THE EFFECT OF LABELING CONTENT AND PROMINENCE ON INFORMATION PROCESSING AMONG OLDER ADULTS DURING SELF-SELECTION OF OVER-THE-COUNTER MEDICATIONS

By

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ABSTRACT

THE EFFECT OF LABELING CONTENT AND PROMINENCE ON INFORMATION PROCESSING AMONG OLDER ADULTS DURING SELF-SELECTION OF OVER-THE-COUNTER MEDICATIONS

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The labeling of non-prescriptions plays a vital role in presenting drug information for older patients to medicate themselves safely and effectively. Due to the current Research was needed to know how packaging and information processing influence older adults' behaviors and decisions when selecting OTC medications.

Eighty-two subjects with age older than 65 years were tested to examine the effect of labeling content and prominence, including: drug selections for appropriateness, eye tracking and health history interview. The results revealed their propensity for polypharmacy and less attention on the drug facts labels. Decision making regarding drug appropriateness was also questionable. Responses from 66 participants (80.5%) were "problematic". And ibuprofen elicited problematic responses more than any other ingredients ($p<0.0001$). Also, the responses for appropriateness changed along with when the information prominent level varied. Participants with higher degree were more likely to maintain consistent in response ($p=0.0165$).

The probability of viewing a certain information significantly depended on its drug category, prominent level and content ($p=0.0027$). For symptom relief and active ingredient, participants were more likely to view the prominently-featured information, while people viewed the brand name information regardless of the changes of its prominent level.

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KEY TO ABBREVIATIONS

ADE	Adverse drug event
AOI	Area of Interest
APCO	Association of Public-Safety Communication Official
ASL	Applied Science Laboratories
CFR	the Code of Federal Regulations
CHPA	Consumer Healthcare Products Association
DFL	Drug facts label
FDA	The US Food and Drug Administration
FFDCA	Federal Food Drug and Cosmetic Act
H-PIM	Human-Package Interaction Model
IRB	Institutional Review Board
MSU	Michigan State University
NCPIE	National Council on Patient Information and Education
NSAID	Nonsteroidal anti-inflammatory drug
ODPHP	the Office of Disease Prevention and Health Promotion
OTC	Over-the-Counter
PDP	Principal Display panel
REALM-R	Rapid Estimate of Adult Literacy in Medicine-Revised
Rx	Prescriptions (Rx)
U.S.	The United States
VHT	Video Head Tracking

CHAPTER 1 INTRODUCTION AND LITERATURE REVIEW

1.1 Trends of Aging Population

The age structure of the overall population in the United States (U.S.) is projected to change greatly over the next four decades, especially in its older populations. According to data from the U.S. Census in 2010, approximately 40 million people were over the age of 65 years or older. (Werner, 2011) Projections indicate that this number will continue increasing as the baby boomer population ages. It has been estimated that the 65+ population will reach 55 million in 2020 and 88.5 million in 2050 (Vincent & Velkoff, 2010). These changes in demographics will impact society in numerous ways, not the least of which is healthcare.

1.2 Use of Over-the-Counter (OTC) Medications among Older Adults

1.2.1 OTC Medication

OTC drugs, also called non-prescription drugs, are defined by the Federal Food Drug and Cosmetic Act (FFDCA) as, "drugs that are safe and effective for use by the general public without a prescription" (US Food and Drug Administration, 2012a). It has been estimated that there are more than 100,000 OTC products currently in the market that utilize approximately 800 different active ingredients. These drugs, which treat varied conditions and comprise over 80 different therapeutic categories, (US Food and Drug Administration, 2012b), are playing an increasingly important role in national health by offering private, convenient, affordable options to treat a variety of conditions.

1.2.2 OTC Use by Older Adults

With age comes a propensity for disease; as a result, many people require more medication (both prescription and OTC) late in their lives. In fact, nearly two thirds of older Americans are afflicted with multiple, chronic conditions (Centers for Disease Control and Prevention, 2013). Among those 65 and older diagnosed as having heart disease (2007-2009), nearly 55% had 5 or more conditions simultaneously.

In light of this propensity, it is not surprising that older adults have a higher per capita usage of medication than any other sector of the population. Studies estimate that somewhere between 31-96% of people 65 and older use OTC medications (Cadigan, Magaziner, & Fedder, 1989; Darnell, Murray, Martz, & Weinberger, 1986; Espino et al., 1998; Hanlon et al., 1992; Hanlon, Fillenbaum, Ruby, Gray, & Bohannon, 2001; Helling et al., 1987; Stoehr, Ganguli, Seaberg, Echemen, & Belle, 1997) (Table 1). Although older adults comprise 13% of the population, they take 34% of all prescriptions and 30% OTCs consumed in the U.S. (Centers for Disease Control, 2004; Sansgiry & Cady, 1995) Moreover, many older adults take multiple medications at the same time; one survey of approximately 17,000 Medicare beneficiaries reported that nearly 40 % took five or more medications. (Wilson et al., 2007)

Other surveys corroborate a tendency for polypharmacy in older adults. The 2008 National Social Life, Health and Aging Project indicated that 29% took five or more prescription medications concurrently. Of those who took prescription drugs (42% of the respondents took at least one OTC medication and 81% took at least one prescription medication), 46% reported using an OTC medication at the same time. (Qato et al., 2008)

Table 1 Prevalence and mean OTC drug use reported by selected community-dwelling samples of older persons in the U.S. by Hanlon et al.

Study	**Date of study**	**Location**	**Sample characteristics**	**% reporting OTC use**	**Mean OTC use(a) of sample**	**Mean OTC use(a) among users**
Helling et al. (1987)	1981/1982	2 counties, Iowa	Total population; n = 3567; age 65+ years; White	65	1.1	1.7
Cadigan et al. (1989)	1984	Baltimore, Maryland	Representative sample; n=609; age 65+ years; White women	77	1.4	1.8
Darnell et al. (1986)	No date	Indianapolis, Indiana	Public housing; n=150; residents; age 50-96 years; race unspecified	96	3.4	3.5
Hanlon et al. (1992)	1986/1987	5 counties, Piedmont, North Carolina	Stratified random sample; Nonblack (all but 26 White); n=2258; age 65+ years;	76	1.4	1.9
			Black; n=1904; age 65+ years	66	1.1	1.7
Stoehr et al. (1997)	1989/1991	Monongahela Valley, Pennsylvania	Random sample; n=1059; age 65+ years; White	87	1.9	2.2
Espino et al. (1998)	1993/1994	Southwest US	Random sample; n=2938; age 65+ years; Hispanic	31	0.4	1.3
(a) Mean number of OTC drugs taken on an average day.						

1.2.3 Benefits and Risks of OTC Medications

The prevalence of OTC medication use among older consumers is not surprising, given the benefits that they offer. The availability of OTC drugs saves limited resources in the healthcare system, and affords the patient convenience, cost savings, flexibility and accessibility. (Consumer Healthcare Products Association, 2012b) Financially, it has

been reported that every dollar spent on OTC medications saved $6-7 for the U.S. healthcare system, resulting in an estimated $102 billion of saving in the year of 2012.(Consumer Healthcare Products Association, 2012b)

Additionally, with the support of government policy, in recent decades accelerating numbers of prescription medicines have been switched to OTC status in the U.S. (Consumer Healthcare Products Association, 2012a, 2014; Francis, Barnett, & Denham, 2005) Since 1976, a total of 106 ingredients, indications or dosage strengths had have been switched from prescriptions (Rx) to OTC status, which translated to more than 700 prescription medicines (Consumer Healthcare Products Association, 2013). It has been estimated that this has led to $13 billion in cost savings for consumers and $20 million for care organizations. (Pawaskar & Balkrishnan, 2007)

Despite the advantages that self-medicating offers, there are risks associated with their use which are more pronounced for older consumers. Reductions in liver and kidney function affect drug absorption and the ability to break drugs down. Changes in cognition and perception can create difficulties in reading, interpreting and remembering medication instructions. Declines in body weight, loss of body fluid and fatty tissue alter the way drugs are distributed and concentrated in the body. (Ghaswalla, 2011; Meadows, 2005) These factors, combined with increased propensities for polypharmacy and complex medical regimens, escalate the likelihood of adverse drug events (ADEs) among older patients.

The Office of Disease Prevention and Health Promotion (ODPHP) defines ADEs as “injuries resulting from drug-related medical interventions (US Food and Drug Administration, 2007).” These include: harm caused by the drug (such as side effects,

drug interactions, as well as overdoses), harm from the use of the drug (dose reductions and discontinuations of drug therapy.) (Singh, 2015; US Department of Health Human Services, 2014).

1.2.3.1 Risk of Drug Interactions

Drug interaction is one of the risks for patients engaged in polypharmacy. It is broken into three broad categories by the US Food and Drug Administration (FDA): drug-drug interactions, drug-condition/disease interactions, and drug-food/beverage interactions. (Table 2) (US Food and Drug Administration, 2013) A survey among 3,005 community-dwelling older adults showed that, "prescription and nonprescription medications were commonly used together, with nearly 1 in 25 individuals potentially at risk for a major drug-drug interaction" (Qato et al., 2008).

Table 2 General Categories of Drug Interactions

Categories	**Description**
Drug-drug interaction	May occur when two or more drugs react with each other. Drug-drug interactions have the potential to result in unexpected side effects.
Drug-condition/disease interaction	May occur when an existing medical condition makes certain drugs potentially harmful. For example, if high blood pressure and nasal decongestants are contraindicated.
Drug-food/beverage interaction	Result from drugs reacting with foods or beverages. For example, mixing alcohol with some drugs may result in fatigue and slowed reaction time.

The state government of California has summarized common drug-drug interactions (Appendix A). It is worth noting that people are put at particular risk when taking prescriptions for common age-related diseases, including: heart and blood pressure problems, diabetes, depression, etc.

1.2.3.2 Risk of Unintentional Overdose

Unintentional overdose is another risk, which is defined as drug injures or poisonings caused when people take excessive amounts of drugs without the intention of doing so. Although most fatal unintentional drug poisonings are associated with cocaine, heroin and opioid painkillers (Centers for Disease Control and Prevention, 2010), a study of OTC pain relievers containing acetaminophen suggested that 24% of adults took more than the recommended maximum dose, and that approximately 33% of self-treating people struggled with dosing timing, such as taking another dose too soon (Wolf et al., 2012). Factors such as these have caused unintentional overdose to surpass viral hepatitis as the leading cause of liver failure when taking acetaminophen. Misuse of acetaminophen contributes to more than 30,000 hospitalizations annually, with half to two thirds of them unintentional. (King et al., 2011)

1.3 The Role of OTC Packaging Labeling

1.3.1 The Importance of OTC Packaging Labeling

There are a myriad of factors that have the potential to contribute to the likelihood of drug-drug interactions, drug condition interactions and unintentional overdoses when selecting and administering drug products. As such, clear communication of proper use of OTCs is paramount.

Expected sources of health information are different for prescription and OTC products. For prescription drugs, two sources typically act as “learned intermediaries” for consumers: the prescribing physician and the pharmacist who dispenses the drug (Alsobrook, 1992; L. L. Bix, 2001). However, when choosing an OTC product, even

though consumers can also seek help from other sources, in the majority of cases, the label is the sole source of comprehensive product information. (Brass & Weintraub, 2003) This makes the labeling a predominant mechanism for communicating information about OTC products.

1.3.2 OTC Packaging Labeling and Regulations

Regulations which address specific labeling requirements for OTC drugs sold in U.S. markets are currently written and administered by the U.S. FDA. These requirements standardize the content and formatting of information for OTC drug product labeling. The regulations are intended to make labeling more efficient for consumers to read and understand to facilitate a drug's safe and effective use. Details are published in Title 21 of the Code of Federal Regulations (CFR) Part 201 Subpart C (21 CFR 201) (US Food and Drug Administration, 2010). More specifically, requirements dictate a:

- **Principal display panel (PDP)** (21 CFR 201.60): Statement of identity (SOI) (21 CFR 201.61); Declaration of net quantity of contents (21 CFR 201.62)
- **Drug facts label (DFL)** (21 CFR 201.66)
- **Others (not completely covered):** Pregnancy/breast-feeding warning (21 CFR 201.63); Labeling requirements for Sodium (21 CFR 201.64), Calcium (21 CFR 201.70), Magnesium (21 CFR 201.71), Potassium (21 CFR 201.72), etc.

Table 3 provides some detail regarding current content and formatting requirements for the PDP and DFL of OTC products. Labeling of the test stimulus (described in the Materials and Methods Chapter) were designed based on these rules. The Guidance is intended to enable better understanding of the OTC labeling requirements presented in 21 CFR 201. 66. (US Department of Health Human Services, 2005).

Table 3 Requirements of Content and Formatting for the Principal Display Panel and Drug Facts Label as Dictating by 21 CFR

Part 1. Content requirements		
Packaging panels	**Contents**	**Details**
Principal display panel or alternative principal display panels (PDP)	Statement of identity (Sec. 201.61)	• The general pharmacological category(-ies) of the drug (Sec. 201.61 (b)) • Or, the principal intended action(s) of the drug (Sec. 201.61 (b)), for example, “antacid”, “analgesic”, “decongestant”
	Declaration of net quantity of contents (Sec. 201.62)	• Weight, measure, numerical count, size (Sec. 201.62 (a)) • Reveal the quantity of drug or device in the package accurately (Sec. 201.62 (f))
Drug facts label	Drug facts label (Sec. 201.66 (c))	• Drug facts; Active ingredients; Purposes; Uses; Warnings; Directions; Other information; Inactive ingredients; Questions (Sec. 201.66 (c) through (1)-(9))

Table 3 (cont'd)

Part 2. Format requirements		
Packaging panels	**Formats**	**Details**
Principal display panel or alternative principal display panels (PDP or alternative PDP)	Principal display panel	• one entire side with the area of height times width (Sec. 201.60 (a))
	Statement of identity (Sec. 201.61 (c))	• bold face type • parallel to the base • size reasonably to the most prominent printed matter
	Declaration of net quantity of contents (Sec. 201.62)	• appear as a distinct item on the PDP • be parallel to the base of the package • be placed on the PDP within the bottom 30 percent of the area of the label panel in lines (Sec. 201.62 (e)) • appear in conspicuous and easily legible boldface print or type in distinct contrast (by typography, layout, color, embossing, or molding) to other matter on the package (Sec. 201.62 (g)) • be in letters and numerals in a type size established in relationship to the area of the PDP of the package and be uniform for all packages, e.g. not less than 3/16 inch in height with the PDP area between 25 to 100 square inches (Sec. 201.62 (h))
Drug facts label	Drug facts label (Sec. 201.66 (d))	• Drug facts; Active ingredients; Purposes; Uses; Warnings; Directions; Other information; Inactive ingredients; Questions (Sec. 201.66 (d) through (1)-(9)) • The FDA-recommended Drug Facts Labeling formats (Appendix B)

1.4 Information Processing on OTC Packaging Labeling

1.4.1 Information Processing Model and Human-Package Interaction

To frame our experiments regarding how older adults interact with labeling information, a common information processing model was employed, which is adapted from DeJoy (1991). This model proposes that five stages of recipient-message interactions must occur to ensure effective information processing.

1) **Exposure**: Users are exposed to information (in our case, labeling).
2) **Perception**: Information is received by users via their five senses; in the case of labeling, this occurs through vision.
3) **Encodation**: Perceived information is converted from the external signal into an internal signal that can be processed by their cognitive systems.
4) **Comprehended**: Encoded information is recognized and assigned meaning by users.
5) **Execution/Action**: Processed signals are externalized as actions by activating related muscles. An action is performed to change the state of things. For instance, after viewing information provided on a package's PDP, older adults may turn the OTC packages for more information, or simply select or reject the product.

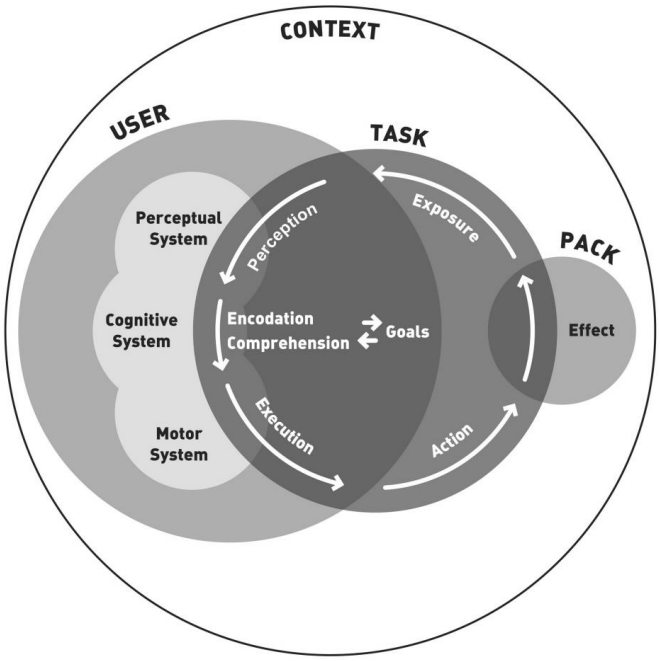


Figure 1 Human-Package Interaction Model (H-PIM) by Javier de la Fuente. Reprinted with permission, de la Fuente CJ (2013) Usability of tabs in semi-rigid packaging (Doctoral Dissertation). School of Packaging, Michigan State University.

de la Fuente (de la Fuente, 2013) further adapted the processing model by combining it with Shackel's Human Tool theory (Shackel, 2009) (Figure 1). Four inputs from Shackel's model directly influence the effectiveness of each processing stage (above), acting as system inputs. These inputs are:

- **User**: the characteristics of the person, such as perceptual and cognitive capabilities, previous behaviors, habits and beliefs.
- **Package/product**: the object of the interaction, the packaging design or contents
- **Context**: the physical and social environment of the interaction
- **Task**: the series of actions and goals to be accomplished

Driven by a given task, the user interacts with the information on the labeling during the five stages of information processing. All the while, these stages are undergirded by a specific context (e.g. the brightly lit aisle of a grocery store) in order to execute an action (e.g. select or reject the product) relating to the task. Once a given task is complete, the information processing circle will restart for the next task.

1.4.2 State of Knowledge Regarding Information Processing and OTC Labels

Clearly, it is important that consumers effectively engage with the information on OTC products. If users, purposefully or otherwise, fail to view/use the information present on OTCs (early stages of the processing model), later stage processing (comprehension) is irrelevant (i.e. the information cannot be used to inform a decision if it is not seen).

Despite this fact, survey results from data collected for the National Council on Patient Information and Education (NCPIE) report that only 41% of people indicated that they looked for usage information, and 34% the active ingredient, when buying an OTC. (Centers for Disease Control, 2004; National Council on Patient Information and Education, 2010; Sansgiry & Cady, 1995) Others conducting research specific to acetaminophen containing products suggest that "the root cause is likely poor understanding of medication labeling or failure to recognize the consequences of exceeding the recommended maximum daily dosage." (King et al., 2011)

More recent surveys suggest lack of engagement with labeling information on OTC continues to be a problem and that label usage varies with demographic characterization. (PR Newswire, 2015) An Association of Public-Safety Communication Official (APCO) Insight online survey of more than 2,000 US adults conducted in July 2015 found that while consumers recognized the importance of OTC labeling, only 20% report re-reading the label of an OTC on repeat use, and there were wide gaps in attitude regarding the importance of OTC labels by age, gender and ethnicity. Women, Millennials, African Americans and Hispanics were reported to be more careful about OTC use and women found label reading (81%) and paying attention to restrictions

(74%) to be significantly more important than their male counterparts (62% and 58%, respectively). Caucasians were about half as likely to think it was very important to read the label of a drug that they had taken before (33%) as African-Americans (60%) and Hispanics (57%). African Americans (72%) and Hispanics (57%) were also significantly more likely than Caucasians (33%) to pay attention to active ingredients present in the OTC.

Of specific interest to us were the age related gaps. While all age groups recognized the importance of reading labels the first time they took a product, only 54% of adults over 70 felt that this was important when reusing a product, compared to 82% of the Millennial (respondents 18-34). (PR Newswire, 2015)

It is not surprising that consumers do not use specific information (e.g. active ingredients, usage information or the DFL) in light of the "Model for consumer in-store navigation and decision making for OTC drugs," (Julie Aker, 2014) which postulates that consumers primarily use visual cues (e.g. signage and brand name) to make decisions related to OTC purchases. Researchers, who tested 204 adults in an online survey meant to illuminate purchase behaviors, reported that a majority of consumers (56%) look for a brand name they trust, while 20% reported looking for color or graphics that they knew to identify the correct shelf. Once the participants had narrowed to the correct shelf, a majority (78%) indicated that they looked for symptom relief to make the selection while 54% reported looking for brand name and 47% for what is on sale. Convenient package size (11%), special displays (7%) and "other" (7%, such as generic of the brand name), were also enumerated as factors for making a decision about whether or not to buy an OTC.

The appropriateness of medicine selection among self-medicating older adults is essential for safe use of drugs and patients' health. Amoako, Richardson-Campbell, and Kennedy-Malone (2003) emphasized lack of awareness of adverse risks among self-medication, older adults as problematic. Many factors can influence older adults' appropriate selection and use of OTC medications. Haider, Johnell, Weitoft, Thorslund, and Fastbom (2009) investigated the influence of educational level on polypharmacy and inappropriate use among older adults in Sweden. People with lower educational levels were more likely to have inappropriate drug uses and excessive polypharmacy. Beyond that, Blalock et al. (2005) identified factors that exhibited associations, including illiteracy, skin color, the use of 4 or more drugs per day, and the use of medications prescribed by a doctor.

Objectively understanding the factors that aid older consumers who do wish to engage the information on the label, is important to know in order to optimize the design of information on OTC labels. Therefore, it is surprising that remarkably little is known about how older consumers interact with and use information on OTC products during the decision making process. (Albert et al., 2014)

Print size is one of the most obvious factors that can be manipulated to enhance information processing for older adults. Vigilante and Wogalter (1999) studied older adults and undergraduates perceptions of the readability of medication labels. To do so, twelve labels that had varied print sizes, leading (space between text lines) and formats (tradition vs. extended) were rank-ordered for ease of reading. In a companion publication (Viglilante & Wogalter, 2003), the research team reported the efficiency of information acquisition, obtained through answers provided on a survey that participants

filled out (some with label present, others with label absent). Among older adults, print size was a very important factor for both perceived readability and acquisition performance. Younger adults, who showed no performance difference in print-size, had significantly better information acquisition performance than the older adults, who performed significantly better in the medium and large print conditions compared the small conditions. Sansgiry, Cady, and Patil (1996) reported similar results when they compared the difference between two age groups asked to rate the importance of several labeling attributes for OTC medications. Older adults were more concerned about print size, the manufacturer and side effects than their younger counterparts.

Sansgiry and Cady (1995) also investigated symbol comprehension and aging in a two-part study. Researchers concluded that older subjects had significantly more difficulty interpreting symbols than younger subjects for all but one symbol. Additionally, subjects could not interpret graphic only (symbols from existing OTC products) but were able to understand the same information when presented in written form (text on existing OTC products). A follow-up study by the same group further explored the use of symbols. (Sansgiry, Cady, & Adamcik, 1997) Authors concluded that participants had less confusion when the label designs were congruent (picture-verbal) or text only as compared with picture only and incongruent picture-verbal.

King et al. (2011) also investigated the use of plain-language text and icons for a specific group of OTC products (containing acetaminophen) but did not specifically focus on older adults. Their study employed guided interviews and focus groups of adults (≥ 18 years). Researchers suggested that changes to OTC labeling for products containing acetaminophen are warranted. Results suggested that few participants recognized the

active ingredient or the potential for ADEs. Focus groups recommended the use of a stop-sign shaped icon to warn of the potential for unintentional overdose, indicating that it would draw the eye and be easily understood to convey the maximum daily dose.

While the previous studies have investigated specific aspects of label design (type size, leading, icon use, etc.) other studies have looked at how to organize the information that is required for the safe and effective use of OTC products. Vigilante and Wogalter (1997) indicated that patients prefer an organized way to present medical information logically and schematically. Their survey of 140 people concluded that participants preferred to have indications and benefits precede those relating to adverse effects and warnings. A similar experiment asked participants from different age groups to sort pieces of medication information (directions, adverse effects, etc.) into an instruction set. Participants created a similar order: name, indication, directions, warnings and side effects.

In the US, Principal display panels (PDPs) combine with the Drug Facts Label (DFLs) on OTCs to provide all the information deemed most necessary for their safe and effective use. PDPs are displayed facing patients during retail, and DFLs contain detailed information specifically required by regulation. Both of their design details are strictly regulated by 21 CFR 201 (as shown in Section 1.3.2). However, PDPs have relatively fewer requirements than DFLs, which gives manufacturers more room for product characterization. For instance, information organization in the DFLs is mandated in an exact order starting from “active ingredient”, followed by “uses”, “warnings”, “directions”, “other information”, “inactive ingredients” and ending with “questions”. In contrast, the requirements for PDPs provide an acceptable range for designs, as opposed

to exact values. For instance, the net content needs to be displayed on the PDP in the lower third of the label, but alignment (left or right) is at the discretion of the manufacturer.

The aforementioned review suggests that while few people interact significantly with the detailed information present on an OTC when making a purchase decision, this information is important for the safe and effective use of these products. A limited number of studies explore how people interact with the detailed information present on OTC products.

L. Bix, Bello, Auras, Ranger, and Lapinski (2009) conducted eye tracking on five different packages of OTC pain reliever randomly presented with five other grocery products to investigate how adults viewed the information present in five zones (brand name, indications, DFL and two warnings). The research team found that participants spent significantly less time viewing information in the warning zones than in the brand name area. During a post-hoc test of recall, participants were asked to record anything that they could remember about the pain relievers that they had viewed. Brand name, indications and package color were recalled significantly more frequently than warning information.

Gawasane, Bix, Sundar, and Smith (2012) conducted an eye tracking study where OTC packages were randomly presented among varied grocery products to objectively evaluate how a warning's design could be manipulated to increase its likelihood of being seen. The research team concluded that warning information was significantly less noticeable than drug name for all three dependent variables reported: time in zone (Figure 2), fixation probability and number of visual hits to a zone); this was despite the fact that

US law requires this warning to be conspicuous. No significant difference was evident for the varied warning designs which were graphically enhanced from standard through the use of boxing and countershading but remained constrained to the same surface area as the traditional warning.

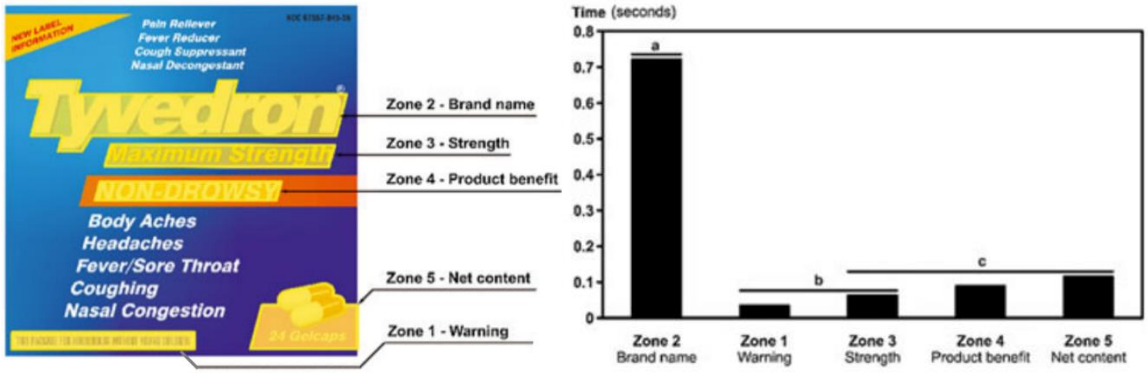


Figure 2 Zones of test stimulus (left) and Estimate of time spent in a zone (right)

JeongSeo Choi et al. (2012) evaluated consumer attention to OTC labeling in Japan. Twenty eight participants were asked to select one drug from a set of cold remedies or vitamin supplements. Visual stimulus was presented on a computer screen and subjects were able to view any side of the package using mouse clicks. (Figure 3) Consistent with the previous two studies (L. Bix et al., 2009; Gawasane et al. (2012)), and the survey work conducted by Julie Aker (2014), researchers concluded that drug name drew a significant amount of time and attention, while information regarding risk and proper use were largely disregarded.

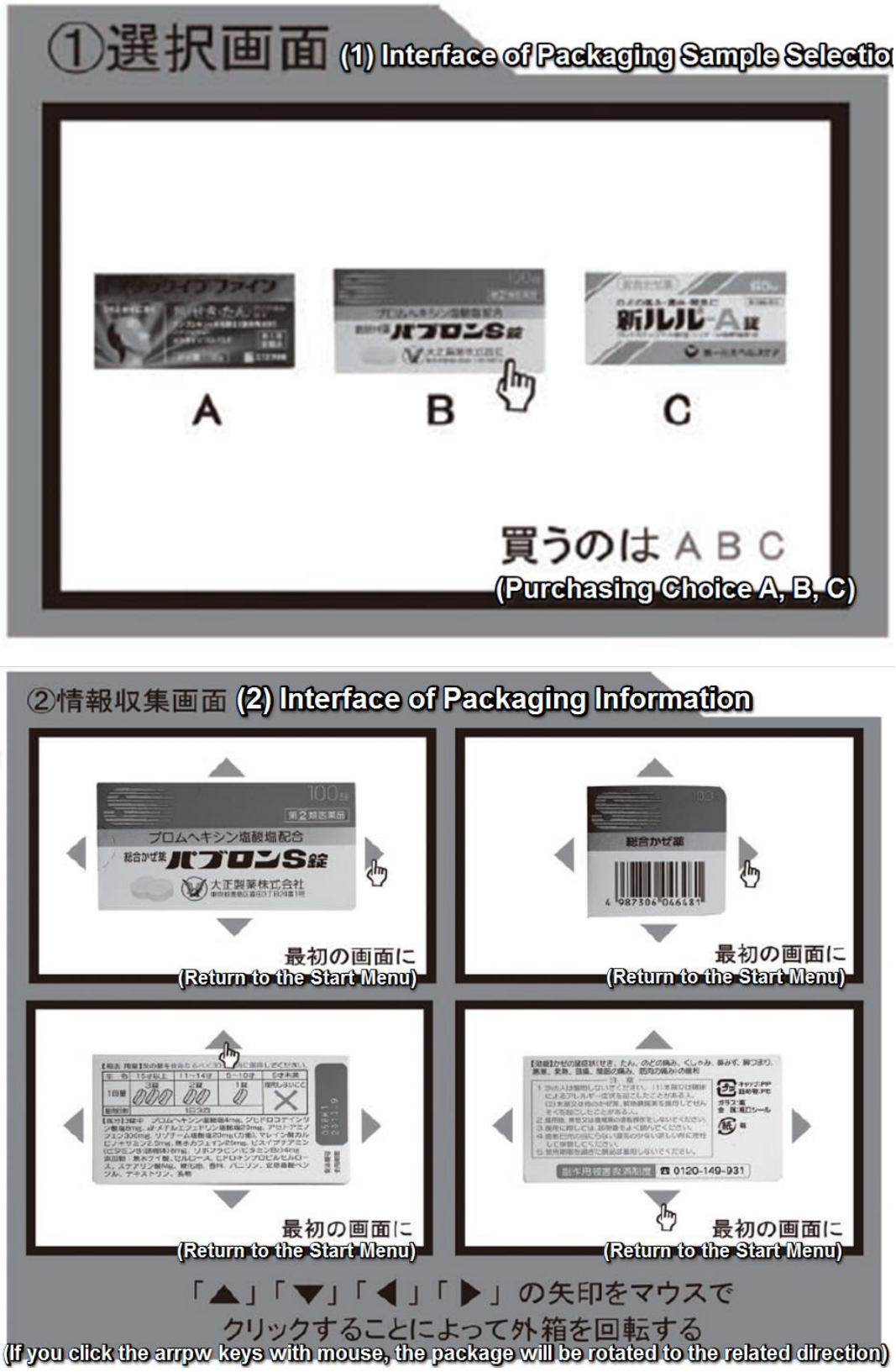


Figure 3 Packaging visual stimulus presenting on a computer screen by Choi et al.

The available research regarding how people interact with specific elements of the label has been conducted with "branded" products. That is, OTCs that place the brand name in a prominent position on the PDP (L. Bix et al. (2009); Gawasane et al., 2012; JeongSeo Choi et al. (2012)). However, Kline & Company (2009) reports that consumers have been increasingly turning to private brands, or store brands, such as Walgreens and CVS. Unlike nationally-branded OTC medications, which exclusively feature the brand name in the most prominent position, it is not uncommon for the store brands to feature a variety of different pieces of information, including: store brand, e.g. Wal-Dryl; active ingredients, e.g. ibuprofen; or symptom relief, e.g. pain reliever. (Figure 4) Yet, little literature exists regarding how featuring different pieces of information impacts the viewing pattern and decision making process.

Figure 4 Types of the store brands layouts

Herein, we attempt to fill several gaps in knowledge identified during the course of the literature review. Specifically, we directly measure how older consumers interact with OTC labeling that has varied information emphasized when assessing whether or not a product is appropriate for them to take. To this end, nine different active ingredients were carefully chosen from three drug categories, namely pain reliever, cough and cold as well as acid reducers.

CHAPTER 2 MATERIALS AND METHODS

2.1 Objectives

The goal of this research is to explore the role of OTC labeling in information processing and decision-making among self-medicating older adults during an OTC selection scenario. In doing so, five specific objectives are listed below:

1. To begin to garner insights regarding the proportion of subjects who examine information beyond the PDP for more when deciding whether (or not) a drug is appropriate for them.

2. To quantify and compare the attention of older adults to specific information present on the Principal Display Panels (PDP) of OTC packages (brand name, active ingredient and symptom relief).

3. To test the effect of information formatting on the attentive behaviors of older adults viewing OTC products (prominently featured information vs. less prominently featured).

4. To begin to benchmark whether or not older consumers make appropriate choices based on their current health status and medication history.

5. To test the effect of information formatting (prominent or non-prominent) on determination of drug appropriateness.

2.2 Participants

Eighty-two older adults (65+) were recruited and tested according to the documents and procedures approved by the MSU Institutional Review Board (IRB#14-679) and ClinicalTrials.gov (NCT02188134). Recruitment flyers (Appendix C) were posted and distributed through a variety of channels including: several clinics throughout the MSU health system, the pharmacy at the Clinical Center, MSU Extension programs targeting seniors, the Family Resource Center list serve, the Learning and Assessment Center's standardized patient list serve and Sparrow Pharmacy Plus. Participants also distributed fliers to interested friends.

Screening criteria was listed on the recruitment flier and reiterated during a scheduling phone call. Eligible participants:

- were at least 65 years of age;
- willing to bring all the medications, herbal remedies and vitamins that they took on either a scheduled or as-needed base within one week of their test date;
- were legally sighted and did not use hard contact lenses (interfere with eye tracking);
- purchased and administered OTC medications by themselves;
- had transportation to the lab, where testing occurred.

Participants were called twenty-four hours prior to their scheduled appointment and reminded to bring all prescription, OTC, herbal supplements and vitamins that they took regularly with them to the testing and provided directions and parking information at that time as well.

Upon arrival, screening criteria were reviewed again and each participant was provided with a printed copy of the IRB approved consent form and a verbal explanation of the experiment (Appendix C). After informed consent was obtained, participants were

assigned a number, and asked to provide any medications that they brought with them to an undergraduate research assistant, who scanned them using an Rx Label Reader (Meditory, LLC; Brighton, MI) while subjects participated in other aspects of the research study.

2.3 Testing Procedures and Related Materials

2.3.1 Participant Characterization:

Subjects were characterized through an assessment comprised of three parts, a demographic survey (Appendix D), visual acuity test and, a measure of health literacy called the Rapid Estimate of Adult Literacy in Medicine-Revised (REALM-R, 2013), (Appendix E).

Basic demographic information was collected including: gender, age, ethnicity, educational level and native language.

Upon completion of the demographic survey, each subject's visual acuity was tested using a near point visual acuity card (Opt-Source, LLC; Bellport NY) (Appendix F). Researchers asked subjects to hold the card at a distance of approximately 16 inch under standard room illumination conditions and read the lowest line of letters that they were able. (Figure 5) Visual acuity was recorded as the lowest line where the participant could correctly identify all letters, corresponding with the appropriate reading on the card (20/20, 20/30, 20/40, etc.).

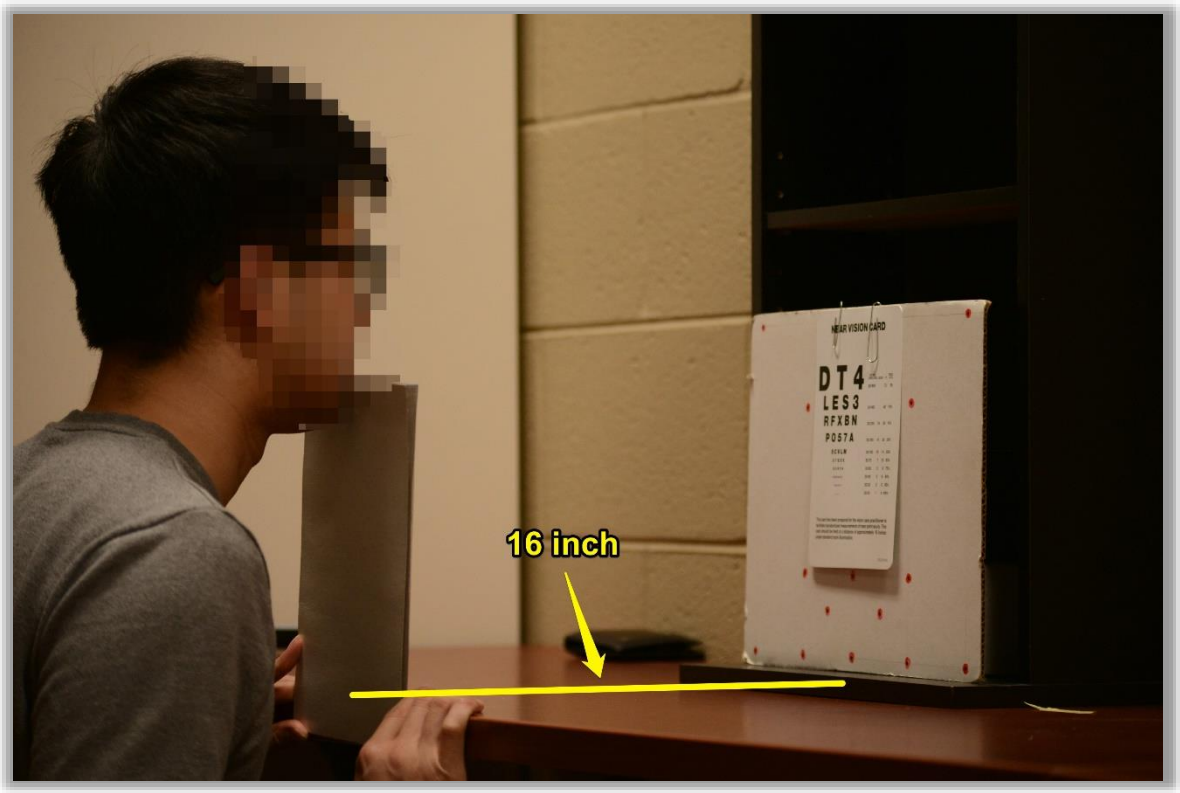


Figure 5 Test for visual acuity with near vision card

Following visual acuity testing, each subject was given a REALM-R card which they held at a convenient reading distance. In accordance with standard, published procedures for the test, subjects were instructed,

> "It would be helpful for us to get an idea of what medical words you are familiar with. What I need you to do is look at this list of words, beginning here (point to the first word with a pencil). Say, out loud, all of the words you know. If you come to a word you don't know, you can sound it out, or indicate, 'Pass.'"

In the event that a participant stopped, researchers indicated,

"Feel free to look down this list and say the other words that you know."

If participants took more than 5 seconds on a word, they were encouraged to move down the list with a prompt like, "Let's try the next word."

An "X" was placed on the scoring sheet (see "Administration and Scoring" in Appendix E) anytime an error occurred. Errors were counted as any word that was not attempted, or mispronounced. Participants at risk for poor health literacy were defined as those with a score of six or less. The first three words were not scored, serving as a warm up period.

2.3.2 Experiment 1: Subsidiary Experiment

2.3.2.1 Materials

- Walgreens® store brand OTC medicines;
- 43cm (Length)*14cm (Width) *58cm (Height) wooden shelf;
- 72cm (Height) desk; 40cm ~ 55cm (Height) office chair;
- Opaque container (corrugated box) with 27cm (Length) * 23cm (Width) * 44cm (Height); White paperboard, served as "shopping cart" to hold consumer's choice in each trial;
- GoPro Hero 4. (GoPro, Inc., San Mateo, CA)

2.3.2.2 Experimental Design

Experiment one was intended to explore, ***Study Objective One***, "To begin to garner insights regarding the pro portion of subjects who closely examine the labeling of an OTC (e.g. turn to the DFL) when deciding whether (or not) a drug is appropriate for them.

As part of a shopping scenario, subjects were shown three different sets of store-brand OTC medicines; each set pertained to a particular drug category, namely: allergy

relief, sleep aids and anti-diarrheas. (Table 4) Each set was comprised of two different medicines (i.e. two active ingredients). For each medicine/active ingredient, two identical packages were displayed on the shelf (a total of four packages per set) with the PDPs facing subjects. Therefore, a total of 12 packages (3 category sets* 2 active ingredients * 2 packages) were shown to each participant during three separate trials. (Appendix G)

Table 4 Category information for the sets in the Experiment 1

Set Order	**Drug Category**	**Trigger Text**	**2 Active Ingredients comprising each set**
1	Allergy	"*Suppose that you have been suffering the effects of seasonal allergies*, and are seeking an over-the-counter medication to alleviate your symptoms. Please select a product for yourself to take from the set that I show you. Once you've decided, please put your selection into the cart."	Diphenhydramine Nasal Strips
2	Sleep Aids	"*Suppose that you have been having difficulty falling asleep...*"	Melatonin Diphenhydramine
3	Anti-Diarrheal	"*Suppose that you have been suffering from diarrhea...*"	Psyllium seed Kusk Fiber

2.3.2.3 Testing Procedures

Subjects were seated in front of the shelf set while wearing a head gear outfitted with a GoPro Hero 4 scene camera. The angle of the camera was adjusted to record the subject's perspective as completely as possible during each trial. (Figure 6)

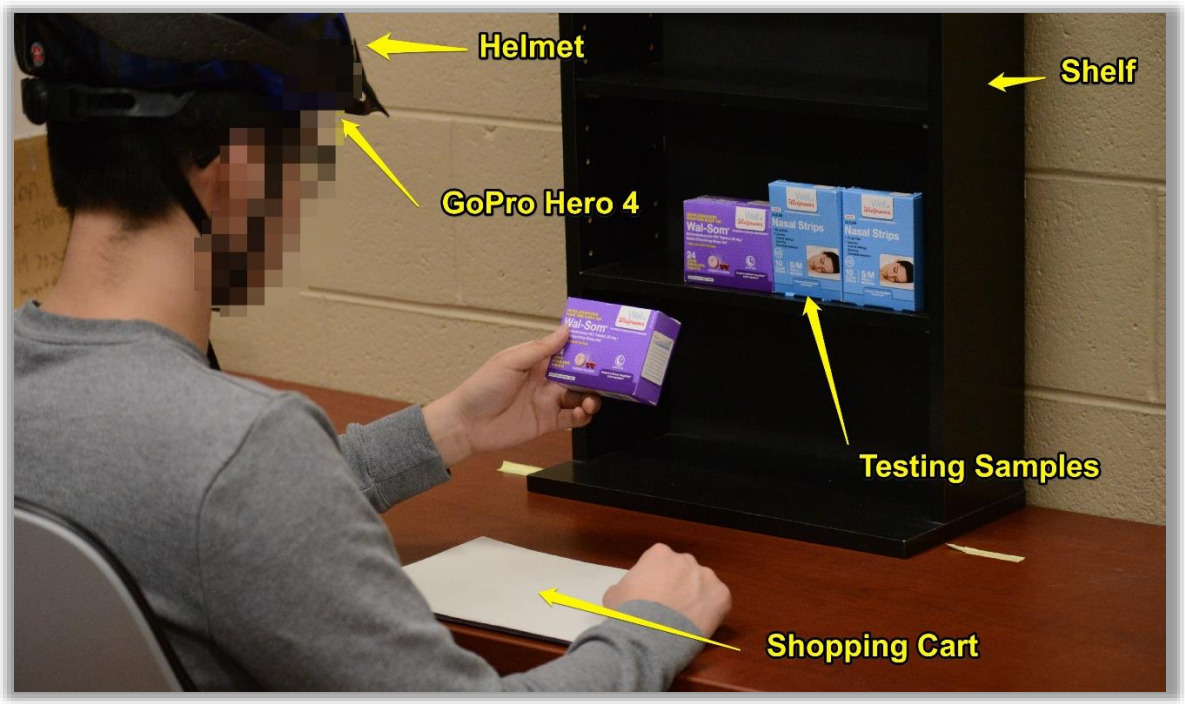


Figure 6 Testing devices for running Experiment 2

Researchers indicated, "Now, we are going to start Experiment One. As you can see, there is an empty shelf in front of you and a container on the table next to it. Imagine that you are in the pharmacy at Meijer or Walgreens, please pretend that the wood shelf is a store shelf, and the container is your shopping cart area. Feel free to ask researchers if you need help."

Following this, subjects were asked to close their eyes while the shelf was loaded with the first set of testing sample. Those testing packages were picked up from an opaque container to preclude the subject's ability to preview the drugs or categories. They were read the trigger text for the appropriate set (Table 4) and asked to open their eyes.

Once the subject finished their selection in the first set, the researcher would empty the shelf and continue with another set.

While the experimenter unloaded the previous set and loaded a new set of samples; the subject was asked to close his/her eyes. Subject were instructed to keep their eyes closed until the researcher finished loading the next sample set and reading its trigger text (Table 4), Then, the subject was asked to open his/her eyes to start the test,

Product selection and viewing behaviors (turning the package to the more complete information comprising the DFL) were recorded on a data collection sheet (Appendix H). Results could also be verified through the post-hoc review of the user view point video that was recorded.

2.3.3 Experiment 2: Main Test

2.3.3.1 Materials

- ASL EYE-TRAC 7 desk mounted optics eye tracking system (Applied Science Laboratories, Bedford, MA)
- Testing program for Experiment 2 driven by Unity 4.0 (Unity Technologies, San Francisco, CA)
- Chin rest with latex-free foam-based paddings (medical closed-cell foam by UFP Technology, Inc., Georgetown, MA)

2.3.3.2 Experimental Design

Experiment two supported all five research objectives. During this experiment, a bright pupil eye tracker was utilized to track the eye movements of participants while they were viewing mock brands of OTCs on a computer screen. Mock brands were comprised of 3 drug categories, each with 3 active ingredients (Table 4). Stimulus were

programed on the computer so that participants could use the mouse to view any of the six faces of the OTC carton on the computer screen. Participants were asked to assume that they had the condition each drug was intended to treat, and assess whether or not the drug would be an appropriate choice for them (binary variable yes/no).

Table 5 Active ingredients by category

Drug Categories based on Symptoms	**Drugs based on Active Ingredients**	**Novel Brand Name based on Active Ingredients**
Analgesic/Pain Reliever	Acetaminophen	Hublenol
	Ibuprofen	Hubidvil
	Naproxen	Hublevel
Cough/Cold	Guaifenesin	Hubrinex
	Dextromethorphan	Hubussin
	Phenylephrine	Hublafed
Acid Reducer	Omeprazole	Hublosec
	Cimetidine	Hublamet
	Ranitidine	Hubantac

2.3.3.2.1 Stimuli:

For each of the nine brands (Table 5) three layouts were created to emphasize the different pieces of information of interest in the study (active ingredient, symptom relief or mock brand name), see Table 6 and Figure 7 for details. As such, each subject examined 27 packages (3 drug categories x 3 active ingredients x 3 graphical layouts (Appendix I).

Table 6 Types of PDP layouts based on prominent level

	Prominent Level		
Layout Type	**Level A Most Prominent**	**Level B Less Prominent (First line + Second line)**	
Type 1	Novel Brand	Active Ingredients	Symptom Relief
Type 2	Active Ingredients	Symptom Relief	Novel Brand
Type 3	Symptom Relief	Novel Brand	Active Ingredients

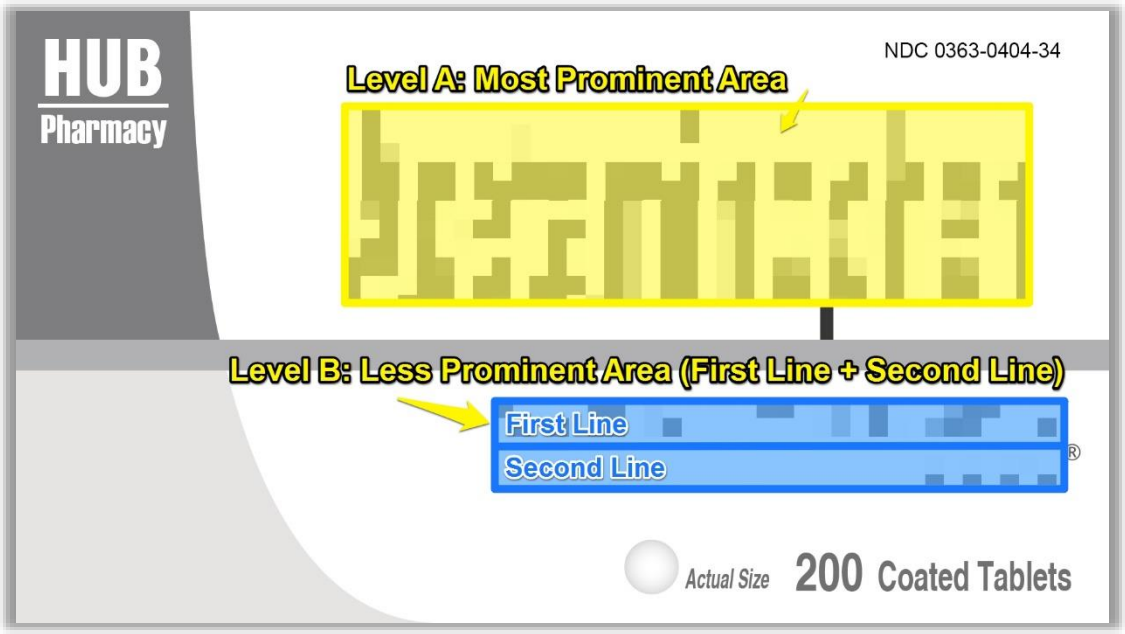


Figure 7 Levels of prominent areas for PDP layouts

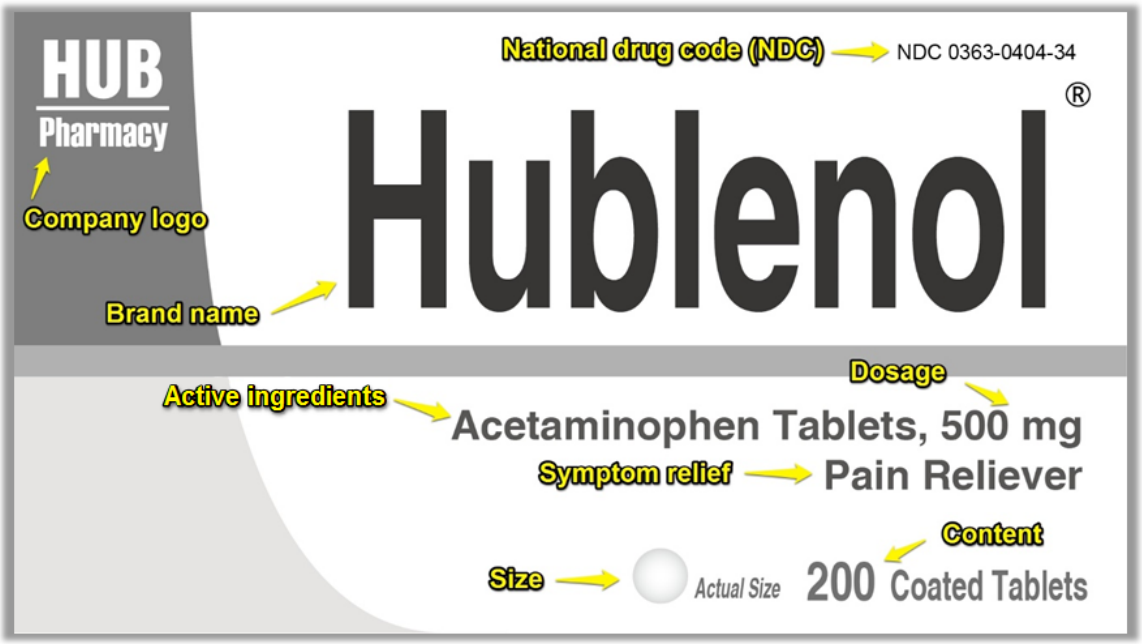


Figure 8 Design template involving the required information on PDP in the U.S market

All stimulus materials were greyscale and were modeled on information that is typically present or required of OTC products sold in US markets. PDP information

included company logo, national drug code (NDC), brand name, active ingredients, symptom relief, dosage, content and pill size. (Figure 8)

Mock products were created such that they had a square cross section. Two of the four major panels comprised the Drug Facts Panel, and were designed following the Code of Federal Regulations for OTC drugs labeling requirements (US Food and Drug Administration, 2010). The other two of the four major panels were PDPs. The remaining two (end) panels utilized other design elements typically found on these products, including bar coding, expiration dating, and manufacturer information. (Appendix J)

All graphics for the package drawings were created using Adobe Photoshop CS6 and Adobe Illustrator CS6, (Adobe Systems Incorporated, San Jose, CA) and then, rendered and converted into 3d package models via ArtiosCAD Version 14.0. (Esko Graphics, Gent, Belgium) in such a way that they seamlessly interfaced with the test program built using Unity 4.0.

