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Randomized Study of Placebo and Framing Information in Direct-to-Consumer Print Advertisements for Prescription Drugs

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Abstract

Background—Research suggests that quantitative information in direct-to-consumer (DTC) prescription drug ads may be helpful for consumers.

Purpose—The objective was to examine the effect of adding placebo rates and framing to DTC ads.

Methods—In Study 1, 2,000 Internet panel members with chronic pain participated in a randomized controlled experiment of DTC ads varying in placebo rate and framing. In Study 2, 596 physicians ranked DTC ads varying in placebo rate and framing by how well they conveyed scientific information and their usefulness for patients.

Results—In Study 1, participants who viewed placebo rates were able to recall them and use them to form certain perceptions. A mixed frame led to lower placebo rate recall and perceived efficacy. In Study 2, overall, physicians preferred a placebo/single frame ad.

Conclusions—Adding placebo rates to DTC ads may be useful for consumers. The evidence does not support using a mixed frame.

Keywords

DTC advertising; placebo; mixed frame; quantitative

Direct-to-consumer (DTC) prescription drug advertisements (ads) are required by law to contain a fair balance of benefit and risk information (1). A content analysis of DTC ads showed that vague and qualitative benefit terminology was used in 87% of the ads whereas only 13% of the ads contained quantitative benefit information (2). Despite a current lack of quantitative benefit information in DTC ads, there is evidence that this information may be useful for consumers. In general, the risk communication literature suggests that certain statistical formats and visuals can help people understand quantitative information (3, 4). Recent studies demonstrated that participants can accurately recall quantitative benefit information from DTC prescription drug print and television ads for a fictitious prescription drug (5, 6). The present research extends these findings by investigating the inclusion of placebo information and the role of single or mixed frames in DTC print ads.

Authors' Statement of Conflict of Interest and Adherence to Ethical Standards: Authors O'Donoghue, Sullivan, and Aikin declare that they have no conflict of interest. All procedures, including the informed consent process, were conducted in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2000.

Placebo Rates

The ability to understand the placebo rate is critical to make an informed decision about the effectiveness of a drug. Research suggests that people do not adequately understand the concept of placebo for the purposes of clinical trial informed consent (7, 8) or scientific literacy (9). Thus it is possible that people will not understand this information in DTC ads. It is also possible that people use placebo rates as a peripheral cue (10) to mean “scientific information” and thus will not process the content of the information. However, Schwartz and colleagues found that most people presented with a placebo rate in a DTC drug ad were able to accurately report it (11). The authors speculate that this led to a better understanding of how well the drug worked, although they did not vary the presence of the placebo rate. In the current studies, we examined the usefulness of placebo rates in DTC ads.

Framing

Framing information in terms of a loss or a gain has been found to influence the choices individuals make (12). There are several ways to frame information about the benefits of a drug. One could provide only the number of people who benefited from a drug (a single, positive frame) or only the number of people who did not benefit (a single, negative frame). Alternatively, one could provide both the number of people who benefited and the number of people who did not benefit (a mixed frame). Although risk communication guides recommend the use of mixed framing to create more accurate perceptions (3, 13), few studies have actually measured this mixed approach (14).

The studies that have examined mixed frames do not present a clear picture. O'Connor asked participants to choose between two treatments after presenting the survival rate (positive frame), the death rate (negative frame), or both (mixed frame) (15). Participants who saw the mixed frame had similar preferences as those who saw the positive frame. But when Bernstein and colleagues compared single frames with mixed frames they did not find a consistent pattern (16). Peters and colleagues asked participants to rate how risky a drug was after reading about how many people experienced a side effect (negative frame), how many people did not experience a side effect (positive frame), or both (mixed frame) (17). Participants in the mixed frame condition reported risk perceptions that were higher than those in the positive frame condition and lower than those in the negative frame condition, suggesting that providing both negative and positive frames may indeed provide a balance of information. Similarly, another study found that participants choosing between lung cancer treatments who saw a mixed frame reported preferences somewhere in between the preferences of those who saw the survival (positive) and mortality (negative) frames (18). However, the same authors found that, when considering the termination of pregnancy for an abnormal genetic test, women responded to the mixed frame as they did to the normal (positive) frame whereas men responded to the mixed frame as they did to the abnormal (negative) frame. Clearly more research is needed to determine whether there are any consistent trends in responding to mixed frame information.

