

Improved Label and Liver Warning for Nonprescription Acetaminophen Products

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BACKGROUND

- Acetaminophen is safe for self-care when used as directed, but has a narrow therapeutic index.^{1,2}
- Acetaminophen-related overdose is currently the number one cause of acute liver failure, and is a leading cause of liver transplant in the United States.^{2,3}
- Appropriate labeling of the over-the-counter (OTC) Drug Facts Labels for nonprescription acetaminophen has been a primary focus of the FDA for over 46 years.⁴

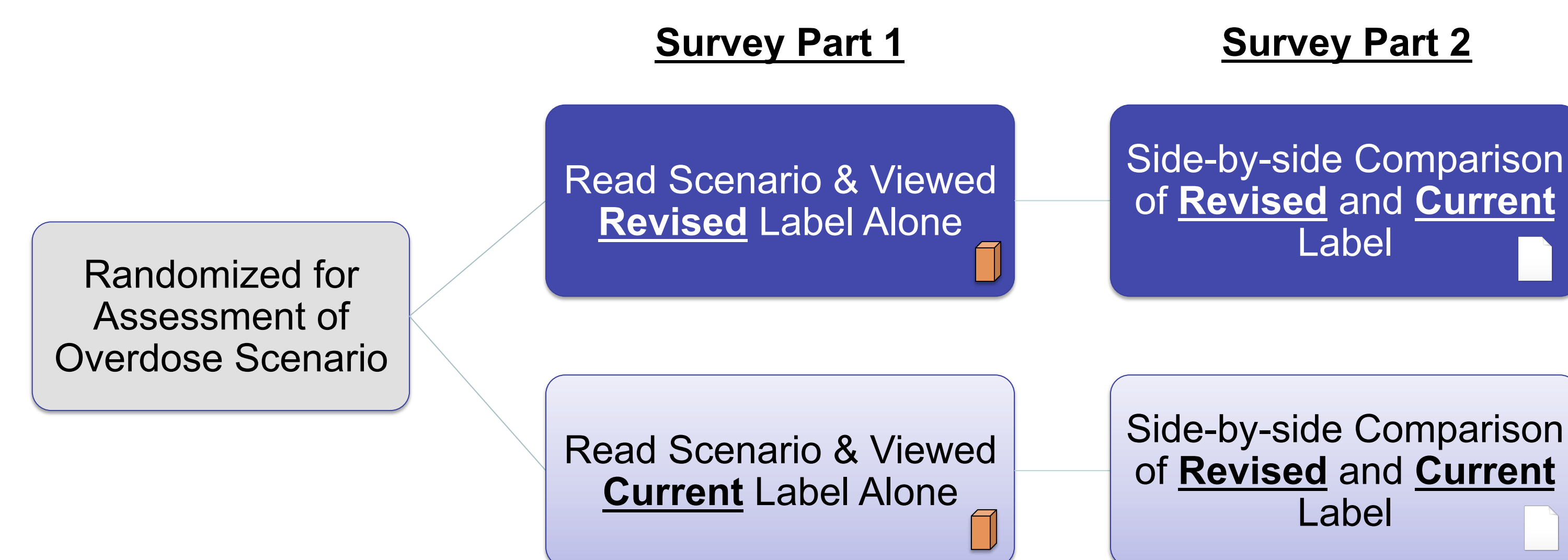
PURPOSE

- Compare consumer preferences for, and comprehension of, the current OTC Drug Facts format versus a revised format for nonprescription acetaminophen labeling, using previously published methodology.
- Compare consumer preferences for a revised cap statement versus the currently marketed cap statement on brand Tylenol (acetaminophen).

METHODS

- Study design:** Prospective label comprehension study using design and implementation from prior published studies.⁵ Study approved by the UCSF Committee on Human Research.
- Revised label:** Development informed by an extensive literature review, expert opinion from liver transplant and Poison Control pharmacists, and focus groups.
- Revised cap statement:** Developed using information already contained on the current OTC Drug Facts label.
- Recruitment:** Community center in San Francisco in September 2013. Participants received a US\$5.00 gift card incentive for survey completion.
- Inclusion criteria:** No history of liver damage due to acetaminophen; between 18 – 90 years of age; able to read English; able to read English in 6-point Helvetica with or without corrective lenses; consent to participate in study.
- Measures:** (a) Label: ease of finding and understanding the liver warning, correct intended action after reading scenario (Table 1), usefulness and overall preference (Figure 3); (b) Cap Statement: likelihood to read label and overall preference (Figure 5).

Figure 1: Schematic of Study Procedure



Sequence of Survey Questions

Part 1: Initial scenario using an actual OTC acetaminophen carton for reference:

- Correct Intended Action Question:** "Based on reading the information on the Drug Facts Label, if you were Henry, what would you tell Dolores to do?"
- Scenario:** "In the past, Dolores used acetaminophen for her arthritis pain. On Saturday her arthritis was getting worse. She bought a bottle of Extra Strength acetaminophen at her local pharmacy. Dolores took the acetaminophen as recommended on the carton label (2 caplets every 6 hours). On Monday morning, she felt that the pain relief from the medication did not last for the 6 hours between doses. She started to take 2 caplets every 3 to 4 hours. Dolores planned to see her doctor on Friday afternoon. Over the next several days, she continued to take her acetaminophen – about 2 caplets every 3 to 4 hours. On Thursday morning, Dolores woke up feeling very tired. She felt like she would throw up and had a dull pain in her stomach. She vomited. Her significant other, Henry, was worried and decided to look at the drug label."
- Additional questions** on accessibility, readability and understandability (Table 1).

Part 2: Side-by-side label and cap comparisons:

- Questions on usefulness and preferences (Figure 3 and 5) were answered after the scenario question.
- Current and revised labeling was excerpted and presented side-by-side in the survey questionnaire.

RESULTS

- N=110 included in final analysis:** 120 participants recruited, 10 were excluded for failure to meet inclusion criteria and early drop out.
- Baseline demographics:** Well-balanced between participants randomized to view the current label first versus the revised label first (p>0.05).
 - Age ≥36 years (71% vs. 55%)
 - Female (69% vs. 65%)
 - Achieved secondary education (91% vs. 81%)
 - Caucasian (85% vs. 80%)
 - Past use of multiple OTC analgesics (acetaminophen [78% vs. 85%], aspirin [60% vs. 75%], ibuprofen [89% vs. 89%])

Figure 2. Current (A) and Revised (B) OTC Label for Side-by-Side Comparisons

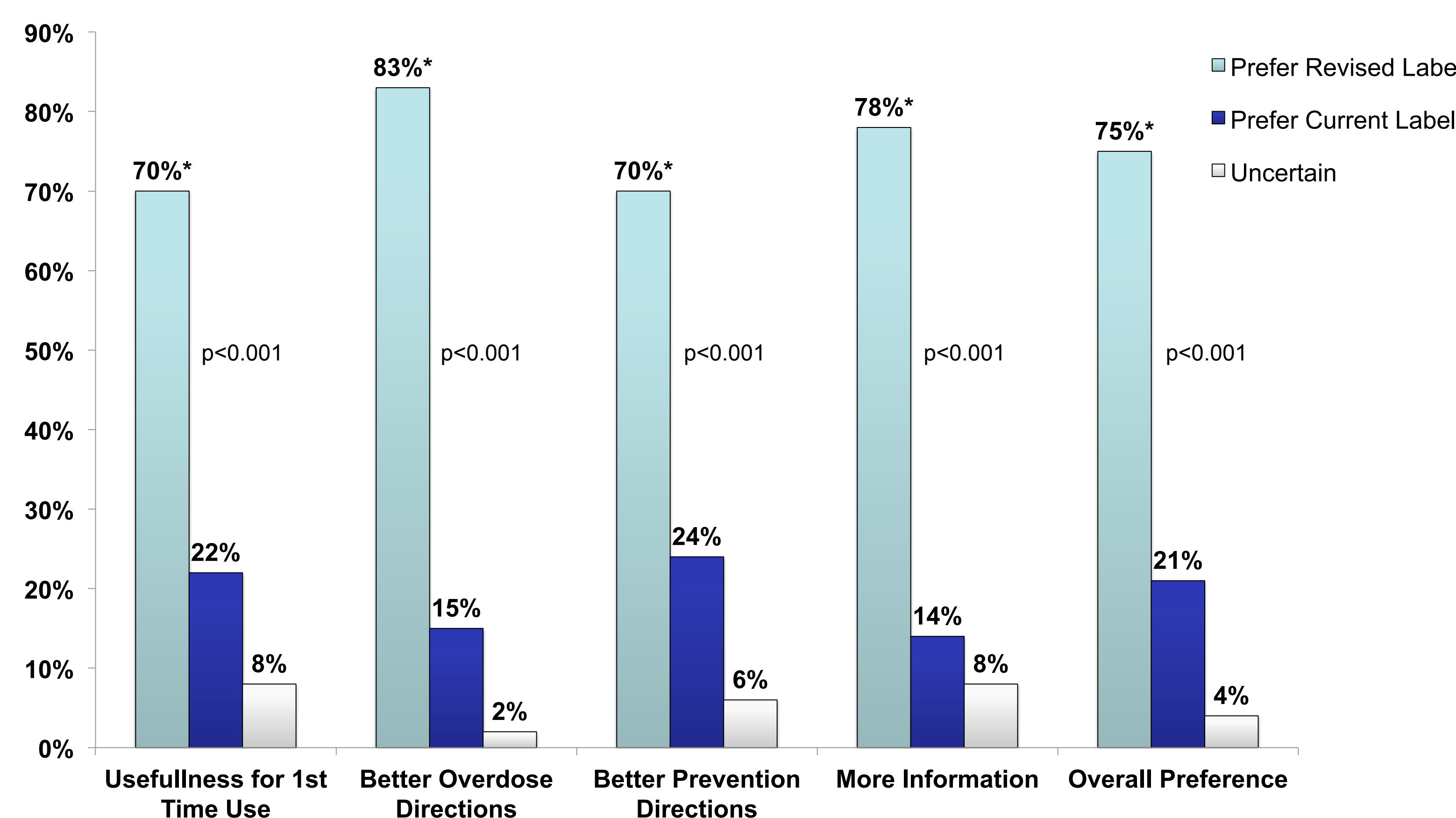
Note: Labels were controlled for length, size, and font to ensure these elements would not confound results. Information on the Drug Facts label was separated into two panels (sides) of the box carton, as they appear on the actual carton. Both labels fit into the existing space allotted by the generic drug manufacturer for the current OTC Drug Facts label.

Table 1. Overdose Scenario: Individual Reviews of Actual Cartons (N=55 per group) [^]

	Group A Rating Current Label, n (%)	Group B Rating Revised Label, n (%)	95% CI Group A	95% CI Group B	p-value for difference
Very easy/easy to find	85% (47)	87% (48)	0.76 – 0.94	0.78 – 0.96	0.8 ^a
Very easy/easy to understand	89% (49)	87% (48)	0.81 – 0.97	0.78 – 0.96	0.8 ^a
Correct Intended Action	76% (42)	91% (50)	0.65 – 0.87	0.83 – 0.99	0.03 ^a

[^]This parameter includes ratings of the individual labels as very easy or fairly easy on a 5-point Likert scale prior to participants viewing both labels side-by-side.
a) Two-sided, two-sample Z-test of proportions between observed percentages in Group A and Group B.

Figure 3. Overall Usefulness and Preference Ratings for Labels (N=110, both groups)



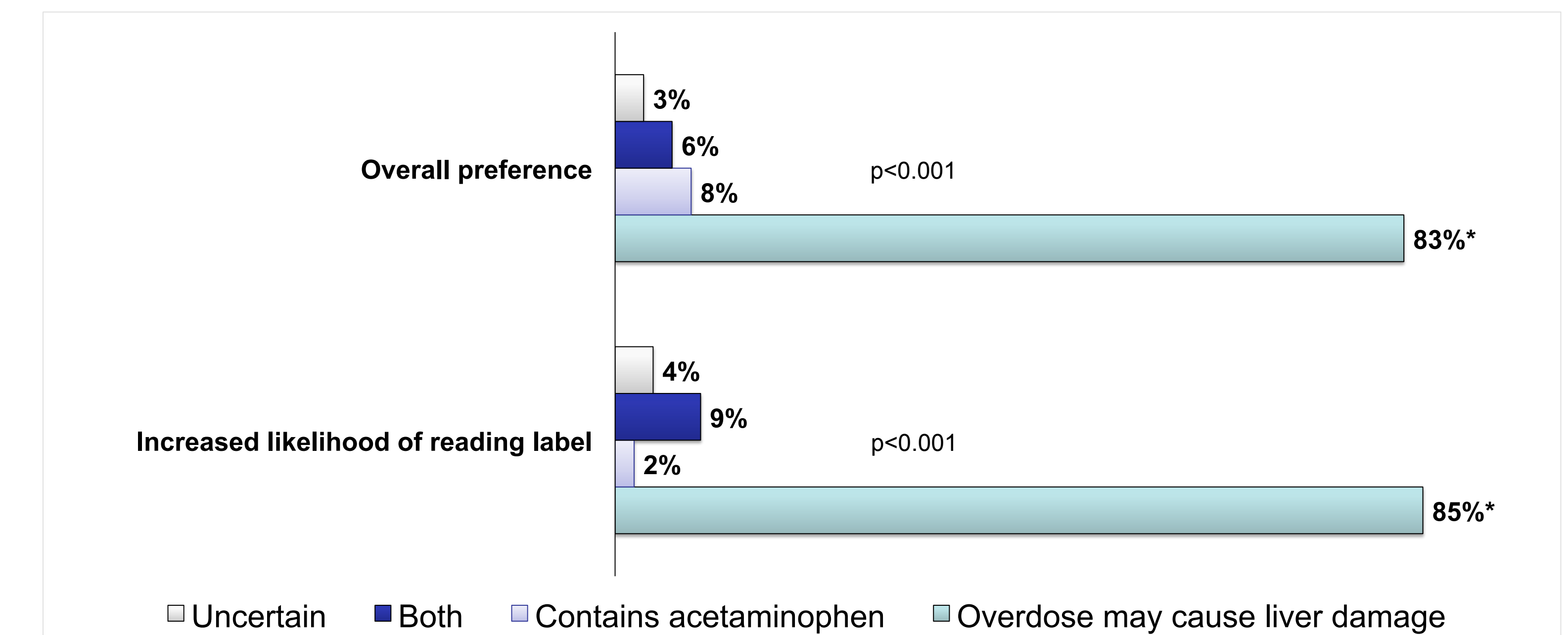
* Two-sided, two-sample, Z-test of proportion between percent who selected revised label vs. percent who selected current label; statistically significant p<0.001, adjusted for multiple tests

RESULTS (continued)

Figure 4. Current (A) and Revised (B) Cap Statement for Side-by-Side Comparison



Figure 5. Overall Increased Likelihood of Reading the Label and Preference



*Percent preferring current vs. revised cap; two-sided, Z-test of proportion, statistically significant p<0.001, adjusted for multiple tests

DISCUSSION, LIMITATIONS, CONCLUSIONS

- Discussion:** To our knowledge, this is the first publicly available post-marketing study on the liver warning in the acetaminophen OTC Drug Facts label.

Consumers preferred the following key revisions to the current liver warning for OTC acetaminophen: signs of overdose, re-location of directions to seek medical help after "severe liver damage," revised headings, and re-organization of information to improve usefulness.

- Potential Limitations:** (a) sample size, although the study demographic matches a large segment of the U.S. consumer population; (b) investigators not blind to randomization although researchers were trained with a standard script and did not interfere with participants completing the survey on their own.
- Conclusions:** Our findings indicate the proposed labeling revisions would help improve consumer awareness and action in the event of an overdose.

The label comprehension model used in this study can serve as a lower cost approach with rapid turn-around for those companies interested in optimizing the likelihood that their product labels will be used to help improve medication safety.

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DISCLOSURES

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