The effectiveness of the drug facts box in communicating the benefits and side effects of prescription drugs

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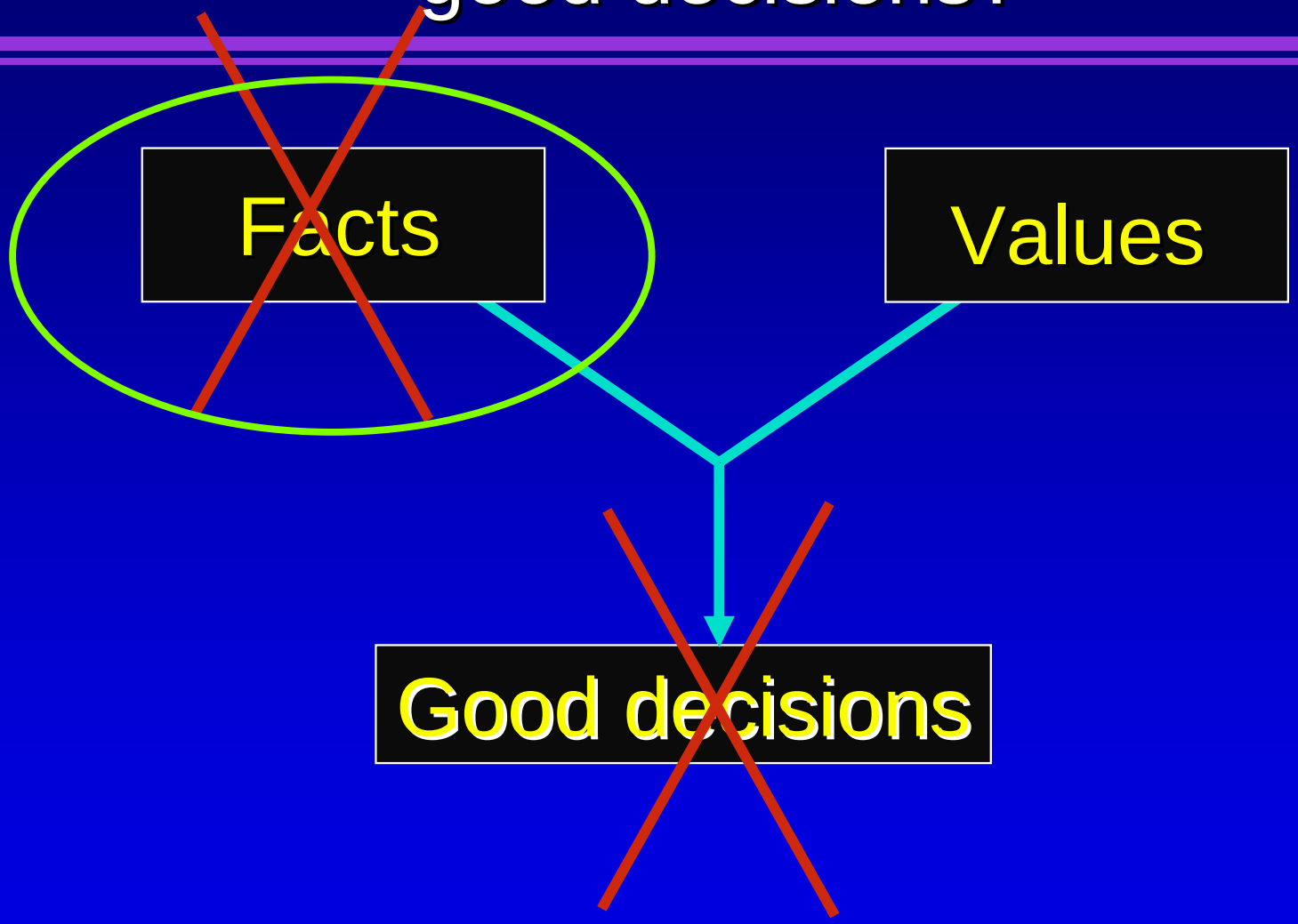
Grant Support: Attorney General Consumer and Prescriber Education Grant program, National Cancer Institute and the Robert Wood Johnson Pioneer Grant Program

Outcomes Group

What do people need to make good decisions?



In the past, people were not the intended audience for drug facts

"… [information in drug label

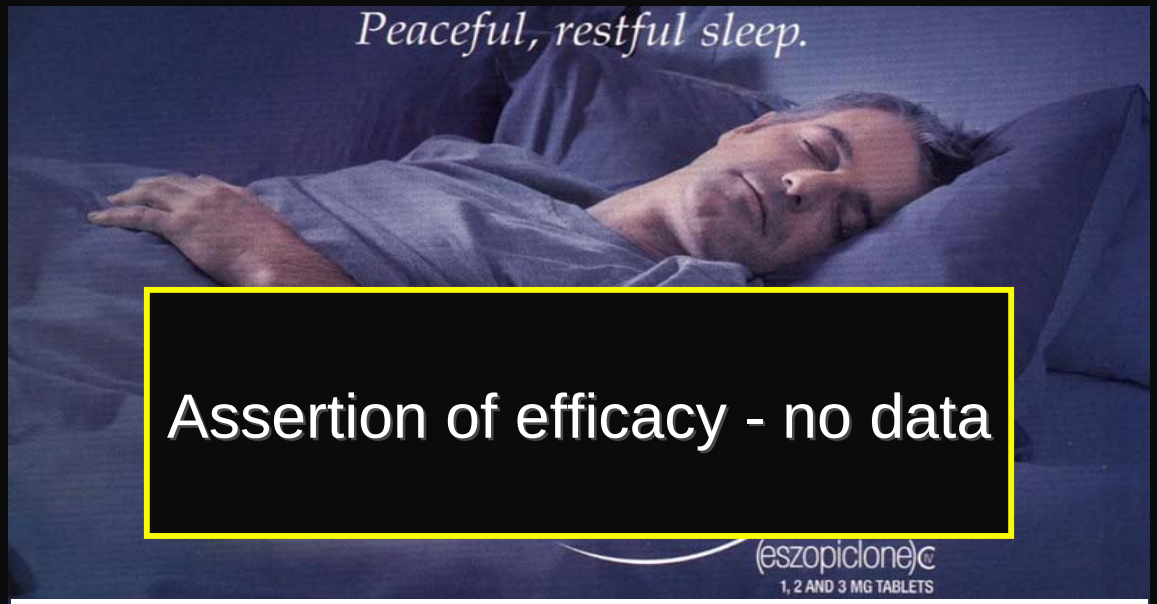
ordinary individual…"

Consumers are now the intended audience for lots of drug information

1938

Federal Food, Drug, and Cosmetic Act, 3 Fed. Reg. 3168 (December 28, 1938)

Direct-to-Consumer Ads



Assertion of efficacy - no data

Lunesta not only helps more people fall asleep fast, it helps you sleep all through the night.

If you've been hesitant to take a prescription sleep aid, be sure to ask your doctor about Lunesta.

See important patient information on the next page.

Leave the rest to Lunesta

Direct-to-consumer advertisements for prescription drugs: what are Americans being sold?

Steven Woloshin, Lisa M Schwartz, Jennifer Tremmel, H Gilbert Welch

Summary

Background Pharmaceutical companies spent US$1·8 billion on direct-to-consumer advertisements for prescription drugs in 1999. Our aim was to establish what messages are being communicated to the public by these advertisements.

Methods We investigated the content of advertisements, which appeared in ten magazines in the USA. We examined seven issues of each of these published between July, 1998, and July, 1999.

Findings 67 advertisements appeared a total of 211 times

Introduction

The first direct-to-consumer advertisement for a prescription drug appeared in *Reader's Digest* in 1981 in USA.[1,2] Over the next few years, other such advertisements were published, and the US Food and Drugs Administration (FDA) became worried that little was known about the potential effect of such advertisements on the public. Consequently, in 1983, the FDA initiated an advertising moratorium while it studied the issues and considered the regulatory options.[3,4] Although they concluded that "direct to the public prescription advertising was not in the public interest,"[4] the FDA lifted the moratorium in 1985, because of concerns about freedom of speech

The rule - not the exception

Efficacy asserted with vague qualitative statement

- only 13% presented data

- when data was presented, typically in exaggerated format - relative risk reductions without absolute risks

Brief Summary

Lunesta®
(eszopiclone)
1, 2 AND 3 MG TABLETS

Please read this summary of information about LUNESTA before you talk to your doctor or start using LUNESTA. It is not meant to take the place of your doctor's instructions. If you have any questions about LUNESTA tablets, be sure to ask your doctor or pharmacist.

LUNESTA is used to treat different types of sleep problems, such as difficulty in falling asleep, difficulty in maintaining sleep during the night, and waking up too early in the morning.

you take LUNESTA only when you are able to get a full night of sleep before you need to be active again. Be sure to talk to your doctor if you think you are having memory problems.

Tolerance

When sleep medicines are used every night for more than a few weeks, they may lose their effectiveness in helping you sleep. This is known as "tolerance." Development of tolerance to LUNESTA was not observed in a clinical study of 6 months' duration. Insomnia is often transient and intermittent, and prolonged use of sleep medicines is generally not necessary. Some people, though, have chronic sleep problems that may require more prolonged use of sleep medicine. If your sleep problems continue, consult your doctor, who will determine whether other measures are needed to overcome your sleep problems.

Dependence

any changes in your behavior, or if you have any unusual or disturbing thoughts, call your doctor immediately.

Pregnancy And Breastfeeding

Sleep medicines may cause sedation or other potential effects in the unborn baby when used during the last weeks of pregnancy. Be sure to tell your doctor if you are pregnant, if you are planning to become pregnant, or if you become pregnant while taking LUNESTA.

In addition, a very small amount of LUNESTA may be present in breast milk after use of the medication. The effects of very small amounts of LUNESTA on an infant are not known; therefore, as with all other prescription sleep medicines, it is recommended that you not take LUNESTA if you are breast-feeding a baby.