Some past and current DTC ads have included quantitative benefit information and in these cases, they have historically contained only a single positive frame (e.g., “...lower bad

cholesterol 39-60%”). The current research examines the use of single and mixed frames to address the inconclusive literature on mixed frames and the lack of data on mixed frames in DTC ads.

Numeracy

Numeracy is the ability to work with numbers, including basic probability and mathematical concepts (19). This individual difference variable may moderate the effects of placebo rates and framing, with individuals higher in numeracy more likely to process drug rate and placebo rate information. A previous study did not find an interaction between numeracy and framing (17). However, it is possible that the mixed frame may help low-numeracy individuals understand the numerical information better; or that the mixed frame may be difficult for low-numeracy individuals to understand due to the additional numbers. In Study 1, we examined whether numeracy moderated the effects of placebo rate and framing information.

Treatment Versus Prevention Claims

Typically, prescription drug ad claims fall into two categories: treatment or prevention. Treatment claims usually involve symptoms that may be alleviated by taking a given prescription drug.

Prevention claims are important but potentially harder to understand due to their long-term nature. A drug that prevents a negative future event may not alleviate any symptoms at all. For many medical conditions, the events being prevented are relatively rare, and thus the numbers used to describe them are very small. For example, a cholesterol drug that reduces the risk of heart attack from 3 out of 100 to 2 out of 100 may not seem large for an individual, but from a public health perspective it has enormous consequences for millions of people and the healthcare system in general (20). Similar to related research (6), we chose to test this type of claim to determine whether people are sensitive to the magnitude of the benefit in these clinically meaningful but objectively small outcomes.

We conducted two studies to examine the role of placebo rates and framing in prevention and treatment claims in DTC ads. The first study examined how laypeople process this information in DTC ads. The second study examined physicians' perceptions of this information in DTC ads.

Study 1

Method

Design—We designed and implemented a randomized, controlled study exposing participants to fourteen different versions of a DTC print ad for a fictitious prescription drug, Gilarix, indicated to reduce chronic pain and swelling and to reduce the risk of heart attack or stroke (for an example of one ad, see Figure 1). We examined treatment claims and prevention claims in two concurrent parts of the study. In the treatment design, the ad claims focused on the chronic pain indication (i.e., “50 out of 100 on Gilarix reported less pain”). In

the prevention design, the ad claims focused on the heart attack prevention indication (i.e., “96 out of 100 people avoided a heart attack while on Gilarix”). The independent variables were placebo rate and framing.

We conducted a pretest with 100 participants with chronic pain to determine the numbers and wording used to create the levels of placebo rate (data not shown). For placebo rate, three levels were examined for both treatment and prevention designs. In all cases, the efficacy rate of Gilarix remained the same (i.e., 50 out of 100 people on Gilarix reported less pain; 96 out of 100 people on Gilarix avoided a heart attack). The three levels included a control condition with no placebo information, a small difference between drug and placebo rate (i.e., “45 out of 100 on placebo reported less pain” or “95 out of 100 people on placebo avoided a heart attack”), and a large difference between drug and placebo rate (i.e., “5 out of 100 people on placebo reported less pain” or “91 out of 100 people on placebo avoided a heart attack”). In an attempt to make our claims as realistic as possible in the prevention design, we maintained fairly low placebo rates in the large difference and small difference placebo conditions. However, in the prevention design we also included conditions in which the placebo rate was very large—higher than could reasonably be expected but large enough to be objectively noticeable (i.e., “75 out of 100 people on placebo avoided a heart attack”).

For framing, we examined the addition of mixed framing to the traditional use of a single positive frame in a DTC ad. In the mixed frame conditions, we added how many people taking the drug did not have better health outcomes (e.g., “50 out of 100 people saw no improvement on Gilarix”). In conditions with a placebo rate and a mixed frame, participants also saw how many people did not have better health outcomes on placebo (e.g., “95 out of 100 people on placebo saw no improvement”).

