Author's response to reviews

Title: A cross-sectional evidence-based review of pharmaceutical promotional marketing brochures and their underlying studies: Is what they tell us important and true?

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Author's response to reviews: see over
Dear Editor,

Below you’ll find our responses and appropriate revisions to each comment made by the reviewers.

**REVIEWER 1**

**Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)**

1. There does not appear to be any substantial review of existing literature pertinent to this topic, which would arguably include: (a) accuracy of print advertisements and (b) accuracy of verbal communications from pharmaceutical detail representatives as well as (c) accuracy of print promotional materials provided directly to physicians by “reps.” Some literature at least is available on (a) and (b). The website, http://www.drugpromo.info/ is an excellent source of material on these topics, at least if published before about 2003, with evidence-based assessments of quality. These authors need to place their findings within the context of this previous literature.

The reviewers’ comments and suggestions were extremely useful. The suggested resources were utilized and another literature review was conducted. The introduction and discussions sections were updated with more supporting evidence. One constraint was the very limited number of studies that assessed accuracy of promotional information. Actually, NO study was found that objectively assessed the accuracy of information provided on brochures.

2. The authors need to make more clear how and why they chose to focus on what they eventually did study, that is, printed promotional information/brochures handed to physicians by reps. Why, for instance, did they not study printed advertisements in medical journals or the actual verbal presentation given by reps that accompanied these printed materials? All, arguably, are forms of “DTP” marketing. The authors in some places imply that they have studied ALL DTP marketing when in fact they have looked only at this small slice of the total marketing operation. In particular, given that these printed materials are intended to be used as part of the rep's presentation, and not given to the physician independently, it is unclear what value an analysis of the materials has in the absence of the rep's oral presentation. What if, for example, only 25% of these PAs refer to non-valid studies; but the rep transmits misleading information to the physician on 75% of all encounters? In what way would the level of validity of these PAs indicate anything useful about the reliance physicians place on using the pharmaceutical rep as a source of information?

This was clarified in the introduction of the manuscript. This study assessed the accuracy and validity of information provided on brochures that accompany a pharmaceutical reps verbal presentation. We studied only the brochure because it provides a visual impact of the data presented and may be re-used by physicians as a resource about a new medication while seeing patients. Moreover, pharmaceutical reps were the most frequent source of information about new medication reported by physicians in previous studies. These brochures are left with physicians, just as pens, notepads, mugs, which function as a subliminal reminder mechanism. We found it extremely important to assess
the accuracy and validity of the data on these brochures. It was not the objective of this study to assess whether these brochures caused a behavioral change.

3. The authors need to explain how they decided that a sample of only 20 PAs was sufficiently powerful for their purposes. To the naive reader this study looks substantially underpowered, especially since many of the disease categories are represented only by a single PA.

The sample size of 20 was selected *a priori*. No studies are available that would enable the calculation of an adequate sample size. This was stated and mentioned in the manuscript. This study will allow researchers to calculate sample sizes in future studies.

4. Table 1 indicates an 8-item instrument to assess an article's validity. Somehow the score on this 8-item instrument was turned into the dichotomous variable, "valid"/"not valid." The authors never explain how this was done.

This was explained in detail in the Methods section. The table was also re-written and categorized by the Major and Minor criteria.

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Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

I was surprised to read the figure $6 billion for the total physician marketing effort by the pharmaceutical industry. More typical estimates are commonly given in the $20-25 billion range; and some estimates (e.g., Angell, The Truth About the Drug Companies) argue that the actual sum is closer to $40 billion.

We updated this figure based on data presented by the IMS Health, a world leader in pharmaceutical information.

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Discretionary Revisions (which the author can choose to ignore)

On p. 9, bottom, the editorial comments about the virtues of the drug industry seem to fly in from out of left field. It is not clear why the authors feel the need for this disclaimer. I would hope that one could agree that the drug industry serves an extremely important social function while still offering criticisms of specific pharmaceutical marketing practices.

We removed the sentences regarding the virtues of the pharmaceutical industry and focus on possible solutions.

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REVIEWER 2

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

There are three significant areas where this paper needs revisions:

1. The authors need to cite previous similar work and discuss their study in light of this previous material. Specifically they should look at Lexchin et al. CMAJ 1994151:47-54 and Cooper et al. CMAJ 2005;172:487-91.
We appreciate the reviewer’s suggestions and have incorporated updated evidence and references as suggested, including an updated literature review. There was a limited number of studies that assessed the accuracy and validity of studies.

2. There are a number of areas where things are unclear or where the authors have not adequately explained what they intend to do:

Page 6, first paragraph:
Although the authors give some examples of direct-to-physician marketing it is not clear what the full extent of DTP means, i.e., does it cover visits by sales reps, company sponsored CME?

**We have addressed this issue in the manuscript in the introduction and methods.**

Page 6, Methods:
In this section the authors do not define: how they determined if study funded by pharmaceutical industry; how patient-oriented versus disease-oriented was determined; how the PA was compared to the original study. The authors also need to add a statement about ethical approval.

**We addressed and explain how these things were done.**

Page 6, third paragraph:
Did the authors a priori decide to stop collecting PAs when they reached 20 or was 20 the entire number that the physicians received?

**We clarified this issue and added a section regarding this sample size. The goal was to collect 20 PA, and the time frame was provided as the time it took to collect these 20 PAs.**

3. There are problems with the organization of the material:

Page 8, first paragraph:
In the Methods section the authors do not mention that they intend to evaluate whether or not the underlying studies compare two active treatments but they are presenting results on this topic.

**We clarified that we wanted to assess whether the therapy (medication) was being compared to another therapy, placebo, or neither in the method section. We did not intend to assess the accuracy of the comparison mediation or treatment. This was also rectified in the Results and Discussion sections.**

Page 9, first paragraph:
The authors comment that the overwhelming majority of data from the underlying studies were based on a desired visual impact. This analysis was not mentioned in either the Methods or Results. Similarly, later in this paragraph they mention that companies selected the outcome with the greatest relative risk reduction. Once again, there was no mention of this in either the Methods or Results.

**We added these sections to the methods section and modified the table to reflect these results.**
Page 9, second paragraph:
The part of this paragraph starting "It should be noted, however, ..." is irrelevant to the purpose of this study. If the authors wish to include this material they need to do a better job of establishing how it is relevant.

This was removed and re-worded to emphasize potential solutions that the paragraph discussed.

Page 10, last paragraph:
There are additional limitations that need to be mentioned: there was a relatively small sample size; the analysis was limited to material that GPs receive, the material that specialists receive may be different; the results only apply to underlying studies that are used to support print material from the companies, studies used to support other types of DTP promotion may yield different results; the material was collected from a single institution and may not reflect material that is distributed in the community or in other geographic areas.

These were all addressed in the limitation section of the manuscript, in addition to other limitations that we felt needed to be mentioned.

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

Page 5, first paragraph:
The figures on the amount spent on promotion to doctors is old. More recent information can be found at [http://www.imshealth.com/ims/portal/front/indexC/0,2773,6599_49695965_0,00.html]

We appreciate the reviewer’s reference. The numbers were updated.

Page 5, second paragraph:
When the authors discuss changes in the promotion of antihypertensives it's unclear what the authors mean - do they mean % of total dollars spent promoting antihypertensives, % of number of advertisements, etc.?

We addressed the confusion by clarifying the number of prescriptions “written” and the number of advertisements of CCB.

Page 6, second paragraph:
The authors need to define what they mean by patient-oriented and disease-oriented.

This was done and added to the Method, Results, and Discussion sections.

Page 6, last paragraph:
The authors seem to be saying that there was only a single underlying study for each PA. If that is true then it should be explicitly stated.

We clarified this in the Method section. The one outcome emphasized on the brochure by the rep was marked by the physician and the one study that reported the data on the brochure was reviewed.

Page 10, last paragraph:
Do the authors mean "subjective" instead of "objective"?

Yes...this was corrected.