

Subject: BMJ - Decision on Manuscript ID BMJ-2019-051174

Body: 28-Aug-2019

Dear Dr. Fabbri,

Manuscript ID BMJ-2019-051174 entitled "Industry funding of patient and health consumer organisations: Systematic review with meta-analysis" which you submitted to BMJ,

Thank you for sending us your paper, manuscript. I apologise sincerely for the delay in sending out this decision letter. Thank you for checking on the paper! Our statistician originally said that he wanted to write a separate note to guide the revision, and I was waiting for that. When I reminded him of this recently, he said that after reflection he thinks the reviews provided are plentiful and helpful and he would like to see the paper and appraise it once it is revised in response to those reviews.

When we discussed this paper at the manuscript meeting, people were interested in the topic and appreciative of the amount of work you put into the appeal. We still were not certain, however, that it will ultimately be right for The BMJ.

We hope therefore that you will be willing and able to revise your paper as explained below in the report from the manuscript meeting, so that we will be in a better position to understand your study and decide whether the BMJ is the right journal for it. We are looking forward to reading the revised version and, we hope, reaching a decision.

Please remember that the author list and order were finalised upon initial submission, and reviewers and editors judged the paper in light of this information, particularly regarding any competing interests. If authors are later added to a paper this process is subverted. In that case, we reserve the right to rescind any previous decision or return the paper to the review process. Please also remember that we reserve the right to require formation of an authorship group when there are a large number of authors.

When you return your revised manuscript, please note that The BMJ requires an ORCID iD for corresponding authors of all research articles. If you do not have an ORCID iD, registration is free and takes a matter of seconds.

Sincerely,

Elizabeth Loder, MD, MPH

*** PLEASE NOTE: This is a two-step process. After clicking on the link, you will be directed to a webpage to confirm. ***

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****Report from The BMJ's manuscript committee meeting****

These comments are an attempt to summarise the discussions at the manuscript meeting. They are not an exact transcript.

Present: Wim Weber (chair); Rafael Perera (statistician); Elizabeth Loder; Jose Merino; Tiago Villanueva; Timothy Feeney

Decision: Request revisions before decisions. Professor Perera to see the revision.

* We acknowledge this is a very important topic, and this version of the paper is more accessible than the original. Your results clearly show that funding of patient groups by industry is frequent, and, moreover, lacks transparency.

* We are less convinced about whether it adds sufficiently above and beyond the individual studies that are included, although we do think that bringing together all of this information in one location probably is useful. But it seems mainly a collection of case reports.

* There continues to be general dissatisfaction with the quality, completeness, and variability of the data. This is not your fault, of course, and is in fact part of the problem, but it limits the conclusions that can be drawn. It does of course point to the need for better reporting of these connections, and more research in the field.

* Our statistician notes: "This was a difficult area to evaluate using this design. In a way, it is mainly highlighting that no adequate research has been carried out and that this is an area that would be relevant to evaluate.

Specifically in the methods, although it is probably not relevant due to only meta-analysing one outcome, you should have considered the potential overlap of organisations included in the studies. This would make the estimates uninterpretable."

* One of our editors who is involved in drug decisions notes that patient groups "are far more influential than the healthcare professional organizations partly because they are professionalized. This is often their day job whereas for doctors this is an extra role. So they are influential, dedicated, and compromised. So they should be no less scrutinized than doctors."

In your response please provide, point by point, your replies to the comments made by the reviewers and the editors, explaining how and where you have dealt with them in the paper.

**** Comments from the external peer reviewers****

Reviewer: 1

Comments:

Any attempt to draw attention to the negative impact of industry funding on the independence of patient groups is a step in the right direction.

However, I can already hear the cacophony of outrage from those groups who spend most of their time trying to rationalize their decision to accept such funding. There are myriad holes that they can erroneously use to both support their position and undermine detractors.

I do not bemoan their attempt to try to make sense of something so poorly studied, understood and subject to spin. This manuscript does its very best to make a silk purse out of a sow's ear.

From an independent patient perspective, it certainly provides more fodder for debate, but it is far from a silver bullet to support independent patient groups.

The biggest problem with the study is related to the source material. The approach to and acceptance of industry funding varies greatly from country-to-country, province-to-province, election-to-election, group-to-group, individual-to-individual and web site-to-web site.

Ultimately, the signal-to-noise ratio is so low that it is difficult to make any clear conclusions, which is a shame.

As an independent patient advocate, I would have liked to have seen some guidance on how to determine the veracity of patient group motives. Or discussion on how to practically study this going forward would have been helpful.

