# Report to Congress

# Implementation of Section 3507 of the Patient Protection and Affordable Care Act of 2010

# Final Report

# Food and Drug Administration

## Executive Summary

The Secretary of Health and Human Services (the Secretary) is providing this final report to Congress in accordance with Section 3507 of the Affordable Care Act of 2010. Under this Section of the Patient Protection and Affordable Care Act, Congress asked the Food and Drug Administration (FDA) to determine whether adding quantitative summaries of the benefits and risks of prescription drugs in a standardized format to promotional labeling or print advertising for drugs would improve health care decision-making by clinicians, patients, and consumers. To make this determination, FDA performed a thorough review of all available scientific evidence and research in the areas of social and cognitive psychology regarding whether the presentation of quantitative risk and benefit information influences people's processing, understanding, and behavior; consulted with outside experts; and conducted three studies. Based on these efforts, the Secretary of the Department of Health and Human Services (HHS) determined that the inclusion of such quantitative information in a standardized format cannot be readily applied to many drugs. Therefore, it is not appropriate to issue new regulations that would require such information to be added to promotional labeling or print advertising for all prescription drugs. The detailed reasoning and analysis for this determination is provided in this report.

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## I. Background

In March 2010, President Obama signed into law a comprehensive health reform bill, the Patient Protection and Affordable Care Act, Pub. L. No. 111-148, 124 Stat. 119 (2010), and a package of amendments to the Affordable Care Act, the Health Care and Education Reconciliation Act of 2010, Pub. L. No. 111-152, 124 Stat. 1029 (2010). These laws are collectively referred to as the Affordable Care Act.

Subsection 3507(a)[1] of the Affordable Care Act requires the HHS Secretary, acting through the Commissioner of FDA, to determine whether the addition of quantitative summaries of the benefits and risks of prescription drugs in standardized format (i.e., similar to the "Drug Facts" box on over-the-counter products) to the promotional labeling or print advertising of such drugs would "improve health care decision-making by clinicians and patients and consumers."

Subsection 3507(b) of the Affordable Care Act requires FDA to consider research in the areas of social and cognitive psychology and to consult drug manufacturers, clinicians, patients, and consumers—specifically "experts in health literacy, representatives of racial and ethnic minorities, and experts in women's and pediatric health."

Finally, Subsection 3507(c) of the Affordable Care Act directs FDA to submit a report to Congress outlining its determination under subsection (a). If FDA determines that adding these types of standardized risk–benefit summary statements (or tables) to advertising or promotional labeling for prescription drugs would improve health care decision-making, subsection 3507(d) of the Affordable Care Act directs FDA to promulgate proposed regulations setting forth such requirements.

When FDA initiated its analysis, available research did not provide a sufficient scientific basis to conclude whether the promulgation of proposed regulations to require the addition of quantitative summaries of the benefits and risks of prescription drugs on promotional labeling or print advertising would improve health care decision-making. FDA estimated that it would take 3 years to conduct the necessary studies, literature review, and consultation with appropriate experts. FDA provided Congress with a report in March 2011 outlining its plan of action. In two subsequent reports, dated May 2012 and June 2013, FDA apprised Congress of its progress. This is FDA's final report as mandated under Subsection 3507(c).

[1] Pub. L. No. 111-148, Section 3507, 124 Stat. 119, 530 (codified at note following 21 U.S.C. Section 352).

## II. Prior Research on Standardized Formats

Since at least the mid-2000s, FDA has considered whether a standardized Drugs Facts box format on prescription drug promotional labeling and advertising, similar to a Drug Facts box on over-the-counter drug labeling, that contained quantitative information about the risks and benefits of prescription drugs, would enhance health care decision-making. Between 2007 and 2008, FDA collaborated on a pilot project with researchers[2] from the Veteran's Administration Outcomes Group at Geisel School of Medicine at Dartmouth, who contributed to the scientific literature on this issue. The pilot project engaged eight volunteer FDA medical officers in the Office of New Drugs (OND) in the Center for Drug Evaluation and Research (CDER) and involved the development of sample Drug Facts boxes containing risk and benefit information for certain approved prescription drug products based on approved label information. After developing sample boxes, FDA volunteers held a workshop to discuss issues with the process and helped develop a hypothetical guidance document to be used by other medical officers.

Although the OND medical officers who volunteered for the pilot study liked the idea of a Drugs Facts box that contained quantitative information about the risks and benefits of prescription drugs, they found that developing a useful, accurate box was difficult for some prescription drugs. These issues included whether it was feasible to accurately summarize the risks and benefits of prescription drug products with multiple indications and/or multiple clinical trials in a single standardized format. In general, prescription drug labeling includes results from several clinical trials, with multiple symptoms and outcomes being measured in different patient populations. Medical officers found that the variable amount and nature of clinical trial data available for different drugs makes developing a standard format a challenge, as prescription drugs may have many critical studies, multiple indications, boxed warnings, many warnings and precautions, or complex dosing instructions. In addition, the complexity of certain study designs may present a challenge for developing a standard format that communicates these results accurately and helpfully (e.g., composite endpoints, comparators versus placebo, multiple doses studied).

These concerns were presented to FDA management in an August 2008 briefing as part of a determination about whether to extend work on the pilot project. Managers in CDER were presented with several options for extending the project, including the potential for taking regulatory action that would require industry stakeholders to provide Drug Facts boxes that contained quantitative information about the risks and benefits of prescription drugs as part of the new drug application process; the potential for issuing nonbinding guidance recommending, but not requiring, industry to provide the boxes; and the potential for requiring that FDA medical officers create Drug Facts boxes themselves as part of the new drug approval process. CDER management agreed that, while the pilot project represented a novel approach to providing medication information, there was not

[2] Lisa M. Schwartz, MD, MS and Steven Woloshin, MD, MS.

enough information about how Drugs Facts boxes for prescription drugs could benefit health care decision-making. At that time, FDA chose not to move forward with requiring a Drugs Facts box for prescription drugs. Section V of this report discusses FDA's current efforts to provide useful benefit-risk information about regulated products to prescribers and consumers.

## III. Current Research

Under the Affordable Care Act, FDA was asked to look at this issue again, and determine if it would be appropriate to take regulatory action to require the addition of such quantitative summaries of prescription drug benefits and risks of in a standardized format on the promotional labeling or print advertising of prescription drug products. As FDA reported to Congress in March 2011, available information at that time did not provide a sufficient scientific basis to conclude whether the promulgation of proposed regulations would improve health care decision-making. In order to obtain more data, FDA conducted a thorough literature review, convened a Risk Communications Advisory Committee (RCAC) meeting to solicit feedback from experts and representatives of racial and ethnic minorities, and conducted three studies regarding prescription drug advertising. These efforts are described in further detail below. FDA has attached the literature review and the executive summaries for the three studies currently being prepared for publication.

### A. Literature Review

In accordance with Subsection 3507(b) of the Affordable Care Act, FDA contracted with a research firm[3] to review all available scientific evidence on decision-making and social and cognitive psychology regarding whether the presentation of quantitative risk and benefit information influences people's processing, understanding, and behavior. The review noted the limitations of the existing body of evidence surrounding this issue. While the review concluded that quantitative information improves people's understanding of risks and benefits, relatively few studies focused on behavior, which is important to consider when evaluating its effect on health care decision-making. Additionally, while relatively simple presentations that use both numeric and other means may be useful, no specific format or visual approach to presenting quantitative information distinguished itself as better than other approaches. The review also noted that more systematic research is needed.

[3] Please see attachment 1 for a copy of the published review.

