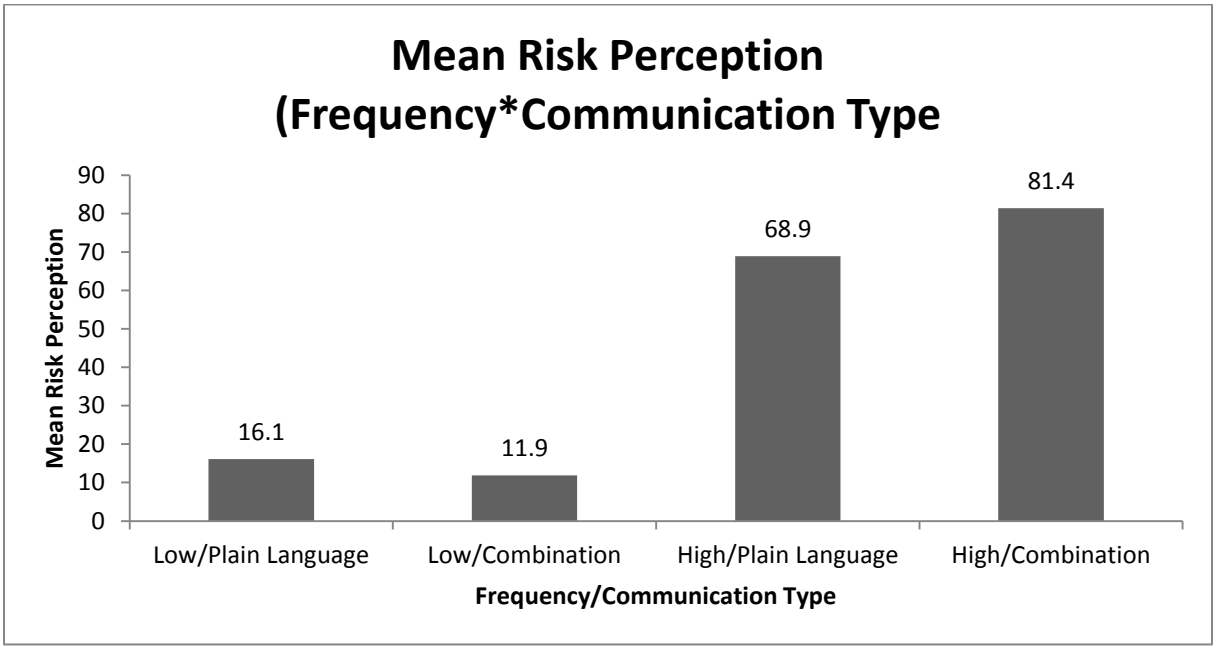
Table 16: Mean Risk Perception Scores for Communication Type*Frequency

Communication Type	**Frequency**	**Mean Risk Perception**	**95% CI**	
Plain Language	Low	16.1	12.7	19.6
Plain Language	High	68.9	65.5	72.3
Combination	Low	11.9	8.5	15.3
Combination	High	81.4	77.9	84.6

Table 17: Significant Effects of Communication Type*Frequency on Risk Perception

Communication Type/Frequency	**Communication Type/Frequency**	**Difference**	**p value**
Plain Language/High	Plain Language/Low	52.8	<0.001
	Combination/Low	57.0	<0.001
	Combination/High	-12.5	<0.001
Combination/High	Plain Language/Low	65.2	<0.001
	Plain Language/High	12.5	<0.001
	Combination/Low	69.5	<0.001

Figure 8: Mean Risk Perception (Frequency*Communication Type)



Effects of Severity*Frequency*Communication Type on Risk Perception

The combined effects of severity, frequency and communication type on risk perception were measured and Tukey post hoc analysis was conducted. When frequency and severity were identical there was no difference between plain language and combination communication type groups except in the high frequency, low severity group. For high frequency, low severity group the mean risk perception score for the combination communication type group was significantly higher (M = 81.7, 95% CI [77.0, 86.4]) compared to the plain language communication type group (M = 56.6, 95% CI [51.5, 61.6]), $p < 0.001$. See Appendix [#] for a full table of comparisons between groups and p-values.

Table 18: Mean Risk Perception Scores for Frequency*Severity*Communication Type

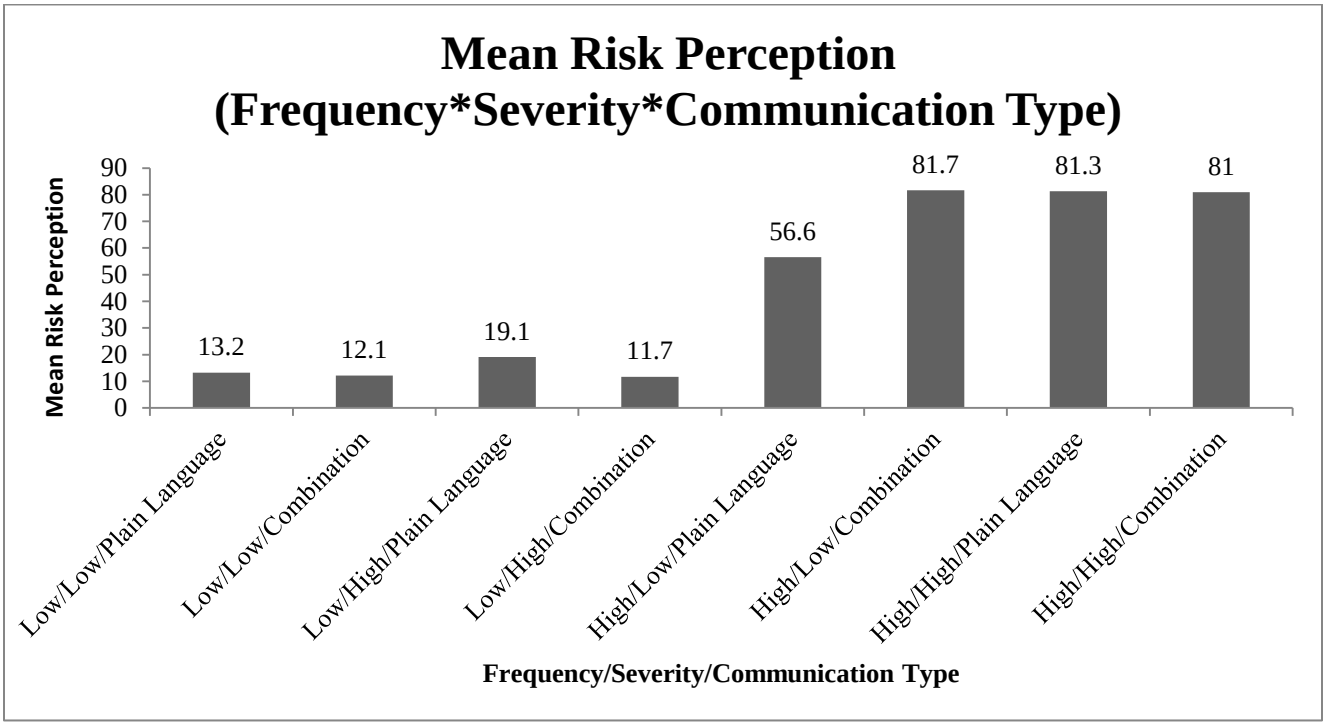
Frequency	Severity	Communication Type	Mean Risk Perception	95% CI	
Low	Low	Plain Language	13.2	8.3	18.0
Low	Low	Combination	12.1	7.2	16.9
Low	High	Plain Language	19.1	14.2	24.0
Low	High	Combination	11.7	6.9	16.4
High	Low	Plain Language	56.6	51.5	61.6
High	Low	Combination	81.7	77.0	86.4
High	High	Plain Language	81.3	76.7	85.8
High	High	Combination	81.0	75.9	86.2

Table 19: Differences Between Combinations of Frequency/Severity/Communication Type on Risk Perception

Combination 1 (i)	Combination 2 (j)	Difference (i-j)	p-value
Low/Low/Plain Language	Low/Low/Combination	1.1	1
	High/Low/Plain Language	-43.4	<.0001
	High/Low/Combination	-68.5	<.0001
	Low/High/Plain Language	-5.9	0.6965
	Low/High/Combination	1.5	0.9999
	High/High/Plain Language	-68.1	<.0001
	High/High/Combination	-67.9	<.0001

Low/Low/Combination	High/Low/Plain Language	-44.5	<.0001
	High/Low/Combination	-69.6	<.0001
	Low/High/Plain Language	-7.0	0.4858
	Low/High/Combination	0.4	1
	High/High/Plain Language	-69.2	<.0001
	High/High/Combination	-69.0	<.0001
High/Low/Plain Language	High/Low/Combination	-25.1	<.0001
	Low/High/Plain Language	37.5	<.0001
	Low/High/Combination	44.9	<.0001
	High/High/Plain Language	-24.7	<.0001
	High/High/Combination	-24.5	<.0001
High/Low/Combination	Low/High/Plain Language	62.6	<.0001
	Low/High/Combination	70.0	<.0001
	High/High/Plain Language	0.5	1
	High/High/Combination	0.7	1
Low/High/Plain Language	Low/High/Combination	7.4	0.3962
	High/High/Plain Language	-62.1	<.0001
	High/High/Combination	-61.9	<.0001
Low/High/Combination	High/High/Plain Language	-69.6	<.0001
	High/High/Combination	-69.4	<.0001
High/High/Plain Language	High/High/Combination	0.2	1

Figure 9: Mean Risk Perception (Frequency*Severity*Communication Type)



Dependent Variable: Intent to Adhere to Therapy

The effects of communication type, severity of side effects and frequency of side effects were analyzed for respondents' intent to adhere to therapy. The overall effect of communication type, severity and frequency on intent to adhere to therapy was significant ($F_{7,392} = 2.6$, $p = 0.01$). There was no significant difference between communication type on the intent to remain adherent ($F_{1,392} = 0.07$, $p = 0.786$). There was a significant difference on intent to remain adherent for severity ($F_{1,392} = 6.84$, $p = 0.009$) and frequency ($F_{1,392} = 8.2$, $p = 0.004$). Interestingly there was no difference for the combined effects of severity*frequency ($F_{1,392} = 0.08$, $p = 0.774$). The primary variable of communication type was not significantly different between groups, nor was the interaction with any of the independent variables.

