Improving Prescription Drug Warnings to Promote Patient Comprehension

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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 simplified 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 \( \text{AOR}=2.64; 95\% \text{ confidence interval [CI]}=2.00-3.49 \), simplified text + icons − \( \text{AOR}=3.26; 95\% \text{ CI}, 2.46-4.32 \)). Patients’ ability to correctly interpret labels was not significantly different with the inclusion of icons (simplified text + icons − \( \text{AOR}=1.23; 95\% \text{ CI}, 0.90-1.67; P = .20 \)). Low literacy was also an independent predictor of misinterpretation (\( \text{AOR}, 0.65; 95\% \text{ CI}, 0.44-0.94 \)). 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 − \( \text{AOR}=2.59; 95\% \text{ CI}, 1.24-5.44; P = .01 \); low literacy − \( \text{AOR}=3.22; 95\% \text{ CI}, 1.39-7.50; P = .006 \)).

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.

Arch Intern Med. 2010;170(1):50-56
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.

**METHODS**

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). Guide-lines established by the International Organization for Standardization (IOS) for the development and testing of universal icons were followed. Other design elements were also implemented, including removal of the use of color and optimizing font size for clarity.

**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.

**ASSIGNMENT**

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
were sequentially assigned to 1 of the 3 regimens to review. Each label
above the warning was repeated 4 times (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. 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 warn-
ings 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 docu-
mented on a separate form. All patient responses to each of 9 drug
warnings were then independently rated as either correct or in-
correct 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 pre-
viously 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 la-
bes placed 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 pa-
tient 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 pri-
mary care physician, a clinical psychologist, and a health ser-
dice researcher with expertise in health literacy. Each panel
member, also blinded to patient information, independently re-
viewed 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 mem-
bers was used to determine the scores.

ANALYSIS PLAN

Descriptive statistics (percentage, mean [SD]) were calculated
for patient demographic characteristics, literacy, and attend-
dance 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 prescrip-
tion medication primary label instructions and also attend-
dance 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
variables 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 coeffi-
cients 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 vari-
able 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 attain-
ment 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,19 and the same
method was used. Site was also entered into the model to ad-
just for any potential differences across study locations. Po-
tential 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 fe-
nal, nearly two-thirds (63.6%) were African Ameri-
can, 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 (mar-
ginal literacy). Patients were taking an average of 2.9 pre-
scription 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 bet-
tween literacy level, sex, or number of prescription medi-
cations 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 pre-
scription drug warnings they were given to review; a non-
response represented patients not attending to and at-
tempting to interpret a warning on the bottle (Table 3).
Overall rates of attendance to drug warnings on the pre-
scription bottles varied significantly among patients view-
ing standard, simplified text, and simplified text + icon
warning labels (70.2%, 73.4%, and 78.3%, respectively;
Plurified text and simplified text

Overall rates of correct interpretation significantly varied, with 403 (12.1%) being coded as incorrect (Table 3). Respondents were more likely to attend to simplified text only or standard labels. "Limit your time in the sun" was significantly more likely to be correctly interpreted compared with standard warnings (95% CI, 2.46-4.32; Table 2). When the reference group was changed to labels with simplified text only, patients were statistically significantly more likely to be correctly interpreted compared with standard labels (simplified text−AOR=2.64; 95% CI, 1.90-3.33; 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.

Among the 3328 patient attempts to interpret drug warnings, 403 (12.1%) were coded as incorrect (Table 3). Simplified text + icon labels instructing patients to "Take with food or milk" and "May cause drowsiness. Be careful when driving a car or using machinery" were better attended by respondents than simplified text only or standard labels. Labels that were not in the most prominent (first) position on the container were less likely to be attended to by patients than their standard warning label counterparts (Table 3). Simplified text + icon labels that cautioned "Use only on your skin," "Talk to your doctor before using any over-the-counter drugs," and "Do not stop taking unless directed by your doctor" were more likely to be attended to by patients than their standard warning labels (98.3% vs 89.3%; P<.001). The same simplification effect was noted between simplified text and simplified text + icons by those with low literacy skills.

In multivariate analyses, both label type and label order were associated with attendance to the auxiliary drug warning labels (Table 2). Simplified text labels, with and without patient-centered icons, were better attended to by patients than standard labels (simplified text−adjusted odds ratio [AOR]=1.17; 95% confidence interval [CI], 1.02-1.36; simplified text + icon−AOR=1.59; 95% CI, 1.38-1.83). When the reference group was altered from standard label to the simplified text label, warnings that included both simplified text and icons were found to be better attended to than the labels with simplified text only (AOR, 1.35; 95% CI, 1.19-1.55; P<.001). Labels 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 with 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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Abbreviation: GED, general education diploma.

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).

**COMMENT**

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.\textsuperscript{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.\textsuperscript{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.

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Abbreviations: AOR, adjusted odds ratio (adjusted for all variables shown); CI, confidence interval; GED, general education diploma; NA, not applicable.
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.2-4 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. A 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 formidably 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.24-26 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.27-29 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).30 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

### Table 3. Attendance to and Correct Interpretation of Drug Warnings by Label Type

<table>
<thead>
<tr>
<th>Warning Label</th>
<th>Standard</th>
<th>Simplified Text</th>
<th>Simplified Text + Icon</th>
<th>P Value</th>
</tr>
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<table>
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<th>Simplified Text + Icon</th>
<th>P Value</th>
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</table>

*See Figure 1 for warnings for each label type.*
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.

Accepted for Publication: August 22, 2009.

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Financial Disclosure: Dr Wolf has received financial support for research, consultation, and grant review services from Pfizer Pharmaceuticals.

Funding/Support: Research and faculty support was provided to Drs Wolf (principal investigator), Davis, and Parker by grants from Target Corp and the Agency for Healthcare Research and Quality (R01HS017687).

Additional Contributions: Mickey Eder, PhD, and Access Community Health Network provided their support of this project.

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Correction

Error in Figure. In the article titled “Improving Prescription Drug Warnings to Promote Patient Comprehension” 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.”