Finally, as someone at the coalface, how do I get the authentic patient voice front-and-centre?

Additional Questions:

Please enter your name: Bill Swan

Job Title: Lead Agitator

Institution: Faces of Pharmacare

Reimbursement for attending a symposium?: No

A fee for speaking?: No

A fee for organising education?: No

Funds for research?: No

Funds for a member of staff?: No

Fees for consulting?: Yes

Have you in the past five years been employed by an organisation that may in any way gain or lose financially from the publication of this paper?: Yes

Do you hold any stocks or shares in an organisation that may in any way gain or lose financially from the publication of this paper?: No

If you have any competing interests (please see BMJ policy) please declare them here:

Reviewer: 2

Comments:

Thank you for the opportunity to review this paper which uses a systematic review and meta analysis to look at issues linked to pharmaceutical industry funding for community-based organisations.

These are very important research concerns and ensuring and expanding transparency for industry funding with both mainstream research and community activity is essential - and has long been a focus for the organisations involved..

The paper by Fabbri et al. is clearly the result of considerable work, with a large and extensive data search and analysis of important questions. However, most of the results do not add to our understanding of the specific questions better than some of the studies it is based on. More importantly, more direct research approaches would be more likely to answer the four key questions outlined as study objectives rather than this approach to use a literature review and meta analysis.

Although many of the referenced studies have used various methods to collect information, including surveys and questionnaires and internet searches (mainly patient and industry websites), the wide heterogeneity in the results makes the outcomes from this meta analysis unclear on some of the four main research questions.

Q1 - The prevalence of industry funding is not addressed with an appropriate denominator, using only data from a small number of studies that themselves only include small numbers of patient organisations.

2 - The percentage of funding within each organisation that comes from industry - a key marker for understanding context of potential influence - is either not available or only low grade quality of evidence.

3 - The percentage of industry-funded groups that report this funding online - roughly 27% - might now be out-dated because of changes in guidelines for industry funding over the 15+ years that data is taken from. Calendar year is not referenced or adjusted for over absolute funding levels which will have changed over this time.

4 - The analysis of policy positions being shared with funders and organisations does include interesting examples that suggest less than independent views. However, this part of the paper doesn't refer to some of the larger studies that also addressed this question. For example, Rose et al reported high organisational importance and awareness of conflict of interest (>80%) and much lower (7%) perceived pressure to conform to interests of corporate donors.

This makes the paper's results too indirect and dissociated from the key primary questions set by the researchers - all of which are critically important to ensure transparency. As an example, five out of the six criteria related to industry funding in Table 2 are graded either low or very low. Many of the key parameters are covered by less than 6 studies. And the large Kopp et al study included in Table 2 doesn't appear to be included in the references.

The concern that industry funding can directly or indirectly influence the independence of community-based patient organisations is a real one. Over the last 15 years, at least in the UK, this has led to more restricted guidelines that govern such funding - and these include a high level of transparency for all financial support. A direct audit of these guidelines might therefore be a more effective and appropriate way to find out how closely they are being followed.

Many other approaches for original research might be a better way to find out the current percentage of community organisations (of which there are thousands in the UK alone) that receive pharmaceutical funding. A similar approach would then find out the percentage of overall budget that come from this source - as this is mandated in producing annual accounts. Charities in the UK have to produce accounts and to highlight and name funders. This would seem a much better way to systematically find out levels of industry funding and the relative proportions each company contributes to the overall budgets. Although it is good practice for charities to include their financial accounts online, these are open access documents on the Charity Commission website.

APBI and other guidelines have also changed probably several times during the years and combining results based on a metric of whether funding is reported on an organisations website are likely to be very different in 2019 compared to 2003, and yet calendar years isn't accounted for in answers to the key questions.

There are also now stricter restrictions on the overall percentage of income that a single company can contribute to an organisations overall budget - I think set at not being more than 20-25%. In the past though, requirements for transparency for funding have been set at much lower thresholds - perhaps when >5% of overall budgets.

Similarly, several aspects of pharmaceutical funding that the paper highlights as being most important including the percentage that this makes to the overall organisations total budget, are either not available or are too poorly detailed to be useful.

Although the paper sets out to look at differences by country (high vs low income etc), all the selected studies are from high income countries (with one also including South Africa). There might be value in looking at difference between high income countries, especially for the US in terms of corporate guidelines.

Although a more minor point, the language of the paper sometimes has a bias that assumes there is a story here to be discovered. It is not scientifically neutral and neither are the assumptions behind the research. While the implications of inappropriate industry funding affecting the perceived independence of community organisations and their related agenda might easily be true, a more scientific approach should be to start from a position that is more neutral.