Table 20: Sum of Squares for Dependent Variable: Intent to Remain Adherent

Variable	**DF**	**Type III SS**	**Mean Square**	**F Value**	**Pr > F**
Communication Type	1	24.906	24.906	0.070	0.786
Severity	1	2306.607	2306.607	6.840	0.009
Frequency	1	2766.418	2766.418	8.210	0.004
Severity*Frequency	1	28.086	28.086	0.080	0.773
Communication Type*Severity	1	389.115	389.115	1.150	0.283
Communication Type*Frequency	1	3.570	3.570	0.010	0.918
Communication Type*Severity*Frequency	1	841.561	841.561	2.500	0.115
Model	7	6126.62	875.23	2.60	0.01
Error	392	132145.91	337.11		
Corrected Total	399	138272.53			

Mean Intent to Remain Adherent Scores

A Tukey post hoc analysis was completed to assess main effects and interactions. Least squares means were obtained for each variable and difference across each level were measured. Scores are on a scale from 0-100 and higher scores indicate greater intent to adhere.

Mean scores for intent to adhere in the combined communication type group were slightly higher (M = 85.5, 95% CI [82.9, 88.0]) compared to the plain language group (M = 84.9, 95% CI [82.4, 87.5]), but were not statistically significant (p = 0.786).

Mean scores in the high severity group were significantly lower (M = 82.8, 95% CI [80.3, 85.4], p = 0.009) than mean scores for the low severity group (M = 87.6, 95% CI [85.1, 90.2]). The mean scores for the high frequency group were also significantly lower (M = 82.6, 95% CI [80.0, 85.2], p = 0.004) compared to means for the low frequency group (M = 87.9, 95% CI [85.3, 90.4]).

Table 21: Least Squares Means of Intent to Adhere to Therapy

Variable	Level	Least Squares Mean (95% CL)	Difference (95% CL)	%	p-Value
Communication Type	Plain Language	84.9			
	Combination	85.5	0.5	0.05%	0.786
Severity of Side Effect	Low	87.6			
	High	82.8	-4.8	-5.49%	0.009
Frequency of Side Effect	Low	87.9			
	High	82.6	-5.3	-6.38%	0.004

Effects of Severity*Communication Type on Intent to Remain Adherent

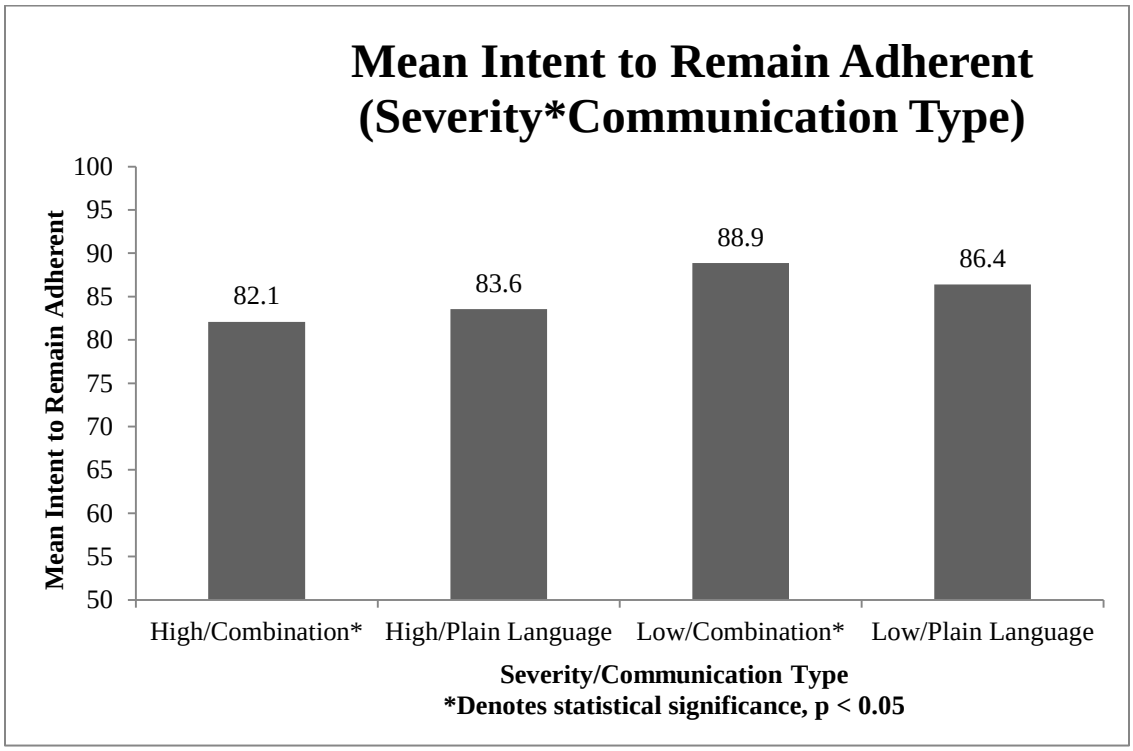
Effects of severity*communication type were compared with Tukey post hoc analysis. The only significant difference was between the high severity, combination communication type group and the low severity, combination communication type group. The mean intent to remain adherent score for the high severity, combination communication

group was significantly lower (M = 82.1, 95% CI [78.4, 85.8], p = 0.046) than the low severity, combination communication group (M = 88.9, 95% CI [85.3, 92.42].

Table 22: Effect of Communication Type*Severity on Intent to Remain Adherent

Communication Type	Severity	Mean Intent to Remain Adherent	95% CI	
Plain Language	Low	86.4	82.7	90.1
	High	83.6	80.0	87.1
Combination	Low	88.9	85.3	92.4
	High	82.1	78.4	85.8

Figure 10: Mean Intent to Remain Adherent (Severity*Communication Type)



Effects of Frequency*Communication Type on Intent to Remain Adherent

Effects of frequency*communication type on the intent to remain adherent were analyzed and post hoc analysis with a Tukey test was conducted. There were no significant differences between groups for the intent to remain adherent.

Table 23: Mean Intent to Remain Adherent Scores for Frequency*Communication Type

Communication Type	**Frequency**	**Mean Intent to Remain Adherent**	**95% CI**	
Plain Language	Low	87.7	84.1	91.4
Plain Language	High	82.2	78.7	85.8
Combination	Low	88.0	84.4	91.6
Combination	High	82.9	79.3	86.6

Effects of Frequency*Severity on Intent to Remain Adherent

Effects of severity and frequency were compared for mean scores of the intent to remain adherent and a Tukey post hoc analysis was conducted. The mean score for intent to remain adherent in the low severity, low frequency group was significantly greater ($M = 90.0$, 95% CI [86.4, 93.6], $p < 0.001$) compared to the mean score for the high severity, high frequency group ($M = 79.9$, 95% CI [76.3, 83.6]). No other combinations of severity and frequency were statistically significantly different.

Table 24: Mean Intent to Remain Adherent for Severity*Frequency

Severity	**Frequency**	**Mean Intent to Remain Adherent**	**95% CI**	
Low	Low	90.0	86.4	93.6
Low	High	85.3	81.6	88.9
High	Low	85.7	82.1	89.3
High	High	79.9	76.3	83.6

Effects of Severity*Frequency*Communication Type on Intent to Remain Adherent

Effects of communication type, severity and frequency combined were compared for mean scores of intent to remain adherent and a Tukey post hoc analysis was conducted.

Table 25: Mean Intent to Remain Adherent for Severity*Frequency*Communication Type

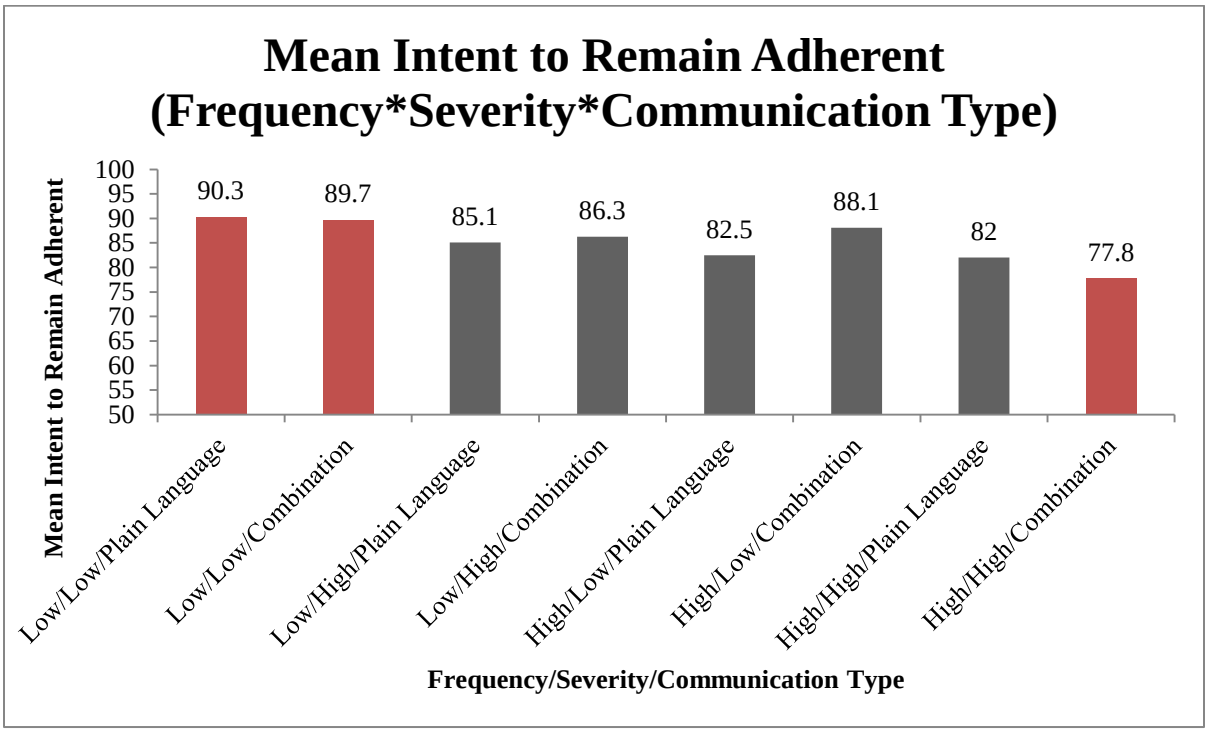
Severity	**Frequency**	**Communication Type**	**Mean Intent**	**95% CI**	
Low	Low	Plain Language	90.3	85.2	95.4
Low	Low	Combination	89.7	84.6	94.8
Low	High	Plain Language	82.5	77.2	87.8
Low	High	Combination	88.1	83.1	93.0
High	Low	Plain Language	85.1	79.9	90.3
High	Low	Combination	86.3	81.3	91.4
High	High	Plain Language	82.0	77.2	86.8
High	High	Combination	77.8	72.4	83.3

The mean score for intent for the high severity, high frequency, combined communication type group was significantly lower (M = 77.8, 95% CI [72.4, 83.3]) than the mean score for the low severity, low frequency, plain language group (M = 90.3, 95% CI [85.2, 95.4], p = 0.02) and the low severity, low frequency, combined group (M = 89.7, 95% CI [84.6, 94.8], p = 0.04). No other combinations of severity, frequency or communication type were significantly different.

