The Influence of Brand and Principle Display for Safe Consumer use of Over the Counter Drugs – Advancing the Science

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1.0 Background

Product names and packaging are important guides for consumers of over-the-counter (OTC) drugs. However, these may also drive consumer behavior, as individuals may rely too heavily on these product identifiers to help address their health needs. In particular, there can be risks when OTC drugs look too familiar. There are situations where consumers mistakenly take something different than they thought they were taking or use an OTC drug in a manner that isn't intended.

Companies apply well-known brand names and packaging to new products. In some cases, the new product may have different active ingredients with different risks or higher doses of what is normally a safe and effective drug. This is known as brand extension. Such practices could create problems when consumer choices lead to overlooking the warnings and safety information on a new OTC drug label.

This research study will look into the extent to which OTC brands and packaging can lead consumers to make mistakes about product use and safety information. We will investigate how aspects of OTC branding and packaging could mislead consumers and lead to drug errors, and for whom these risks are the greatest. A better understanding of consumer OTC decision making and product use can then lead to new policies and strategies that will make things safer.

2.0 Purpose

Aim 1: Determine the prevalence of brand-name recognition and associations with consumer misunderstanding of OTC drug use among well-known products when the brand is extended.

> **H_1**: Among recognized OTC brands, consumers will demonstrate high rates of awareness of these products' symptoms they are primarily used to treat, but low rates of knowing active ingredient(s).
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> **H_2**: Participants will recognize differences in design attributes of the principal display panel (PDP) in brand extended products (e.g. color, font differences) prior to differences in symptoms treated and/or active ingredients, if identified at all.
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> **H_3**: Brand extended products will be at greater risk for self-selection errors compared to non-brand extended products, especially in participants more familiar with the brand.
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> **H_4**: Consumers will be less likely to identify differences in active ingredient and/or symptoms treated when the PDP 1) contains the familiar base brand name and 2) the PDP is the same color.

Aim 2: Explore consumers' knowledge, beliefs, and assumptions about brand name OTC drugs as well as consumer perspectives on how these elements affect their intended use and attention to safety information.

> **H_5**: We expect interview data will show that heuristic processing accentuated by the branding and display preempts or distracts consumer attention from significant safe-use information.

Aim 3: Analyze and synthesize quantitative and qualitative findings to provide a more comprehensive and secure basis for regulatory decisions.

> **H_6**: The integration of qualitative and quantitative data and analyses from this study will provide a more secure basis for ongoing decision making about proprietary naming of OTC drugs and labeling negotiations.
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> **H_7**: The mixed methods results, along with existing literature, will provide a strong basis for guidance development on the topic of brand extension in OTC drugs.

H_8: The results will more broadly inform brand considerations in other regulated products and enhance the Agency's body of knowledge on risk communication

Investigational Plan

3.0 Study design

We will conduct a cross-sectional, mixed-methods study consisting of structured, one-time in-person interviews among 400 adults in the Chicago area. Participants will be recruited through four methods. Patients (n=240) will be approached in-person at one primary care setting in Chicago Northwestern Lastly, we will recruit participants (n=100) from Craiglist posts. Scripts for research assistants (RAs) for approaching potential participants in person will be embedded in the screener/battery questionnaire. We will submit the Craigslist ad language for IRB approval.In-person appointments will be completed in clinic dedicated research space where space is available or scheduled and held on-site at Northwestern. All participants will interact with common OTC products to determine the prevalence of misunderstanding and unintentional potential misuse. Interviews will qualitatively explore how individuals correctly or incorrectly think about OTC products, labeling, and think about brands in general.

4.0 Sample

Inclusion criteria

The inclusion criteria for subjects participating in the study will be 1) age 18-80 and 2) English-speaking.

Exclusion criteria

Exclusion criteria include any participant with visual, cognitive, or hearing impairments as determined by direct communication with the participant, Snellen eye chart, and a six-item screener cognitive assessment.

5.0 Recruitment, Eligibility Screening and Informed Consent

The research assistants (RAs) will approach potential subjects in the Northwestern primary care clinic space to briefly asess interest. Interested participants will be screened for eligibility and if eligible, given informed consent. Once the participant agrees to participate and signs the consent form they will be given the option to complete the interview immediately in clinic (where space is available) or scheduled to come in to Northwestern offices at a later time.

An IRB approved advertisement for this research study will be posted on Craigslist. Participants will see a brief description of the study and requirements, and asked to email their name and phone number to the research staff. Research staff will call the potential participant, assess interest, and ask permission to screen. The screener consists of questions to confirm eligibility (confirm age, does not self-report having visual, hearing, cognitive impairment). If the patient is eligible and interested, the RA will schedule a time for the patient to come back for an in-person appointment.

