Improving Prescription Drug Warnings to Promote Patient Comprehension

Michael S. Wolf, PhD, MPH; Terry C. Davis, PhD; Patrick F. Bass, MD, MPH; Laura M. Curtis, MS; Lee A. Lindquist, MD, MPH; Jennifer A. Webb, MA; Mary V. Bocchini, BS; Stacy Cooper Bailey, MPH; Ruth M. Parker, MD

Background: Prior studies have documented a high prevalence of patients who misunderstand prescription drug warning labels, placing them at risk for medication error. We evaluated whether the use of “enhanced print” drug warnings could improve patient comprehension beyond a current standard.

Methods: An evaluation of enhanced print warning labels was conducted at 2 academic and 2 community health primary care clinics in Chicago, Illinois, and Shreveport, Louisiana. In total, 500 adult patients were consecutively recruited and assigned to receive (1) current standard drug warning labels on prescription containers (standard), (2) drug warnings with text rewritten in plain language (simplified text), or (3) plain language and icons developed with patient feedback (simplified text + icon). The primary outcome was correct interpretation of 9 drug warning labels as determined by a blinded panel review of patients’ verbatim responses.

Results: Overall rates of correct interpretation of drug warnings varied among standard, simplified text, and simplified text + icon labels (80.3%, 90.6%, and 92.1%, respectively; P < .001). Warnings with simplified text and simplified text + icons were more likely to be correctly interpreted compared with standard labels (simplified text − adjusted odds ratio [AOR] = 2.64; 95% confidence interval [CI], 2.00-3.49; simplified text + icons−AOR = 3.26; 95% CI, 2.46-4.32). Patients’ ability to correctly interpret labels was not significantly different with the inclusion of icons (simplified text + icons−AOR = 1.23; 95% CI, 0.90-1.67; P = .20). Low literacy was also an independent predictor of misinterpretation (AOR, 0.65; 95% CI, 0.44-0.94). Patients with marginal and low literacy were better able to correctly interpret warning labels with simplified text + icons compared with labels with simplified text only (marginal literacy−AOR = 2.59; 95% CI, 1.24-5.44; P = .01; low literacy−AOR = 3.22; 95% CI, 1.39-7.50; P = .006).

Conclusions: Simple, explicit language on warning labels can increase patient understanding; the addition of appropriate icons is particularly useful for adults with lower literacy skills. Evidence-based standards are needed to promote patient-centered prescription labeling practices.

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Author Affiliations: Health Literacy and Learning Program, Division of General Internal Medicine, Feinberg School of Medicine, Chicago (Drs Wolf and Lindquist and Ms Curtis, Webb, and Bailey); and Department of Learning Sciences, School of Education and Social Policy (Dr Wolf), Northwestern University, Evanston, Illinois; Department of Medicine–Pediatrics, Louisiana State University Health Sciences Center at Shreveport (Drs Davis and Bass and Ms Bocchini); and Department of General Medicine, Emory University School of Medicine, Atlanta, Georgia (Dr Parker).
all literacy levels. To date, little progress has been made by these organizations to improve or standardize warning labels for prescription drug containers.

We recently developed and pilot tested a set of “enhanced print” prescription drug warning labels that we hypothesized would be more easily understood by a diverse set of individuals, including those with limited literacy skills. This process involved patients in the writing of the warning messages and design of complementary graphic icons. We evaluated whether the use of these enhanced drug warnings improved patient comprehension beyond a current practice standard.

A 3-arm, cross-sectional evaluation was conducted testing the efficacy of enhanced auxiliary drug warning labels. Specifically, patients were assigned to receive (1) the current standard drug warning labels on prescription containers (standard), (2) enhanced drug warnings with text rewritten in plain language (simplified text), or (3) the enhanced language on drug warnings and also icons developed with patient feedback to support the text messages (simplified text + icon).

STUDY PARTICIPANTS

Adult patients who attended 1 of 4 outpatient primary care clinics were recruited in 2 distinct cities (Shreveport, Louisiana, and Chicago, Illinois). One clinic in each city was a general medicine academic practice; a second clinic was a safety net community health center. Participant recruitment took place from June through August 2007. Patients were considered eligible for the study if they were at least 18 years old, and ineligible if the clinic nurse or study research assistant identified a patient as having 1 or more of the following conditions: (1) had severely impaired vision, (2) had hearing problems, (3) was too ill to participate in the survey, or (4) was non-English speaking. Institutional review boards for all locations approved the study. A total of 562 patients were approached in the order they arrived at the clinics and prior to the medical encounter; 530 consented to be enrolled in the study. Thirteen patients were excluded based on self-reported impairments with hearing (n=3) or vision (n=10). Ten patients were excluded owing to limited English proficiency, and 7 others were excluded based on incomplete information. In all, 500 patients participated in the study; the sample was evenly split across the 2 study locations (n=250 per city) and practice setting (academic, community; n=125 within each study location). A response rate determined according to the American Association for Public Opinion Research standards estimated that 92.8% of approached eligible patients participated in the study.