2.3.3.2.2 ASL EYE-TRAC 7 desk mounted optics eye tracking system

The ASL EYE-TRAC 7 desk mounted optics eye tracking system was used to measure participants' point of gaze during the experiment. The system is composed of three main components: a system for displaying stimulus material (the 3D rendering), a desk-mounted optics module, and processing unit. The stimulus system consisted of a monitor, stimulus computer and audio system. (Figure 9) The test program (created in Unity) was shown to participants on this system.

The desk mounted optics module consisted of the tracking mirror mechanisms, the camera optics, the illuminator module and Video Head Tracking (VHT) unit. The

adjustable aiming mirror directed the eye camera and illumination source so that the near infrared lights generated by the illuminator assembly are coaxial with the camera's imaging path towards the participant. The image from the eye camera was the one used to compute the line of gaze. The head tracking camera in VHT unit was also aimed towards the participant, the image from which was used to help direct the eye camera (via the moving mirror) in order to correct the measurement regarding to the changes of head position.

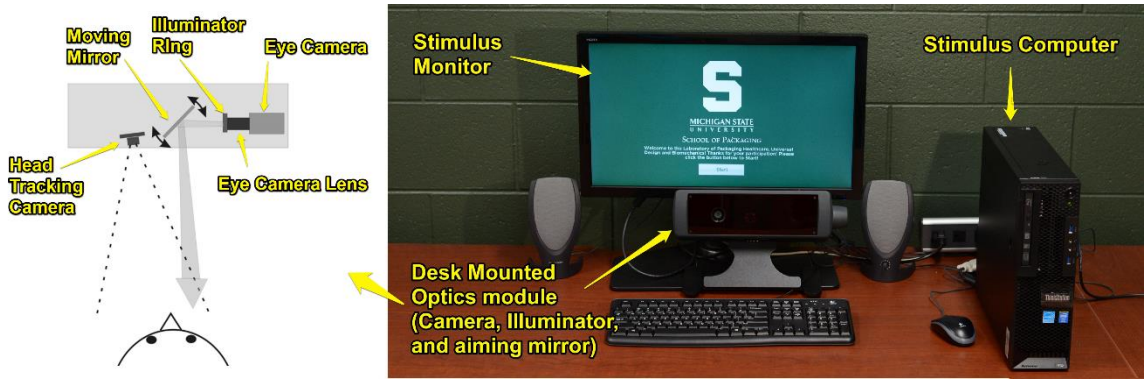


Figure 9 ASL EYE-TRAC 7 desk mounted optics module and stimulus system

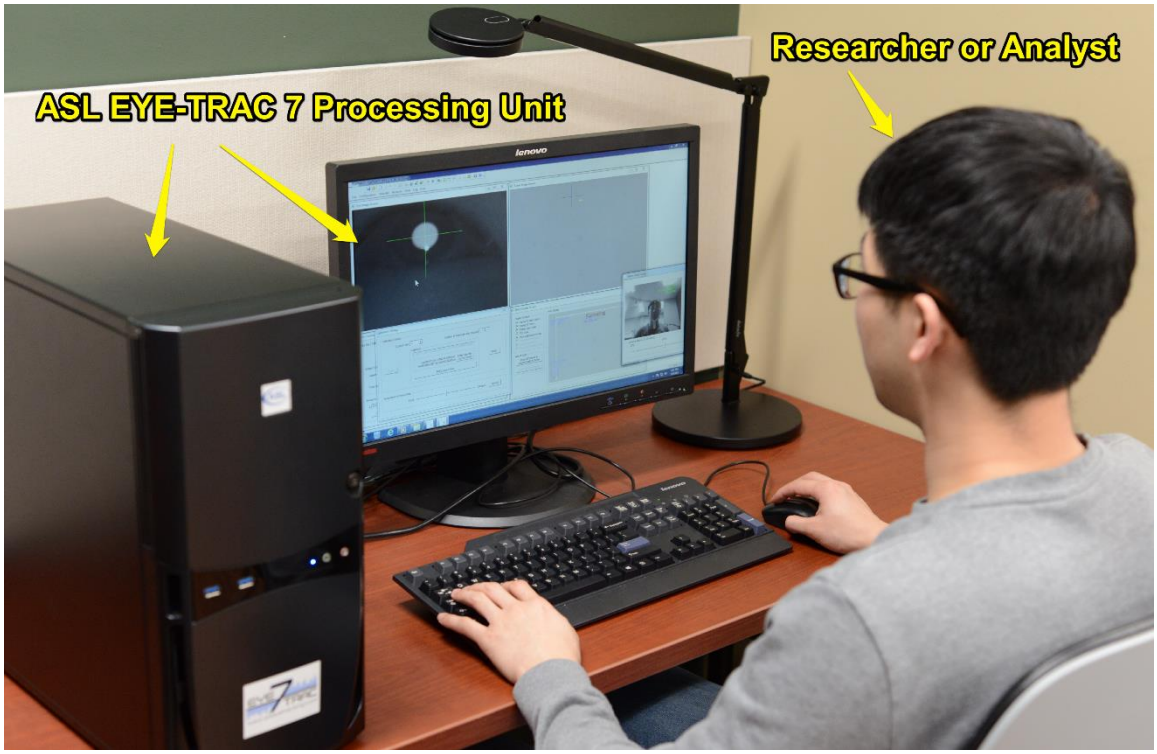


Figure 10 ASL EYE-TRAC 7 processing unit

The ASL EYE-TRAC 7 processing unit (Figure 10) contains all the processing electronics for the eye tracker, including the user interface application, the gaze computations, record data, etc. Also, ASL Results Pro (Applied Science Group Company, Bedford, MA) was installed for processing and analyzing data collected by ASL eye tracker.

2.3.3.2.3 Testing Program for Experiment 2

The testing program participants interfaced with when viewing stimulus material was built using Unity 4.0. It included three main parts: (Appendix K)

- A computer mouse tutorial (optional for participants who were not comfortable using a computer mouse)

- Two test trials that served as an instructional piece regarding how to interact with stimulus materials and
- Twenty seven trials with visual stimuli that comprised the main test

(a) Computer Mouse Tutorial (Part A, Appendix K)

The computer mouse tutorial was designed to familiarize subjects with the basic operations of computer mouse. These operations included moving the mouse pointer and using the mouse to click buttons in order to provide information input. Subjects were able to skip this portion of the testing if they were comfortable in doing so. Textual instructions with audio voice over directed participants through this section of the orientation.

(b) Testing Program Instructions (Part B, Appendix K)

Upon completion of the mouse tutorial (or having skipped it), both textual and audio instructions guided participants through two trials that depicted food packages. This portion of the orientation was intended to provide participants with basic operations for successfully using the program. Questions that were asked of the subjects included information that forced them to turn the package to a face other than the PDP in order to have a correct answer, so that they were aware of this feature within the program.

(c) Main Test

As shown in the Part C of Appendix K, the main test consisted of a total 27 trials (3 drug categories x 3 ingredients x 3 layouts- see PDP layouts section). In each trial, the "Shelf view section" (comprised of the PDP only) was the first to be shown. Subjects were asked to answer the question "If you had the condition that this product treats, is it appropriate for you?" by clicking either yes or no. The subject could either click on the

package, which enabled them to view any of the six faces of the OTC, or answer the question. The subject could answer the question when viewing any of the faces of the packages. Once the question had been answered, the subject began a new trial.

To prevent subjects missing any trials due to fast clicking, mouse function was prohibited during the intervals of trial switching, and the screen showed "Please move your mouse to continue" (Part C, Appendix K).

Trials were randomized using a carefully devised randomization scheme which minimized the likelihood that the same active ingredient would appear in back to back trials (i.e. formatted differently with the same active ingredients) and made it impossible for the same active ingredient to appear in three simultaneous trials. Nine arrays, each of which was comprised of the packages that contained the same active ingredient (marked as A-C (pain reliever category), M-O (cough and cold category) and X-Z (acid reducer category) (Figure 11)), with critical information at varied prominence levels (1 Symptom Relief, 2 Active Ingredient and 3 Novel Brand Name), were used as part of the randomization scheme. After a single trial was selected from each of the arrays for a block (i.e. one trial for the green, one for the orange, the last for the blue), the order of the nine trials (represented as groups) was randomized as well. Using such a scheme minimized the likelihood that participants could access information regarding these novel brand names through short-term memory because it was not likely that multiple trials containing the same active ingredient (and brand name) would appear serially.

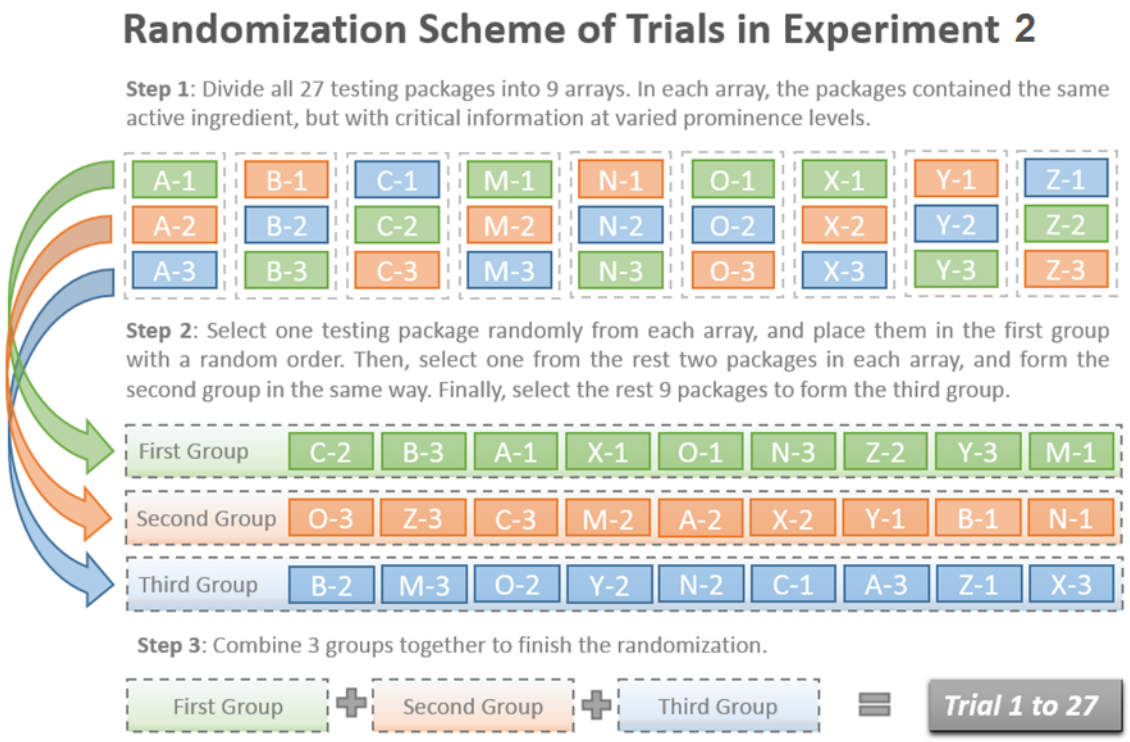


Figure 11 Randomization scheme of trials in Experiment 2

2.3.3.3 Testing Procedures

Subjects were seated at the eye tracking station where their chair was adjusted for comfortable viewing of the computer screen. Throughout the orientation process (described above), researchers were available for questions. Upon completion of the orientation materials (mouse tutorial and two trial test), subjects were asked if they had any questions.

This was followed by general instructions relating to the experimental trials. These instructions consisted of the following text with voice-over audio:

"*For this experiment, we are going to show you 27 samples of medications one by one. Some will be for head and muscle aches; some will be for upset stomach; some for cold symptoms. For each package, please decide whether the product would be an*

appropriate choice for you to use, assuming that you have aches, or upset stomach, or cold symptoms. Feel free to ask researcher if you have any questions."

Once existing questions had been clarified for subjects, a calibration sequence was conducted. To assist them in this endeavor, the researcher assisted to adjust a foam covered chin rest for their comfort. To calibrate the system to the subject's eye, a nine-point calibration technique was used. Calibration points were dispersed throughout the viewing field for maximum accuracy. Subjects were instructed to sit as still as possible and avoid large head movements. (Figure 12)

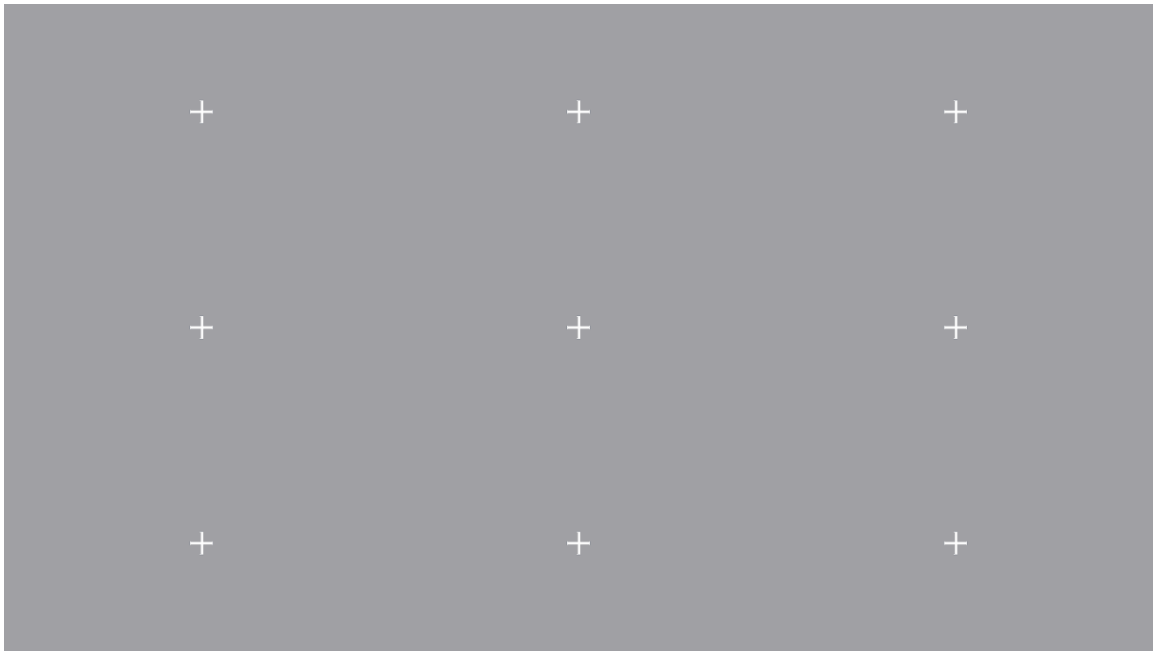


Figure 12 Nine-point calibration image

Once calibration was completed, a general instruction page was shown again to reiterate the task. By clicking the "Start" button, testing commenced. (Figure 13) The system captured stimulus presentation and eye movement data simultaneously. Subjects were able to spend as long (or as little) time as they wished answering the question for each of the 27 trials; as described previously, they could rotate to any of the six faces of

the package to access information that the labeling provided in order to make an informed decision regarding the drug/active ingredient being tested.

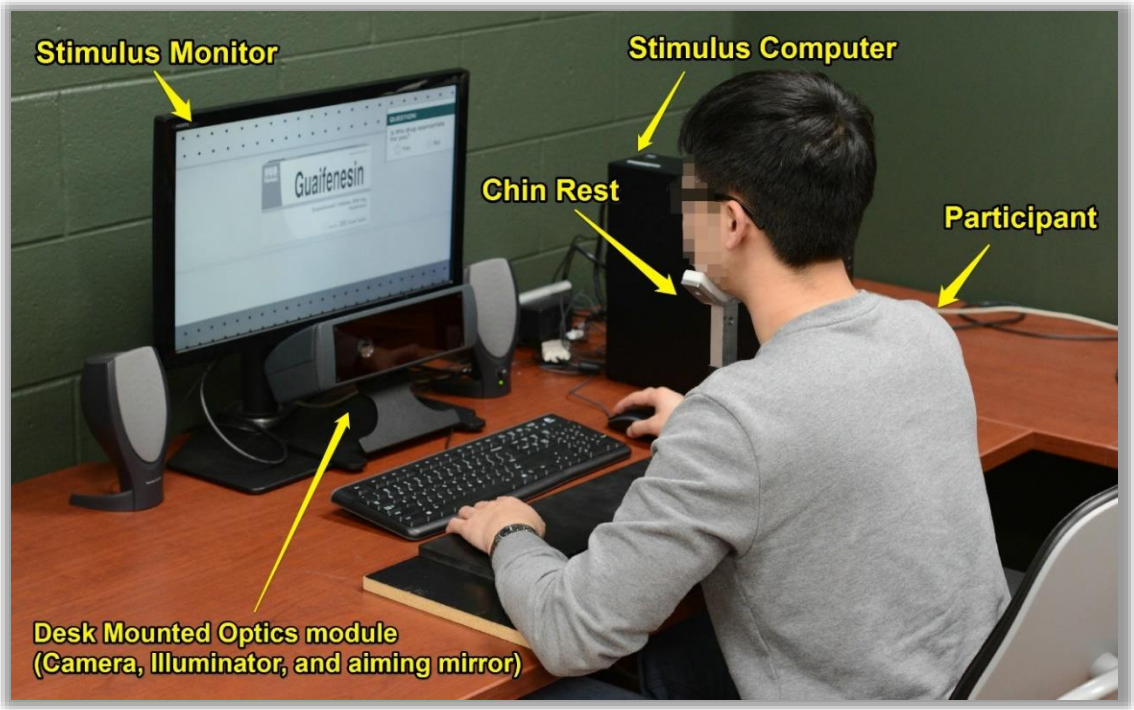


Figure 13 Testing with ASL EYE-TRAC 7 desk mounted optics eye tracking system

2.3.4 Post-test Survey:

After the eye tracking study was complete, subjects took part in a survey and guided interview.

2.3.4.1 Materials

- Post-test survey form (Appendix L)

2.3.4.2 Experimental Design and Testing Procedure

As shown in Appendix L, subjects were firstly asked to indicate all active ingredients that they recognized by circling those that they could remember from the eye tracking study. These were coded (post-hoc) in a binary fashion (correctly remembered or

correctly rejected vs. incorrect response). Following this, participants were shown a mock OTC label with typical information sections called out. They were asked to report (using a 1-5 Likert scale) how frequently they used each piece of information and how important the information was to them. They were also asked to record (for all active ingredients that were present in the study) whether or not they were familiar with each active ingredient prior to the study and whether (or not) each (of the nine active ingredients tested) was appropriate for them to take. Following this, participants were asked about medications they had taken within the past week (supported by the presence of the medications that they had brought with them) and a series of questions about their health status using a guided interview process.

2.3.5 Health History Interview

2.3.5.1 Materials

- Rx Label Scanner (Meditory Corporation, Dallas, TX)
- Health History Survey (Appendix M)

2.3.5.2 Testing Procedures

All the medications that the subjects brought (including prescription and OTC medications, herbal and vitamin supplements) were scanned and saved as digital images using Rx Label Scanner. (Appendix N) The Rx Label Scanner allowed quick and simple capture of label information and subsequent edit of the required label information. (Figure 14) Scanning of all medications was conducted while subjects were participating in the first two portions of the experiment.

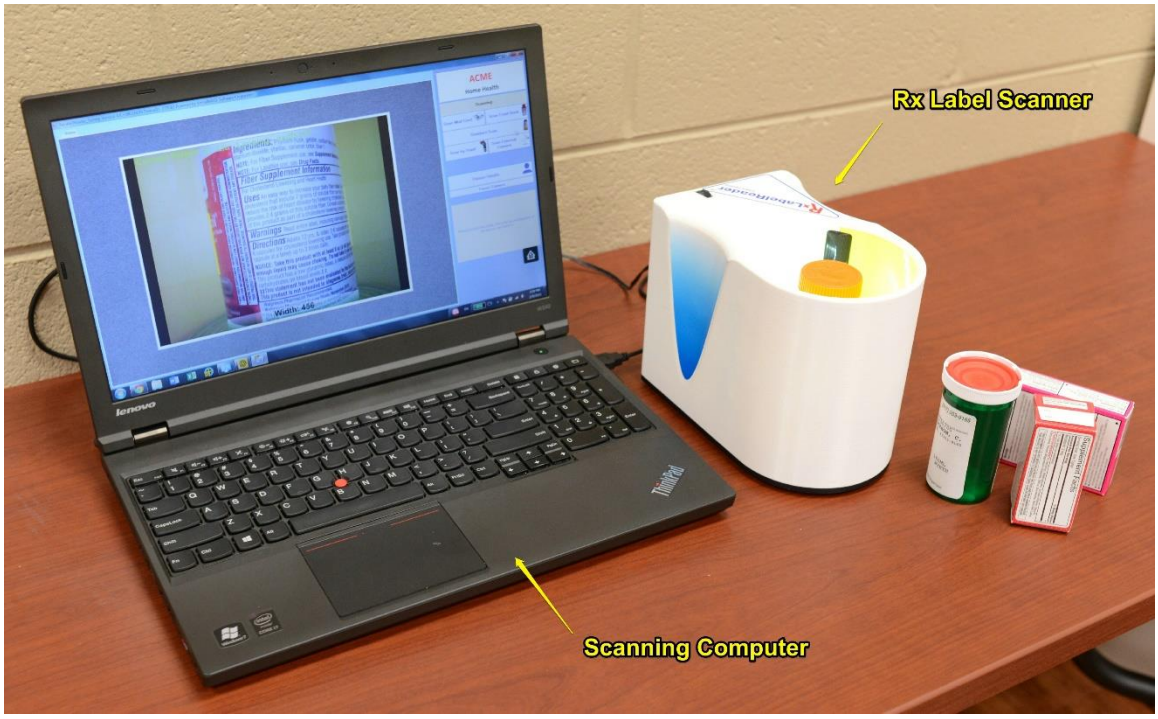


Figure 14 Rx Label Scanner system for health history survey

The Rx label scanning system was customized so that data was saved locally on a password protected laptop and the OCR software was set to obscure names and addresses on the prescription drug packaging. As a second check, researchers verified collected files as they were scanned and made adjustments to what the system had done so that no data that could be used to identify participants was present. Researchers used this information to populate the medication history form which was adapted from a form provided by a team of pharmacists' at University of Wisconsin (Appendix M). This information served as a basis for the guided interview which took place after the subjects were done with the eye tracking portion of the study.

During the guided interview, undergraduate researchers asked participants about how they took the medications (i.e. if they deviated from the instructions provided on the labeling) and use occasions. Participants were also questioned about any medications

that they took on a regular basis that they may have forgotten to bring using a series of prompts.

The purpose of this portion of the study was to gather information from the subjects about their health status and the types of medicines that they took. De-identified data regarding the items subjects brought and how they took them as well as their health histories were provided to pharmacists at University of Wisconsin. Based on the information provided by the participants (i.e. medications that were scanned and the health history that they reported in the survey and guided interview), pharmacists assessed whether (or not) an active ingredient was appropriate for the subject to take. Pharmacists' responses that were indicated to be a "no" were further characterized into five main reasons. Specifically, they were drug-drug interaction, drug-disease interaction, anticholinergic load, duplicate therapy and cognitive impairment (Table 7).

Table 7 Reasons for the negative assessments summarized by the pharmacists at University of Wisconsin

Reason name	**Description**
Drug-drug interaction (D-D or D)	One drug interacts with other drugs.
Drug-disease interaction (D-Dx or Dx)	One drug interacts with other diseases. Primary D-Dx are high blood pressure and asthma with Nonsteroidal anti-inflammatory drugs (NSAIDs).
Anticholinergic Load (ACL)	Usually with ranitidine and/or cimetidine based on other medications on the profile.
Duplicate therapy (Dup)	Duplicate drug class with a medication the patient is already taking. If the participant indicated frequency of use as 1 time per month or longer, the duplication will not be designated.
Cognitive impairment (Cog)	Interaction with cimetidine and age-related factors. It is designated > 70 year as the chronological value.

CHAPTER 3 DATA ANALYSIS AND RESULTS

3.1 Subject Demographics

3.1.1 Basic Information

A total of 82 adults (65 and older) were tested in the HUB research lab at the School of Packaging at Michigan State University during the fall semester 2014. The average age of participants was 74.2 years old (ranging from 65 to 91, median: 73.5). Figure 15 presents the age distribution of the test population.

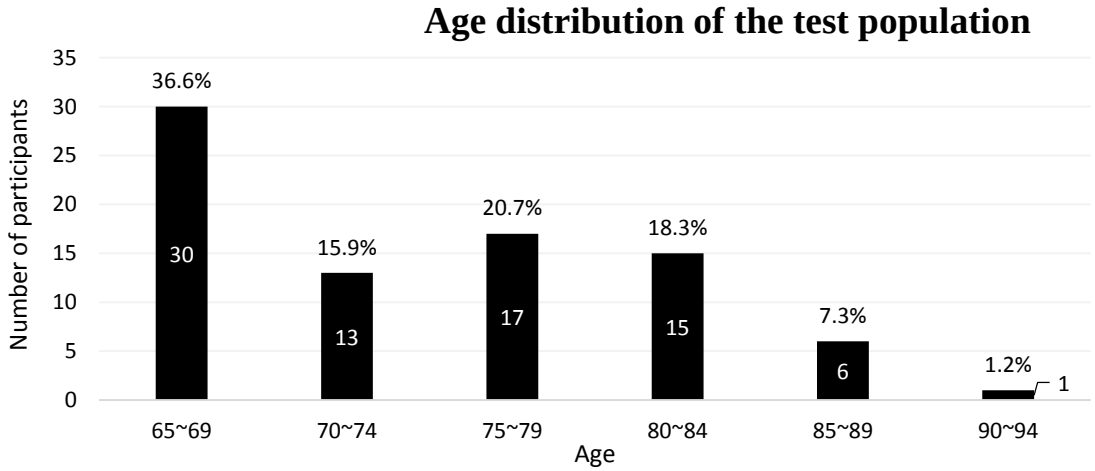


Figure 15 Age distribution of the test population

Of the 82 participants, 56 were female and 26 were male. Eighty participants spoke English as their native language. More complete demographic characterization of the test population is depicted in Figure 16.

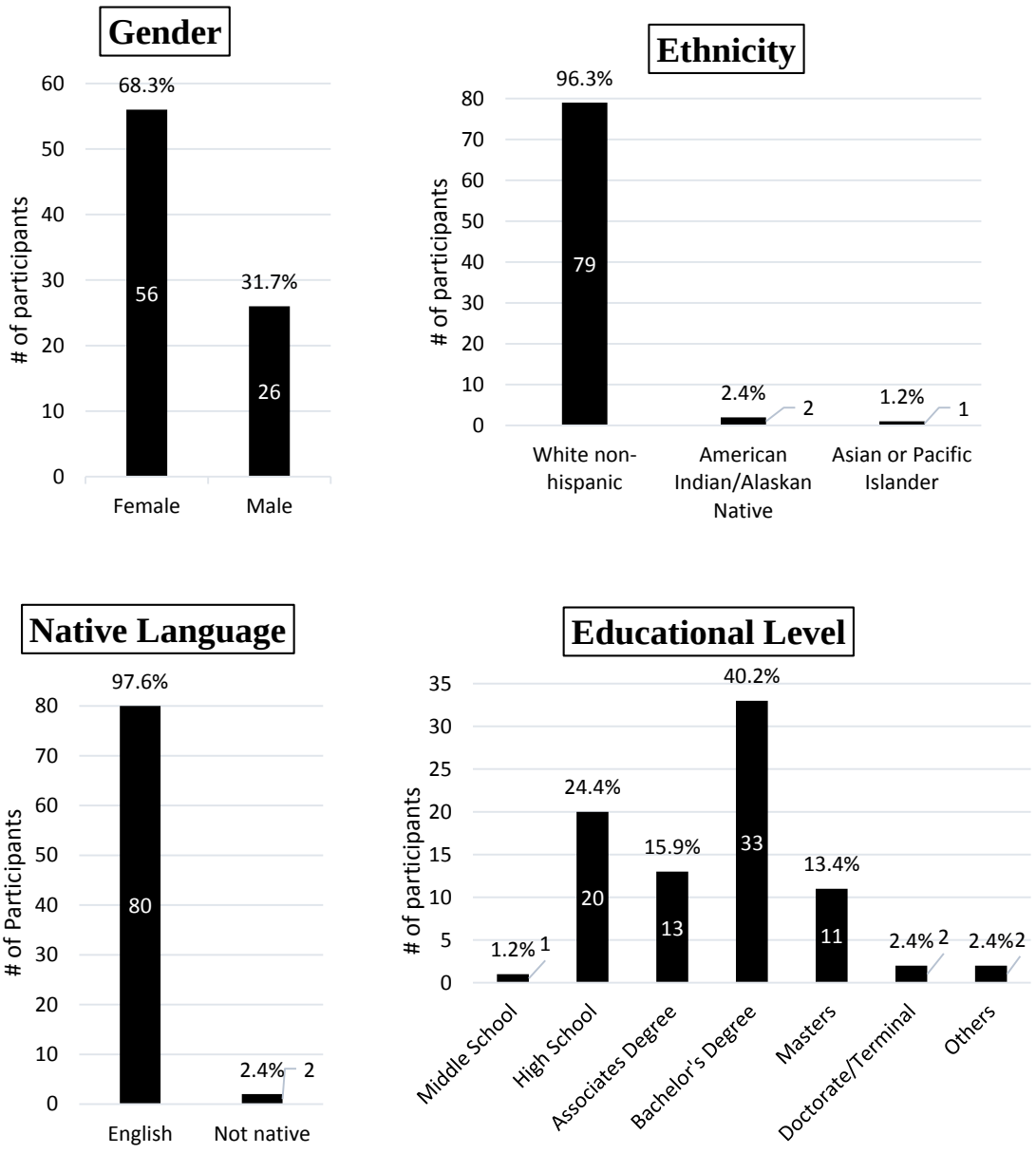


Figure 16 Demographics information (percentage and frequency) of participants by gender, ethnicity, native language and education (highest level achieved)

Pre-tests regarding visual acuity and health literacy were conducted prior to the main experiments. Results are presented in Figure 17.

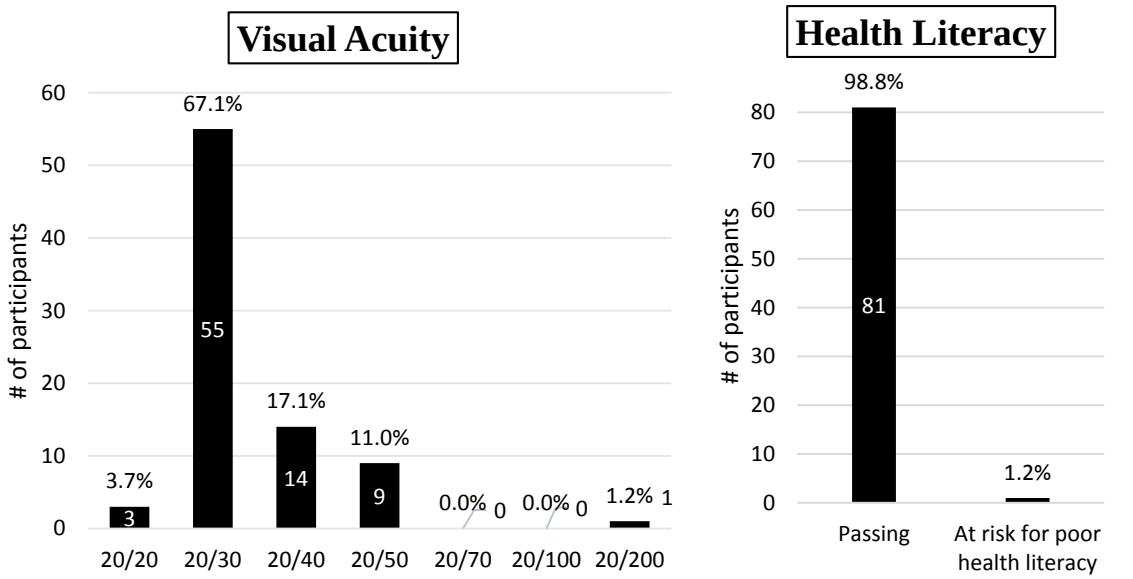


Figure 17 Subject characteristics (percentage and frequency) for visual acuity and health literacy

Despite the fact that 21 participants (25.6%) reported a High School Diploma or less as the highest level of education that they had achieved, overall, the participant population performed very well on the REALM-R test of health literacy. In fact, only one participant (1.2% of the test population) was recorded as at risk for poor health literacy.

3.1.2 Medication Usage and Health History Information

To provide insight regarding potential drug-diagnosis interactions and drug-drug interactions, researchers further characterized the test population using the information gathered from the health history, medication scans and the guided interview process. Participants were asked to bring any medicines which they took on an as-needed basis or regular schedule within one week before testing date. The vast majority of test participants brought at least one prescription medication (77 of 82; 93.9%), OTC medication (80 of 82; 97.6%), or vitamin preparation (71 of 82; 86.6%), indicating that

they take them on either a scheduled or as-needed basis (Figure 18). Additionally, 37 (45.1%) of the study population brought at least one herbal supplement to testing.

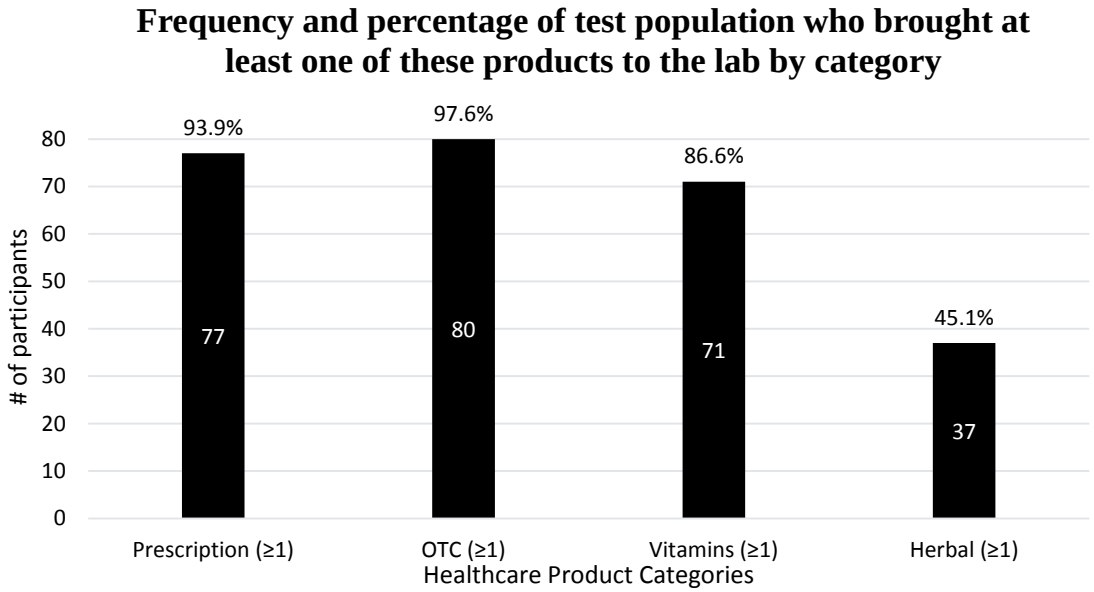


Figure 18 Frequency and percentage of test population who brought at least one of these products to the lab by category.

Participants were directed to bring products from these categories that they recently took, either on a scheduled or as-needed basis. The number of unique products within a product grouping (prescription, OTC, vitamins or herbal supplements) that participants brought was also recorded and analyzed. Forty-three participants (52.4%) brought 5 or more unique prescriptions, while 34 (41.5%) brought 5 or more OTCs, 14 (17.1%) brought five or more vitamins, and 6 (7.3%) brought five or more herbal products. More details are summarized in Figure 19.

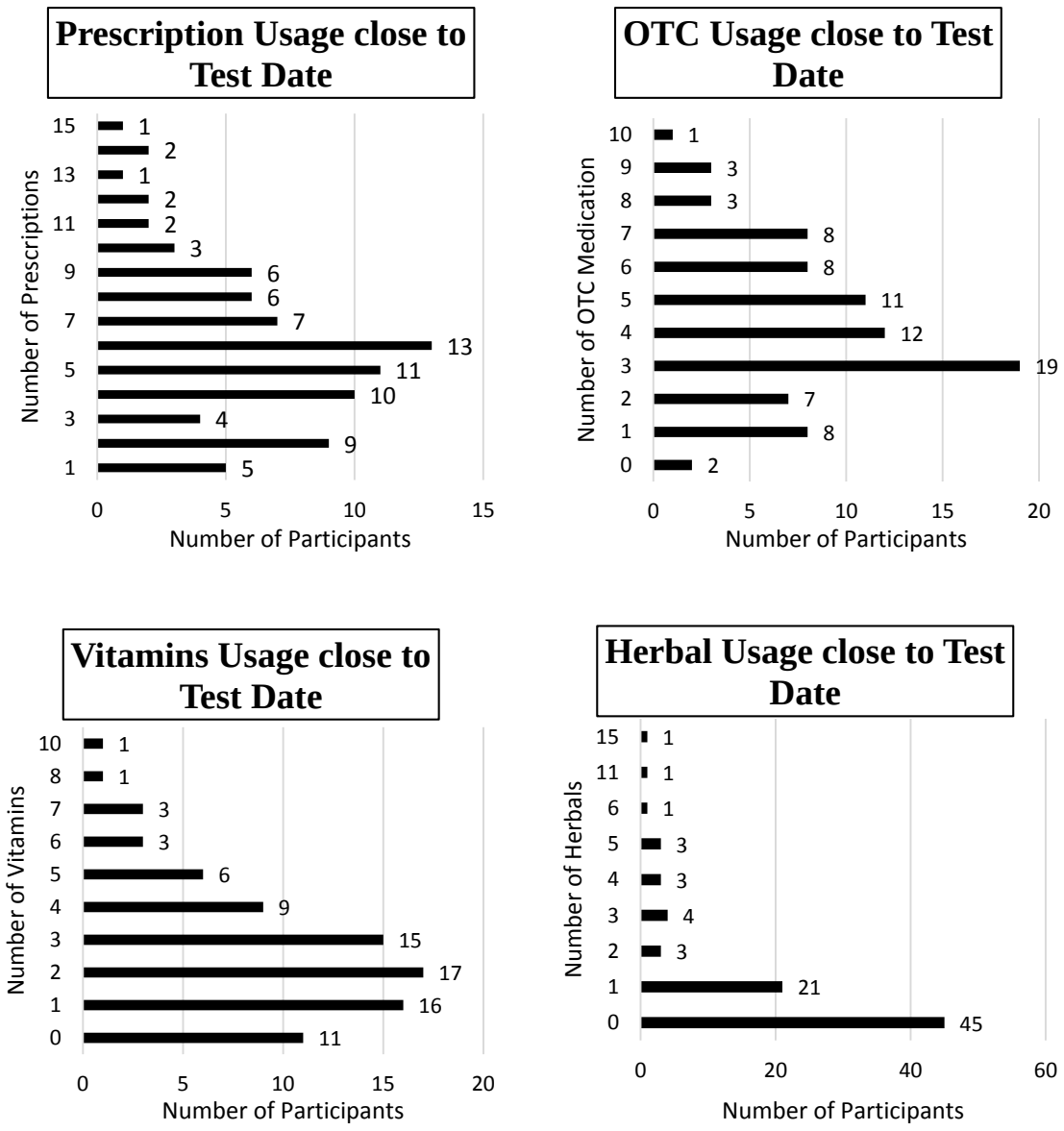


Figure 19 Numbers of each type of the healthcare products taken by participants on scheduled or as needed basis within one week before their test date

3.2 Statistical Methods, Data Analysis and Results

3.2.1 Data Analysis for Objective 1:

- ***Objective 1:*** *To begin to garner insights regarding the proportion of subjects who examine beyond the PDP for more information during OTC selection.*

Data from both Experiments 1 and 2 can be used to investigate Objective 1. For both experiments, subjects were asked to assess whether (or not) a given product was appropriate for them while viewing various OTC packages (commercially available packages in Experiment 1 and 3D renderings of novel brands created for Experiment 2). In the first experiment, where subjects interacted with actual packages, the researcher recorded, in binary fashion, whether or not participants turned the package beyond the PDP, by both observing their behaviors during the test and reviewing videos (post-hoc). Similarly, during the eye tracking portion of the study (Experiment 2), the researchers analyzed the "click path" recorded by the Unity 3D software as a record of whether or not each subject turned beyond the PDP during each of their 27 trials.

In the Experiment 1, three sets of store-brand OTC medicines were shown to participants set by set. (See more details about experiment procedures in 3.3.2 Experiment 1). In each set, if the subjects turned *any package* from the PDP to another panel for more information, the response for the set was recorded as "yes", otherwise "no" was recorded. The frequencies of the number of sets recorded as "yes" is described in Figure 20. Just over half of the participants (43; 51.8%) never looked beyond the PDP for any package in any set that they examined when assessing the appropriateness of the products in the sets. By contrast, a relatively small proportion of the test population, 12 participants (14.5%), looked beyond the PDP for at least one package in every single set of the three that they were shown.

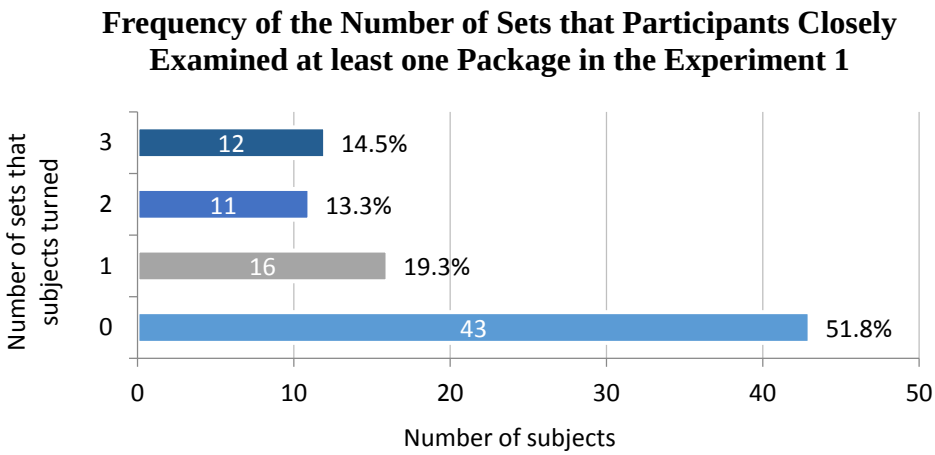


Figure 20 Frequency of the number of sets that participants closely examined at least one package in the Experiment 1

In Experiment 2, the same 82 participants were each presented 27 3D renderings of different OTC medications in random order, and asked to decide whether or not the medicines were appropriate for them to take. (See more details about experiment procedures in the Method chapter). In each trial, if the subjects clicked any panels other than the PDPs (PDPs were shown in shelf, front and top views), "Yes" was recorded, otherwise "No." The frequency of "yes" (turned) responses are depicted in Figure 21. Fifty-one participants (62.2%) exclusively used the PDPs (i.e. they did not turn to another panel during *any* trials) during Experiment 2. Only 7 participants (8.5%) turned each package beyond the PDP views for every single trial, and a total of 20 participants (24.4%) turned packages during 25 trials or more.

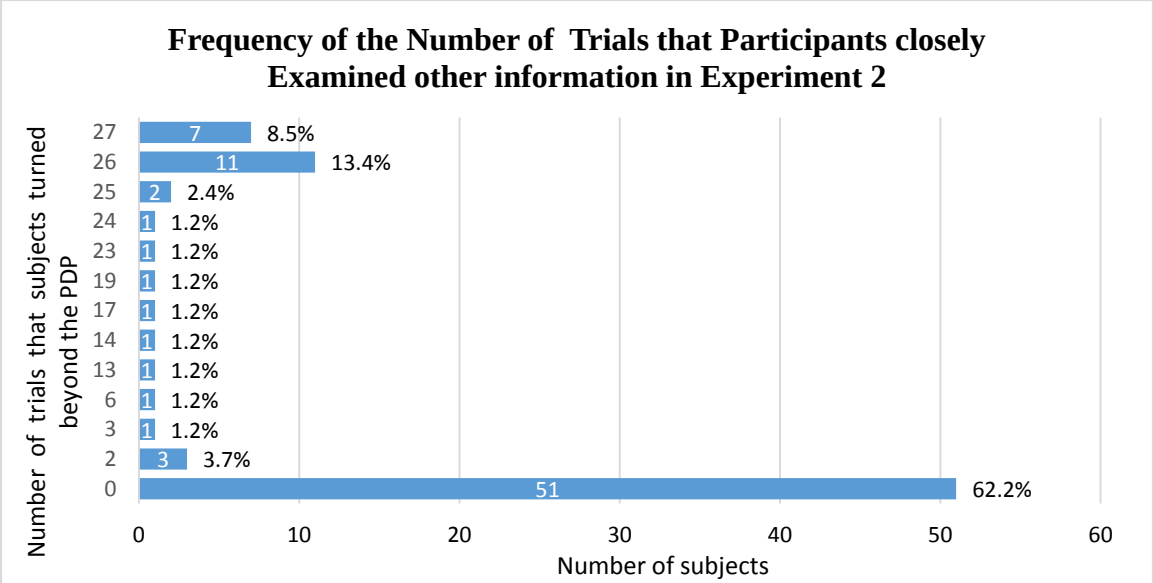


Figure 21 Frequency of the number of trials that participants closely examined packages in Experiment 2

It is worth noting that the proportion of subjects who focused solely on the PDP information exceeded 50% for both experiments, and 36.6% (30 out of 82) of the subjects never turned any package in both experiments. Our data is lower than data reported in the National APCO Insight Survey (PR Newswire, 2015). The survey indicates that 20% of participants (adults from the US) self-reported rereading OTC labels on the repeated use, while our data suggest a smaller percentage of study participants (14.5% in the Experiment 1 and 8.5% in the Experiment 2) turned packages beyond the PDP in every set (Experiment 1) or trial (Experiment 2).

3.2.1.1 Statistical Modeling Approach:

To analyze data from Experiment 1, two chi-square tests were conducted respectively to assess whether participants' educational level (above high school vs. high school or below), or gender (male vs. female), was associated with their viewing behavior (viewing at least one package in a set beyond the PDPs, vs. viewing only PDPs for all

packages). The Chi-square testing procedure of SPSS (Version 20, IBM SPSS Statistics, Armonk, NY) was used.

3.2.1.2 Data Analysis and Results:

Tests of statistical effects provided no evidence for any relationships between participants' viewing behaviors and their educational level ($\chi^2 = 0.129, df = 1, p = 0.720$) or gender ($\chi^2 = 0.555, df = 1, p = 0.456$).

3.2.2 Data Analysis for Objective 2 and Objective 3:

- ***Objective 2:*** *To quantify and compare the attention of older adults to specific information present on the Principal Display Panels (PDP) of OTC packages (brand name, active ingredient and symptom relief).*

- ***Objective 3:*** *To test the effect of information formatting on the attentive behaviors of older adults viewing OTC products (prominently featured information vs. less prominently featured).*

For the first ten subjects of the study, a chin rest was not used; large amounts of eye data were lost and, as a result, a chin rest was then employed for subjects 11-82. As such, useable data was obtained from the last 72 subjects, among which 50 were female and 22 were male. Figure 22 presents the age distribution of the population reported for eye tracking trials. Seventy participants spoke English as their native language. More complete demographic characterization of the test population is depicted in Figure 23.

