

PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Pharmaceutical Industry Funding of Events for Healthcare Professionals on Non-vitamin K Oral Anticoagulants in Australia: An Observational Study
AUTHORS	Behdarvand, Behrad; Karanges, Emily; Bero, Lisa

VERSION 1 - REVIEW

REVIEWER	David J. Rothman Columbia College of Physicians & Surgeons
REVIEW RETURNED	04-Apr-2019

GENERAL COMMENTS	<p>The major finding of this paper is that drug companies spend considerable money and effort to promote their products to physicians. The details are overwhelming and impressive; the research is thorough, including compilations of money spent and where they were spent. The authors "suggest" that the events "had a promotional purpose." (p.12) However, the analysis of only 2 sessions' content is disappointing. And so is the absence of information by name of speakers paid by the companies to deliver talks. The relationship of event to sales is also left open. The tables do inform the reader of content but there is very little analysis the information in the text . Nor is there much discussion of the two "complaints,"</p> <p>Questions for authors:</p> <ol style="list-style-type: none">1. What is new and important about your findings? What have you added to the extensive literature?2. Why did you bury the discussions of two sessions and the conflicts of interests to "boxes" rather than analyze them in the text?3. Why were you not more detailed and specific about presenters conflicts of interest?"
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REVIEWER	Stöllberger Claudia KA Rudolfstiftung, Wien, Austria
REVIEW RETURNED	14-Apr-2019

GENERAL COMMENTS	<p>The title is confusing and should be modified</p> <p>Abstract: The abbreviation "AUD" should be explained. The results regarding NAOC dispensing rates should be described in more detail.</p>
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	<p>The content analysis, reported in the results, is not indicated in the methods part.</p> <p>Methods: The methods section is quite long and shortening this part of the manuscript would be useful.</p> <p>Results: The data regarding events are very impressive and I recommend to omit the content analysis, since it does not add substantial information for the reader. Instead I recommend to mention the close ties between the manufacturer of the NOAC and the authors of the studies as a reference (Stöllberger C, Schneider B, Finsterer J. There is a need for independent studies about new oral anticoagulants in atrial fibrillation patients. <i>Int J Cardiol.</i> 2014;172(1):e119-20. doi: 10.1016/j.ijcard.2013.12.118).</p>
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REVIEWER	<p>Inmaculada Hernandez University of Pittsburgh USA I have received scientific advisory fees from Pfizer</p>
REVIEW RETURNED	14-May-2019

GENERAL COMMENTS	<p>My review is focused on the statistics and methods, since I was specifically asked to provide a statistical review.</p> <p>I have no major comments. The manuscript presents some descriptive statistics, and analyses are appropriate. I only have two minor suggestions</p> <ul style="list-style-type: none"> -Total cost of events seems to be defined over time instead of by year—I wonder whether costs are highest for Boehringer because dabigatran was approved earlier ? maybe the authors could add a variable defined as average annual costs of events, where the period differs for each industry, and equals the time after approval of each drug and until the end of the period of observation -I am just wondering whether there may be a better way to display the events in the figures—I wonder whether it may make more sense to show numbers of events by quarter? This is just a suggestion, I defer to the authors.
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VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

Reviewer Name: David J. Rothman

Institution and Country: Columbia College of Physicians & Surgeons

The major finding of this paper is that drug companies spend considerable money and effort to promote their products to physicians. The details are overwhelming and impressive; the research is thorough, including compilations of money spent and where they were spent. The authors "suggest" that the events "had a promotional purpose." (p.12) However, the analysis of only 2 sessions' content is disappointing.. And so is the absence of information by name of speakers paid by the companies to deliver talks.

Response: Our analysis was largely dictated by the content of the Educational Events database. The database contains information on payments and general information on events (example event

descriptions are provided in Fabbri et al, 2017. A cross-sectional analysis of pharmaceutical industry-funded events for health professionals in Australia, *BMJ Open* 7: e016701). It does not contain detailed information on the content of events. Therefore, we sought detailed information on specific events from a variety of sources (see p8 methods. Content of educational events: Illustrative case studies) and describe the 2 cases with the most information available. Unfortunately, there was sparse information available on additional events. We have clarified this in the limitations (page 15 – tracked version; page 13 – clean version).

The database also does not include the names of sponsored healthcare professionals. Companies only disclose the number of healthcare professionals sponsored to attend/speak and the amount of money paid. For the events we analysed, the company only mentioned sponsoring healthcare professionals to attend; there was no mention of any speaker fees, which suggests that the sponsored healthcare professionals may not have presented at the meeting. As the speakers themselves were often not from Australia, and our information on their pharmaceutical industry ties was drawn from their conflict of interest declarations within their presentations or other documents, we have not elaborated further on their profiles.

The relationship of event to sales is also left open.

Response: Our analysis of NOAC use was based on the only data available to us – publically-available, aggregated, national dispensing data. Therefore events could not be directly linked to NOAC prescribing, whether by individual prescriber or in an ecological analysis based on region. However, we have refined our section on NOAC dispensing in the results (page 12-13 – tracked version; page 10-11 – clean version) to more strongly convey the relationship between events and prescribing, to the extent that our data permits.

The tables do inform the reader of content but there is very little analysis the information in the text.

Response: We have expanded the description of the case studies in the results section (p13).

Nor is there much discussion of the two "complaints,"

Response: We have provided most of the information on the complaints that was available. We have not elaborated further due to space limitations and the fact that the complaints were dismissed by the regulatory agency.

Questions for authors:

1. What is new and important about your findings? What have you added to the extensive literature?

Response: We have now elaborated on this point in the introduction (page 5 – tracked version):

In the United States, pharmaceutical industry payments directly to physicians have previously been associated with higher NOAC prescribing within hospital referral regions,²⁵ but direct payments to physicians are just one way that the pharmaceutical industry interacts with prescribers. Industry-sponsored events as a source of promotion have not been examined. Australian transparency databases provide a unique opportunity to examine the potential role of pharmaceutical industry sponsorship of educational events for healthcare professionals in NOAC promotion.²⁶ Medicines Australia, the pharmaceutical industry trade organisation, requires member companies to submit reports on sponsorship of events for physicians and other healthcare professionals, including spending on food and beverages, trade displays, sponsorship of healthcare professional attendance, speaker fees and other associated costs. Here, we use these reports to...

2. Why did you bury the discussions of two sessions and the conflicts of interests to "boxes" rather than analyze them in the text?

Response: We used the boxes to draw attention to our cases studies rather than bury them. We believe the use of boxes achieves this but have included some additional text in the results to summarise our key findings and help draw the attention of the reader to the boxes (page 13-14 – tracked version).

3. Why were you not more detailed and specific about presenters conflicts of interest?"

Response: As mentioned above, our information on the speaker's conflicts of interest was drawn from the conflict of interest declarations within their presentations or other documents. We do not have any information on the speakers or their conflicts within our database.

Reviewer: 2

Reviewer Name: Stöllberger Claudia

Institution and Country: KA Rudolfstiftung, Wien, Austria

Please state any competing interests or state 'None declared': None declared

The title is confusing and should be modified

Response: We have modified the title to: Pharmaceutical Industry Funded Funding of Events for Healthcare Professionals on Non-vitamin K Oral Anticoagulants in Australia: An Observational Study

The abbreviation "AUD" should be explained.

Response: We have removed all references to AUD and replaced it with the standard symbol for Australian dollar, \$A. We define the abbreviation the first time it appears in the abstract and text.

The results regarding NAOC dispensing rates should be described in more detail.

Response: We have expanded our discussion of the changes in NOAC dispensing in the results.

The content analysis, reported in the results, is not indicated in the methods part.

Response: We had included the content analysis in the methods, but have clarified this section by modifying the heading and refining the text. The content analysis methods were previously split over two sections (on data source and extraction) and we have now combined these two sections into one. This also shortens the methods in line with the reviewer's comment below.

Methods:

The methods section is quite long and shortening this part of the manuscript would be useful.

Response: We have shortened the methods in various places as indicated in the text.

Results:

The data regarding events are very impressive and I recommend to omit the content analysis, since it does not add substantial information for the reader. Instead I recommend to mention the close ties between the manufacturer of the NOAC and the authors of the studies as a reference (Stöllberger C, Schneider B, Finsterer J. There is a need for independent studies about new oral anticoagulants in atrial fibrillation patients. *Int J Cardiol.* 2014;172(1):e119-20. doi: 10.1016/j.ijcard.2013.12.118).

Response: We have decided to retain the content analysis as we believe it provides a useful example of the type of information presented at the events and its promotional content, and provides insights into the reasons the pharmaceutical industry sponsors healthcare professional education. We also received positive feedback on this section from the other reviewer.

Thank you for providing the valuable reference. We have now included it and some other related references in the introduction (page 4, paragraph 3 – tracked version).

Reviewer: 3

Reviewer Name: Inmaculada Hernandez

Institution and Country: University of Pittsburgh, USA

Please state any competing interests or state 'None declared': I have received scientific advisory fees from Pfizer

My review is focused on the statistics and methods, since I was specifically asked to provide a statistical review.

I have no major comments. The manuscript presents some descriptive statistics, and analyses are appropriate. I only have two minor suggestions

-Total cost of events seems to be defined over time instead of by year—I wonder whether costs are highest for Boehringer because dabigatran was approved earlier ? maybe the authors could add a variable defined as average annual costs of events, where the period differs for each industry, and equals the time after approval of each drug and until the end of the period of observation

Response: We have further looked into the changes in spending by each company over the study period and the potential impact of the timing of TGA approval and PBS listing on costs. For all companies, regardless of the time of initial PBS/TGA approval, there was a pronounced increase in spending in the months preceding the expansion of PBS subsidy in August/September 2013. This is reflected in our Figures (shown as number of events). Although we attempted to do the analysis suggested, we felt it was not informative due to this increase in spending in 2013, as well as the long period of time between the original approval of dabigatran and rivaroxaban (November 2008) and the start of the educational events data (October 2011).

-I am just wondering whether there may be a better way to display the events in the figures—I wonder whether it may make more sense to show numbers of events by quarter? This is just a suggestion, I defer to the authors.

Response: Thank you for this excellent suggestion. We have changed the graphs to show events and dispensing by quarter, as suggested. This makes the graphs, and the potential association between events and payments, much clearer.