Procedure—In May and June of 2012, a research firm recruited participants from an opt-in online panel of approximately 1.2 million individuals. Invitations were sent to a random sample of 40,000 panel members. Participants were asked a series of questions at the beginning of the survey to assess whether they were eligible to participate: i.e., if they had reported experiencing chronic pain in the last six months and were at least 18 years of age. Questions were included to ensure a reasonable representation of gender, race, and ethnicity, and that at least 20% of the sample had achieved a high school education or less.

Panelists who agreed to participate gave their informed consent and were randomly assigned via computer program to view one of fourteen versions of the fictitious DTC prescription drug print ad, consisting of a display page and the accompanying brief summary page. The two pages of the ad (the display page and the brief summary page) appeared on the screen together. Participants could click on each section of the ad to enlarge the section (e.g., the risk information on the display page). Participants were told that they would be asked questions about the ad after they had explored it, but were not given any particular instruction on what to look for in the ad. After first viewing the ad, participants answered a series of questions. After answering these questions, participants were shown the ad again and told to look at the ad again, this time focusing specifically on how effective the drug is. Participants again answered a series of questions. The questionnaires for the treatment and prevention designs were identical except that some questions in the treatment design referred

to reducing chronic pain and some in the prevention design referred to preventing a heart attack.

The study protocol can be obtained from the corresponding author. This study was granted an exemption from review by the US Food and Drug Administration's (FDA) Research Involving Human Subjects Committee.

Measures

Accuracy.: After participants viewed the ad for the second time, we measured whether participants could accurately report how well the drug worked (drug rate accuracy). To do so, we asked "If 100 people take Gilarix, how many will (report less pain/ avoid a heart attack)?" The correct answer was "50" in the treatment design and "96" in the prevention design.

We also measured whether participants could accurately report the placebo rate (placebo rate accuracy), with the question, "If 100 people take a placebo, how many will (report less pain/ avoid a heart attack)?" In the treatment design, the correct answer was "45" for the small difference placebo conditions and "5" for the large difference placebo conditions. In the prevention design, the correct answer was "95" for the small difference placebo conditions, "91" for the large difference placebo conditions, and "75" for the very large difference placebo conditions.

For both questions we scored responses as correct or incorrect. If participants cannot process and recall placebo rates, we would expect participants who view placebo rates to be no more accurate than participants who have to guess the placebo rates because they did not view them. Thus, we considered the responses of participants in the no placebo condition (who did not see a placebo rate), as correct if they were able to correctly guess the placebo rates viewed by other participants. This allowed us to test whether participants who viewed placebo rates were more accurate than guessing.

Perceived benefit.: After the first ad viewing, we asked participants three questions to measure perceived benefit: how effective they thought the drug would be for them, how well it would work for them, and how effective the drug is compared with other drugs for the condition. The reliability among these items was high in the treatment and prevention designs (Cronbach's alphas = 0.90) and therefore they were averaged to create one measure of perceived benefit (1 = *low perceived benefit*, 7 = *high perceived benefit*). After the second ad viewing, we asked participants how much the drug would reduce either symptoms of pain or heart attack risk (1 = *not much at all*, 7 = *a great deal*).

Perceived risk.: After the first ad viewing, we asked participants three questions to measure perceived risk: how risky they thought the drug would be for them, how safe they thought the drug would be for them, and how safe the drug is compared with other drugs for the condition. The reliability among these items was high in the treatment and prevention designs (Cronbach's alphas = 0.82) and therefore they were averaged to create one measure of perceived risk (1 = *low perceived risk*, 7 = *high perceived risk*).

Behavioral intention.: After the first ad viewing, we asked participants how likely they were to take the drug if their doctor prescribed it (1 = *very unlikely*, 4 = *very likely*).

Numeracy.: The numeracy measure consisted of the sum of correct responses to three fill-in-the-blank items, as used in previous research (21).

Demographic and health characteristics.: The demographic variables used in this study were age, gender, race, ethnicity, and educational level. We also asked participants to report the severity of their chronic pain and whether they were currently taking prescription medication for chronic pain.