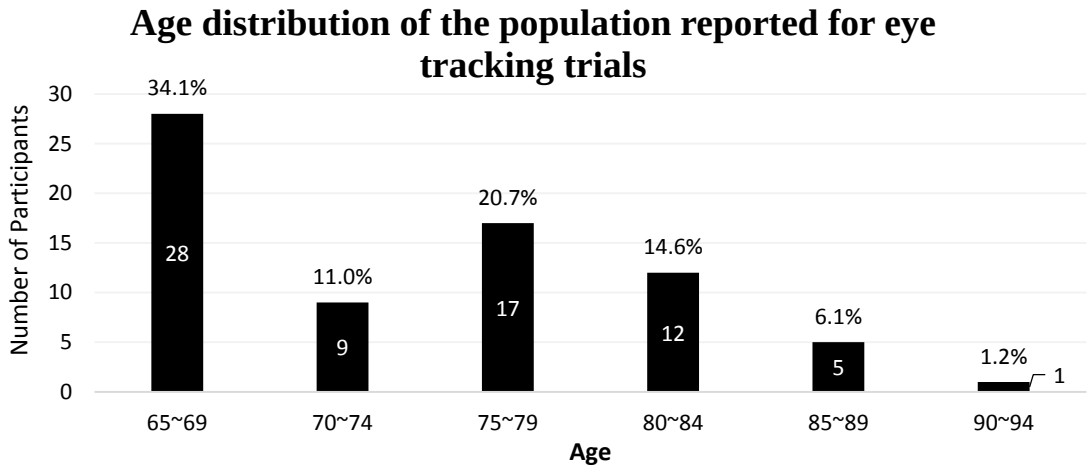


Figure 22 Age distribution of the population reported for eye tracking trials

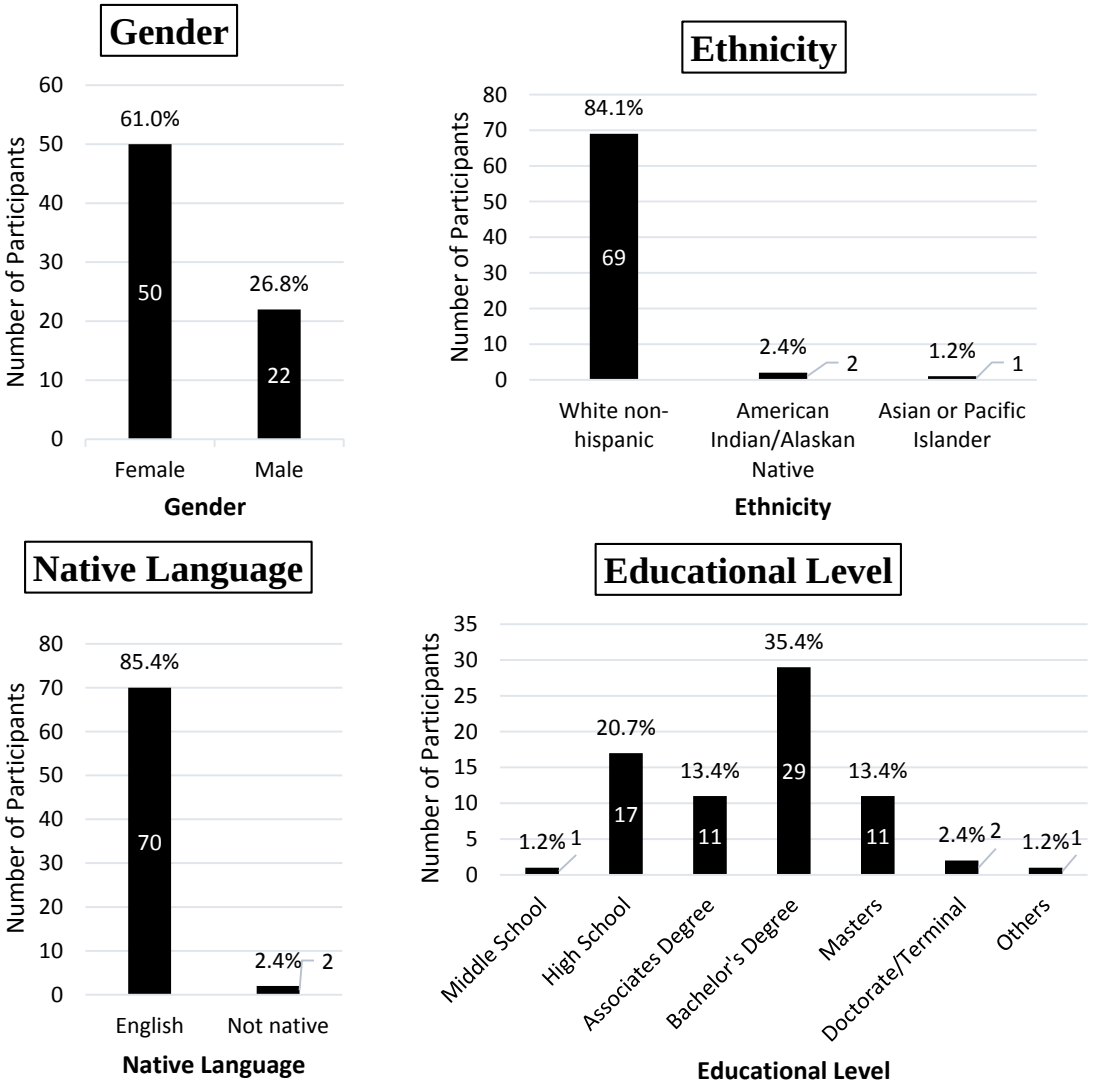


Figure 23 Demographics information (percentage and frequency) of participants by gender, ethnicity, native language and education (highest level achieved)

Pre-tests regarding visual acuity and health literacy were conducted prior to the main experiments. Results are presented in Figure 24.

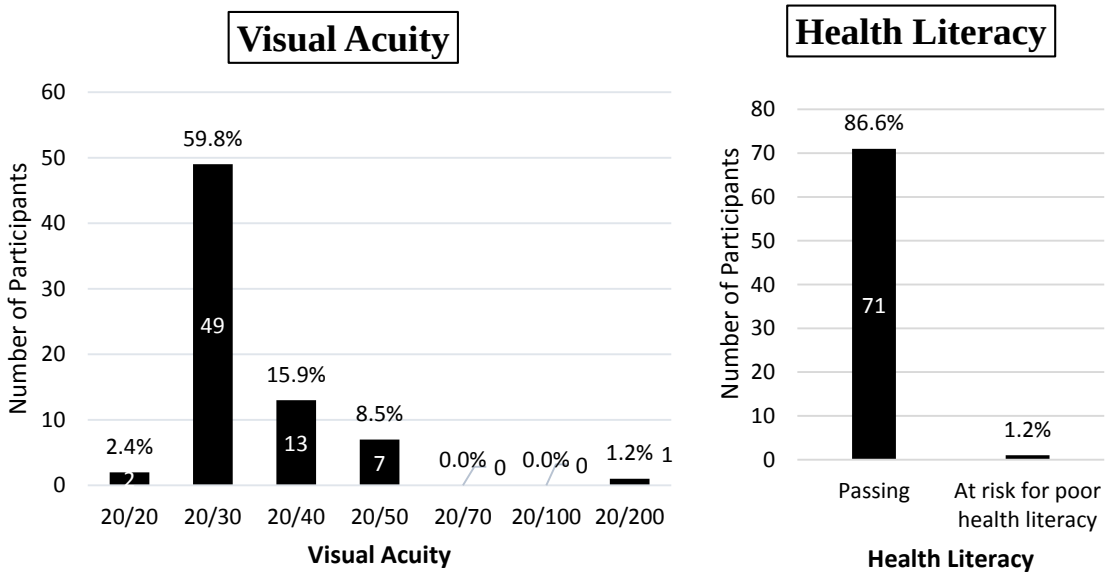


Figure 24 Subject characteristics (percentage and frequency) for visual acuity and health literacy

Possible demographic factors for inclusion in the model were: Native Language (English=70, other=2), Ethnicity (White=69, American Indian=2 and Asians=1), Health Literacy (Pass=71, Failure=1), and the outcomes of interest. Insufficient information was available to assess the relationship between a number of demographic factors, as such, only a subset of the factors were considered for further analysis. These included: gender, educational level and visual acuity.

To investigate Objectives 2 and 3, subjects' eye movement data while viewing the three PDP views (i.e. shelf view, front panel or top panel) were collected and analyzed. Dependent variables were analyzed (time on the information and whether or not a participant viewed the information) for three pieces of information (active ingredient, symptom relief and brand name) on PDPs (shelf, front and top). We used ASL Results

software to identify the coordinates where each of these pieces of information were drawn; these zones are referred to as "Areas of Interest (AOIs)" (see Figure 25). Data from an AOI containing one of the three pieces of information (symptom relief, active ingredient or brand name) were combined for three faces of the stimulus (shelf, front and top) to develop dependent variables for analysis (e.g. the time the participant spent in the AOI that contained a specific piece of information was added across the three views). AOIs were categorized as "prominent" (Area A) or "subordinate" (Areas B and C). The size and surface area of the AOI for Area A (the prominent area) was fixed, which meant that information within was resized to fit. In contrast, the size of the AOIs comprising Area B and Area C depended on the length of the information being presented. For all the AOI zones, zones were drawn such that they bounded half of the space between Area B and Area C without overlapping. Participants' attentive behaviors to the PDP were measured in the following ways:

- Probability of viewing or fixating a given AOI (which contained the information: active ingredient, symptom relief or brand name) on any of the PDP views possible for a given treatment (shelf, top or front; i.e., binary variable)
- Time spent on a specific AOI (which contained active ingredient, symptom relef or brand name) summed across all of the PDP views (shelf, top or front; i.e., a continuous variable)

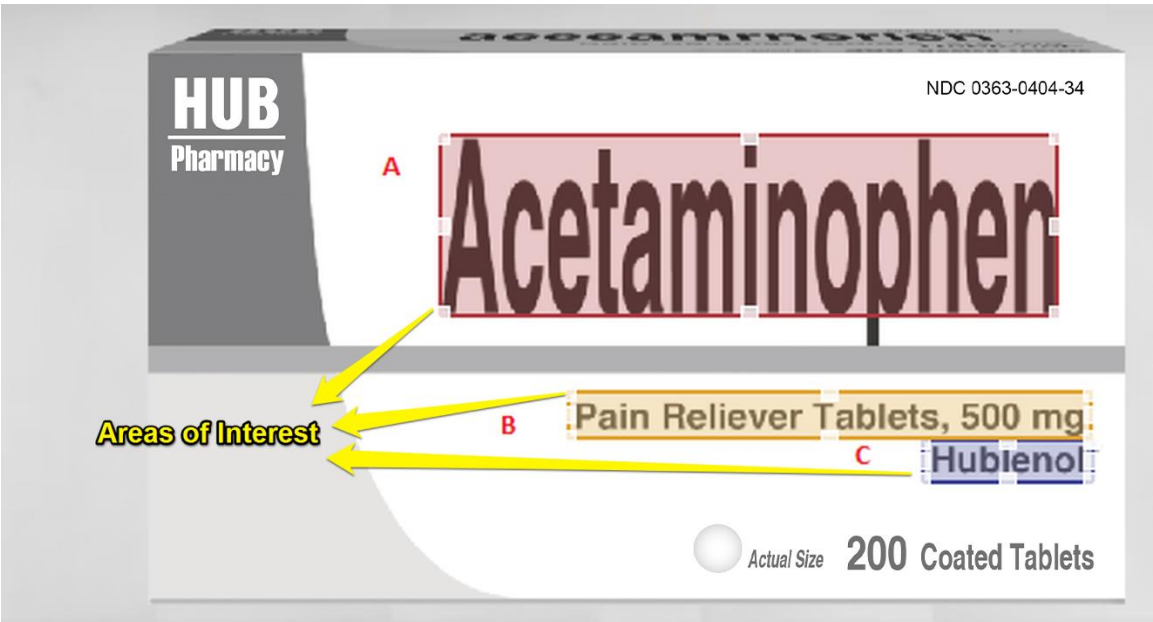


Figure 25 Illustration of the three Areas of Interest (AOIs); one prominent (Area A) and two subordinates (Areas B and C). Positioning of the information of interest (symptom relief, active ingredient and brand name) varied by trial in the Experiment 2

3.2.2.1 Probability of Fixating the PDPs

Each of the 72 subjects completed 27 trials (3 drug categories x 3 active ingredients x 3 AOIs). This made for a total of 1,944 trials reviewed in total (72 subjects x 27 trials). For all trials, the relevant dependent variable (binary; viewed yes/no and continuous; time in a given zone) was aggregated across the three PDPs (shelf, top and front) to arrive at the variable used in the analysis. In other words, for a given trial, if a subject fixated the symptom relief on any of the potential views (shelf, front or top), the information was coded as a "yes." For the continuous variable, time in zone, the time that they spent on a given area of interest (e.g. brand name) was summed for all three faces (shelf, front and top).

3.2.2.1.1 Statistical modeling approach:

A generalized linear mixed model was fitted to the binary response defined as whether a given piece of information was viewed ("fixated") or not using a Bernoulli distribution and a logit link function. The linear predictor in the model considered the fixed effects of drug category (i.e. acid reducer, pain reliever, cough and cold), active ingredient nested within drug category (3 active ingredients within each drug category), prominent information and area of interest (AOI) as well as all 2-way and 3-way interactions. Demographic variables, previously discussed, were also considered for model inclusion, but did not improve model fit or provide evidence for a significant association with the response and thus, were removed from the final model. The linear predictor also included the random effect of subject as an overall blocking factor. Other random effects were considered, including the blocking effect of package and its cross product with subject, but their variance components converged to zero and thus, they were removed from the model.

Over-dispersion was evaluated using the maximum-likelihood based fit statistic Pearson Chi-Square/DF. No evidence for over-dispersion was apparent. The final statistical model used for inference was fitted using residual pseudo-likelihood. Degrees of freedom for inference were estimates using Kenward-Roger's approach. The model was fitted using the GLIMMIX procedure of SAS (Version 9.4, SAS Institute, Cary, NC) implemented using Newton-Raphson with ridging as the optimization technique. Relevant pairwise comparisons were conducted using a Bonferroni adjustment to avoid inflation of Type I error rate due to multiple comparisons at the cell means level.

3.2.2.1.2 Data Analysis and Results:

The results provided evidence (P = 0.0103) for a 3-way interaction between **drug category, prominence and area of interest** on the probability that a given piece of information was viewed. Not unexpectedly, for all 3 drug categories, the prominent areas were the areas that were most likely to be fixated (P<0.05) in all cases, though the relative magnitude of the effect of prominence and information of interest varied across drug categories. Figure 26 provides the mean estimates on the probability of viewing each AOI when the differing pieces of information were in the prominent position.

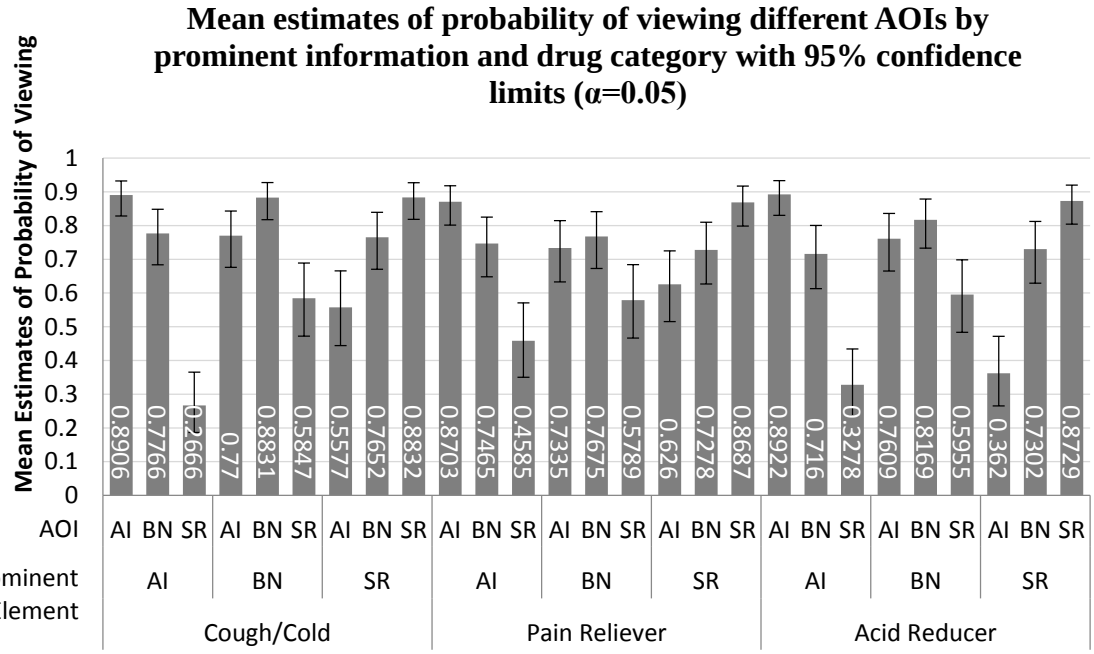


Figure 26 Mean estimates of probability of viewing different AOIs by prominent information and drug category with 95% confidence limits (α=0.05)

Pairwise comparisons have been conducted and presented to interpret the meaning of this three-way interaction. The following figures (Figure 27 to Figure 35) compare the least square means of the probability of fixating the AOI for treatments by the AOI prominence and drug category. The same data has been reorganized to be presented in three ways (figures #a, #b, #c) for each category.

- The **#a figures** present the pairwise comparisons among the probabilities of viewing the ***different*** information (AOIs for active ingredients, brand name ***and*** symptom relief) on PDPs of the ***same*** information is prominently featured. (e.g. Does a significant difference exist in the likelihood that symptom relief is viewed as compared to the likelihood that active ingredient will be viewed when brand name is prominently featured?)
- The **#b figures** present the pairwise comparisons among the probabilities of viewing the ***same*** information (AOIs for active ingredients, brand name ***or*** symptom relief) where ***different*** pieces of information are prominently featured. (e.g. Is the likelihood of viewing the active ingredient significantly affected by what is prominent (brand name, active ingredient or symptom relief?)
- The #c figure present all of the comparisons in one single figure; comparisons related to the **#a figures** are viewed ***vertically*** while those related to the **#b figures** are viewed ***horizontally***.

Pairwise comparisons were compared across the treatments within the category of cough and cold. As shown in the Figure 27 (#a), every comparison was found to be significant at $\alpha=0.01$. Information that was prominently featured was significantly more likely to be fixated than the other pieces of information in the same trial, regardless of what information it was.

For trials that had the active ingredient prominently featured within the cough and cold category, participants were the least likely to view symptom relief information (LSM=0.2666, UCL=0.3654, LCL=0.1866). Brand name was significantly more likely to be viewed (LSM=0.7766, UCL=0.8482, LCL=0.6838) than symptom relief, but less likely to be viewed than the active ingredient (LSM=0.8906, UCL=0.9321, LCL=0.8284), when active ingredient was prominently featured.

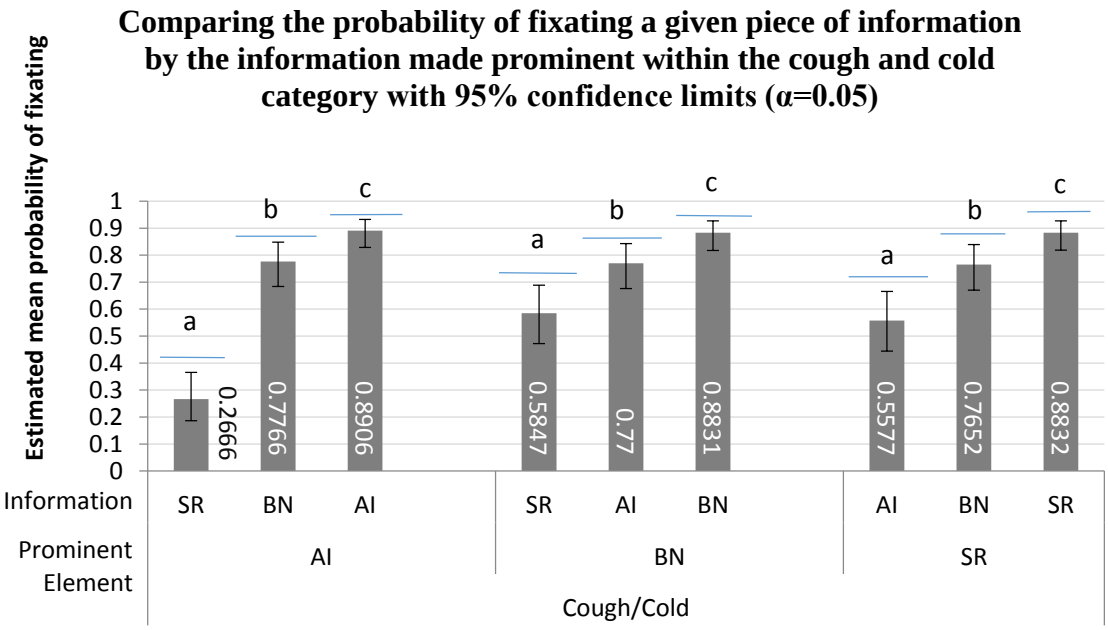


Figure 27 (#a) Comparing the probability of fixating a given piece of information by the information made prominent within the cough and cold category with 95% confidence limits (α=0.05)

As with the trials that prominently featured the active ingredient (within the cough and cold category), symptom relief was significantly less likely to be fixated (LSM=0.5847, UCL=0.6889, LCL=0.4722) in the trials that featured the brand name. Not surprisingly, brand name was the information that was significantly most likely to be fixated when it was featured LSM=0.8831, UCL=0.9273, LCL=0.8174) and active ingredient fell intermediate to the other two pieces of information (LSM=0.7700, UCL=0.8430, LCL=0.6761); that is, it was significantly more likely than the symptom relief and less likely than the brand name.

When symptom relief was prominently featured, it was the information most likely to be fixated (LSM=0.8832, UCL=0.9270, LCL=0.8183), with brand name intermediate (LSM=0.7652, UCL=0.8393, LCL=0.6703) and active ingredient significantly less likely than the other two (LSM=0.5577, UCL=0.6655, LCL=0.4442).

Where Figure 27 (#a) looked at comparisons regarding how the varied information performed when a specific piece of information was prominently displayed, we also examined how people viewed a specific piece of information when differing information was prominently displayed. To further explore the interaction, comparisons were also made regarding the likelihood of fixating a given piece of information when other pieces of information were prominent by drug category. Figure 28 (#b) compares the likelihood of a specific piece of information being viewed as what was prominently displayed changed.

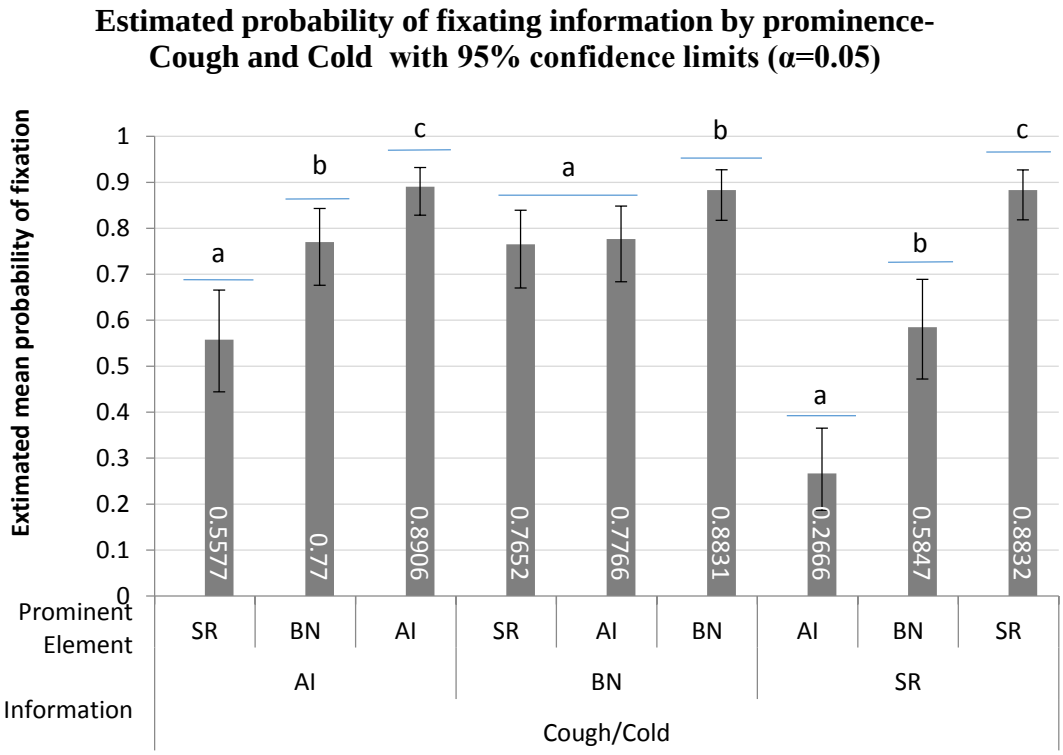


Figure 28 (#b) Estimated probability of fixating information by prominence-Cough and Cold with 95% confidence limits (α=0.05)

Generally speaking, the probability of viewing a specific piece of information significantly varied depending on what information was prominently displayed in the labels.

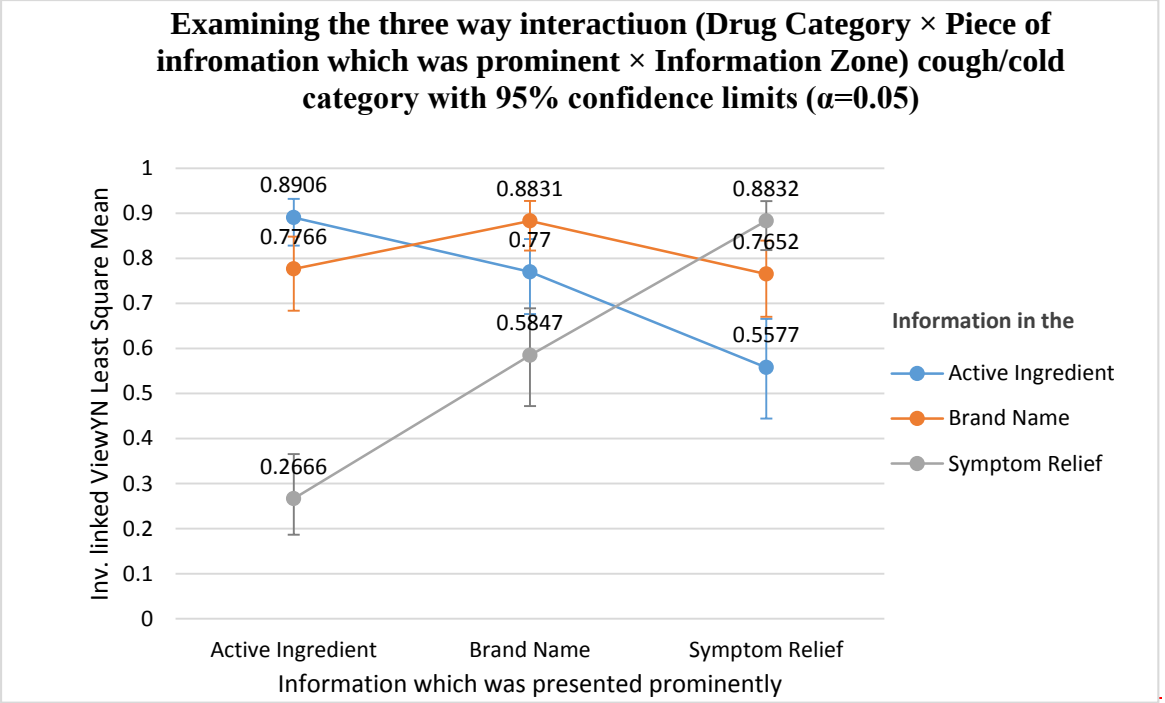


Figure 29 (#c) Examining the three way interaction (Drug Category × Piece of information which was prominent × Information Zone) cough/cold category with 95% confidence limits (α=0.05)

As with the cough and cold category, pairwise comparisons were conducted within trials that prominently featured a given piece of information (active ingredient, pain reliever, or symptom relief) for the pain relievers (Figure 30, #a). Just like the cough and cold products, *symptom relief was the least likely piece of information to be fixated unless it was prominently featured, in which case it was more likely to be fixated*. For treatments where the active ingredient was prominently featured, all pairwise comparisons were significantly different at α=0.01. There was no evidence of a difference in the likelihood of fixating either the active ingredient (LSM=0.6260, UCL=0.7250, LCL=0.5152) or the brand name (LSM=0.7278, UCL=0.8099, LCL=0.6265) when the symptom relief was prominently featured on the label. Additionally, when the brand name was prominently featured for the pain relieving

products (LSM=0.7675, UCL=0.8413, LCL=0.6727), the active ingredients was just as likely to be viewed (LSM=0.7335, UCL=0.8145, LCL=0.6330).

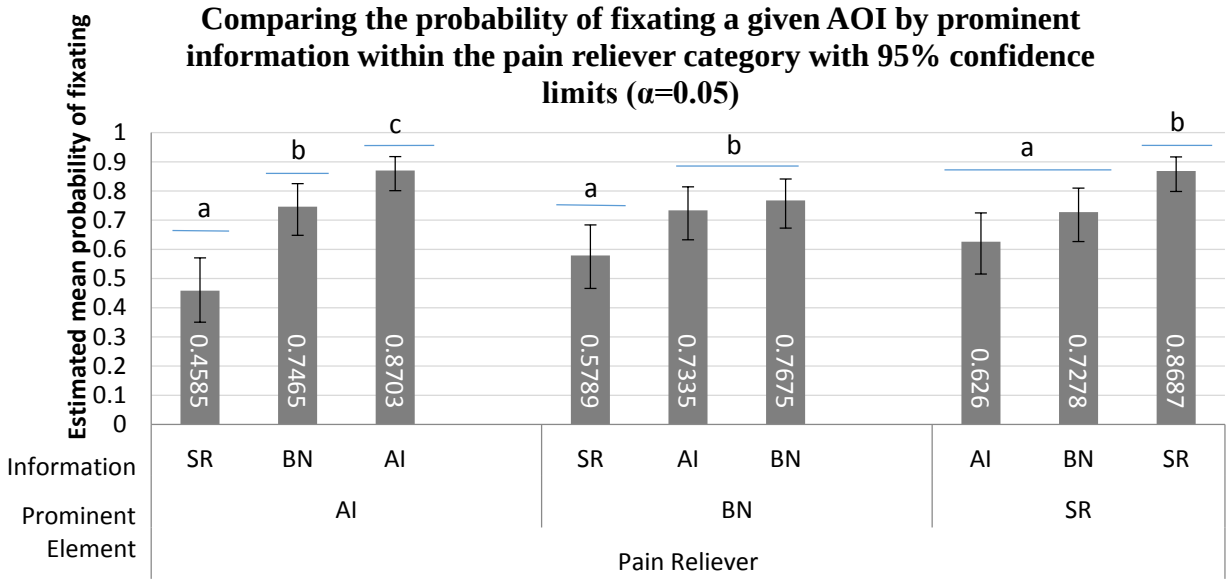


Figure 30 (#a) Comparing the probability of fixating a given AOI by prominent information within the pain reliever category with 95% confidence limits (α=0.05)

Pairwise comparisons were also conducted to look at how participants' probability of fixating specific information changed as a function of what was prominent within the pain reliever category. (Figure 31, #b) For the pain relievers, the information "brand name" behaved differently than the other two pieces of information. Specifically, there was no evidence for a statistical difference on the probability of fixating the brand name, regardless of the information that was prominently displayed. In other words, *people were as likely to fixate the brand name when active ingredient or symptom relief was prominently featured as they were when the brand name itself was prominent*. This was in contrast to the other two pieces of information, which were statistically significantly more likely to be seen when they were prominent than when the other two pieces of information were prominent.

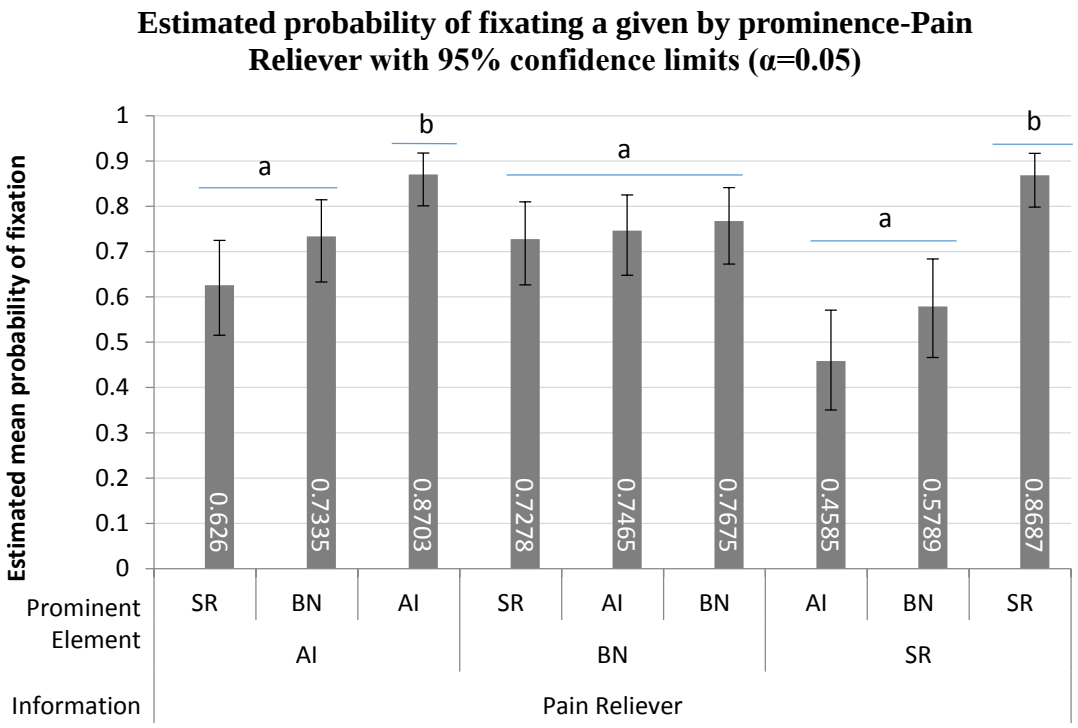


Figure 31 (#b) Estimated probability of fixating a given AOI by prominence-Pain Reliever with 95% confidence limits (α=0.05)

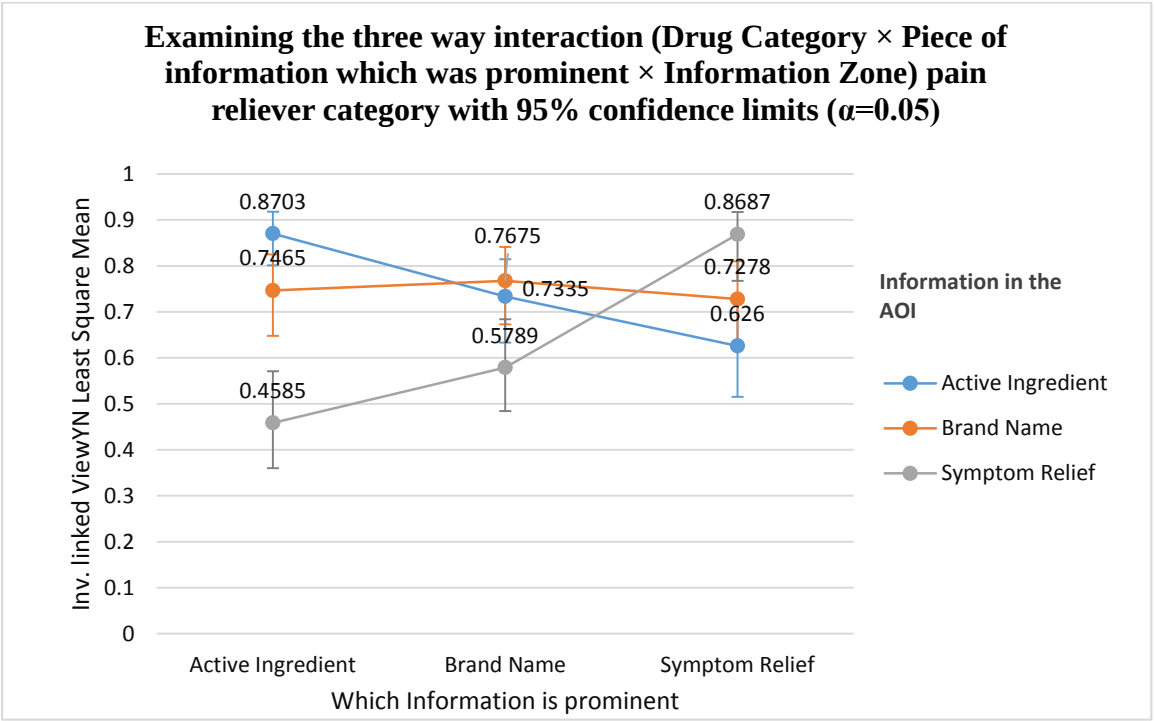


Figure 32 (#c) Examining the three way interaction (Drug Category × Piece of information which was prominent × Information Zone) pain reliever category with 95% confidence limits (α=0.05)

With the trials that involved acid reducers, symptom relief continued to be the least likely information to be fixated, unless it was presented prominently, at which point it was significantly more likely to be fixated than other information. (Figure 33, #a) Trials involving acid reducers followed a very similar pattern to that of the pain relievers when brand name was the information prominently featured. In the case of these trials, there was no evidence of a significant difference when the probability of fixating the active ingredients (LSM=0.7609, UCL=0.8360, LCL=0.6650) was compared with that of fixating the brand name (LSM=0.8169, UCL=0.8787, LCL=0.7331), with symptom relief significantly less likely to be fixated than either of the other two pieces of information (LSM=0.5955, UCL=0.6983, LCL=0.4836)

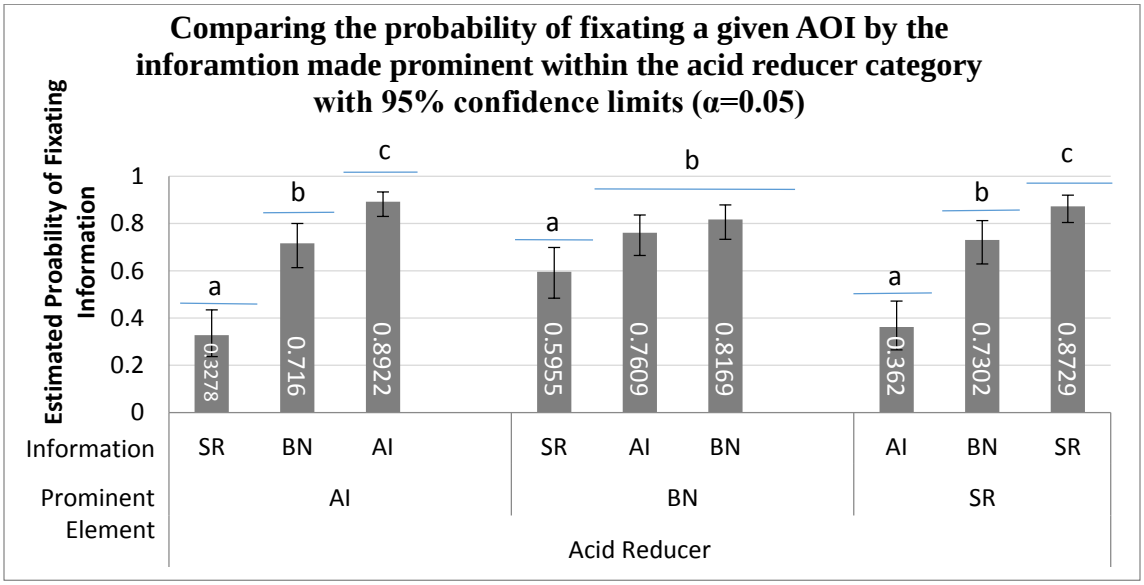


Figure 33 (#a) Comparing the probability of fixating a given AOI by the information made prominent within the acid reducer category with 95% confidence limits (α=0.05)

When considering how a particular piece of information performed within the acid reducer category of products when different pieces of information were prominently featured, brand name showed the same pattern that was evident in the pain relievers (Figure 34, #b). Both symptom relief and active ingredient were more likely to be

viewed when they were the featured piece of information than when another piece of information was prominently featured. *Acid reducers followed an identical pattern to the pain reliever category with regard to the performance of brand name; that is, its performance (the likelihood of it being viewed) was independent of the information prominently featured*.

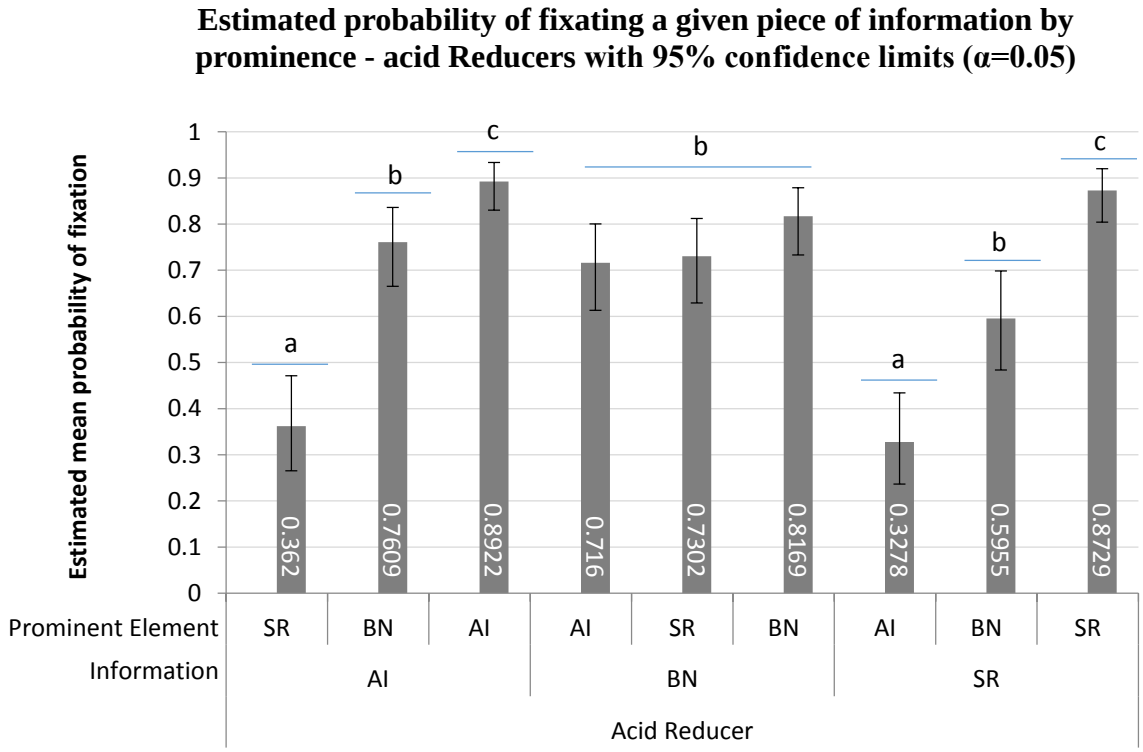


Figure 34 (#b) Estimated probability of fixating a given piece of information by prominence - acid reducer with 95% confidence limits (α=0.05)

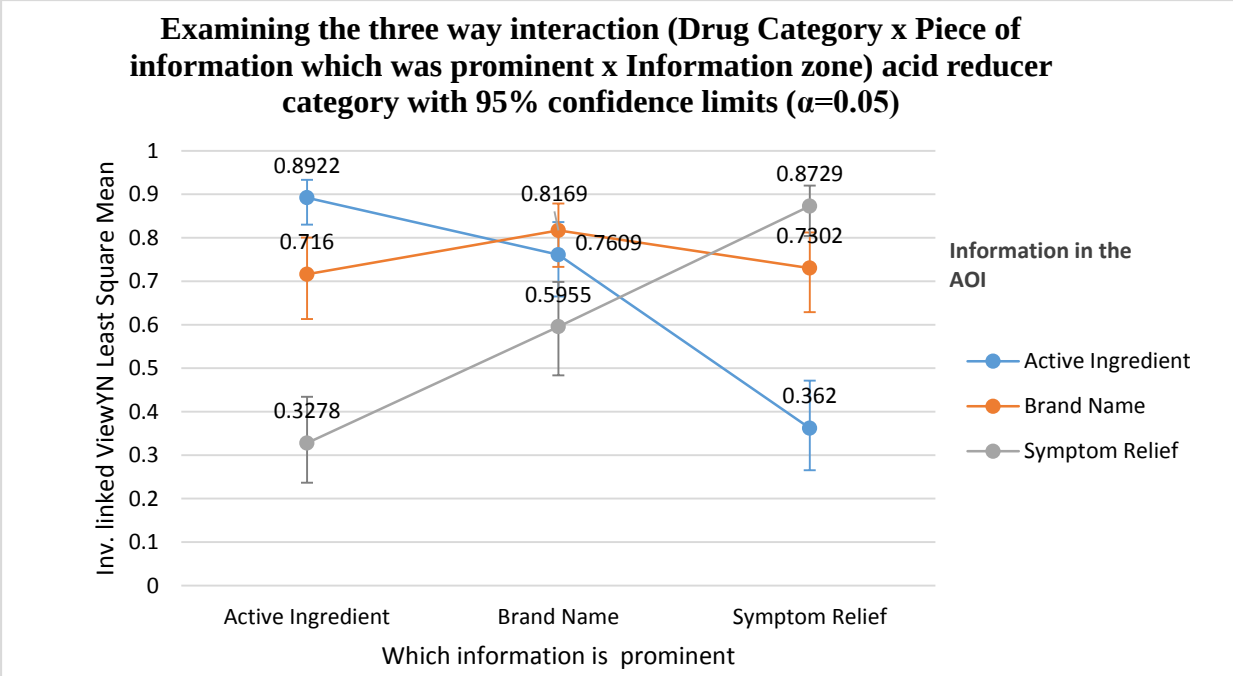


Figure 35 (#c) Examining the three way interaction (Drug Category x Piece of information which was prominent x Information zone) acid reducer category with 95% confidence limits (α=0.05)

No evidence was found for any differences between genders, ages, educational levels, visual acuity groups or familiarity group on the probability of viewing the PDPs, regardless of prominence and drug category (P>0.30).

3.2.2.2 Time spent on the PDPs

In addition to the probability of viewing a given piece of information, the time that participants spent on a particular piece of information was also used as a dependent variable for analysis.

3.2.2.2.1 Statistical modeling approach:

A general linear mixed model was fitted to the response total time spent on a given piece of information from the PDPs summed from all views where they were present (front, top and shelf). The response was expressed in the log transformed scale to stabilize variances. The linear predictor in the model included the fixed effects of drug

category (i.e. acid reducer, pain reliever, cough and cold), active ingredient nested within drug category (3 active ingredients within each drug category), information prominently featured and information within the AOI, or the information viewed (i.e. active ingredient, symptom relief or brand name), as well as all 2-way and 3-way interactions. Demographic variables, including gender, age, visual acuity group, educational level group and prior familiarity were also considered for model inclusion, though none seemed to help in explaining the behavior of the response (neither showed any evidence for a significant association with the response), and thus, were removed from the final model. The linear predictor also included the random effect of subject as an overall blocking factor. Other random effects were considered, including the blocking effect of package and its cross product with subject, but their variance components converged to zero and thus, they were removed from the model. Variance components were estimated using restricted maximum likelihood. Kenward Roger's method was used to estimate degrees of freedom and make the corresponding adjustments the in estimation of standard errors. Model assumptions were evaluated using externally studentized residuals and were considered to be reasonably met.

The model was fitted using the GLIMMIX procedure of SAS (Version 9.4, SAS Institute, Cary, NC) implemented using Newton-Raphson with ridging as the optimization technique. Estimated least square means ("EstimateOS") and 95% confidence intervals ("LCL_OS" and "UCL_OS") for each treatment are presented in the original scale following back-transformation. Relevant pairwise comparisons were conducted using Tukey-Kramer or Bonferroni adjustment, as appropriate, to avoid inflation of Type I error rate due to multiple comparisons.

3.2.2.2.2 Data analysis and results:

Main effects having to do with the participants, namely education level and prior familiarity were noted at α=0.01. Active ingredient (nested within category) also significantly affected the time that participants spent viewing labeling information. Further, the results provided evidence of a 3-way interaction between **drug category, prominence, and information in the AOI** on the time spent viewing specific information (active ingredient, symptom relief or brand name) (P = 0.0027).

Figure 36 explores the main effect of education. Pairwise comparisons of the data suggest *evidence for a significant difference in the viewing time spent by those who had some level of graduate school training (LSM=0.50384, UCL=0.60997, LCL=0.41617), as compared to those who had achieved a high school degree or less (LSM=0.67799, UCL=0.80147, LCL=0.57353).*

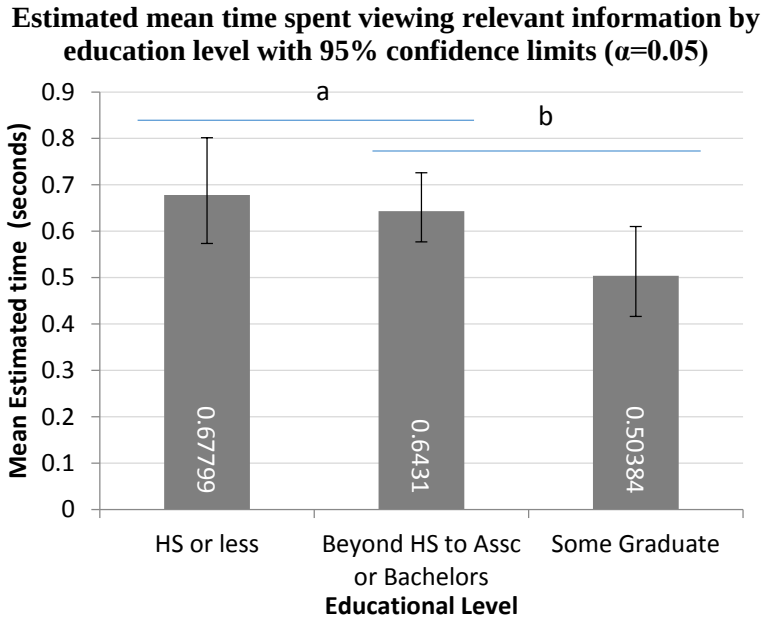


Figure 36 Estimated mean time spent viewing relevant information by education level with 95% confidence limits (α=0.05)

A significant main effect of prior familiarity was also noted on the time participants spent viewing information of relevance (active ingredient, symptom relief and active ingredient) (p=0.0244). (Figure 37) Specifically, *people spent significantly less time on the information of interest (active ingredient, brand name and symptom relief) for products containing active ingredients that they reported being familiar with (LSM=0.56817, UCL=0.63058, LCL=0.51194) than those that they were uncertain of (LSM=0.65181, UCL=0.73281, LCL=0.57976; P =0.0179).* For the products that contained active ingredients which they reported as unfamiliar prior to the study (LSM=0.59706, UCL=0.66083, LCL=0.53945), there was no evidence of any significant difference in time spent viewing information compared with those in the familiar category (P= 0.1666) or those which people were not sure about (P=0.4884).