The RA will review the consent form with the participant and ask the participant if they have any questions. The participant will be reminded that the RA will will be audio-recording the interview to ensure that no data is lost. Participants will be told they are participating in a study of how consumers identify and use over-the-counter products.

6.0 Interview

During the interview patients will be asked about their demographic information, socioeconomic status, health status, and current and prior use or experience with OTC products. Health literacy will also be assessed using the Newest Vital Sign (NVS). A series of tasks will then be administered to test patients' functional understanding of a range of OTC products of varying indication and brands via 1) proper identification of symptoms treated and active ingredient(s), and 2) risk of misuse, as measured by self-selection errors in simultaneously taking two OTC products containing the same underlying active ingredient.

Specifically for Task 1, partipants will be shown a list of brand names for OTC products and asked if they recognize the brand name. For each brand participants recognize, they will then be asked 1) if/how often they have used that brand's products, 2) if they can choose from a list the symptoms that products under that brand name typically treat and 3) if they can choose from a list the active ingredients found in that brand's products.

For Task 2, participants will be presented with hypothetical purchasing scenarios where they are shown OTC products and asked which they would take if they had a specific symptom or set of symptoms. In each scenario, participants will be shown 8 common brand name OTC products that treat various conditions. Each question will contain a 'BE' answer of a brand extended product. Within each question, there will be a varying number of overall correct choices (between 1 and 4). The position of the 8 OTC product choices will be fixed across participants. Interviewers will record any behaviors the participant employs to answer the question (if the participant picks up the boxes, looks at the back of the box, looks up information on phone).

For Task 3, participants will be shown 12 sets of 2 PDPs at a time and asked to report as many similarities and differences they see in the 2 products. Interviewers will write verbatim the participants responses and after the interview they will standardize the participants responses and record 1) what similarities and differences the participant mentioned and 2) the order in which they answered the question. Ten of the 12 pairs are brand extended products and 2 are manipulated labels (i.e. Tylenol PM – Simply Sleep and Midol – Menstridol). Specific aspects of the final 2 PDPs will be altered in order to isolate whether particular characteristics (i.e. similar vs different colors, presence/absence of 'makers of' statement) affect participant response. 4 versions of each medication will be tested: 1) original packaging for both where color differs and extended product includes "makers of", 2) color manipulated to be the same, extended product includes "makers of", 3) color differs, "makers of" removed from extended product, and 4) color manipulated to be the same and makers of" removed from extended product. Participants will be randomized to 1 of 4 groups and only receive 1 of the 4 options.

To counterbalance potential order effects, the sequence in which the scenarios (Task 2) and brands (Task 3) are presented to subjects will also be randomized.

The interview will include questions pertaining to 1) how participants read product labeling, 2) the diversity of factors that affect decisions related to purchase and use, and 3) other salient factors that reflect decision making around choosing and using OTC branded products. At the end of the tasks, questions will include followup,"think aloud" probes that explore and expand on the verbatim responses, contextualizing and validating the derived categorical data. This portion of the interview interview will be audio recorded and transcribed to allow for analysis of textual data.

7.0 Reimbursement

All participants will be paid $30 for their participation in the study. Participants may withdraw at any time during the study at no penalty. If participants withdraw at any time after consent, they will be paid the full $30. Participants who complete the interview will be paid in cash immediately after the conclusion of the interview.

Evaluation Phase (months 19-24)

During this phase, we will analyze the data and prepare reports and manuscripts. Deidentified or aggregate preliminary interim analyses will be conducted in order to provide progress reports to FDA.

Aim 1: Determine the prevalence of brand-name recognition and associations with consumer misunderstanding of OTC drug use among well-known products when the brand is extended.

Analysis Plan. Descriptive statistics (percentage, mean and standard deviation) will be calculated for familiarity with brand names, indication, or active ingredient, and potential misuse as well as the following patient characteristics: age, gender, race/ethnicity, socioeconomic status (educational attainment, employment, household income) current and prior use/experience with OTC products, health status, cognitive function, and literacy level. Chi-square and Student's t-tests will be used to evaluate associations between patient characteristics and medication familiarity and potential misuse. Generalized linear models with a Poisson distribution and log link function will be used to estimate risk ratios for included covariates compared to each referent condition. A Generalized Estimating Equation (GEE) approach will be used to adjust model coefficients and standard errors for within-patient correlation because tasks will be repeated using multiple medications within multiple scenarios. All models, described in more detail per hypothesis below, will include the potential confounding variables and risk factors of age, gender, race (black, white, other), literacy (limited (< 9th grade or low + marginal) vs. adequate (≥ 9th grade)), household income, OTC use (non, moderate, heavy), and recruitment site. Since education is strongly associated with literacy, it will be examined separately to avoid overadjustment in final models. Interaction terms between covariates will be included in models to determine whether associations vary according to these characteristics. All statistical analyses will be performed using STATA software version 10.0 (StataCorp, College Station, TX).