B. 2011 RCAC Meeting[4] and Other Outreach Activities

In accordance with Subsection 3507(b) of the Affordable Care Act, FDA convened a meeting of the RCAC, which included members who are experts in health literacy, representatives of racial and ethnic minorities, and experts in women's and pediatric health. For example, FDA requested the appointment of Dr. Hsiang Yin, an expert in pediatric health at the Bellevue Hospital Center, and confirmed participation by experts already appointed to the RCAC, including Dr. Vicki S. Freimuth, the Director of the Southern Center for Communication, Health, and Poverty; Dr. Michael S. Wolf, a health literacy specialist with the Feinberg School of Medicine at Northwestern University; Dr. Kala L. Paul, an expert in medical risk communication and health literacy; and Dr. Valerie Reyna, who has extensive experience in women's health issues including 2 years as research director at the University of Arizona's Center of Excellence in Women's Health.

Committee members discussed the quality of the studies analyzed in the literature review, and how to present information of differing quality in risk communication. The RCAC observed that the difficulty inherent in scientifically determining the best practices for communicating risk and benefit information, particularly regarding prescription drugs with complex profiles (e.g., multiple indications, warnings, or contraindications, and complex clinical trial data), has resulted in research gaps.

A significant amount of discussion regarding a standardized format centered around the potential creation of a Drug Facts box format similar to that found on over-the-counter products. The following quotations from the RCAC meeting transcript characterize the discussion:

- Dr. Col: "How do we decide what gets in the box and what doesn't get in the box? There might be some critical risk that—are we looking at things according to severity, the difference in the treatment versus control, the magnitude of the difference? Are we looking at statistical significance,

[4] The Drug Facts box format was also discussed at a 2009 meeting of the RCAC in the context of Patient/Consumer Medication Information (CMI/PMI). CMI/PMI is delivered to an individual patient at point of sale, making it conceivable that the information could be individuated by indication. That could be consistent with efforts toward the much-desired "one document solution" where the goal is a single, useful, usable, and relevant document for the patient about his/her prescribed drug. The 2009 RCAC recommended that FDA adopt a standard format for CMI/PMI. The RCAC recommended the Drug Facts box format be adopted as that standard, with the caveat "…it is not clear how a Drug Facts box format might best be integrated with tiered information, how it might affect subsequent consumer decision-making, and what further development might be needed. The recommendation should be read in the spirit of a Drug Facts box being a conceptual standard, that further work should address how to provide more detailed information, and that any adoption should be supported by rigorous evaluation building on existing research." At the 2011 RCAC meeting, however, the focus was prescription drug promotional material, which is individuated by product, not indication.

the strength of the effect, the certainty, how strong the signal is, the duration of the effect, whether it's reversible or not, getting at some of those issues, things that you wouldn't want to go? How do you decide which factors go in that box? That's huge."

- Dr. Brewer: "But let's take the other situation, where there is substantially conflicting data, where you have some kind of a cohort study, another one that's a randomized, controlled trial, but it's small, and then the dosing regimen was sort of screwed up along the way, so that there wasn't really the right kind of dosing that maybe would have given the full story. You can come up with these sorts of peculiarities among studies. I agree that it would take an expert to really yield an opinion about these, and I think some digested form that would be a sentence or two—maybe each study would be described in a sentence, a narrative sentence—would probably be substantially more helpful than one of these enumerations of all these numbers without some kind of context to understand them. So I guess I sort of lean towards, when there's something that we can say with confidence, the number makes sense to me, but when there's a great deal of uncertainty around it, having a narrative description instead of the number would be far preferable. Of course, that then starts to raise the question—you have this ideal situation of A and B, these two polar extremes. Where do you draw the line? When have you crossed that point into being uncertain about being able to combine it into a single point estimate?"

- Dr. Huntley-Fenner: "The questions that one should ask if you are not a perfectly healthy individual don't sort of pop out of a structure like this. I think that's something we ought to be thinking about as we are considering recommendations for a standardized format."

- Dr. Andrews: "You have to pick your poison here. It's a very difficult situation. We have different populations, different duration issues, different types of risks, and different severity. How do you deal with that? Do you include a Drug Facts box with bold disclosures talking about different populations and duration issues? Or do you deal with the population and duration issues with line graphs? Some of you might have seen that for multiple ones, for different types of risks. Yet you are running out of space in the brief summary. And don't even think about that with the commercials."

C. Scientific Studies

FDA conducted three studies in the area of direct-to-consumer (DTC) prescription drug advertising to gather further information regarding whether the addition of quantitative

summaries of benefit and risk information to prescription drug advertising would improve health care decision-making:

- **Presentation of Quantitative Effectiveness Information to Consumers in DTC Television and Print Advertisements for Prescription Drugs (Quantitative Study).** The purpose of this study was to investigate whether adding quantitative benefit and risk information to DTC advertisements for prescription drugs would affect consumers' opinions about the benefits and risks of prescription drugs, and whether it would improve the ability of consumers to make informed decisions about those drugs. The study explored a variety of ways to present that information, including numerical and graphical (visual) presentations. The study found that adding absolute frequency (e.g., 85 out of 100) and percentage (e.g., 85%) information about benefits and risks to DTC ads may help consumers more accurately recall a drug's risks and benefits. Visual aids also helped participants accurately recall how well a drug works, with bar charts and tables demonstrating advantages over other visual aids. However, the addition of quantitative information did not change consumers' attitudes towards the prescription drug, their perception of the drug's benefits or risks, or their intentions to get more information about the drug or to take the drug. More detailed information is contained in the executive summary for this study found in attachment 2.

- **Study of Format Variations in the Brief Summary of DTC Print Advertisements (Format Study).** The purpose of this study was to systematically examine the type of quantitative risk and benefit information that could be presented in a standardized box format to prescription drug advertising, and whether such information would benefit consumer decision-making. The study found that adding absolute frequencies and percentages of risks and benefits in a box format to DTC advertising may help consumers recall that information. Absolute differences (e.g., 3 percentage points higher) and qualitative labels (e.g., more likely), which were included in a previous study on a Drug Facts box-type of format on prescription drug labeling, did not improve consumer recall more than the inclusion of absolute frequencies and percentages. Please see attachment 3 for the executive summary.

- **Study of Clinical Efficacy Information in Professional Labeling and DTC Print Advertisements for Prescription Drugs (Display Page Study).** The purpose of this two-part study was to determine how physicians and consumers, respectively, make risk–benefit assessments for prescription drugs from prescription drug advertising. In particular, the study examined how consumers and physicians make such judgments in response to variations in the efficacy presentations in the display (first) page of a DTC print advertisement. The study found that adding placebo rates (information about the rates of clinical trial subjects who appeared to obtain benefits or risks from a placebo) to DTC ads may help consumers and physicians recall information and form perceptions about prescription drugs. The study did not show a benefit to including quantitative information about both the number of people who benefited from the drug as well as the number of people who did not benefit from the drug,

known as a "mixed frame," as has been suggested by research in the past. The executive summary for this study is captured in attachment 4.

## IV. Reasoning and Analysis for Determination

As discussed above, FDA was asked to determine whether the addition of quantitative summaries of the benefits and risks of prescription drugs in a standardized format added to the promotional labeling or print advertising for such drugs would improve health care decision-making by clinicians, patients, and consumers. The results of a literature review revealed that this type of quantitative information can improve consumer understanding of risks and benefits of prescription drugs. Similarly, FDA conducted three studies which found evidence that the presentation of quantitative information about the risks and benefits of prescription drugs, including percentages of subjects in clinical trials who experienced risks or obtained benefits from a drug, absolute frequencies of risks and benefits, and placebo rates, may help consumers recall information and better understand a drug's risks and benefits. The literature review and studies found evidence that certain types of quantitative information can be helpful in some limited circumstances, such as with drugs that have a single indication and straightforward clinical trial data.