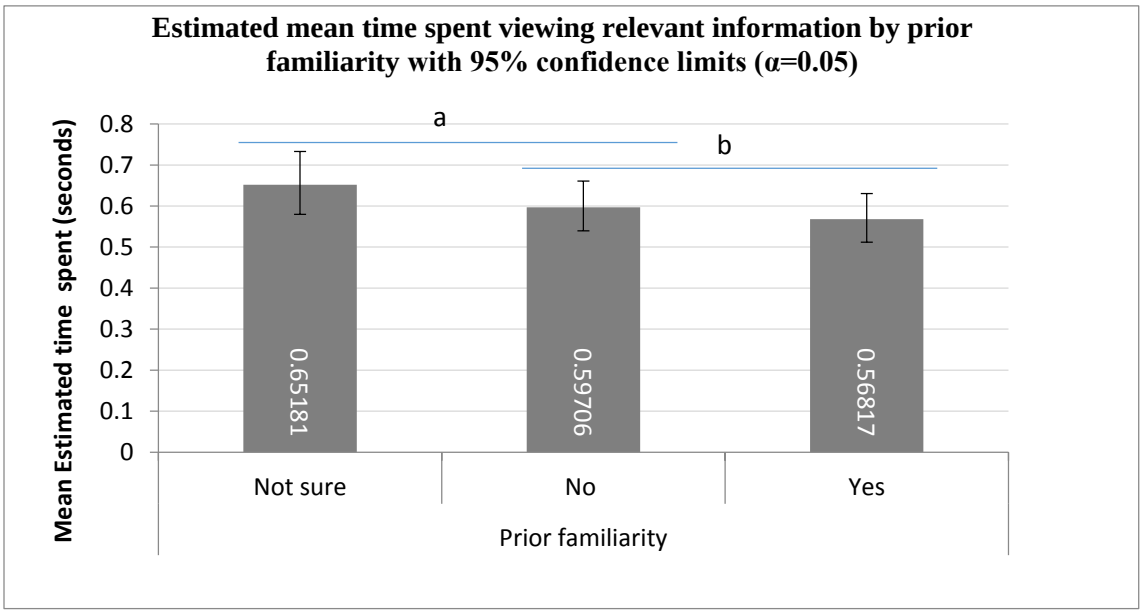


Figure 37 Estimated mean time spent viewing relevant information by prior familiarity with 95% confidence limits (α=0.05)

As mentioned previously, a 3-way interaction between drug category, prominence and AOI was indicated (P = 0.0027) when the time spent viewing specific information (active ingredient, symptom relief or brand name) was the resultant variable (Figure 38).

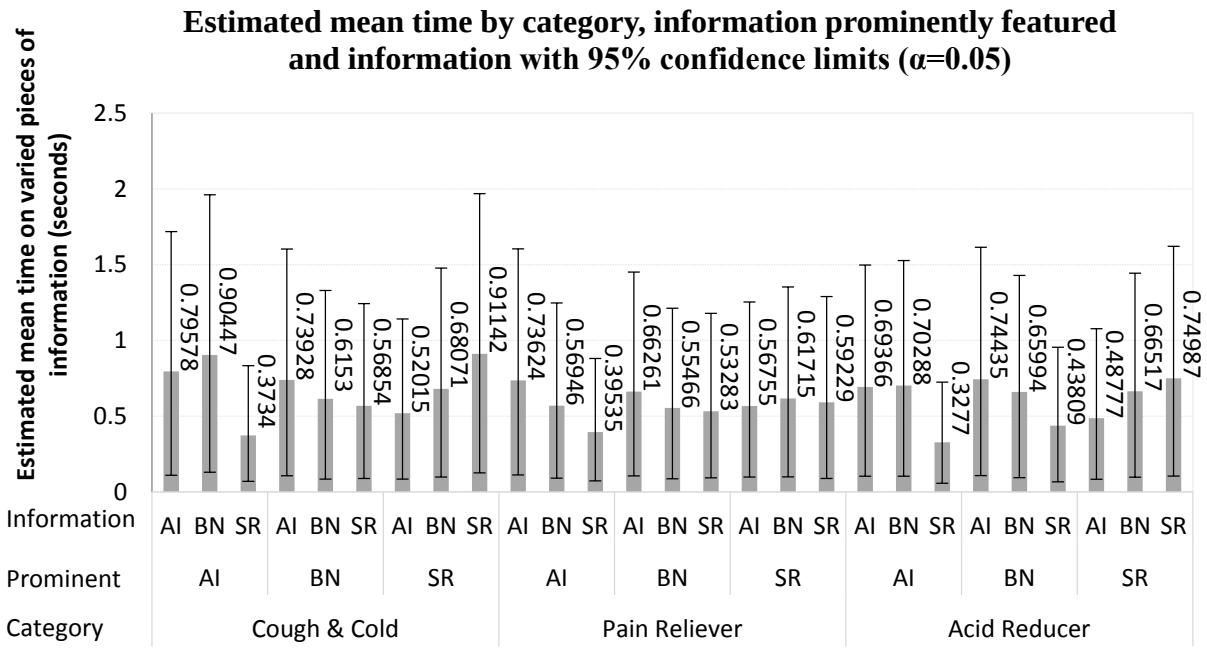


Figure 38 Estimated mean time by category, information prominently featured and information viewed with 95% confidence limits (α=0.05)

As with the previous dependent variable (probability of viewing a specific piece of information), the data was plotted in multiple ways to help explore and explain the complex, 3-way interaction. The following figures (Figure 39 to Figure 47) compare estimated least square means of total time spent on specific pieces of information viewed for packages with a given prominent element for each drug category.

Specifically, pairwise comparisons were conducted to characterize data in three ways:

- The **#a Figures** present how time was allocated to ***different pieces of information*** when the ***same*** information was prominently displayed. (e.g. How long did viewers spend on active ingredient compared to symptom relief when active ingredient was prominently featured information?).
- The **#b Figures** present how time devoted to a given piece of information (the ***same*** information*)* changed when ***different*** information was prominently featured in trials (e.g. How long was the active ingredient attended when it was prominent compared with how

much time was spent viewing it when symptom relief or brand name were prominently featured).

- The **#c Figures** present (within each drug category) all of these comparisons in a single graphic.

The analysis of the time spent on a given piece of information yielded a different pattern of results than the analysis of the probability of viewing a given piece of information. *With regard to the probability of viewing (discussed in the previous section), in every single case, the mean estimate of probability of viewing information was at its largest value for the information that was prominently featured.* In other words, a piece of information that was prominently featured was most likely to be viewed, though it was not always significantly more likely to be viewed relative to other pieces of information. When the dependent variable was the time spent viewing a piece of information, this was frequently not the case see Figure 39a- active ingredient and brand name; Figure 42a brand name and symptom relief; Figure 45a active ingredient and brand name). That is, participants did not show a consistent pattern of spending more time on the prominently featured information (though they had been more likely to view it).

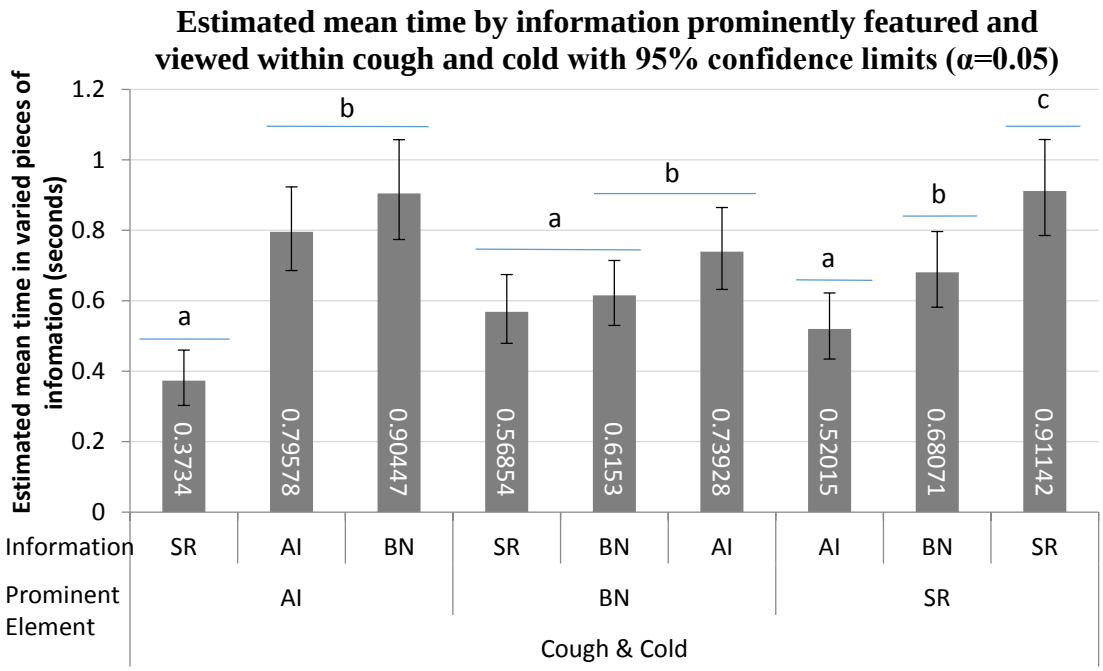


Figure 39 (#a) Estimated mean time by information prominently featured and viewed within cough and cold with 95% confidence limits (α=0.05)

Figure 39 (#a) examines how people's allocation of attention (as measured by time) to varied pieces of information changed when a given piece of information was prominently displayed. As was mentioned previously, just because a piece of information was prominently featured, it did not necessarily translate into participants spending significantly longer on the information than others we examined (See Figure 39, #a, Brand Name). Surprisingly, brand name was viewed for the longest period (in trials of cough and cold products) of time not when it was prominently featured, but when active ingredient was prominently featured (LSM= 0.90447, UCL= 1.05734, LCL= 0.77371) (Figure 39, #a). There was no evidence of a difference in the time spent viewing brand name when it was featured (LSM= 0.61530, UCL= 0.71428, LCL= 0.53003) compared with time spent on symptom relief (LSM= 0.68071, UCL= 0.79663, LCL= 0.58167 P=1.00) when branding information was prominently featured.

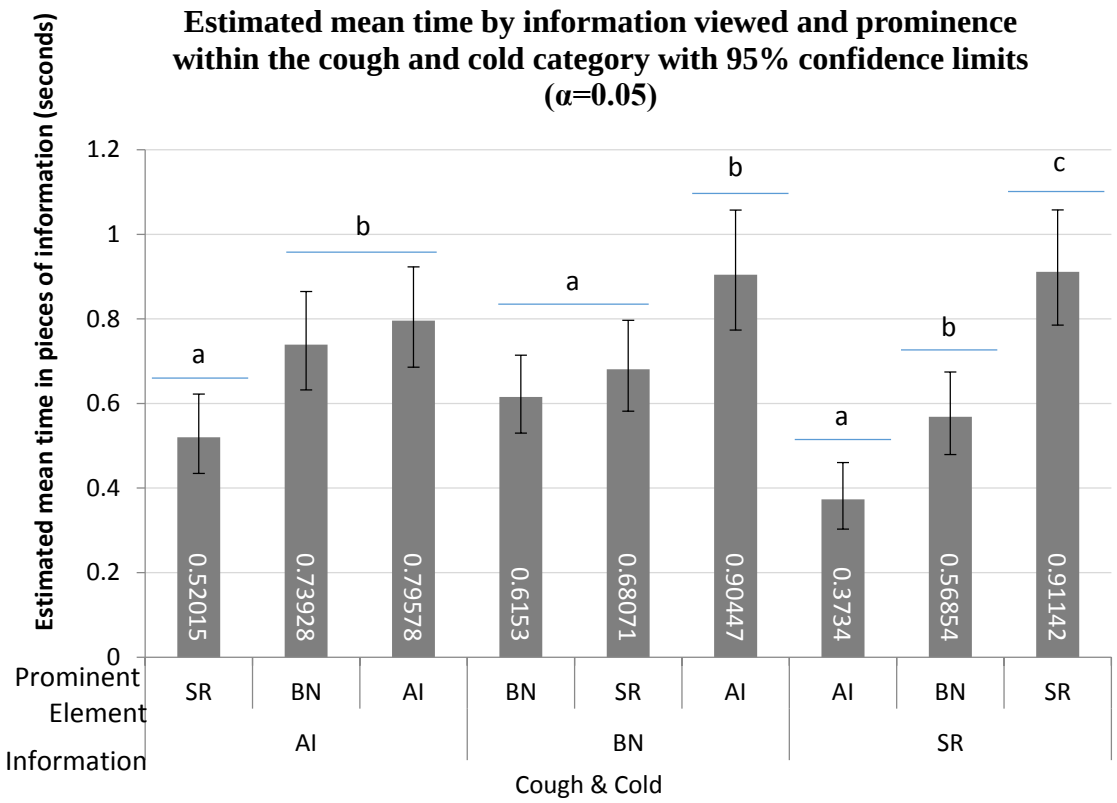


Figure 40 (#b) Estimated mean time by information viewed and prominence within the cough and cold category with 95% confidence limits (α=0.05)

While Figure 39 (#a) looked at comparisons regarding how much time was spent on different information when a specific piece of information was prominently displayed, we also examined how attention to a given piece of information within an AOI (as measured by time) varied as a function of the information that was prominently displayed (Figure 40, #b). In the case of active ingredient, there was no evidence of a difference in performance (time spent viewing) when it was prominently featured (LSM=0.79578, UCL=0.92318, LCL=0.68597) vs. when the brand name was prominently featured on cough and cold products (LSM=0.73928, UCL=0.86466, LCL=0.63207; P=1.00). However, when symptom relief was prominent, the AOI containing the information active ingredient was viewed for significantly less time (LSM=0.52015, UCL=0.62232,

LCL=0.4347) than it was when brand name was prominent (P=0.0019) or when the information itself (active ingredient) was prominent (P<0.0001).

Symptom relief was viewed for significantly longer than other information in treatments which prominently featured it (LSM= 0.91142, UCL= 1.05791, LCL= 0.78522); that is, symptom relief was viewed for less time when brand name was the prominently featured information (LSM= 0.56856, UCL= 0.67455, LCL= 0.47923 (P<0.0001)) and for the least amount of time (relative to the other two zones of interest) on treatments where the active ingredient was prominently featured on cough and cold products (LSM= 0.37340, UCL= 0.46014, LCL= 0.30302). Figure 41 (#c) provides all comparisons simultaneously.

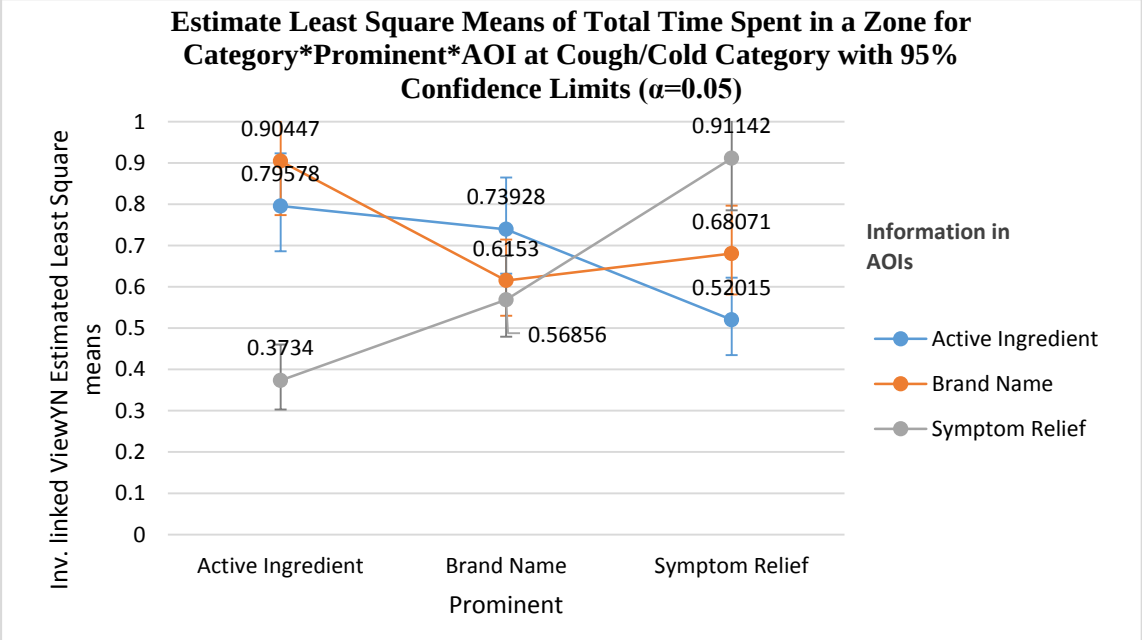


Figure 41 (#c) Estimated least square means of total time spent in a zone for Category*Prominent*AOI at cough/cold category with 95% confidence limits (α=0.05)

For the pain relievers, when brand name and symptom relief were prominently featured, there was no evidence of difference in the time spent on the varied AOIs (Figure 42, #a). For trials that prominently featured the active ingredient, participants spent

significantly longer on that information (LSM= 0.73624, UCL= 0.86820, LCL= 0.62434) than the brand name (LSM= 0.56946, UCL=0.67851, LCL= 0.47793) and significantly longer on the brand name than the symptom relief (LSM= 0.39535, UCL= 0.48555, LCL= 0.32191).

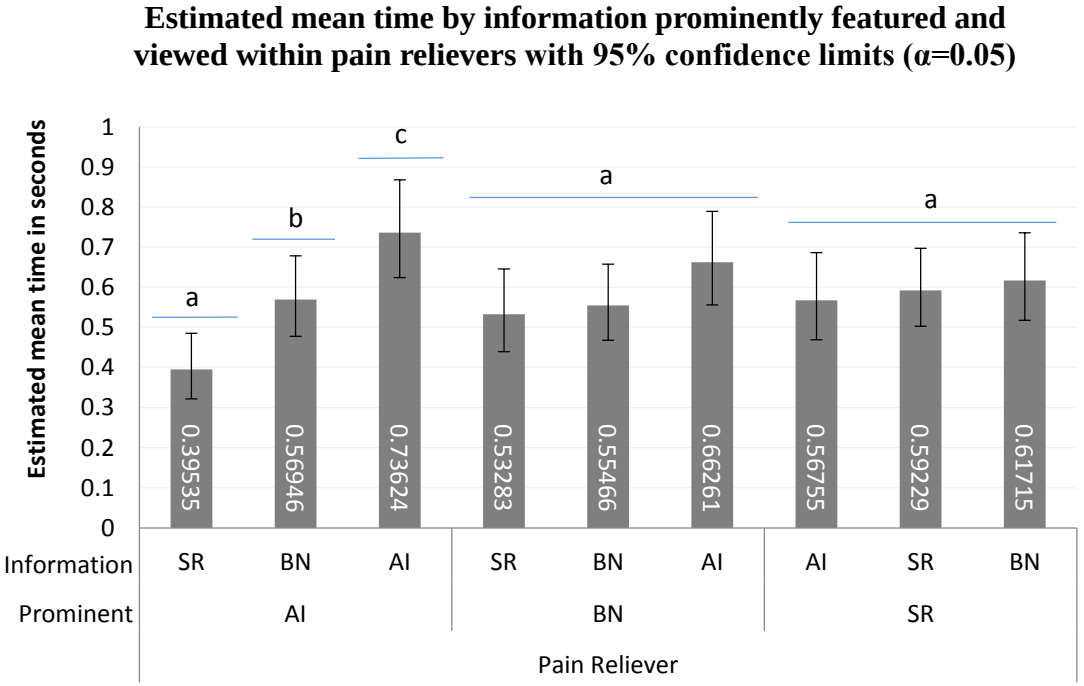


Figure 42 (#a) Estimated mean time by information prominently featured and viewed within pain reliever with 95% confidence limits (α=0.05)

For trials involving pain relieving products, people viewed the brand name and the active ingredient for the same amount of time (no evidence of statistical significance) regardless of the information that was prominently featured on the package. (Figure 43, #b) The amount of time participants spent viewing the AOI, symptom relief, was significantly impacted by the information that was prominently featured.

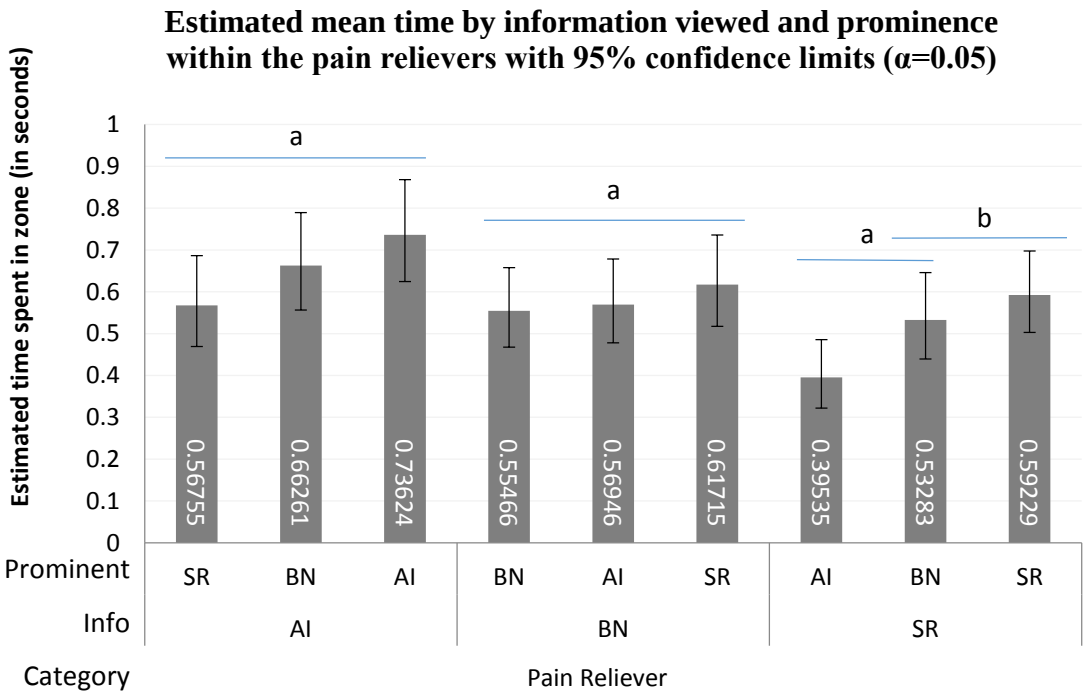


Figure 43 (#b) Estimated mean time by information viewed and prominence within the pain reliever with 95% confidence limits (α=0.05)

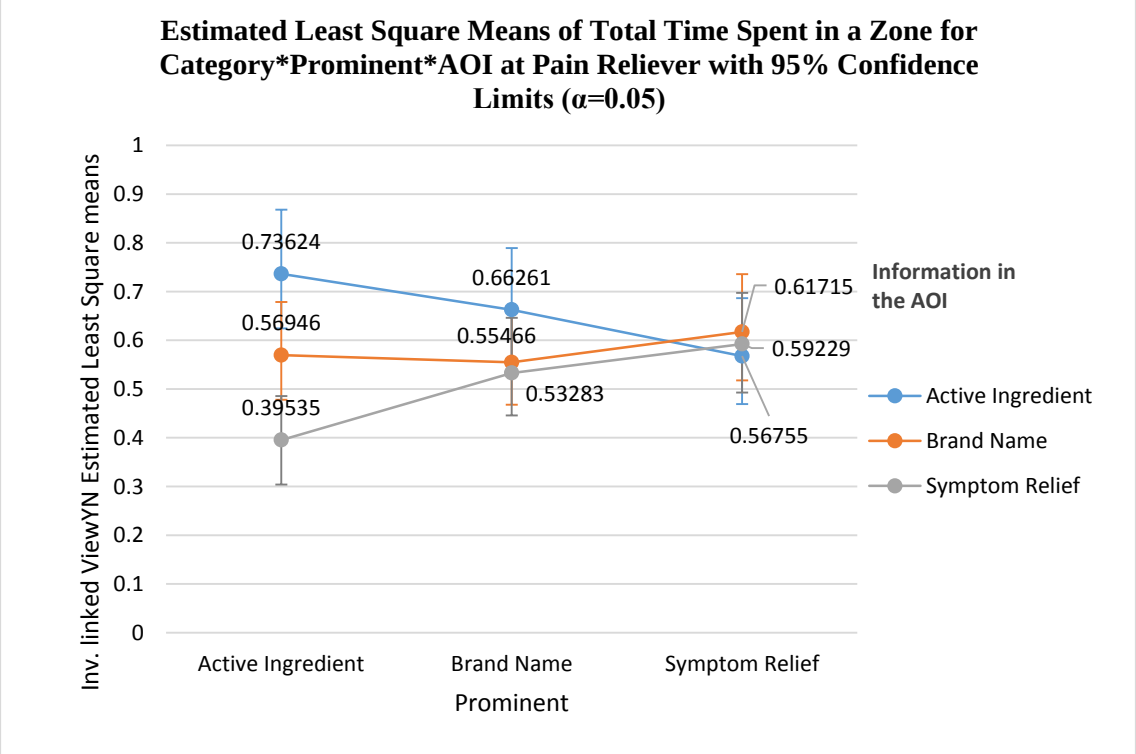


Figure 44 (#c) Estimated least square means of total time spent in a zone for Category*Prominent*AOI at pain reliever category with 95% confidence limits (α=0.05)

When the information, active ingredient, was prominently featured for trials that related to acid reducing products, the active ingredient (LSM= 0.69366, UCL= 0.80463, LCL= 0.59800) and the brand name (LSM= 0.70288, UCL= 0.82438, LCL= 0.59929) were attended significantly longer than the symptom relief (LSM= 0.32770, UCL= 0.39729, LCL= 0.27031) (both P<0.0001). (Figure 45, #a) For trials where the brand name was emphasized, the active ingredient (LSM= 0.74435, UCL= 0.87071, LCL= 0.63632) and the brand name (LSM= 0.65994, UCL= 0.76948, LCL= 0.56600) were again attended significantly longer than the symptom relief (LSM= 0.43809, UCL= 0.51746, LCL= 0.37089) (both P<0.0001). By contrast to all other trials, when symptom relief was emphasized, this information (P<0.0001) and brand name (LSM= 0.66517, UCL= 0.77896, LCL= 0.56801 P=0.0123) were viewed significantly longer than the active ingredient (LSM= 0.48777, UCL= 0.58975, LCL= 0.40342).

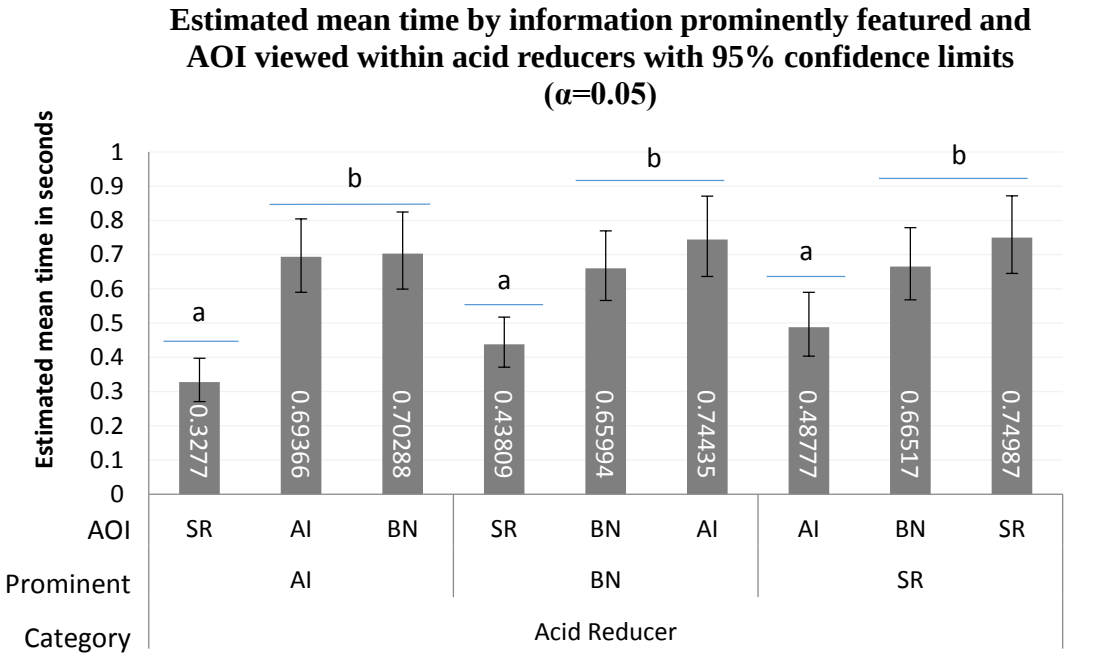


Figure 45 (#a) Estimated mean time by information prominently featured and AOI viewed within acid reducer with 95% confidence limits (α=0.05)

Time that participants spent attending to the brand name was not influenced by which information was prominently displayed for the acid reducers (Figure 46, #b) or pain reliever trials (Figure 43, #b). This type of relationship held for the active ingredient within the pain reliever category as well (i.e. time spent on the information was not affected by the formatting of the other information) (Figure 43, #b).

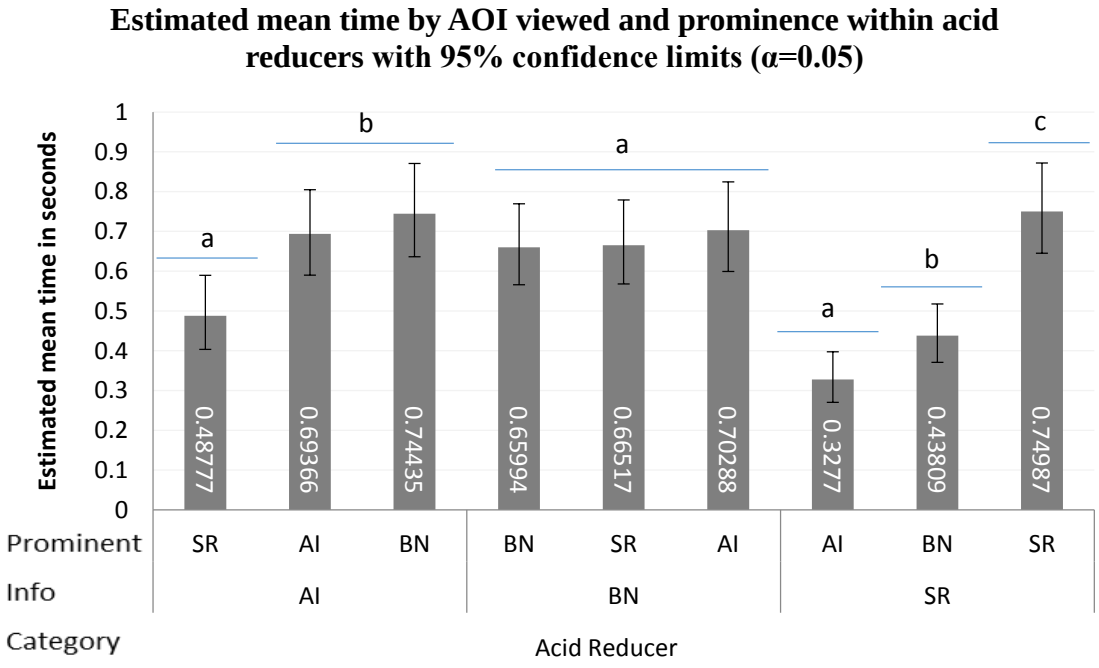


Figure 46 (#b) Estimated mean time by AOI viewed and prominence within the acid reducer with 95% confidence limits (α=0.05)

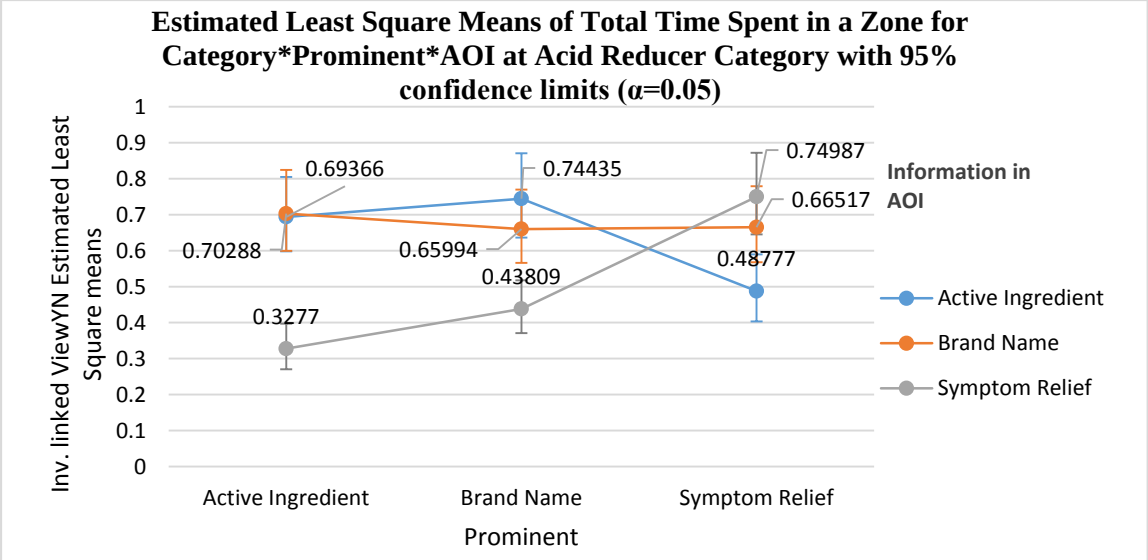


Figure 47 (#c) Estimated least square means of total time spent in a zone for category*Prominent*AOI at acid reducer category with 95% confidence limits (α=0.05)

3.2.3 Data analysis for Objective 4:

- ***Objective 4:*** *To begin to benchmark whether or not older consumers make appropriate choices based on their current health status and medication history (survey, or event data).*

Participants were asked to assess an active ingredients' appropriateness for their use during the post-test survey, by answering the question, "If you had the condition which this drug treats, would it be appropriate for you to take?" As mentioned in the Methods Chapter, this was termed, survey data or *event* level data, and responses were recorded as "yes, no, or maybe." Data collected during the medication scans, informed by the guided interview, and health histories, gathered in the form of the survey, were coded and uploaded to a secured cloud space. Two pharmacists from University of Wisconsin assessed whether (or not), based on the reported history and medications collected, each of the nine active ingredients was appropriate for each subject. As such,

there were several possible combinations of response when comparing patient and pharmacists answers (see Table 8).

It is important to note that not all disagreements result in the same level of concern from a health perspective. For instance, when a patient indicates that the drug is not appropriate (N), and the pharmacist indicates it is (Y), the primary risk is that the patient will forego an OTC treatment that could help with their ailments. Conversely, when the patient indicates appropriateness (Y) and the pharmacist indicates no (N), there is the potential for drug-drug interactions, drug-diagnosis interactions, etc. that could result in adverse reactions.

There were 738 possible observations in this study (9 active ingredients x 82 patients= 738). However, participants did not provide responses for eight different events.[1] As such, a total of 730 events were evaluated by pharmacists. Of these, one-hundred and twenty-seven (17.4%) yielded the most concerning response, yes/no (i.e. patient indicates appropriate, pharmacist not). Figure 48 summarizes the frequency and percentage of all possible combinations.

Directly following, we present analysis of appropriateness data on the basis of all responses that we collected; however, it can be argued that a more appropriate denominator for the analysis is only the population of responses where the pharmacist suggests a "no." Consider, for example, a very healthy individual that realizes that they can take anything because they have no health conditions or take any other products; in the case of this person, it may be completely reasonable that they would not examine the

[1] Specifically, Subject 06 for dextromethorphan, Subject 15 for cimetidine and guaifenesin, Subject 17 for acetaminophen, Subject 38 for naproxen, and Subject 50 for phenylephrine and Subject 66 for acetaminophen and dextromethorphan.

product labeling more closely. Nonetheless, we have analyzed the data conservatively (with the complete set of responses) and present that analysis in this chapter.

In addition, we have conducted some analysis based only on the events which pharmacists claimed as "not appropriate" in terms of the patient's health conditions. In order to minimize confusion regarding the basis of the analysis, the analysis that was conducted on the basis of the pharmacists "no"s is presented in Appendix O.

Table 8 Combined possibilities of patient and pharmacist responses to the question, "If you had the condition which this drug treats, would it be appropriate for you to take"? (Event data from the survey)

	Possible Participant Responses (N=82); total possible responses =730			
Pharmacists Response	**Yes**	**No**	**Maybe**	**SUM**
Yes	Y, Y (103, 13.4%)	N, Y (49, 6.6%)	M, Y (237, 32.1%)	389 (53.3%)
No	**Y, N (127, 17.2%)**	N, N (55, 7.5%)	M, N (152, 20.6%)	334 (45.8%)
Maybe	Y, M (2, 0.3%)	N, M (0, 0.0%)	M, M (5, 0.7%)	7 (0.9%)
SUM	232 (31.8%)	104 (14.2%)	394 (54%)	730 (100%)

*Participant response is listed first, followed by pharmacist

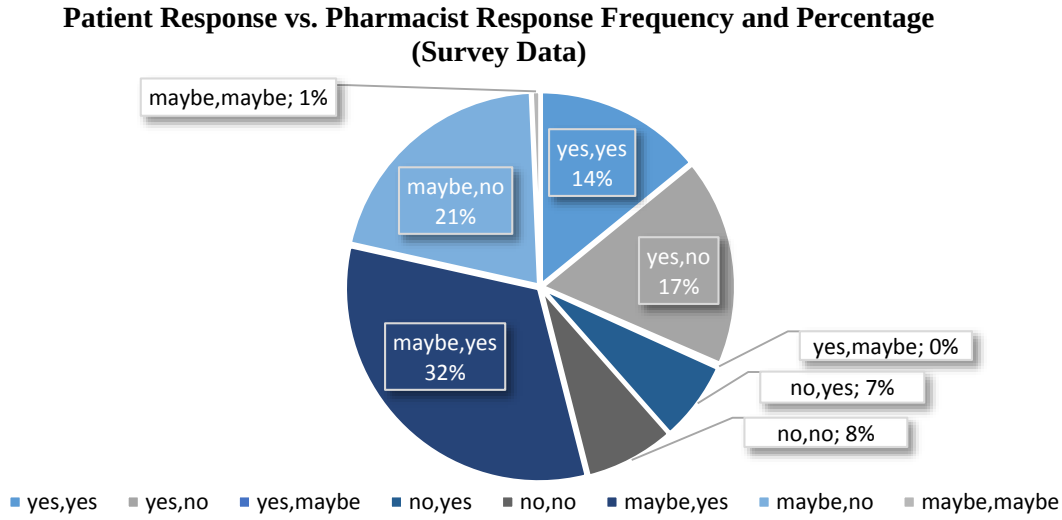


Figure 48 Patient response vs. pharmacist response frequency and percentage (survey data)

Sixty-six of the 82 (80.5% of the population tested) participants had at least one yes/no response combination for one or more of the nine active ingredients that they reviewed with a total of 127 events. Figure 49 provides information regarding how many problematic events (defined as patients indicates "yes appropriate" while pharmacist indicates "no, not appropriate") these 66 participants generated. Thirty participants had just one active ingredient that proved problematic, while 36 participants had more than one problematic combination.

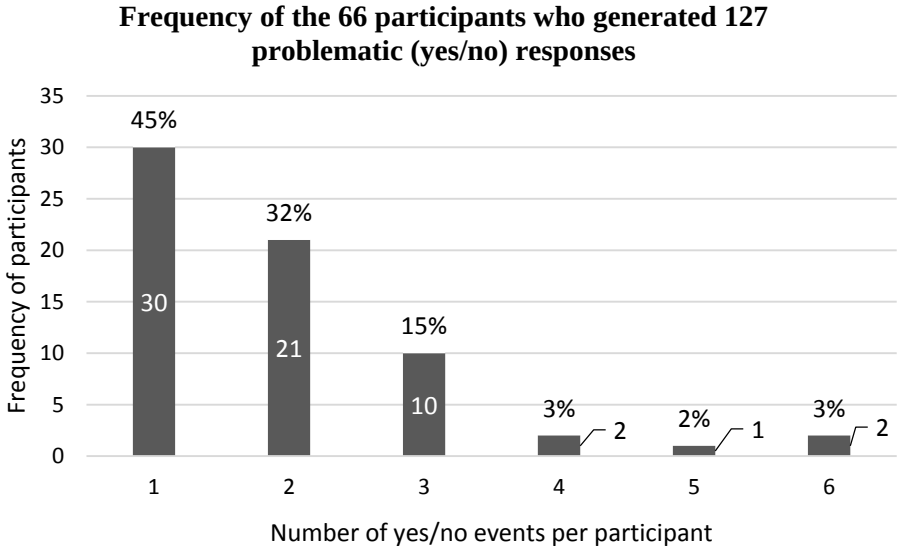


Figure 49 Frequency of the 66 participants who generated 127 problematic (yes/no) responses

The frequency of problematic (yes/no) disagreements was investigated by drug category and by active ingredient. Of the total number of yes/no disagreements that occurred, approximately 2/3s (85/127; 66.9%) were contributed by products from the pain reliever category, 52 (52/85 61.1%) of these related to subjects' responses to ibuprofen (see Figure 50).

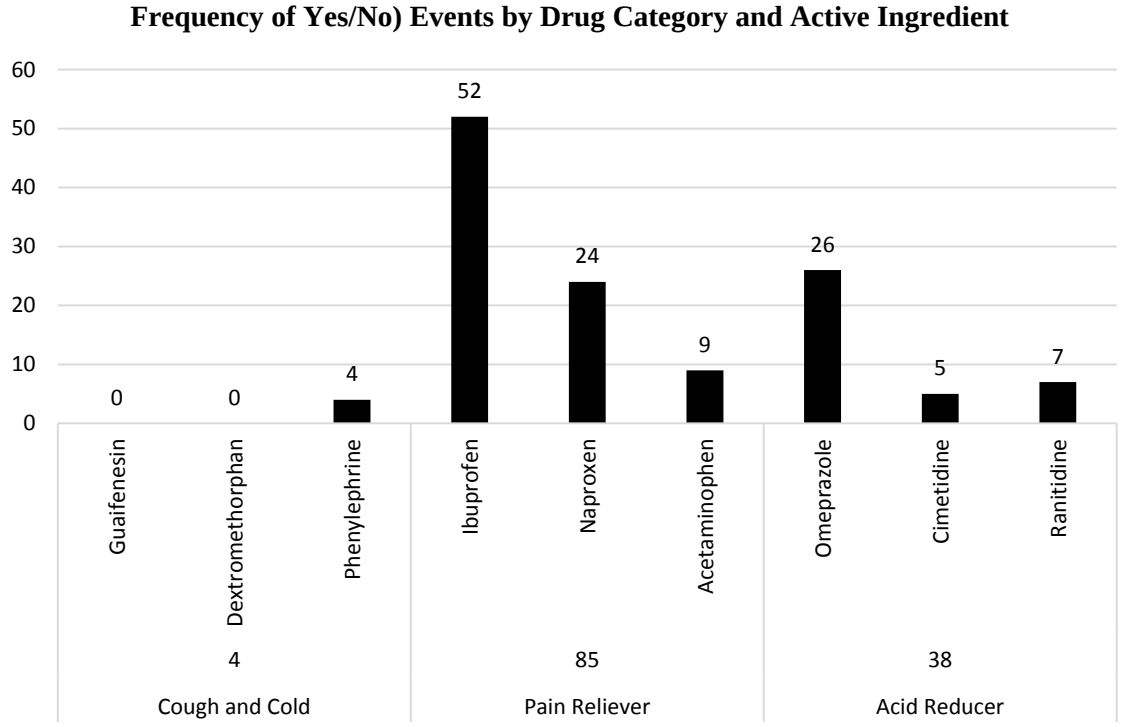


Figure 50 Frequency of yes/no events by drug category and active ingredient

To develop a sense of the role of prior familiarity and problematic (yes/no) disagreements, 728 events were analyzed (2 responses were excluded due to dual answers for prior familiarity). Figure 50 shows the frequency of problematic (yes/no) disagreement survey events by the participants' indication of prior familiarity with the active ingredient; surprisingly, 118 (93%) of the concerning responses were generated from active ingredients that subjects reported that they *were* familiar with prior to participating in the study.

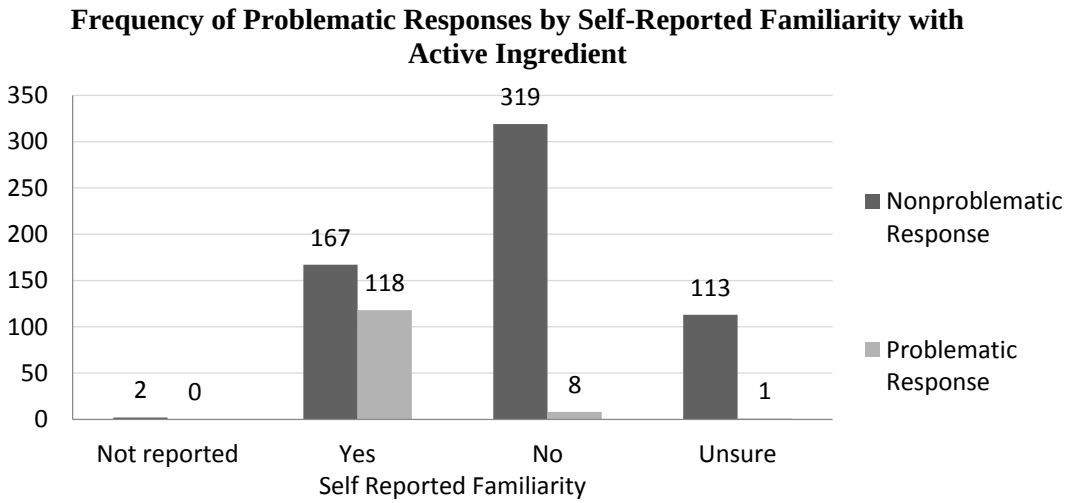


Figure 51 Frequency of problematic responses by self-reported familiarity with active ingredient

3.2.3.1 Event-Level (Post survey based): Disagreement between patient's and pharmacist's assessments

To statistically investigate the problematic (yes/no) disagreements presented by the survey responses, the data were converted into a binary response (yes/no); That is, the 127 responses of this type were keyed in binary fashion as "problematic" vs. the remainder of responses (601) from the survey which were keyed as "not problematic."

3.2.3.1.1 Statistical modeling approach

A generalized linear mixed model was fitted to the binary response defined as "problematic disagreement between pharmacist and patient" (yes=1; no=0) using a Bernoulli distribution and a logit link function to model the probability of response change. The linear predictor in the model considered the fixed effects of drug category (acid reducer, pain reliever, cough and cold) and active ingredient nested within drug category (3 active ingredients within each drug category). The linear predictor also included the random effect of subject as an overall blocking factor and its cross product

with drug category to account for over-dispersion in the data. In addition, demographic descriptors were considered for inclusion in the model, including gender, age, education level (i.e. 1 = high school or below; 2 = above high school) and visual acuity (i.e. 1 = 20/20 or 20/30; 2 = else), though none seemed to help in explaining the behavior of the response.

Over-dispersion was evaluated using the maximum-likelihood based fit statistic Pearson Chi-Square/DF. No evidence for over-dispersion was apparent. The final statistical model used for inference was fitted using Laplace approximation to maximum likelihood, as it was not possible to reach convergence using residual pseudo-likelihood estimation. The model was fitted using the GLIMMIX procedure of SAS (Version 9.4, SAS Institute, Cary, NC) implemented using Newton-Raphson with ridging as the optimization technique. Estimated least square mean probability of response change and corresponding standard errors and 95% confidence intervals are reported in the columns labeled "Mean", "Standard Error Mean", “Upper Mean” and “Lower Mean”, respectively, in the LSMean Estimates sections below. Relevant pairwise comparisons were conducted using a Tukey-Kramer adjustment to avoid inflation of Type I error rate due to multiple comparisons.

3.2.3.1.2 Data analysis and results

The results provided evidence for the effects of drug category (P=0.0002) and active ingredient (nested within category) (P<0.0001) on the probability of a problematic disagreement with the pharmacist. (Figure 52) With regard to demographic descriptors, there was no evidence for any differences between gender, ages, educational levels or

visual acuity groups on the probability of a problematic\ disagreement event between pharmacists and patients (P>0.10).

To further investigate the effect that drug category and active ingredients had on the response, pairwise comparisons were conducted for the three categories of drug (Figure 52) as well as the nine active ingredients tested (Figure 53). *Pain relievers (LSM=.0.2705, LCL=0.1884, UCL=0.3719) were significantly more likely to result in problematic disagreements than acid reducers (LSM=0.08195, LCL=0.04397, UCL=0.1477, P<0.0001).* Meaningful comparisons could not be made with the cough and cold category because of an extreme category problem within the data. That is, because there were a very low degree of problematic survey events (patient says yes; pharmacist says no) in the drug category of cough and cold, the resultant lack of variability causes the estimation process to fail. *Regardless, data suggest that the maximum probability of a problematic disagreement occurred within the pain reliever category, was intermediate for acid reducers and least likely to occur with products we tested from the cough and cold category.*

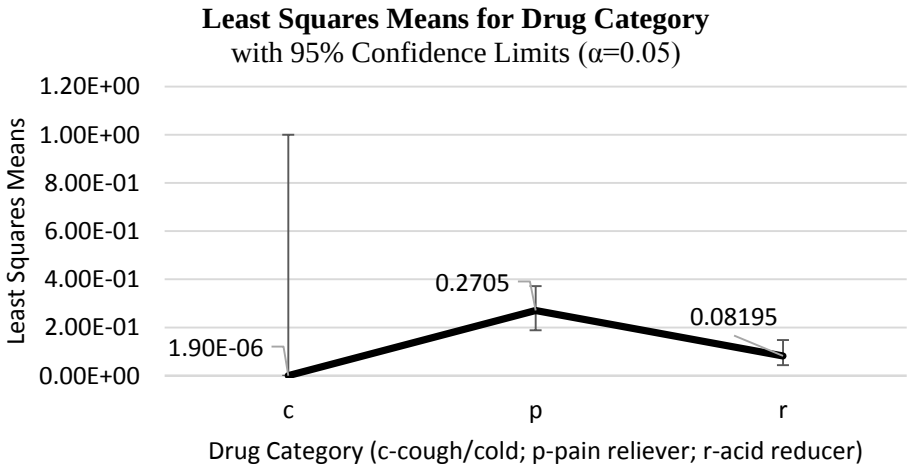


Figure 52 Least squares means for drug category with 95% confidence limits (α=0.05)

To further investigate the main effect we found regarding how active ingredient (nested within drug category) impacted the probability of a problematic disagreement between patients and pharmacists in the survey data, pairwise comparisons were performed using Tukey-Kramer techniques (described in Section 4.2.1.1.1). Figure 53 provides visual comparisons by active ingredient. Two drugs from the cough and cold category (guaifenesin and dextromethorphan) had an extreme category problem. For these drugs, there were no problematic disagreements (patient says yes; pharmacist says no); as a result of the lack of problematic disagreements, the estimation process fails so subsequent, pairwise testing is not meaningful. For the remaining comparisons between active ingredients, the lines represent statistical significance at $\alpha=0.05$. For example, the ibuprofen was significantly more likely to result in a problematic disagreement when compared to all other ingredients tested.