For example, the implication of bias, whether conscious or unconscious, is never balanced by an awareness that community organisations might have the capability to construct their own agenda based on their direct experience of patient needs. And that they might similarly be able to independently analyse and report results on new treatments or indeed work with independent investigators and researchers to highlight any possible bias from industry-presented data.

Similarly, and it is a point that runs throughout the paper, there is no recognition that community and industry goals can be independently similar for different reasons: patients who are desperately in need of treatment want better and more effective drugs, and the financial interests of manufacturers are of little concern to them (other than when prices prevent access to new drugs). The paper frames overlapping or similar goals as directional, actually saying that community "echo" industry, rather than independently setting out own agenda.

Similarly, the analysis of "shared positions" doesn't include examples of when funded organisations actively disagree or criticise those of the pharmaceutical funders. One easy metric would be to see which organisations challenge inappropriate pricing for drugs. The paper doesn't include a discussion of where challenging company pricing strengthens an organisation's independence. In research areas with many drugs, many companies accept that over time new data might sometimes show their drugs in a more favourable light and sometimes highlight new concerns. Independent community organisations (who take positions that are different to that of their funders) have the potential to be seen as more stable and less partisan - as should be their true role.

So an analysis that looks at the presence or absence of comment about drug prices in an organisations work might be a useful surrogate for whether their funding has allowed them to remain independent. And there will be many industry-funded organisations where an absence of comment on pricing, shouts much larger than anything that proactively supports one drug or another.

Finally, if the paper is published, I suggest that the two current final bullet points for what this study are are not appropriate. Perhaps one new bullet summary would refer to the limited data that this study could find for this analysis, I also thought that the health fields analyzed were strange for not including any studies from the field of HIV, where activism significant;t affected the research agenda, but where the relationship with industry funding has also been complex and sometimes controversial.

In the interest of transparency, I have been working for charities that over the last 20 years has including funding from both independent trusts and charities and from pharmaceutical companies.

The funding has been critical to whether these services have continued and they have been run without direct input from funders into the programmes they support. In contrast, public funding - whether from the NHS or the complex history of commissioning bodies over that time - might have been preferable or carried advantages, but in practice has either not been available or not been sufficiently flexible to respond urgently to new situations.

I work for an organisation that accepts industry support - but which also has policies for how this funding can only be used for specific projects. For example, industry funding is used to support some direct services but is never used to support either publications or printing. Advertising is not allowed in publications for either health professional or lay readers (patients) - online or for any publication.

We also have a history of taking positions that directly challenge funders over both pricing and marketing policies. All funding is reported online and itemised in the online annual accounts.

Additional Questions:

Please enter your name: simon collins

Job Title: advocate

Institution: HIV I-base

Reimbursement for attending a symposium?: No

A fee for speaking?: No

A fee for organising education?: No

Funds for research?: No

Funds for a member of staff?: Yes

Fees for consulting?: No

Have you in the past five years been employed by an organisation that may in any way gain or lose financially from the publication of this paper?: No

Do you hold any stocks or shares in an organisation that may in any way gain or lose financially from the publication of this paper?: No

If you have any competing interests (please see BMJ policy) please declare them here: I have no personal financial conflict of interest. My organisation receives some industry funding for some projects.

Reviewer: 3

Comments:

Importance

This study explored the crucial and influential relationship between patient groups and industry sponsors. Financial transparency in healthcare has always been a seminal issue, and the influence of capital on the actions of those within healthcare organizations cannot be denied.

This work is of particular importance to patients and policymakers. The general reach of the BMJ will provide this study with a good platform from which to reach its desired audience. However, this study may also be well suited to a Public Health Journal.

Originality

This systematic review with meta-analysis is a first of its kind study which explores the issue of industry funding of health consumer organizations. While there have been many individual studies and compelling incidents which expose the entanglement between patient advocacy organizations and for-profit companies, a high-quality systematic review has not yet been produced.

Research Question

The research question has been clearly defined under the sub-headings of

- i) Prevalence of industry funding
- ii) Transparency
- iii) Positions

However, it is not noted explicitly if this study sought to explore the industry-patient group relationship within a particular country/political jurisdiction (for example, the U.S vs. the E.U). Instead, it is left to the reader to elucidate this information on their own as it appears in the results section. This is an important dimension which should be addressed explicitly, and is relevant because different healthcare systems and governments have differing policies (if any) regarding the industry-patient group relationship.

Abstract

The abstract should include a brief overview of the importance of this topic in order to better represent the subject and convey to the reader why the study was undertaken.