INTERVENTION

The intervention was the use of enhanced auxiliary prescription drug warning labels, with or without patient-centered icons to support comprehension. Previously, 9 of the most commonly used drug warnings and/or precautions placed directly on prescription medication bottles were revised with patient feedback and pilot tested. Specifically, text was rewritten using more clear, concise, and explicit language. The icons supporting comprehension of the text message were altered to more accurately reflect the mental representations patients identified with each warning, or to use a default, universal cautionary symbol when not deemed possible (Figure 1). Guidance

<table>
<thead>
<tr>
<th>Label</th>
<th>Standard</th>
<th>Simplified Text</th>
<th>+Icon</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Shake well before stirring.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Use only on your skin.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Do not stop taking unless directed by your doctor.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>Take with food or milk.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>Do not use if you are pregnant, think you are pregnant, or breastfeeding.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>May cause drowsiness. Be careful when driving a car or using machinery.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>Do not drink alcohol.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>Limit your time in the sun.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>Talk to your doctor before using any over-the-counter drugs.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Figure 1. Warning labels by type.

Nine drug warnings were used in this study. Each warning had 3 versions (standard, simplified text, and simplified text + icon) for a combined total of 27 labels under evaluation. Within each label version, warnings were randomly organized into groups of 3 labels and then placed on the back of Target Pharmacies ClearRx flat-panel prescription bottles (Target Corp, Minneapolis, Minnesota) (Figure 2). Each bottle therefore had 3 labels, all of which were either standard, simplified text, or simplified text + icon. We viewed 3 warnings on a bottle to be a realistic portrayal of the number of warnings commonly found on pill bottles, many pharmacies allot space for as many as 3

METHODS

Structured Interview

A structured “cognitive” interview protocol was developed to assess patient understanding of the drug labels, a process previously used by our research team. After patients consented to the study, a trained research assistant administered the structured interview that included self-report of sociodemographic information (age, sex, race or ethnicity, education, number of prescription medications currently taken daily). Actual prescription pill bottle containers with drug warning labels attached were then shown to all of the patients for review. Once the patient provided their interpretations, the research assistant administered the Rapid Estimate of Adult Literacy in Medicine (REALM), a reading recognition test comprised of 66 health-related words. The REALM is the most commonly used test of patient literacy in medical settings. It is highly correlated with standardized reading tests and the Test of Functional Health Literacy in Adults.
The initial order of the warnings on the back of the bottle (eg, first, second, or third position) was also randomly assigned and replicated across all label versions (Figure 2). The bottles were then randomly grouped into 3 sets, every set containing 1 bottle from each label version and all of the 9 warnings (Figure 1). Patients were thereby exposed to all of the drug warnings and each label type, seeing only 1 version of each warning message. Consecutive patients scheduled for medical appointments at each of the clinics who consented to the study were sequentially assigned to 1 of the 3 regimens to review.

OUTCOMES

Correct interpretation by patients of the 9 prescription drug warnings placed on container vials was evaluated. A trained research assistant at each location would direct patients to the back of 1 of 3 prescription vials and ask, “In your own words, what do these labels mean to you?” The patient’s verbatim responses were documented on a separate form. All patient responses to each of 9 drug warnings were then independently rated as either correct or incorrect by 3 general internal medicine attending physicians from 3 different academic medical centers.

BLINDING AND CODING

Each physician rater was blinded to all patient information and was trained to follow stringent coding guidelines agreed on previously by the research team. Specifically, correct scores were to be given only if the patient’s response included all aspects of the label’s message. Responses were given an incorrect score if they were inaccurate, or if they did not contain all aspects of the warning. During the coding process it was noted that many participants did not attempt to interpret all of the warning labels on a bottle. If a patient did not respond to a warning label, this was coded as “nonattendance.”