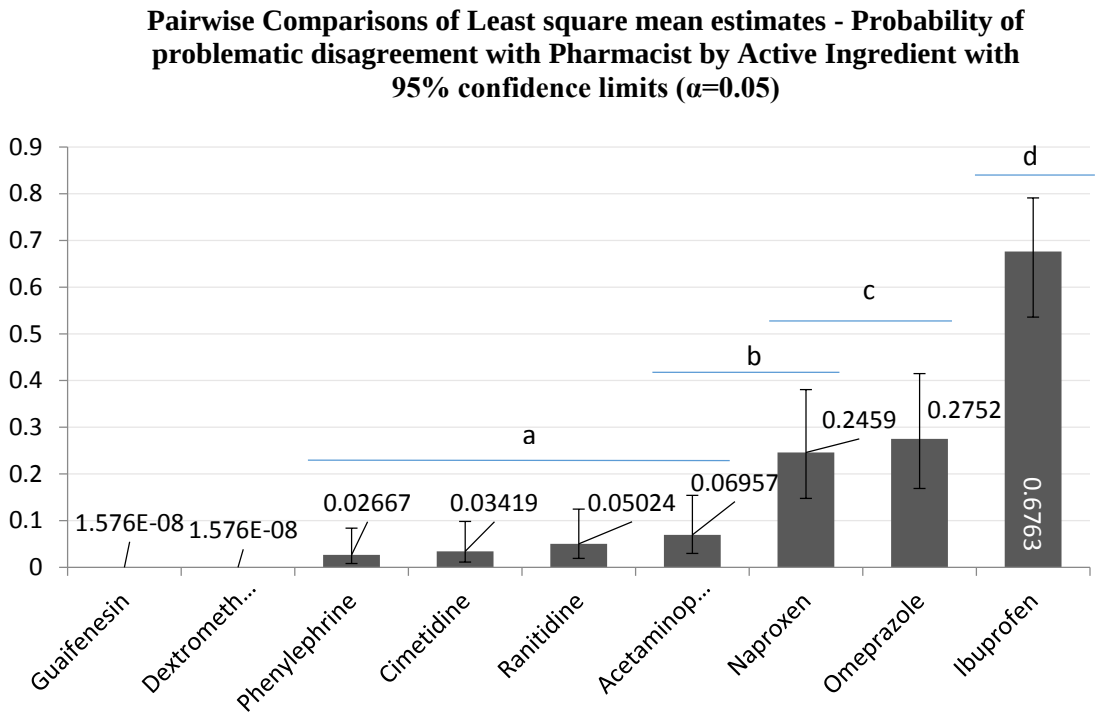


Figure 53 Pairwise comparisons of least square mean estimates - probability of problematic disagreement with pharmacist by active ingredient with 95% confidence limits (α=0.05)

3.2.4 Data analysis for Objective 5:

Objective 5: *To test the effect of information formatting (prominent or non-prominent) on determination of drug appropriateness (trial level/eye tracking data).*

Even though 10 participants' eye data could not be used due to large head movements exacerbated by the lack of a chin rest, all 82 participants answered questions regarding the appropriateness choice for each trial. Each participant saw stimulus with a given active ingredient three times, with each of the three trials emphasizing different information on the PDP (i.e. brand name, symptom relief and active ingredient), see Figure 54 and Appendix I for details. This resulted in 27 trials per participant (3 pieces of information x 3 drug categories x 3 active ingredients). During each trial, participants were asked to answer, "If you had the condition which this drug treats, would it be

appropriate for you to take?" in binary fashion (yes/no). Because each subject viewed the same active ingredient in three different trials, there was an opportunity for them to provide a different answer for each trial, despite the fact that they were viewing the same (theoretical) product.

Figure 54 Illustration depicting the three presentations of information for a single active ingredient (acetaminophen) with "Base Trial" and other trials

To investigate whether information formatting impacted participants' assessments of drug appropriateness, this study analyzed data for changes in response to the question by comparing responses to the question in trials where active ingredient or symptom relief was prominent to a "base trial," where the brand name was prominent (Figure 54).Trials with the brand name in the most prominent position were considered a "base response" due to the fact that this information is most commonly emphasized commercially. Changes in response for the other two trials (active ingredient emphasized and symptom relief emphasized) relative to the base trial response were recorded in binary fashion (changed/not changed). We also coded and analyzed the "directionality" of the change. When the response from the base changed from "no, this is not appropriate for me" to "yes, this is appropriate for me" it was coded as a change to positive. By contrast, when the response from the base changed from "yes, this is appropriate for me" to "no this is not appropriate," researchers coded it as a change to negative. In this way, researchers were able to begin to develop a sense of how the information, itself,

potentially impacted decision making (e.g. did emphasis on chemical name result in a conservative answer of appropriateness while symptom relief resulted in responses that embraced use?)

Participants were eye tracked during a total of 2,214 trials (82 participants x 3 drug categories x 3 active ingredients x 3 formats of label); the ten participants who were previously excluded due to excessive loss of eye data were retained here because the responses to each question were not affected by their eye tracking data. Base trials comprised 1/3 of this data, resulting in a total of 1,476 trials (2,214/3) where the response could be changed.

Of the 1,476 trials that had the potential to be changed, 269 were (18.2%). Specifically, an estimated 18.7 ±2.4% (95% CI= [14.4, 24.0]) change in response to trials was found (relative to the brand name response) when active ingredient was present on the label, and an estimated 19.1 ±2.5% (95% CI= [14.7, 24.5]) when symptom relief was prominent. Both probabilities are significantly lower than a coin toss (probability of 50%; $P < 0.0001$) and also greater than 0 (i.e. note the lower bound of the 95% confidence interval), meaning that the data would suggest that the observed changes relative to brand name is deliberate, not random. Therefore, even though there was no evidence for any difference in changes in behavior between prominent active ingredient and prominent symptom relief, *our evidence suggests that presenting the active ingredient or symptom relief as prominent can significantly change behavior compared to trials where the brand name was prominent.*

When examining the proportion of changed responses as the dependent variable, a main effect of education level ($p=0.0165$) was indicated. *Subjects with a high school*

degree or less were more likely than those that continued their education beyond high school to change their response (see Figure 55) *when either symptom relief or active ingredient were prominent.* This difference in the probability of response change between educational levels was apparent regardless of the directionality of changing responses (negative or positive).

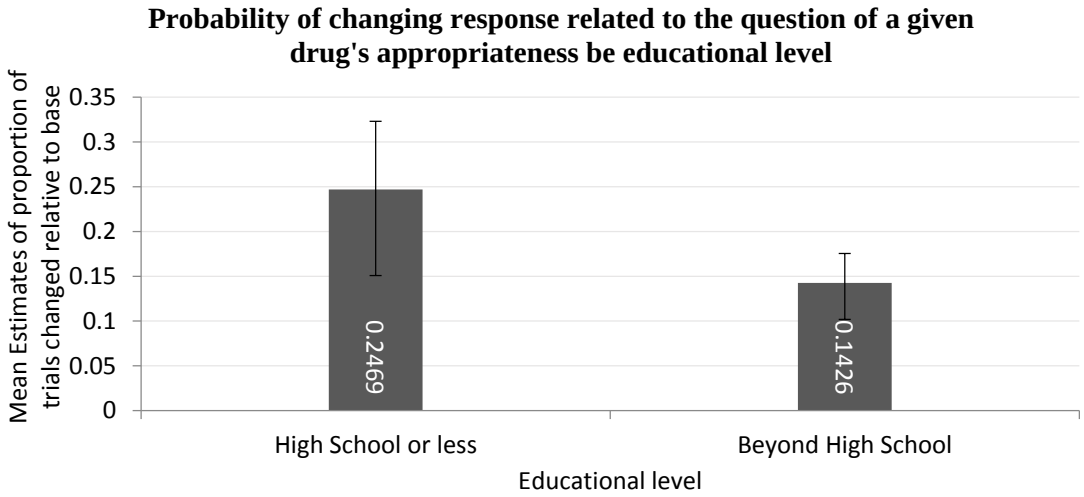


Figure 55 Probability of changing response related to the question of a given drug's appropriateness by educational level

Within the treatments of a given directionality (i.e. a change to negative or a change to positive), the probability of changing response were also compared between the subjects with a High School degree or less to those that had gone to school beyond High School. There was no evidence of difference between the two levels of education when answers changed from no to yes (P=0.1722), a change in the positive direction. *When subjects changed their answers from yes to no, a change in the negative direction, a significant difference was noted between the two levels of education (P = 0.0046).* An estimated 22% of trials (LCL 14.5%; UCL 33.1%) were changed when a person with a High School Diploma or less changed from yes to no compared with the more educated group, who only changed trials 10.5% (LCL 7.7%; UCL 14.1%) (Figure 56).

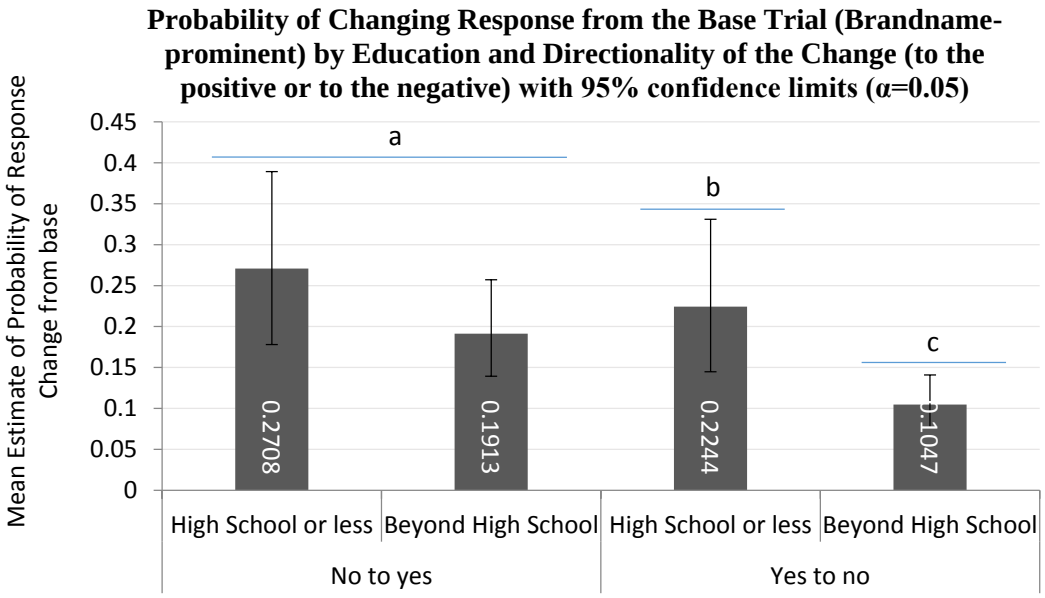


Figure 56 Probability of changing response from the base trial (brandname-prominent) by education and directionality of the change (to the positive or to the negative) with 95% confidence limits (α=0.05)

Additionally, a significant interaction, drug category by the directionality of change in response (to the positive or negative) (p=0.0219) was also indicated by the analyses. To investigate, we compared the proportion of trials that were a change in the positive direction (that is, no to yes) and compared them to those that were changed in the negative direction (i.e. from yes to no) to test for difference in the proportion of changed trials. For pain relievers, participants were significantly more likely to change their response if they had originally considered a drug as "not appropriate" during the base trial (P=0.0035) regardless of what information was prominently displayed (symptom relief or active ingredient) when compared changes to the negative in the same category. In other words, *changes from no to yes were more likely than changes from yes to no when participants considered the appropriateness of pain relievers (see Figure 57 and 58).* For the cough and cold category, comparisons could not be made for reasons discussed previously. Within the acid reducers, there was no evidence of a difference in

the likelihood of a change based on the directionality of the response (no to yes vs. yes to no) (P= 0.2253).

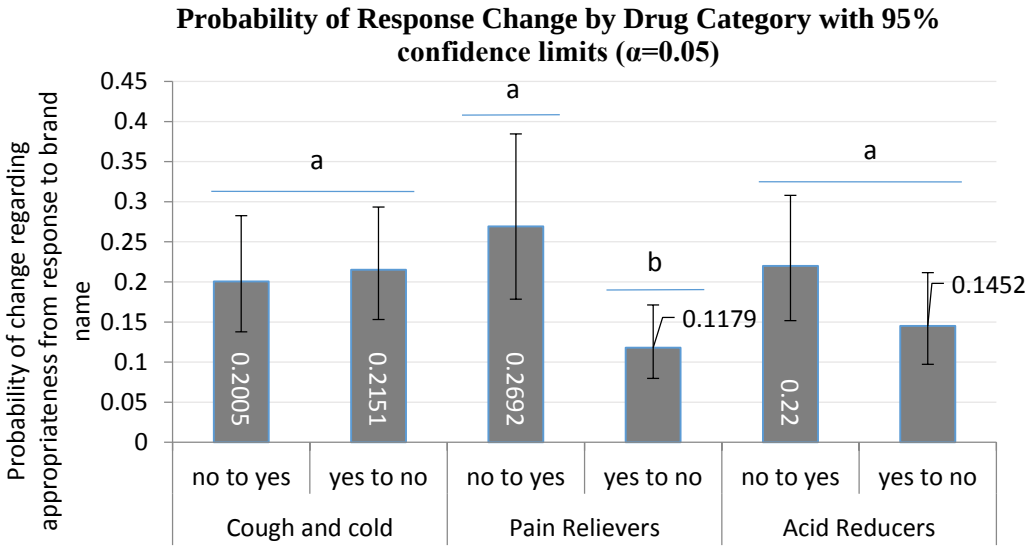


Figure 57 Probability of response change by drug category with 95% confidence limits (α=0.05)

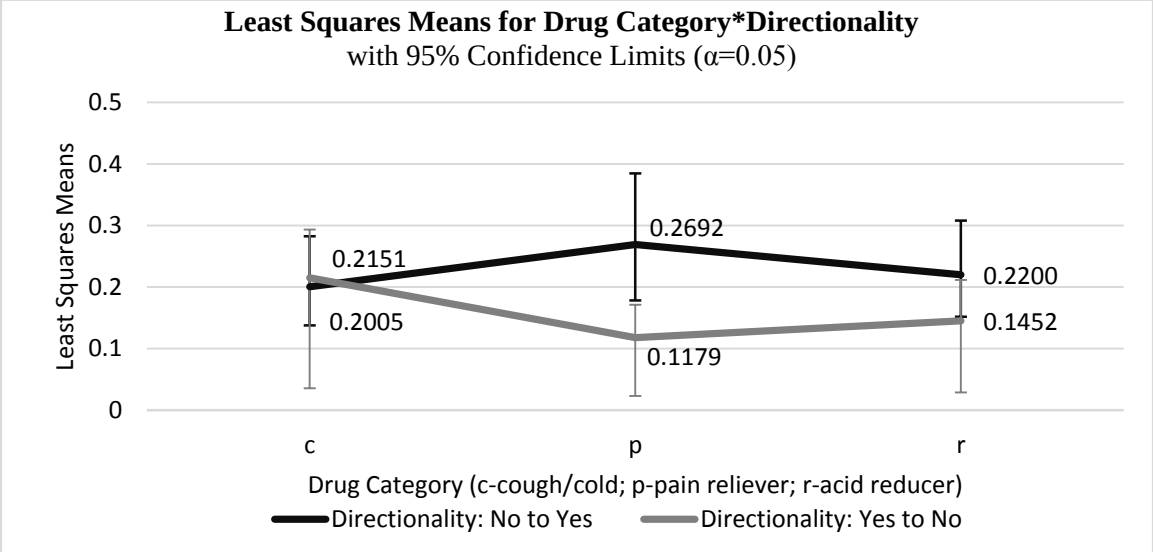


Figure 58 Least squares means for drug category*directionality with 95% confidence limits (α=0.05)

3.2.4.1 Trial-Level (Eye tracking test based): the effects of information formatting on appropriate choice

As mentioned previously, pharmacists from the University of Wisconsin reviewed data coded from the scanned medications and guided interview and health history and made assessments regarding the appropriateness of each of the nine ingredients studied for each patient. In the previous sections of the analyses, the pharmacist's response was compared to the survey/event data, which asked the patient to assess each of the active ingredients (yes, no or maybe). Study participants were also asked to assess appropriateness during each of the 27 eye tracking trials (82 x 27= 2,214 trials total). This section comprises this information.

Table 9 Combined possibilities of patient and pharmacist responses to the question, "If you had the condition which this drug treats, would it be appropriate for you to take?" (Trial data from the eye tracker)

	Participant Responses		
Pharmacists Response	**Yes**	**No**	**SUM**
Yes	Y, Y (738, 33.3%)	N, Y (447, 20.2%)	1185
No	**Y, N (648, 29.3%)**	N, N (359, 16.2%)	1008
Maybe	Y, M (19, 0.9%)	N, M (2, 0.1%)	21
SUM	1406	808	2214

*Subject response is listed first, followed by pharmacist

During the eye tracking trials, participants were limited to a binary response regarding the question, "If you had the condition which this drug treats, is it appropriate for you to take?" Table 9 shows the possible combinations of patient/pharmacist response and Figure 59 provides frequencies and percentages of response combinations. It is important to note that the pharmacists assessed each active ingredient a single time (as the active ingredient), while patients assessed each active ingredient three times (once for

each trial), and, as noted in the previous analysis, occasionally changed their responses from trial to trial.

As was the case with the event data previously reported, not all disagreements result in the same level of concern from a health perspective. The most troubling combination occurs when the patient indicates that the drug is appropriate, and the pharmacist does not (i.e. a yes/no combination). A total of 649 trials were observed in this category (29% of the total trials collected). Figure 59 summarizes the frequency and percentage of all possible combinations. Here, analysis present the problematic yes/no responses in light of the entire set of trails collected; however, as with the survey/event data, it can be argued that the relevant way to analyze is as a function of the pharmacists' "no"s (the only trials where there is the potential for such a mistake to occur). Limited analysis of the data on this basis can be found at the end of Appendix O.

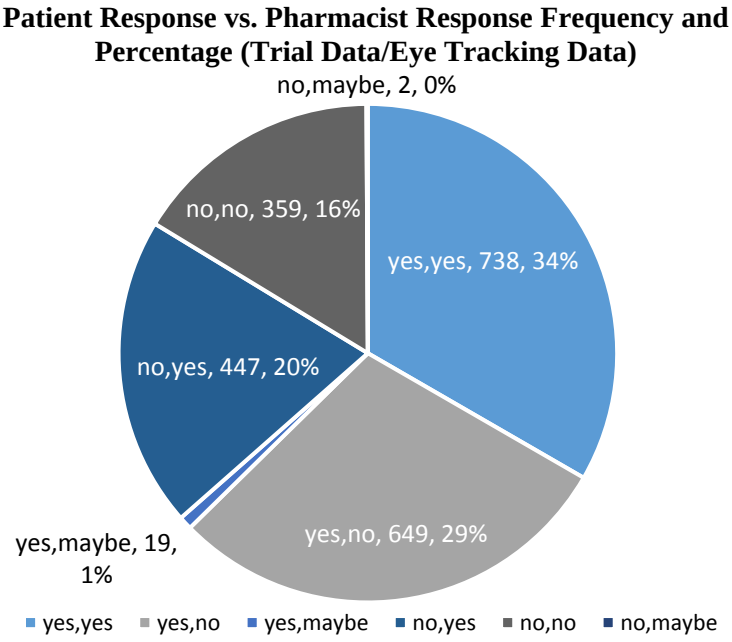


Figure 59 Patient response vs. pharmacist response frequency and percentage (trial/eye tracking data)

As with the survey/event data, the combination of responses were coded in a binary fashion (problematic being the yes/no response combination and all other responses coded as non-problematic). This binary data was then analyzed using generalized linear mixed model.

Regardless of what information was prominently displayed, there was evidence of a main effect of active ingredient (nested within drug category) on the probability of a problematic disagreement between the patient and pharmacist (P=<0.0001). (Figure 60) Additionally, a significant interaction was noted between drug category and prior familiarity on the likelihood that a problematic disagreement would occur (P=0.0114).

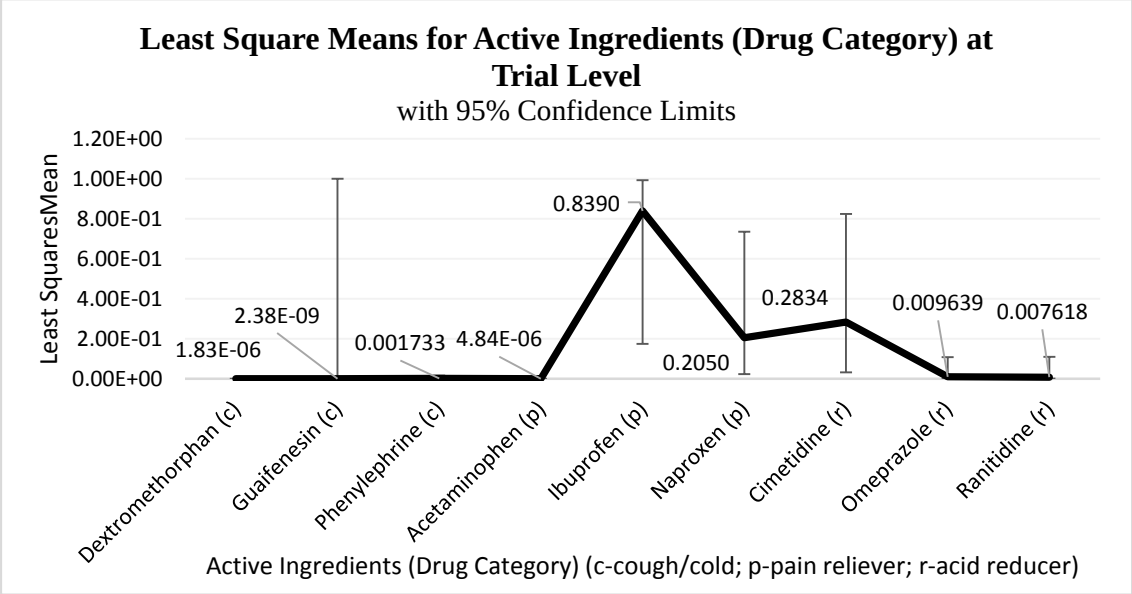


Figure 60 Least square means for active ingredients (drug category) at trial level with 95% confidence limits

As within the survey/event level data, the trial level (eye tracking) suggested that the maximum probability of a problematic response was observed for ibuprofen (Mean Estimate 83.9%, [17.4, and 99.2]). (Figure 60 and 61)Within cough and cold category, the probability of a problematic disagreement was estimated to be < 0.1% for all active ingredients considered. Within acid reducers, although there was no evidence of a

significant difference compared with omeprazole, maximum likelihood of a problematic disagreement was observed for cimetidine (28.3% [3.2, 82.4]). And disagreement estimated at less than 1% for both omeprazole and ranitidine. Pairwise comparisons were also conducted between each active ingredient.

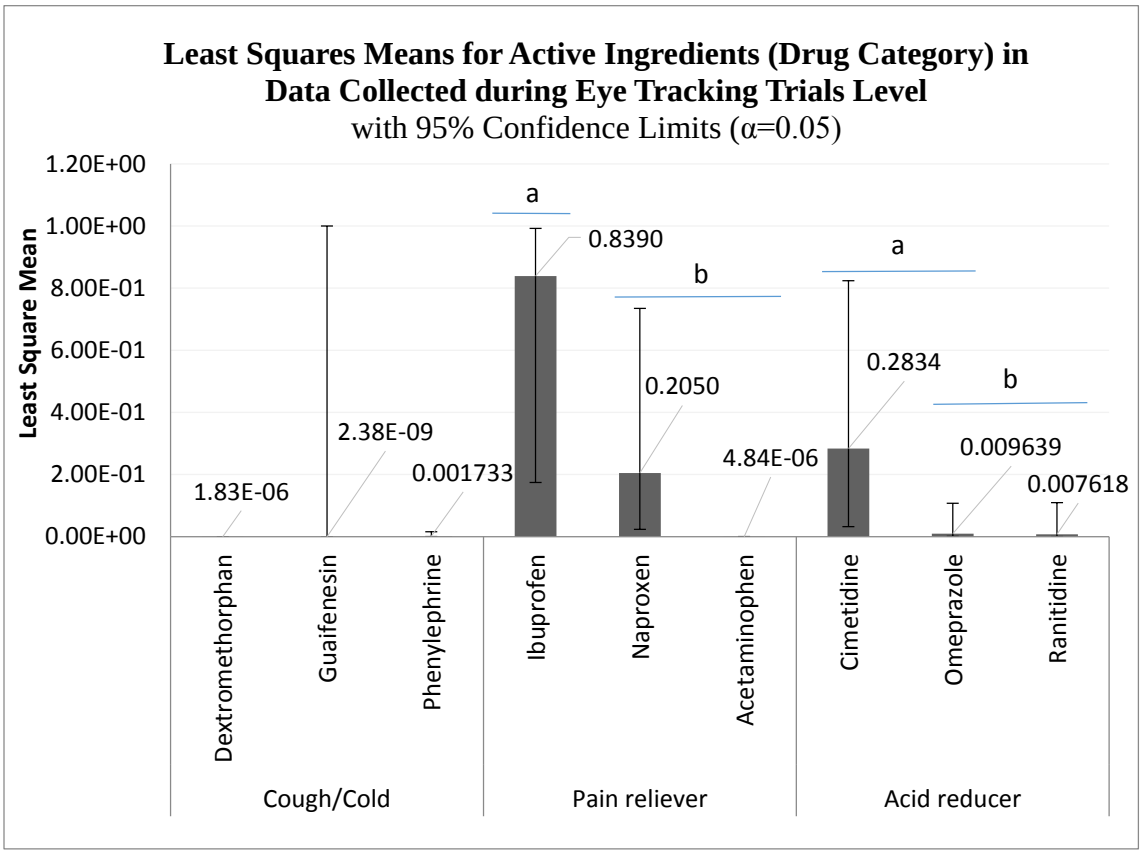


Figure 61 Least squares means for active ingredients (drug category) in data collected during eye tracking trials level with 95% confidence limits (α=0.05)

In addition to the main effect of active ingredient (drug category) on the probability of a problematic disagreement, a significant interaction of prior familiarity and drug category was also noted (P=0.0114). That is, the probability of a problematic disagreement between patient and pharmacists significantly differed by the drug category and patient familiarity (Figure 62). As with previous analyses, comparisons regarding the cough and cold category could not be made due to the low number of problematic y/n

responses generated within the category. Pain relievers indicated no evidence of a difference in the probability of a problematic disagreement across familiarity conditions. By contrast, within the acid reducer category, patients were more likely to have a problematic disagreement if they had prior familiarity with the drug (P<0.0015).

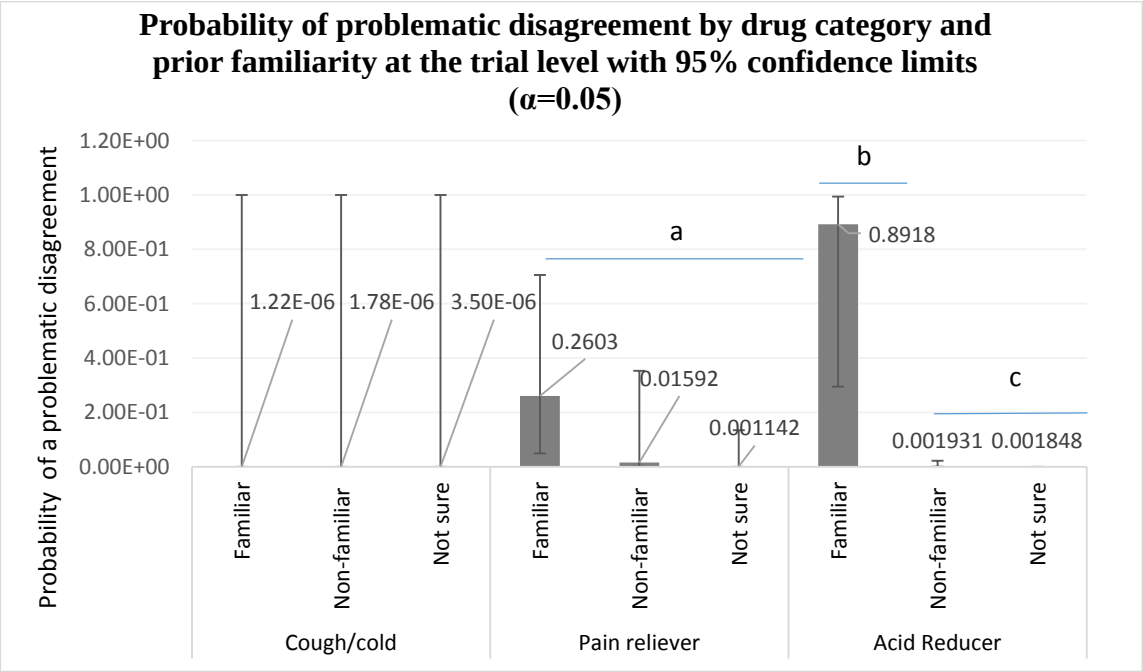


Figure 62 Probability of problematic disagreement by drug category and prior familiarity at the trial level with 95% confidence limits (α=0.05)

3.3 Descriptive Statistics on Questionnaire Evaluation

3.3.1 Memory test for active ingredients

A memory test was conducted immediately following the eye tracking portion of the study. Responses of participants' memory test are shown in Figure 63. The percentage of the number of participants who believed that the active ingredient had been shown in the main test were recorded.

The black columns and capitalized ingredients represent the active ingredients that were tested during the course of the main test, while the grey columns served as

products intended to be fillers. Nearly all participants circled acetaminophen (75; 91.5%) and ibuprofen (78; 95.1%).

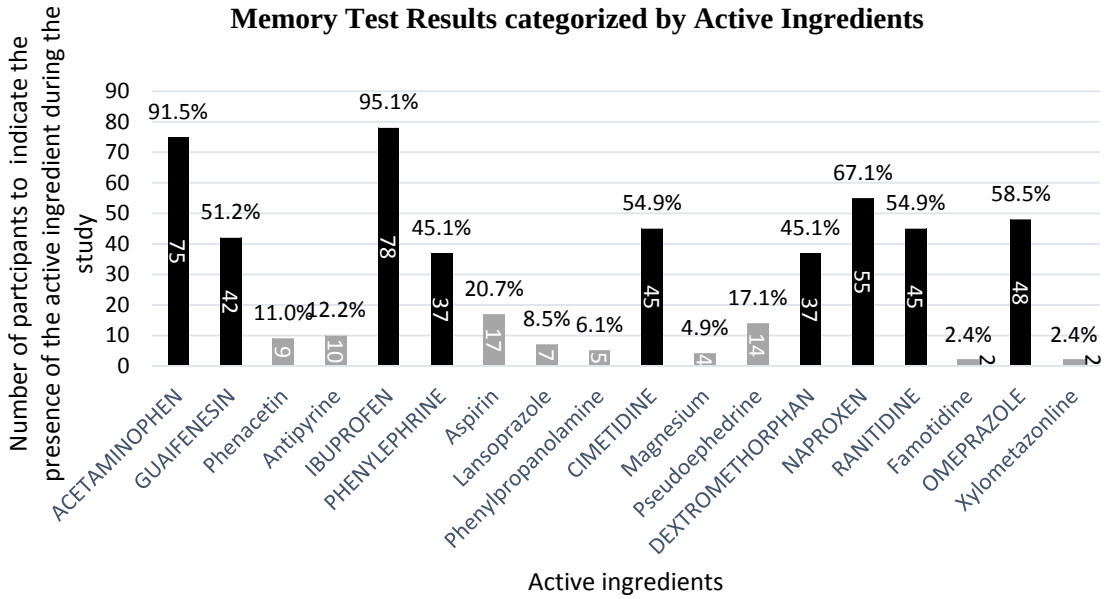


Figure 63 Memory test results categorized by active ingredients

Also, the percentages of participants who circled the correct active ingredients are characterized by numbers of correct circle, shown in Figure 64. Almost 45 (55%) of total participants correctly identified 6 or more active ingredients in the post hoc test.

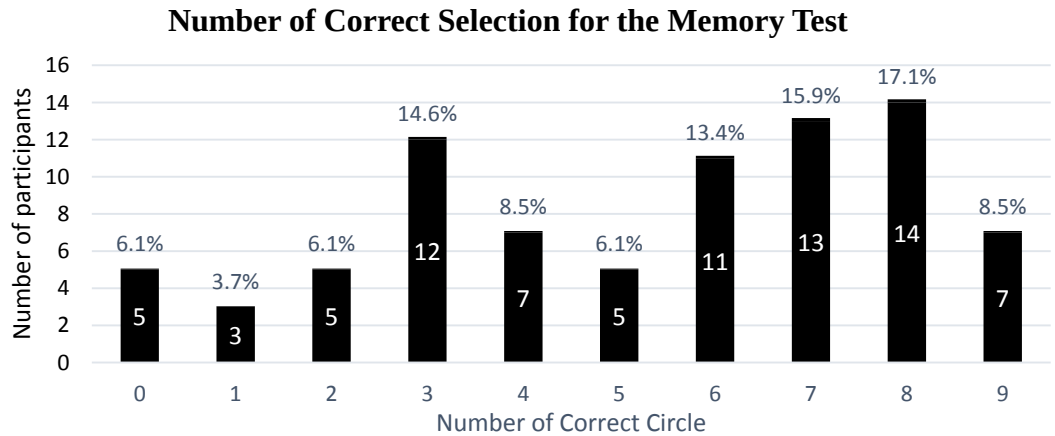


Figure 64 Number of correct selection for the memory test

3.3.2 Elements Ranking Survey

Participants reported the frequency of use regarding specific information present on OTC labels during the post-testing survey. Figure 65 provides an overview of answers to the question “how often do you use the information?” from all the participants. Responses were collected in a Likert fashion with levels of frequency from 1 (never) to 5 (always). “Directions” on the Drug Facts Label (DFL) was ranked as level 5 among 51 (62.2%) of all the participants, followed by “Tablet concentration and Brand name” (45; 54.9%), “Uses” (42; 51.2%) and “Warnings” (42; 51.2%), etc.

Participants also reported the importance of specific packaging elements during the post survey. In Figure 66, it characterizes an overview of answers to the question “how important is the information during a purchase for yourself?” from all the participants. Similar to the previous question, most of the participants ranked the highest level on the elements: “Tablet concentration and brand name” (62; 75.6%), “Directions” (60; 73.2%) , “Warnings” (56; 68.3%), “Uses” (53, 64.6%), “Active ingredient on DFL”(52; 63.4%), “Active ingredients on PDP” (45; 54.9%), “Pill size number and type” (40; 48.4%), “LOT and expiration date” (32; 39.0%) , “TE warning” (23; 28.0%).

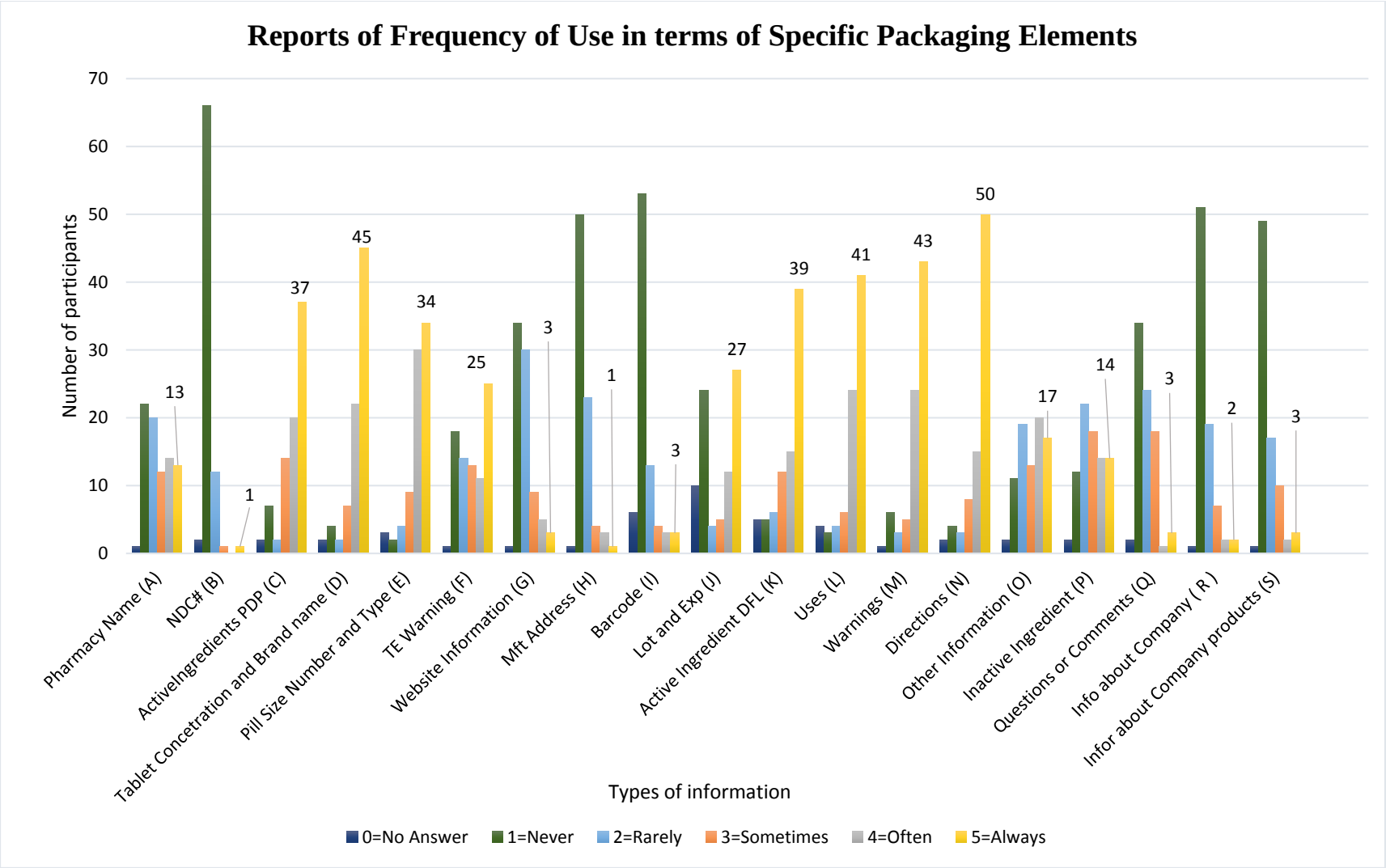


Figure 65 Reports of frequency of use in terms of specific packaging elements

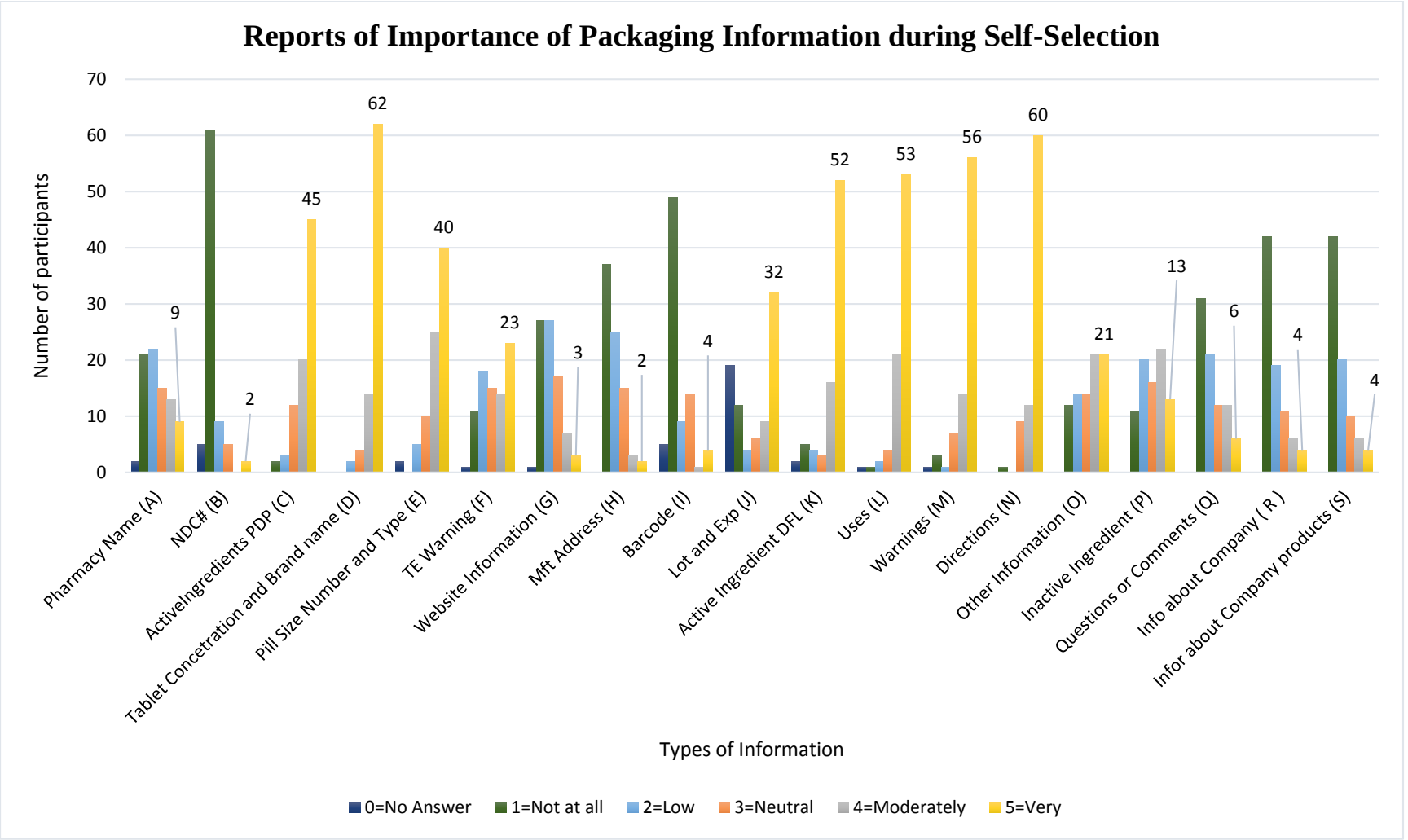


Figure 66 Reports of importance of packaging information during self-selection

CHAPTER 4 DISCUSSION AND CONCLUSION

4.1 Discussion and Conclusion

Our data, which directly measured the behaviors of older adults while assessing the appropriateness of OTCs, closely corroborate reported findings regarding label use previously collected through survey, observational study, self-reports and guided interviews.

1. Propensity for polypharmacy:

The propensity for polypharmacy, which catalyzes the likelihood of ADEs in a physiologically vulnerable population, was found in this study. As expected and supported by the work of others (Martin, Jones, & Gilbert, 2013), every member of the test population (n=82) brought at least one of the products that the researchers enumerated (prescription, OTC, vitamin and herbal remedy) to the testing, indicating that they had taken it in the week prior to the study. Compared to 29% of the respondents of the 2008 National Social Life, Health and Aging Project (Qato et al., 2008), who reported taking 5 or more prescriptions concurrently, over half of our test population brought 5 or more unique prescriptions and 41.5% brought 5 or more OTCs.

2. Behaviors on accessing OTC labeling information

Consumers access information limitedly from OTC labeling. The APCO Insight survey reports only 20% of the participants report rereading the label of an OTC on repeat use; also, that seniors are less likely than Millennials to report label use as important, despite the fact that they are at increased risk for ADEs for varied reasons. (PR Newswire, 2015) Consistent with these findings, a minimal number of the participants

examined OTC labeling beyond the PDP, and this was true for both of the experiments during this research: Specifically, in Experiment One, only 12/82 participants (14.5%) looked beyond the PDP for at least one package in each set while making selections from sets comprised of various drug categories, and 43 (51.8%) never looked beyond the PDP for any package in any selection set. Experiment one's purpose was to develop baseline data regarding the attentive behaviors of subjects when they didn't have the constraints imposed by the eye tracking experiment. Specifically, we had concerned that the use of a mouse and computer might be daunting to some seniors, thereby limiting the information that they viewed. However, results collected during the eye tracking test (Experiment Two) were consistent with Experiment One and the existing literature. That is, they provided further evidence that older adults rely quite heavily on the PDP during decision making. A majority, 63.4% of the test population, exclusively focused on the PDP, not investigating other information for *any* of the 27 trials that they viewed, and only 13 participants (15.8% of the test population) used information beyond the PDP for every single trial. Furthermore, a total of 30 participants (36.6% of the test population) never turned any OTC packages in *either* of the two experiments of this research.

This highlights the fact that the most heavily regulated, comprehensive information, the DFL, was never exposed for many participants when they assessed the appropriateness of the OTCs they were viewing. This is concerning in light of research that suggests that less than half of consumers seek the advice of a learned intermediary when purchasing an OTC (Harris Interactive, 2002). It could be argued that this result was because participants were familiar with the products being viewed; however, the study was comprised of novel brands, so any prior familiarity (and associated knowledge

regarding the risks of the same) was limited to those associated with the active ingredient. Regardless, in the most positive scenario, it suggests that more than one third of the older adults in the study depended on their memory to make every decision regarding the appropriateness of the drugs, since there was no drug information on the PDPs relating to directions or warnings.

3. Assessment of appropriateness is questionable at best

Decision making regarding drug appropriateness was questionable. Nearly 20% of the total responses collected from participants on the survey for the nine active ingredients tested (127/730) fell into the "problematic" category (subjects says, yes, it is appropriate while the pharmacist says no). These 127 responses were generated by 66 participants or 80.5% of the test population, more than half (36) whom had more than one response in this category. If familiarity with the active ingredient was the reason that so few people failed to seek more detailed information, it could be construed as "false bravado." Of the 127 problematic disagreements recorded, 118 (92.9%) occurred with active ingredients that participants reported as familiar, with drug category and active ingredient significantly impacting the likelihood of a problematic response. Pain relievers were significantly more likely to trigger a problematic response (LSM=0.2705, UCL=0.3719, LCL=0.1884) than acid reducers (LSM=0.02527, UCL=0.1477, LCL=0.04397), and Ibuprofen significantly more likely to elicit a problematic response than any of the other active ingredients in the study.

Nonsteroidal anti-inflammatory drugs (NSAIDs), such as Ibuprofen, have been implicated in studies examining drug-drug interactions previously, with published research suggesting that it may not be cause for tremendous alarm. Hersh, Pinto, and

Moore (2007) suggest that case reports and clinical trial reviews revealed evidence of relatively well known drug-drug interactions between prescription/OTC NSAIDs and alcohol, antihypertensive drugs, high-dose methotrexate and lithium in addition to frequently prescribed narcotics and other central nervous system depressants. Despite the reports of many potential interactions, the research team concluded that it doesn't necessarily result in a significant impact on public health,

> "Considering the widespread use of analgesic agents, the overall incidence of serious drug-drug interactions involving these agents has been relatively low. The most serious interactions usually involved other interacting drugs with low therapeutic indices or chronic and/or high-dose use of an analgesic and the interacting drug." (Hersh et al., 2007)

5. Information formatting matters and should be objectively evaluated further

The rising number of private label products, which tend to emphasize varying pieces of information on the PDP (brand name, active ingredient and symptom relief), coupled with previous research (Harris Interactive, 2002) suggesting many healthcare providers think the potential for inappropriate use of OTCs is a concern (79%) because consumers have a lack of understanding regarding active ingredients (69%), catalyzed our investigation into how the formatting of this information affects consumer assessment of a drug's appropriateness. Answers were found to significantly change relative to base) with formatting and a main effect of education level was evident. Specifically, those with a high school degree or less were significantly more likely to change their answer from base than those that had some education after high school ($p=0.0165$). This would suggest that less educated consumers are more likely to be swayed by changes in the

arrangement of the PDP; that more educated consumers are less likely to change their response, regardless of the information highlighted.

We also directly measured how the formatting of information influenced the attentive behaviors of older adults using eye tracking. Previous research relying on self-reports collected with surveys suggests that very few consumers (34%) can correctly identify the active ingredient in their brand of pain reliever, and that only 21% report using warnings when purchasing an OTC for the first time, despite the fact that 78% report using them. (Harris Interactive, 2002)

We directly measured the information that older consumers viewed when assessing a products appropriateness using eye tracking, and considered the probability of viewing a given piece of information as the dependent variable. A three-way interaction (drug category x prominence x information of interest) was evident. One relatively consistent behavior related to how people interacted with brand name. Specifically, for two of the three drug categories (pain reliever and acid reducer) there was no evidence in a change in the proportion of people that viewed the brand name regardless of whether or not it was prominent. For other information, namely symptom relief and active ingredient, people were more likely to view in the information when it was prominently featured than when it was not. This suggests that people may have been actively seeking the brand name information (despite the fact that these were mock brands).

4.2 Limitations and Future Work

Work presented here represents an important first step in objectively measuring some of the behaviors that occur when older adults make decisions regarding the appropriateness of an OTC drug. As with any study, there are several limitations.

For both Experiments 1 and 2, even though the subjects were told to presume that they were in a store making assessments, they were tested using laboratory experiments under the supervision of researchers, which potentially impacts behaviors. One possible approach to the creation of a more realistic experience while maintaining the experimental control achieved herein, is the use virtual reality technology and wearable devices, such as Oculus Rift, Leap Motion in combination with Eye tracking.

For Experiment 2, even though the researchers added the basic tutorial for using the mouse as well as the audible instructions with demos to familiarize subjects with the testing program, it was still possible that subjects didn't turn the package samples for more information due to the complexity and difficulty using the computer. However, results reported for the first experiment (which used real packages) provide similar rates of examination to those reported in the literature and collected during Experiment 2.

It is possible that people became fatigued during the eye-tracking test, since there were 27 similarly-designed samples for each subject to view and assess. The focus of this study were on the effect of labeling content and formatting, and therefore the factors of packaging color and PDP design layout, which could have further influenced results, were not include. More studies are needed in the future to specifically test other design factors more realistically.

Moreover, in order to simulate real products, the PDP designs for the drugs in the cough and cold category were confounded with 3 different words for symptom relief ("expectorant" for guaifenesin, nasal decongestant for phenylephrine, and "antitussive" for dextromethorphan). This was inconsistent with the other two drug categories, where the terms "pain reliever" and "acid reducer" were used as the symptom relief description for all products in each of the respective categories... This could be provide some insight into the nuances of the date from the cough and cold category.

In addition, the use of mock brands in this study does not reflect real world situations where consumers may be familiar with, and have prior experience with, brands, the active ingredients that they contain and the conditions that they treat. It is possible that the patients' prior familiarity of those well-known brands might lead to different results. Therefore, the effect of real brand could be a research topic in future studies.

APPENDICES

Appendix A. Drug-Drug Interactions of Common OTC Drugs

Access from the government documentation of the State of California. (Co-Occurring Joint Action Council, 2014)

Table 10 Drug-Drug Interactions of Common OTC Drugs: Pain Relievers, Antihistamines, Decongestants and Cough Medicines

Pain Relievers		
OTC Drug	**Prescription Drug**	**Adverse Effect**
Acetaminophen (brand name: Tylenol)	Antibiotics rifampin (brand names: Rifadin, Rimactane) and isoniazid (INH)	Gets in the way of how the liver processes acetaminophen and increases the risk of liver problems when taking acetaminophen.
Aspirin (two brand names: Bayer, St. Joseph)	Diabetes medicines such as chlorpropamide (brand name: Diabinese), insulin and others Anti-seizure drugs such as phenytoin (brand name: Dilantin) and valproic acid (brand name: Depakene)	Aspirin increases the blood-sugar-lowering effects of diabetes medicines. Aspirin gets in the way of the anti-seizure drugs binding with proteins in the blood and leads to increased anti-seizure drug levels in your blood.
Nonsteroidal anti-inflammatory drugs (NSAIDs), including: * Aspirin * Ibuprofen (two brand names: Advil, Motrin) * Ketoprofen (brand name: Orudis KT) Naproxen (one brand name: Aleve)	Anti-cancer drug methotrexate (one brand name: Trexall) Drugs to suppress the immune system, such as cyclosporine (brand names: Neoral, Sandimmune) Heart medicines such as digoxin Blood pressure drugs, such as propranolol (brand names: Inderal, Innopran XL), metoprolol (brand names: Lopressor, Toprol-XL) and atenolol (brand name: Tenormin	NSAIDs reduce how the kidneys clear methotrexate out of the body. This can lead to having too much methotrexate in your blood. NSAIDS reduce how the kidneys clear the mmune system or heart drugs out of the body. This can lead to having too much of the drugs in your blood. NSAIDS reduce the blood pressure-lowering effects of the blood pressure drugs.