Introduction

While this article has done a good job of consolidating available evidence regarding industry sponsorship of patient groups, some specific examples of this relationship at play in the introduction section might help provide some context about the scope of the issue and to ease the reader into the subject. Additionally, it is suggested that examples of patient groups be provided in the introduction. For instance, some readers may not be aware that large influential organizations such as the American Heart Association and the American Diabetes Association are, in fact, patient groups.

Lines 91-93: reference needed here. Patient and health consumer groups are defined without a supporting citation.

Methods and study design

The study design was robust. The methods are adequately described and transparency has been assured by the provision of supplementary material where needed. The relevant reporting standard is met. No ethical objections are evident.

In addition to sponsorship from the pharmaceutical and medical device industries, another source of financial support and potential conflict of interest for some organizations (such as the American Heart Association and the American Diabetes Association) is from health insurance companies. It would be helpful to know if the studies included in this meta-analysis addressed this.

Page 9, line 235 – ‘Patient involvement’ should be changed to ‘Investigator involvement in patient groups’ since this section describes the involvement of the investigators of this study in various patient consumer groups.

Results

Scientific reliability

Why were p-values not reported for the results?

Lines 50-51 ‘Estimates of prevalence of organizational policies ranged from 2% to 64%’. Needs clarification; would make more sense if it read ‘Estimates of prevalence of organizational policies regarding industry sponsorship ranged from 2% to 64%’.

Discussion

While the discussion section expresses the practical applications and implications of the results of this study, the overall message is somewhat scattered and unclear. It is suggested that a ‘Conclusions’ section be included so as to focus the main takeaways from this article.

Key findings

This section is a summary of the key results and should be included in the results section as opposed to the discussion section.

Lines 434 – 436: ‘Four studies focused on a selected population of patient groups; prevalence ranged from 34% to 436 75%’. To which ‘selected population’ are the authors referring?

Lines 444 - 451: The discussion of how industry-funded groups generally supported sponsors’ interests more often than non-funded groups is an important one. While the ensuing paragraph provides reasons as to why these results should be interpreted with caution, the discussion is incomplete without an exploration of whether or not the policy positions/sponsors interests are in opposition to available evidence (from the perspective of evidence-based medicine), or potentially harmful to the patient.

Implications for policy and practice

While the implications of the results of this study on patients, patient groups and the medical industry are explored in depth, the implications of these findings on physicians are not discussed in sufficient detail. Since a majority of the readership for this article is expected to be healthcare practitioners, a detailed discussion of the physician related consequences of these findings is suggested.

Page 18, line 522-524 - citation needed here: Two studies examining disclosure in patient group submissions to consultations with US governmental agencies reported very different disclosure rates: 0%, in submissions to the CDC and 91% in submission to the FDA.

Tables and figures

Table 2. GRADE summary of findings: Industry funding of patient groups – a legend should be included for the interpretation of the ☹☹ symbols.

Table 3. Details of industry funding – under the ‘mean amount’ column, the time period for this amount should be mentioned (e.g., per calendar year or fiscal year)

Figure 1. Study flow diagram – should be labeled the PRISMA study flow diagram

References

Areas which need references have been mentioned separately under each sub-heading in this review. Please see above for specific recommendations.

Additional Questions:

Please enter your name: Anum Fasih

Job Title: Associate Consultant

Institution: The Indus Hospital

Reimbursement for attending a symposium?: No

A fee for speaking?: No

A fee for organising education?: No

Funds for research?: No

Funds for a member of staff?: No

Fees for consulting?: No

Have you in the past five years been employed by an organisation that may in any way gain or lose financially from the publication of this paper?: No

Do you hold any stocks or shares in an organisation that may in any way gain or lose financially from the publication of this paper?: No

If you have any competing interests (please see BMJ policy) please declare them here:

Reviewer: 4

Comments:

<i>Relevant for patients:</i>

Yes, highly.

<i>Areas of relevance that are missed:</i>

Given what the authors have written and changed the only thing missing is the part in the first article on the surveys on the opinion from patient groups about receiving industry funding. If it is still good data, I might be good to include it again, as it shows the discussions and ideas on industry funding. The articles quoted in the this section are no longer included in the reference list. I'm OK with it if the authors can give a clear reason for this, but if not I would like it to be re-included. It is an indication about the internal (patient organisations) discussions on the subject of industry funding.

<i>Methods used:</i>

I don't know enough of the statistics to judge if the changes made fit the questions asked in the first round of comments.

<i>What can be improved:</i>

Compared to the previous version of the article, this one is clearer in its statements based on what can be found in the studies and does not add conclusions that can't be made (like the implication of bias by the patients organisation because of industry funding). The inclusion of the advice that this type of study would be needed is helpful.