Safe Use Of Sleep Medicines

No data on efficacy
(or side effects)

- Lightheadedness
- Difficulty with coordination

Sleep medicines can make you sleepy during the day. How drowsy you feel depends upon how your body reacts to the medicine, which sleep medicine you are taking, and how large a dose your doctor has prescribed. Daytime drowsiness is best avoided by taking the lowest dose possible that will still help you sleep at night. Your doctor will work with you to find the dose of LUNESTA that is best for you. Some people taking LUNESTA have reported next-day sleepiness.

To manage these side effects while you are taking this medicine:

- When you first start taking LUNESTA or any other sleep medicine, until you know whether the medicine will still have some effect on you the next day, use extreme care while doing anything that requires complete alertness, such as driving a car, operating machinery, or piloting an aircraft.
- Do not drink alcohol when you are taking LUNESTA or any sleep medicine. Alcohol can increase the side effects of LUNESTA or any other sleep medicine.
- Do not take any other medicines without asking your doctor first. This includes medicines you can buy without a prescription. Some medicines can cause drowsiness and are best avoided while taking LUNESTA.
- Always take the exact dose of LUNESTA prescribed by your doctor. Never change your dose without talking to your doctor first.

Special Concerns

There are some special problems that may occur while taking sleep medicines.

Memory Problems

Sleep medicines may cause a special type of memory loss or "amnesia." When this occurs, a person may not remember what has happened for several hours after taking the medicine. This is usually not a problem since most people fall asleep after taking the medicine. Memory loss can be a problem, however, when sleep medicines are taken while traveling, such as during an airplane flight and the person wakes up before

stopped suddenly after being used daily for a long time. In some cases, these symptoms can occur even if the medicine has been used for only a week or two. In mild cases, withdrawal symptoms may include unpleasant feelings. In more severe cases, abdominal and muscle cramps, vomiting, sweating, shakiness, and, rarely, seizures may occur. These more severe withdrawal symptoms are very uncommon. Although withdrawal symptoms have not been observed in the relatively limited controlled trials experience with LUNESTA, there is, nevertheless, the risk of such events in association with the use of any sleep medicine.

Another problem that may occur when sleep medicines are stopped is known as "rebound insomnia." This means that a person may have more trouble sleeping the first few nights after the medicine is stopped than before starting the medicine. If you should experience rebound insomnia, do not get discouraged. This problem usually goes away on its own after 1 or 2 nights.

If you have been taking LUNESTA or any other sleep medicine for more than 1 or 2 weeks, do not stop taking it on your own. Always follow your doctor's directions.

Changes In Behavior And Thinking

Some people using sleep medicines have experienced unusual changes in their thinking and/or behavior. These effects are not common. However, they have included:

- More outgoing or aggressive behavior than normal
- Confusion
- Strange behavior
- Agitation
- Hallucinations
- Worsening of depression
- Suicidal thoughts

How often these effects occur depends on several factors, such as a person's general health, the use of other medicines, and which sleep medicine is being used. Clinical experience with LUNESTA suggests that it is rarely associated with these behavior changes.

It is also important to realize it is rarely clear whether these

sleep medicine, until you know whether the medicine will still have some effect on you the next day, use extreme care while doing anything that requires complete alertness, such as driving a car, operating machinery, or piloting an aircraft.

8. Be aware that you may have more sleeping problems the first night or two after stopping any sleep medicine.
9. Be sure to tell your doctor if you are pregnant, if you are planning to become pregnant, if you become pregnant, or if you are breastfeeding a baby while taking LUNESTA.
10. As with all prescription medicines, never share LUNESTA or any other sleep medicine with anyone else. Always store LUNESTA or any other sleep medicine in the original container and out of reach of children.
11. Be sure to tell your doctor if you suffer from depression.
12. LUNESTA works very quickly. You should only take LUNESTA immediately before going to bed.
13. For LUNESTA to work best, you should not take it with or immediately after a high-fat, heavy meal.
14. Some people, such as older adults (i.e., ages 65 and over) and people with liver disease, should start with the lower dose (1 mg) of LUNESTA. Your doctor may choose to start therapy at 2 mg. In general, adults under age 65 should be treated with 2 or 3 mg.
15. Each tablet is a single dose; do not crush or break the tablet.

Note: This summary provides important information about LUNESTA. If you would like more information, ask your doctor or pharmacist to let you read the Prescribing Information and then discuss it with him or her.

Rx only

SEPRACOR

Medication Guide

MEDICATION GUIDE
LUNESTA® (lū'-nes"-tā) Tablets, Coated C-IV
(eszopiclone)

Read the Medication Guide that comes with LUNESTA before you start taking it and each time you get a refil[redacted] the place of talking to y[redacted]

What is the m[redacted]

After taking L[redacted] nd do an activity that y[redacted] ember that you did a[redacted] ctivities if you drink alco[redacted] orted activities inclu[redacted]

No data on efficacy

(or side effects)

- driving a car ("sleep-driving")
- making and eating food
- talking on the phone
- having sex
- sleep-walking

Call your doctor right away if you find out that you have done any of the above activities after taking LUNESTA.

Currently Approved Label

21476 FDA approved labeling text 1.24.08

Chronic Insomnia (Adults And Elderly)

The effectiveness of LUNESTA was established in five controlled studies in chronic insomnia. Three controlled studies were in adult subjects, and two controlled studies were in elderly subjects with chronic

No data on efficacy
(lots of side effect data)

Adults

In the first study, adu double-blind, parallel-group trial of mg with placebo. Objective endpoints were measured for 4 weeks. Both 2 mg and 3 mg were superior to placebo on LPS at 4 weeks. The 3 mg dose was superior to placebo on WASO.

In the second study, adults with chronic insomnia (n=788) were evaluated using subjective measures in a double-blind, parallel-group trial comparing the safety and efficacy of LUNESTA 3 mg with placebo administered nightly for 6 months. LUNESTA was superior to placebo on subjective measures of sleep latency, total sleep time, and WASO.

FDA Review Documents

FDA U.S. Food and Drug

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Lunesta (Esz
Company:
Application
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- Approval Letter(s)
- Printed Labeling
- Medical Review(s)
- Chemistry Review(s)
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- Statistical Review(s)
- Microbiology Review(s)
- Clinical Pharmacology Biopharmaceutics Review
- Administrative Document(s) & Correspondence

021476_Lunesta_medr~1.PDF (403 pages)

403 pages

will offer a brief review of the relevant data, and the recommendation of the division for action on this application.

Effectiveness

As noted abov ; 5 in patients with c

1) Study 045 days of treatment, employing doses of 1, 2, 2.5, 3 mg of esz, zolpidem 10 mg, and placebo.
2) Study 046 was a parallel group study in which patients with chronic insomnia were randomized to receive 2 mg, 3 mg, or placebo for 44 days.
3) Study 049 was a parallel group study in which patients with chronic insomnia were randomized to receive either 3mg or placebo for 6 months.
4) Study 047 was a parallel group study in which elderly patients with chronic insomnia were randomized to receive 2 mg or placebo for 2 weeks.
5) Study 048 was a parallel group study in which elderly patients with chronic

Search

96
97
98
99

Table VIC21. Efficacy Results on Subjective Sleep Latency from the 6- month Doub Blind Phase of Study 190-049 (A subjective sleep study in non-elderly patients with Chronic Insomnia).
ITT Population

p. 306

Time Interval	Statistic		Esopiclone 3 mg (n=593)	P-value
Month 4-6 Average [primary endpoint]	Mean (SD)	64.7 (56.4)	46.7 (45.6)	<0.0001
	Median	44.8	31.7	
	Min, Max	4.1, 330.0	2.1, 565.0	
Month 1-3 Average	Mean (SD)	66.1 (54.8)	45.3 (40.0)	<0.0001
	Median	50.8	32.1	
	Min, Max	5.0, 330.0	4.8, 373.3	
Month 1	Mean (SD)	71.3 (59.8)	44.3 (36.5)	<0.0001
	Median	52.5	31.3	
	Min, Max			
Month 2	Mean (SD)	65.4 (56.9)	45.1 (46.2)	<0.0001
	Median	50.0	30.0	
	Min, Max			
Month 3	Mean (SD)	63.2 (57.1)	46.3 (53.9)	<0.0001
	Median	45.0	30.0	
	Min, Max			
Month 4	Mean (SD)	64.3 (59.8)	47.8 (49.8)	<0.0001
	Median	45.0	30.0	
	Min, Max			
Month 5	Mean (SD)	66.6 (74.6)	45.3 (45.4)	<0.0001
	Median	43.8	30.0	
	Min, Max			
Month 6	Mean (SD)	63.1 (57.9)	47.0 (50.6)	<0.0001
	Median	45.0	30.0	
	Min, Max			

Note: This table summarizes data for Population A + C, see Figures 9.7.1.2-1 and 10.1-2 for the description of the populations.

Note: For each subject, "Month 1-3 Average" represents the average over Months 1-3 of the double-blind period, and "Month 4-6 Average" represents the average over Months 4-6 of the double-blind period based on the last observation carried forward algorithm. For

Precedent: FDA nutrition facts box a better job getting the facts to consumers?

Prescription Drug Facts: AMCID (amoditine)

What is this drug for?	To relieve heartburn
Who might consider taking it?	Men and women bothered by heartburn or acid reflux disease
Who should NOT take it?	Women who are pregnant or breastfeeding
Recommended testing	None
Other things to consider doing	Eat frequent small meals; avoid fatty foods (and others which trigger your symptoms); excessive alcohol and eating close to bedtime; don't smoke; look into other

How long has the drug

Amcid was approved by FDA in 1991 - Studies show that most serious side effects or recalls of new drugs happen during their first 5 years of approval.

How well does the drug work?

What is the chance of the outcome

if I take or do not take the drug?

What side effects does the drug cause?

What is the chance of different problems

if I take or do not take the drug?