Analyses—We conducted analyses for the main study separately for the treatment and prevention designs. For the continuous dependent variables, we conducted 2 (frame: single, mixed) by 3 (placebo: none, small difference, large difference) ANOVAs in the treatment design and 2 (frame: single, mixed) by 4 (placebo: none, small difference, large difference, very large difference) ANOVAs in the prevention design. For the categorical dependent variables, we conducted logistic regressions with forward selection. The predictor variables were frame, placebo, and the interaction between frame and placebo. We conducted these analyses both with and without covariates (i.e., demographic and health characteristics) included in the model. The results did not change when covariates were included; therefore, we present the results from analyses without covariates only. In addition, we tested whether effects were moderated by numeracy. If a main effect or interaction was significant, we conducted pairwise comparisons to determine which conditions were significantly different from one another. For pairwise comparisons, we used Bonferroni-adjusted p values, defining significance as $p < 0.017$ for comparisons among placebo rates in the treatment design and $p < 0.008$ for comparisons among placebo rates in the prevention design. For all other tests we defined significance as $p < 0.05$.

Results

Participants—A total of 40,000 panelists were invited to participate in the study. Of those panelists, 2,000 ultimately consented to and completed the study (with 840 in the treatment design and 1,160 in the prevention design based on a priori power analyses; see Figure 2). All participants reported having experienced chronic pain in the last six months. See Table 1 for participant characteristics.

Results from Study 1 are summarized in five sub-sections according to dependent variable: placebo rate and drug rate accuracy, benefit and risk perceptions, and behavioral intentions.

Placebo Rate Accuracy

Treatment.: Participants in the single frame conditions (31.3%) were significantly more likely to report the correct placebo rate than were participants in the mixed frame conditions (25.2%; $p = 0.03$; Figure 4). Participants in the small (40.2%) and large (43.0%) difference placebo conditions were significantly more likely to report the correct placebo rate than were participants in the no placebo condition (1.4%; $ps < 0.001$). The interaction between frame and placebo was not significant.

Numeracy moderated the effect of frame ($p = 0.03$). An examination of the means suggests that the single frame led to better placebo rate accuracy than the mixed frame for lower numeracy participants but this was reversed for the highest numeracy participants. Numeracy also moderated the effect of placebo ($p < 0.001$). An examination of the means suggests that the difference between the no placebo conditions and all other placebo conditions was smallest for participants with the lowest numeracy.

Prevention.: Participants in the single frame conditions (32.8%) were significantly more likely to report the correct placebo rate than were participants in the mixed frame conditions (24.3%; $p = 0.001$; Figure 4). Participants in the small (40.7%), large (34.1%), and very large (37.6%) difference placebo conditions were significantly more likely to report the correct placebo rate than were participants in the no placebo condition (1.7%; $p < 0.001$; Figure 4). The interaction between frame and placebo was not significant.

Numeracy moderated the effects of placebo ($p = 0.001$). An examination of the means suggests that the difference between the no placebo conditions and all other placebo conditions was smallest for participants with the lowest numeracy.

Drug Rate Accuracy

Treatment and prevention.: For drug rate accuracy, the main effects of frame and placebo and the interaction between frame and placebo were not significant in the treatment or prevention designs. Numeracy did not moderate the effects of frame or placebo. Overall, 56.7% of participants in the treatment design and 39.2% of participants in the prevention design reported the correct drug rate.

Perceived Benefit

Treatment.: After the first ad viewing, participants in the single frame conditions had significantly higher perceived benefit than did participants in the mixed frame conditions ($p = 0.01$; Figure 5). The main effect of placebo and the interaction between frame and placebo were not significant. Numeracy did not moderate the effects of frame or placebo.

After the second ad viewing, participants in the single frame conditions thought the drug would lead to a greater reduction in pain than did participants in the mixed frame conditions ($p = 0.01$; Figure 5). There was also a main effect of placebo ($p = 0.001$). Participants in the no placebo conditions and large placebo conditions thought the drug would lead to a greater reduction in pain than did participants in the small difference placebo conditions ($p = 0.001$). The interaction between frame and placebo was not significant. Numeracy moderated the effect of frame ($p = 0.02$). An examination of the means suggests that frame did not affect low-numeracy participants; however, high numeracy participants in the single frame conditions thought the drug would lead to a greater reduction in pain than did high numeracy participants in the mixed frame conditions.