Table 26: Significant Differences Between Combinations of Severity/Frequency/Communication Type

Severity/Frequency/Communication Type		Difference	95% CI		p-value
High/High/ Combination	Low/Low/Plain Language	-12.5	-0.93	-24.1	0.02
	Low/Low/Combination	-11.9	-0.31	-23.5	0.04

Figure 11 Mean Intent to Remain Adherent (Frequency*Severity*Communication Type)



Dependent Variable: Perceived Harm of Side Effects

The effect of communication type, severity and frequency of side effects was analyzed for the effect on perceived harm of the side effects. Type III sum of squares was calculated for the effects of all the variables and the interactions between the variables. The overall model of communication type, severity and frequency and the effect on perceived harm was significant ($F_{7,392}$= 91.46, $p < 0.0001$), but most of this effect was from the

variables of severity and frequency. There was no significant effect of communication type on perceived harm ($F_{1,392} = 0.2$, $p = 0.659$). There was a significant effect of severity ($F_{1,392} = 586$, $p < 0.0001$), frequency ($F_{1,392} = 38.41$, $p < 0.0001$) and the combination of severity*frequency ($F_{1,392} = 13.9$, $p = 0.0002$).

Table 27: Sum of Squares for Dependent Variable: Perceived Harm

Variable	**DF**	**Type III SS**	**Mean Square**	**F Value**	**Pr > F**
Communication Type	1	87.8188	87.8188	0.2	0.659
Severity	1	263864	263864	586.12	<.0001
Frequency	1	17291.7	17291.7	38.41	<.0001
Severity*Frequency	1	6258.59	6258.59	13.9	0.0002
Communication Type*Severity	1	236.804	236.804	0.53	0.4687
Communication Type*Frequency	1	158.323	158.323	0.35	0.5535
Communication Type*Severity*Frequency	1	484.282	484.282	1.08	0.3003
Model	7	288233	41176.1	91.46	<.0001
Error	392	176474	450.189		
Corrected Total	399	464707			

Mean Scores for Perceived Harm

Least squares means for communication type, severity of side effect and frequency of side effect were calculated for the effect on perceived harm of side effect. A Tukey post hoc

analysis was conducted. Scores for perceived harm are scored on a 0-100 scale, with higher scores indicating greater perceived harm. Scores of perceived harm for the plain language communication group slightly lower (M = 40.7, 95% CI [37.8, 43.7], p = 0.66), compared to the combined language group (M = 41.7, 95% CI [38.7, 44.6]) but the difference was not statistically significant. The mean score for perceived harm in the high severity group was significantly higher (M = 66.9, 95% CI [64.0, 69.9], p < 0.001) compared to the low severity group (M = 15.4, 95% CI [12.5, 18.4]). Perceived harm scores for the high frequency group were significantly higher (M = 47.8, 95% CI [44.8, 50.8], p < 0.001) compared to the low frequency group (M = 34.6, 95% CI [31.7, 37.6]).

Table 28: Least Squares Means of Perceived Harm

Variable	Level	LS Mean (95%CL)	Difference	%	p-value
Communication Type	Plain Language	40.7 (37.8-43.7)			
	Combination	41.7 (38.7-44.6)	0.94 (-3.2 - 5.1)	2.31%	0.66
Severity of Side Effect	Low	15.4 (12.5-18.4)			
	High	66.9 (64.0-69.9)	51.5 (47.3-55.7)	333.4%	<0.001
Frequency of Side Effect	Low	34.6 (31.7-37.6)			
	High	47.8 (44.8-50.8)	13.2 (9.0-17.4)	38.1%	<0.001

Effects of Severity*Communication Type on Perceived Harm

The effects of severity and communication type on perceived harm were compared and a post hoc Tukey analysis was conducted. There were no significant differences amongst the same level of severity between communication type. However, the mean score for perceived harm in the low severity, plain language group was significantly lower (M = 14.2, 95% CI [9.9, 18.5], $p < 0.0001$) than the score for the high severity, plain language group (M = 67.3, 95% CI [63.2, 71.4], $p < 0.0001$) and the score for the high severiy, combination group (M = 66.7, 95% CI [62.4, 70.9], $p < 0.0001$). Also, mean perceived harm scores for the low severity, combination group were significantly lower (M = 16.7, 95% CI [12.6, 20.8], $p < 0.0001$) compared to the high severity, plain language group (M = 67.3, 95% CI [63.2, 71.4], $p < 0.0001$) as well as the high severity, combination group (M = 66.7, 95% CI [62.4, 70.9], $p < 0.0001$).

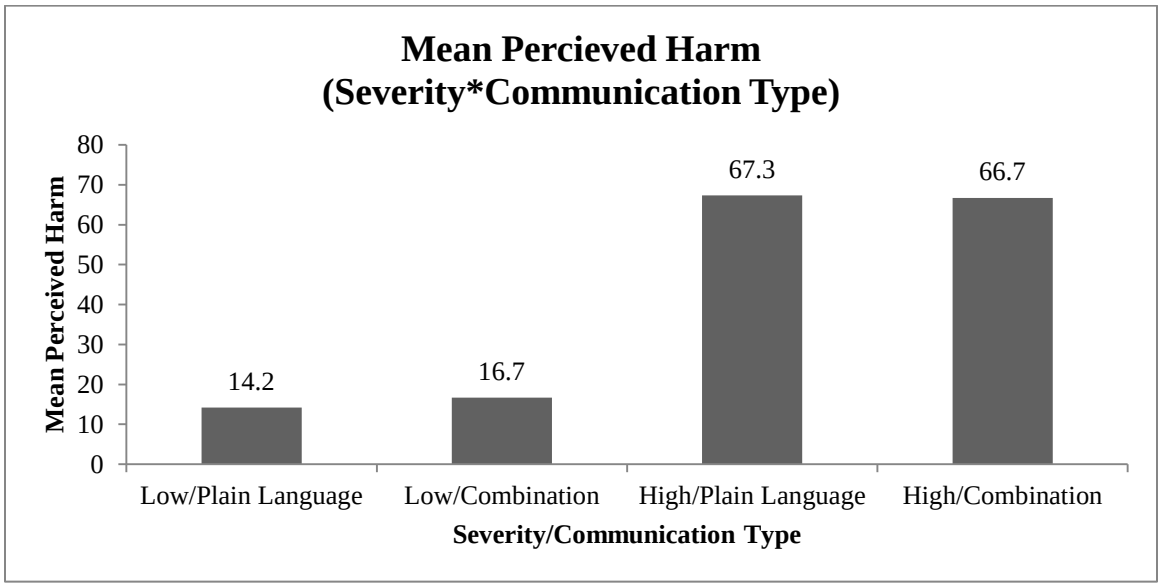
Table 29: Mean Scores for Perceived Harm of Severity*Communication Type

Severity	Communication Type	Mean Percieved Harm	95% Confidence Limits	
Low	Plain Language	14.2	9.9	18.5
Low	Combination	16.7	12.6	20.8
High	Plain Language	67.3	63.2	71.4
High	Combination	66.7	62.4	70.9

Table 30: Significant Differences in Perceived Harm between Combinations of Severity*Communication Type Groups

Combination 1 (i)	Combination 2 (j)	Difference (i-j)	95% CI		p-value
Low/Plain Language	High/Plain Language	-53.1	-60.8	-45.3	<.0001
	High/Combination	-52.5	-60.4	-44.5	<.0001
Low/Combination	High/Plain Language	-50.6	-58.2	-43.0	<.0001
	High/Combination	-50.0	-57.7	-42.2	<.0001

Figure 12: Mean Perceived Harm (Severity*Communication Type)



Effects of Frequency*Communication Type on Perceived Harm

The effects of frequency*communication type on scores for perceived harm were compared across groups and a post hoc Tukey analysis was completed. Mean scores for perceived harm were not significantly difference between plain language and combined communication groups when frequency was held constant. However, scores for perceived harm for low frequency, plain language communication were significantly lower (M = 34.8, 95% CI [30.6, 39.0]) than scores for the high frequency, plain language group (M = 46.7, 95% CI [42.5, 50.8], $p < 0.001$) and the high frequency, combination group (M = 48.9, 95% CI [44.7, 53.1], $p < 0.001$). Also, scores for perceived harm in the low frequency, combination communication type group were significantly lower (M = 34.5, 95% CI [30.3, 38.6]) compared to the high frequency, plain language group (M = 46.7, 95% CI [42.5, 50.8], $p < 0.001$) and the high frequency, combination language group (M = 48.9, 95% CI [44.7, 53.1], $p < 0.001$).