Descriptive information

Simple tabular display of quantitative info

Benefit data

Side effect data

New drug warning

Drug Facts Box
Progress Report

Four studies testing the box

1. **Boston Study** (2003)
2. **Vermont Study** (2007)
3. **National Randomized Trial: Symptom Drug Box Trial** (2009)
4. **National Randomized Trial: Prevention Drug Box Trial** (2009)

Implementing the box at the FDA

A story: The box goes to Washington

FDA U.S. Food and Drug Administration — Department of Health and Human Services

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Division of Drug Marketing,

CDER

DDMAC

Organization within the Di

Regulatory Information

Submission Information

FAQs

Research

Presentations

Contact us

Invited to FDA & met with 20 officials who:

* Liked drug box idea
* Challenged us to show that consumers want, value, and understand benefit data

ponsibility for
advertising

enforcement and education program, and by fostering better communication of labeling and promotional information to both healthcare professionals and consumers."

Information About What DDMAC Reviewers Do

DDMAC reviewers have responsibility for reviewing prescription drug advertising and promotional labeling to ensure that the information contained in these promotional materials is not false or misleading. They engage in a variety of tasks to perform this responsibility, including: providing written comments to pharmaceutical sponsors on proposed promotional materials to ensure clear and unambiguous communication of the laws and regulations relating to prescription drug promotion; reviewing complaints about alleged promotional violations; initiating enforcement actions on promotional materials that are false or misleading; comparing the product labeling and promotional materials of various closely related products to ensure that the

1. Boston Study

Prescription Drug Facts: PRIDCLO (pricogrel)

What is this drug for?	To reduce clotting in order to reduce the chance of having or dying from a heart attack
Who might consider taking it?	Men and women with heart or vascular disease (a stroke or narrowed blood vessel in the leg)
Who should not take it?	People with bleeding problems, liver or kidney problems
Recommended testing	None
Other things to consider doing	Eat a low saturated fat/low cholesterol diet, don't smoke, exercise more, talk to other medications

PRIDCLO STUDY FINDINGS

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

What difference did PRIDCLO make?	**People given Aspirin (325mg a day)**	**People given PRIDCLO (75mg a day)**
Did PRIDCLO help?		
Fewer people had a heart attack (0.6% fewer)	3.3% 33 in 1000	2.7% 27 in 1000
No difference in dying from a heart attack	About 1.4% in both groups 14 in 1000	
No difference in dying from anything	About 5.5% in both groups 55 in 1000	
Did PRIDCLO have side effects?		
Life threatening side effects		
No difference in strokes from bleeding into brain	About 0.5% 5 in 1000	
Fewer people had major stomach bleeding (0.7% fewer)	2.7% 27 in 1000	2.0% 20 in 1000
Symptom side effects		
Fewer people had abdominal pain (1.5% fewer)	7.1% 71 in 1000	5.6% 56 in 1000
More people had bruising (1.6% more)	3.7% 37 in 1000	5.3% 53 in 1000
More people had diarrhea (1.1% more)	3.4% 34 in 1000	4.5% 45 in 1000
More people had a rash (0.7% more)	2.9% 29 in 1000	4.2% 42 in 1000

How long has the drug been in use?

Pridclo was approved by FDA in 1997. Studies show that most serious side effects or recalls of new drugs happen during the first 5 years of approval.

Study Features (n=203)

-Test simple "benefit box"

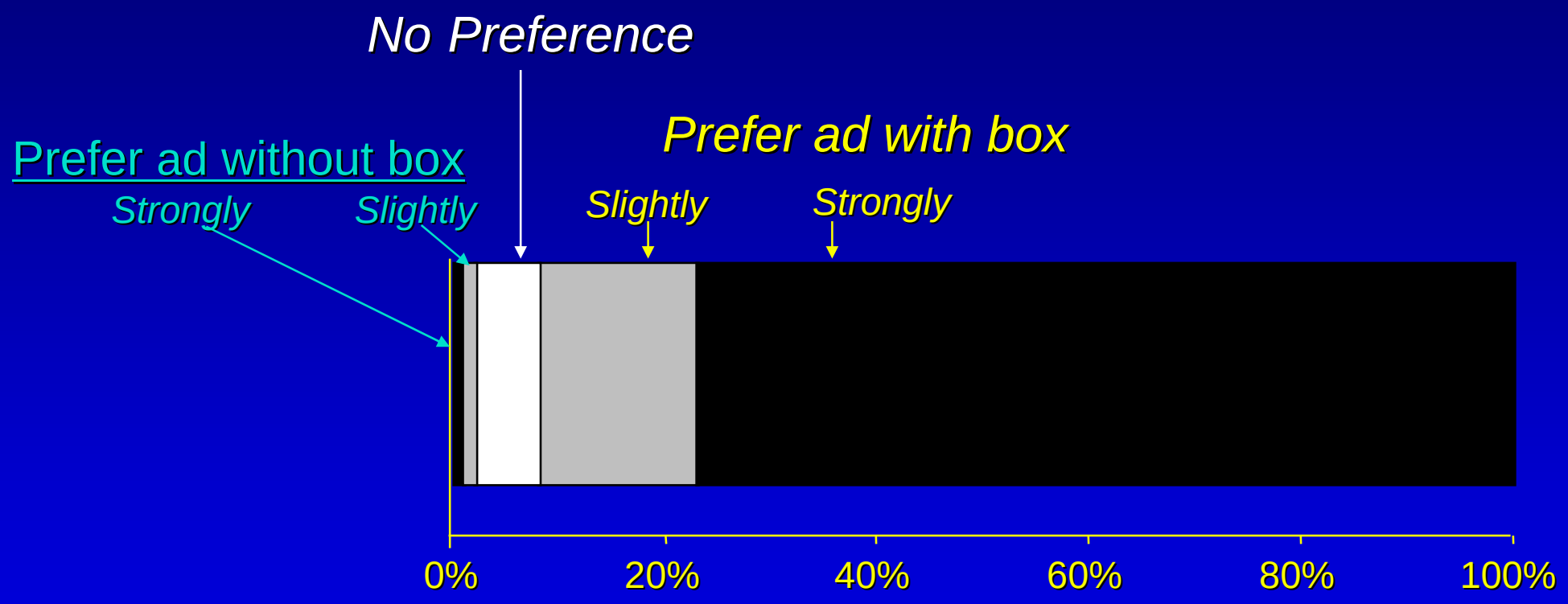
-Interviewer study

orient participants to box

ask how they like it

simple comprehension tasks

Would you prefer to see this ad with or without the facts box?



Read related papers by Joel Weissman et al., Pat Kelly, David Riggs et al., James Jeffords, Henry Waxman, and Peter Pitts.

DATAWATCH

The Value Of Benefit Data In Direct-To-Consumer Drug Ads

Simple tables showing drugs' expected outcomes are understood and valued by consumers.

by Steven Woloshin, Lisa M. Schwartz, and H. Gilbert Welch

ABSTRACT: Direct-to-consumer (DTC) pharmaceutical ads typically describe drug benefits in qualitative terms; they rarely provide data on how well the drug works. We describe an

"Most people we interviewed want benefit data in drug ads, can understand these data, and are influenced by them."

2. Vermont Study

Prescription Drug Facts: NOLVADEX (tamoxifen)

What is this drug for?	Reduce the chance of getting breast cancer
Who might consider taking it?	Women at high risk of getting breast cancer (1.7% or higher risk over 5 years). You can calculate your breast cancer risk at http://bcra.nci.nih.gov/btc.
Who should not take it?	Women who are pregnant or breastfeeding
Recommended testing	Have a yearly checkup that includes a gynecological examination and blood tests
Other things to consider doing	No other medicines are approved to reduce breast cancer risk for women who have not had breast cancer

NOLVADEX STUDY FINDINGS

13,000 women at high risk of getting breast cancer were given NOLVADEX or a sugar pill for 6 years. Here's what happened:

What difference did NOLVADEX make?	**Women given a sugar pill**	**Women given NOLVADEX (20 mg a day)**
Did NOLVADEX help?		
Fewer women got invasive breast cancer	2.7%	1.4%
Fewer women died from breast cancer	0.09%	0.05%
Did NOLVADEX have side effects?		
Life threatening side effects		
More women had a blood clot in their leg or lungs	0.4%	0.8%
More women had a stroke	0.4%	0.6%
More women got invasive uterine cancer	0.2%	0.5
Symptom side effects		
More women had hot flashes	69%	81%
More women had vaginal discharge	35%	55%
More women had cataracts needing surgery	1.1%	1.7%
Other things to know		
Dying for any reason	1.1%	0.9%

How long has the drug been in use?
Nolvadex was first approved by the FDA in 1982 - Studies show that most serious side effects or recalls of new drugs happen during their first 5 years of approval.

Study Features (n=274)

-More complex box: table with 9 rows of 2 columns of data.

-No instructions or training on how to use the box

-More demanding tasks

The Drug Facts Box: Providing Consumers with Simple Tabular Data on Drug Benefit and Harm

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

"Most participants – even those with lower formal educational attainment – were able to understand and use the tabular data."