Prevention.: The main effects of frame and placebo and the interaction between frame and placebo were not significant for perceived benefit measured after the first ad viewing ($p > 0.05$; Figure 5). Numeracy did not moderate the effects of frame or placebo ($p > 0.05$).

After the second ad viewing, there was a main effect of placebo ($p < 0.001$). Participants in the no placebo, large placebo, and very large placebo conditions thought the drug would lead to a greater reduction in heart attacks than did participants in the small difference placebo conditions ($p = 0.001$). In addition, participants in the no placebo and very large placebo conditions thought the drug would lead to a greater reduction in heart attacks than did participants in the large placebo conditions ($p = 0.001$). This main effect of placebo was qualified by an interaction with frame ($p = 0.01$; Figure 5), such that the differences among placebo conditions were not as great in the mixed frame, compared with the single frame conditions. Specifically, in both the single and mixed frame conditions, participants in the no placebo and very large placebo conditions thought the drug would lead to a greater reduction in heart attacks than did participants in the small difference placebo conditions ($ps < .008$). Only in the single frame conditions, participants in the no placebo and very large placebo conditions thought the drug would lead to a greater reduction in heart attacks than did participants in the large placebo conditions ($ps < .001$). The main effect of frame was not significant. Numeracy moderated the effect of placebo ($p = 0.02$). An examination of the means suggests that the differences between placebo conditions increased as numeracy increased.

Perceived Risk

Treatment.: There was a significant main effect of placebo ($p = 0.03$). Participants in the small difference placebo conditions had higher perceived risk ($M = 4.34$, $SD = 1.47$) than did participants in the large difference placebo conditions ($M = 4.01$, $SD = 1.53$; $p = 0.01$). The main effect of frame and the interaction between frame and placebo were not significant. Numeracy did not moderate the effects of frame or placebo.

Prevention.: The main effects of frame and placebo and the interaction between frame and placebo were not significant. Numeracy did not moderate the effects of frame or placebo.

Behavioral Intention

Treatment and prevention.: The main effects of frame and placebo and the interaction between frame and placebo were not significant. Numeracy did not moderate the effects of frame or placebo.

Study 2

Method

Study 2 examined physicians' perceptions of placebo and framing in DTC ads. A research firm invited a total of 3,000 physicians from an opt-in Internet panel of over 100,000 physician members of the American Medical Association to participate in the study in May and June of 2012 (see Figure 3). To be included in the study, they had to report their primary area of specialization as "family practice," "general practice," or "internal medicine." They also had to report spending 50% or more of their time in an average week on direct patient care. Five hundred and ninety-six physicians ultimately consented to, and completed, this task. The sample size was based on a priori power analyses. See Table 2 for participant characteristics.

Participants first completed an unrelated task that involved reviewing the Prescribing Information label for a prescription drug (described in a separate paper). For this study, participants then saw four versions of a print DTC ad for a fictitious prescription drug. To respect participants' time, they were randomly assigned via computer program to see either four ad versions with treatment claims (lowering bad cholesterol) or four ad versions with prevention claims (preventing heart attacks). The versions varied in terms of the presence or absence of placebo information and a single or mixed frame. Participants then ranked the ads in order of how well the ads represented scientific information (Task 1) and how easy the ads would be for patients to understand (Task 2).

To determine whether rankings differed, we examined non-parametric Friedman tests for Tasks 1 and 2 in the treatment conditions and in the prevention conditions. Significant Friedman tests were followed by post-hoc analyses to determine which rankings differed. We used Wilcoxon signed rank tests with Bonferroni-adjusted p -values (< 0.008).

This study was granted an exemption from review by FDA's Research Involving Human Subjects Committee.

Results

All four Friedman ranking tests were significant ($ps < 0.001$; Table 3).

Task 1—For both treatment and prevention claims, physicians ranked the placebo/single frame ad higher than all others when asked how well the ads represented scientific information ($ps = 0.001$). For prevention claims, physicians also ranked the placebo/mixed frame ad higher than the no placebo/single frame ad ($p = 0.006$).