<i>What is missing:</i>

- *Are the questions the paper addresses relevant and important to patients and/or carers?*

Yes. Industry funding is an important issue that needs more research on the impact. Having the meta-analysis done in this study is already very helpful.

- *Are there topics or issues that are missing, or need to be highlighted more?*

Just the part on the *surveys about the opinion on industry funding between patient organisations* that was in the previous version of article. (p 17/100 previous version of the article.)

- *Is the treatment or intervention suggested or guidance given something which patients/carers can readily take up? or does it present challenges?*

Yes patients and patient organisations need to think about industry funding and the effect it has on their organisation and the freedom of expressing their opinions. As a patient involved in a patient organisation you need to think about the effects and consequences it has.

- *Are the outcomes described/measured in the study important to patients/carers?*

Yes. For this article these are the right outcomes to highlight and report upon.

- *Do you have any suggestions that might help the author(s) strengthen their paper?*

I think the new version of the article is sufficient improvement.

Two small remarks for improvement:

(1) In the CONCLUSIONS (p4 L55-56) and in WHAT THIS STUDY ADDS (P4 l82-83) the authors write that "industry funding of patient groups is common in many higher income countries and disease areas". This sentence is unclear. What disease areas do you mean? How many patients groups are there in middle and low income countries? What exactly are you saying? Later in the article the authors write that with the exception of South Africa all studies were conducted in high-income countries. Please amend the sentence in the article.

(2) Why has the part on the studies on survey data on the opinion of patients groups about industry funding been left out in the new article? It is an important section on the discussion about industry funding.

- *Do you think the level of patient/carers involvement in the study could have been improved?*

Yes it could have been improved, but they have improved some of it between the first and second version of the paper.

The authors have stated the of two of the authors engagement in women's health, consumers and community involved.

A representative of a patient groups commented on the findings.

The dissemination of the findings to patient groups through publicly accessible conferences, workshops and the media has been added. Which is positive. It would be good to do this both in the US and in Europe.

Additional Questions:

Please enter your name: Dominique Hamerlijnck

Job Title: patient/consumer experience expert, tobacco control expert

Institution: Dutch Lung Foundation, EUPATI fellow

Reimbursement for attending a symposium?: Yes

A fee for speaking?: Yes

A fee for organising education?: Yes

Funds for research?: Yes

Funds for a member of staff?: No

Fees for consulting?: Yes

Have you in the past five years been employed by an organisation that may in any way gain or lose financially from the publication of this paper?: No

Do you hold any stocks or shares in an organisation that may in any way gain or lose financially from the publication of this paper?: No

If you have any competing interests (please see BMJ policy) please declare them here: I have been given grants to come to the HTAi, ISPOR, European Respiratory Society and IMI PARADIGM conferences and symposia.
I have been given a fee for speaking at IMI PARADIGM, EUPATI.BE,
I have been given a fee for co-developing the EUPATI.NL EUPATI training course.
I am the patient co-chair for an ERS clinical research consortium that receives money from 5 industry partners.
I am an independent consultant for NOVARTIS in improving the level of patient involvement as advisors.
I am a consultant for the Dutch Patient Federation, the Dutch Lung Foundation and Dutch Government organisations in advising on research applications.

Reviewer: 5

Comments:

Overall this article is important and useful. Should be published.
Independence of interested parties that participate in EU decision-making and policy development need to be investigated and documented.

However important points need to be revisited (major comments):
Line 98-99: This view seems rather partial and oriented. Patient groups' actions target both public authorities (reimbursement/coverage) and industry (for example advocacy campaigns to lower the price of medicines (closing-down Wall Street on September 14, 1989 (seven ACT UP members infiltrated the New York Stock Exchange to protest the high price of the only approved AIDS drug, AZT. Several days following this demonstration, Burroughs Wellcome lowered the price of AZT from \$10,000 to \$6,400 per patient per year).
Other actions in favour of generic products met to advocacy towards the World Trade Organisation which adopted rules on Compulsory Licensing and this advocacy movement was conducted by patient organisations that were largely funded by the pharmaceutical industry

237-241 Methods

Analysis by location of study sample is missing. Location of study sample reflects a large dominance of anglo-saxon culture: United Kingdom, USA, New-Zealand, Canada, Australia, Ireland mentioned 25 times out of a total of 37 locations.

Given the very different practices/cultures in the anglo-saxon world (and also laws and practices on financial relations etc.) a separate analysis should have been done to account for contextual influence of different legal systems/sets of rules.