Dartmouth's "Community Medical School" public lecture series and Dartmouth Hitchcock's Center for Shared Decision Making and 88 veterans and their families recruited from waiting rooms in the Veterans Affairs outpatient clinic, White River Junction, Vermont. ***Design.*** *Cross-sectional survey. Participants were tested on their comprehension of the study findings table about the drug tamoxifen got breast cancer in the tamoxifen v. the placebo group. Most participants were also able to use the table to make comparisons.* ***Conclusion.*** *Most participants—even those with lower formal educational attainment—were able to understand and use the tabular data.* ***Key words:*** *risk communication; decision aids; pharmaceutical decision making.*
(Med Decis Making 2007;27:655–662)

Direct-to-consumer pharmaceutical advertisements have been criticized for how they present data on drug benefit and side effects.[1,2] Drug benefit is rarely quantified, and when quantitative data are provided, they are typically provided in a format that tends to exaggerate perceptions of the effect size—namely, a relative change with no base rate (e.g., "lowers heart risk by 40% v. placebo," without stating the risk in the placebo group).[2] Although side effect data often appear in ads, they are generally

"*Gold standard*" trials to generate the highest quality evidence in the target audience: US consumers

Nationally representative sample of US adults ages 35-70
(identified by random digit dialing)

↓

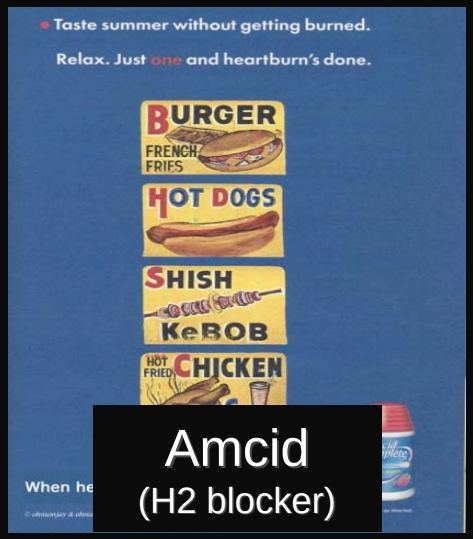
Randomization
(second page of ad)

↙ Drug Facts Box Second Page

↘ Brief Summary Second Page

NCT 00450931, NCT00753857

3. Symptom Drug Box Trial



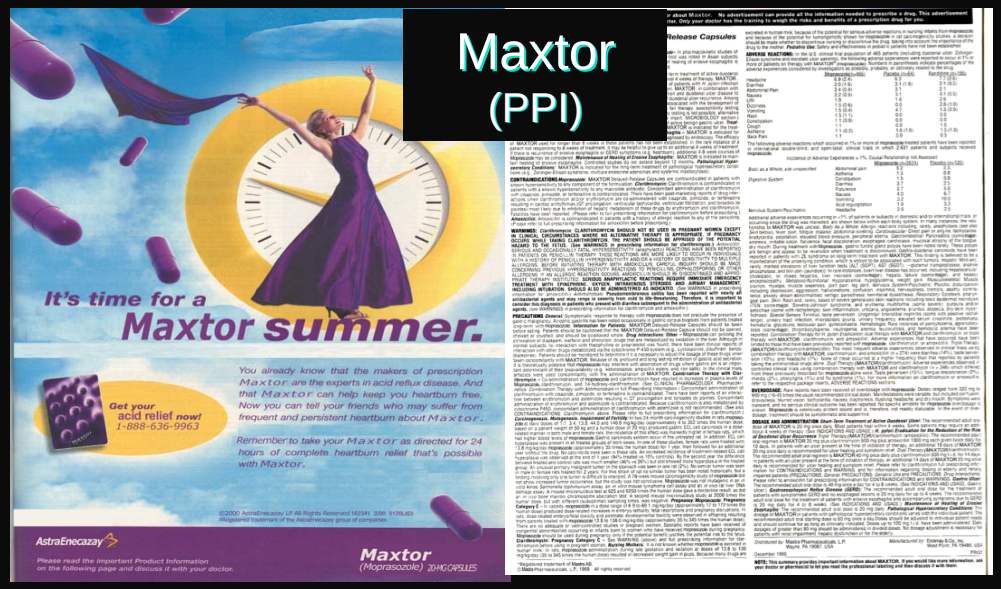
Study Features (n=231)

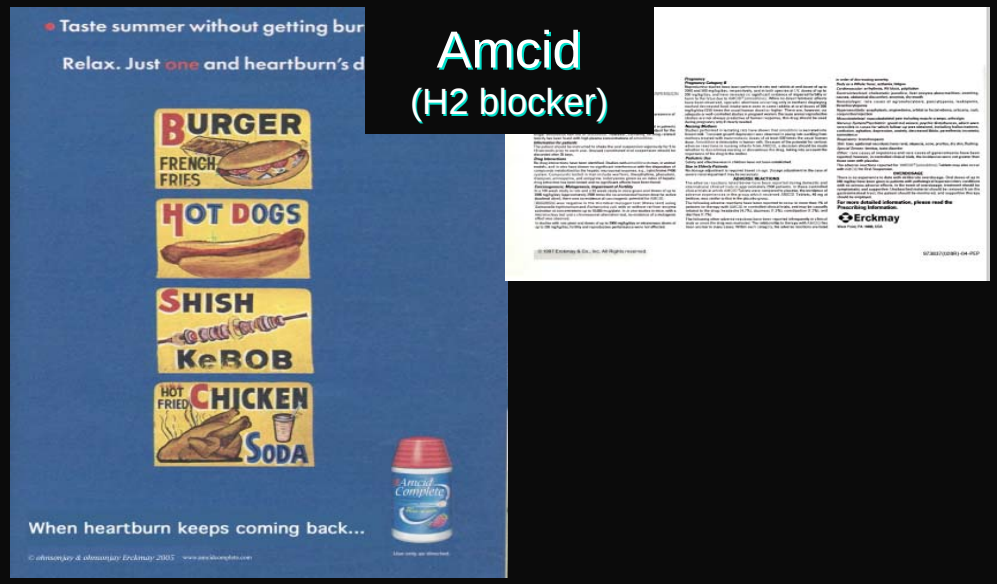
Real world challenge: Show people ads for 2 drugs treating the same condition.

The drugs have similar side effects but one is substantially more effective.

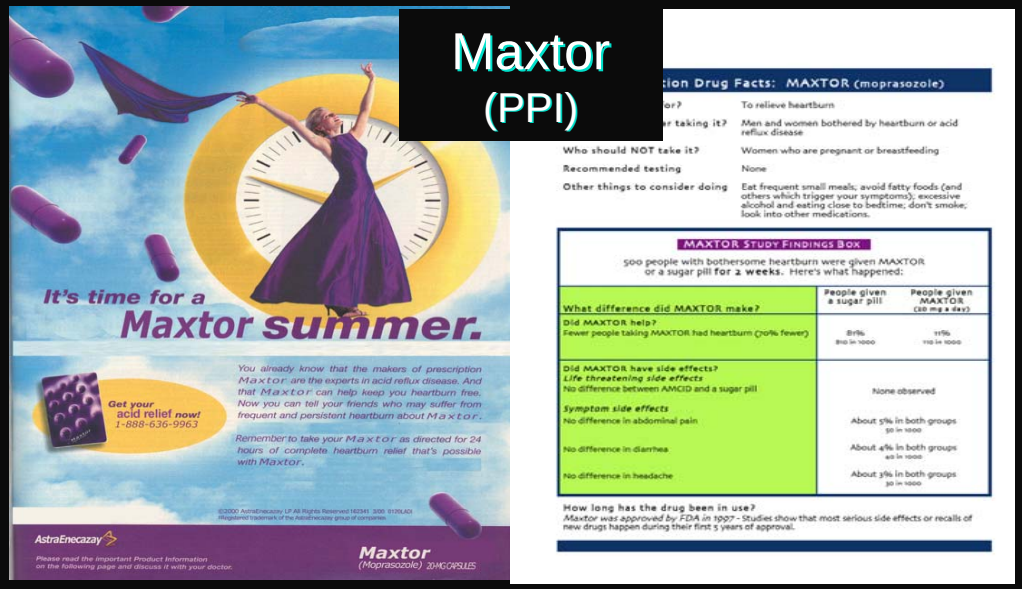
Can people choose the objectively *better* drug?

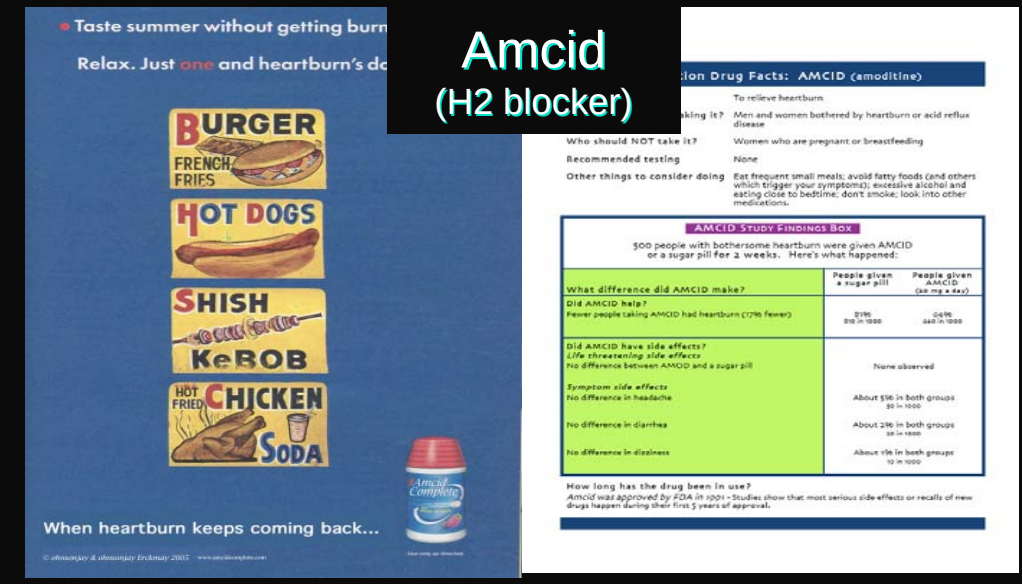
Control: Ads + Brief Summaries





Drug Box: Ads + Drug Boxes





In your opinion, how does MAXTOR compare to **AMCID** in relieving heartburn?