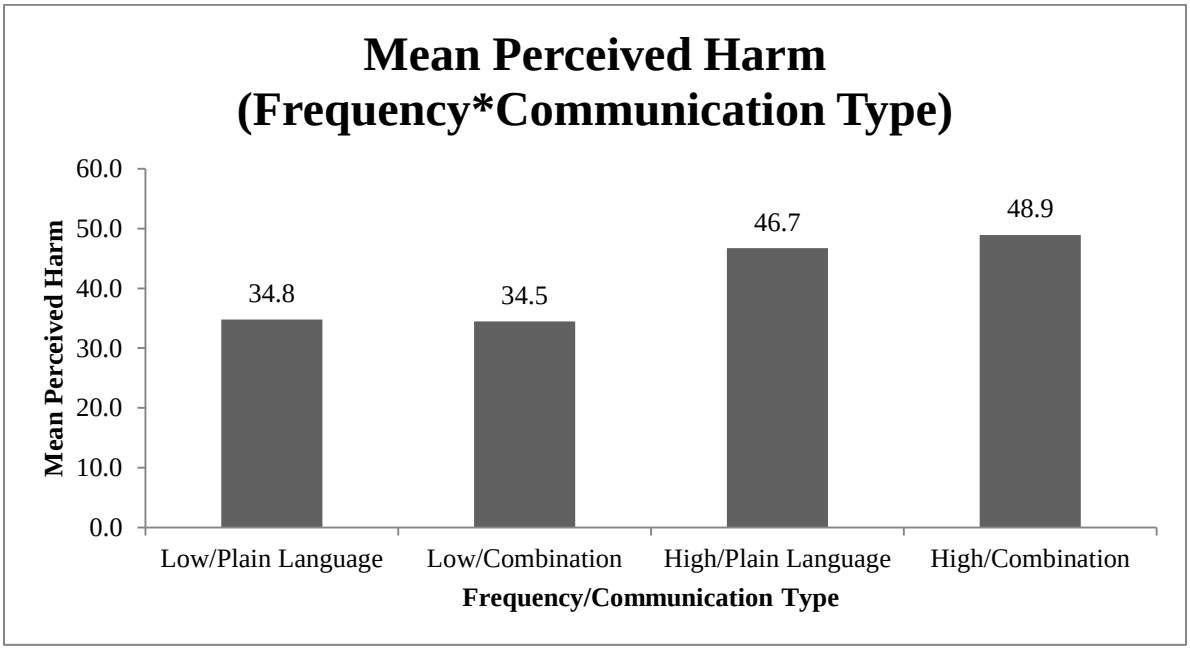
Table 31: Mean Perceived Harm Scores for Frequency*Communication Type

Frequency	Communication Type	Mean Perceived Harm	95% CI	
Low	Plain Language	34.8	30.6	39.0
Low	Combination	34.5	30.3	38.6
High	Plain Language	46.7	42.5	50.8
High	Combination	48.9	44.7	53.1

Table 32: Significant Differences in Perceived Harm Between Combinations of Frequency*Communication Type

Combination 1 (i)	Combination 2 (j)	Difference (i-j)	95% CI		p value
Low/Plain Language	High/Plain Language	-11.9	-19.7	-4.2	<0.001
	High/Combination	-14.1	-22.0	-6.3	<0.001
Low/Combination	High/Plain Language	-12.2	-19.9	-4.6	<0.001
	High/Combination	-14.4	-22.2	-6.7	<0.001

Figure 13: Mean Perceived Harm (Frequency*Communication Type)



Effects of Frequency*Severity on Perceived Harm

Effects of frequency and severity on perceived harm were compared and a post hoc Tukey analysis was conducted. Mean scores for perceived harm in the low severity, low frequency group were significantly lower (M = 12.8, 95% CI [8.7, 17.0]) compared to the high severity, low frequency group (M = 56.4, 95% CI [52.2, 60.6], $p < 0.001$) as well as the high severity, high frequency group (M = 77.5, 95% CI [73.3, 81.7], $p < 0.001$). Mean perceived harm scores for the low severity, high frequency group were significantly lower (M = 18.1, 95% CI [13.9, 22.3]) compared to the high severity, low frequency (M = 56.4, 95% CI [52.2, 60.6], $p < 0.001$) group as well as the high severity, high frequency group (M = 77.5, 95% CI [73.3, 81.7], $p < 0.001$). Finally, scores for perceived harm in the high severity, low frequency group were significantly lower (M = 56.4, 95% CI [52.2, 60.6], $p < 0.001$) compared to the scores for the high severity, high frequency group (M = 77.5, 95% CI [73.3, 81.7], $p < 0.001$).

Table 33: Mean Perceived Harm for Severity*Frequency Combinations

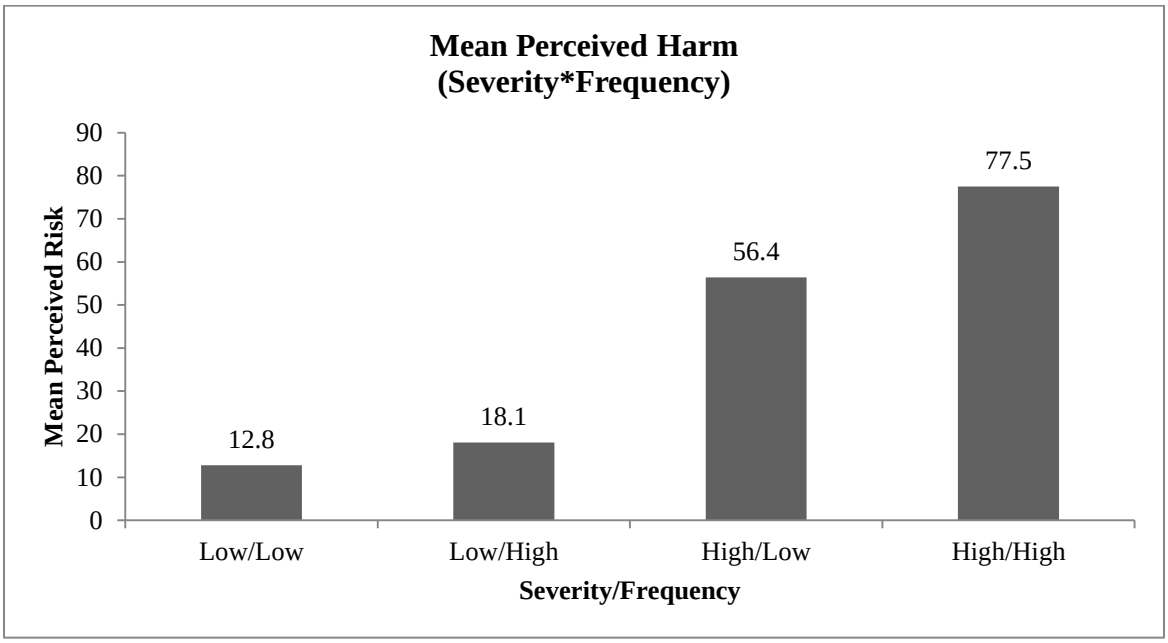
Severity	**Frequency**	**Mean Perceived Harm**	**95% CI**	
Low	Low	12.8	8.7	17.0
Low	High	18.1	13.9	22.3
High	Low	56.4	52.2	60.6
High	High	77.5	73.3	81.7

Table 34: Significant Differences for Perceived Harm Between Severity*Frequency

Combination 1 (i)	**Combination 2 (j)**	**Difference (i-j)**	**95% CI**		**p-value**
Low/Low	High/Low	-43.6	-51.3	-35.8	<0.001
	High/High	-64.7	-72.5	-56.9	<0.001

Low/High	High/Low	-38.3	-46.1	-30.6	<0.001
	High/High	-59.4	-67.2	-51.7	<0.001
High/Low	High/High	-21.1	-28.9	-13.3	<0.001

Figure 14: Mean Perceived Harm (Severity*Frequency)



Effects of Severity*Frequency*Communication Type on Perceived Harm

Effects of severity*frequency*communication type on perceived harm were compared and a post hoc Tukey analysis was conducted. When levels of severity and frequency were held constant there were no significant differences in scores of perceived harm between plain language and combination language groups. Though in general, combination group scores were slightly higher than plain language scores, albeit not significantly. There were significant differences between different levels of severity and frequency as is evident in Table 35 and Chart 1 below.

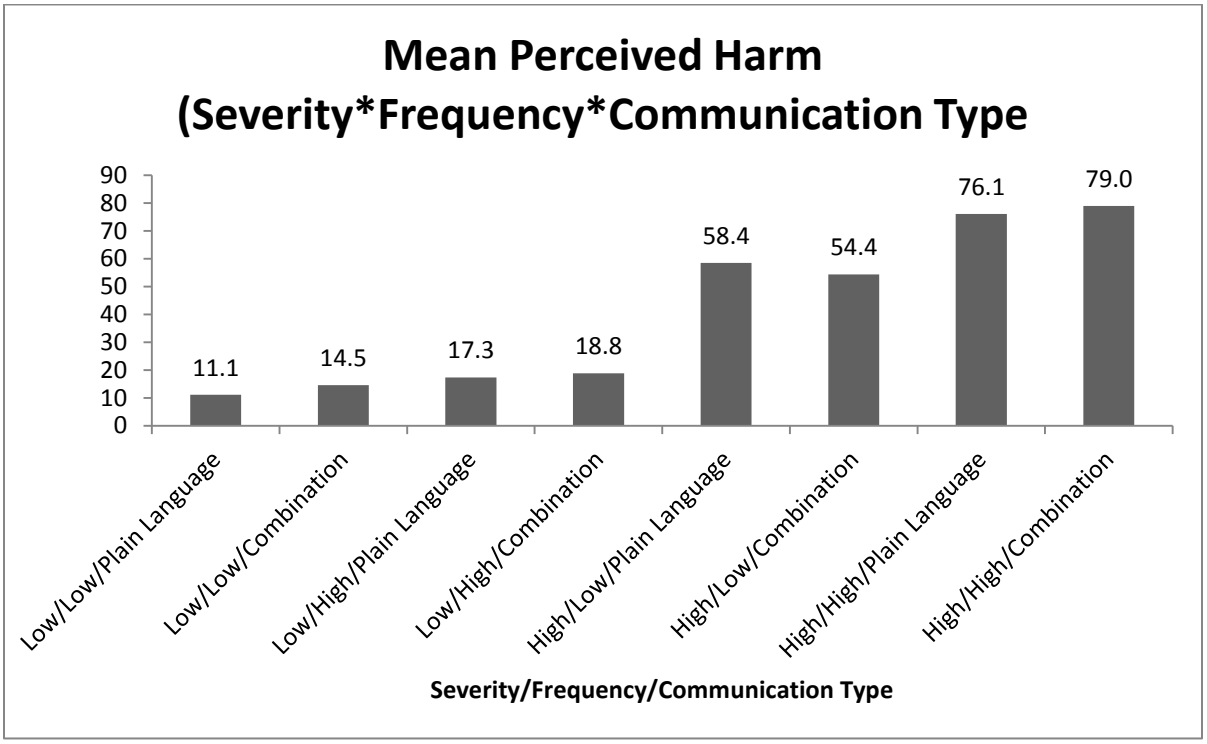
Table 36: Mean Perceived Harm for Severity*Frequency*Communication Type