Interrater reliability among the 3 physicians coding the patient responses was high (κ=0.87). The 380 responses (8.4%) that received discordant ratings between the 3 reviewers were sent for further review to an expert panel that included a primary care physician, a clinical psychologist, and a health services researcher with expertise in health literacy. Each panel member, also blinded to patient information, independently reviewed and coded the responses as correct or incorrect. For 327 of the 380 responses (86.1%), a consensus ruling was achieved among the expert panel for a final ruling on the coding of those responses. For the remaining 53 patient responses, a majority rule was imposed, and the rating by a minimum of 2 panel members was used to determine the scores.

ANALYSIS PLAN

Descriptive statistics (percentage, mean [SD]) were calculated for patient demographic characteristics, literacy, and attendance to and correct interpretation of each individual warning label. χ² Tests were used to evaluate the association between label type and patient understanding of each of the 9 prescription medication primary label instructions and also attendance to the auxiliary labels. The latter was viewed as an unexpected but important outcome of interest with significant implications to clinical practice. For that reason, multivariate analyses were conducted, first modeling attendance to each of the warnings, followed by correct interpretation. The 9 binary repeated responses of attendance or correct interpretation per participant were modeled using a generalized linear model with a binomial distribution and logit link function. A generalized estimating equation approach was used to adjust model coefficients and standard errors for within-patient correlation. An unstructured correlation structure was specified. The primary independent variable of interest for both models was label type (simplified text, simplified text + icon vs current standard). The final multivariate model included the potential confounding variables age, sex, race (African American vs white), literacy (low [sixth grade or below], marginal [seventh to eighth grade], or adequate [ninth grade or higher]), education, and number of medications currently taken daily. While educational attainment is associated with literacy, it was examined separately but included in the final model to present conservative estimates of the effect of literacy on rates of understanding. This issue has previously been reviewed by Wolf et al, and the same method was used. Site was also entered into the model to adjust for any potential differences across study locations. Potential interactions between label type and literacy as well as all combinations of age, education, race, literacy, and label type were tested in additional models. All statistical analyses were performed using Stata software (version 10.0; College Station, Texas).

RESULTS

The mean (SD) age of respondents (n=500) was 48.9 (14.4) years (range, 18-83 years). Sixty percent were female, nearly two-thirds (63.6%) were African American, and one-third (32.8%) were white; 19.4% reported having less than a high school level of education (Table 1). Patient literacy was limited; 20.1% were reading below a seventh grade level (low literacy), and 32.0% were reading at the seventh to eighth grade level (marginal literacy). Patients were taking an average of 2.9 prescription medications. Lower literacy was associated with older age (P < .001), African American race (P < .001), less education (P < .001), and the Shreveport study site (P < .001). No significant differences were reported between literacy level, sex, or number of prescription medications taken daily (see Table 2 for P values).

Overall, patients gave a total of 3328 responses out of a possible 4500 (74.0% response rate) across the 9 prescription drug warnings they were given to review; a non-response represented patients not attending to and attempting to interpret a warning on the bottle (Table 3). Overall rates of attendance to drug warnings on the prescription bottles varied significantly among patients viewing standard, simplified text, and simplified text + icon warning labels (70.2%, 73.4%, and 78.3%, respectively;
Among the 3328 patient attempts to interpret drug warnings, 403 (12.1%) were coded as incorrect (Table 3). Overall rates of correct interpretation significantly varied by label type; with simplified text + icon and simplified text-only warnings more likely to be understood compared with standard warnings (92.1%, 90.6%, and 80.3%, respectively; P < .001). The same significant differences were found between simplified text and patient-centered icons and standard labels (which included both text and icons) among patients with low literacy skills.

Belts that were not in the most prominent (first) position on the container were less likely to be attended to by patients (second position−AOR=0.79; 95% CI, 0.70-0.90; third position−AOR=0.70; 95% CI, 0.62-0.79). In addition, older age, male sex, and fewer years of schooling were statistically significant independent predictors of poorer attendance to drug warnings. A significant interaction was found between label type and literacy level. Patients with low literacy skills were more likely to attend to simplified text labels compared with the standard warning (AOR, 1.60; 95% CI, 1.09-2.33; P = .02); no significant differences (P = .39) were noted between attendance to labels with simplified text vs simplified text + icons by those with low literacy skills.