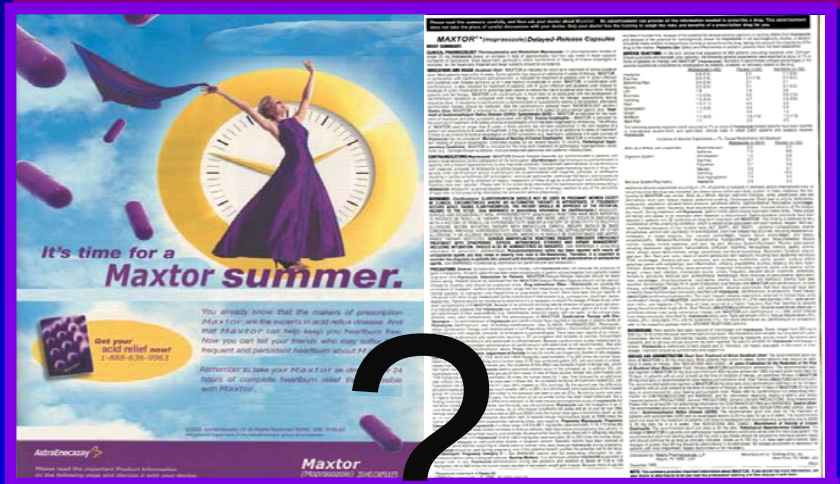
a. MAXTOR is a lot more effective

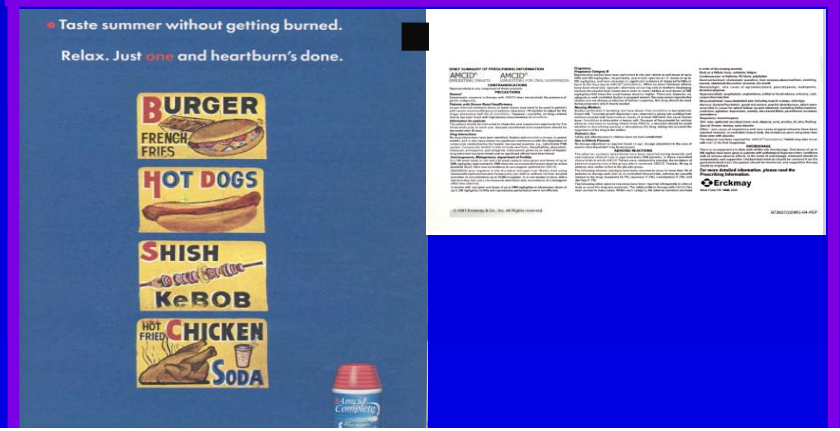
b. MAXTOR is a little more effective

c. MAXTOR is about the same

d. MAXTOR is a little less effective

e. MAXTOR is a lot less effective





?

MAXTOR STUDY FINDINGS BOX

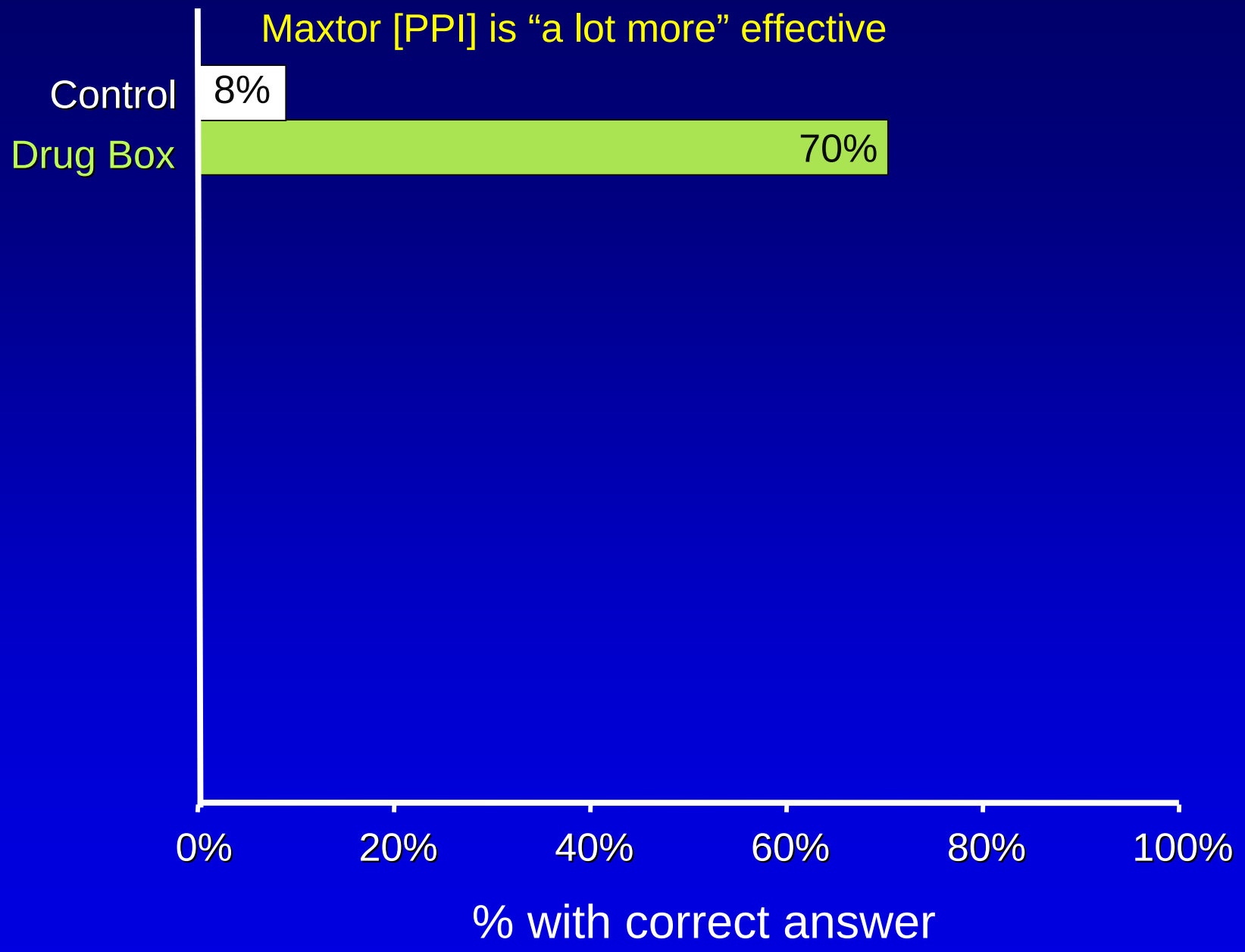
500 people with bothersome heartburn were given MAXTOR or a sugar pill **for 2 weeks.** Here's what happened:

What difference did MAXTOR make?	People given a sugar pill	People given MAXTOR (20 mg a day)
Did MAXTOR help? Fewer people taking MAXTOR had heartburn (70% fewer)	81% 810 in 1000	11% 110 in 1000

AMCID STUDY FINDINGS BOX

500 people with bothersome heartburn were given AMCID or a sugar pill **for 2 weeks.** Here's what happened:

What difference did AMCID make?	People given a sugar pill	People given AMCID (20 mg a day)
Did AMCID help? Fewer people taking AMCID had heartburn (17% fewer)	81% 810 in 1000	64% 640 in 1000

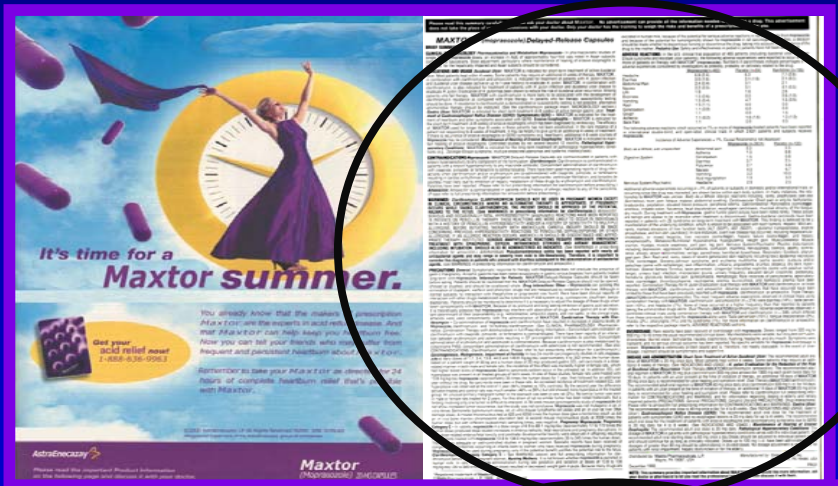

Maxtor [PPI] is “a lot more” effective
Control
8%
Drug Box
70%
0%
20%
40%
60%
80%
100%
% with correct answer

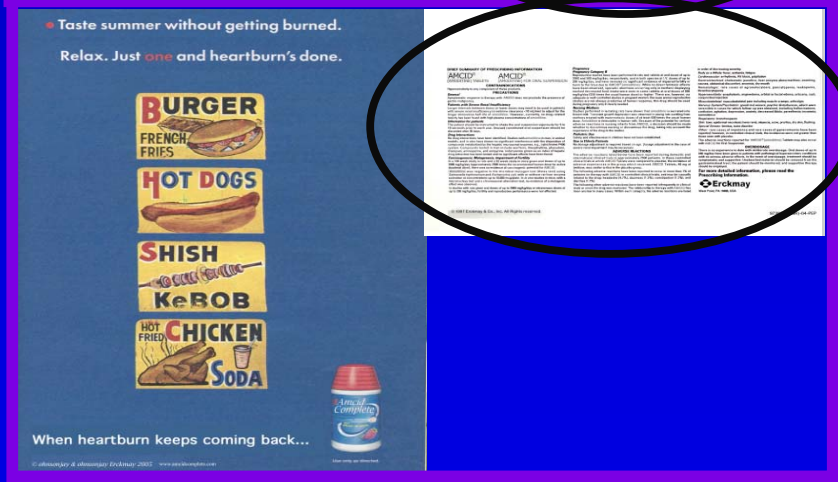
In your opinion, how do the side effects of MAXTOR compare to AMCID?