H_1: Among recognized OTC brands, consumers will demonstrate high rates of awareness of these products' symptoms they are primarily used to treat, but low rates of knowing active ingredient(s).

The prevalence of recognition for each brand presented in Task 1 will be calculated. The proportion of patients who are able to correctly identify symptoms treated and active ingredients of recognized brands will also be examined descriptively and used as a covariate in analyses described below.

H_2: Participants will recognize differences in design attributes of the PDP in brand extended products (e.g. color, font differences) prior to differences in symptoms treated and/or active ingredients, if identified at all.

Task 3 trials will be used to test H2. The order differences in active ingredients, symptoms treated, and other characteristics of the PDP (e.g. color, font) are noticed will be recorded. The order of noticing symptoms treated vs. active ingredient differences, if at all, will first be noted for each trial and summarized across trials for each participant. The order of differences in symptoms treated and/or active ingredient vs. differences in other characteristics will be summarized similarly. Associations between order variables and familiarity variables created for H1, per brand, will also be examined to determine whether brand familiarity affects differences recognized.

H_3: Brand extended OTC products will be at greater risk for self-selection errors compared to non-brand extended products, especially in participants more familiar with the brand.

Task 2 will be used to test H2 and will be analyzed as a three-level GEE model with each possible response nested in scenario, and each scenario nested in participant. The possible product response

options will be coded to indicate whether it is considered a brand extension for that scenario. The outcome will indicate whether a self-selection error occurred (yes/no) per response. Two separate models will be run using Task 2 trials: the first outcome indicates selection errors due to product type (Trials 1-6) and the second indicates errors due to double-dipping (trials 7-10). Product brand extension (yes/no) will be the primary independent variable of interest for these models. A familiarity variable will be created for each brand on a scale from 0-3 using responses from Task 1. Specfically, 1 point will be given if the participant recognized the brand name, 1 point if they were able to identify the symptoms it typically treats, and a third possible point for correctly identifying the active ingredient. An interaction term between brand extension and familiarity will determine whether more familiarity with a brand indicates higher risk of incorrectly selecting a brand-extended product compared to less risk for non-extended products. The familiarity variable may need be collapsed into familiar/not familiar depending on its distribution.

H_4: Consumers will be less likely to identify differences in active ingredient and/or symptoms treated when the PDP 1) contains the familiar base brand name and 2) the PDP is the same color.

Task 3 will be used to test H3. Each of the 12 brand combinations will be coded to indicate whether 1) the brand name is the same, 2) the brand name is different and includes "makers of" original brand, and 3) the brand name is different and there is no mention of the original brand. A second variable for each brand combination will indicate color differences: 1) same colors used (both background and secondary), 2) background colors are the same with different secondary colors, 3) the products have completely different coloring. The outcomes of interest are whether participants notice differences in active ingredients (yes/no) or symptoms treated (yes/no) for each pair presented (n=12). The order differences in active ingredients and/or symptoms treated are noticed with be recorded. Patterns defined in H2 will be examined to determine whether the outcome should be defined as noticing active ingredient and/or symptoms at all (if infrequently noticed) or prior to other differences (if frequently noticed). Separate GEE models with pairs nested within participant will be run for each outcome. Unadjusted models will first be run for each independent variable of interest (brand, color) predicting each outcome (symptoms, active ingredient) to determine whether the 3 category independent variables should be collapsed in multivariable models. For example, if #2, the category for "different brand name but includes 'Maker of Brand'" performs similarly to trials coded as #1 where the same brand name is used, these will be combined into one group "contains the same base brand name". Estimates for brand and color variables described above will be examined to test H3.

Aim 2: Explore consumers' knowledge, beliefs, and assumptions about brandname OTC drugs as well as consumer perspectives on how these elements affect their intended use and attention to safety information.

H_5: We expect interview data will show that heuristic processing accentuated by the branding and display preempts or distracts consumer attention from significant safe-use information.

Analysis Plan for Aim 2. Verbatim responses throughout the questionnaire (OTC Use and Frequency of Use, Product labeling, and After Task Questions) will be analyzed. The qualitative research team will generate *a priori* codes based on known barriers from the study team's prior research and those identified in the literature. During pilot testing these will be further refined and additional probing questions will be added as needed. After research completion, the coding team will read through transcripts to become familiar with common responses. We will utilize 2 cycle coding strategy for the data proposed and validated by Saldana. The first cycle analyses will be to apply predefined overarching codes to all the data. Any emergent codes will be added and prior codes may be removed or altered. Second cycle coding will focus within each overarching code to further refine sub-themes. Analysis will be facilitated using N-Vivo Software (QSR International, Burlington, MA).

Aim 3: Analyze and synthesize quantitative and qualitative findings to provide a more comprehensive and secure basis for regulatory decisions.

Analysis Plan for Aim 3. Synthesis and analysis of quantitative and qualitative findings under Objective 3 will involve integrated presentation and discussion of results from both components of the study. Synthesis will focus on identification of concordances, discordances, and new learnings from the combination of the cross-sectional testing with the embedded qualitative study. In addition to concrete dissemination products, including both reporting and publications, we expect to establish a more comprehensive and secure basis for regulatory decisions around proprietary naming and OTC labeling negotiation. Feasibility for this research is enhanced by our collaboration with accomplished health services researchers who have undertaken similar studies, using the same clinical contexts previously Overall, the proposed study has minimal risk for participants. Researchers will nonetheless maintain the anonymity of participants with identification numbers in analysis datasets.

8.0 Projected Time Lines

The entire length of the study will be two years. In the first 3 months, we will develop the protocol and battery and submit final materials for IRB approval as well as FDA approval. Recruitment, data management, and interim analyses will last from months 7-18. Final analyses will be conducted and reported in months 19-24.

Tasks	**Year 1**				**Year 2**			
Months	**1-3**	**4-6**	**7-9**	**10-12**	**13-15**	**16-18**	**19-21**	**22-24**
Develop protocol and study instrumentation in advance of final determination of support								
Submit protocol and instrumentation for human subjects review, OMB approval and public comment, contract management and any additional permissions								
Conduct cross-sectional study, including quantitative testing and embedded semistructured interviewing (Objectives 1 & 2)								
Data management and analysis—ongoing								
Final analysis of both study components								
Synthesis of data, final reporting, policy formulation, and planning for “next-steps” research or study extension (Objective 3)								

Risks, Benefits, and Confidentiality

9.0 Risks and Benefits to Participants

Although it is possible that there could be negative consequences to participating in the interview and answering the questions, we expect this to be unlikely. Participants will be told they can skip any questions and withdraw at any time without penalty. Patients may feel discomfort with being audio-recorded. We do not expect this to happen often, but if participants refuse to be audio-recorded, they will still be allowed to participate in the study – the interviewer will be trained to skip audio recording and record verbatim responses as best as possible..In addition, participants are at risk for loss of confidentiality. Steps in place to minimize this risk are detailed in the next section. There are no unforeseeable risks. There are no risks to those who do not choose to participate. All respondents will be provided with an assurance of privacy to the extent allowable by law.

Participants will not receive a direct benefit from this research study. Results from this research may help researchers to understand if there are risks to consumers when brand names are extended to include different active ingredients. Potential risks seem reasonable in light of the potential benefit.

10.0 Recorded names and safeguarding of confidential data

Participants' names (first and last) and contact information will be recorded on the Northwestern server for tracking purposes. Names will also be recorded in the consent forms and will be uploaded to Northwestern secure Study Tracker.

At the time of consent, all subjects will be given a unique study code (PIN) and all study data and personal information collected for research purposes will be linked to that number, not to any other identifier. Subjects' names will be linked with their PIN in a single file, which will be stored on a password protected computer. All documents that include identifiers (i.e. Consent Forms) will be stored in a locked, secure location that only key authorized study personnel (i.e. PI, Study Coordinator) will have access to.

11.0 Audio recordings and survey data

For this study, audio will be used primarily for recording responses to open ended questions. Language to this effect will be in the consent form. All audio files will be saved under the participant ID number.

The tapes will be converted to a digital format and uploaded directly to secure servers within General Internal Medicine. The PI will have responsibility for maintaining the data and ensuring that all protections and in place and protocols are being followed. Storage of and destruction of identifiable data can be found below.

Responses to the questionnaire items will be recorded in Snap 11 Interviewer software loaded onto study laptops. Survey responses will be linked to PIN’s and stored on the password-protected computers used by the RAs, which will be kept in a locked room at the study site when not in use. At the close of each day, all collected data will be transferred to a secure server at Northwestern University. Only NU employees listed as authorized study personnel with Northwestern's IRB will have access to all study data.

12.0 Storage of and the destruction of identifiable data

All data collected for this study will be kept in a locked, secure location. After completion of data analysis and