Communication of Quantitative Risks and Benefits Summaries in Promotional Labeling or Print Advertising of Prescription Drugs: A Literature Review

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What is the impact of adding quantitative risks and/or benefits information to drug ads?

Will adding quantitative summaries impact informed decision making?
Background: The FDCA

Under the Food, Drug, and Cosmetic Act (FDCA), all promotional materials for prescription drugs must:

1. Strike a fair balance in presenting risks and benefits.
2. Contain a brief summary of the product label.
3. Contain a true statement of the side effects, contraindications, and effectiveness of the advertised product.
Background: Current Controversies

- What is the best way to present the necessary information?
- No uniform standards
- Logical equivalence is not equal to cognitive equivalence
- Can format impact informed decision making?
**KQ1.** What is the value of quantitative information or summaries about the risks and benefits of medical interventions for consumers, patients, and clinicians?

**KQ2.** How does presentation of the quantitative information influence consumers’, patients’, and clinicians’ processing and understanding of the risks and benefits of medical interventions?
### Background: Possible Relevant Variables

<table>
<thead>
<tr>
<th>Independent Variables</th>
<th>Potential Outcomes</th>
<th>Potential Moderators</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exposure to numeric vs. non-numeric risks and/or benefits information</td>
<td>Attitude toward prescription drug choice and use</td>
<td>Health literacy</td>
</tr>
<tr>
<td></td>
<td>Knowledge</td>
<td>Numeracy</td>
</tr>
<tr>
<td></td>
<td>Information format and style preferences</td>
<td>Socioeconomic status</td>
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<tr>
<td></td>
<td>Perceived risks and benefits</td>
<td></td>
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<tr>
<td></td>
<td>Behavioral intention</td>
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</tr>
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<td></td>
<td>Behavior</td>
<td></td>
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</tbody>
</table>
Quantitative Information

Numeric
- Probabilities: There is a 0.20 probability of experiencing nausea.
- Frequencies: 1 out of every 3 women reported experiencing nausea.
- Percentages: 10% of women reported experiencing nausea.

Non-Numeric
- Descriptive: Women “rarely” experience nausea.
- Visual: Bar graphs, Pie charts, Icon arrays, Face icons

There is a 0.20 probability of experiencing nausea. 1 out of every 3 women reported experiencing nausea. 10% of women reported experiencing nausea. Women “rarely” experience nausea.
Methods: Systematic Literature Search

- Develop and refine key questions and inclusion/exclusion criteria
- Convene a technical expert panel (TEP)
- Conduct PubMed searches
- Conduct hand searches
- Remove duplicate citations

674 citations reviewed
# Methods: Inclusion & Exclusion Criteria

<table>
<thead>
<tr>
<th>Study population</th>
<th>Adults</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study settings and geography</td>
<td><strong>KQ1</strong>: Studies were not limited by geography</td>
</tr>
<tr>
<td></td>
<td><strong>KQ2</strong>: Studies conducted in the United States or New Zealand (i.e., where direct-to-consumer [DTC] advertising is allowed)</td>
</tr>
<tr>
<td>Time period</td>
<td>Published from 1990 until February 23, 2011</td>
</tr>
<tr>
<td>Publication criteria</td>
<td>Full-text article in English</td>
</tr>
<tr>
<td>Comparisons</td>
<td><strong>KQ1</strong>: Risks and/or benefits information provided in numeric vs. non-numeric (text or narrative) format</td>
</tr>
<tr>
<td></td>
<td><strong>KQ2</strong>: Graphics such as pictographs and survival curves; numeric formats such as frequencies, probabilities, NNT, and others</td>
</tr>
<tr>
<td>Admissible evidence</td>
<td><strong>KQ1</strong>: Original research that focused on communicating information on risks and/or benefits comparing numeric vs. non-numeric presentations of this information</td>
</tr>
<tr>
<td></td>
<td><strong>KQ2</strong>: Original research conducted in the United States or New Zealand, used an experimental design, and focused on comparing numeric formats for conveying risks and/or benefits information of medication use</td>
</tr>
</tbody>
</table>
Methods: Article Selection