a. MAXTOR side effects are more serious

b. AMCID side effects are more serious

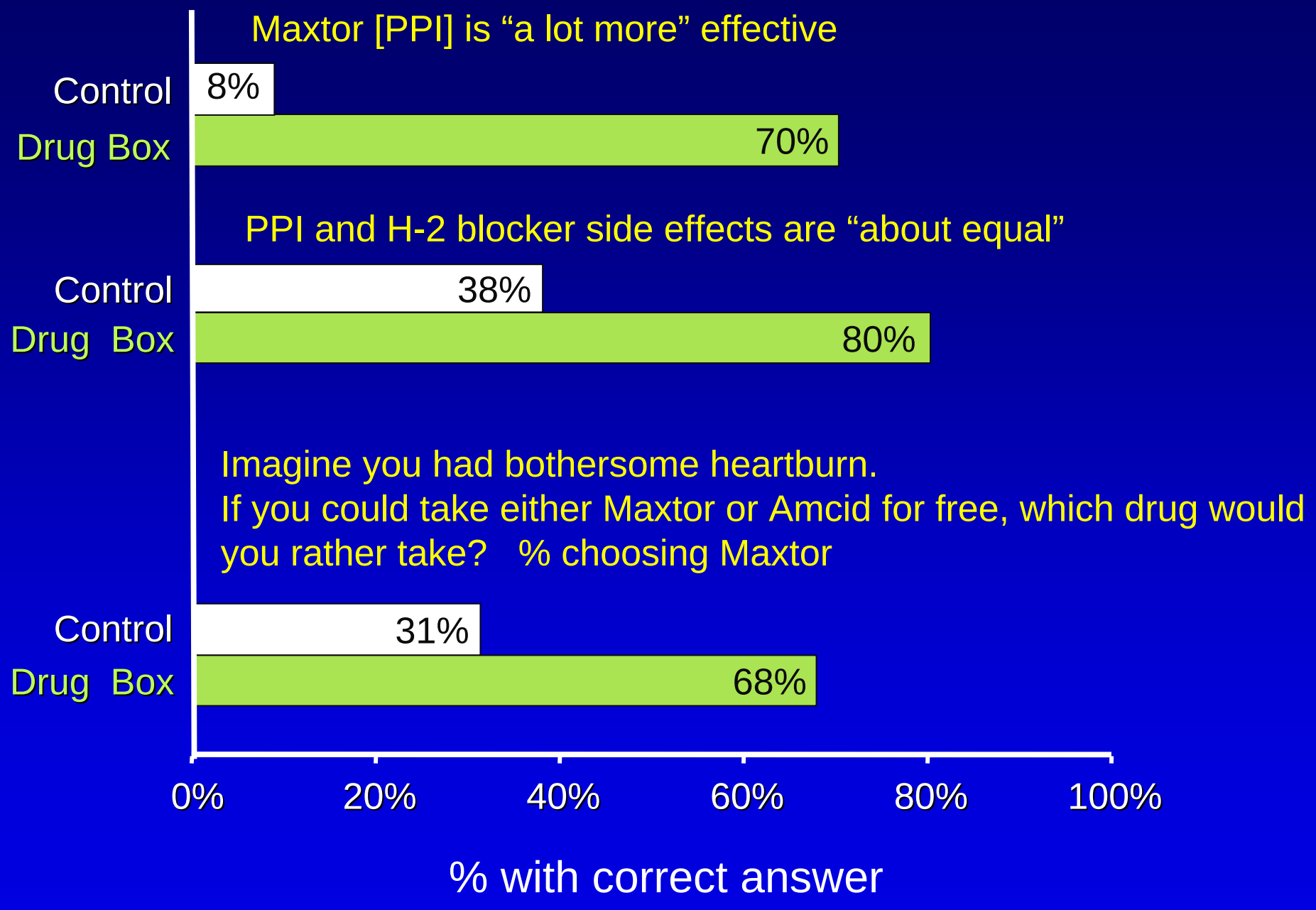
c. The side effects are about equal





Did MAXTOR have side effects?	
Life threatening side effects	
No difference between AMCID and a sugar pill	None observed
Symptom side effects	
No difference in abdominal pain	About 5% in both groups 50 in 1000
No difference in diarrhea	About 4% in both groups 40 in 1000
No difference in headache	About 3% in both groups 30 in 1000

Did AMCID have side effects?	
Life threatening side effects	
No difference between AMCID and a sugar pill	None observed
Symptom side effects	
No difference in headache	About 5% in both groups 50 in 1000
No difference in diarrhea	About 2% in both groups 20 in 1000
No difference in dizziness	About 1% in both groups 10 in 1000


Maxtor [PPI] is “a lot more” effective
Control
8%
Drug Box
70%
PPI and H-2 blocker side effects are “about equal”
Control
38%
Drug Box
80%
Imagine you had bothersome heartburn.
If you could take either Maxtor or Amcid for free, which drug would you rather take? % choosing Maxtor
Control
31%
Drug Box
68%
0%
20%
40%
60%
80%
100%
% with correct answer

4. Prevention Drug Box Trial

Concor
(statin)

Pridclo
(clopidogrel)

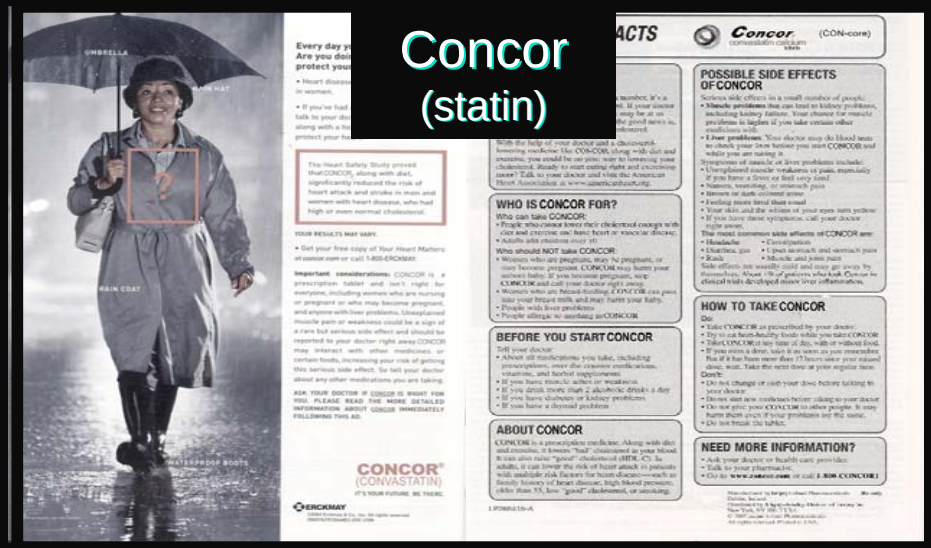
Study Features (n=219)

Two drugs used to reduce the risk for future events that are important but relatively rare.

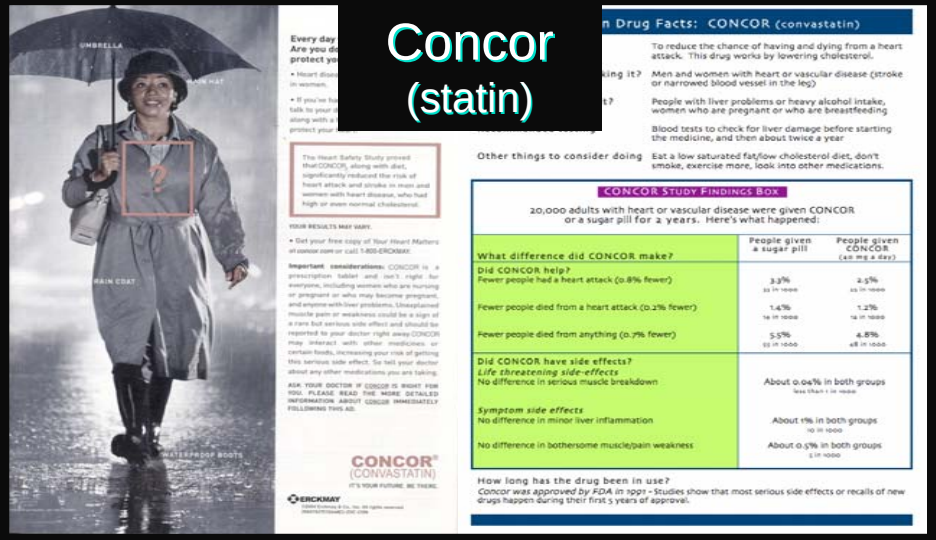
Current ads for statin and clopidogrel for preventing second heart attacks.

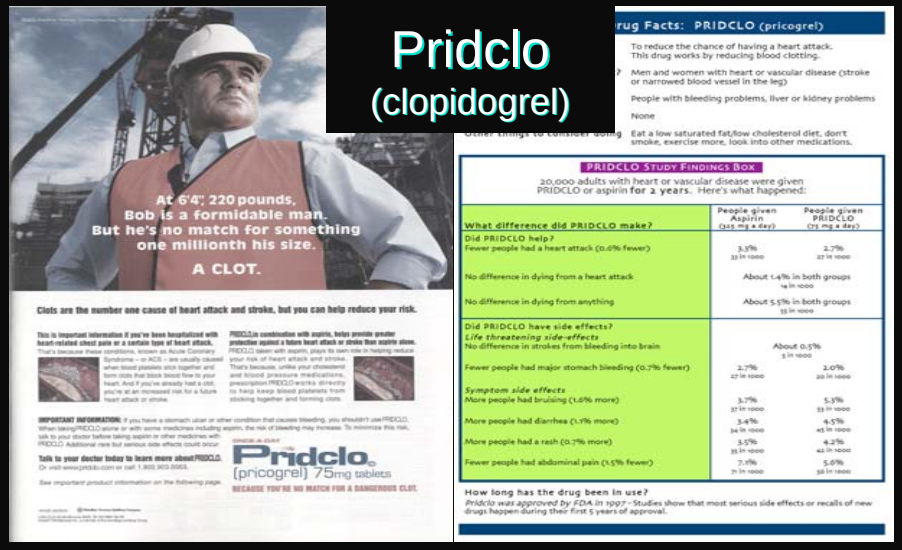
Does the box result in more *accurate perceptions* of drug benefits and side effects?

Control: Ads + Brief Summaries



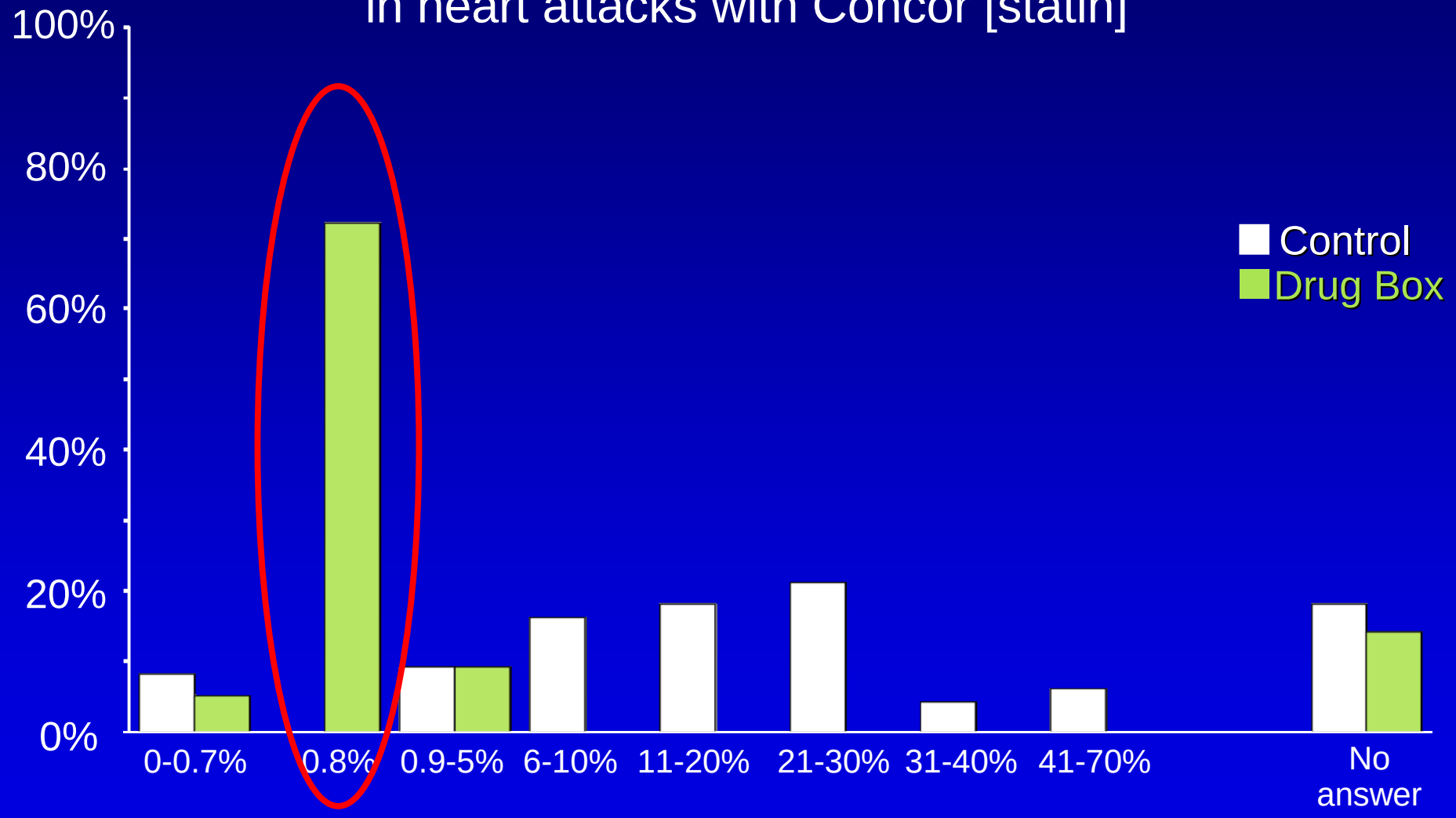
Drug Box: Ads + Drug Boxes





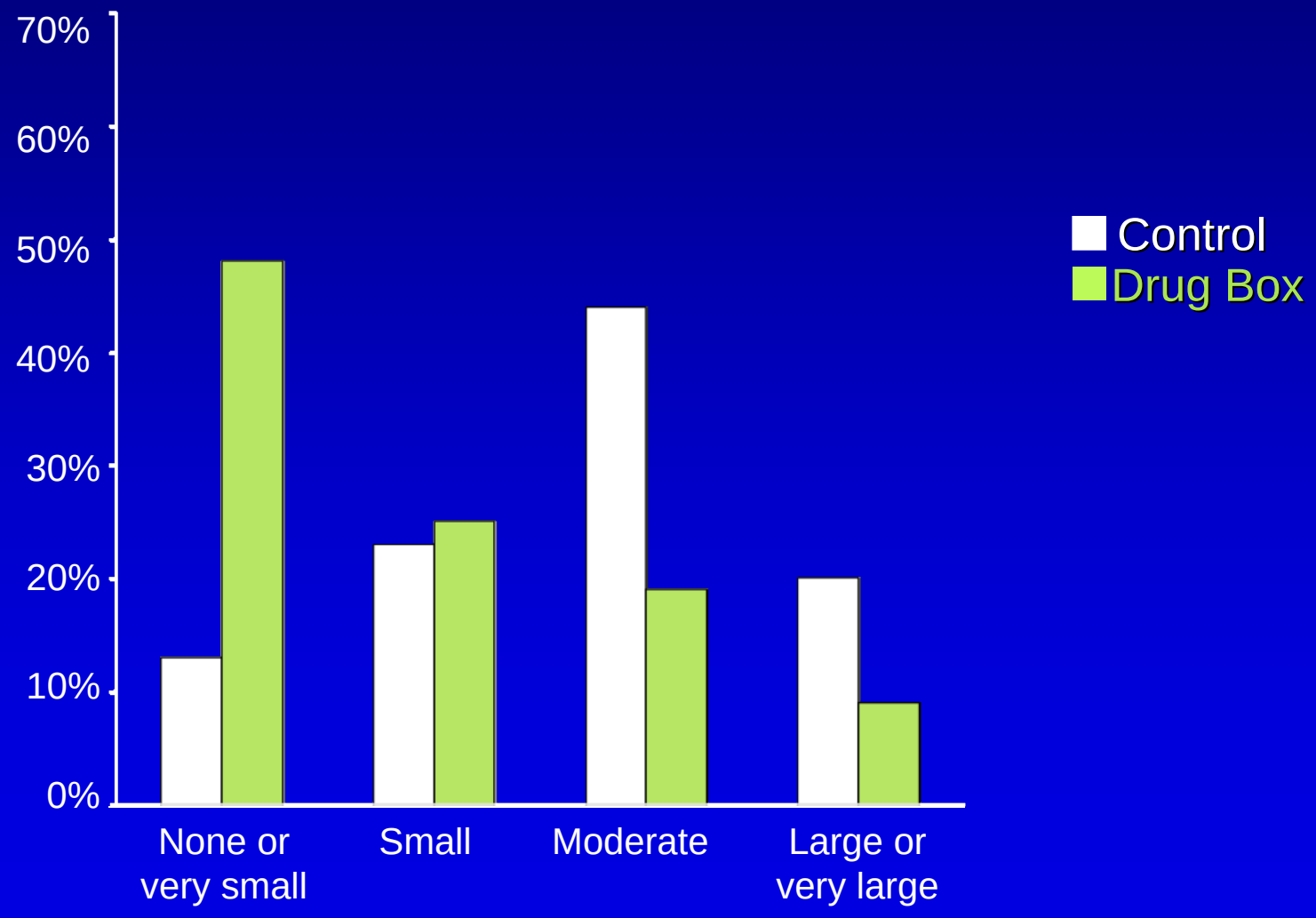
Benefit

Perceived absolute risk reduction(calculated)
in heart attacks with Concor [statin]



Side Effects

"How would you describe the side effects of Concor [statin] for people with heart or vascular disease?"



"Are the benefits of Concor [statin] worth the possible side effects for people with heart or vascular disease?"

	Control	Drug Box
% Yes	86%	72%

Cautions

While comprehension was high, the information in the box was not accessible to everyone.

The trials tested drug boxes in only 4 direct-to-consumer ads. If other ads communicated outcome data better, the effect of the drug box would be reduced.

Summary: Effectiveness of the Drug Facts Box

Annals of Internal Medicine | ARTICLE

Communicating Drug Benefits and Harms With a Drug Facts Box: 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 do not provide data on how well the drug works. Consumers require this fundamental information to make informed decisions.

Participants: Adults age 35 to 70 years who completed a mailed survey; the final samples comprised 231 participants with completed surveys in the symptom drug box trial (49% response rate) and 219 in the prevention drug box trial (46% response rate).

Intervention: In both trials, the control group received 2 actual drug ads (including both the front page and brief summary). The drug box group received the same ads, except that the brief summary was replaced by a drug facts box.

Measurements: Choice between drugs (primary outcome of the symptom drug box trial) and accurate perceptions of drug benefits and side effects (primary outcome of the prevention drug box trial).

Results: In the symptom drug box trial, 70% of the drug box group and 8% of the control group correctly identified the PPI as being "a lot more effective" than the histamine-2 blocker ($P <$ 0.001), and 80% and 38% correctly recognized that the side

outcome data better, the effect of the drug box would be reduced.

Conclusion: A drug facts box improved U.S. consumers' knowledge of prescription drug benefits and side effects. It resulted in better choices between drugs for current symptoms and corrected the overestimation of benefit in the prevention setting.

Funding: National Cancer Institute and Attorney General Consumer and Prescriber Education Program.

Ann Intern Med. 2009;150:* * * FILL THIS IN * * *. www.annals.org
For author affiliations, see end of text.
ClinicalTrials.gov registration numbers: NCT00450931, NCT00753857.
This article was published at www.annals.org on 17 February 2009.

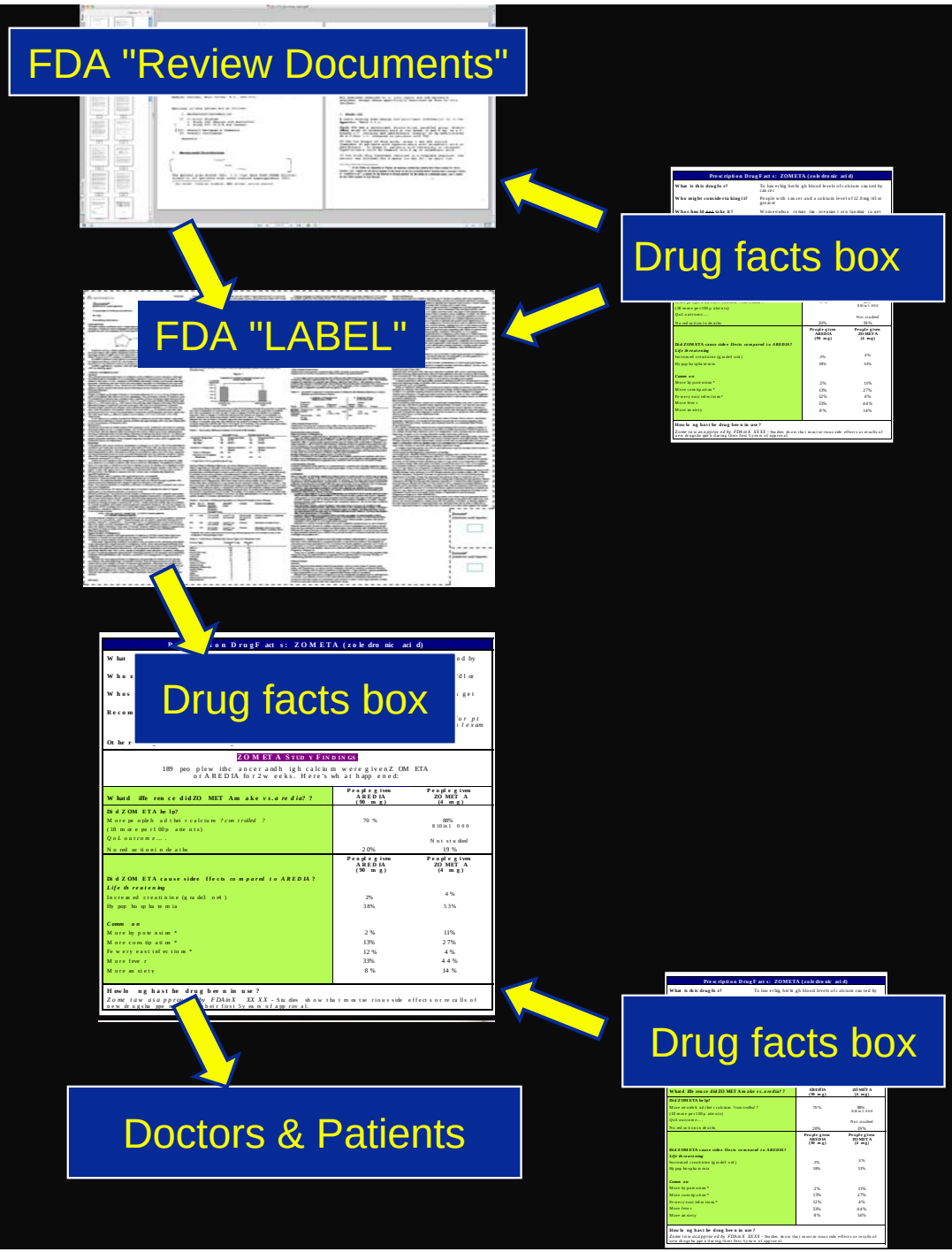
"A drug fact box improved US consumers' knowledge of prescription drug benefits and side effects. It resulted in better choices between drugs for current symptoms and corrected the overestimation of benefit in the setting of prevention."

Drug Facts Box
Progress Report

Four studies testing the box

1. Boston Study (2003)
2. Vermont Study (2007)
3. National Randomized Trial: Symptom Drug Box Trial (2009)
4. National Randomized Trial: Prevention Drug Box Trial (2009)

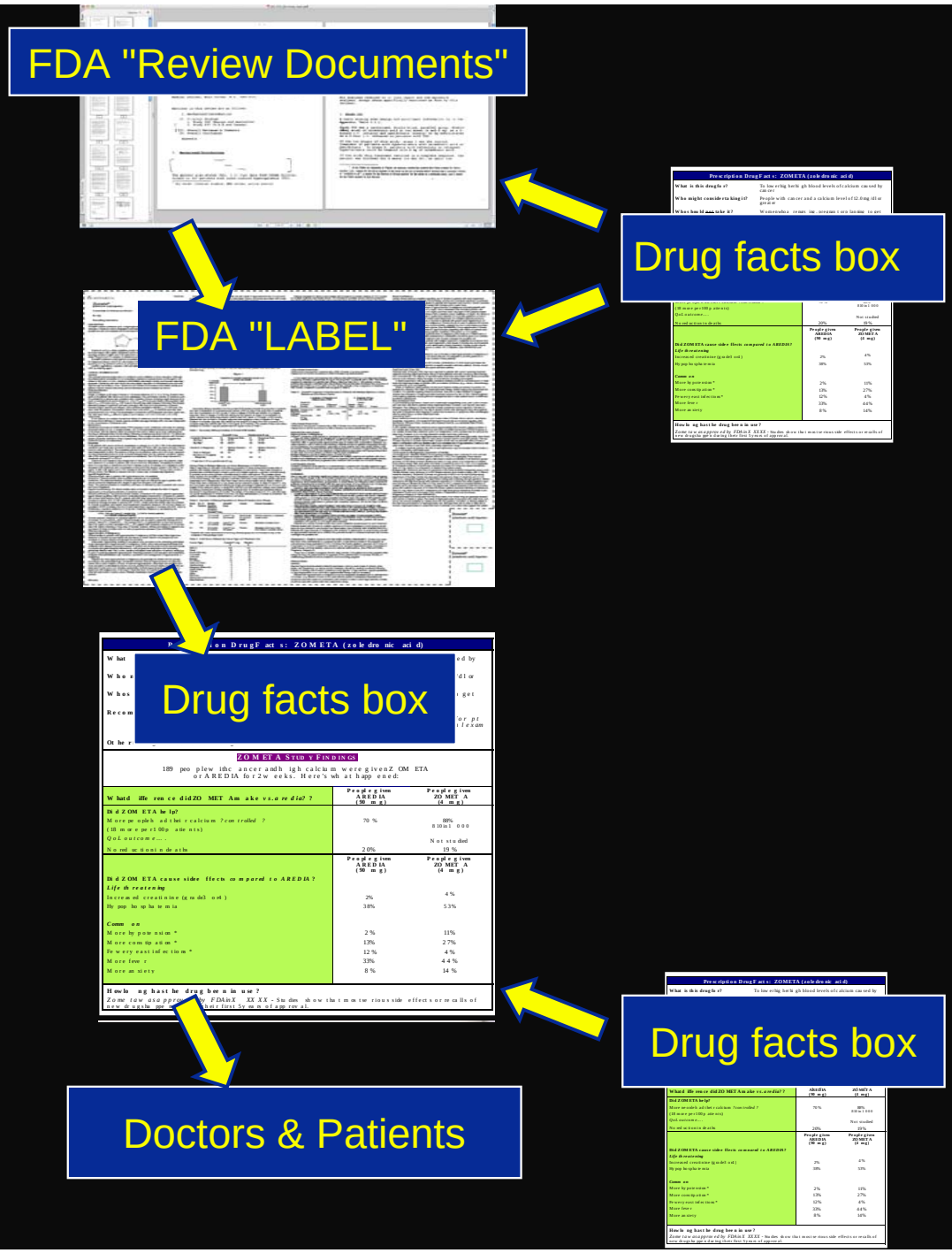
Implementing the box in the FDA



FDA official suggested an earlier role for the box.

- Reviewers are independent clinician experts who know the drugs better than anyone else.

- They have access to totality of published and unpublished data.



The drug facts box could promote structure in both the review documents and the label.

* Highlights what is missing

* Highlights what is known

* Creates a hierarchy for dealing with multiple side effects

P A

For 2 year eligman and D Safety, Policy cal review

- produce

- develop r making presc duct.

Drug Box Handbook for Reviewers

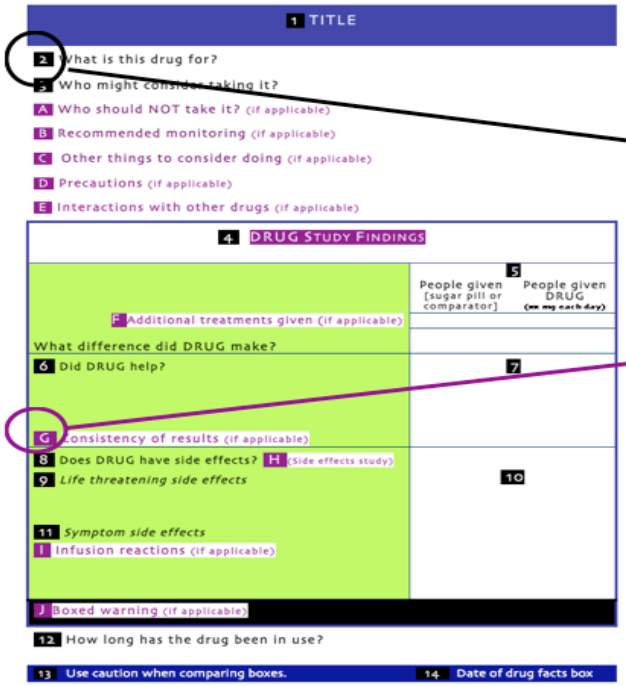
Overview

The goal of the drug box is provide an efficient summary of drug benefit and side effects. This synthesis will convey efficacy and safety data in a single table ideally on a single page. The box will allow reviewers to represent their synthesis of drug information **to a consumer with no special technical background**.

Because of space constraints, reviewers cannot include every aspect of drug performance; a big challenge for reviewers will be in selecting the most important information to convey.

Disclaimer: This handbook is a draft -- it is not meant to address every drug box issue, it does not solve every drug box challenge, and it will evolve based on feedback from reviewers as they gain experience building boxes.

The rest of this document is organized around the schematic drug box found on the next page. Here is how to use the schematic:



Small black squares are used to number **required** elements.

Small violet squares are used to indicate elements to include **only if applicable** (these elements are labeled with letters).

Our recommendations

FDA should start producing drug facts boxes as part of the review process for new drugs now - either in a stand-alone form or as part of other CMI efforts.

Consumers want and understand data on drug efficacy and side-effects as presented in drug facts boxes.

No one is better positioned than FDA reviewers to write boxes.

Drug facts boxes are an effective way for FDA to ensure that it communicates what it knows about drugs to the public.