Table 10 (cont'd)

	Diuretics	NSAIDS decrease effectiveness of diuretics.
Acetaminophen NSAIDs	Blood thinners such as warfarin (brand name: Coumadin)	Acetaminophen and NSAIDs increase blood-thinning effect of blood thinners.
Ibuprofen Naproxen sodium	Lithium	Ibuprofen and Naproxen reduce how the kidneys clear lithium out of the body. This can lead to having too much lithium in your blood.
Antihistamines		
OTC Drug	**Prescription Drug**	**Adverse Effect**
* Brompheniramine (some brand names: Dimetapp Cold & Allergy Elixir, Robitussin Allergy & Cough Liquid) * Chlorpheniramine (one brand name: Robitussin Flu Liquid) * Dimenhydrinate (brand name: Dramamine Original) * Diphenhydramine (some brand names: Benadryl Allergy, Nytol, Sominex) * Doxylamine (two brand names: Vicks NyQuil, Alka-Seltzer Plus Night-Time Cold Medicine)	Sleeping pills, sedatives, muscle relaxants, anti-anxiety drugs, including alprazolam (brand name: Xanax), diazepam, lorazepam (brand name: Ativan), temazepam (brand name: Restoril) and others	These antihistamines increase the depressant effects (for example, sleepiness) of sleeping pills, sedatives, muscle relaxants or anti-anxiety drugs on the central nervous system (brain).

Table 10 (cont'd)

Decongestants		
OTC Drug	**Prescription Drug**	**Adverse Effect**
Pseudoephedrine (some brand names: Contac Non-Drowsy, Efidac 24, Sudafed)	Monoamine oxidase inhibitors (MAOIs),* including isocarboxazid (brand name: Marplan), phenelzine (brand name: Nardil), selegiline (one brand name: Eldepryl) and tranylcypromine (brand name: Parnate) High blood pressure drugs	Pseudoephedrine can cause dangerous increases in blood pressure and heart rhythm problems when taken with MAOIs. Pseudoephedrine reduces the blood-pressure-lowering effects of high blood pressure drugs.
Pseudoephedrine (some brand names: Contac Non-Drowsy, Efidac 24, Sudafed)	Stimulants, such as diet pills	Pseudoephedrine can increase the side effects of stimulants on the central nervous system (brain), such as anxiety.
Cough Medicines		
OTC Drug	**Prescription Drug**	**Adverse Effect**
Dextromethorphan (some brand names: Delsym, Robitussin Maximum Strength, Vicks 44 Cough Relief)	MAOIs* Sedatives or tranquilizers	Dextromethorphan, when taken with MAOIs, can cause "serotonin syndrome" with symptoms such as agitation, high body temperature, sweating, rapid heart rate, and trouble moving. Dextromethorphan increases the sedative effects of the sedatives or tranquilizers.
*-- Note that pseudoephedrine and dextromethorphan may cause serious drug-drug interactions and should never be taken while you are taking anMAOI or within 2 weeks of taking one.		

Appendix B. Examples of Graphic Enhancement Used by FDA

Available at: http://www.gpo.gov/fdsys/pkg/CFR-2011-title21-vol4/pdf/CFR-2011-title21-vol4-part201-appA.pdf

Figure 67 Examples of Graphic Enhancement Used by FDA

(2) At least as large as the size of the ''Drug Facts'' title, as required in §201.66(d)(2). The new warnings information statement must remain on the PDP of the drug product for at least 1 year from the date the product is initially introduced into interstate commerce.

(c) *Requirements to supplement approved application.* Holders of approved applications for OTC drug products that contain internal analgesic/antipyretic active ingredients that are subject to the requirements of paragraph (a) of this section must submit supplements under §314.70(c) of this chapter to include the required information in the product's labeling. Such labeling may be put into use without advance approval of FDA provided it includes at least the exact information included in paragraph (a) of this section.

[74 FR 19407, Apr. 29, 2009, as amended at 74 FR 31180, June 30, 2009; 74 FR 61514, Nov. 25, 2009]

APPENDIX A TO PART 201—EXAMPLES OF GRAPHIC ENHANCEMENTS USED BY FDA

I. SECTION 201.66 STANDARD LABELING FORMAT

A. Overall

1. The ''Drug Facts'' labeling is set off in a box or similar enclosure by the use of a barline with all black type printed on a white, color contrasting background.

B. Typeface and size

1. ''Drug Facts'' is set in 14 point Helvetica Bold Italic, left justified.
2. ''Drug Facts (continued)'' is set in 8 point Helvetica Bold Italic for the words ''Drug Facts'' and 8 point Helvetica Regular for the word ''(continued)'' and is left justified.
3. The headings (e.g., ''Directions'') are set in 8 point Helvetica Bold Italic, left justified.
4. The subheadings (e.g., ''Ask a doctor or pharmacist before use if you are'') are set in 6 point Helvetica Bold, left justified.
5. The information is set in 6 point Helvetica Regular with 6.5 point leading, left justified.
6. The heading ''Purpose'' is right justified.
7. The bullet is a 5-point solid square.
8. Two em spacing separates bullets when more than one bullet is on the same line.
9. A table format is used for 3 or more dosage directions.
10. A graphic appears at the bottom of the first panel leading the reader to the next panel.

C. Barlines and hairlines

1. A 2.5-point horizontal barline extends to each end of the ''Drug Facts'' box (or similar enclosure), providing separation between each of the headings.
2. A 0.5-point horizontal hairline extends within 2 spaces on either side of the ''Drug Facts'' box (or similar enclosure), immediately following the title and immediately preceding the subheadings.
3. A 0.5-point horizontal hairline follows the title, immediately preceding the heading, when a heading appears on a subsequent panel immediately after the ''Drug Facts (continued)'' title.

D. Box or Enclosure

1. All information is enclosed by a 2.5-point barline.

II. SECTION 201.66 MODIFIED LABELING FORMAT

A. Overall

1. The ''Drug Facts'' labeling is presented in all black type printed on a white color contrasting background.

B. Typeface and size

1. ''Drug Facts'' is set in 9 point Helvetica Bold Italic, left justified.
2. The headings (e.g., ''Directions'') are set in 8 point Helvetica Bold Italic, left justified.
3. The subheadings (e.g., ''Ask a doctor or pharmacist before use if you are'') are set in 6 point Helvetica Bold, left justified.
4. The information is set in 6 point Helvetica Regular with 6.5 point leading, left justified.
5. The heading ''Purpose'' is right justified.
6. The bullet is a 5-point solid square.
7. Bulleted information may start on same line as headings (except for the ''Warnings'' heading) and subheadings, with 2 em spacing separating bullets, and need not be vertically aligned.

C. Barlines and hairlines

1. A 2.5-point horizontal barline extends to each end of the ''Drug Facts'' box (or similar enclosure), providing separation between each of the headings.
2. A 0.5-point horizontal hairline extends within 2 spaces on either side of the ''Drug Facts'' box (or similar enclosure), immediately following the title and immediately preceding the subheadings.

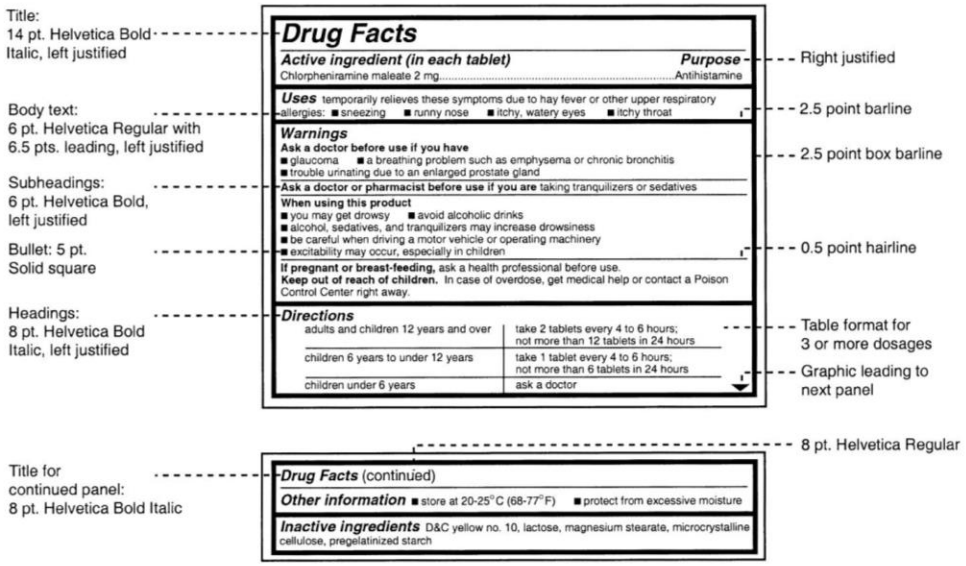
D. Box or Enclosure

1. All information is set off by color contrast. No barline is used.

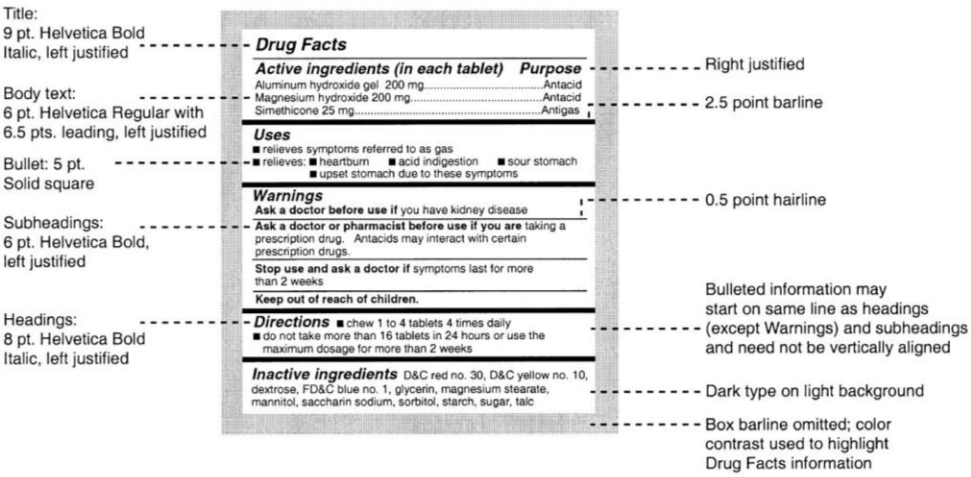
III. EXAMPLES OF §201.66 STANDARD LABELING AND MODIFIED LABELING FORMATS

Figure 67 (cont'd)

A. SECTION 201.66 STANDARD LABELING FORMAT



B. SECTION 201.66 MODIFIED LABELING FORMAT



PART 202—PRESCRIPTION DRUG ADVERTISING

AUTHORITY: 21 U.S.C. 321, 331, 352, 355, 360b, 371.

§ 202.1 Prescription-drug advertisements.

(a)(1) The ingredient information required by section 502(n) of the Federal Food, Drug, and Cosmetic Act shall appear together, without any intervening

Appendix C. Recruitment Flyer and the Consent Form approved by MSU Institutional Review Board (IRB)

1. Recruitment Flyer

Figure 68 Recruitment Flyer

2. Research Participant Information and Consent Form

Figure 69 IRB Approved Consent Form

Research Participant Information and Consent Form

You are being asked to participate in a research study. Researchers are required to provide a consent form to inform you about the research study, to convey that participation is voluntary, to explain risks and benefits of participation, and to empower you to make an informed decision. You should feel free to ask the researchers any questions you may have.

Study Title: Quantifying the attentive behaviors of older adults during selection of an over-the-counter (OTC) medication
Principal Investigator: Laura Bix, Associate Professor, 517-355-4556, bixlaura@msu.edu
Secondary Investigator: Lanqing Liu, Graduate Student, 517-775-6283, liulanqi@msu.edu
Department and Institution: School of Packaging, Michigan State University
Address: 153 Packaging Building East Lansing MI 48824

1. PURPOSE OF RESEARCH

- **Eligibility:** To participate in this study you MUST:
  - Be at least 65 years of age
  - Be willing to bring all prescriptions and OTC products that you are regularly taking to the experiment
  - Not be legally blind
  - Not wear hard contact lenses
  - Purchase and administer OTC medications by yourself
  - Have transportation to the School of Packaging at MSU or the MSU Extension offices (within the Ingham County Human Services Building on Cedar Street), where the testing will take place

- **Purpose of research:** You are being asked to participate in a research study which investigates the how older adults view and select OTC drugs.

- **Time of duration:** This study will take no more than 2 hours of your time.

2. WHAT YOU WILL DO

- **Pre-test (About You):** You will be provided a survey that gathers basic information about you, including your gender, ethnicity, educational background, and age. After this we will also provide you with a series of images made up of colored dots. These dots form numbers. We will ask you to read aloud any numbers that you can see. This provides us with an estimate of your ability to see color. We will then provide you with a second printed card and you will be asked to read the smallest text on the card that you are able as a measure of your visual acuity (20/20, 20/30, etc.). We will then provide you with a list of medical words. You will be asked to read the words from the list aloud to provide us with an idea of how familiar you are with medical terminology.

- **Main Test (Selection of Product and Eye Tracking):** This portion of the research is made up of two stages. In the first stage, we will ask you to put a pair of glasses on that contain a very small camera. This camera will film what you are seeing, but will not film you. We will set a series of packages in front of you and ask you to choose products that are appropriate for you to take.

This consent form was approved by a Michigan State University Institutional Review Board.
Approved 07/2/2014 - valid through - 07/01/2015. This version supersedes all previous versions. IRB #14-679

Figure 69 (cont'd)

In the second stage, you will be asked to view several packages that appear on a computer screen to assess whether or not the product (an OTC drug) is appropriate for you to use (given you current health status) while using eye tracker. The software we use will allow you to turn to any face of the package that you wish while the eye tracker tracks what you are looking at. Prior to starting with the eye tracker, we will do a short training with you to show you how to use the software to rotate packages that appear on the screen.

- **Calibration**
  You will be asked to sit in front of our computer and set your head on a chin rest; we will adjust the position of the chin rest and the chair to make you as comfortable as possible. While you look at the computer screen, we will adjust a small camera sitting in front of the computer so that it can track the position of your eye. While holding your head as still as possible, we will ask you to look at a series of the dots on the screen.
- **Eye Tracking Procedure**
  After calibration, you will be asked to view totally 27 package samples one by one on the monitor and decide whether (or not) each of the 27 is appropriate for you to take given your current health status.

- **Post-test:** After the eye tracking test, we will ask you a series of questions regarding your health history and the research team will go over the medications that you have brought. They will record the name of the drugs and prescribing information. With regard to the OTCs that you have brought, we will record how frequently you take them**. Your name will not be affiliated with any of the information collected.**

A description of this clinical trial will be available on http://www.ClinicalTrials.gov. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

3. POTENTIAL BENEFITS

Even though there is no direct benefit from your participation in this study, it is our hope that the data gathered can be used to provide guidance for the improvement of OTC labeling so that it can better assist consumers during decision making.

4. POTENTIAL RISKS

Risks associated with this research would be minor discomfort stiffness/or soreness from remaining still and resting your chin on the chin rest during this study. If you are uncomfortable and need anything adjusted, or if you need a break, please let the research team know.

You will be asked to read a series of words related to healthcare aloud. It is normal that you may not be familiar with some of these words, but this may be embarrassing to you.

We will also be collecting a substantial amount of information related to your current health status and a complete list of the medications that you take. This information will be recorded with a subject number, not your name. Individual data will only be available to the research team and members of MSUs Human Risk Protection Program (HRPP).

Figure 69 (cont'd)

If you are injured as a result of your participation in this research project, researchers from Michigan State University will assist you in obtaining emergency care, if necessary, for your research-related injuries. If you have insurance for medical care, your insurance carrier will be billed in the ordinary manner. As with any medical insurance, any costs that are not covered or in excess of what are paid by your insurance, including deductibles, will be your responsibility.

The University's policy is not to provide financial compensation for lost wages, disability, pain or discomfort unless required by law to do so. This does not mean that you are giving up any legal rights you may have.

5. PRIVACY AND CONFIDENTIALITY

The data for this project will be kept confidential. All information will be tied to a subject number; collected information will not be identified by name and your confidentiality will be maintained to the maximum extent of the law. Information retrieved during this entire study will be protected on a password protected computer or in a locked file cabinet on the campus of Michigan State University for a minimum of three years after the close of the project.

Only the appointed researchers and the Human Risk Protection Program (HRPP)will have access to the research data. Within these restrictions, results of the study will be made available to you at your request.

The results of this study may be published or presented at professional meetings, but the identities of all research participants will remain anonymous.

6. YOUR RIGHTS TO PARTICIPATE, SAY NO, OR WITHDRAW

Participation is voluntary. Refusal to participate in this study will involve no penalty or loss of benefits to which you are otherwise entitled. It is your right to choose whether to participate or not. Also, you may refuse to participate in certain procedures or to answer certain questions, or discontinue your participation at any time.

7. COSTS AND COMPENSATION

There is no cost for being in this study. You will be given $40 as compensation for participation.

8. CONFLICT OF INTEREST

This research is being sponsored by the Education Foundation of the Consumer Healthcare Products Association (CHPA). The CHPA is a trade association whose members produce and sell OTC drugs.

9. CONTACT INFORMATION

If you have concerns or questions about this study, such as scientific issues, how to do any part of it, or to report an injury, please contact the researcher (Laura Bix 517-355-4556; 153 Packaging Building East Lansing, MI 48824 bixlaura@msu.edu).

This consent form was approved by a Michigan State University Institutional Review Board.
Approved 07/2/2014 - valid through - 07/01/2015. This version supersedes all previous versions. IRB #14-679

Figure 69 (cont'd)

If you have questions or concerns about your role and rights as a research participant, would like to obtain information or offer input, or would like to register a complaint about this study, you may contact, anonymously if you wish, the Michigan State University's Human Research Protection Program at 517-355-2180, Fax 517-432-4503, or e-mail irb@msu.edu or regular mail at Olds Hall, 408 West Circle Drive #207, MSU, East Lansing, MI 48824.

9. DOCUMENTATION OF INFORMED CONSENT.

Your signature below means that you voluntarily agree to participate in this research study.

---------- ----------

Signature Date

(You will be given a copy of this form to keep.)

10. DOCUMENTATION OF RECEIPT OF INCENTIVE

I have received the $40 incentive _____

_____

Date

This consent form was approved by a Michigan State University Institutional Review Board.
Approved 07/2/2014 - valid through - 07/01/2015. This version supersedes all previous versions. IRB #14-679

Appendix D. Pre-Test Survey Form

PRE-TEST **SUBJECT #:_____**

Subject #		Visual Acuity		Health Literacy	

SECTION A	1	2	3	4	5
ANSWERS					

----------No answers in the tables above----------

SECTION A: DEMOGRAPHIC INFORMATION

( ) 1. What is your gender?

☐ Female ☐ Male ☐ Transgendered

( ) 2. What is your current age?

_____

( ) 3. What is your ethnicity?

☐ White, non-Hispanic
☐ Asian or Pacific Islanders
☐ African Americans, non-Hispanic
☐ American Indian/Alaskan Natives
☐ Hispanic
☐ Others: _____

( ) 4. What is your highest educational level?

☐ Middle School
☐ High School
☐ Associate Degree
☐ Bachelor Degree
☐ Master Degree
☐ Doctor Degree

( ) 5. What is your native language?

☐ English ☐ Russian ☐ Others:
☐ Spanish ☐ Chinese _____
☐ French ☐ Japanese

SECTION B: NEAR POINT VISUAL ACUITY AND HEALTH LITERACY

PART I. Near Point Visual Acuity

Visual Acuity	

----------No answers in the tables above----------

Visual Acuity: I want you to hold this card at about 16 inches from your eyes and try to read the lowest line on this card.

20/800: D T 4

20/400: L E S 3

20/250: R F X B N

20/200: P O 5 7 A

20/100: 8 C V L M

20/70: 3 7 S Z K

20/50: E X R T N

20/40: D M P R O F

20/30: F H G J X V

20/20: 3 A S R E P

Result: 20/____

PART II. REALM-R Examiner Record

fat		fatigue	_____
flu		directed	_____
pill		colitis	_____
allergic	_____	constipation	_____
jaundice	_____	osteoporosis	_____
anemia	_____		

Fat, Flu, and Pill are not scored. We have previously used a score of 6 or less to identify patients at risk for poor literacy.

Score _____

Appendix E. Rapid Estimate of Adult Literacy in Medicine-Revised (REALM-R)

Available at: http://www.ahrq.gov/sites/default/files/wysiwyg/professionals/quality-patient-safety/pharmhealthlit/REALM-R.pdf

Description of the Test

The REALM-R is a brief screening instrument used to assess an adult patient's ability to read common medical words. It is designed to assist medical professionals in identifying patients at risk for poor literacy skills. The REALM-R is a ***word recognition*** test – not a reading comprehension instrument. Adults are asked to de-code or pronounce words. The test takes less than 2 minutes to administer and score.

Preliminary data regarding the REALM-R has been published in the *Journal of General Internal Medicine* December 2003; 18:1036-1038.

Administration and Scoring:

1. Give the patient the laminated copy of the REALM-R word list. Attach the examiner record form to the clipboard. Hold the clipboard at an angle such that the patient is not distracted by your scoring procedure.

In your own words, introduce the REALM-R to the patient:

In a research setting or for research purposes:

"It would be helpful for us to get an idea of what medical words you are familiar with. What I need you to do is look at this list of words, beginning here [point to first word with pencil] *. Say all of the words you know. If you come to a word you don't know, you can sound it out or just skip it and go on."*
If the patient stops, say, *"Look down this list* [point] *and say the other words you know."*

In a clinical setting:

"Sometimes in this office, we may use medical words that patients aren't familiar with. We would like you to take a look at this list of words to help us get an idea of what medical words you are familiar with. It will help us know what kinds of patient education to give you. Start with the first word [point to 1st word with pencil]*, please say all of the words you know. If you come to a word you do not know, you can sound it out or just skip it and go on."* If patient stops do as above.

**Special Note: Do not use the words "read" and "test" when introducing and administering the REALM-R. These words may make patients feel uncomfortable and unwilling to participate.

"Please <u>say</u> these words for me?"

2. If the patient takes more than 5 seconds on a word, encourage the patient to move along by saying,

"Let's try the next word."

If the patient begins to miss every word or appears to be struggling or frustrated, tell the patient,

"Just look down the list and say the words you know."

3. Count as an error any word that is not attempted or mispronounced (see "Special Considerations" for pronunciation/scoring guidelines).

4. Scoring options:

1) Place a check mark on the line next to each word the patient pronounces correctly.

OR

2) Place an X on the line next to each word the patient does not attempt or mispronounces.

Scoring should be strict, but take into consideration any problems which could be related to dialect or articulation difficulties. Use the dictionary if in doubt. Count as correct any self-corrected word. ***In our study we chose to define 'at risk patients' as those with a score of six or less.***

Special Considerations for Administration and Scoring:

Examiner Sensitivity:

Many low literate patients will attempt to hide their deficiency. Ensure that you approach each patient with respect and compassion. You may need to provide encouragement and reassurance.

A positive, respectful attitude is essential for all examiners. (Remember, many people with low literacy feel ashamed.) Be sensitive.

***Visual Acuity*:**

If the patient wears glasses, ask him/her to put them on for this test. The REALM-R is designed to be read by persons with 20/100 vision or better. For vision of 20/100 or better I have used a font size of 18. In my studies we have excluded patients with worse vision. The REALM has a visually impaired version using a font size of 28.

***Pronunciation*:**

Dictionary pronunciation is the scoring standard.

***Dialect, Accent or Articulation Problems*:**

Count a word as correct if the word is pronounced correctly and no additions or deletions have been made to the beginning or ending of the word. For example: A patient who says "jaundiced" would not receive credit for the word "jaundice"; "directs" would not receive credit for the word "directed"; "colon" would not receive credit for "colitis". Words pronounced with a dialect or accent should be counted as correct provided there are no additions or deletions to the word. Particular attention should be paid for patients who use English as a second language.

REALM-R Examiner Record

Reading Level _____

Patient Name/
Subject # _____ Date of Birth _____

Grade Completed _____

Date _____ Clinic _____ Examiner _____

fat		fatigue	____
flu		directed	____
pill		colitis	____
allergic	____	constipation	____
jaundice	____	osteoporosis	____
anemia	____		

Fat, Flu, and Pill are not scored. We have previously used a score of 6 or less to identify patients at risk for poor literacy.

Score _____

fat

flu

pill

allergic

jaundice

anemia

fatigue

directed

colitis

constipation

osteoporosis

Appendix F. Near Point Visual Acuity Card

Figure 70 Near Point Vision Acuity Card

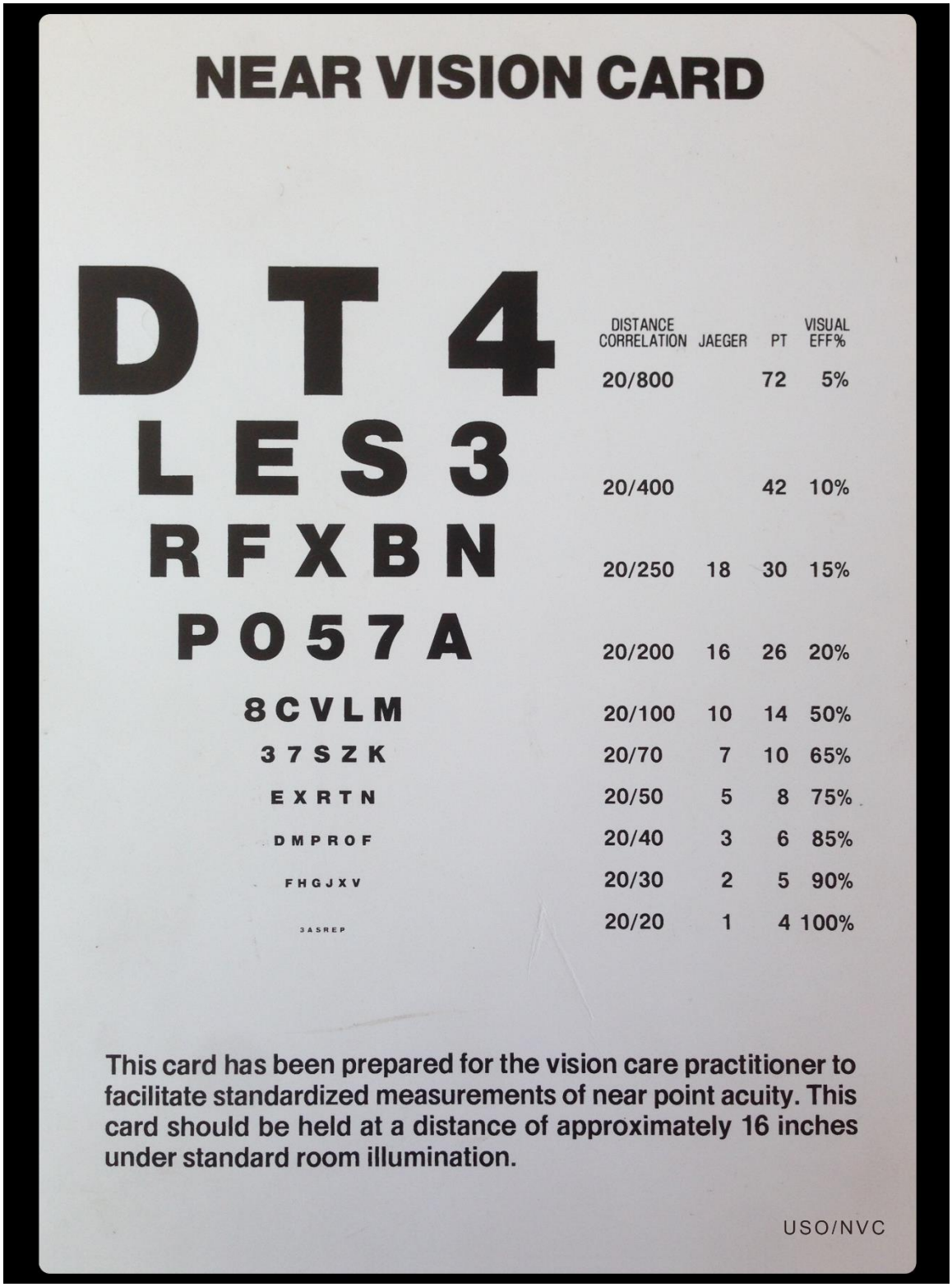
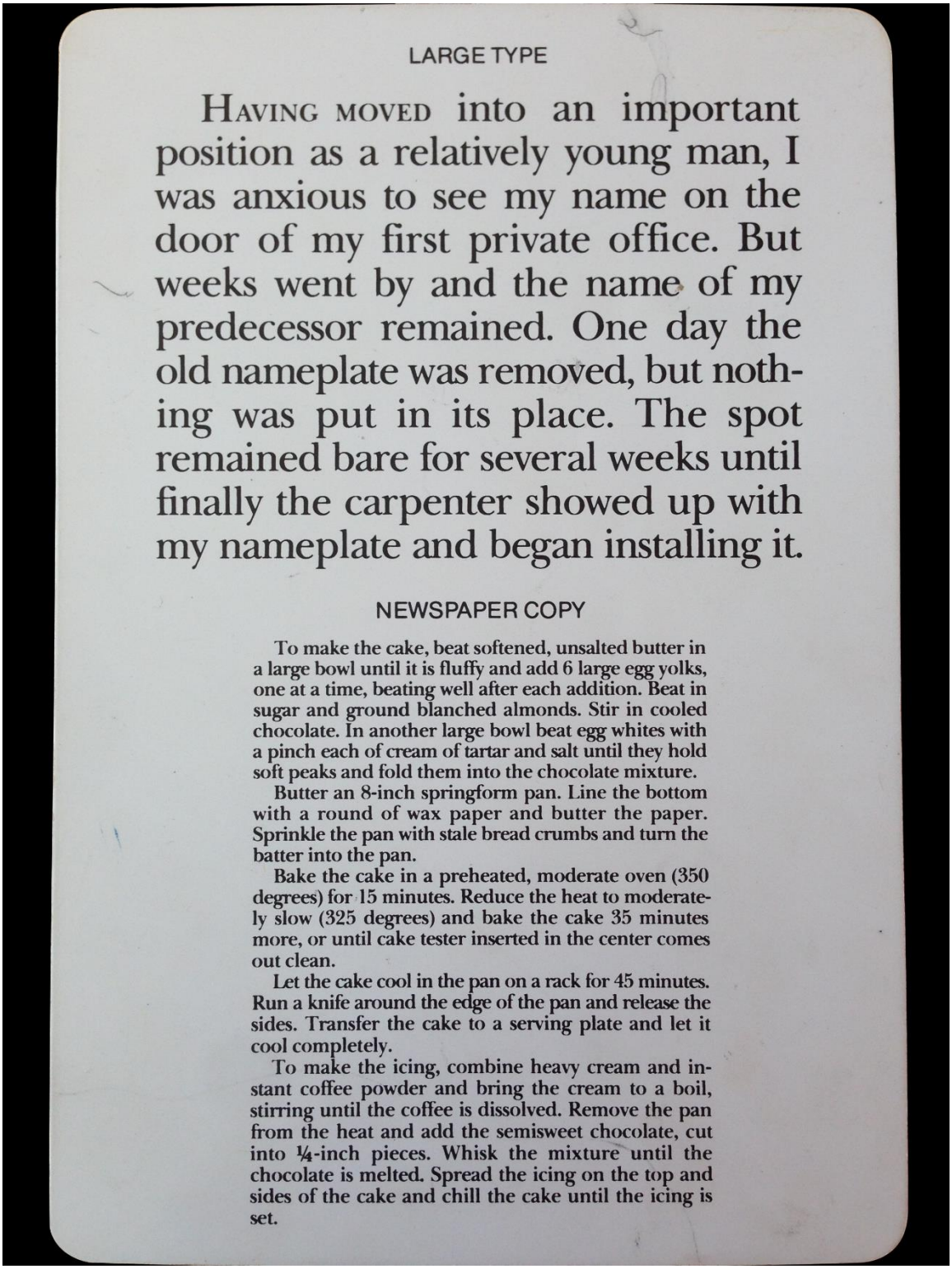


Figure 70 (cont'd)



LARGE TYPE

HAVING MOVED into an important position as a relatively young man, I was anxious to see my name on the door of my first private office. But weeks went by and the name of my predecessor remained. One day the old nameplate was removed, but nothing was put in its place. The spot remained bare for several weeks until finally the carpenter showed up with my nameplate and began installing it.

NEWSPAPER COPY

To make the cake, beat softened, unsalted butter in a large bowl until it is fluffy and add 6 large egg yolks, one at a time, beating well after each addition. Beat in sugar and ground blanched almonds. Stir in cooled chocolate. In another large bowl beat egg whites with a pinch each of cream of tartar and salt until they hold soft peaks and fold them into the chocolate mixture.

Butter an 8-inch springform pan. Line the bottom with a round of wax paper and butter the paper. Sprinkle the pan with stale bread crumbs and turn the batter into the pan.

Bake the cake in a preheated, moderate oven (350 degrees) for 15 minutes. Reduce the heat to moderately slow (325 degrees) and bake the cake 35 minutes more, or until cake tester inserted in the center comes out clean.

Let the cake cool in the pan on a rack for 45 minutes. Run a knife around the edge of the pan and release the sides. Transfer the cake to a serving plate and let it cool completely.

To make the icing, combine heavy cream and instant coffee powder and bring the cream to a boil, stirring until the coffee is dissolved. Remove the pan from the heat and add the semisweet chocolate, cut into ¼-inch pieces. Whisk the mixture until the chocolate is melted. Spread the icing on the top and sides of the cake and chill the cake until the icing is set.

Appendix G. Medication Samples for Experiment 1

Figure 71 Medication Samples for Experiment 1

Appendix H. Data Recording Sheet for Experiment 1

Table 11 Data Recording Sheet for Experiment 1

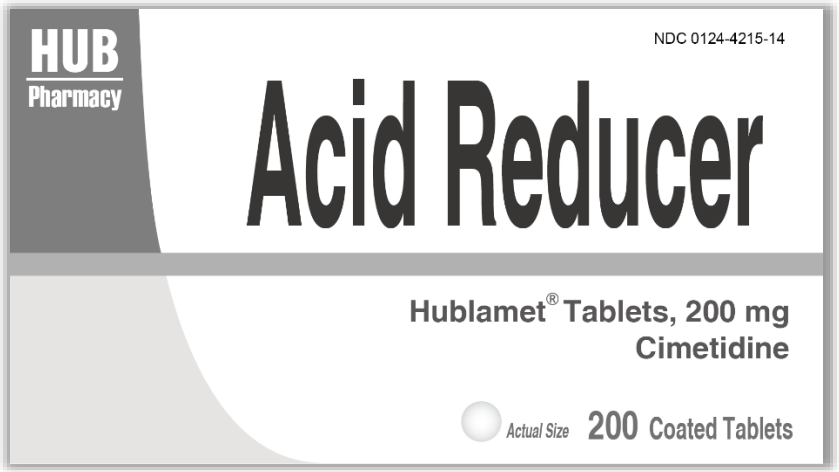
Subject # _____ Date: _____

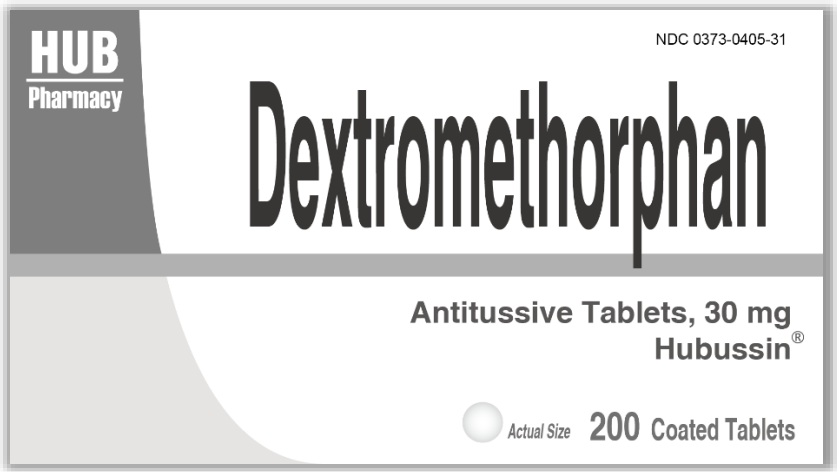
Questions	Drug Choice	Rotate or not
Set 1: You have been suffering the effects of seasonal allergies. You are seeking an over-the-counter medication to alleviate your symptoms. Please select a product for yourself to take from the set that I show you.	☐ Wal-Dryl ☐ Nasal Strips ☐ Wal-Som ☐ Melatonin ☐ Soothe ☐ Wal-Mucil	☐ Yes ☐ No
Set 2: You have been having difficulty falling asleep. You are seeking an over-the-counter medication to help you. Please select a product for yourself from the set that I show you."	☐ Wal-Dryl ☐ Nasal Strips ☐ Wal-Som ☐ Melatonin ☐ Soothe ☐ Wal-Mucil	☐ Yes ☐ No
Set 3: You have been suffering from diarrhea. You are seeking an over-the-counter medication to help. Please select a product for yourself from the set that I show you.	☐ Wal-Dryl ☐ Nasal Strips ☐ Wal-Som ☐ Melatonin ☐ Soothe ☐ Wal-Mucil	☐ Yes ☐ No

Appendix I. PDP Designs for Experiment 2

Figure 72 PDP Designs for Experiment 2

Figure 72 (cont'd)





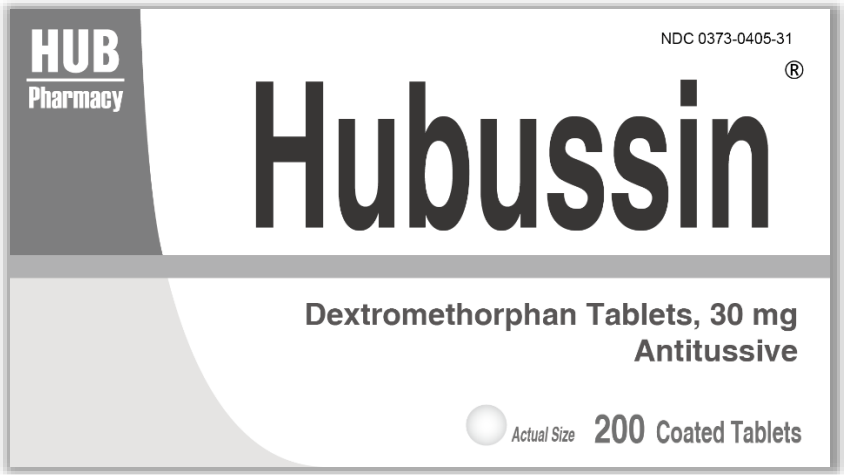


Figure 72 (cont'd)

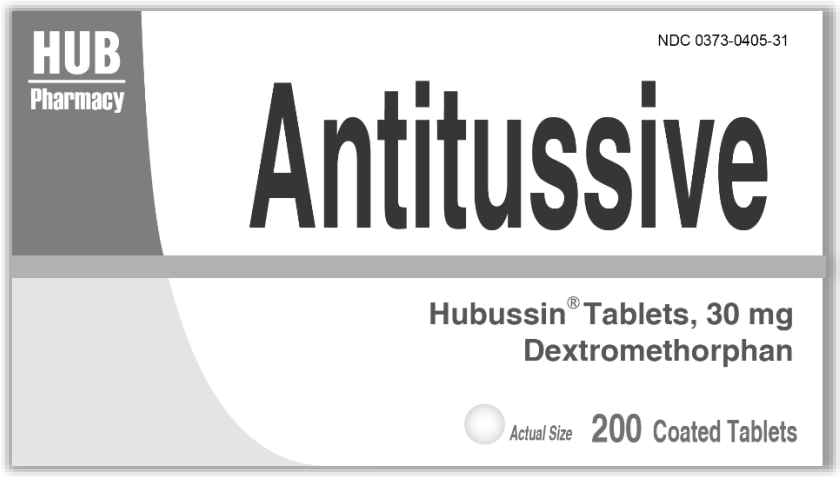


Figure 72 (cont'd)

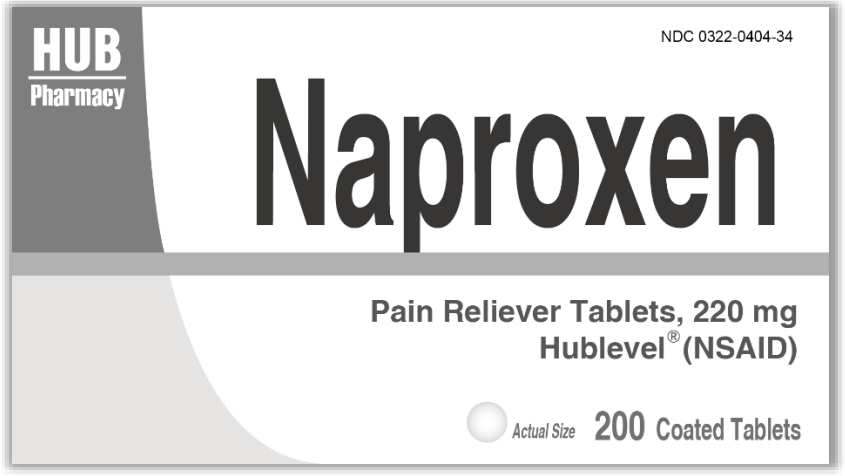


Figure 72 (cont'd)

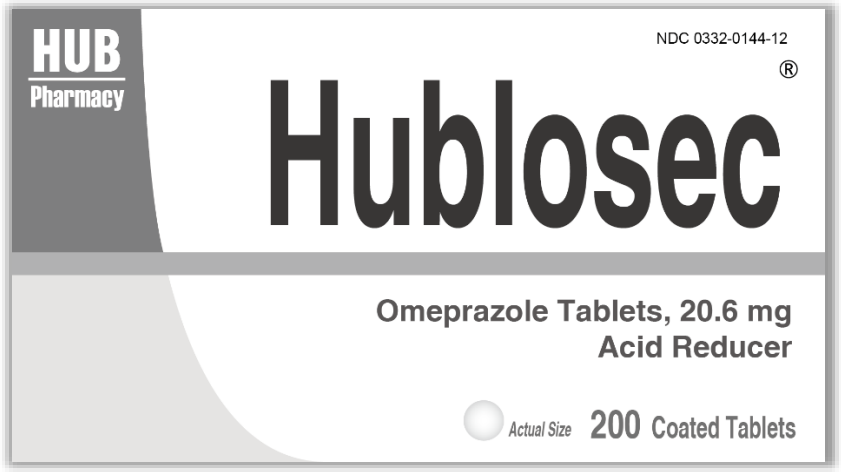


Figure 72 (cont'd)

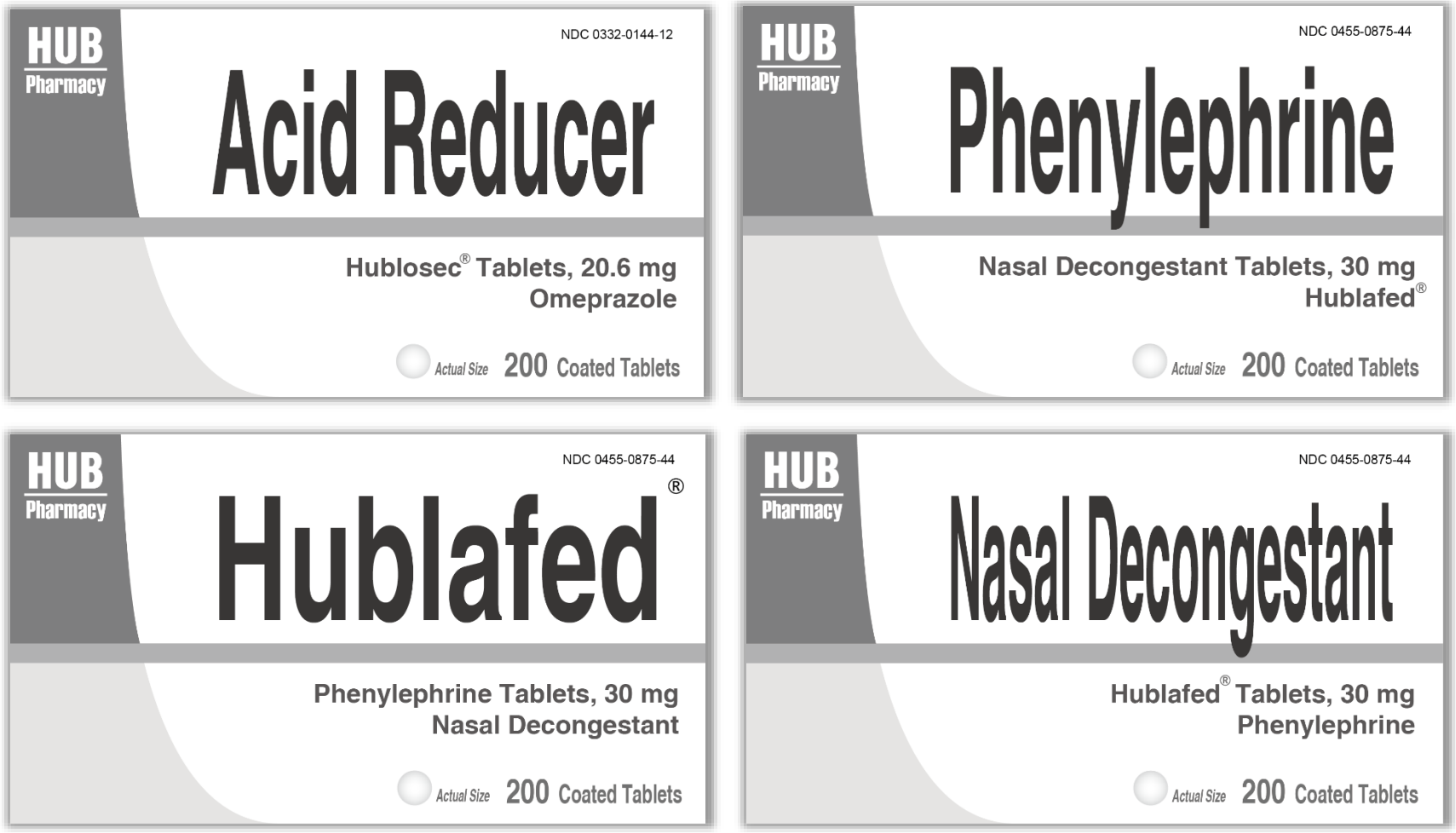
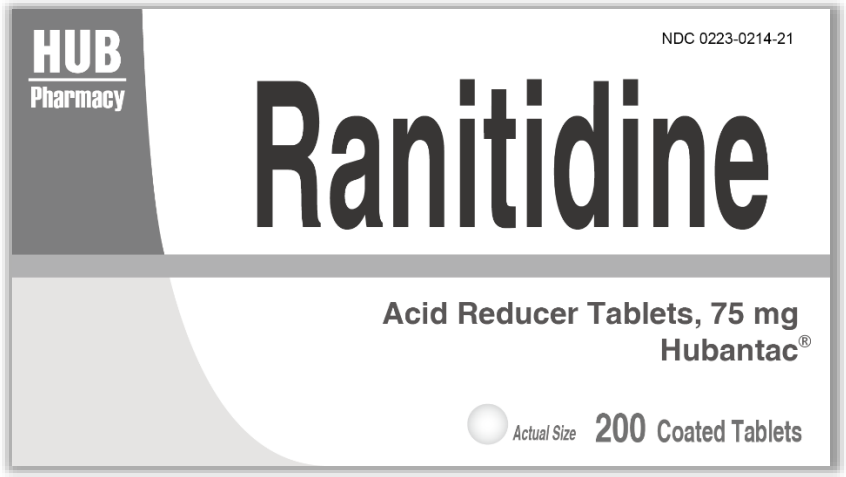
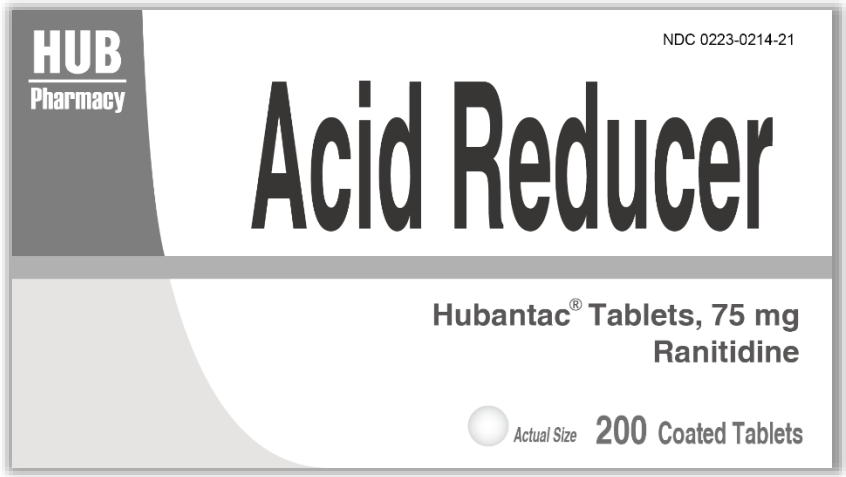


Figure 72 (cont'd)





Appendix J. Expansion Drawings for Sample Design in Experiment 2

To avoid repetition, only the expansion drawings for each active-ingredient-emphasized sample designs (totally 9 designs) are listed below. The PDP design is the only difference between an active-ingredient-emphasized sample and a sample with other information emphasized.