Unduplicated citations (n = 674)

- Background articles (n = 30)
- Includes for KQ1 and/or KQ2 (n = 107)
- Review articles (n = 11)

Includes for KQ1 (n = 29)

- KQ1 only (n = 13)
- KQ1 & KQ2 (n = 16)

Includes for KQ2 (n = 78)

- KQ2 only (n = 23)
- Excluded (n = 55)
Results: Overview

- Reviewed 52 studies (37 on prescription drugs or hypothetical drugs)
- Topics ranged from decisions about immunizations and other screenings, risk of disease, treatment decisions, environmental health issues
- Diverse populations, but mostly adults
- Most studies focused on patient or consumer behavior
Results: Key Outcomes of Interest

- Information Format & Style Preferences
- Knowledge & Comprehension
- Perceived Risk
- Behavioral Intentions & Behaviors
What format do people prefer?

Example study
- Knapp, Raynor, & Berry, 2004
Comparison of two methods of presenting risk information to patients about the side effects of medicines

P Knapp, D K Raynor, D C Berry

See editorial commentary, p 169


Objective: To determine whether the use of verbal descriptors suggested by the European Union (EU) such as “common” (1–10% frequency) and “rare” (0.01–0.1%) effectively conveys the level of risk of side effects to people taking a medicine.

Design: Randomised controlled study with un concealed allocation.

Participants: 120 adults taking simvastatin or atorvastatin after cardiac surgery or myocardial infarction.

Setting: Cardiac rehabilitation clinics at two hospitals in Leeds, UK.

Intervention: A written statement about one of the side effects of the medicine (either constipation or pancreatitis). Within each side effect condition half the patients were given the information in verbal form and half in numerical form (for constipation, “common” or 2.5%; for pancreatitis, “rare” or 0.04%).

Main outcome measure: The estimated likelihood of the side effect occurring. Other outcome measures related to the perceived severity of the side effect, its risk to health, and its effect on decisions about whether to take the medicine.
Results: Information Format & Style Preference

“Atorvastatin is associated with some side effects. It can cause pancreatitis.”

<table>
<thead>
<tr>
<th>Numeric</th>
<th>Non-Numeric</th>
</tr>
</thead>
<tbody>
<tr>
<td>“This side effect occurs in 0.04% (that is, 4 in 10,000) people who take this medicine.”</td>
<td>“This is a rare side effect of the medicine.”</td>
</tr>
</tbody>
</table>

Overall, people were more satisfied with the information when it contained numeric information.
Summary of findings overall

- Favor numerical presentation of risks and benefits information
  - Numeric presentation vs. simple verbal descriptions
  - Numeracy

Do these preferences translate to better comprehension or behavioral intention?
Results: Knowledge & Comprehension

- Presentation format → knowledge acquisition
- Range of studies
  - Compared numeric with non-numeric formats
  - Compared various numeric formats
  - Compared various non-numeric formats
  - Compared framing techniques
- Example study
  - Schwartz et al., 2009
Using a Drug Facts Box to Communicate Drug Benefits and Harms

Two Randomized Trials

Lisa M. Schwartz, MD, MS; Steven Woloshin, MD, MS; and H. Gilbert Welch, MD, MPH

Background: Direct-to-consumer prescription drug ads typically fail to provide fundamental information that consumers need to make informed decisions: data on how well the drug works.

Objective: To see whether providing consumers with a drug facts box—a table quantifying outcomes with and without the drug—improves knowledge and affects judgments about prescription medications.

Design: Two randomized, controlled trials conducted between October 2006 and April 2007: a symptom drug box trial using direct-to-consumer ads for a histamine-2 blocker and a proton-pump inhibitor to treat heartburn, and a prevention drug box trial using direct-to-consumer ads for a statin and clopidogrel to prevent cardiovascular events.

Being “a lot more effective” than the histamine-2 blocker ($P < 0.001$), and 80% and 38% correctly recognized that the side effects of the 2 drugs were similar ($P < 0.001$). When asked what they would do if they had bothersome heartburn and could have either drug for free, 68% of the drug box group and 31% of the control group chose the proton-pump inhibitor, the superior drug ($P < 0.001$). In the prevention drug box trial, the drug box improved consumers’ knowledge of the benefits and side effects of a statin and clopidogrel. For example, 72% of the drug box group and 9% of the control group correctly quantified the benefit (absolute risk reduction) of the statin ($P < 0.001$). Most of the control participants overestimated this benefit, and 65% did so by a factor of 10 or more.
### PRIDCLO Study Findings Box

20,000 adults with heart or vascular disease were given PRIDCLO or aspirin for 2 years. Here’s what happened:

<table>
<thead>
<tr>
<th>What difference did PRIDCLO make?</th>
<th>People given Aspirin (325 mg a day)</th>
<th>People given PRIDCLO (75 mg a day)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Did PRIDCLO help?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fewer people had a heart attack (0.6% fewer)</td>
<td>3.3% in 1000</td>
<td>2.7% in 1000</td>
</tr>
<tr>
<td>No difference in dying from a heart attack</td>
<td>About 1.4% in both groups</td>
<td>14 in 1000</td>
</tr>
<tr>
<td>No difference in dying from anything</td>
<td>About 5.5% in both groups</td>
<td>55 in 1000</td>
</tr>
<tr>
<td>Did PRIDCLO have side effects?</td>
<td>[Table continues]</td>
<td></td>
</tr>
<tr>
<td>Life threatening side-effects</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No difference in strokes from bleeding into brain</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fewer people had major stomach bleeding (0.7% fewer)</td>
<td>2.7% in 1000</td>
<td>2.0% in 1000</td>
</tr>
<tr>
<td>Symptom side effects</td>
<td></td>
<td></td>
</tr>
<tr>
<td>More people had bruising (1.6% more)</td>
<td>3.7% in 1000</td>
<td>5.3% in 1000</td>
</tr>
<tr>
<td>More people had diarrhea (1.1% more)</td>
<td>3.4% in 1000</td>
<td>4.5% in 1000</td>
</tr>
<tr>
<td>More people had a rash (0.7% more)</td>
<td>3.5% in 1000</td>
<td>4.3% in 1000</td>
</tr>
<tr>
<td>Fewer people had abdominal pain (1.5% fewer)</td>
<td>7.1% in 1000</td>
<td>5.6% in 1000</td>
</tr>
</tbody>
</table>
Results: Knowledge & Comprehension

Resulted in more accurate understandings of the side effects/benefits of the different medications.
Results: Knowledge & Comprehension

- Summary of findings overall
  - Advantages of numeric formats
  - Advantages of non-numeric formats
  - Include both numeric and non-numeric formats?
  - Implications for cognitive load
  - Numeracy

- Is there a particular format that is ideal across numerous topics?
Results: Perceived Risks & Benefits

- Presentation format → personal risks/benefits perception
- Range of studies
  - Main effects of presentation format
  - How people engage numeric risk presentations
  - Why non-numeric vs. numeric formats differ in their effects on risk perceptions
- Example study
  - Berry et al., 2004
Over the counter medicines and the need for immediate action: a further evaluation of European Commission recommended wordings for communicating risk

Dianne Berry\textsuperscript{a,}\textsuperscript{*}, Theo Raynor\textsuperscript{b}, Peter Knapp\textsuperscript{b}, Elisabetta Bersellini\textsuperscript{a}

\textsuperscript{a} School of Psychology, University of Reading, Earley Gate, Whiteknights, Reading RG6 6AL, UK
\textsuperscript{b} Pharmacy Practice and Medicines Management Group, University of Leeds, Leeds, UK

Received 20 March 2002; received in revised form 5 February 2003; accepted 4 March 2003
Presented information leaflet that described the side effect associated with the medicine.

<table>
<thead>
<tr>
<th>Numeric</th>
<th>Non-Numeric</th>
</tr>
</thead>
<tbody>
<tr>
<td>“This effect occurs in 6% of people (that is, 6 in every 100 people) who take these tablets.”</td>
<td>“This effect is common in people who take these tablets.”</td>
</tr>
</tbody>
</table>

Patients are more likely to perceive greater likelihood of side effects, more risks to health, and greater side effect severity.
Results: Perceived Risks & Benefits

- Summary of findings overall
  - Format affects assessments of personal risk
  - Numeric vs. non-numeric formats
    - Non-numeric $\rightarrow$ more extreme risk perceptions
    - Numeric $\rightarrow$ increased precision
  - Importance of absolute numbers
    - Ex: 1 in 10 vs. 48 in 100
  - Numeracy
Results: Behavioral Intentions & Behaviors

- Presentation format → behavior
- Range of studies
  - Variety of outcome measures
- Example study
  - Man-Son-Hing et al., 2002
The effect of qualitative vs. quantitative presentation of probability estimates on patient decision-making: a randomized trial

Malcolm Man-Son-Hing MD MSc,*,† Annette M. O’Connor RN PhD,* Elizabeth Drake BA MHA,* Jennifer Biggs RN,* Valerie Hum BSc* and Andreas Laupacis MD MSc‡

*Clinical Epidemiology Unit, Loeb Health Research Institute, Ottawa Hospital, Ottawa, †Institute on Health of the Elderly, Sisters of Charity Health Service, Ottawa and ‡Institute for Clinical Evaluative Sciences and Faculty of Medicine, University of Toronto, Toronto, Canada

Abstract

Background Given the greater uncertainty surrounding probability estimates associated with qualitative (use of words or phrases) descriptions, the use of quantitative (numerical) information to communicate the risks and benefits of therapies is recommended but the impact of its use in decision aids is unexplored.
For moderate risk participants: More likely to make an actual choice at the extremes of available options (warfarin vs. no therapy).
Results: Behavioral Intentions & Behaviors

- Summary of findings overall
  - Numeric format prompts decisions
  - Impact on informed decision making
  - Paucity of behavioral outcomes
Overall, numeric information has a positive impact on various outcomes.
There is a 0.20 probability of experiencing nausea.

1 out of every 3 women reported experiencing nausea.

10% of women reported experiencing nausea.

Women “rarely” experience nausea.

Bar graphs
Pie charts
Icon arrays
Face icons
Observations & Conclusions

Quantitative Information

Numeric

Probabilities

There is a 0.20 probability of experiencing nausea.

Frequencies

1 out of ever 3 women reported experiencing nausea.

Percentages

10% of women reported experiencing nausea.

Non-Numeric

Descriptive

Women “rarely” experience nausea.

Visual

Bar graphs

Pie charts

Icon arrays

Face icons
Observations & Conclusions

- No format, structure, or graphical approach emerged as superior
- Range of quality of studies and study outcomes
- Intervention framing
- Numeracy
Limitations & Future Research

- Lack of consistency in testing formats
- Lack of critical tests
- Lack of theoretical progress
- Lack of consideration of important moderators
- Too few studies addressed the end point of the health communication spectrum (i.e., actual behaviors)
Conclusions

- Call for future studies
- What is the impact of adding quantitative data or summaries to drug ads on informed decision making?
Contact Information

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### Evidence Table Information

#### Study characteristics
- Objective
- Country in which study population recruited
- Study design
- Start date (for enrollment)
- Duration
- Communication format and brief description of content

#### Inclusion and exclusion criteria
- Eligibility criteria
- Sampling frame, if applicable
- Inclusion/exclusion criteria
- Intervention description
- Number of individuals in each intervention group

#### Participant characteristics
- Demographic information (e.g., age, gender, race/ethnicity)

#### Outcomes evaluated
- Primary outcomes
- Secondary outcomes

#### Results
- Qualitative and quantitative outcome and intervention group with summary statistics

#### Bottom line
- Brief summary of study design, methods, and findings