Beyond attendance, prescription drug warning labels with simplified text and simplified text + icons were also significantly more likely to be correctly interpreted compared with standard labels (simplified text−AOR=2.64; 95% CI, 2.00-3.48; simplified text + icons−AOR=3.26; 95% CI, 2.46-4.32; Table 2). When the reference group was changed to labels with simplified text only, patients’ ability to correctly interpret labels was not significantly different from the inclusion of the patient-centered icon (simplified text + icons−AOR=1.23; 95% CI, 0.90-1.70; P = .20). Low literacy level was also a significant independent predictor of misinterpretation (AOR, 0.65; 95% CI, 0.44-0.94). Similar to the outcome of attendance, an interaction between label type and literacy level was found. Patients with marginal and low literacy skills were better able to correctly interpret warning labels with simplified text and icons compared with labels with simplified text only (marginal literacy−AOR=2.59; 95% CI, 1.24-5.44, P = .01; low literacy−AOR=3.22; 95% CI, 1.39-7.50; P = .006). Similar differences were found between simplified text and patient-centered icons and standard labels (which included both text and icons) among

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Table 1. Characteristics of Study Sample

<table>
<thead>
<tr>
<th>Variable</th>
<th>All Participants (N=500)</th>
<th>Low (n=101)</th>
<th>Marginal (n=160)</th>
<th>Adequate (n=239)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (SD), y</td>
<td>48.9 (14.4)</td>
<td>48.1 (13.3)</td>
<td>45.6 (14.6)</td>
<td>51.5 (14.2)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Male</td>
<td>39.6</td>
<td>44.6</td>
<td>38.8</td>
<td>38.1</td>
<td>.34</td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>&lt;.001</td>
</tr>
<tr>
<td>African American</td>
<td>63.6</td>
<td>90.1</td>
<td>83.1</td>
<td>39.3</td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>32.8</td>
<td>6.9</td>
<td>15.0</td>
<td>55.7</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>3.6</td>
<td>3.0</td>
<td>1.9</td>
<td>5.0</td>
<td></td>
</tr>
<tr>
<td>Education</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>&lt;.001</td>
</tr>
<tr>
<td>&lt;High school</td>
<td>19.4</td>
<td>37.0</td>
<td>30.0</td>
<td>5.0</td>
<td></td>
</tr>
<tr>
<td>High school/GED</td>
<td>33.2</td>
<td>54.0</td>
<td>36.2</td>
<td>22.7</td>
<td></td>
</tr>
<tr>
<td>Some college</td>
<td>20.4</td>
<td>7.0</td>
<td>21.9</td>
<td>25.1</td>
<td></td>
</tr>
<tr>
<td>≥College graduate</td>
<td>26.6</td>
<td>2.0</td>
<td>11.9</td>
<td>47.1</td>
<td></td>
</tr>
<tr>
<td>Medications taken daily, mean (SD), No.</td>
<td>2.9 (3.1)</td>
<td>2.8 (3.5)</td>
<td>2.6 (2.9)</td>
<td>3.1 (3.1)</td>
<td>.05</td>
</tr>
<tr>
<td>Site</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>.002</td>
</tr>
<tr>
<td>Chicago, Illinois</td>
<td>50.0</td>
<td>31.7</td>
<td>54.4</td>
<td>54.8</td>
<td></td>
</tr>
<tr>
<td>Shreveport, Louisiana</td>
<td>50.0</td>
<td>68.3</td>
<td>45.6</td>
<td>45.2</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Practice setting</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Academic</td>
<td>50.0</td>
<td>33.7</td>
<td>33.1</td>
<td>68.2</td>
<td></td>
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<tr>
<td>Community</td>
<td>50.0</td>
<td>66.3</td>
<td>66.9</td>
<td>31.8</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviation: GED, general education diploma.

a All data are given as percentages except where indicated.
individuals with limited literacy skills (marginal literacy – AOR=1.99; 95% CI, 1.01-3.90; P = .05; low literacy – AOR=2.13; 95% CI, 1.04-4.40; P = .04).

In our study, many patients did not attend to or correctly interpret potentially important warning information commonly placed on prescription drug containers to support proper understanding and use. However, auxiliary warning labels that had explicit, easy-to-read messages significantly improved rates of attendance and comprehension among patients. The inclusion of icons on warning labels, developed with patient feedback, was found to further improve attendance and correct interpretation among individuals with low literacy skills. The use of both explicit language and icons has previously been found to support comprehension of health materials.15,20-23 While the study further confirms the value of these enhanced print attributes to increase patient understanding, our findings may offer additional guidance to clinical practice as follows.