Results

361: At that time, HAI, Perehudoff is member of, adopted strong views that the directive proposal was a partial introduction of direct-to-consumer advertising in Europe which raises the impartiality of this analysis. Can you objectively assess/judge other's opinion when yourself adopted a strong one?

The work done by Perehudoff was based on 11 groups in official relations with the European Medicines Agency (EMA) out of 22 contacted, when there were 25 eligible organisations among 41 actually involved in EMA activities as of June 2009.

362-363: This statement can largely be discussed, it is partly false. The organisation I work for, for example, did not support an increased role for industry. It supported the view that pushed information for prescription medicines should continue to be banned (communication/advertisement from industry), but pulled information (when patients or their organisations contact the marketing authorisation holder to obtain information) should become possible (this was the case in some member states but not all, introducing large disparity in access to life-saving information).

Another proposal was to authorise industry to provide product information on websites in the jurisdiction of EU institutions, as most of these websites were registered/hosted in the US, and European authorities had no legal power to intervene in the information they provided (European users having to navigate on US based web sites to find information on a product, information which might differ from the European authorised reference documents), where my organisation thought the European Commission had a point there, but which did not mean my organisation advocated for industry to be authorised to post anything they wanted on Internet.

430 - 533, Discussion section

The systematic review with meta-analysis as proposed here is interesting, however the discussion eliminated other works on the same topic. Their absence questions the completeness of the literature search on what is already known on this topic and/or the discussion. Publications from experts on conflicts of interests in the health care sector and on the financial links between patient organisations and industry funding include:

- Sebastien Dalgarrondo "Sida : la course aux molécules", Paris, EHESS, 2004
- Daniel Carpenter & David A. Moss (dir.), Preventing Regulatory Capture. Special Interest Influence and How to Limit it, Cambridge University Press, 2013.
- David Demortain, "The tools of globalization. Ways of regulating and the structure of the international regime for pharmaceuticals", Review of International Political Economy, 2015, 22, 6, 1249-1275.
- James Ferguson, «The uses of neoliberalism», Antipode, 2010, 41, S1, 166-184.
- Boris Hauray, Emmanuel Henry & Sébastien Dalgarrondo, «Conflit d'intérêts», dans Emmanuel Henry, Claude Gilbert, Jean-Noël Jouzel & Pascal Marichalar (dir.), Dictionnaire critique de l'expertise. Santé, travail, environnement, Presses de SciencesPo, 2015, p.71-79.
- Deborah Cohen & Philip Carter, «Conflicts of Interest: WHO and the pandemic flu "conspiracies"», BMJ, 2010, 340, c2912.

441-444: To discuss possible publication biais here. Many patient groups, if not most, do not publish their position on policy proposals, often because of lack of resources. They use other advocacy methods to make their voice heard.

So what are these studies measuring ? The relation between industry funding and the position of patient groups? Or the relation between industry funding and the likelihood that a group publishes its position, thanks to the additional resources? This would favour the hypothesis of a link between industry funding and the group position when the group

position is in favour of industry (and thus is more likely to receive funds from industry afterwards).

In other words, does industry fund a patient group to influence its position towards industry interests?

Or is the industry funding a "reward" to groups that adopt views that seem to be closer to industry interests? This would exclude groups that are against industry interests and therefore not likely to receive such rewards. The causality industry funding therefore favourable organisation position is not demonstrated.

The competing interest exist, but this does not demonstrate the patient groups were influenced by industry.

This is briefly discussed lines 449-451 but 3 lines do not really balance all what is explained above and after.

487-488: another indication of uncompleted literature search. Equivalent legislations were adopted in other jurisdictions, e.g. Belgium (betransparent.be), France (Décret 2013-414 of May 21st 2013) and probably many others.

More minor comments:

Line 59-61: In Discussion, authors should address biases that might also exist among other interested parties, healthcare professional organisations in particular, also playing important roles in advocacy, education and research vis-à-vis funds they receive from industry, probably in higher proportions/amounts than patient organisations.

Line 68-69: more importantly patients groups are part of the decision-making and scientific evaluation§. This is important to recognise their role/impact, and also for the purpose of this research. The more sensitive aspects of dependency to industry, if there is one, are when this can influence decision-making (although no such case reported, but concern raised)

98-99: patient groups are not only advocating for access to new medicines and devices, but sometimes older ones also.