Task 2—For both treatment and prevention claims, physicians ranked the placebo/single frame and the no placebo/single frame ads as equally good when asked how easy the ads would be for patients to understand; moreover, both were ranked higher than the no placebo/mixed frame and placebo/mixed frame ads ($ps < 0.001$). For treatment claims, physicians also ranked the no placebo/mixed frame ad higher than the placebo/mixed frame ad ($p < 0.001$).

Discussion

Our designs manipulated both placebo information and framing, providing novel quantitative information on the understanding of placebo and contributing to the question of whether mixed frames help or hinder the understanding of drug efficacy. We examined these questions within the context of treatment and prevention claims and with the issue of numeracy in mind as a potential moderating factor.

In Study 1, we varied whether the difference between the drug effect and the placebo effect was large or small, in addition to using a no placebo control group. We did this without changing the drug effect, thus ensuring that any differences we saw were a result of the placebo information. If participants did not pay attention to the placebo rates or used them as peripheral cues, we would not expect to see differences between the placebo conditions and

the no placebo conditions. Instead, approximately 40% of participants were able to accurately report the placebo rate seen in the DTC ad. When asked specifically about placebo rate information, participants in the small and large placebo difference groups were significantly more accurate than those in the no placebo control group, consistent with prior research showing that people can accurately report quantitative information in DTC ads (11). Further, the presence of placebo rates did not decrease participants' ability to recall the drug rate.

Participants' perceived benefit differed depending on placebo rates. When they were asked to look at the ad for information about effectiveness, a consistent pattern emerged across treatment and prevention conditions whereby participants in the large placebo difference conditions and the no placebo conditions thought the drug would work better than participants in the small placebo difference. These results, seen even with clinically meaningful but objectively small outcomes, suggest that participants used placebo rates to arrive at their perceptions.

Noteworthy is the finding that participants who did not receive placebo information responded similarly to those who saw large differences between the drug and the placebo. This suggests that, in the absence of placebo context, people assume prescription drugs work well. This finding is consistent with previous research (11) and supports the addition of placebo rates in DTC ads to encourage accurate perceptions of benefit and risk. Future research should evaluate whether this finding stands when the placebo rates are consistently low and the drug rates vary.

The other major contextual information we examined was the use of a single versus mixed frame. Past research has been inconclusive regarding the benefits of the additional context. We found that participants who viewed the single positive frame were more accurate in recalling quantitative information than those who saw the mixed frame. At the same time, those who saw the single frame perceived the drug as more beneficial than those who saw the mixed frame. Although adding a mixed frame may help participants consider the number of people who do not receive the benefit of a prescription drug, it is important to note that studies show negative information is often given disproportionate precedence over positive information in a range of situations (22, 23). Therefore, instead of helping consumers interpret the risks and benefits of a drug in a balanced manner, mixed-frame quantitative information may lead consumers to overvalue the negative.

An interesting finding arose in the treatment condition: as effectiveness increased, perceived risk decreased. Participants in the large difference placebo condition reported lower perceived risk than those in the small difference placebo condition. This finding is consistent with previous research showing that drug efficacy level changes perceptions of identical risk profiles (5) and consistent with the affect heuristic hypothesis (24, 25). According to this hypothesis, affect is unavoidable when making decisions, resulting in perceptions that as benefits increase, risks decrease. Our findings provide additional support that this hypothesis applies to the processing of prescription drug advertising as well.

As expected, numeracy played a role in understanding the information in the ad. In two instances, numeracy muted the differences between placebo rate groups, such that lower numerate individuals showed smaller differences than those with higher levels of numeracy. It appears that participants with lower numeracy were less able to recall placebo rate information. This is consistent with past research which has shown that higher numeracy levels are associated with easier processing of different types of medical and numerical information (26). In the treatment condition, participants were generally more accurate with single frame information than with mixed frame information. Numeracy moderated this relationship, such that this finding was reversed for high numerate individuals. Those who were facile with numbers found the addition of the extra frame more useful although overall, the mixed frame was not helpful.

The findings of Study 2 support those of Study 1. When physicians viewed DTC ads that varied in placebo rate and framing information, they reported that the placebo/single frame condition was both a more accurate way to communicate scientific information and one of the most easily understandable presentations for their patients.

Limitations and Future Directions

As with all research studies, ours had some limitations. First, our samples originated from an opt-in Internet panel, making the sample non-representative of the U.S. population. Moreover, we did not record from which groups quits and quality concerns stemmed (see Figures 2 and 3), so we do not have that specific information. Instead, the strength of our studies lies within the internal validity of the experimental conditions. By controlling extraneous factors, we were able to draw conclusions about the cause of differences between conditions. Second, our studies examined reactions to one prescription drug product. For each study, we created a fictitious drug that allowed us to look at both treatment of symptoms and prevention of negative events, but we do not know how participants would react to a drug for a more or less serious medical condition, one with more or less serious risks, or one with a different benefit profile. The effects of placebo rate and framing should be examined with other populations to determine how generalizable the results are.

Although we contributed to the discussion of single versus mixed frame, note that we did not include a negative frame. Previous research included conditions with positive, mixed, and negative frames (15, 17, 18). Although a completely balanced design would also include a negative framing condition (which would provide only the number of people who did not benefit), we felt it was unrealistic to create a DTC ad that would claim only, for example, that “Gilarix did not work for 50% of people in clinical trials,” so we chose not to include negative framing in this study. Studies of how people react to medical information outside of DTC advertising could include a negative frame as well to extend our research.

Placebo rate information affected some participants' accuracy and benefit perceptions, but we did not find that it influenced participants' intentions to take the drug if their doctor prescribed it. This is consistent with previous research (5). This is likely because many factors outside the scope of this research (such as the relationship between the participant and his or her healthcare professional, cost, and other personal characteristics) contribute to

those behaviors. More research on what drives these intentions would expand our understanding of what factors in DTC ads may influence intentions.

Conclusion

Previous research examined placebo information in other contexts (7, 8) and touched upon the use of placebo information in the context of prescription drug advertising (6), but the current studies are the first to thoroughly explore the use of placebo rate information in DTC ads. By manipulating not only the presence of placebo information but the size of the difference in efficacy between the placebo and the drug, we were able to determine that participants were able to process placebo information in their assessment of a prescription drug. Physician measures from Study 2 supported the inclusion of placebo rate information.

We also examined the use of a single or a mixed frame of information in prescription drug advertising, expanding upon the inconclusive literature on framing in other areas (14). Our findings demonstrated that participants were more likely to recall the placebo rate information in the single frame condition, consistent with physicians' assessments. Given these findings, it appears that a mixed frame does not add value to the communication of prescription drug information in this context. The presence of placebo rates, however, may be an important piece of information for the understanding of a prescription drug's benefit/risk profile.

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If chronic pain is a part of your life, talk to your doctor about Gilarix. Gilarix is a prescription medicine used to help relieve chronic pain by reducing inflammation and swelling associated with injury, surgery, or arthritis.

New Help for Chronic Pain

In a clinical study, Gilarix reduced the amount of pain people reported.

- 50 out of 100 people on Gilarix reported less pain
- 50 out of 100 people saw no improvement on Gilarix
- 5 out of 100 people on placebo reported less pain
- 95 out of 100 people on placebo saw no improvement

To learn how Gilarix can help you manage your chronic pain visit www.gilarix.com.

Important risk information
Gilarix is not for everyone, including people with liver problems and women who are nursing, pregnant, or may become pregnant. You need simple blood tests to check for liver problems. Skin reactions, or stomach and intestine problems such as bleeding and ulcers, can occur without warning and may be life threatening. If you develop fever, unexplained weakness, or confusion, tell your doctor right away as these may be signs of a rare but potentially life threatening condition called TTP, which has been reported sometimes in less than 2 weeks after starting therapy. Also tell your doctor if you are taking other medications, or if you have any muscle pain or weakness, as this may be a sign of another rare but serious side effect. Common side effects include diarrhea, joint pain, and tiredness.

Please see next page for additional risk information.

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You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch or call 1-800-FDA-1088.

Figure 1.

Example Study 1 ad for a fictitious chronic pain prescription drug, with a mixed frame and a large difference between placebo and drug rates.

Figure 2.
CONSORT diagram for Study 1.

Figure 3.
CONSORT diagram for Study 2.

Figure 4.

Placebo rate accuracy in the Study 1 treatment and prevention designs by frame and placebo.

Figure 5.

Perceived benefit in the Study 1 treatment and prevention designs by frame and placebo.

Note. Perceived benefit was measured on a 7-point scale (*1 = low perceived benefit, 7 = high perceived benefit*). Perceived reduction in pain/heart attacks was measured on a 7-point scale (*1 = not much at all, 7 = a great deal*).

Table 1.

Study 1 Participant Characteristics

		2,000 (100%)	
Characteristics		Treatment Design	Prevention Design
Chronic Pain Sufferers		840 (100%)	1160 (100%)
Gender			
	Male	420 (50%)	576 (49.7%)
	Female	420 (50%)	584 (50.3%)
Ethnicity			
	Hispanic or Latino	43 (5.1%)	64 (5.5%)
	Not Hispanic or Latino	797 (94.9%)	1096 (94.5%)
Race			
	American Indian or Alaska Native	16 (1.9%)	13 (1.1%)
	Asian	27 (3.2%)	36 (3.1%)
	Black or African American	65 (7.7%)	82 (7.1%)
	Native Hawaiian or Pacific Islander	2 (0.2%)	2 (0.2%)
	White	682 (81.2%)	977 (84.2%)
	Other	13 (1.5%)	23 (2.0%)
	Multi-racial	35 (4.2%)	27 (2.3%)
Education			
	Less than high school	11 (1.3%)	24 (2.0%)
	High school graduate	204 (24.3%)	361 (31.1%)
	Some college	285 (33.9%)	353 (30.4%)
	Bachelor's degree	225 (26.8%)	278 (24.0%)
	Some postgraduate work	36 (4.3%)	43 (3.7%)
	Postgraduate degree	79 (9.4%)	101 (8.7%)
Taking prescription medication for chronic pain		383 (45.6%)	475 (40.9%)
		Mean (SD)	
Age (Years)		49.5 (14.6)	48.1 (15.2)
Chronic pain severity		3.2 (0.9)	3.1 (0.9)
Numeracy (0-3)		1.7 (0.9)	1.6 (0.9)

Note. *SD* = standard deviation. Chronic pain severity was rated on a 5-point scale (1= *very mild*, 5 = *very serious*).

Table 2.Study 2 Participant Characteristics ($N = 596$)

Characteristics		Number	Percent
Gender			
	Male	450	75.5
	Female	146	24.5
Ethnicity			
	Hispanic or Latino	29	4.9
	Not Hispanic or Latino	567	95.1
Race			
	American Indian or Alaska Native	2	0.3
	Asian	124	24.8
	Black or African American	11	1.8
	Native Hawaiian or Pacific Islander	1	0.2
	White	407	68.3
	Other	19	3.2
	Multi-racial	10	1.7
	Prefer not to answer	22	3.7
Primary Area of Specialization			
	Family Practice	271	45.5
	General Practice	32	5.4
	Internal Medicine	293	49.2
		Mean (SD)	Range
Age (Years)		47.41 (10.5)	26-78
Years in Practice		16.5 (9.2)	1-48
Time per Week for Patient Care (%)		95.5 (8.1)	50-100

Note. SD = standard deviation.

Table 3.

Mean Physician Ranking of Prevention and Treatment Claims in Study 2, by Placebo and Frame

	Prevention (<i>n</i> = 300)				<i>p</i> -value	Treatment (<i>n</i> = 296)				<i>p</i> -value
	No Placebo		Placebo			No Placebo		Placebo		
	Single Frame	Mixed Frame	Single Frame	Mixed Frame		Single Frame	Mixed Frame	Single Frame	Mixed Frame	
Task 1	2.77	2.68	2.11	2.45	<0.001	2.50	2.75	2.19	2.56	<0.001
Task 2	2.27	2.69	2.12	2.92	<0.001	1.92	2.72	2.12	3.24	<0.001

Note. Participants in both the prevention and treatment conditions were asked to rank the four versions from best (1) to worst (4) in terms of how well the ads represented the scientific information (Task 1) and ease of understanding for the typical patient (Task 2).