Severity	**Frequency**	**Communication Type**	**Mean Perceived Harm**	**95% CI**	
Low	Low	Plain Language	11.1	5.2	17.0
		Combination	14.5	8.6	20.4
	High	Plain Language	17.3	11.2	23.5
		Combination	18.8	13.2	24.5
High	Low	Plain Language	58.4	52.4	64.5
		Combination	54.4	48.6	60.2
	High	Plain Language	76.1	70.5	81.7
		Combination	79.0	72.7	85.2

Table 37: Significant Differences of Mean Perceived Harm Scores Between Severity*Frequency*Communication Type Combinations

Combination 1 (i)	**Combination 2 (j)**	**Difference (i-j)**	**95% CI**		**p-value**
Low/Low/Plain Language	High/Low/Plain Language	-47.3	-60.4	-34.3	<0.001
	High/Low/Combination	-43.3	-56.1	-30.5	<0.001
	High/High/Plain Language	-65.0	-77.6	-52.4	<0.001
	High/High/Combination	-67.8	-81.2	-54.5	<0.001
Low/Low/Combination	High/Low/Plain Language	-43.9	-57.0	-30.8	<0.001
	High/Low/Combination	-39.8	-52.6	-27.0	<0.001
	High/High/Plain Language	-61.6	-74.1	-49.0	<0.001
	High/High/Combination	-64.4	-77.8	-51.1	<0.001
Low/High/Plain Language	High/Low/Plain Language	-41.1	-54.5	-27.8	<0.001
	High/Low/Combination	-37.1	-50.1	-24.0	<0.001
	High/High/Plain Language	-58.8	-71.6	-45.9	<0.001
	High/High/Combination	-61.6	-75.3	-48.0	<0.001
Low/High/ Combination	High/Low/Plain Language	-39.6	-52.4	-26.8	<0.001
	High/Low/Combination	-35.5	-48.1	-23.0	<0.001
	High/High/Plain Language	-57.2	-69.6	-44.9	<0.001
	High/High/Combination	-60.1	-73.2	-47.0	<0.001
High/Low/Plain Language	High/High/Plain Language	-17.7	-30.4	-4.9	0.001
	High/High/Combination	-20.5	-34.0	-7.0	<0.001
High/Low/ Combination	High/High/Plain Language	-21.7	-34.2	-9.3	<0.001
	High/High/Combination	-24.6	-37.8	-11.3	<0.001

Figure 15: Mean Perceived Harm (Severity*Frequency*Communication Type)



Hypothesis Testing

H_1: There is no difference in risk perception, perceived harm of side effects and intent to adhere to therapy between plain language and combined language groups.

A multivariate analysis of variance (MANOVA) was conducted, controlling for the independent variables of communication type, severity and frequency of side effect and with risk perception, perceived harm and intent to remain adherent as dependent covariates. A significant difference between all covariates was identified ($F_{3,390} = 4.33$, $p = 0.005$).

The first hypothesis is further subdivided into three hypotheses:

A post hoc Tukey analysis was conducted to determine the outcome of the hypotheses. The table below shows the differences between plain language and combination

language across the dependent variables of perceived risk, perceived harm and intent to remain adherent.

Table 38: Differences in Perceived Risk, Harm and Intent to Remain Adherent Between Communication Types

Dependent Variable	Mean Scores (95% CI)		Difference	p-value
	Plain Language	Combination		
Perceived Risk	42.5 (40.1 – 44.9)	46.6 (44.2 – 49.1)	4.1	0.018
Perceived Harm	40.7 (37.8 – 43.7)	41.7 (38.7 – 44.6)	0.94	0.66
Intent to Remain Adherent	84.9	85.5	0.5	0.786

H_{1a}: There is no difference in risk perception between plain language and combined language groups.

Risk perception for the plain language group was significantly lower (M = 42, 95% CI [40.1, 44.9], p = 0.018) compared to the combination group (M = 46.6, 95% CI [44.2, 49.1]). The difference is statistically significant, thus the null hypothesis H_{1a} can be rejected.

H_{1b}: There is no difference in perceived harm of side effects between plain language and combined language groups.

Perceived harm for the plain language group was lower (M = 40.7, 95% CI [37.8, 43.7]) compared to the combination group (M = 41.7, 95% CI [38.7, 44.6]) but the difference was not statistically significant (p = 0.66). Thus, the null hypothesis H_{1b} is accepted.

H_{1c}: There is no difference in intent to adhere to therapy between plain language and combined language groups.

Mean scores for intent to adhere in the combined communication type group were slightly higher (M = 85.5, 95% CI [82.9, 88.0]) compared to the plain language group (M = 84.9, 95% CI [82.4, 87.5]), but were not statistically significant (p = 0.786). Thus the null hypothesis H_{1c} is accepted.

Correlation Analysis

H_2: There is no association between perceived risk of side effects and the intent to remain adherent.

$$H_2: \rho = 0$$

Where,

ρ = Spearman correlation coefficient

A spearman product-moment correlation coefficient was computed to assess the relationship between the variables perceived risk and intent to remain adherent. Perceived risk was positively correlated with perceived harm ($r = 0.298$, $n = 400$, $p < 0.001$). There was a negative correlation between perceived risk and intent to remain adherent ($r = -0.189$, $n = 400$, $p = < 0.001$). A spearman product-moment correlation coefficient was computed to assess the relationship between the variables perceived harm and intent to remain adherent. There was a negative correlation between perceived harm and intent to remain adherent ($r = -0.261$, $n = 400$, $p = < 0.001$). Thus, the null hypotheis H_2 is rejected.

Table 39: Spearman Correlation Coeffecients Between Perceived Risk & Harm And Intent

Variables	**Correlation with Intent**	**95% CI**		**p-value**
Perceived Risk	-0.189	-0.282	-0.093	< 0.001
Perceived Harm	-0.261	-0.350	-0.167	< 0.001

CHAPTER FIVE

Discussion, Limitations, Implications and Conclusion

This chapter includes a discussion of the results of the study, implications of the findings, limiations of the study and conclusions that can be drawn.

Discussion

Communication about health information effects the way patients perceive their medications in every way from safety, efficacy and even the role of the FDA (Schwartz and Woloshin, 2011). Studies continually show that patient-physician (Hall, Roter and Katz, 1988) and patient-pharmacist (Raynor et al., 2000) communication leads to greater understanding and greater medication adherence. The primary aim of this study was to apply principles of the Health Belief Model to examine how individual's respond to the communication of risk information about medication side effects. The Health Belief Model proposes that amongst other factors, barriers toward taking health action play a large role in health decisions. Medication adherence is one such health behavior. Side effects of medications play a major role in medication adherence. Risk information was communicated in either plain language or a combination of plain language and natural frequency risk probability. Because individuals interpret language statements with wide variety, it was hypothesized that adding natural frequency risk information to a plain language statement would decrease risk perception of side effects and lead to higher intended medication adherence.

The study participants were mostly young (M = 24.6 years) and white or Asian. Participants had an overall high level of education and were all students at the University of Houston College of Pharmacy. It is not clear that age, race or gender would affect risk assessment but is likely in the case of this study since most participants were unlikely to have personal experience of many of the side effects/medications used as part of the study.

Generally, participants perceived the higher risk side effects as being more risky and more harmful. The same was found when side effects were perceived to be occurring more frequently, despite vague plain language descriptors.

Multivariate analysis of communication type across the dependent variables (perceived risk, perceived harm and intent to remain adherent) was not significant ($F_{3,390}$ = 1.97, p = 0.118). It is very likely that because of the similarities between perceived risk and perceived harm, any significant differences in communication type were washed out of the model. Perceived risk was positively correlated with perceived harm (r = 0.298, n = 400, p < 0.001). When severity and frequency were added to the model with communication type, a significant interaction was found ($F_{3,390}$ = 4.33, p = 0.005).

This study showed that pairing natural frequency risk information with plain language statements can actually lead to a 10% increase in the risk perception of side effects. However, there was no difference in the perceived harm of side effects or in respondents' intent to remain adherent. Despite communication style, side effects that were perceived as occurring more frequently or that were more severe led to decreased intent (6.4% & 5.5%). Severity and frequency of side effects plays a large role in influencing the perceived risk of the side effects. If either factor is strong enough, this seems to wash out the effect of

communication style. Overall, the reported intention to remain adherent was over 80% across all levels of variables and risk information. This is in the range of what is generally considered acceptable adherence. It is likely that because the participants were primarily pharmacy students they are biased toward intentional medication use and may not be as influenced by risk information as the general public.

Correlation of Perceived Risk and Harm with Intent to Adhere

The health belief model predicts that as barriers to medication use increase, adherence should decrease. Risky and harmful medications are perceived as barriers to medication use. As such, it was shown that in this population that intent to adhere is negatively correlated to perceived risk and perceived harm of medication side effects. This is seemingly in line with the health belief model.

Limitations

All but two subjects were students at the University of Houston College of Pharmacy. It may be that the knowledge pharmacy students have skews the perception of risk about side effects and the harm of such side effects. It is also possible that pharmacy students put a different emphasis on the importance of medication adherence than people without extensive drug knowledge would. Another limitation is inherent to survey studies. This study only measured intent for adherence rather than actual adherence, and was not presented in a real life situation. Additionally, the effects of psychological framing have significant consequences on how people evaluate information, including health risk information (Tversky and Kahneman, 1981). It is possible that the design of the drug facts boxes were framed in a way that influenced the perception of risk on the part of the participants.

Implications

Implications from this study do support the notion that communication style plays a role in perception of risk of medications. Interestingly, even in a sample of individuals receiving training in pharmacology and medication use, communication style had such an impact. It suggests that individuals do respond to such styles even with having prior background knowledge. This could lend support to patient education initiatives even with patients that have been on long term therapies and may have an attitude of being knowledgeable about risks. This information is valid even in a context of written material and could even be applicable to electronically available resources.

Recommendations for Future Research

The next logical step for this research would be to apply it in a "real world" setting such as a clinic, pharmacy, hospital or physician's office with a more representative population. Further areas for research on this topic could be devoted to teasing out response rates amongst patients making new decisions and patients perceptions of medications they have already been taking.

Conclusion

In conclusion, there does seem to be an effect on the risk perception of side effects when information is distributed in plain language and natural frequencies as opposed to only plain language. People are diverse and like to receive information in multiple formats and this can aid in the decision making process as well as the risk-benefit analysis patients do every time they take a medication. Also, it should be noted that pharmacy education may be

having a positive effect on the importance of adherence and that even pharmacy students (not yet experts in the field of medication use) are protected from the effects of risk information and can make rational decisions despite conflicting information. This supports the idea that patient education is important in helping patients make good decisions not guided by emotional information, but by the facts. Further research is needed to define the best ways for distributing this information and to which populations that would receive the most benefit.

CHAPTER SIX

Summary

The primary purpose of this study was to determine the effects of combining plain language risk information with natural frequency risk information on perceived risk and perceived harm of medication side effects, as well as the effect on the intention to remain adherent to medication therapy. The secondary aim was to determine the correlation of perceived risk and harm with the intent to remain adherent. The study uses the tenets of the Health Belief Model that lowering barriers to preventive health behavior will lead to an increase in the desired health behavior. In the study, the desired health behavior is medication adherence (taking medications as prescribed). The barriers to this behavior were defined as side effects of medications and were measured by the perceived risk and harm of the medications.

This was a 2 x 3 factorial study with independent variables of communication type, severity of side effects and frequency of side effects. Each had two levels (plain language or combined, and high or low). In order to estimate the effects of communication type on perceived risk and harm, a drug facts box was developed and shown to participants. The drug facts box described the uses and side effects of a medication. The severity and frequency of side effects were manipulated to be either high or low. Frequency of side effects was described in either plain language terms only or in plain language with additional natural frequencies for the side effects. Then participants were asked to rate how risky they perceived the side effects to be, how harmful the side effects were and then how likely they would be to adhere to the medication.

400 invitations to participate in the survey were emailed via University of Houston College of Pharmacy listserv groups. 168 individuals responded. Of those, 100 completed the survey for an overall response rate of 25%. The mean age for participants was 24.65 (SD 2.89) years. Age of the participants ranged from 20 to 39 years. The study sample consisted of a majority of females and white (53%) or Asian (38%). Majority of the participants reported at least some college (26%) or a bachelor's degree (62%). All of the participants were students at the University of Houston College of Pharmacy.

Multivariate analysis was conducted and a post-hoc Tukey analysis for significant effects was conducted. Multivariate effects of the independent variables communication type, severity of side effect and frequency of side effect were measured across the dependent variables of perceived risk, perceived harm and intent to remain adherent. There were no significant effects for the variable of communication type (plain language or combination) alone ($F_{3,390} = 1.97$, $p = 0.118$). When combined with severity, frequency, and severity*frequency, significant effects were found for communication type. The rest of the effects of the independent variables were found to be significant at $p < 0.05$. Analysis of the dependent variable perceived risk was conducted. The overall effects of communication type, severity and frequency had a significant effect on the dependent variable perceived risk ($F_{7,392} = 190$, $p < 0.0001$). The effect of communication type on perceived risk was significantly different ($F_{1,392} = 5.5$, $p = 0.0195$). There was also a difference between severity ($F_{1,392} = 17.87$, $p < 0.0001$) and frequency ($F_{1,392} = 1225$, $p < 0.0001$).

Tukey post-hoc analysis indicated that the combination communication type group had significantly higher risk perception scores (M = 46.6, 95% CI [44.2, 49.1]), compared to

the risk perception scores for the plain language group (M = 42.5, 95% CI [40.1, 44.9]), p = 0.019. Risk perception scores were significantly higher in the "high severity" group (M = 48.3, 95% CI [45.8, 50.7]) compared to the "low severity" group (M = 40.9, 95% CI [38.5, 43.3]), p < 0.001. Risk perception scores were significantly higher in the "high frequency" group (M = 75.1, 95% CI [72.7, 77.6]) as compared to the "low frequency" group (M = 14, 95% CI [11.6, 16.4]), p < 0.001.

A spearman product-moment correlation coefficient was computed to assess the relationship between the variables perceived risk and intent to remain adherent. Perceived risk was positively correlated with perceived harm (r = 0.298, n = 400, p < 0.001). There was a negative correlation between perceived risk and intent to remain adherent (r = -0.189, n = 400, p = < 0.001). A spearman product-moment correlation coefficient was computed to assess the relationship between the variables perceived harm and intent to remain adherent. There was a negative correlation between perceived harm and intent to remain adherent (r = -0.261, n = 400, p = < 0.001).

Results of this study validate the model of the HBM and the correlation of barriers with preventive health behavior. Education seems to play a significant role in removing some of the risk bias that can be imposed by different methods of communication. Still, adding natural frequency information about side effects led to higher perceived riskiness of the side effects compared to only plain language information. Further studies in real world population may extrapolate finer differences in risk communication techniques for patients and providers and help improve medical outcomes.

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Appendix A: Complete Statistical Tables

Table 40: Mean Scores Across All Variables

Severity	Frequency	Communication Type	N	Variable	Mean	Std Dev
Low	Low	Plain Language	50	risk	13.1720000	13.5358035
				harm	11.1080000	14.4690640
				intent	90.3200000	14.4412109
		Combination	50	risk	12.0800000	14.7341613
				harm	14.5360000	17.7999514
				intent	89.7000000	16.1779013
	High	Plain Language	46	risk	56.5869565	28.8186484
				harm	17.3065217	20.5933582
				intent	82.4782609	19.0014492
		Combination	54	risk	81.7037037	16.2092795
				harm	18.8444444	14.1050997
				intent	88.0555556	16.7269037
High	Low	Plain Language	48	risk	19.1041667	16.4410482
				harm	58.4375000	27.3043573
				intent	85.1041667	17.8781212
		Combination	52	risk	11.6730769	14.8439215
				harm	54.3653846	28.9062235
				intent	86.3461538	14.3224554
	High	Plain Language	56	risk	81.2500000	16.4208847
				harm	76.0892857	19.9947964
				intent	82.0178571	18.1523763
		Combination	44	risk	81.0454545	14.6159431
				harm	78.9545455	22.3189924
				intent	77.8204545	28.2920778

Table 41: Combined Effects of Severity-Frequency-Communication Type on Intent to Remain Adherent

ivrisk	ivfreq	ivcomm	intent LSMEAN	LSMEAN Number
1	**1**	**0**	90.32	1
1	**1**	**1**	89.7	2
1	**2**	**0**	82.4783	3
1	**2**	**1**	88.0556	4
2	**1**	**0**	85.1042	5
2	**1**	**1**	86.3462	6
2	**2**	**0**	82.0179	7
2	**2**	**1**	77.8205	8

Least Squares Means for effect ivrisk*ivfreq*ivcomm Pr > |t| for H0: LSMean(i)=LSMean(j) Dependent Variable: intent								
i/j	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**
1		1	0.4229	0.9985	0.8543	0.9581	0.2832	0.0238
2	1		0.5343	0.9998	0.9199	0.9838	0.3845	0.0393
3	0.4229	0.5343		0.7997	0.9972	0.9679	1	0.9308
4	0.9985	0.9998	0.7997		0.9925	0.9997	0.6714	0.1125
5	0.8543	0.9199	0.9972	0.9925		1	0.9897	0.5512
6	0.9581	0.9838	0.9679	0.9997	1		0.9245	0.3147
7	0.2832	0.3845	1	0.6714	0.9897	0.9245		0.9488
8		0.0393	0.9308	0.1125	0.5512	0.3147	0.9488	

ivrisk	ivfreq	ivcomm	intent LSMEAN	95% Confidence Limits	
1	**1**	**0**	90.32	85.2151	95.4249
1	**1**	**1**	89.7	84.5951	94.8049
1	**2**	**0**	82.4783	77.156	87.8005
1	**2**	**1**	88.0556	83.1433	92.9678
2	**1**	**0**	85.1042	79.894	90.3144
2	**1**	**1**	86.3462	81.3404	91.352
2	**2**	**0**	82.0179	77.1942	86.8416
2	**2**	**1**	77.8205	72.3786	83.2623

Least Squares Means for Effect ivrisk*ivfreq*ivcomm				
i	j	Difference Between Means	Simultaneous 95% Confidence Limits for LSMean(i)-LSMean(j)	
1	2	0.62	-10.57	11.8103
1	3	7.84174	-3.5892	19.2727
1	4	2.26444	-8.7166	13.2455
1	5	5.21583	-6.0904	16.5221
1	6	3.97385	-7.1083	15.056
1	7	8.30214	-2.5843	19.1885
1	8	12.4995	0.93408	24.065
2	3	7.22174	-4.2092	18.6527
2	4	1.64444	-9.3366	12.6255
2	5	4.59583	-6.7104	15.9021
2	6	3.35385	-7.7283	14.436
2	7	7.68214	-3.2043	18.5685
2	8	11.8795	0.31408	23.445
3	4	-5.5773	-16.804	5.64896
3	5	-2.6259	-14.17	8.91859
3	6	-3.8679	-15.193	7.45723
3	7	0.4604	-10.673	11.5941
3	8	4.65781	-7.1407	16.4563
4	5	2.95139	-8.1478	14.0506
4	6	1.7094	-9.1615	12.5803
4	7	6.0377	-4.6336	16.709
4	8	10.2351	-1.1281	21.5983
5	6	-1.242	-12.441	9.95725
5	7	3.08631	-7.9193	14.0919
5	8	7.28371	-4.394	18.9614
6	7	4.3283	-6.4469	15.1035
6	8	8.5257	-2.9352	19.9866
7	8	4.1974	-7.0743	15.4691

Appendix B: Consent to Participate In Survey

UNIVERSITY OF HOUSTON
Learning. Leading.

Consent to Participate in Research Study
Effect of Verbal and Numerical Risk Information on Individual Risk Perception of Medication Side Effects

Dear Participant,

You are being invited to participate in a research project conducted by Collin Beatty from the College of Pharmacy at the University of Houston, as part of his thesis. This project is being conducted under the supervision of Sujit Sansgiry, Ph.D.

Your participation is voluntary and you may refuse to participate or withdraw at any time without penalty or loss of benefits to which you are otherwise entitled. You may also refuse to answer any question. If you are a student, a decision to participate or not or to withdraw your participation will have no effect on your standing.

The purpose of this research is to evaluate the effect of different combinations of risk information about medication side effects on an individual's perceived risk of experiencing medication side effects. You will be one of approximately 1000 subjects to be asked to participate in this project. It is estimated that it will take approximately 10-15 minutes of your time to complete the information requested and you will not be asked to complete any additional information for this project once you have finished the survey.