First, not all of the patient-centered icons were effective at improving comprehension beyond the revised text. In particular, a few of the icons provided abstract imagery for messages that were more difficult to visually depict in such a small size, such as “Use only on your skin.” It may not be possible or necessary to create icons for every warning message. Rather, one approach might be to use established thresholds for rates of comprehension, as in the process detailed by the IOS (ie, >80%), to determine the adequacy of a particular icon or drug warning.13 Given the limited space for content on prescription drug containers, it would be helpful to include only those icons that have been shown in consumer testing to significantly improve comprehension beyond simplified text alone.
Second, patients were less likely to attend to drug warnings, regardless of label type, if they were in the second or third position on the prescription container. In broad terms, it is possible that warnings are not perceived as essential information to aid patients in their use of a medication. Patients might give only a cursory glance at the content of these labels, not believing that the task requires considerable attention. Previous research has reported that patients do not seem to expend a great deal of cognitive effort in reviewing medication instructions and precautions, and as a result they may be at greater risk for making errors. Yet this finding could indicate a level of distraction imparted to patients by the considerable content placed on a relatively limited amount of space. A practical solution may be to limit the number of auxiliary warnings to only the 1 or 2 deemed most critical to a prescribed drug’s safe and appropriate use. Any other warnings could be referenced in supplemental patient medication information materials. Note to that regard could also be placed on the container label to direct patients to the accompanying patient leaflets or medication guides. To accomplish this, a detailed investigation of the current pharmacological evidence supporting each of the warnings and precautions associated with each prescription drug would need to be performed.

Third, it is important to note that patient literacy level remained a significant independent predictor of correct interpretation of drug warnings. The use of patient-centered icons along with clear, concise instructions and/or precautions may improve comprehension among patients with lower literacy skills. However, it is likely that enhanced print materials alone are insufficient for addressing literacy disparities. Patient counseling, in addition to better labeling practices, will be necessary in order to comprehensively respond to health literacy problems. Previous research has shown that physicians do not commonly review medication instructions at the time of prescribing, nor do pharmacists routinely verbally counsel patients when filling prescriptions. More effective communication strategies should be devised to ensure that both prescribing clinicians and pharmacists can adequately counsel patients and provide simple, clear, and explicit information on how to safely use their medicine.

There are several limitations to our study that should be recognized. To begin, we investigated patient comprehension of different styles of writing warning instructions and precautions and the effectiveness of icons to support understanding only. The association between misinterpretation of these warning labels and medication error was not examined. We also did not study patients’ actual prescription drug-taking behaviors. Patients’ motivation, concentration, and comprehension might have been greater if they were reporting on their own medicine given by their physician for conditions they actually had. Because the study design did not include a medical chart review, we also did not have information on patients’ health information, in particular, whether they had actual experience with medication use. While labels were randomly grouped, patients themselves were not randomized. However, no differences were noted by demographic characteristics or literacy level across study arms. Other elements of the study container and labels (ie, Target’s ClearRx flat panel bottle, use of color on warning labels, number of warnings per bottle) were not directly evaluated in this investigation but also might influence comprehension. Finally, the generalizability of our findings is further limited by the fact that patients were predominantly African American and female (an accurate depiction of the clinic patient populations) and that participation was limited to patients who spoke English. This was due in part to criteria for using the REALM as our literacy assessment. Because many pharmacies are limited in their ability to provide language concordant services, it is of increasing importance for studies to examine ways to communicate prescription warning information to patients with limited English proficiency (LEP). The use of the patient-centered icons, in particular, may be especially helpful and should be evaluated among populations with LEP.

In summary, prescription warnings placed on the container label may be particularly valuable to patients as the most tangible source of medication information. Presently, there are several companies that produce auxiliary warning labels (as part of a software package or as container stickers) for use among community pharmacies, including the pharmacies themselves. As a result, different messages and icons may be used to convey similar messages regarding medication administration. A large
number of these instructions and precautions remain unnecessarily complex and are seldom tested for comprehension among consumers to include their feedback in the development process. We offer additional evidence for setting forth best practices in the design and development of patient-centered prescription drug warnings for use on container labels. Regulatory and policy-setting entities, including the FDA, US Pharmacopeia, and state boards of pharmacy, should consider setting standards for ensuring the use of a single recommended list of prescription drug warnings that include comprehensible language and icons.

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Correspondence: Michael S. Wolf, PhD, MPH, Division of General Internal Medicine, Feinberg School of Medicine, Northwestern University, 750 N Lake Shore Dr, 10th Floor, Chicago, IL 60611 (mswolf@northwestern.edu).


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Correction

Error in Figure. In the article titled “Improving Prescription Drug Warnings to Promote Patient Compre-
hension” by Wolf et al, published in the January 11, 2010, issue of the Archives (2010;170[1]:50-56), there was an
error in Figure 1. The simplified text for Label 1 should have read “Shake well before using.”