Figure 73 Expansion Drawings for Sample Design in Experiment 2

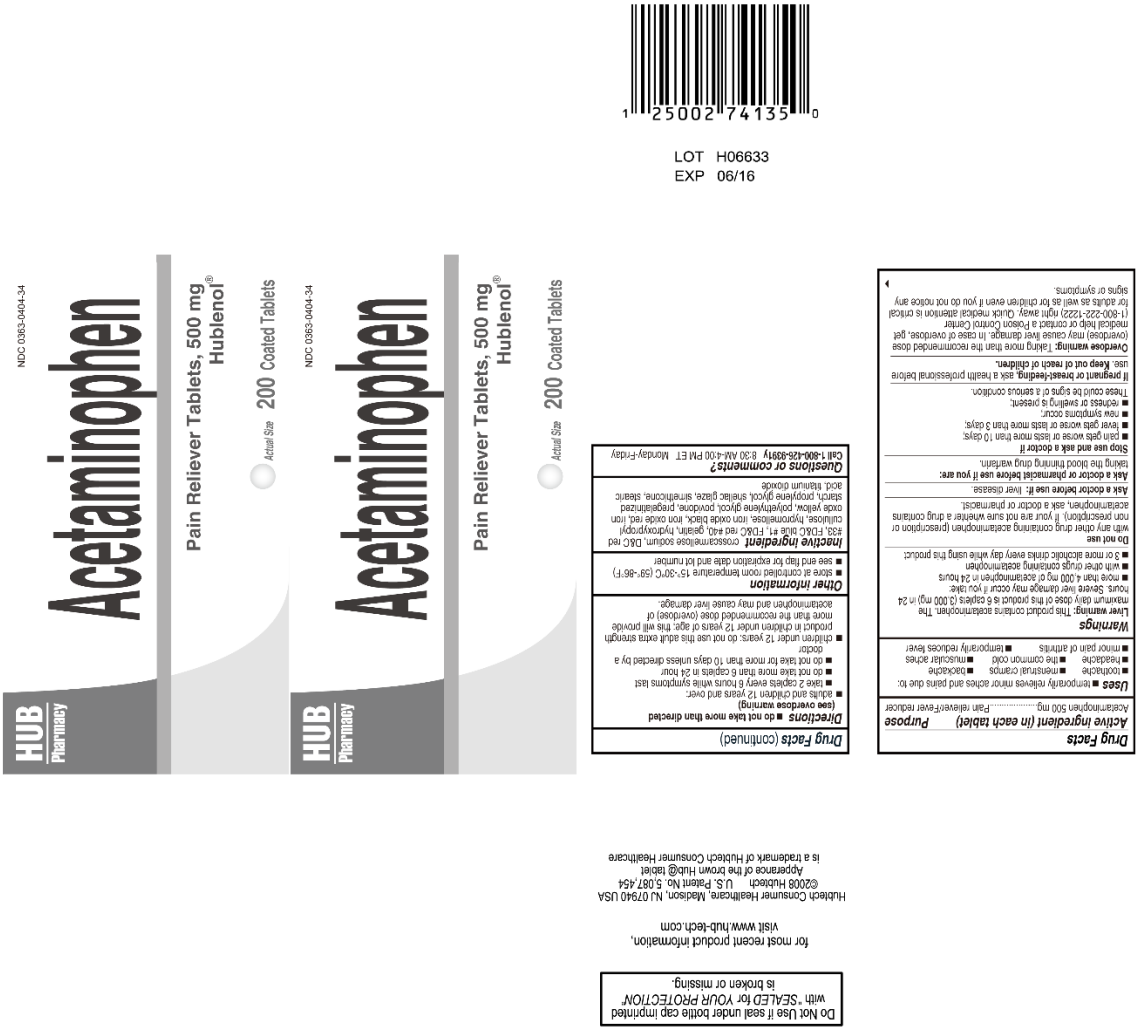


Figure 73 (cont'd)

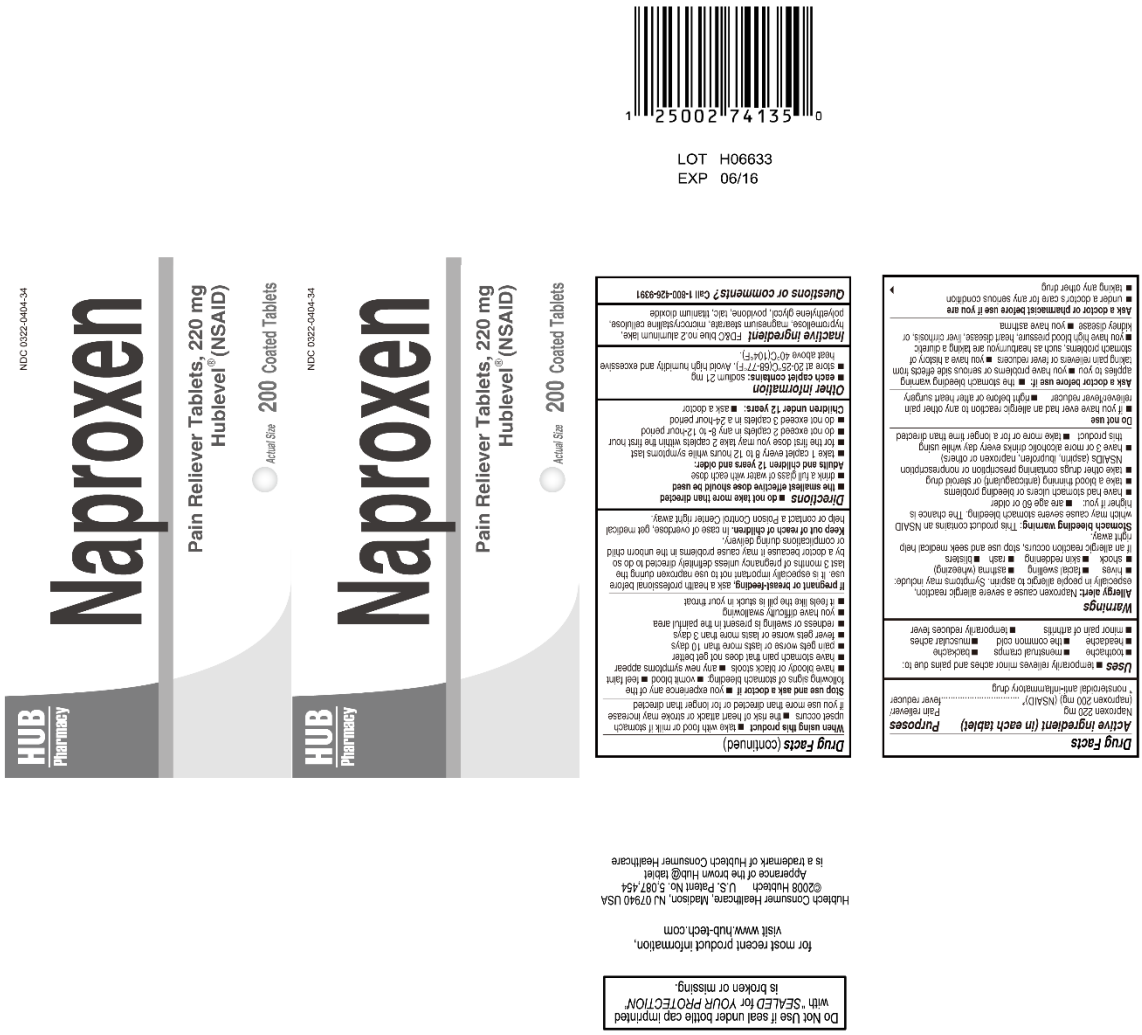


Figure 73 (cont'd)

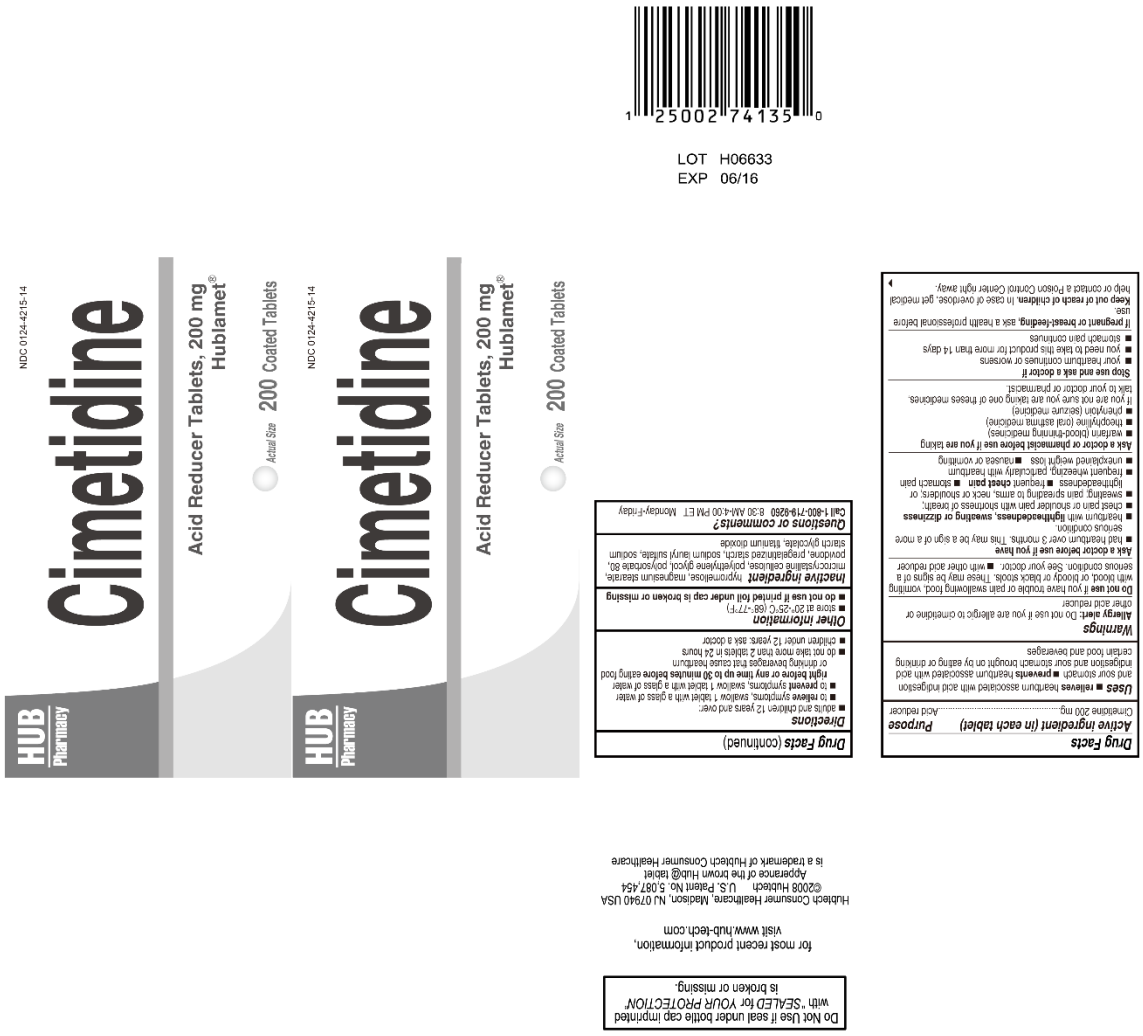


Figure 73 (cont'd)

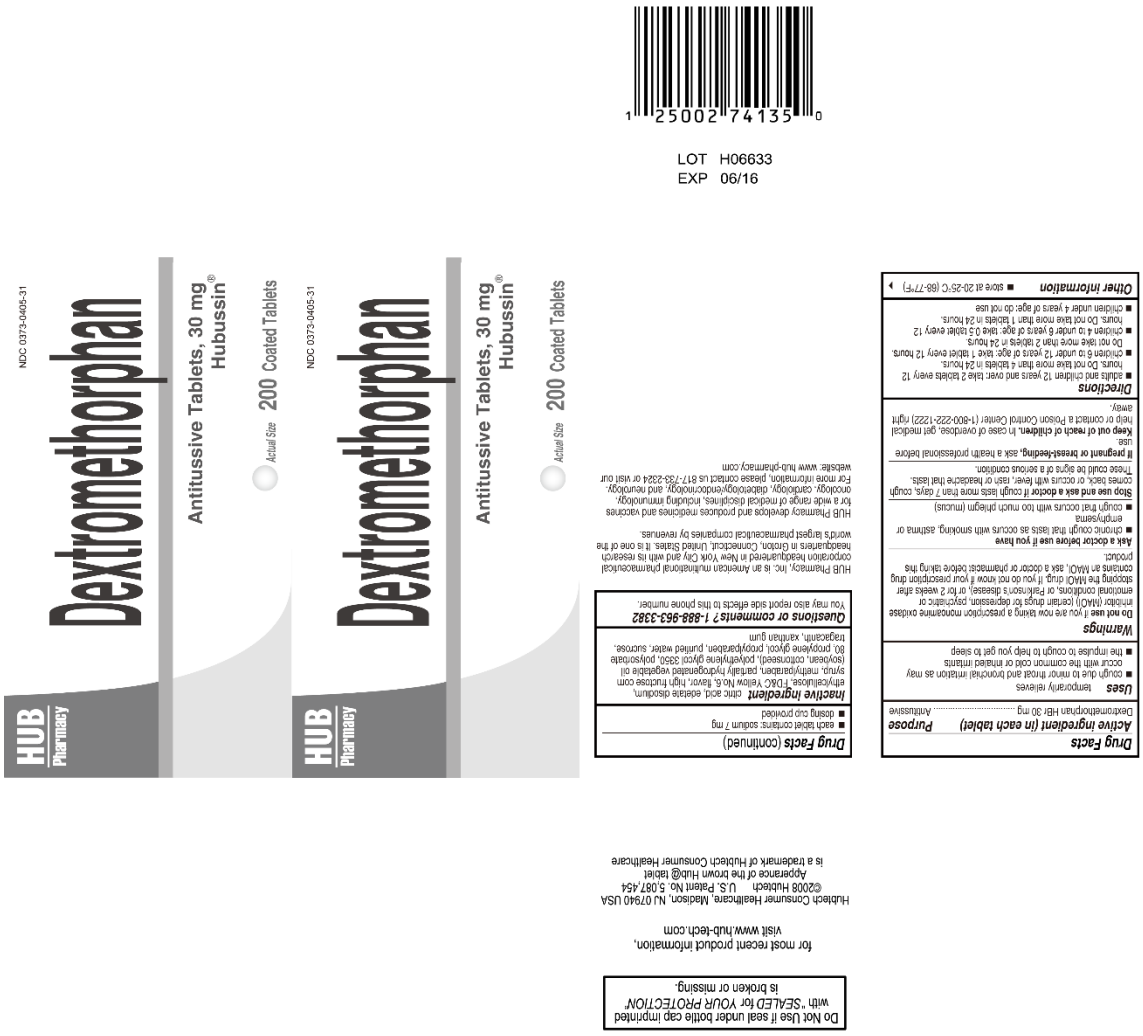


Figure 73 (cont'd)

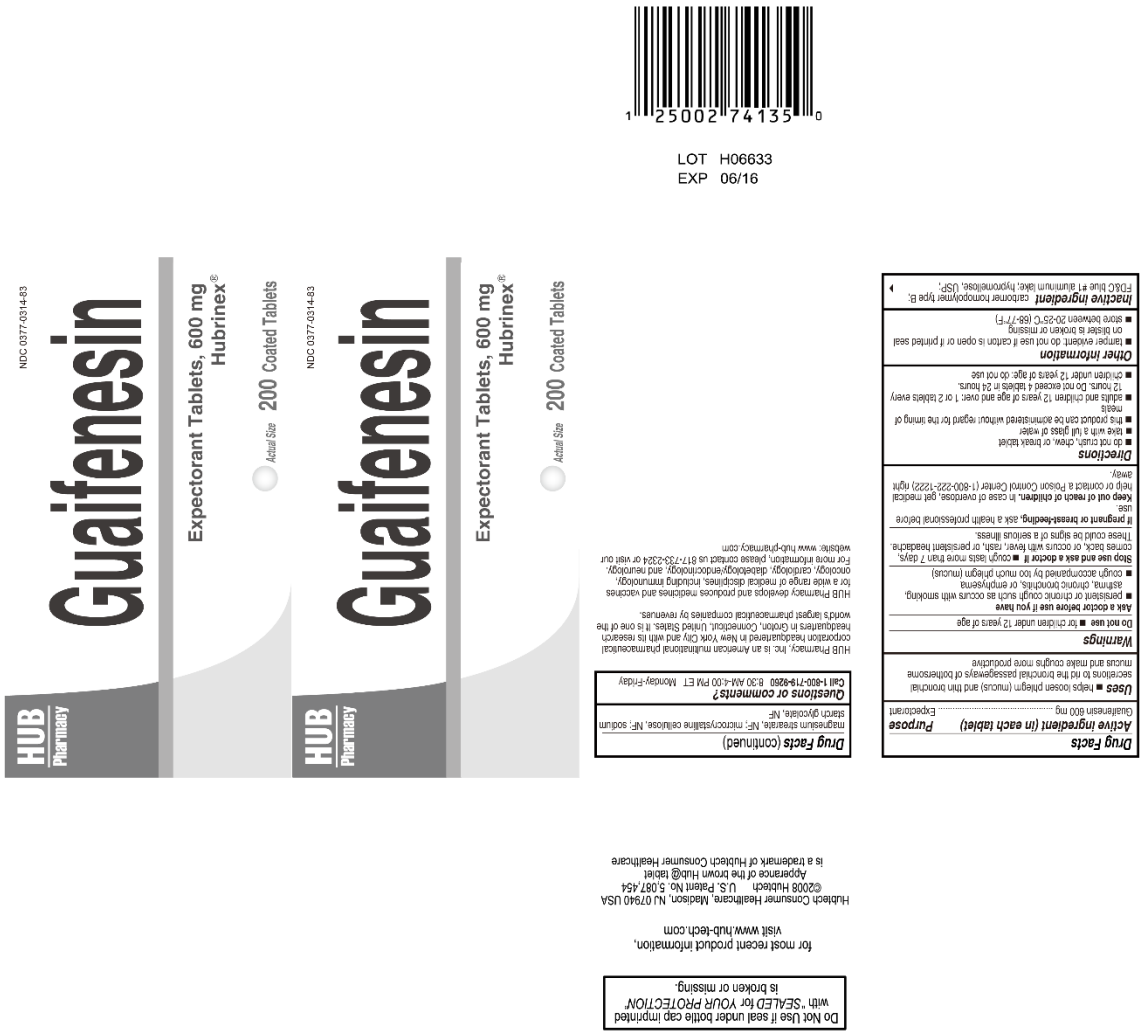


Figure 73 (cont'd)

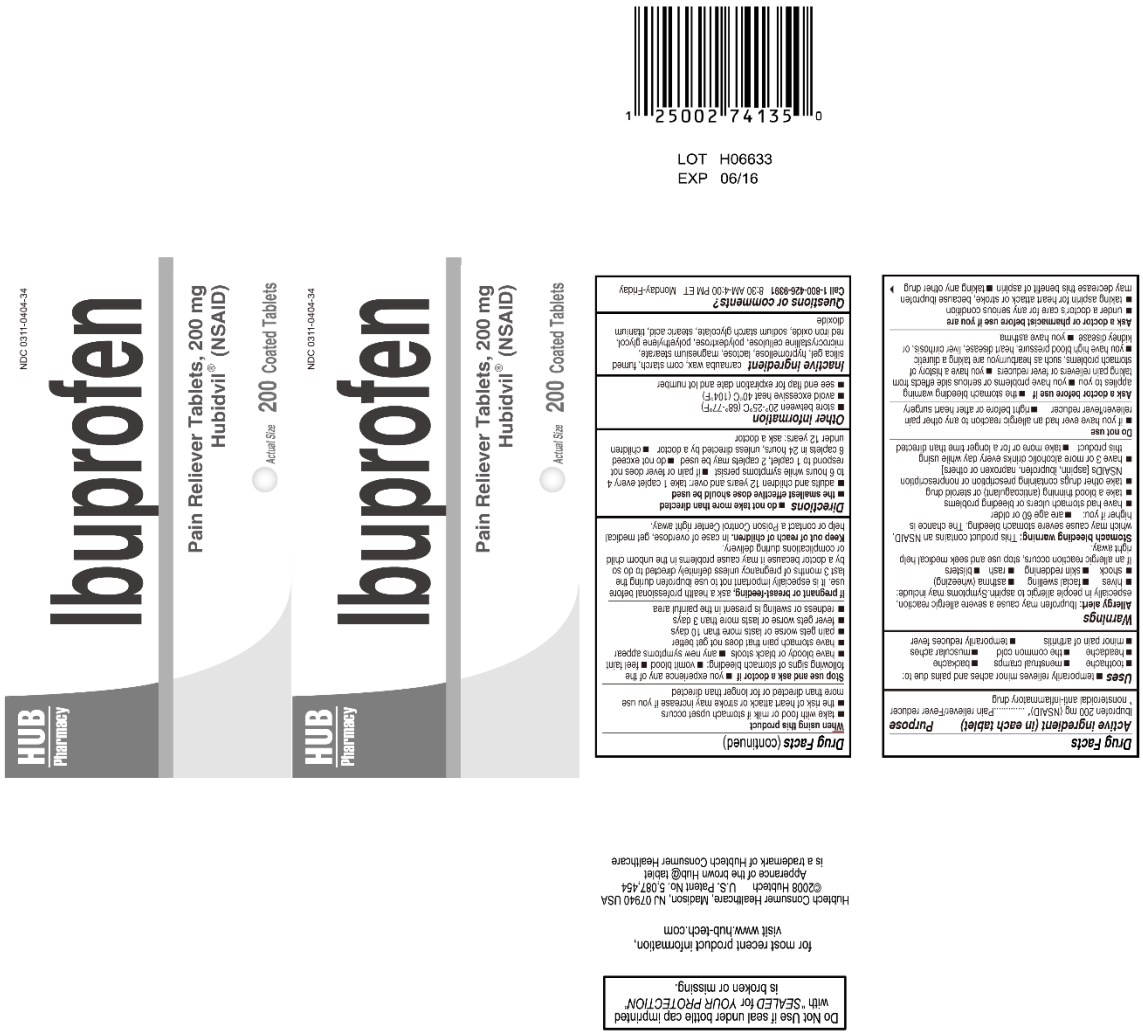


Figure 73 (cont'd)

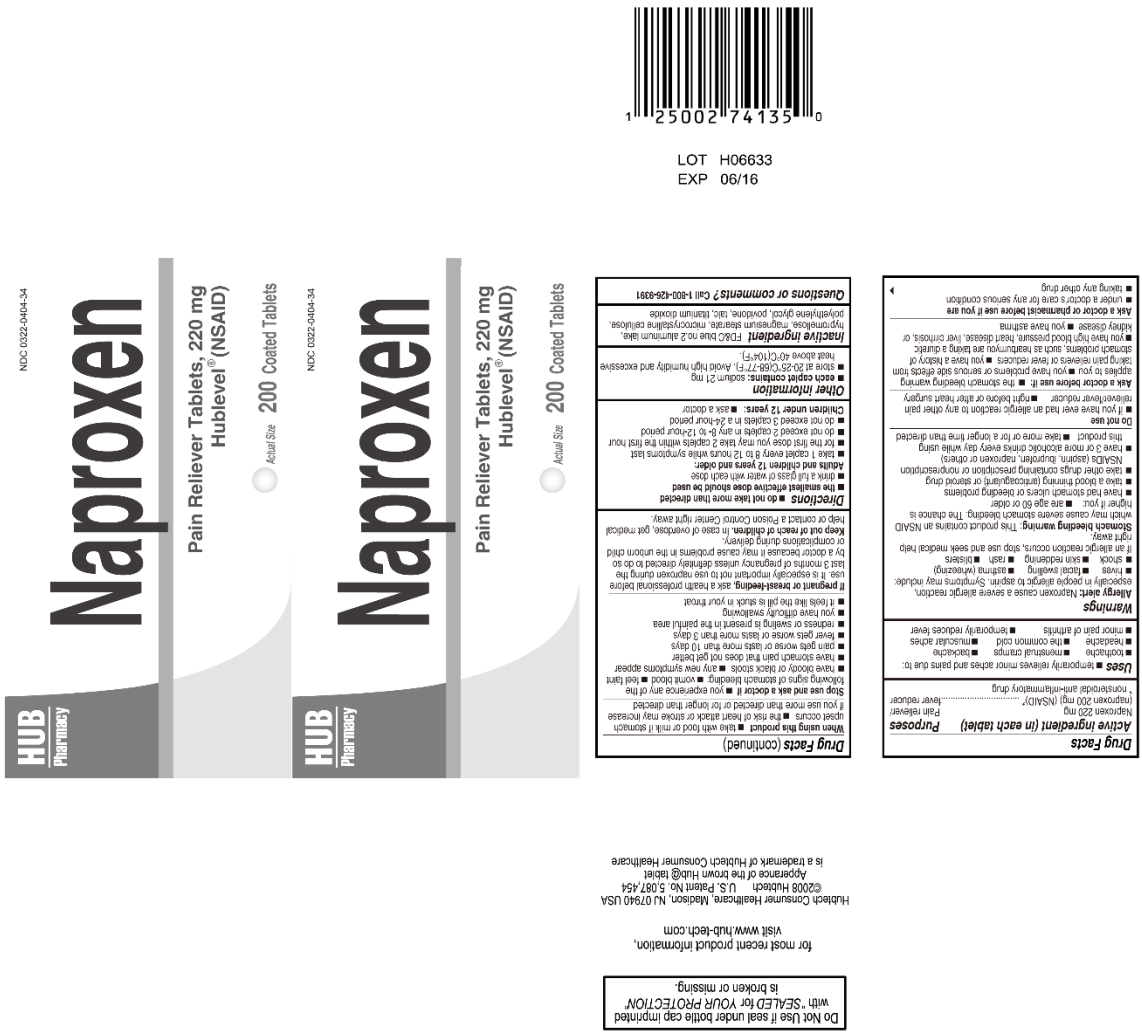


Figure 73 (cont'd)

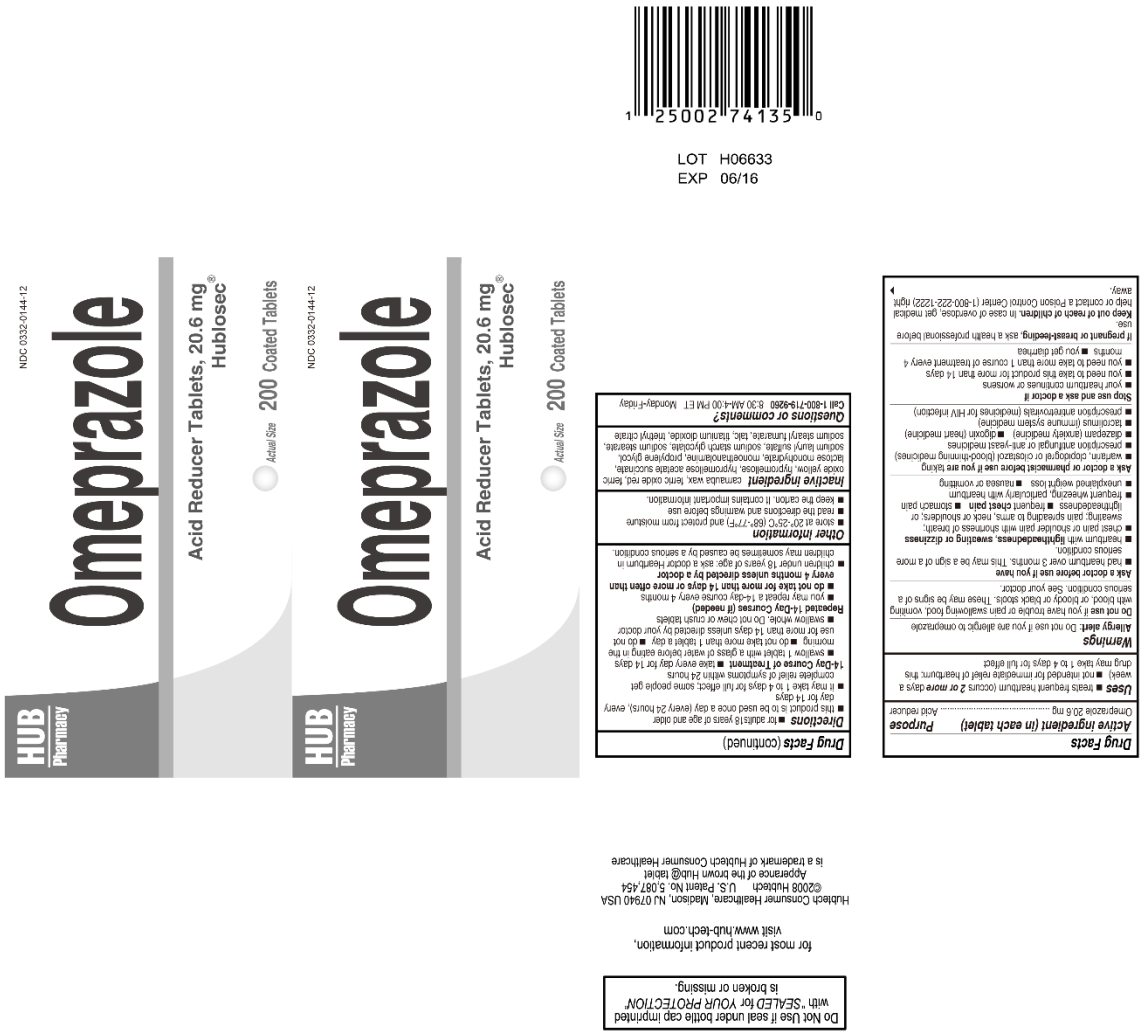


Figure 73 (cont'd)

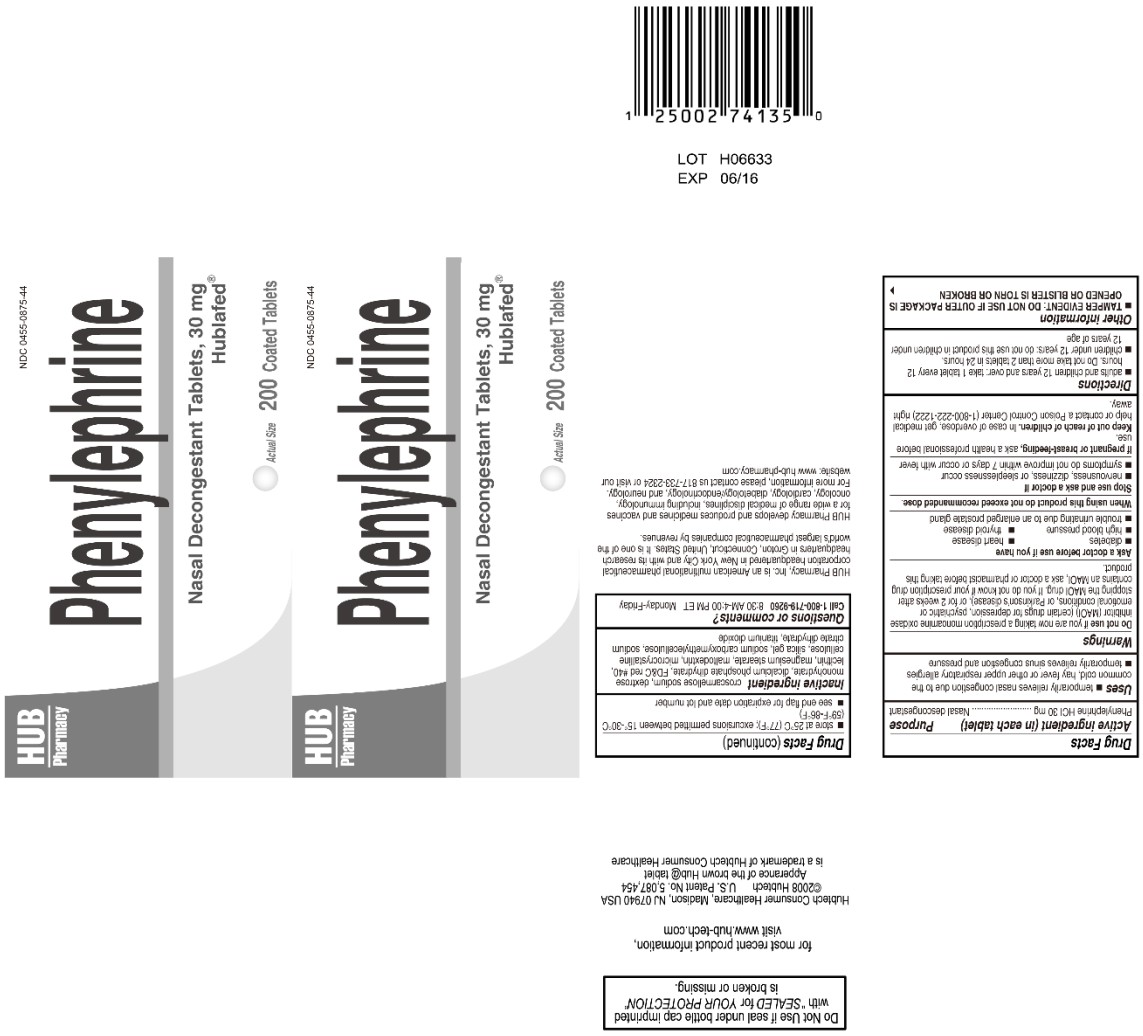
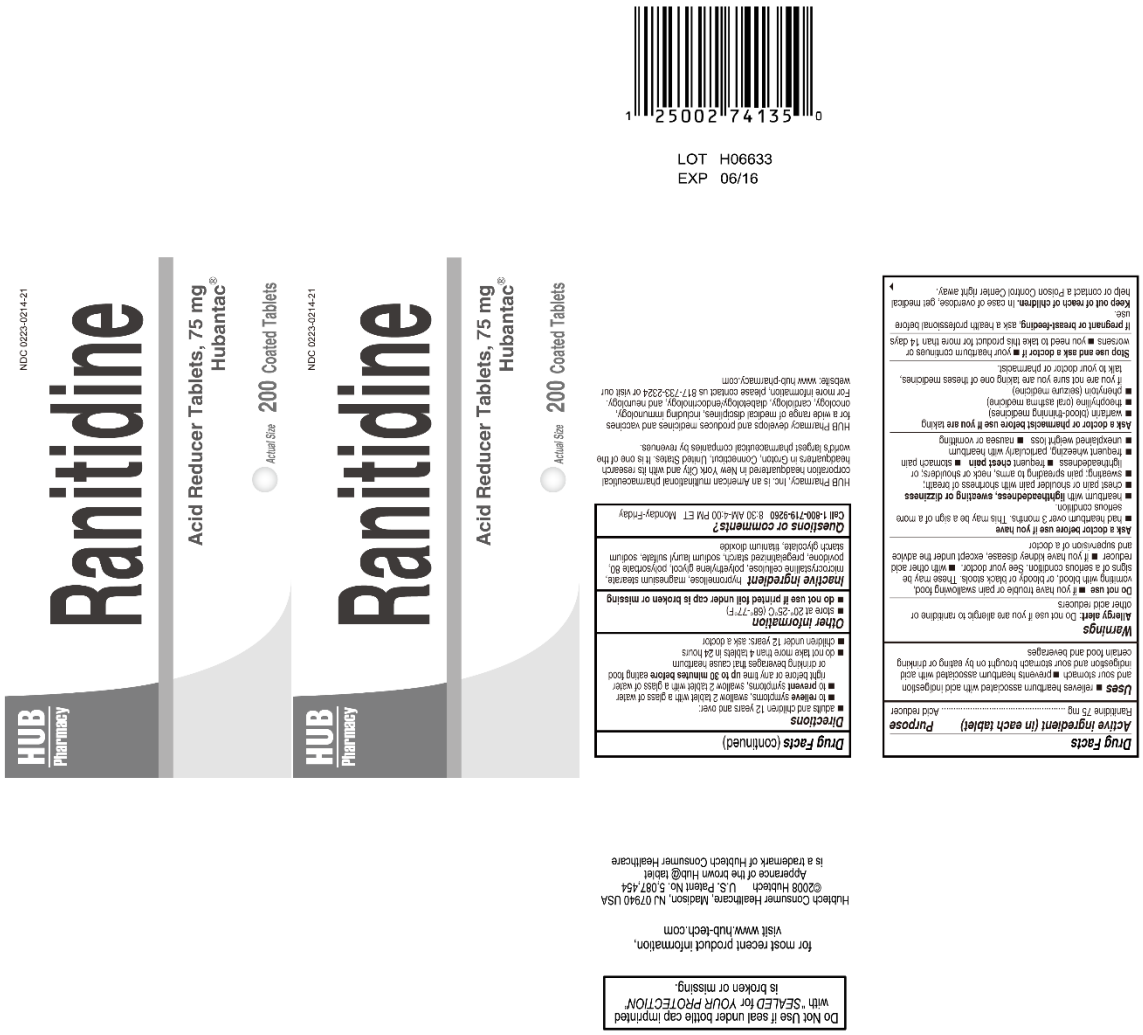


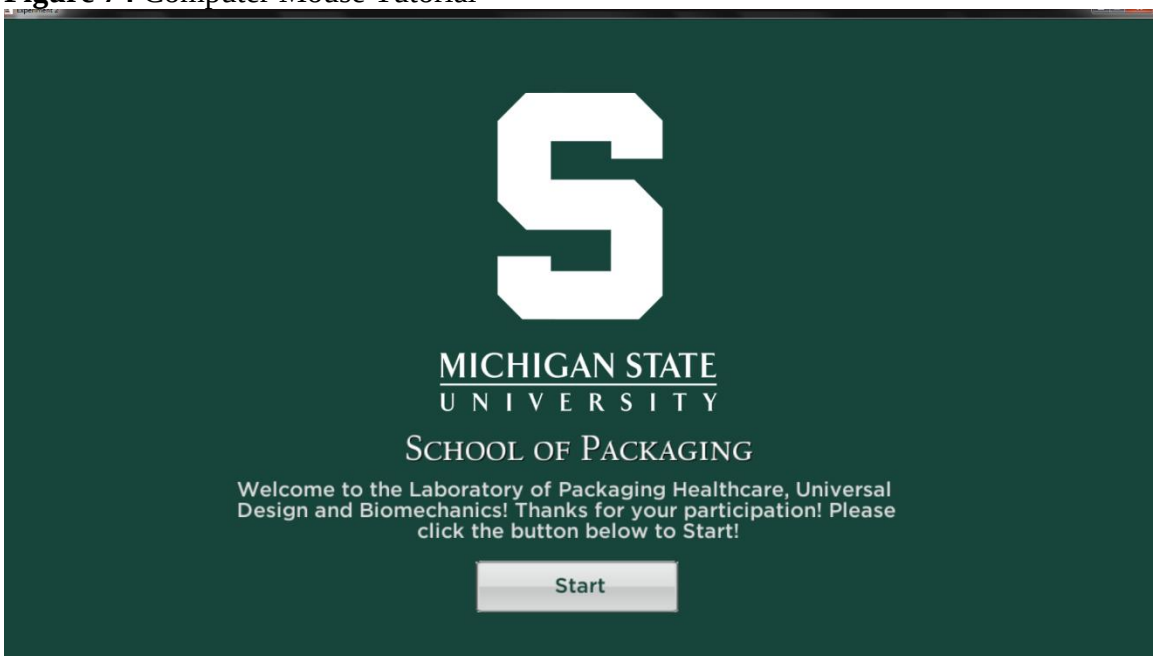
Figure 73 (cont'd)



Appendix K. Testing Program for Experiment 2

Part A Computer Mouse Tutorial

Figure 74 Computer Mouse Tutorial



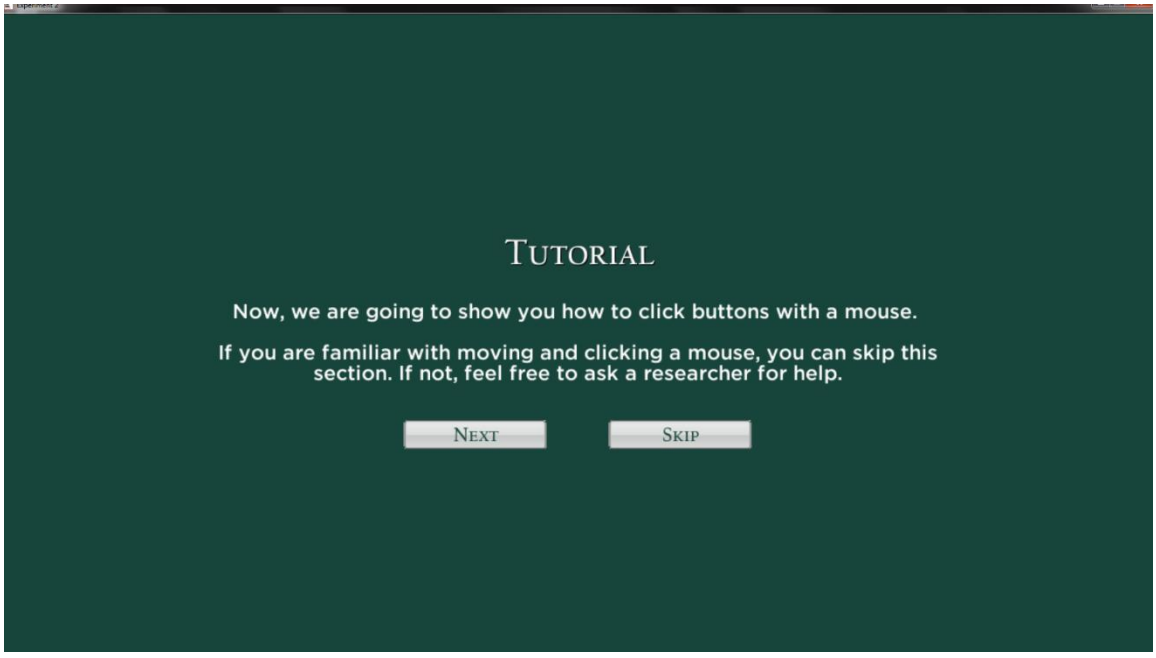
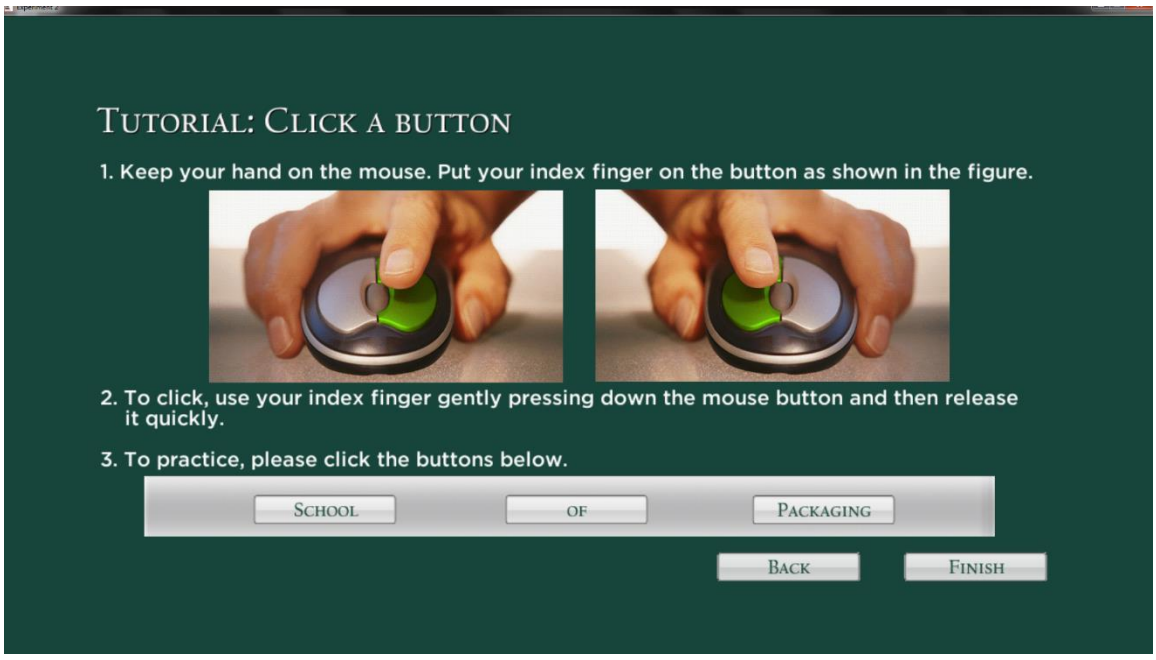


Figure 74 (cont'd)



Part B Testing Program Instructions

Figure 75 Testing Program Instructions

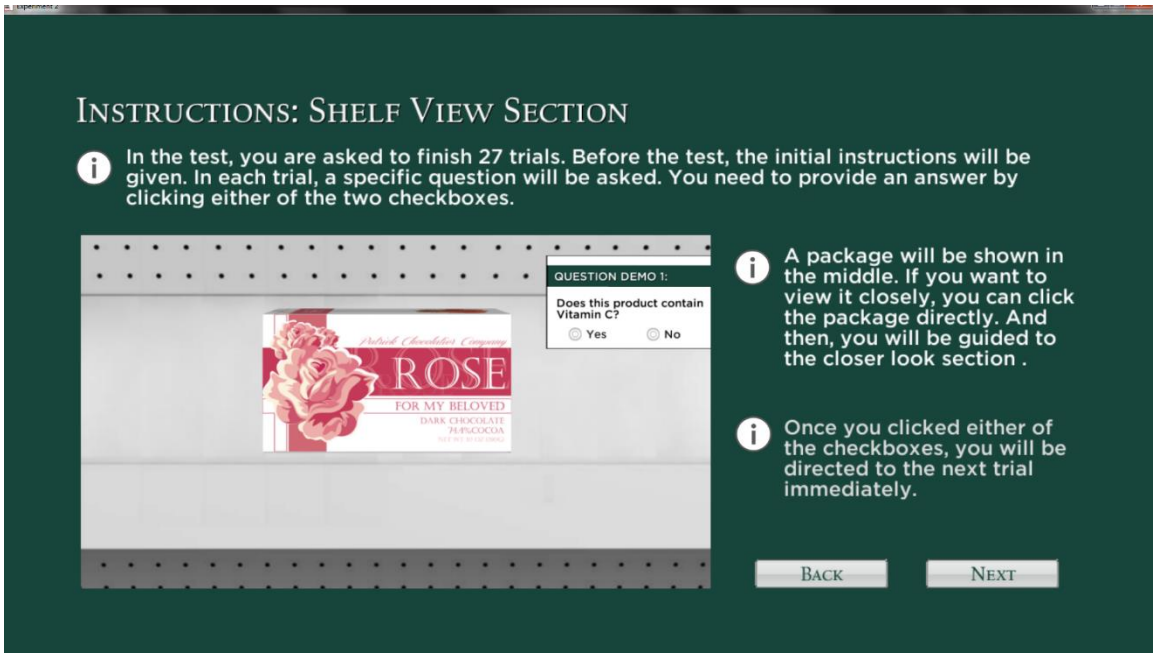
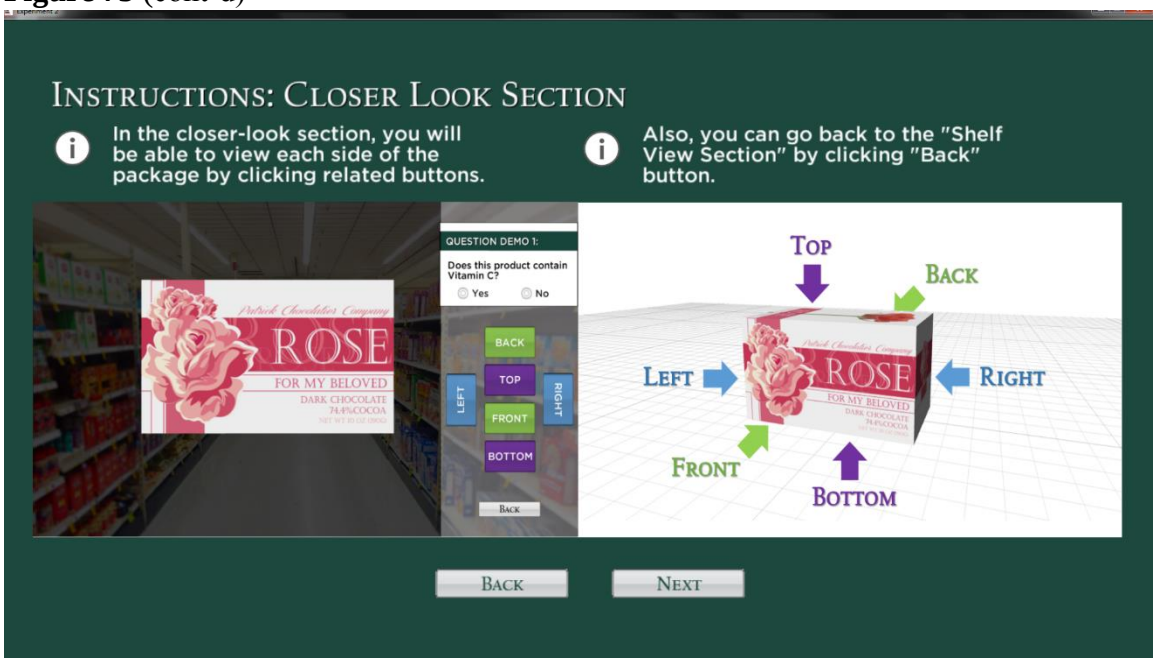


Figure 75 (cont'd)



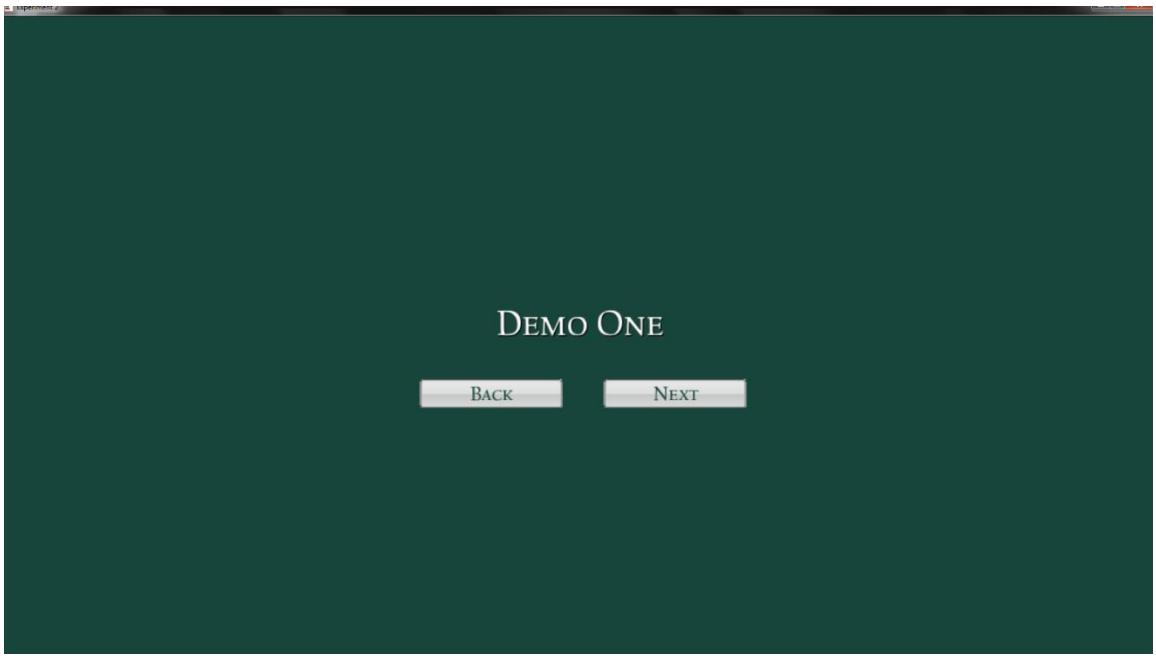


Figure 75 (cont'd)

Figure 75 (cont'd)