FDA has determined that any format for standardized quantitative information, as directed by Section 3507, would have to be:

(1) consistent and broadly applicable across all promotional labeling and advertising materials;
(2) usable by clinicians, patients, and consumers; and
(3) an improvement to health care decision-making.

Because of the great variability in the amount and complexity of quantitative information about prescription drugs, promulgating regulations for a blanket standardized format that would be implementable for all drug products is not feasible.

For drugs with a single indication or straightforward clinical trial data, it may be possible to meet these criteria; the study results discussed above show how this information could be summarized in a way that is useful for consumers and clinicians. However, for many prescription drugs, the usability of standardized information may be sharply reduced because of the additional information needed to convey the appropriate benefit and risk information. Moreover the space and context required to reflect multiple, potentially conflicting clinical trials, for one complex indication would not lend itself to a single, space-limited box. Simply picking the largest or most recent trial from FDA-approved labeling to summarize, for example, would not necessarily represent the drug's true risk–benefit profile and may present a skewed or unbalanced presentation of the data. The Agency also considered its determination on the need for a regulation in the context of CDER's ongoing efforts to better inform providers and patients. Therefore, based on this information, FDA determined that adding these types of standardized risk-benefit summary statements to prescription drug advertising would not broadly improve health care decision-making. Furthermore, it is not feasible to promulgate regulations that

cannot be applied across all products. Therefore, FDA is not promulgating new regulations requiring a single standardized format across all products.

## V. Current Efforts to Provide Useful Benefit-Risk Information about Regulated Products

CDER collaborates with a broad spectrum of groups to improve information for prescribers and consumers. While the Secretary has determined that the inclusion of quantitative information about the risks and benefits of prescription drugs in a single standardized format in prescription drug promotional labeling or adverstising does not warrant new regulations, FDA encourages sponsors to include quantitative information in promotional materials and labeling and continues to look for ways to improve communication regarding prescription drugs to both health care professionals and consumers.

FDA plays a critical role in providing health professionals and consumers information to use drugs appropriately and safely. FDA is devoting substantial resources to other, more promising, communication vehicles that will be appropriate and useful for CDER-regulated products. These efforts are directed to health care professionals, patients and consumers and will improve the communication of important information to these audiences. These vehicles are described below.

For health care professionals: FDA issued several guidances regarding prescription drug labeling and is actively developing guidance in other areas. For example, the "Clinical Studies Section of Labeling for Human Prescription Drug and Biological Products – Content and Format" guidance is intended to assist applicants in deciding:

(1) what studies should be included in the CLINICAL STUDIES Section of prescription drug labeling,
(2) how to describe individual studies, and
(3) how to present study data, including presentation of data in graphs and tables.

In addition, this guidance is intended to make the CLINICAL STUDIES Section of labeling more useful and to promote consistency in content and format of the Section across drug product classes and within drug classes and indications. This guidance is an important tool in ensuring that health care professionals receive important quantitative information regarding prescription drugs. FDA is also engaged in developing a publicly available framework for benefit-risk assessment in the human drug and biological product review process entitled "Structured Approach to Benefit-Risk Assessment in Drug Regulatory Decision-Making." This framework will summarize the relevant facts, uncertainties, and key areas of judgment, and clearly explain how these factors influence a regulatory decision. Such a framework can provide transparency regarding the basis of conflicting recommendations made by different parties using the same information. When the final decision is made, a single framework provides a standardized, predictable, and accessible form that communicates the basis for FDA's regulatory decision to the public, while also documenting the decision for reference as FDA considers similar benefit-risk assessments in the future. The goal of this effort is to make the Agency

assessment of benefit-risk and regulatory decisions for drug and biologic approvals more accessible and transparent to health care providers and the public.

For patients and consumers: In addition to Medication Guides and required Patient Package Information (PPIs), FDA is actively developing guidances designed to improve communication in patient- and consumer-directed materials. These include "Presenting Risk Information in Prescription Drug and Medical Device Promotion," "Direct-to-Consumer Television Advertisements — FDAAA DTC Television Pre-review Program," and "Brief Summary and Adequate Information for Use: Disclosing Risk Information in Consumer-Directed Print Advertisements and Promotional Labeling for Prescription Drugs." These draft and final guidance documents are intended to enhance communication about prescription drugs by:

(1) providing recommendations on the presentation of benefit and risk in advertising and promotional labeling, and
(2) describing a program that will help ensure that certain high risk products and high-impact TV ads accurately and effectively communicate key information about advertised products.

FDA is also actively working on an initiative to improve Patient Medication Information (PMI) that is provided to patients.

Within CDER, the Office of Prescription Drug Promotion's mission is to protect the public health by assuring prescription drug information is truthful, balanced and accurately communicated. This is accomplished, in part, by fostering better communication of labeling and promotional information to both health care professionals and consumers. FDA remains committed to working with sponsors to improve the quality of prescription drug advertising and promotional labeling. While the results of the studies described in this report will not be used as the basis to promulgate a regulation, they do provide a valuable contribution to efforts to improve risk-benefit communications. Therefore, FDA is seeking publication of these studies so that sponsors and advertising agencies can readily access information that will help them to provide valuable quantitative information for certain drugs. In addition, FDA routinely provides advisory comments on proposed promotional materials that are sent in by sponsors who request recommendations prior to dissemination. The information from these studies will also be used to help inform FDA's advisory comments. FDA is also planning to continue researching approaches to communicate information in advertising and promotional labeling.

## VI. Conclusion

In conclusion**,** FDA performed a thorough review of all available scientific evidence and research in the areas of social and cognitive psychology regarding whether the presentation of quantitative risk and benefit information influences people's processing, understanding, and behavior; consulted with outside experts, including the RCAC; and conducted three studies in the area of DTC prescription drug advertising. The Agency also considered the need for a regulation in the context of CDER's ongoing efforts to

better inform providers and patients about the risks and benefits of prescription drugs. Although the research found that the addition of simple quantitative information could help consumers recall and understand the risks and benefits of prescription drugs, FDA determined that implementing a single, standardized format across all products is not feasible given the complexities of many existing drug products. FDA is particularly concerned about presentations of information based on complex clinical trial data that may be confusing to consumers. Based on these efforts, FDA determined that the inclusion of quantitative information about the risks and benefits of prescription drugs in a single standardized format would not broadly improve health care decision-making, and thus does not warrant new regulations. Therefore, because of the problems posed by developing a single format for all drugs and FDA's ongoing efforts to improve the communication of drug risks and benefits, FDA is not promulgating new regulations requiring a single standardized format for the presentation of risk-benefit information in prescription drug promotional labeling or advertising. However, FDA remains committed to ensuring that accurate and understandable information is communicated to clinicians, patients, and consumers. FDA is actively developing guidance for industry on "Presenting Risk Information in Prescription Drug and Medical Device Promotion," "Direct-to-Consumer Television Advertisements — FDAAA DTC Television Pre-review Program," and "Brief Summary and Adequate Information for Use: Disclosing Risk Information in Consumer-Directed Print Advertisements and Promotional Labeling for Prescription Drugs." These draft guidance documents are intended to enhance and improve communication about prescription drugs. FDA is also planning to continue researching different approaches to communicate prescription drug information in advertising and promotional labeling.

FDA is committed to ensuring that accurate and understandable information is communicated to clinicians, patients and consumers through labeling and advertising. FDA recognizes its critical role in providing health professionals and consumers information to use drugs appropriately and safely.

**Attachment 1: Literature Review**

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REVIEW

# Communicating quantitative risks and benefits in promotional prescription drug labeling or print advertising

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ABSTRACT

**Purpose** Under the Food, Drug, and Cosmetic Act, all promotional materials for prescription drugs must strike a fair balance in presentation of risks and benefits. How to best present this information is not clear. We sought to determine if the presentation of quantitative risk and benefit information in drug advertising and labeling influences consumers', patients', and clinicians' information processing, knowledge, and behavior by assessing available empirical evidence.

**Methods** We used PubMed for a literature search, limiting to articles published in English from 1990 forward. Two reviewers independently reviewed the titles and abstracts for inclusion, after which we reviewed the full texts to determine if they communicated risk/benefit information either: (i) numerically (e.g., percent) versus non-numerically (e.g., using text such as "increased risk") or (ii) numerically using different formats (e.g., "25% of patients", "one in four patients", or use of pictographs). We abstracted information from included articles into standardized evidence tables. The research team identified a total of 674 relevant publications, of which 52 met our inclusion criteria. Of these, 37 focused on drugs.

**Results and conclusions** Presenting numeric information appears to improve understanding of risks and benefits relative to non-numeric presentation; presenting both numeric and non-numeric information when possible may be best practice. No single specific format or graphical approach emerged as consistently superior. Numeracy and health literacy also deserve more empirical attention as moderators. 

KEY WORDS risk; benefit; communication; drug advertising; literature review; pharmacoepidemiology

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## INTRODUCTION

Under the Food, Drug, and Cosmetic Act all promotional materials for prescription drugs must strike a fair balance in the presentation of risks and benefits and contain a true statement about side effects, contraindications, and effectiveness. However, meeting the current minimum requirements for fair balance set by Food and Drug Administration does not ensure that information appears in a format easily understood by the average consumer. The question of how to best present risk and benefit information warrants further inquiry. In light of that, we examined available literature to determine if the presentation of quantitative risk and benefit information influences people's processing, understanding, and behavior.

We focused on quantitative information, i.e., any information that numerically addresses the likelihood of different risks or benefits (e.g., "approximately 1 in 500 patients experience a side effect"). The specificity of quantitative information can vary. Risks can either be described using numbers (e.g., "30% of patients," "one in four patients") or through descriptive labels (e.g., "increased," "many," or "frequently"). We can refer to

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the former as *numeric* formats and the latter as *non-numeric*. The most commonly used numeric formats are probabilities, frequencies, and percentages; specific numbers detailing risk reduction associated with a treatment appear as well.[1 3] Likelihood information also can be presented using non-numeric, descriptive terms like *often* or *rare*.[4]

## METHODS

Our team of scientists used the PubMed database, consulted with our technical expert panel, and conducted hand searching of review bibliographies. We searched the PubMed database for articles published between January 1, 1990, and February 23, 2011, on the communication of risks or benefits using either numeric or non-numeric presentation. We limited our pool to studies that (i) involved adult humans, (ii) appeared in English, (iii) used quasi-experimental designs, randomized controlled studies, cross-sectional studies, focus group research, or other explicit research designs, and (iv) appeared in PubMed's core clinical journals or the journals most frequently publishing risk communication research. Team members reviewed abstracts to determine if they met our inclusion criteria and categorized studies as addressing (i) information format and style preferences, (ii) knowledge and comprehension, (iii) perceived risks and benefits, or (iv) behavioral intentions and behaviors.

## RESULTS

Figure 1 is a flowchart showing the source of our citations, our exclusions at each stage of the review process, the reasons for exclusion, and the number of citations we included in our final review.

Of the 52 studies that met the inclusion criteria, 37 focused on prescription or hypothetical drugs. Populations studied were diverse, encompassing university student populations, patients with selected illnesses, jurors, parents or other surrogate decision makers, and the general population of adults, among others. Most of the studies focused on patient or consumer behavior rather than on health care provider behavior. Table 1 provides an overview of articles focused on knowledge and comprehension and perceived risks and benefits.

### *Information format and style preferences*

A minority but sizable proportion of studies focused on preferences for information format and style. These

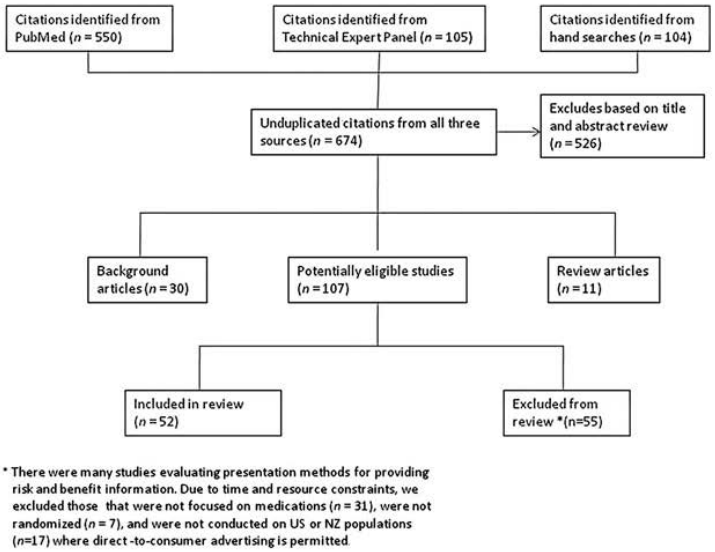


Figure 1. Flowchart of review process




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Table 1. Studies focusing on knowledge and comprehension and perceived risks and benefits

| Reference | Information being communicated | Communication format | | | Findings |
|---|---|---|---|---|---|
| | | Non-Numeric | Numeric | Mixed | |
| ***Studies Focusing on Knowledge and Comprehension*** | | | | | |
| Armstrong et al., 2002[23] | Probabilities of survival or mortality | Survival and mortality graphs | NA | NA | Accuracy of understanding risk and selection of treatment affected by presentation format, with survival curves better than mortality curves. **Moderators**: Effects of survival compared to mortality curves are greater for those with less education and with ethnicities other than Caucasian. |
| Brundage et al., 2005[6] | Health-related quality of life | Descriptive text; Line and bar graphs | NA | NA | Line graphs interpreted correctly most often; however, text summaries better understood than bar graphs. |
| Chao et al., 2003[24] | Breast cancer prognosis | NA | RRR; ARR; ASB; NNT | NA | Presenting all four formats increased confusion. The prognosis was best understood when data was presented in ASB format. |
| Char et al., 2010[15] | Prognostic information for patients in intensive care | Descriptive text | Percentage of surviving; Percentage of dying | NA | No difference in understanding of prognosis based on format. |
| Cuite et al., 2008[25] | Risk of disease and treatment success along with operations performed with the risks | NA | 1-in-*n*; Frequency; Percentages | NA | Overall, accuracy was higher for percentage and frequency formats than the 1-in-*n* format. **Moderators**: Accuracy rates by format varied by the mathematical operation performed (add, sequence, trade-off, triple, halve, compare). Accuracy was greater for those with more education. |
| Garcia-Retamero & Galesic, 2009[26] | Reduced risk of a heart attack if using a hypothetical statin | Icon arrays | Use of different numerators and denominators to achieve a RRR of 50% | NA | Providing icon arrays in addition to the numerical information resulted in greater accuracy of risk understanding, in both high and low numeracy groups. **Moderators**: Participants with lower numeracy less likely to use denominators in the assessment of risk. |
| Garcia-Retamero & Galesic, 2010[27] | Reduced risk of a heart attack or stroke if using a hypothetical drug | Icon arrays (showing sick only); Icon arrays (showing everyone);Bar graph (sick only); Bar graph (overall) | ARR; RRR | NA | Providing icon arrays and bar graphs in addition to numerical information improved understanding of medical information. **Moderators**: Nonnumeric formats were most useful for participants |

(*Continues*)

*Pharmacoepidemiology and Drug Safety*, 2013
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Table 1. (Continued)

| Reference | Information being communicated | Communication format | | | Findings |
|---|---|---|---|---|---|
| | | Non-Numeric | Numeric | Mixed | |
| ***Studies Focusing on Knowledge and Comprehension (Continued)*** | | | | | with low numeracy.Participants from United States were less likely to provide accurate assessments of treatment risk reduction than German participants. |
| Gattellari & Ward, 2003[46] | Prostate cancer screening information | Pamphlet (conventional information that is non-numeric) | Evidence-based booklet with numeric risk information | NA | Participants in evidence-based booklet condition felt more informed, had an overall greater understanding of PSA screening and had more accurate estimates of lifetime incidence and mortality from cancer. |
| Hawley et al., 2008[25] | Risk and benefit information of hypothetical bypass surgery | Table; Pictograph; Pie Chart; Bar graph; Modified pictograph (sparkplug); Modified pie graph (clock) | NA | NA | The pictograph was the most effective at conveying both verbatim knowledge and gist across numeracy levels. **Moderators:** For low numeracy respondents, pictographs, bar charts, and tables were equally effective in conveying verbatim knowledge; the other formats were less effective. |
| Knapp et al., 2010[47] | Perceived risk of tamoxifen side effects | Descriptive text | Absolute frequency; Frequency band | Descriptor+absolute frequency; Descriptor+frequency band | Participants in frequency format significantly more accurate at estimating risk of side effects than participants receiving frequency band information. Combination of non-numeric and numeric did not increase accuracy. |
| Mar-Son-Hing et al., 2002[18] | Risk of stroke | Descriptive text | NA | Decision aid providing risk information, frequency information, and a pictograph | No significant differences in knowledge of options or accuracy of risk perceptions between the non-numeric and mixed conditions. Participants in the mixed format condition felt more informed and had more realistic estimates of treatment outcomes. |
| Marteau et al., 2000[19] | Screening test results for Down syndrome to pregnant women | Descriptive text | NA | Simple frequency+descriptive anchor | Mixed format slightly more effective in helping women understanding the test result, especially for women with lower education. |
| Schwartz et al., 2009[29] | Risks and benefits of prescription medications | NA | Numeric control (Information typically found in drug | Drug fact box quantifying outcomes with and | Participants exposed to drug facts box had more accurate understanding |




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Table 1. (Continued)

| Reference | Information being communicated | Communication format | | | Findings |
|---|---|---|---|---|---|
| | | Non-Numeric | Numeric | Mixed | |
| ***Studies Focusing on Knowledge and Comprehension (Continued)*** | | | | | medications: one to treat symptoms and the other for disease prevention. |
| Sheridan & Pignone, 2002[30] | Benefits of medications to treat a hypothetical disease | NA | RRR; ARR; NNT; Combination | NA | No statistically significant difference in ability to interpret comparative information by format; however, respondents had more difficulty interpreting quantitative data when presented in the NNT format. |
| Sheridan et al., 2003[31] | Benefits of medications to treat a hypothetical disease | NA | RRR; ARR; NNT; Combination of the above | NA | Benefits of treatment are best understood by patients when presented in RRR formats (as well as ARR formats) with a given baseline risk of disease, and are least understood when presented in an NNT format. |
| Steiner et al., 2003[22] | Effectiveness of contraceptives | Descriptive text | Percentages | Descriptive information + percentages | Although the non-numeric condition communicates relative effectiveness better than the numeric- and mixed-format conditions, those in the non-numeric condition were more likely to overestimate the risk of getting pregnant when using a particular contraceptive. |
| Tait, Voepel-Lewis et al., 2010[32] | Risks and benefits of two hypothetical drugs for postoperative pain in children | NA | Percentages | Tabular format; pictograph | Pictographs significantly better than tables and percentages in providing both adequate gist and verbatim understanding. |
| Tait, Voepel-Lewis et al., 2010[33] | Risks and benefits of two drugs | Descriptive text | NA | Tabular format; Pictograph | Parents who received the medication information in the form of a table or pictograph as opposed to text were more likely to demonstrate greater gist and verbatim knowledge of the medication risks and benefits. |
| Tait, Zikmund-Fisher et al., 2010[34] | Risks and benefits related to postoperative pain in children | NA | Four complex risk/benefit trade-off scenarios using percentages and frequencies | NA | Parents presented only with quantitative information about improved outcomes had better understanding of information than parents presented with only quantitative information about reductions in risk. **Moderators**: Better understanding associated with being white, a college education, and higher numeracy. |

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Table 1. (Continued)

| Reference | Information being communicated | Communication format | | | Findings |
|---|---|---|---|---|---|
| | | Non-Numeric | Numeric | Mixed | |
| ***Studies Focusing on Knowledge and Comprehension (Continued)*** | | | | | |
| Ubel et al., 2010[35] | Risks and benefits of tamoxifen | NA | Decision aid that varied the order of risk and benefit information (frequencies and percentages), and the presence or absence of contextual information about risk. | NA | Women who did not receive contextual information demonstrated order effects (women who were presented risks of medication first answered fewer questions about the risks/benefits of the medications correctly); when contextual information was presented with the decision aid, women did not display this order effect. |
| Waters et al., 2006[36] | Risk trade-offs for hypothetical illness | Graph | Frequencies (three levels of cognitive effort); Probabilities (two levels of magnitude of change) | Descriptive text + graph | Using a graphical display, expressing numbers in percentages rather than frequencies, using large net changes in risk, and increases (rather than decreases) in total risk improved accuracy and helped laypeople evaluate medical trade-offs. |
| Waters et al., 2004[37] | Risk trade-offs for hypothetical illness | Bar graph; Array of sick figures | Frequencies | NA | Using arrays of stick figures for graphic representation of probabilities reduces side effect aversion and slightly increases accuracy in evaluating changes in risk. |
| Weymiller et al., 2007[20] | Risks and benefits of using statin medications | Pamphlet described cholesterol management | NA | Decision aid presented tailored cardiovascular risks; benefits and risks of taking statins using pictographs + frequencies | Participants who received quantitative information on ARR (decision aid) had more accurate risk estimates, more accurate estimates of absolute risk reduction, and higher levels of knowledge about statins when compared to participants in pamphlet condition. |
| Woloshin et al., 2004[21] | Benefits of prescription medications | Standard version of a drug ad that did not contain descriptive labels of drug benefits | NA | Drug benefit box with efficacy data presented using percentages + descriptive labels | Including quantitative risk and benefit information decreases adults' perceived effectiveness of drug and increases adults' ability to correctly estimate the drug's effectiveness. |
| Zikmund-Fisher et al., 2008[38] | Risk statistics for tailored estimates of mortality and recurrence risks for breast cancer patients | NA | NA | Frequency + pictograph (showing four possible outcomes); frequency + pictograph (showing only survival-related outcomes) | The simpler mixed format (showing only survival information) had the greatest effect on improving comprehension. |




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Table 1. (Continued)

| Reference | Information being communicated | Communication format: Non-Numeric | Communication format: Numeric | Communication format: Mixed | Findings |
|---|---|---|---|---|---|
| Zikmund-Fisher et al., 2008[39] | Side effect risks concerning prophylactic use of tamoxifen to prevent primary breast cancers | Pictograph | Frequency + percentage; Incremental risk (vs. total risk); 1000 risk denominator (vs. 100) | Pictograph x incremental risk; Pictograph x denominator; Incremental risk x denominator | Whether risk information is presented as incremental risk or total risk, pictograph formats are better for increasing knowledge than numeric text. **Moderators**: Higher numeracy scores associated with lower perceived risk and higher knowledge of risks. |
| ***Studies Focused on Perceived Risks and Benefits*** | | | | | |
| Berry et al., 2004[45] | Adverse events from ibuprofen | Descriptive text | Percentages | NA | Patients more likely to perceive greater likelihood of side effects, more risk to health, and greater side effect severity when risk is presented in a non-numeric format. |
| Gurmankin et al., 2004[43] | Risk of four different types of cancer | Descriptive text | NA | Descriptive + percent; Descriptive + fraction | Risk perceptions are highly variable across the three risk presentation formats. Inclusion of a numeric statement of risk reduced the degree of variation in risk perception. **Moderators**: Overestimation of risk was associated with lower education level, greater worry, and lower numeracy. |
| Halpern et al., 1989[44] | Oral contraceptive safety | NA | Probabilities (two variations); Frequencies three variations); Percentages | NA | When base rates were given, the event was perceived as less likely to occur than when base rates were not given. The "size" of the number affected risk perceptions (e.g., 415% seems bigger than 4.15 times greater). |
| Knapp et al., 2004[45] | Risk of medication side effects | Descriptive text | Percentages | NA | Patients who were provided descriptors overestimated the probability of side effects. Perceptions about likelihood of side effects affected patients' perceived risk of having side effects and potentially their decisions about whether to take the medication. |
| Knapp et al., 2009[46] | Risk of side effects to tamoxifen | Descriptive text | Frequencies | Descriptive text + frequencies | Descriptive text resulted in higher perceived likelihood of a side effect and higher perceived risk to health than frequencies or the mixed format; |

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Table 1. (Continued)

| Reference | Information being communicated | Communication format | | | Findings |
|---|---|---|---|---|---|
| | | Non-Numeric | Numeric | Mixed | |
| ***Studies Focused on Perceived Risks and Benefits (Continued)*** | | | | | the frequency format produced the most accurate estimate of risk of side effects. |
| Knapp et al., 2010[47] | Perceived risk of tamoxifen side effects | Descriptive text | Frequencies (two variations) | Descriptive text + frequencies | Participants in the absolute frequency format were significantly more accurate at estimating risk of side effects than were participants receiving frequency band information. The mixed format did not increase the accuracy of risk estimation. |
| Peters et al., 2011[47] | Benefits and risks of headache medication | NA | Percentages; Frequencies | NA | **Moderators.** Less numerate individuals perceived higher risk when numbers were presented in frequency formats (vs. percentage formats). Also a moderating effect of framing (negative vs. positive); positive frame resulted in lower risk perceptions than negative frame. |
| Shaw & Dear, 1990[33] | Common newborn problems | Descriptive text | Frequency | NA | Large variations in interpreting descriptive expressions of probability by mothers and health care providers; when provided with a frequency format, mothers and health care providers differed significantly in assigning text-based expressions to the numeric probabilities. |
| Tait, Zikmund-Fisher et al., 2010[34] | Risks and benefits related to postoperative pain in children | NA | Frequencies + Percentages | Table; Pictograph | Pictographs resulted in patients perceiving there to be lower perceived risk.<br>**Moderator**: Pictographs may be better for presenting comparative research risk/benefit information and in aiding decision making for individuals with differing levels of numeracy. |
| Tan et al., 2005[48] | Vaccine risk | NA | Frequencies; Percentages | NA | Presenting risk using percentages (probabilities) resulted in less perceived risk as compared to a frequency format. |

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Table 1. (Continued)

| Reference | Information being communicated | Communication format | | | Findings |
|---|---|---|---|---|---|
| | | Non-Numeric | Numeric | Mixed | |
| Teigen & Brun,1999[49] | Efficacy of acupuncture as a treatment for migraine headaches | Descriptive text (positive vs. negative frame) | Percentages | NA | Positively framed descriptive text led to predictions in a positive direction; negative phrases led to fewer positive predictions (of person X performing the recommended behavior). Descriptive expressions provide more information from a linguistic perspective (re: directionality) than numerical expressions. |
| Zikmund-Fisher, et al., 2010[4] | Side effect risks concerning prophylactic use of tamoxifen to prevent primary breast cancers | Pictograph | Frequencies; Percentages; Incremental risk (vs. total); 1000 risk denominator (vs. 100) | Pictograph x incremental risk; Pictograph x denominator; Incremental risk x denominator | Risk perceptions lower when incremental risk (as opposed to total risk of experiencing the complication) presented. |

papers reveal a general preference among the lay public for numerical presentation.[5 10] Several other studies looked at preferences among physicians and health care professionals, who also often appear to prefer numerical presentation.[11 13]

Some evidence suggests that aspects of preferences might be a function of numeracy skills, with those lower in numeracy, i.e., how facile people are with mathematical concepts and their applications, trusting numeric presentation less.[14] What these data cannot tell us, however, is whether those preferences for numeric risk information translate into better comprehension or behavioral intention.

### *Knowledge and comprehension*

Roughly half of the studies examined how the numeric presentation of quantitative information affected study participants' knowledge in comparison with non-numeric presentation. Many specifically focused on the *accuracy* of knowledge retained.[6,13,15 22] Most studies of numeric versus non-numeric comparisons found that numeric presentation resulted in more accurate knowledge or understanding.

Numerous studies assessed which type of numeric presentation had the most desirable influence on risk or benefit knowledge.[22 39] Whether a particular numeric statement of risk or a graphical approach is ideal across numerous topics remains empirically unclear. Sheridan and Pignone,[30] for example, found no significant differences in interpretation accuracy among different numeric risk reduction formats among medical students. Other studies have found education or numeracy skills act as moderating variables in this regard, suggesting that simple graphics such as pictographs might be useful specifically for those with low numeracy skills.[25,26,28,34,39 41] Several studies in our review[26,27,29,32,33] found a combination of numeric and non-numeric information to be useful. The additional presentation of non-numeric guidance might assist some people in discerning *relative or comparative* risk among various options by offering anchoring or orientation.

### *Perceived risks and benefits*

Researchers have examined whether information format affects personal risk and benefit perceptions[5,13,17,34,39,42 49], some of whom have found that numeric presentation reduces unwarranted extreme perceptions of side effect risk.

Our review suggests at least two possible reasons why non-numeric and numeric risk descriptors operate differently. Numbers may simply offer greater precision to people as they develop risk perceptions.[13,43]




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Teigen and Brun[49] offer a different hypothesis, suggesting that descriptive non-numeric probabilistic phrases are different from numeric probabilities because they have more power to be overtly *directive* in suggesting the types of inferences to be drawn. These perceived risk and benefit effects, like others in our review, appear to be tempered by numeracy skills and education. Those with greater levels of numeracy and education are less likely to be affected by the type of risk information presented. In Gurmankin, Baron, and Armstrong,[14] for example, those at higher levels of numeracy and education were less likely to overestimate risks.

### *Behavioral intentions and behaviors*

Only a minority of studies assessed participants' behavioral intention, behavior, or decision making.[5,7,9,18,20,41,48,50 56] The nature of the outcomes studied also varied considerably. Among studies that assessed simple willingness or intention to take a particular medication, we saw some evidence suggesting an effect of numeric information (versus non-numeric) exposure on intention to take a particular drug and other evidence suggesting no effect differences. We nonetheless face limitations in drawing conclusions about intention or behavior effects because many of the studies focused on *hypothetical* engagement with a medication without necessarily accounting for patient circumstance or real-world behavior.

Studies that look at actual (versus hypothetical) circumstances have examined the concordance of decisions with patients' stated preferences or evidence-based recommendations. Findings from these studies again suggest some utility for numeric information presentation regarding outcomes such as making a decision consistent with one's own values.[51] Our review suggests that exposure to numeric presentations might facilitate informed decision making by reducing decisional conflict and uncertainty. The overall paucity of behavioral outcomes in many studies nonetheless leaves us unable to offer a definitive conclusion and signals a need for further research.

## DISCUSSION

Our review is noteworthy in part for the limitations about the existing body of evidence that it highlights. While the vast majority of studies involved a carefully defined intervention, addressed statistical power, and employed a randomized experimental design, some suffered from comparison group constraints or problematic order effects. Importantly, a disproportionate share of studies addressed outcomes at the preliminary stages of the consumer behavior continuum—that is, information preferences, knowledge, understanding, or risk perceptions. Relatively few studies focused on behavioral intentions and actual behaviors. Moreover, of the studies in our review that examined behavioral outcomes, most focused on hypothetical situations. Whether these findings apply outside of the experimental laboratory is unknown. Moreover, researchers in some studies manipulated multiple information features simultaneously to create comparison groups, making it difficult to tease apart the specific reason for a significant effect. Last, studies in our review examined risk information alone more frequently than they examined both risk and benefit information.

Several themes and conclusions nonetheless emerged from our review. First, exposure to numeric presentation of risk or benefit information positively predicts several key outcomes relative to non-numeric presentation. The pattern was clearest for studies that examined the impact of risk/benefit information on knowledge gain. Second, no single specific format, structure, or graphical approach emerged as consistently superior. The apparent superiority of numeric information with regard to various outcomes did not suggest that a *particular visual format* for the presentation of numeric information is superior. Presenting *both* numeric and non-numeric information may offer a useful approach in some circumstances because of the combination of the precision of numeric data and the qualitative or directive context provided by non-numeric information.

Studies included in our review assessed a wide range of different format possibilities but failed to provide a single crucial test of multiple format types at once. Some studies advocated for certain approaches, such as using pictographs (versus tables and text), but the field needs more comprehensive studies comparing a large set of format options. Third, numeracy and health literacy skills are variables that deserve more empirical attention because results varied for different people depending on their numeracy or health literacy levels. We need more evidence to confirm the role of these moderating factors.

While no single method for presentation of risk and benefit information currently enjoys overwhelming support in available literature, relatively simple presentations that employ both numeric and non-numeric information may be warranted, as is the need to acknowledge potential variation in consumer and patient engagement as a function of health literacy and numeracy. At the same time, we clearly also need more systematic study of available formats using well designed and carefully controlled studies using populations who need to make these risk and benefit decisions




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rather than using a more general population presented with hypothetical risk and benefit scenarios.

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## CONFLICT OF INTEREST

None of the authors have any conflicts to declare.

### Key Points

- Numeric presentation of risk/benefit information was associated with a positive impact on several outcomes relative to non-numeric presentation of risk/benefit information.
- No single specific format, structure, or graphical approach emerged as consistently superior.
- Few studies considered how age, race, ethnicity, and culture might influence understanding and interpretation of risk and benefit presentations.
- Numeracy and health literacy are variables that deserve more empirical attention, because results may vary for different people depending on their numeracy or literacy levels.
- Among the studies we reviewed, few addressed outcomes such as actual behaviors.

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**Attachment 2**

**Presentation of Quantitative Effectiveness Information to Consumers in DTC Television and Print Advertisements for Prescription Drugs: Executive Summary**[5]

**Purpose**

FDA is committed to fostering the safe and effective use of prescription drugs and believes that improvement in peoples' understanding of risk and benefit information is essential to this commitment. This study evaluated the effect of including quantitative benefit information in various statistical and visual formats (e.g., relative or absolute frequency, bar graphs, tables) in DTC print and television advertisements (ads). FDA was interested in evaluating, for example, to what extent viewers of quantitative benefit information understood and could accurately recall such information and whether including such information changed their attitude toward the drug, their perception of how well the drug works, or how risky the drug is. FDA was also interested in whether including quantitative benefit information affected viewers' intentions to get more information about the drug or to take the drug. Finally, it was important to determine if including quantitative benefit information had a detrimental effect on the recall of risk information.

The study was guided by the following research questions:

> (1) Does presenting quantitative benefit information in a statistical format in DTC ads help people recall quantitative benefit information in DTC ads? If so, which statistical formats are most helpful?
>
> (2) Do visual aids help people recall quantitative benefit information in DTC ads? If so, which types of visuals are most helpful?

**Methods**

To answer these questions, FDA designed and implemented a randomized, controlled study exposing participants to a DTC prescription drug ad for a mock drug containing quantitative benefit information. Participants saw either a print DTC ad or a television DTC ad; note that the television and print ad conditions were not designed for comparison with one another and some differences existed in the administration of these two conditions. The ad contained information about either a high-efficacy or a low-

[5] O'Donoghue, A.C., Sullivan, H.W., Aikin, K.J., Chowdhury, D., Moultrie, R.R., & Rupert, D.J. (2013). Presenting efficacy information in direct-to-consumer prescription drug advertisements. *Patient Education and Counseling, 95*(2), 271-280.

efficacy cholesterol drug. This benefit information about the drug was presented either in a statistical format or a visual format. The statistical formats tested were absolute frequency (for example, 65 out of 100), percent (for example, 65%), relative frequency (for example, 33 times more likely), a combination of absolute frequency and percent, and a combination of relative frequency and percent. The visual formats tested were pie charts, bar charts, tables, pictographs, and no visual display. All visual formats were accompanied by absolute frequency information. Participants in a control condition saw an ad without quantitative benefit information. Participants were asked a series of questions to measure how accurately they could report the drug's efficacy and risks. Participants were not able to look back at the ad while answering questions. Approximately 4,800 participants who had been diagnosed with high cholesterol responded to the study via the Internet.

**Results**

The results can be grouped into three categories: the effects of statistical format, the effects of visual format, and the effects of drug efficacy level.

Statistical format:

- Participants who did not see any quantitative benefit information about the drug were the least likely to accurately report how well the drug worked.

- Descriptively, presenting information using absolute frequency and percent formats appears to be best at helping participants accurately recall how well a drug works. For instance, 42% of participants presented with an absolute frequency and percentage in a print ad, compared with 3% of participants presented with no quantitative benefit information in a print ad, were able to accurately report the number of people out of 100 taking the drug who would lower their bad cholesterol to normal levels.

- There was a match between the kind of quantitative information participants viewed and the kind of quantitative information participants were able to accurately report. For instance, participants who viewed the benefit information as an absolute frequency (for example, 65 out of 100), compared with those who did not see any quantitative benefit information, were better able to report how well the drug worked as an absolute frequency and a percent but not as a relative frequency (for example, 33 times better).

- In general, participants who saw the benefit information presented in two formats (for example, 65 out of 100 and 65%) were the most likely to accurately report how well the drug worked.

- The statistical format that participants saw did not affect their ability to recall the drug's risks, their attitude toward the drug, their perceptions of how well the drug

works and how risky it is, or their intentions to get more information about the drug or to take the drug.

Visual format:

- When viewing print ads, participants who saw a bar chart or table, compared with those who saw no visual display, were more likely to accurately recall how well the drug worked. For instance, participants who viewed a print ad with a bar chart (53%) or table (52%), compared with participants who viewed a print ad with no visual display (38%), were more likely to accurately report the number of people out of 100 taking the drug who would lower their bad cholesterol to normal levels. The bar chart was also better than the pictograph, and the table was better than the pie chart at helping participants accurately recall how well the drug worked.

- When viewing television ads, participants who saw any visual display, compared with those who saw no visual display, were more likely to accurately recall how well the drug worked. For instance, participants who viewed a television ad with a bar chart (69%), table (52%), pie chart (56%), or pictograph (48%), compared with participants who viewed a television ad with no visual display (28%), were more likely to accurately report the number of people out of 100 taking the drug who would lower their bad cholesterol to normal levels. The bar chart was also better at helping participants accurately recall how well the drug worked than the pictograph and the table.

- The type of visual display that participants saw did not affect their ability to recall the drug's risks, their attitude toward the drug, their perceptions of how well the drug works and how risky it is, or their intentions to get more information about the drug or to take the drug.

Drug efficacy level:

- Participants who saw quantitative information describing the high-efficacy drug had a more positive attitude toward the drug, thought the drug worked better, and reported more intentions to do things like get more information about the drug compared with participants who saw quantitative information describing the low-efficacy drug.

- Participants generally thought that the high-efficacy drug was less risky than the low-efficacy drug, despite identical risk profiles.

- The efficacy of the drug (high or low) did not affect participants' ability to recall the drug's risks.

Overall, the results showed that benefit recall was low, regardless of the particular presentation of information. This is likely an effect of the procedure, in which

participants were not able to refer back to the print ad or television ad as they were answering the questions.

## Conclusions

The study's findings demonstrate that participants can accurately recall quantitative benefit information from DTC prescription drug print and television ads for a mock prescription drug, and that providing this information does not adversely influence their recall or perceptions of the product's risk. Overall, presenting information using absolute frequency and percent formats may be best at helping participants accurately recall how well a drug works. Presenting a visual aid also appears to help participants accurately recall how well a drug works, with bar charts and tables demonstrating advantages over other visual formats. In general, providing information to participants enables them to see the information and answer questions about it correctly, although it does not necessarily change:

(1) their attitude toward the drug,
(2) their perception of how well the drug works and how risky it is, or
(3) their intentions to get more information about the drug or to take the drug.

At the same time, including quantitative benefit information did not have a detrimental effect on the recall of risk information. Thus, the inclusion of quantitative benefit information in DTC print and television ads has the potential to help people make informed decisions about speaking with their health care professional about prescription drugs.

A major contribution of this research is that, to the Agency's knowledge, it is the first study to systematically examine the addition of quantitative information in television DTC ads. In fact, to our knowledge, the risk communication literature has focused only on print (or online text) modalities, making this the first study to examine the addition of quantitative information in a dynamic, television modality.

**Attachment 3**

**Randomized Study of Format Variations in the Brief Summary of DTC Print Advertisements: Executive Summary**

**Purpose**

There have been recent requests to create a "Drug Facts box" for prescription drug ads similar to the one currently used for over-the-counter drug labels. However, it is unclear which data—whether numeric, qualitative, or a combination of the two—best aids consumer understanding. The statement "50 out of 100 people reported less pain" is an example of numeric data whereas "more people had pain relief" is an example of qualitative data. For this study, we tested combinations of numeric and qualitative data to find out what information may be most useful in a Drug Facts box.

**Methods**

Using DTC print ads for a fictitious prescription heartburn drug, we tested 5,068 Internet panelists who reported suffering from heartburn. We randomly assigned these panelists to view 1 of 20 different ads. The ads varied in the type of numeric and qualitative information they included. For instance, some ads contained a Drug Facts box filled with all tested data using numbers and qualitative labels and some ads had boxes that contained no numbers or qualitative labels at all. The numbers we provided included absolute frequencies and percentages ("18% [180 in 1,000]") and absolute differences ("18 percentage points more"). In some cases, we also provided qualitative labels ("more people had heartburn relief"). The participants were then asked a series of questions to measure how accurately they could report the effectiveness of the drug and the drug's risks. Participants were able to look back at the ad while answering questions.

**Results**

The study demonstrates that the majority of participants who viewed numeric data were able to accurately report it. When people were provided with absolute frequencies and percentages, they were able to use this numeric data to report benefit and risk information regardless of whether they also saw absolute differences or qualitative information. The percentage of participants who were able to accurately report the numeric data when viewing an ad with absolute frequencies and percentages ranged from 75% (when answering a question about the percentage of people who took a placebo and had a serious risk) to 89% (when answering a question about the percentage of people who took the drug and had heartburn relief). In comparison, the percentage of participants who were able to accurately report the numeric data when viewing an ad with no numeric data ranged from 0% (when answering a question about the percentage of people who took a placebo and had heartburn relief) to 23% (when answering a multiple choice question about how much the drug increase the chance of heartburn relief compared to placebo). These findings suggest that a simpler Drug Facts box may be useful for people trying to make decisions about prescription drugs.

**Attachment 4**

## Study of Clinical Efficacy Information in DTC Print Advertisements for Prescription Drugs: Executive Summary[6]

### Purpose

Research suggests that quantitative information in DTC prescription drug ads (such as "50 out of 100 people reported less pain") may help consumers understand the benefits and risks of these drugs. Although this sort of data may be useful for consumers, there is little agreement on how best to present it. For this study, we tested a variety of ways to present data with a particular focus on placebo rates and message framing.

When researchers want to know if a drug works, they conduct a clinical trial. In some clinical trials, some people are given the real drug and others are given a "fake drug" (a placebo). No one knows who gets which. The researchers then look to see if people who took the real drug do better than people who took the placebo. By comparing how many people who took the real drug show improvement (the drug rate) versus how many people who took the placebo show improvement (the placebo rate), researchers can measure how well a drug works (also called "efficacy").

In addition, there are different ways to frame the information about how well a drug works. One could provide only the number of people who benefited from a drug (a single, positive frame; for example, "55 patients showed improvement on the drug,") or only the number of people who did not benefit (a single, negative frame; for example, "45 patients saw no improvement on the drug"). Alternatively, one could provide both the number of people who benefited and the number of people who did not benefit (a mixed frame; for example, "while 55 patients showed improvement on the drug, 45 patients saw no improvement"). Some researchers have suggested that mixed frames can help people understand data.

### Methods

Using print ads for a fictitious prescription drug called Gilarix, we conducted a two-part study to find out whether laypeople could understand placebo rates and how this quantitative information was best framed. For the first part of the study, we asked 2,000 Internet panelists who reported having chronic pain to view different versions of the Gilarix ad. The ads had either a single, positive frame or a mixed frame. The ads also

[6] O'Donoghue, A.C., Sullivan, H.W., & Aikin, K.J. (2014). Randomized study of placebo and framing information in direct-to-consumer print advertisements for prescription drugs. *Annals of Behavioral Medicine*. doi: 10.1007/s12160-01409603-1

displayed either no placebo rate, a small placebo rate, or a large or very large placebo rate. The participants were asked questions about the quantitative information presented in the ads and measured their responses.

In the second part of the study, 596 physicians ranked different versions of the Gilarix ad based on how well the ads conveyed scientific information and their usefulness to patients. Similar to the first study, the ads had either a single, positive frame or a mixed frame, and the placebo rate was either present or absent.

**Results**

The study's findings suggest that adding placebo rates to DTC ads may be useful for consumers. The participants who viewed placebo rates were able to recall them and use them to form certain perceptions. For instance, approximately 40% of participants were able to accurately report placebo rates when provided with them (compared to less than 2% who did not see placebo rates), and participants who saw large or no differences between drug and placebo rates consistently reported greater perceived benefits than those who saw small differences between drug and placebo rates. However, the evidence does not support using a mixed frame when communicating placebo information. Compared to the single frame, a mixed frame led to lower placebo rate recall and perceived efficacy. The Agency's survey of physicians supported these findings, with most preferring the ad that included placebo data but contained only a single frame.