Your participation in this project is anonymous. No personal information including your name or email addresses will be collected.

There are no foreseeable risks associated with your participation in this project. While you will not directly benefit from participation, your participation may help investigators better understand the effect of risk information on drug information labels and how that effects patient adherence to medication.

Participation in this project is voluntary and the only alternative to this project is non-participation.

The results of this study may be published in professional and/or scientific journals. It may also be used for educational purposes or for professional presentations. However, no individual subject will be identified. If you have any questions, you may contact Collin Beatty at crbeatty@uh.edu. You may also contact Sujit Sansgiry, Ph.D. faculty sponsor, at 713-795-8392.

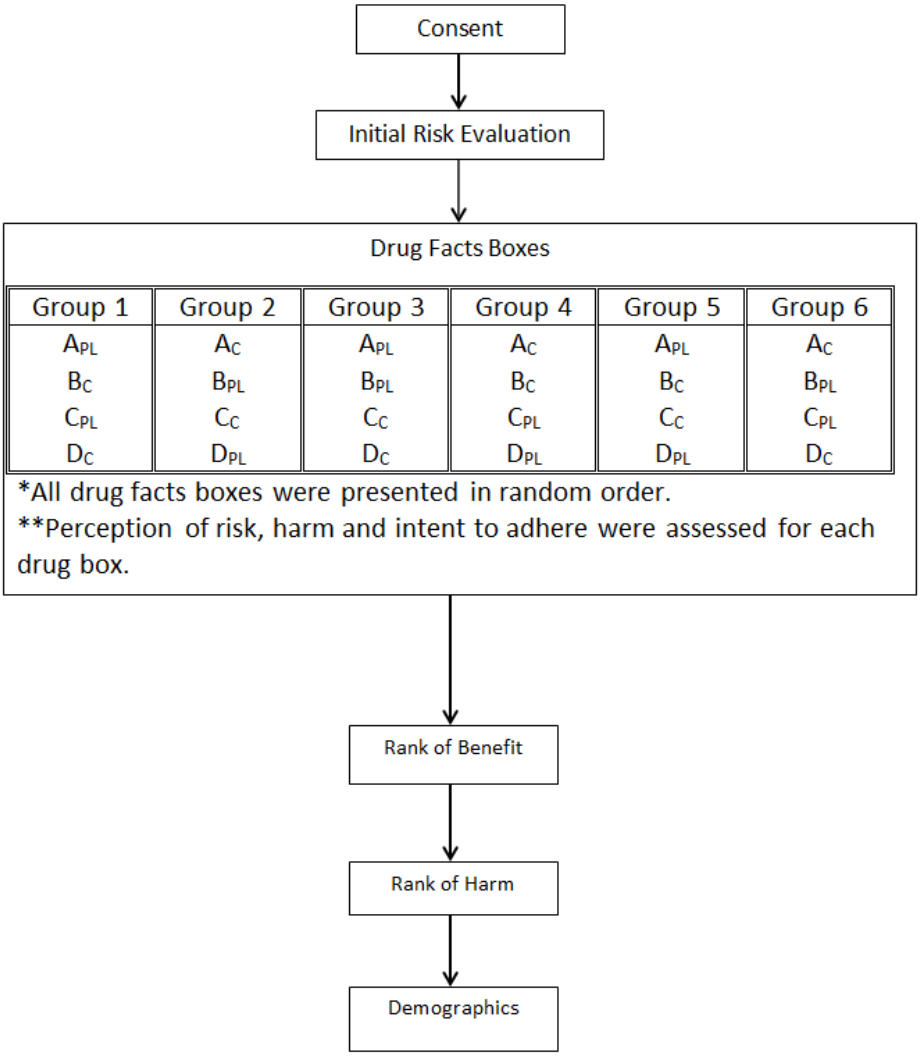
ANY QUESTIONS REGARDING YOUR RIGHTS AS A RESEARCH SUBJECT MAY BE ADDRESSED TO THE UNIVERSITY OF HOUSTON COMMITTEE FOR THE PROTECTION OF HUMAN SUBJECTS (713-743-9204).

Sincerely,

Collin Beatty
Principal Investigator
Pharm.D./M.S. Candidate 2013

Sujit S. Sansgiry, Ph.D.
Faculty Sponsor
Associate Professor

Appendix C: Study Flow


Consent
Initial Risk Evaluation
Drug Facts Boxes
Group 1 Group 2 Group 3 Group 4 Group 5 Group 6
APL AC APL AC APL AC
BC BPL BPL BC BC BPL
CPL CC CC CPL CC CPL
DC DPL DC DPL DPL DC
*All drug facts boxes were presented in random order.
**Perception of risk, harm and intent to adhere were assessed for each drug box.
Rank of Benefit
Rank of Harm
Demographics

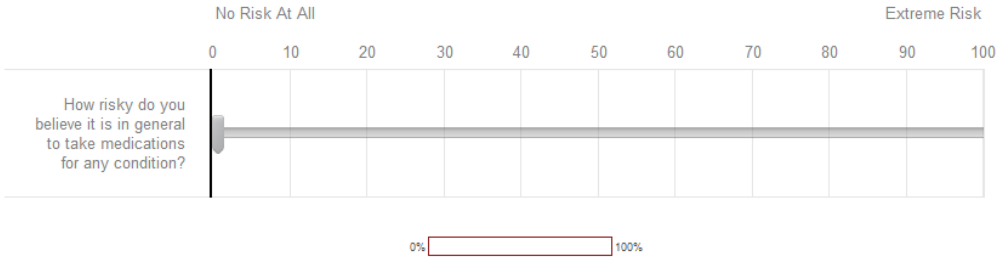
Appendix D: Questionnaire Screenshots

Initial Risk Assessment

Please read the questions below and select the answer that best represents your opinion for each question.

	Strongly Disagree	Disagree	Somewhat Disagree	Neither Agree nor Disagree	Somewhat Agree	Agree	Strongly Agree
I believe that in general medications approved by the FDA are safe.	○	○	○	○	○	○	○
I believe that medications prescribed by my physicians are less risky.	○	○	○	○	○	○	○
In general medications do not have many side effects.	○	○	○	○	○	○	○
I believe that there is no risk if medications are taken appropriately.	○	○	○	○	○	○	○
I believe in general that I am vulnerable to side effects from the use of medications.	○	○	○	○	○	○	○
I believe that in general taking medications to treat any disorder is very risky.	○	○	○	○	○	○	○
I believe that in general I can avoid risk associated with the use of medications.	○	○	○	○	○	○	○

Please answer the question below about risk on the scale from 0 to 100.



Drug Facts Box: Drug A

Drug A **What is this drug for?** Drug A is used to prevent stroke after certain surgical procedures. **What are some side effects of this drug?** Drug A can rarely cause stomach bleeding.	Drug A **What is this drug for?** Drug A is used to prevent stroke after certain surgical procedures. **What are some side effects of this drug?** Drug A can rarely cause stomach bleeding. Out of 100 people taking Drug A for one year, 2 will experience stomach bleeding.

Drug Facts Box: Drug B

Drug B **What is this drug for?** Drug B is used to lower LDL or "bad" cholesterol and raise HDL or "good" cholesterol. **What are some side effects of this drug?** Drug B will very likely cause flushing.	Drug B **What is this drug for?** Drug B is used to lower LDL or "bad" cholesterol and raise HDL or "good" cholesterol. **What are some side effects of this drug?** Drug B will very likely cause flushing. Out of 100 people taking Drug B, 88 will experience flushing.

Drug Facts Box: Drug C

Drug C **What is this drug for?** Drug C is used to treat certain types of cancer. **What are some side effects of this drug?** Drug C will very likely cause a loss of immune function.	Drug C **What is this drug for?** Drug C is used to treat certain types of cancer. **What are some side effects of this drug?** Drug C will very likely cause a loss of immune function. Out of 100 people taking Drug C, 84 will experience loss of immune function.

Drug Facts Box: Drug D

Drug D **What is this drug for?** Drug D is used to treat the symptoms of pollen allergies. **What are some side effects of this drug?** Drug D can rarely cause headache.	Drug D **What is this drug for?** Drug D is used to treat the symptoms of pollen allergies. **What are some side effects of this drug?** Drug D can rarely cause headache. Out of 100 people taking Drug D, 4 will experience headache.

Drug Facts Box (example) with measurement of Risk, Harm and Intent

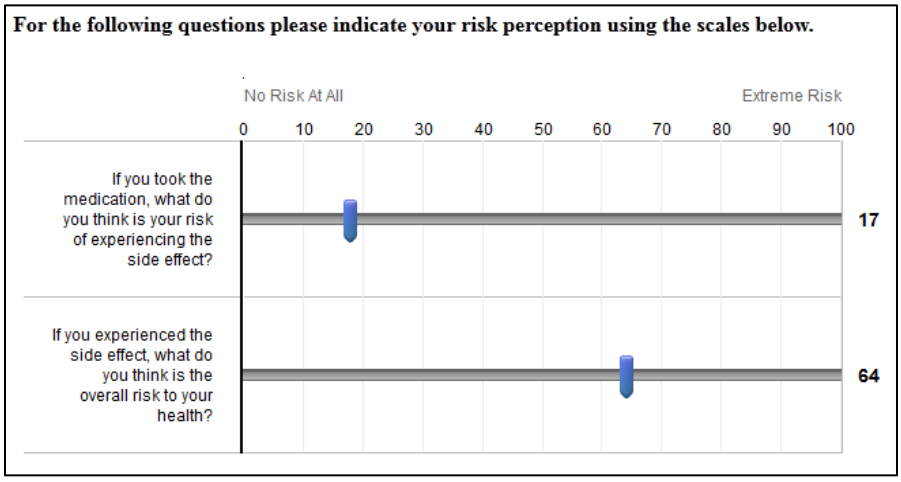
Drug D

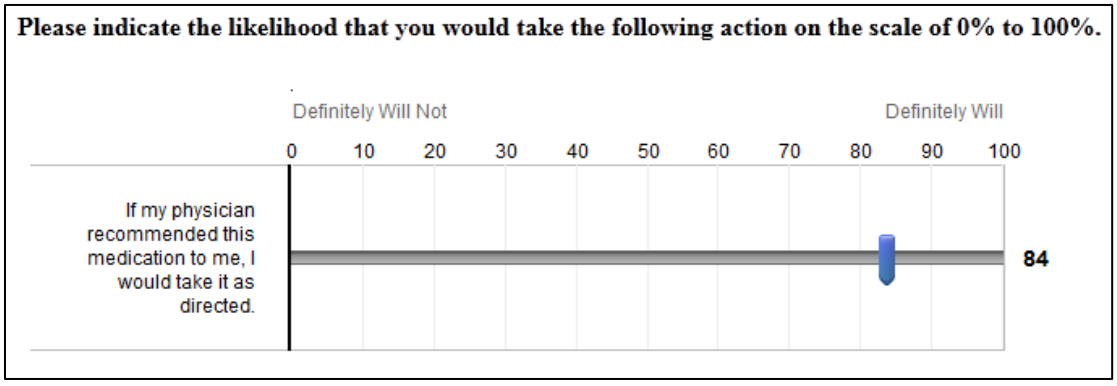
What is this drug for?

Drug D is used to treat the symptoms of pollen allergies.

What are some side effects of this drug?

Drug D can rarely cause headache.





Rank of Side Effect Harm and Medication Benefit

For the following questions, use your cursor to click and drag the items to reorder them as specified by the question. The original order of the items is randomly determined.

Based on your knowledge and perception, please rank the following medication side effects in order of *greatest harm to health*, with "1" being most harmful and "4" being least harmful.

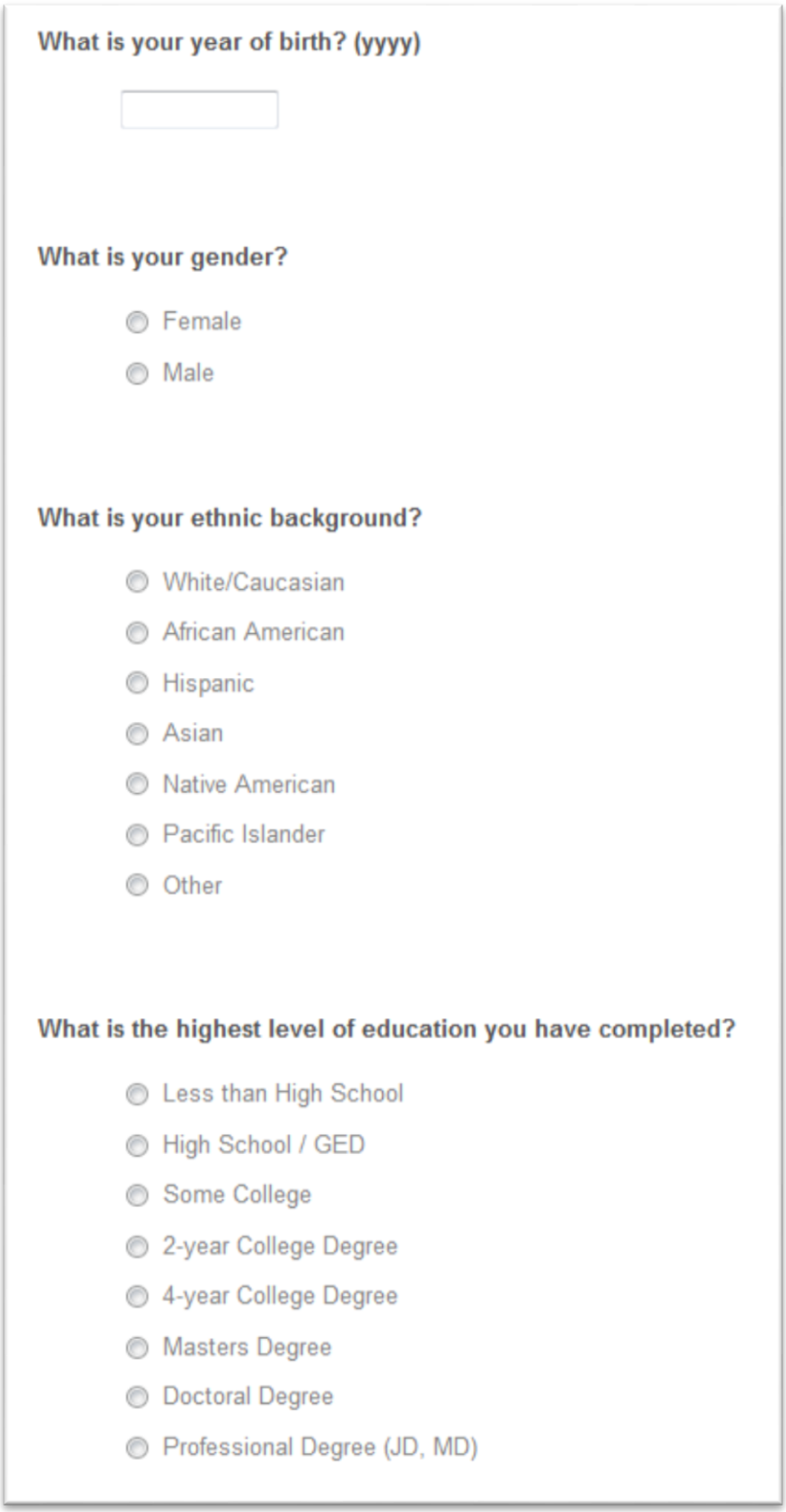
Facial flushing (redness, warmth, sweating)	1
Stomach bleeding	2
Loss of immune function	3
Headache	4

Based on your knowledge and perception, please rank the disease states below in order of *greatest benefit from successful treatment*, with "1" being most benefit and "4" being least benefit.

Preventing stroke	1
Treating cancer	2
Improving levels of cholesterol	3
Treating symptoms of pollen allergies	4

0% 100%

Demographic Information



What is your year of birth? (yyyy)

What is your gender?

- Female
- Male

What is your ethnic background?

- White/Caucasian
- African American
- Hispanic
- Asian
- Native American
- Pacific Islander
- Other

What is the highest level of education you have completed?

- Less than High School
- High School / GED
- Some College
- 2-year College Degree
- 4-year College Degree
- Masters Degree
- Doctoral Degree
- Professional Degree (JD, MD)

Appendix E: Codebook

Variable	Variable Description	Meaning of Codes (Response Codes)
ID	Participant identification number	
IPAddress	IP address collected by qualtrics (non-identifiable)	
Start	Date and time survey was started	
End	Date and time survey was completed	
Group	Group to which participant was randomized. (101 - 601)	
Safe	I believe that in general medications approved by the FDA are safe. (1-7)	1 = strongly disagree 2 = disagree 3 = somewhat disagree 4 = neither agree nor disagree 5 = somewhat agree 6 = agree 7 = strongly agree
RxRisk	I believe that medications prescribed by my physicians are less risky. (1-7)	Same as above.
SideEffect	In general medications do not have many side effects. (1-7)	Same as above.
CorrectUse	I believe that there is no risk if medications are taken appropriately. (1-7)	Same as above.

Variable	Variable Description	Meaning of Codes (Response Codes)
Vulnerable	I believe in general that I am vulnerable to side effects from the use of medications. (1-7)	Same as above.
TxRisk	I believe that in general taking medications to treat any disorder is very risky. (1-7)	Same as above.
Avoid	I believe that in general I can avoid risk associated with the use of medications. (1-7)	Same as above.
riskscore	Continuous risk score. Max of 28. Perceived general riskiness of medications.	
catriskscore	Categorical risk score. Perceived general riskiness of medications.	1 = high (riskscore >16) 0 = low (riskscore <= 16)
vulnscore	Continuous vulnerability score. Max of 21.Perceived general vulnerability to experiencing side effects.	
catvulnscore	Catetorical vulnerability score. Perceived general vulnerability to experiencing side effects.	1 = high (vulnscore >12) 0 = low (vulnscore <=12)
GlobalRisk	How risky do you believe it is in general to take medications for any condition? (0-100)	0 = no risk 100 = extreme risk
ivrisk	Categorical level of the independent variable severity of side effect.	1 = low severity

Variable	Variable Description	Meaning of Codes (Response Codes)
		2 = high severity
ivfreq	Categorical level of the independent variable frequency of side effect.	1 = low frequency 2 = high frequency
ivcomm	Categorical level of the independent variable communication type.	0 = plain language 1 = combination
risk	Continuous score for the dependent variable perceived risk (0 – 100).	0 = no risk 100 = extreme risk
harm	Continuous score for the dependent variable perceived harm (0 – 100).	0 = no risk 100 = extreme risk
intent	Continuous score for the dependent variable intent to remain adherent (0 – 100).	0 = no risk 100 = extreme risk
Harm_A	Ordinal rank of how harmful the side effect for Drug A would be to health (1 to 4).	1 = most harmful 4 = least harmful
Harm_B	Ordinal rank of how harmful the side effect for Drug B would be to health (1 to 4).	1 = most harmful 4 = least harmful
Harm_C	Ordinal rank of how harmful the side effect for Drug C would be to health (1 to 4).	1 = most harmful 4 = least harmful
Harm_D	Ordinal rank of how harmful the side effect for Drug D would be to health (1 to 4).	1 = most harmful 4 = least harmful

Variable	Variable Description	Meaning of Codes (Response Codes)
Benefit_A	Ordinal rank of how much benefit would be gained by using Drug A (1 to 4).	1 = most benefit 4 = least benefit
Benefit_B	Ordinal rank of how much benefit would be gained by using Drug B (1 to 4).	1 = most benefit 4 = least benefit
Benefit_C	Ordinal rank of how much benefit would be gained by using Drug C (1 to 4).	1 = most benefit 4 = least benefit
Benefit_D	Ordinal rank of how much benefit would be gained by using Drug D (1 to 4).	1 = most benefit 4 = least benefit
YOB	Year of birth	YYYY
Age	Calculated age of participant in years. '=Start-YOB'	
Sex	Gender of participant.	1 = Male 2 = Female
Race	Ethnicity of the participant.	1 = white 2 = black 3 = Hispanic 4 = Asian 5 = native American 6 = pacific islander 7 = other

Variable	Variable Description	Meaning of Codes (Response Codes)
Education	Highest level of education completed by the participant.	1 = less than HS 2 = high school/GED 3 = some college 4 = 2-yr college degree 5 = 4-college degree 6 = master's 7 = doctoral 8 = professional degree
Healthcare	Does the participant work or study in a health-related field?	1 = yes 2 = no