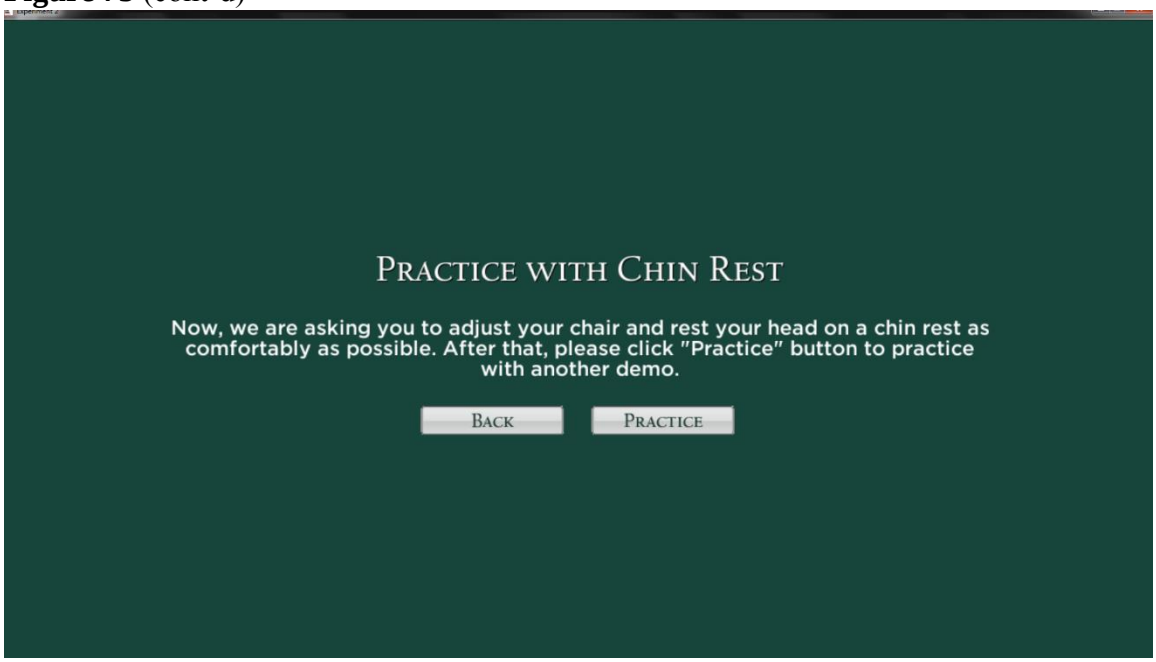
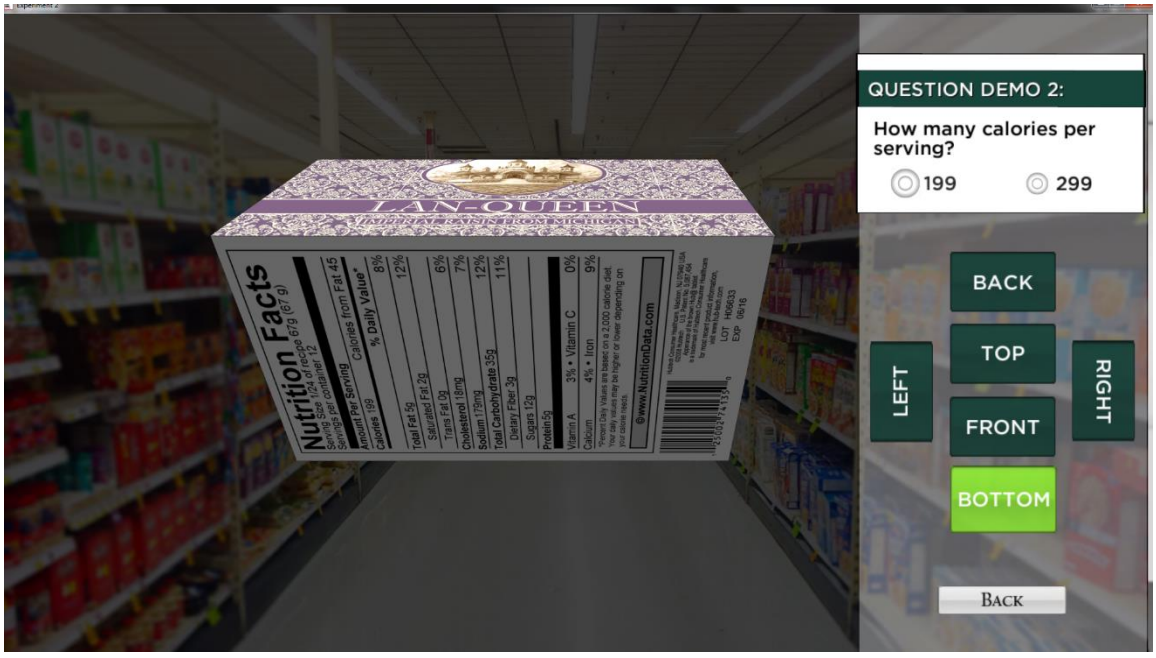


Figure 75 (cont'd)



Part C Main Test

Figure 76 Main Test

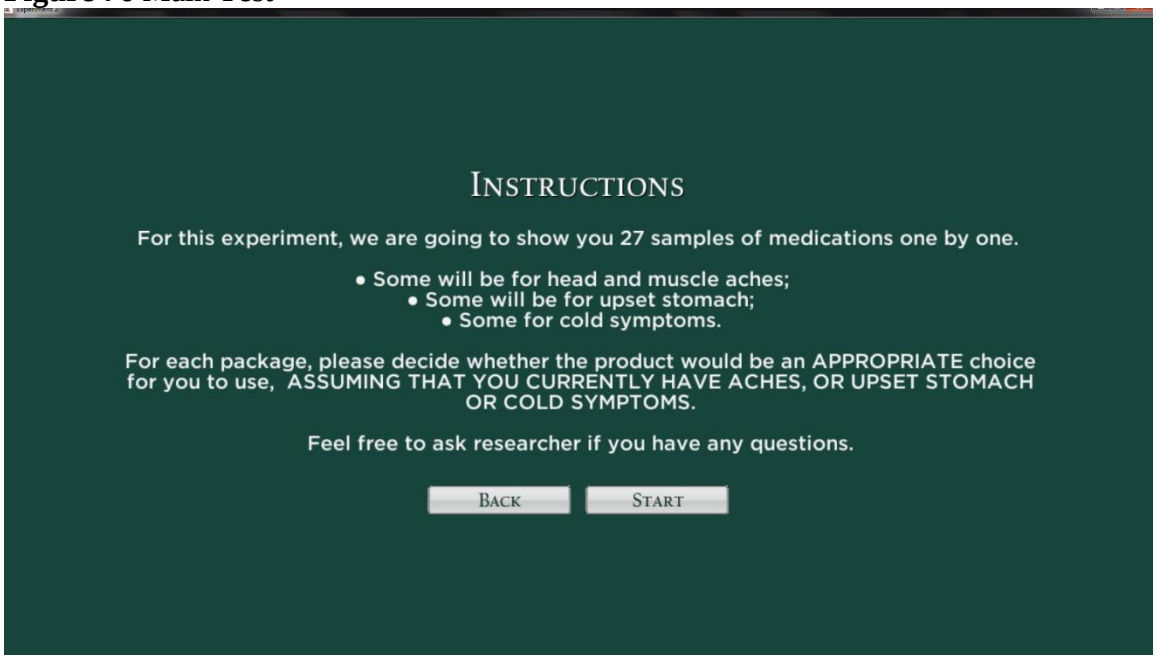


Figure 76 (cont'd)

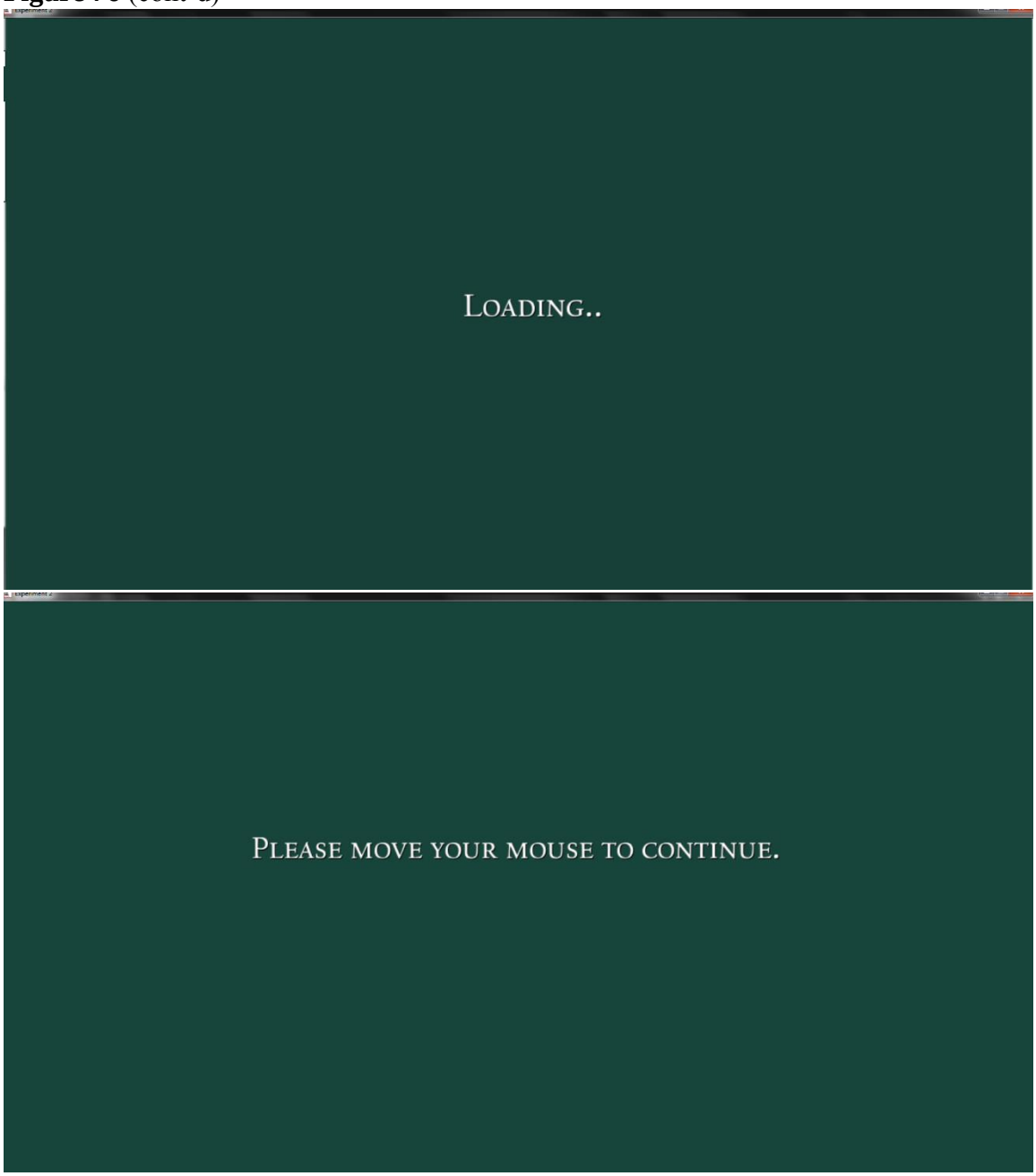
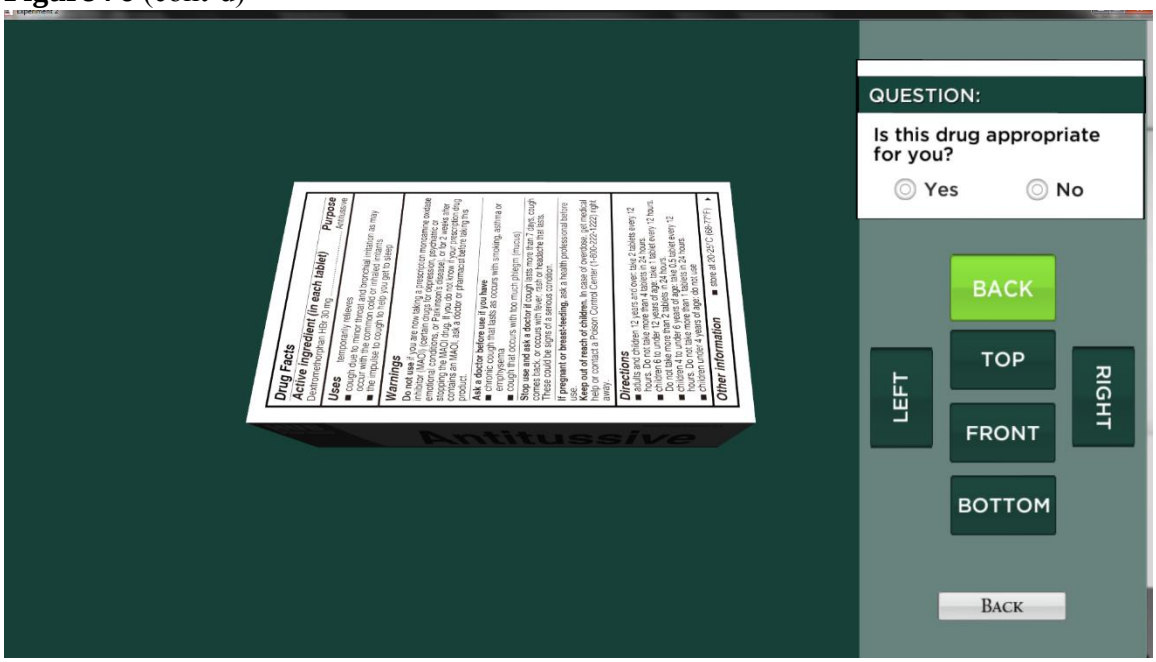


Figure 76 (cont'd)

Figure 76 (cont'd)



Appendix L. Post-test Survey Form

Figure 77 Post-test Survey Form

POST-TEST: **SUBJECT #:_____**

Sect.	Part	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19
A	I																			
	II-a																			
	II-b																			
	III-a										b									
B	I																			
	II																			

----------No answers in the tables above----------

When you answering the following questions, please **DO NOT RETURN** to look at any information in the previous sections.

SECTION A: In this section, you are invited to answer a list of questions regarding to the previous experiment. The general ideas about the questions will be:

PART I. Please circle all drugs which you remember were tested during the eye tracking portion of this study

☐ Acetaminophen	☐ Guaifenesin	☐ Phenacetin
☐ Antipyrine	☐ Ibuprofen	☐ Phenylephrine
☐ Aspirin	☐ Lansoprazole	☐ Phenylpropanolamine
☐ Cimetidine	☐ Magnesium	☐ Pseudoephedrine
☐ Dextromethorphan	☐ Naproxen	☐ Ranitidine
☐ Famotidine	☐ Omeprazole	☐ Xylometazoline

Figure 77 (cont'd)

PART II. Check a **SINGLE** box regarding the frequency with which you use the referenced information (e.g. item A, B, C, etc) and the importance of this information when making a selection for yourself. Information on the package may be referenced more than once, so please answer specific to the location in the graphic.

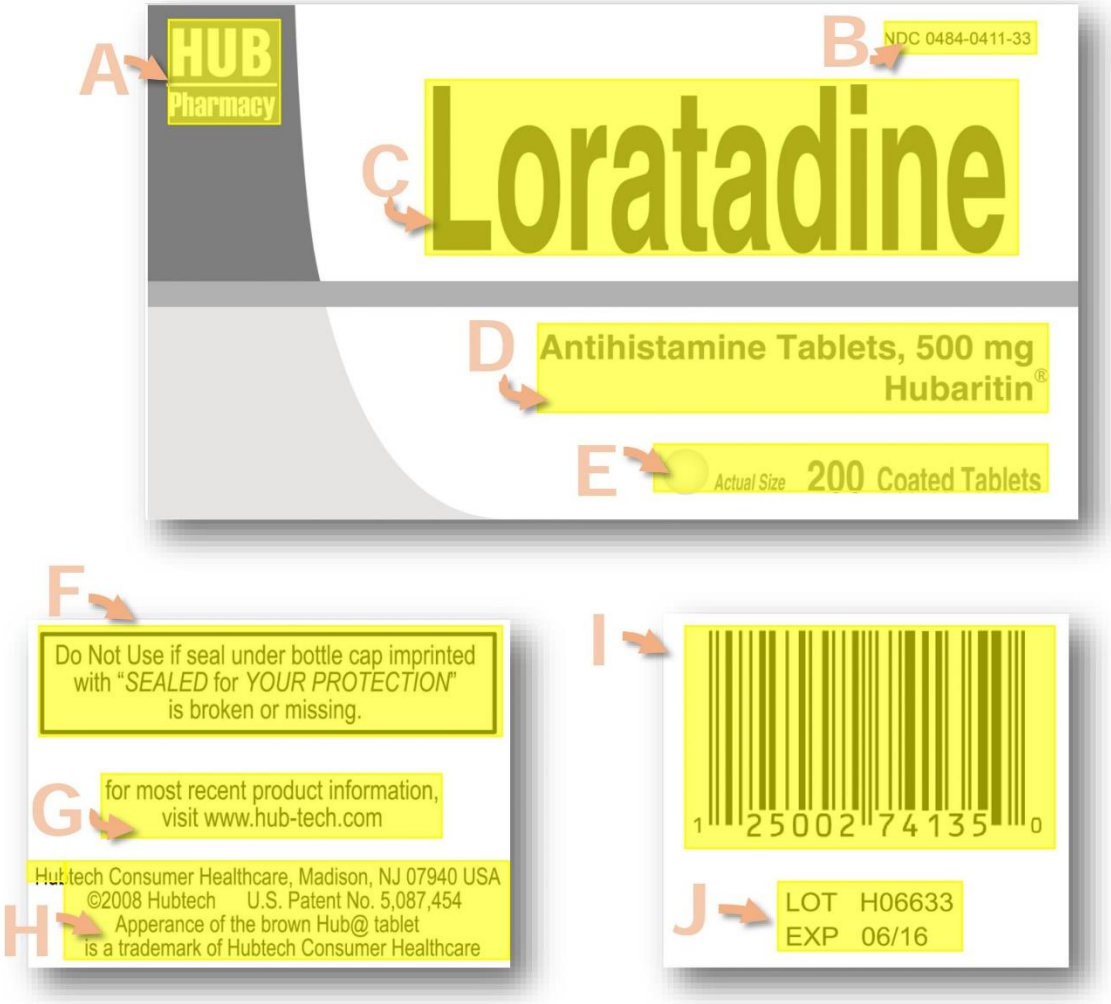


Figure 77 (cont'd)

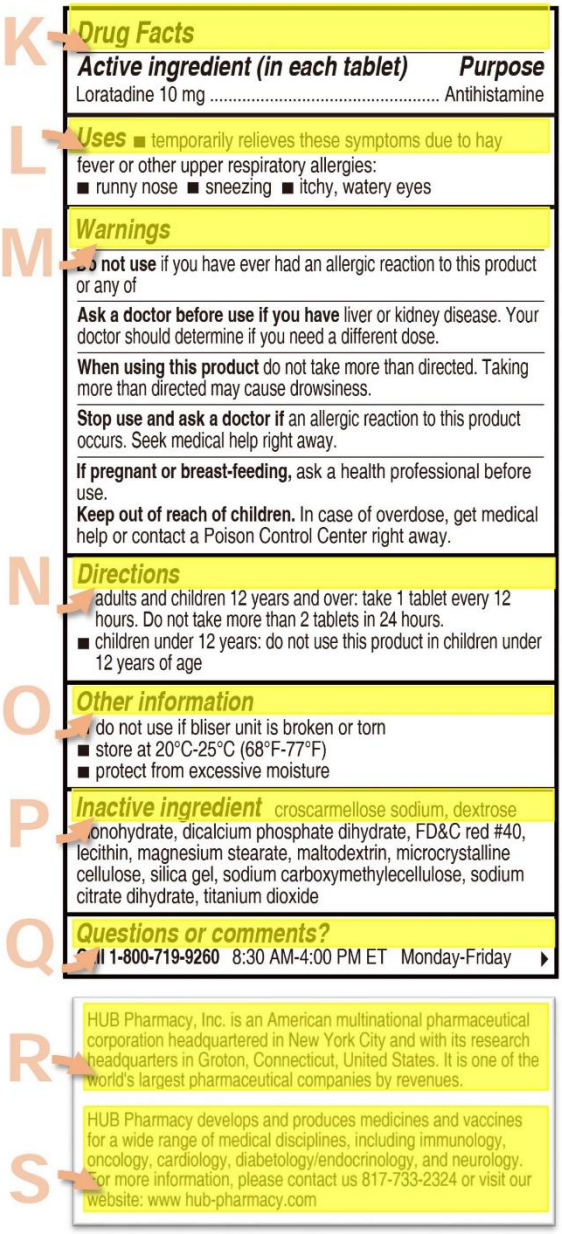


Figure 77 (cont'd)

Check **ONE** box for each of the informational items related to each question						
Table 1		How **frequently do you use the information** that is represented by each letter (please answer relative to the highlighted area as some information appears in more than one place on the label)				
		Never	**Rarely**	**Sometimes**	**Often**	**Always**
A	HUB Pharmacy					
B	NDC 0484-0411-33					
C	Loratadine					
D	Antihistamine Tablets, 500 mg Hubaritin®					
E	Actual Size 200 Coated Tablets					
F	Do Not Use if seal under bottle cap imprinted with "*SEALED* for *YOUR PROTECTION*" is broken or missing.					
G	for most recent product information, visit www.hub-tech.com					
H	Hubtech Consumer Healthcare, Madison, NJ 07940 USA ©2008 Hubtech U.S. Patent No. 5,087,454 Apperance of the brown Hub@ tablet is a trademark of Hubtech Consumer Healthcare					
I	1 25002 74135 0					

Figure 77 (cont'd)

J	LOT H06633 EXP 06/16					
K	***Active ingredient (in each tablet)*** ***Purpose*** Loratadine 10 mg ..... Antihistamine					
L	***Uses*** ■ temporarily relieves these symptoms due to hay fever or other upper respiratory allergies: ■ runny nose ■ sneezing ■ itchy, watery eyes					
M	***Warnings*** **Do not use** if you have ever had an allergic reaction to this product or any of **Ask a doctor before use if you have** liver or kidney disease. Your doctor should determine if you need a different dose. **When using this product** do not take more than directed. Taking more than directed may cause drowsiness. **Stop use and ask a doctor if** an allergic reaction to this product occurs. Seek medical help right away. **If pregnant or breast-feeding,** ask a health professional before use. **Keep out of reach of children.** In case of overdose, get medical help or contact a Poison Control Center right away.					
N	***Directions*** ■ adults and children 12 years and over: take 1 tablet every 12 hours. Do not take more than 2 tablets in 24 hours. ■ children under 12 years: do not use this product in children under 12 years of age					
O	***Other information*** ■ do not use if bliser unit is broken or torn ■ store at 20°C-25°C (68°F-77°F) ■ protect from excessive moisture					
P	***Inactive ingredient*** croscarmellose sodium, dextrose monohydrate, dicalcium phosphate dihydrate, FD&C red #40, lecithin, magnesium stearate, maltodextrin, microcrystalline cellulose, silica gel, sodium carboxymethylecellulose, sodium citrate dihydrate, titanium dioxide					
Q	***Questions or comments?*** **Call 1-800-719-9260** 8:30 AM-4:00 PM ET Monday-Friday					
R	HUB Pharmacy, Inc. is an American multinational pharmaceutical corporation headquartered in New York City and with its research headquarters in Groton, Connecticut, United States. It is one of the world's largest pharmaceutical companies by revenues.					
S	HUB Pharmacy develops and produces medicines and vaccines for a wide range of medical disciplines, including immunology, oncology, cardiology, diabetology/endocrinology, and neurology. For more information, please contact us 817-733-2324 or visit our website: www hub-pharmacy.com					

Figure 77 (cont'd)

Table 2		How **important is the information regarding a purchase for yourself** (please answer relative to the highlighted area as some information appears in more than one place on the label)				
		Not at all	**Low**	**Neutral**	**Moderately**	**Very**
A	HUB Pharmacy					
B	NDC 0484-0411-33					
C	Loratadine					
D	Antihistamine Tablets, 500 mg Hubaritin®					
E	Actual Size 200 Coated Tablets					
F	Do Not Use if seal under bottle cap imprinted with "*SEALED* for *YOUR PROTECTION*" is broken or missing.					
G	for most recent product information, visit www.hub-tech.com					
H	Hubtech Consumer Healthcare, Madison, NJ 07940 USA ©2008 Hubtech U.S. Patent No. 5,087,454 Apperance of the brown Hub@ tablet is a trademark of Hubtech Consumer Healthcare					
I	1 25002 74135 0					

Figure 77 (cont'd)

J	LOT H06633 EXP 06/16					
K	***Active ingredient (in each tablet)*** ***Purpose*** Loratadine 10 mg ..... Antihistamine					
L	***Uses*** ■ temporarily relieves these symptoms due to hay fever or other upper respiratory allergies: ■ runny nose ■ sneezing ■ itchy, watery eyes					
M	***Warnings*** **Do not use** if you have ever had an allergic reaction to this product or any of **Ask a doctor before use if you have** liver or kidney disease. Your doctor should determine if you need a different dose. **When using this product** do not take more than directed. Taking more than directed may cause drowsiness. **Stop use and ask a doctor if** an allergic reaction to this product occurs. Seek medical help right away. **If pregnant or breast-feeding,** ask a health professional before use. **Keep out of reach of children.** In case of overdose, get medical help or contact a Poison Control Center right away.					
N	***Directions*** ■ adults and children 12 years and over: take 1 tablet every 12 hours. Do not take more than 2 tablets in 24 hours. ■ children under 12 years: do not use this product in children under 12 years of age					
O	***Other information*** ■ do not use if bliser unit is broken or torn ■ store at 20°C-25°C (68°F-77°F) ■ protect from excessive moisture					
P	***Inactive ingredient*** croscarmellose sodium, dextrose monohydrate, dicalcium phosphate dihydrate, FD&C red #40, lecithin, magnesium stearate, maltodextrin, microcrystalline cellulose, silica gel, sodium carboxymethylecellulose, sodium citrate dihydrate, titanium dioxide					
Q	***Questions or comments?*** **Call 1-800-719-9260** 8:30 AM-4:00 PM ET Monday-Friday					
R	HUB Pharmacy, Inc. is an American multinational pharmaceutical corporation headquartered in New York City and with its research headquarters in Groton, Connecticut, United States. It is one of the world's largest pharmaceutical companies by revenues.					
S	HUB Pharmacy develops and produces medicines and vaccines for a wide range of medical disciplines, including immunology, oncology, cardiology, diabetology/endocrinology, and neurology. For more information, please contact us 817-733-2324 or visit our website: www hub-pharmacy.com					

Figure 77 (cont'd)

PART II. For each line of the following table, please indicate if you were familiar with each of these drugs (prior to this study). **AND**, considering your current health status (and the drugs you take), whether or not each is an appropriate choice for you.

Ingredients	Familiar with this drug prior to the study?		
	Yes	No	Not Sure
Acetaminophen			
Ibuprofen			
Naproxen			
Dextromethorphan			
Phenylephrine			
Guaifenesin			
Omeprazole			
Ranitidine			
Cimetidine			

Ingredients	Is this drug appropriate for you to take?		
	Yes	No	Not Sure
Acetaminophen			
Ibuprofen			
Naproxen			
Dextromethorphan			
Phenylephrine			
Guaifenesin			
Omeprazole			
Ranitidine			
Cimetidine			

Figure 77 (cont'd)

SECTION B: USING YOUR MEMORY, answer the following questions related to medications that you are taking.

Within the last week, I have taken at least one dose of a drug product (either prescription or OTC) with the following active ingredient(s) or indications	Yes	No	Not sure
(1) Acetaminophen			
(2) NSAIDs (ibuprofen, naproxen, aspirin or others)			
(3) Acid reducers (cimetidine; ranitidine, omeprazole)			
(4) Guaifenesin			
(5) Phenylephrine			
(6) Dextromethorphan			
(7) Any seizure medicine like phenytoin			
(8) Any antifungal or anti-yeast medicines			
(9) Any anxiety medicine like diazepam			
(10) Any immune system medicine like tacrolimus			
(11) Any medicines for HIV infection like prescription antiretrovirals			
(12) Any prescription monoamine oxidase inhibitor (MAOI) (certain drugs for depression, psychiatric or emotional conditions, or Parkinson's disease)			
(13) Any blood thinning drug like warfarin			
(14) Any heart medicine like digoxin			
(15) Any oral asthma medicine like theophylline			
(16) Any diuretic medicines			

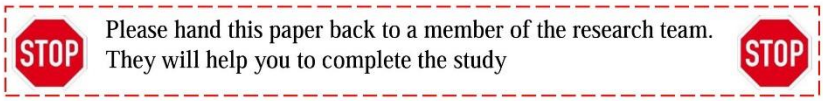
Figure 77 (cont'd)

SECTION C: Please check all that apply to your CURRENT health status

Health condition inquiry	Yes	No	Not sure
(1) 3 or more alcoholic drinks everyday			
(2) have trouble or pain swallowing food, vomiting with blood, or bloody or black stools			
(3) diabetes			
(4) high blood pressure			
(5) any thyroid disease			
(6) any kidney disease			
(7) any liver disease like liver cirrhosis			
(8) any heart surgery			
(9) any stomach problems like ulcers or bleeding			
(10) any troubles with urinating due to an enlarged prostate gland			

Appendix M. Health History Survey Form

Figure 78 Health History Survey Form



SECTION D: Health History.

Please provide the research team with any prescription drugs/OTC drugs that you have brought today.

Researcher:

"The purpose of this portion of the study is to gather information from you about your health status and the types of medicines that you take. I am going to record the conversation to be sure that I get everything down. Everything that you tell me will remain confidential; we will only record your information by participant number, not your name. Also, if you would like to opt out of answering a specific question, feel free to do so."

- If questions regarding medication come up during the course of the conversation, that is good. Remind participants that our goal is to create labeling that provides critical information in the best way possible to consumers and that you are not a healthcare professional. Encourage the participant to discuss the question with their doctor and their pharmacist.
- If participants do not wish to answer any of the following questions, indicate DNA next to the question

"**Let's start with your prescription medications; those are the medicines that a doctor or other medical provider has prescribed to you.**"

Figure 78 (cont'd)

"**Which prescription medicines do you take on a scheduled basis? Are there others that you take that aren't here?**" And, for each one they have brought: "**How often and when do you take (medication name)?**"

Prescription medications- Scheduled			
Drug name	Concentration	Dosing instructions	Differently than prescribed? (If yes, note how it is taken)

"**Which prescription medicines do you take on an as needed basis"? Are there others that you take that aren't here?**" And, for each one they have brought: "**How often and when do you take (medication name)?**"

Prescription medications- As needed			
Drug name	Concentration	Dosing instructions	Differently than prescribed? (If yes, note how it is taken)

Figure 78 (cont'd)

"**Sometimes people will forget to bring a couple of things, so I am going to ask you about some products that people sometimes forget when they think about the medicines that they use**."

Do you use:

- ☐ Eye drops?
- ☐ Patches?
- ☐ Creams or ointments?
- ☐ Inhalers?

If they indicate yes, try to get as much information about the products as you can.

"**Over-the-counter medicines (OTC) are medicines that you can purchase without a prescription. Let's do the same thing with OTC drugs that we just did with the prescription drugs.** " And, for each one they have brought: "**How often and when do you take (medication name)**?"

OTC medications						
Drug name	Strength	Dose	Frequency	To treat what?	Any problems	Differently than directed? (If yes, note how it is taken)

Appendix N. Scanning and Saving Labels using Rx Label Scanner

This appendix includes: (1) Standard Scan mode; (2) Scan Front Back mode; (3) Scan by Hand; (4) Annotations, Zooming, and Cropping Labels; (5) Accepting Scans and Patient Approved Images, which is cited from Rx Label Reader Users Guide provided by Meditory Corporation (2015), available at: http://smg-dev.com/rxlabelreader/images/RxLabelReader_Users%20Guide_2015CvFCC.pdf

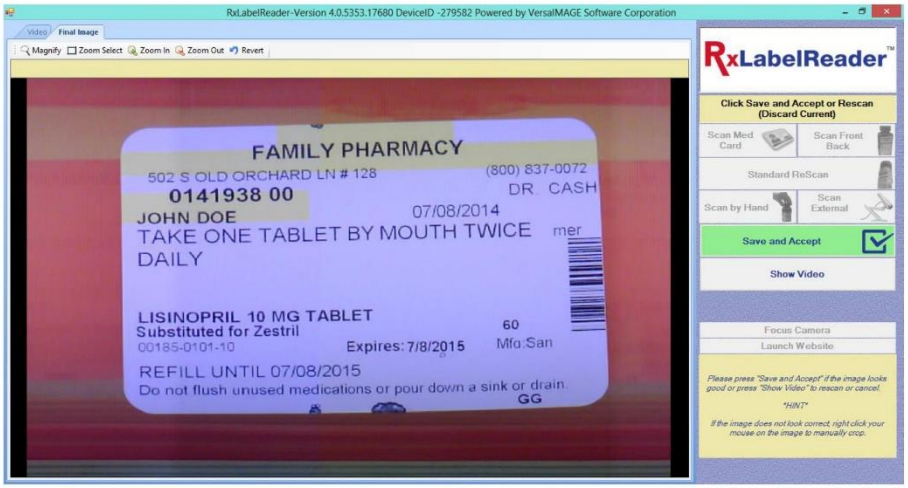
Figure 79 Scanning and Saving Labels using Rx Label Scanner

Standard Scan: Rotary scan label scan mode

Select Standard Scan to scan and capture an image of the label.

Use the Standard Scan mode for standard prescription bottles, most vitamin bottles, and most square and triangular bottles. Select 'Standard Scan' and the bottle is rotated 360 degrees to produce a flat, digital image of the label.

The software automatically switches from the Video tab to the Final Image tab (upper left corner) to show you the scanned label image (Above picture is the Video tab, below picture is the Final Image tab).



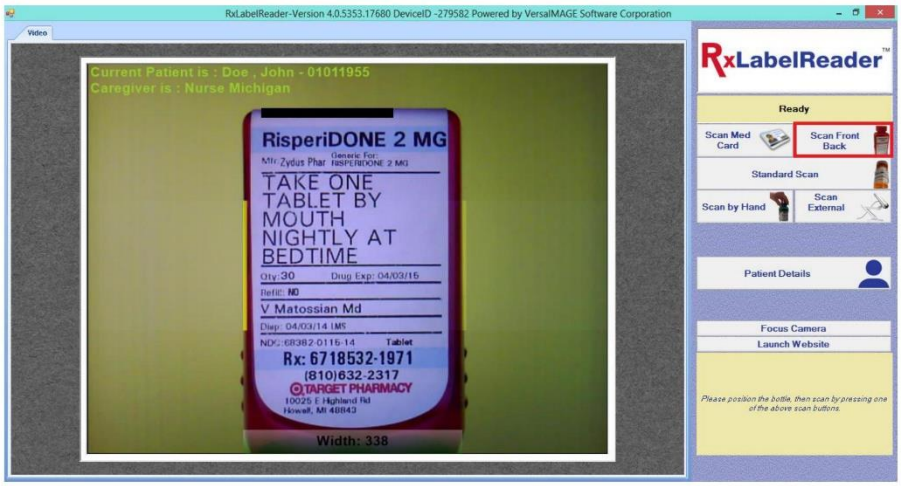
8

Figure 79 (cont'd)

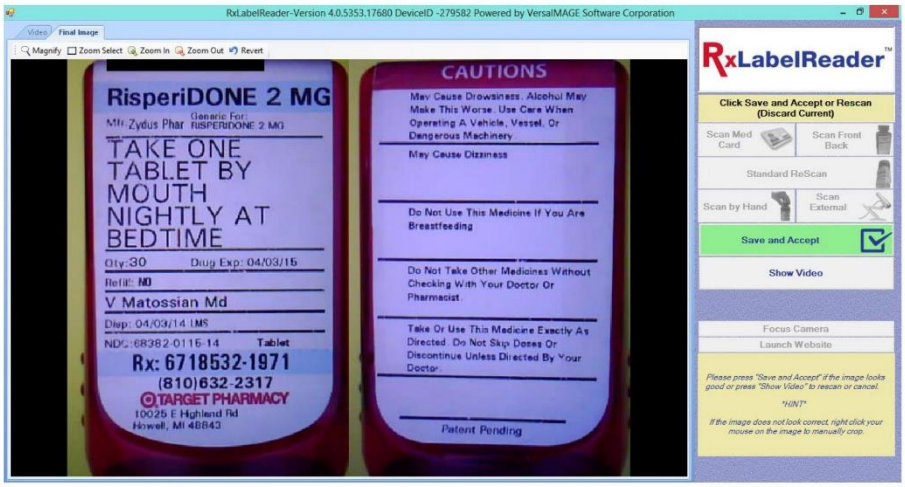
Scan Front Back: Image the Front and Back of a bottle

Select Scan Front Back to image a bottle with labels only on the front and back sides.

If a bottle has labels only on the front and back sides, place it into the bottle receptacle with the front or back label facing the camera so you can clearly see the whole label on that side. Once positioned properly, select 'Scan Front Back' and an image of the label facing the camera is taken, the bottle is rotated 180 degrees, and an image of the opposite label is taken.



After the scan, you are brought to the Final Image tab, where both images have been combined to make a single image. Now you have easy access to a single image of both front and back labels.



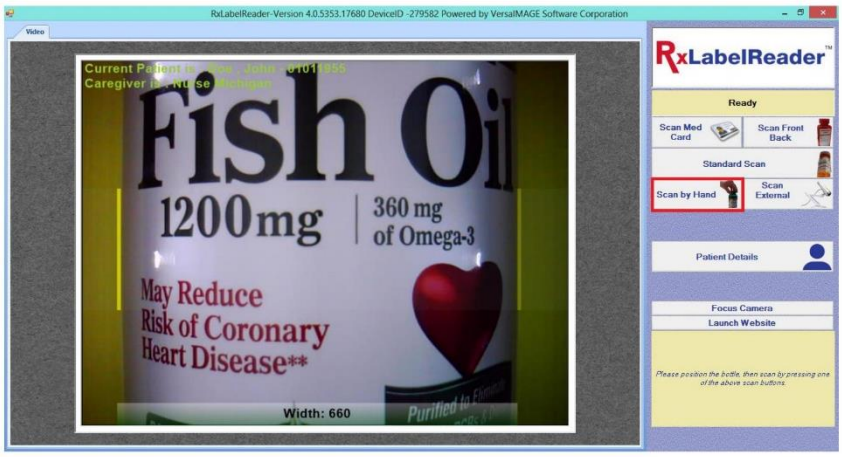
9

Figure 79 (cont'd)

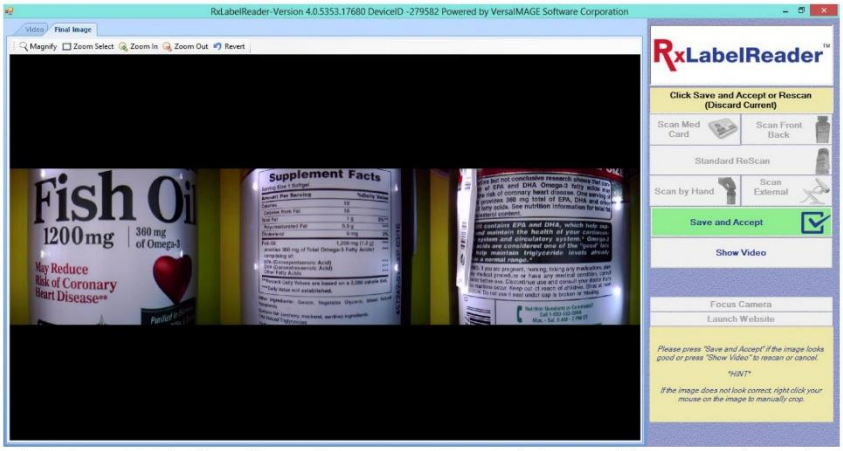
Scan by Hand: Manually Image Labels

Select Scan by Hand to manually image the portion(s) of the label you wish.

If a bottle/box is too big or oddly shaped to scan properly with 'Standard Scan', use the 'Scan By Hand' mode. Select 'Scan by Hand' and Insert the bottle or box into the label reader. Manually rotate the object and use the Thumb-wheel to orient the vertical position of the camera as necessary until the first portion of the label you wish to image is clearly visible. Once you are ready to take the first image, select 'Scan Image Part #1'.



After you have captured Image Part #1, position the bottle to show the next portion of the label you wish to scan. Select 'Scan Image Part #2', and repeat this process until you have captured all portions of the label desired. Click 'Stop and Join' to finish.



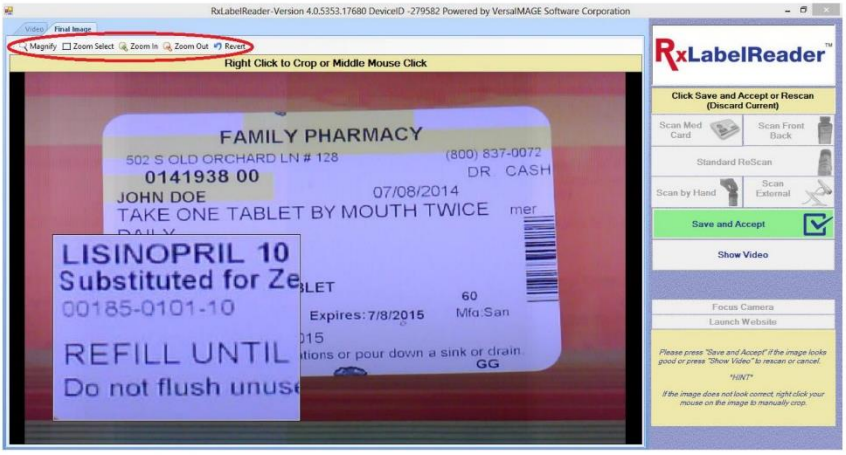
'Stop and Join Image Parts' will combine each Image Part into a single image and bring you to the Final Image tab, showing the Final Image for your review.

10

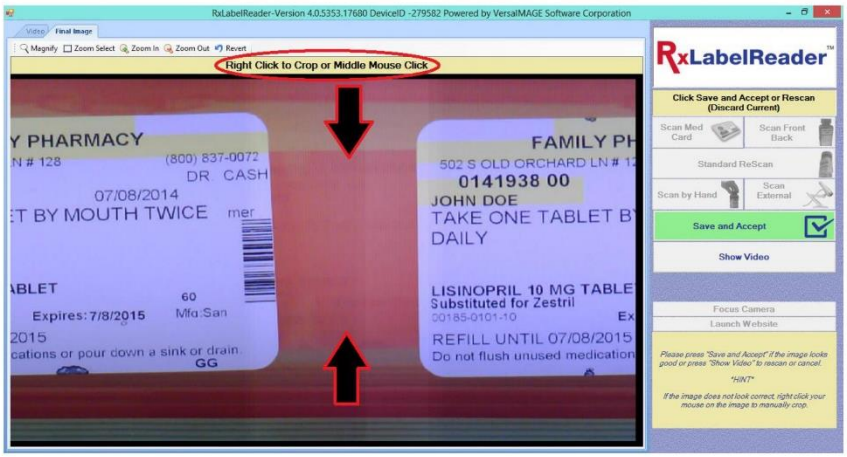
Figure 79 (cont'd)

Annotations, Zooming, and Cropping Labels

Annotations and Zoom features are located in the Toolbar above the label image in the Final Image tab.



These features give you the capability to Magnify portions of the label, Zoom in and Out, Add redactions, and Revert to the original scanned image. This can allow anyone to easily read fine print, check label data to ensure it was read correctly by the OCR, and manipulate the image as desired.



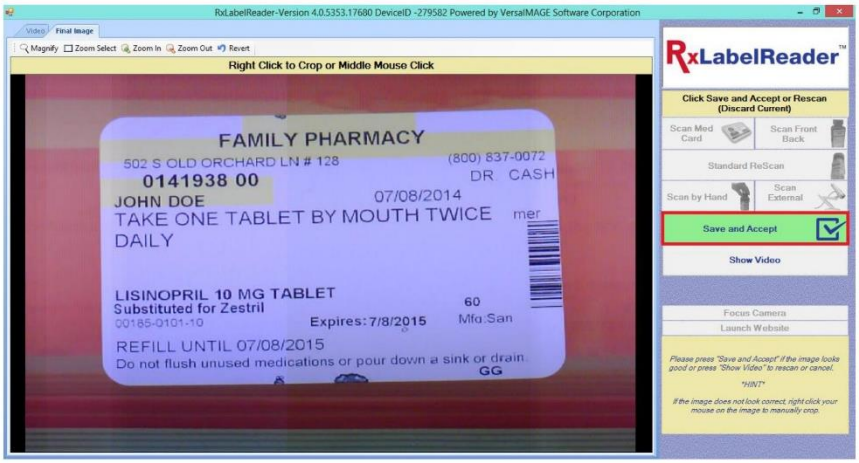
If the image is not cropped (cut) correctly at the true beginning of the label, move the mouse pointer to the actual start of the label image and Middle Mouse or Right click. The label image will be cut at that position and refreshed to show the newly cropped label image.

12

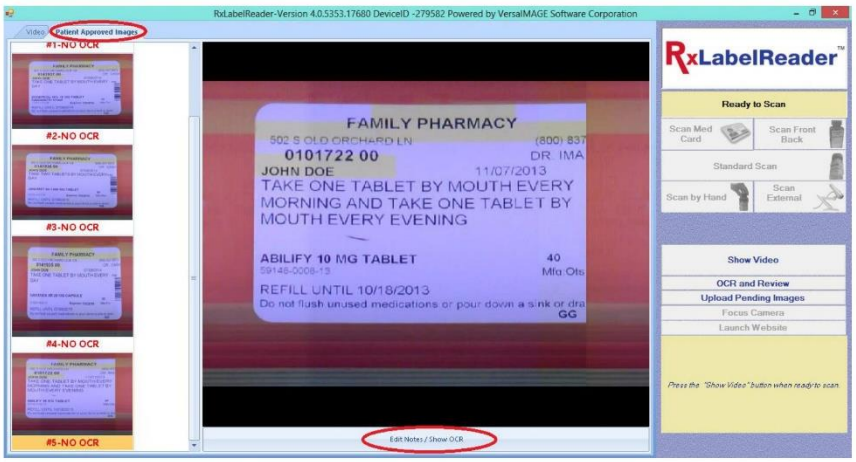
Figure 79 (cont'd)

Accepting Scans and Patient Approved Images

In the Final Image tab, once you have reviewed the label image click Save and Accept.



Once you have Saved and Accepted the scan, the label image is stored in the Patient Approved Images tab where it is pending OCR and/or upload. You can review your accepted scans at any time by clicking the Patient Approved Images tab.

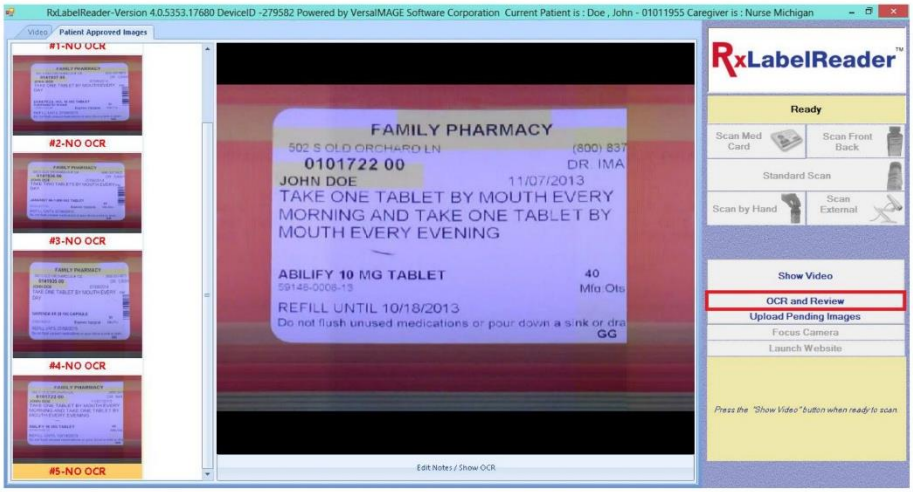


The Patient Approved Images tab allows you to review all labels that have been Saved and Accepted and are pending upload. Click on the thumbnails on the left to view the corresponding label image, and attach a personalized note to any accepted scan by clicking 'Edit Notes / Show OCR' below the label image and entering text into the Notes field.

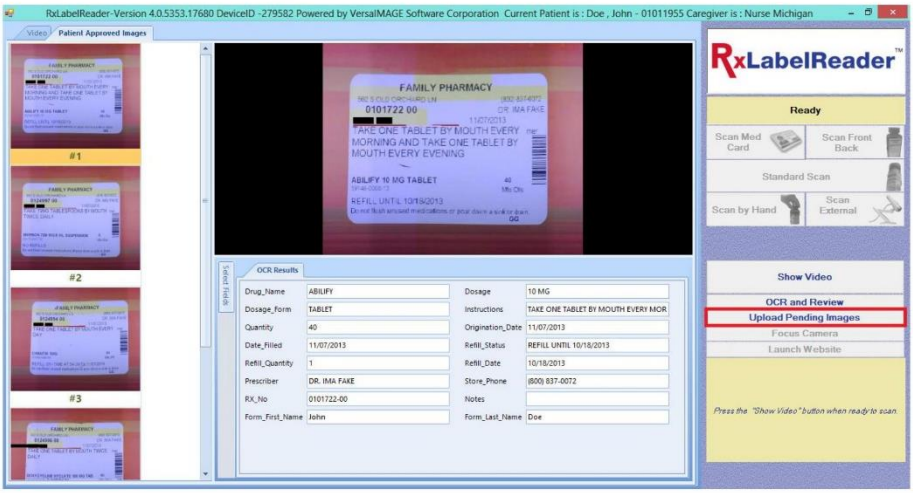
13

Figure 79 (cont'd)

You can OCR your scans locally from the Patient Approved Images tab at any time by clicking the 'OCR and Review' button. (Any labels that do not have OCR when uploaded will be processed automatically on the server.)



The OCR will process the labels and give their corresponding OCR values in data fields below the label image for easy label data review and correction as needed, a personalized note can be added in the 'Notes' field.



Select the 'Upload Pending Images' button at any time to upload all pending images and data for all patients. This can be done before or after 'OCR and Review'. Any labels that are uploaded without first being OCRed will have the OCR processed automatically on the Patient Medication Profile Form on the cloud. This allows you to skip the OCR processing via the RxLabelReader application and instead review OCR data on the PMP Form.

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Appendix O. Preliminary statistics of participant's behaviors on examining packaging samples from the post survey data (event-level) and the eye-tracking test data (trial-level)

(1) Preliminary statistics from post survey data (event-level)

Realizing that not all participants necessarily had a risk of adverse drug event, that is, the pharmacist did not code a drug as inappropriate for a given subject, we characterized the number of "no responses" from the pharmacists more thoroughly. Pharmacists returned a "No" response for a total of 334 of the 730 records (45.8%) reviewed for the 82 participants. Seventy-nine of the 82 participants (96%) had at least one active ingredient that pharmacists reported as inappropriate for use for that individual, coded for one (or more) of four possible reasons: (1) a drug-drug interaction, a drug disease interaction, an anticholinergic load problem, a duplicate therapy or drug class to one that is already reported as taken and/or an age-related cognitive impairment associated with the reported drug (e.g. ≥70 years of age for cimetidine).

(2) Preliminary statistics from eye tracking test data (trial-level)

Table 12 Overview of participant's behaviors on examing trials in Experiment 2

Total number of participants:	82
Total number of trials:	2214
Total number of participants who turned sample beyond PDP at least one of the 27 trials:	31
Total number of trials that the sample had be turned beyond PDP:	852
Number of participants with at least one "No" from pharmacist's comment:	79
Number of trials that pharmacist commented "No":	1008
Number of participants who had turned the sample beyond PDP with a "No" from pharmacist's comment:	13
Number of trials that the sample had be turned beyond PDP and with a "No" from pharmacist's comment:	356
Number of participants with at least one "Patient-Yes/Pharmacist-No" trial:	75
Number of trials with "Patient-Yes/Pharmacist-No" combination:	649
Number of participants who had turned the sample beyond PDP with a "Patient-Yes/Pharmacist-No" combination:	11
Number of trials that the sample had be turned beyond PDP and with a "Patient-Yes/Pharmacist-No" combination:	210

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