Discussion

The discussion part should address biases that might also exist among other interested parties, healthcare professional organisations in particular, also playing important roles in advocacy, education and research vis-à-vis funds they receive from industry, probably in higher proportions/amounts than patient organisations

103: it is good practice to cite older references. Authors should refer to full literature on the topic (some publications in 2004), not the most recent one (2017). One of the 26 studies was published in 2003 by one of the authors (Mosconi), and it certainly refers to documents relating concerns about financial relationships between patient groups and industry. The concern still can persist today, even if not new, and remedy measures have been implemented in some cases.

148-151: Definitions are not so clear. An AIDS patient organisation can advocate for the rights of people who are at risk of acquiring HIV to access effective prophylaxis (they're health services users, they're not defined by a specific disease/condition). Furthermore, later in the article patient groups that include multiple conditions are described. Definitions should be changed.

323: Given the period during which most studies were conducted (from 2003 to 2018), email communication should have been the method of choice. Why not mentioned/measured?

327-329: This seems to indicate communication only took place at the initiative of industry. This does not seem to take into consideration situations where patients/consumers disagree with industry, or need to contact them to advocate for the interests of patients to access a product, a compassionate use programme, to improve a clinical trial, to reduce the price of a medicine etc.

359: Results

Not only consumer but also patient organisations

411-413: This seems to be an extremely small sample, out of a total number of patient groups in Germany that can approximate or exceed 8,000.

510-512: not clear what this says. NICE has a procedure to involve patients in its discussion which includes a declaration of interests. See <https://www.nice.org.uk/Media/Default/About/Who-we-are/Policies-and-procedures/declaration-of-interests-policy.pdf>. So does this mean NICE does not use its procedure, or declarations are not complete?

512-515: Other interests that could influence the opinion of patients/experts should be mentioned. Public funding can also exert a strong influence on an organisation or an expert.

525-526: The authors could also add that ten Patients and Consumers' organisations eligible to work with the EMA published a Code of Practices guiding the Relations between Organisations and the Health Care Industry, as an illustration that indeed they are very aware of the importance to critically evaluate this role.

See :

<https://www.eurordis.org/sites/default/files/thumbnails/0904-PO-Code%20of%20practice.pdf>

532: There is no such thing as a neutral source of funding. Even crowdfunding activities or membership base funding impose certain conditions on an organisation strategy or action plan.

548-549: The author in question could have declared being part of an organisation that hold strong positions against patient organisations being funded by industry. This might have affected the capacity to assess neutrally and objectively the link between industry funding and independence of patient groups.

See Hayes, L. and Mintzes B (1997) 'The ties that bind: drug industry sponsorship'. HAI Lights, 3(2-3):1-3

Shouldn't this have been declared as a potential intellectual conflict of interest?

556: Is there a potential conflict here, as Katrina Perehudoff published several articles largely commented in this article and was also part of HAI, with strong views against patient organisations funded by industry?

Additional Questions:

Please enter your name: François Houyez

Job Title: Director of Treatment Information and Access

Institution: European Organisation for Rare Diseases

Reimbursement for attending a symposium?: Yes

A fee for speaking?: No

A fee for organising education?: No

Funds for research?: No

Funds for a member of staff?: No

Fees for consulting?: No

Have you in the past five years been employed by an organisation that may in any way gain or lose financially from the publication of this paper?: No

Do you hold any stocks or shares in an organisation that may in any way gain or lose financially from the publication of this paper?: No

If you have any competing interests (please see BMJ policy) please declare them here: My organisation is a patient group and as such, in theory could be impacted by the publication of this article, one way or the other. Very unlikely, but I preferred to declare this.

See Eurordis policy on funding:

<https://www.eurordis.org/financial-information-and-funding#tabs-1>

Reviewer: 6

Comments:

Overall impression: As the authors state, a major contribution of this study is that it is the first systematic review of a complex but important topic. They do a nice job summarizing the available data while also acknowledging some of the major limitations. In doing so, they raise some important questions, offer potential implications and establish a clear need for further research.

Intro: This section is well-written and clearly defines the terms, what is known on the subject, the goals of the paper, and why this review is necessary.

Results: How were the studies in different languages reviewed (translated or reviewed by native speakers)? How many languages were included and were discrepancies all resolved in the same manner (by consensus between investigators)?

Is there any way to weight high-quality studies heavier than low-quality studies in the analysis? If so, would this alter the discussion in any kind of meaningful way?

The section titled "Relationship between industry funding and organizational positions" is also nicely organized and flows well. The second paragraph addressing legislative change to increase the industry's role is interesting but has a very small sample size (11). This seems like an interesting area for future research but could be potentially biased given the small n.

In the fourth paragraph of this section, the authors state, "110/147 (75%) of patient groups that sided with pharmaceutical companies and opposed the proposal received industry funding (33)." Was this statistically significant in the original paper? What percent of the total of each group (industry vs non-industry funded groups) did these numbers represent? i.e. if the majority of patient groups surveyed had received funding then this percentage (and its significance) could be misleading.

Discussion: Very strong overall. It is both a strength and a weakness that this paper compares studies across so many different countries with drastically different laws/regulatory policies. Ideally, this degree of inclusion would make the results more generalizable but it's also difficult to draw any meaningful conclusions from the reported outcomes when they vary so greatly between studies and countries. That said, I think the authors do a really nice job acknowledging this and don't overstate their conclusions.

Consider eliminating/changing the last sentence as it feels like a little bit of an afterthought and the preceding sentence is stronger.

Additional Questions:

Please enter your name: Sarah M. Bernstein, MD

Job Title: Physician - neonatal-perinatal medicine fellow

Institution: Duke University Medical Center

Reimbursement for attending a symposium?: No

A fee for speaking?: No

A fee for organising education?: No

Funds for research?: No

Funds for a member of staff?: No

Fees for consulting?: No

Have you in the past five years been employed by an organisation that may in any way gain or lose financially from the publication of this paper?: No

Do you hold any stocks or shares in an organisation that may in any way gain or lose financially from the publication of this paper?: No

If you have any competing interests (please see BMJ policy) please declare them here: none

Reviewer: 7

Comments:

Thank you for the opportunity to review this revised manuscript.

In this new version, the study authors address a key weakness in the previous draft and acknowledge that in recent years, there has been increasing attention to the development of patient advocacy educational programs, codes and guidelines, referencing EUPATI, WECAN, and EFPIA. (lines 114-118 and references 3-6). This is a helpful addition and sets the landscape more clearly.

In the first draft the authors stated that "no patients were involved in planning and conducting this review". It is a positive step that the authors now disclose that "Two of the study authors (PM and BM) have been involved for many years with women's health and consumer groups and maintain strong community engagement," and that the first draft has since been reviewed and commented on by the representative of a Canadian patient group. Although I would personally have preferred to have seen one of the umbrella organisations consulted over the study design and planning, it is clearly unrealistic to do so at this stage. I hope that the authors will consider this approach for future studies.

It is puzzling that the number of studies reviewed in this paper has been reduced from 27 to 26 studies. On closer examination it appears that the Leto di Priolo study referred to in the earlier draft has been taken out. The authors give as their reason for excluding it that there

were "no outcomes of interest". The conclusion of the Leto di Priolo study that "Despite ongoing concerns about the openness and transparency of relations between pharmaceutical companies and patient groups, there is scope for these two sectors to work together on issues of common interest," seems to me both interesting and relevant to the scope of the review, it is therefore disappointing that it has been excluded at this stage.

I do not personally agree with all of the findings in this review article but this second draft has certainly benefited from the remarks made by myself and previous reviewers and the authors have clearly done their best to address the key points. Publication of this review article would facilitate healthy discussion with patient organisations and industry representatives.

Additional Questions:

Please enter your name: Judith Taylor

Job Title: Director and Secretary

Institution: Thyroid Cancer Alliance (patient organisation)

Reimbursement for attending a symposium?: No

A fee for speaking?: Yes

A fee for organising education?: No

Funds for research?: No

Funds for a member of staff?: No

Fees for consulting?: No

Have you in the past five years been employed by an organisation that may in any way gain or lose financially from the publication of this paper?: No

Do you hold any stocks or shares in an organisation that may in any way gain or lose financially from the publication of this paper?: No

If you have any competing interests (please see BMJ policy) please declare them here: The Thyroid Cancer Alliance has received support from Bayer Healthcare and Sanofi Genzyme in previous years. I have received speaker fees for presentations to Eisai staff in 2016 and 2017.

Reviewer: 8

Comments:

In my opinion, this is an important study that deserves publication. As the patient voice grows, organizations need to be cognizant of how their funding sources impact their influence, as well as the public's perceptions.

Thank you,

Barbara

Additional Questions:

Please enter your name: Barbara Lewis

Job Title: Founder

Institution: Joan's Family Bill of Rights

Reimbursement for attending a symposium?: Yes

A fee for speaking?: Yes

A fee for organising education?: Yes

Funds for research?: Yes

Funds for a member of staff?: Yes

Fees for consulting?: Yes

Have you in the past five years been employed by an organisation that may in any way gain or lose financially from the publication of this paper?: No

Do you hold any stocks or shares in an organisation that may in any way gain or lose financially from the publication of this paper?: No

If you have any competing interests (please see BMJ policy) please declare them here: