BMJ - Decision on Manuscript ID BMJ-2019-049540
Body:
18-Apr-2019

Dear Dr. Fabbri,

BMJ-2019-049540 entitled "Industry funding of patient and health consumer organisations: Systematic review with meta-analysis"

Thank you for sending us this paper and giving us the chance to consider your work. We sent it out for external peer review and discussed it at a recent manuscript meeting with editors and our statistical consultant in attendance. There was considerable interest in the topic, as indicated by the comments from the meeting, which are summarised below. However, we did not feel that the manuscript is right for The BMJ in its current form.

While we recognise that the comments from editors and reviewers may help guide a revised paper, we think the revisions would essentially amount to a new paper. You may wish to send your paper to a different venue rather than taking on a substantial revision, especially as we are not able to guarantee that we will pursue it.

If you do wish to resubmit a revised paper amended in the light of our and/or reviewers' comments, please use the resubmission link below. When submitting your revised manuscript please provide a point by point response to our comments and those of any reviewers. I must stress that resubmitting your manuscript does not guarantee eventual acceptance, and that your resubmission may be sent again for review.

As you will appreciate we receive a large number of articles and often have to reject valuable and worthwhile work. When making an editorial decision we take the comments of the reviewers into account and also consider whether a piece will interest and inform our readers and whether it adds sufficiently to previous work. We have a large volume of Analysis submissions competing for limited space at the moment and have to make difficult decisions about which papers to accept.

I'm very sorry for any disappointment caused and hope that the outcome of this submission does not deter you from future submissions to The BMJ.

Sincerely,
Elizabeth Loder, MD, MPH
eloder@bmj.com

Below are comments from the manuscript meeting. Please note that these are a summary of the discussion. They are not an exact transcript.

Present: Jose Merino (chair); Jamie Kirkham (statistician); Elizabeth Loder; Wim Weber; Tiago Villanueva; Daoxin Yin; Timothy Feeney; John Fletcher

Decision: Reject and offer

* We note that you have applied conventional systematic review and meta-analysis methods but along with some of the reviewers we were not convinced that the data lends itself to these approaches. For example, is the RoB methods used really appropriate for these types of studies? Our statistician was not persuaded. We also wonder if pooling of data is wise given the not unexpected high levels of heterogeneity. The forest plots without pooling give a very nice summary of the range of prevalence of industry funding to patient groups across studies and other outcomes considered. Moreover, few of the (if any) planned subgroup analyses could explain any of this heterogeneity so there is a lot if uncertainty about where this is all coming from.

* Despite this we thought that the paper has value but should probably be reworked. As presently written it lacks focus.

One of our editors tried to summarize the questions that are asked here (and added the numbers) and given suggestions about the way forward.

"In particular, we sought to answer the following questions:
1. how prevalent is pharmaceutical or medical device industry funding of patient groups?
2. how transparent are patient groups about industry funding?
does industry funding influence the positions of patient groups on specific issues?
3. what do representatives of patient groups think about receiving industry funding?"

He notes the following: Q1 is a quantitative one that lends itself to descriptive studies. The question might be better specified as % of patient groups that accept industry funding; % of all funding that is from industry industry and % from just one company. Q2 is two different questions. 2a could be % patient groups that report the source of their funding and again a descriptive study would do but 2b is an analytic question asking whether presence or absence of funding affects an outcome such as "recommendation of a specific therapy" Q3 is a qualitative question and can hardly be tackled any way other than through in depth interviews.

The result of this unfocused set of objectives is a search that misses the relevant studies for RQ 3 (because you exclude qual studies) and a real mixture of studies, many of which don't address the same RQ. We looked at 3 research titles to see what they were about.

A. Presentation on websites of possible benefits and harms from screening for breast cancer: cross sectional study. Jorgensen et al. They used internet search engines to find patient information on breast cancer and restricted themselves to Scandanavian and English speaking countries. They extracted data on whether the information was balanced and reflected current research. Although the text mentions funding this wasn't the focus of the data collection and is not reported in any detail or in tables.

B. Assessing stakeholder opinion on relations between cancer patient groups and pharmaceutical companies in Europe. Leto di Priolo et al. This was a telephone survey of "161 policy makers, cancer healthcare group representatives, and cancer patient group leaders from France, Germany, Hungary, Italy, Latvia, the Netherlands, Poland, Portugal, Romania, Spain, Sweden, and the UK".

C. Financial Conflicts of Interest and the Centers for Disease Control and Prevention’s 2016 Guideline for Prescribing Opioids for Chronic Pain. Lin et al. After CDC published its guidelines on pain it invited comments on its website because of criticisms raised about conflicts of interest. This letter in JAMA Int Med reports data extracted from comments made by the 151 organisations leaving comments on the website. (This article is classified as "Peer reviewed journal"...)

These studies are so different it doesn't make much sense to try and combine them numerically. We did not think they are even addressing the same RQ except in a very general way in that they are about conflicts of interest and health information (Study A is about patient information, Study B is about professional, policy and patient views about industry, Study C is about a government sponsored professional guideline).

What to do? A more narrative style of review would be one way to go but would require quite a different writing style. An alternative would be to tighten up (restrict the sope of) the objectives and research question. This would require removing many of the studies and perhaps running a more focused search to bring in more appropriate study designs. Of all the research we see surely this one needed patient participation more than most, so you might consider involving some patients in any reworking of the paper. Several editors mentioned they favor the "more limited scope" idea.

Instructions for resubmission, should you choose that option:

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

https://mc.manuscriptcentral.com/bmj?URL_MASK=60f3f31a4bd04c6e8f0b73afa0975a8f

IMPORTANT: Your original files are available to you when you upload your revised manuscript. Please delete any redundant files before completing the submission.

IMPORTANT INFORMATION TO INCLUDE IN A RESUBMISSION

Instead of returning a signed licence or competing interest form, we require all authors to insert the following statements into the text version of their manuscript:

Licence for Publication
The Corresponding Author has the right to grant on behalf of all authors and does grant on behalf of all authors, an exclusive licence (or non exclusive for government employees) on a worldwide basis to the BMJ Publishing Group Ltd to permit this article (if accepted) to be published in BMJ and any other BMJPGL products and sublicences such use and exploit all subsidiary rights, as set out in our licence (http://group.bmj.com/products/journals/instructions-for-authors/licence-forms).

Competing Interest
Please see our policy and the unified Competing Interests form http://resources.bmj.com/bmj/authors/editorial-policies/competing-interests. Please state any competing interests if they exist, or make a no competing interests declaration.

Reviewer(s)' Comments to Author:

Reviewer: 1

Comments:
Thank you for the opportunity to review this systematic review and meta-analysis. The topic is timely, important, and has been an ongoing focus of BMJ campaigning (e.g. Sophie Arie's report in 2014, the recent Mandeville piece on NICE HTAs, and Jeremy Taylor's reasoned response in BMJ opinion). So the question remains, is *this* study and approach shedding new light?

Reviewing the literature systematically the authors describe a spotty literature that finds that at least half of medical non-profits have received at least $1 of industry funding and that recipients may be more likely to tow the industry line than non-recipients (albeit in a small sample). While the methods are clearly described and the statistical approach appears careful given the potential for bias, I suspect most readers will be unsurprised of the findings and conclusions from prior reporting.

Methodologically I am not quite convinced that describing industry funding only in terms of "prevalence" or "exposure" as if it were an infection quite works. Industry funding in some form or another (whether sponsoring a small regional meeting or sponsoring a survey or taking out advertising space) is so prevalent that the charities who don't receive it are more exceptional – is it because they've "taken a stand", because they are so small they don't register on industry's radar, or that there are no drugs for their disease?

I find the estimates in Table 3 to be quite low; "Platinum" sponsorship of key conferences often weighs in at six figures just to secure the position, for instance.

It's a shame there wasn't better data on the % of funding streams received from industry as giving a $20k donation to the ALS Association who are sitting on $100m from the Ice Bucket Challenge is probably less of a threat to integrity than a larger sum to a smaller organization.

Some non-profits are set up in a HQ & local (e.g. state) chapter model of affiliates, so local vs. central funding is hard to tease out and I've seen the local branches roped in on local issues by their industry liasions e.g. lobbying their elected politicans on biosimilars or generics.

Focussing solely on money misses the fact that much influence (which can be in shorter supply than money) is informally reciprocated "in kind" for instance inviting non-profit staff to sit on industry's adivisory committees or combine forces on a sponsor's advocacy efforts which may lend credibility but is in fact budgeted from marketing and executed by a communications agency.

Industry support often has a lifecycle associated with its products – therefore cross-sectional studies across a broad swathe of diseases may give an uneven picture. For instance in the multiple sclerosis world there are a number of highly competitive biotechs with patented products trying to build a portfolio of products, whereas in cystic fibrosis there is one dominant company that (for now) has a somewhat unique relationship with non-profits in the space. The cycle often starts with "awareness raising" around the disease which is a shared objective but then may mutate as products make their way through the pipeline and particularly at the point of approvals or market access (e.g. NICE) is when the influence has the most chance of being problematic.

While I agree with the authors conclusions that more transparency is warranted and that governments should "do something" it might be informative to point to initiatives that have been successful (or at least a good start) such as the "sunshine initiative" around physician payment.

Additional Questions:
Please enter your name: Paul Wicks

Job Title: VP of Innovation

Institution: PatientsLikeMe

Reimbursement for attending a symposium?: Yes

A fee for speaking?: Yes

A fee for organising education?: No

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 <A HREF='http://www.bmj.com/about-bmj/resources-authors/forms-policies-and-checklists/declaration-competing-interests'target='_new'> (please see BMJ policy) please declare them here: Disclosures

PW is an employee of PatientsLikeMe and holds stock options in the company.

PW is an associate editor at the Journal of Medical Internet Research and is on the Editorial Boards of The BMJ, BMC Medicine, and Digital Biomarkers.

The PatientsLikeMe Research Team has received research funding (including conference support and consulting fees) from Abbvie, Accorda, Actelion, Alexion, Amgen, AstraZeneca, Avanir, Biogen, Boehringer Ingelheim, Celgene, EMD, Genentech, Genzyme, Janssen, Johnson & Johnson, Merck, Neuraltus, Novartis, Otsuka, Permobil, Pfizer, Sanofi, Shire, Takeda, Teva, and UCB.

The PatientsLikeMe R&D team has received research grant funding from Kaiser Permanente, the Robert Wood Johnson Foundation, Sage Bionetworks, The AKU Society, and the University of Maryland.

PW has received speaker fees from Bayer and honoraria from Roche, ARISLA, AMIA, IMI, PSI, and the BMJ.

Reviewer: 2

Comments:
• Are the questions the paper addresses relevant and important to patients and/or carers?
Yes, the questions are relevant for patients and carers. As the paper states patients and carers are dependent on the patient organisation for information, support, education and lobbying on many subject like health policy, reimbursement decisions, HTA etc. that have a direct impact on (quality of) care, availability and quality of medication and devices, selection and funding of research etc. on a national and international level. This directly and indirectly influences quality of life and the options of dealing with the consequences of the disease on a daily basis for patients and carers. The influence of patient organisations in designing the future of health care is increasing. This makes this research even more relevant.
The selection and range of outcome measures is broad enough to give insight on the consequences, results of industry funding of patient organisations.
The study makes clear that better reporting of links/funding with industry is needed. Not just on the yes or no questions, but also the impact of the funding, dependency of the funding from industry and the contacts with industry. A way of monitoring of the influence of the industry involvement in the policy and action of the patient organisations would not be amiss.
We have seen in other areas (like tobacco control) the impact industry can have on policy development by perverting the proposal consultancy process by influencing the input of certain groups and people.
As stated in the study better regulation and monitoring of industry funding and contacts is needed. National and international standards are needed.

• Are there topics or issues that are missing, or need to be highlighted more?
It would be good if they define what they mean with multiple disease areas as the focus of the patient organisations. Would an organisations on lung diseases be multiple or one area. Is cancer one type of cancer or multiple? Are the multiple disease organisations umbrella organisations, where the members are not patients but patient organisations? Are the disease specific organisations umbrella organisations? Is it within one country or on a super national/super state level? It would be good to better describe the type of patient organisation in this way if possible. If this information is not available, please indicate this as well.

The study is quite comprehensive, but does raise questions on how to move forward.
It would be good to formulate an advice to patients and carers on the influence of industry funding on patient organisations and what questions to ask of your own organisation on the subject of industry funding and industry influence.
It would be very interesting to have a study done on this subject in low- and middle income countries and patient organisations in other disease areas.

• Is the treatment or intervention suggested or guidance given something which patients/carers can readily take up? or does it present challenges?
The study is not about a treatment or intervention. It is however important in the development and acceptance of treatments by both doctors and patients/carers.

• Are the outcomes described/measured in the study important to patients/carers? Are there others that should have been considered?
Given the scope of the study, it is a good starting point. For the future it might be good to involve patients in developing relevant criteria for measuring the influence of industry on the policies of patient organisations and behaviour of the people working for patient organisation.

• Do you have any suggestions that might help the author(s) strengthen their paper and make it more useful for doctors to share and discuss with patients/ carers?
Not at this moment.
• Do you think the level of patient/carer involvement in the study could have been improved? If there was none do you have ideas on how they might have done so?
On the one hand it was good that no patients were involved as most of us are a volunteer for one or more patient organisations. I would however advise to involve patient experience experts in developing policies and information material for patients on financial and other links with industry.

Additional Questions:
Please enter your name: Dominique Hamerlijnck

Job Title: patient 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 <A HREF='http://www.bmj.com/about-bmj/resources-authors/forms-policies-and-checklists/declaration-competing-interests'target='_new'> (please see BMJ policy) please declare them here: I have been reimbursed for attending the European Respiratory Society congress, an ERS scientific symposium and received a fee for speaking at the conference in 2018, I was reimbursed for attending the 2018 EU ISPOR conference. I have received a grant for attending the 2019 HTAi conference.
I will be reimbursed for developing the HTA part for the Dutch EUPATI course. This is government funded.
I am co-chair of an ERS Clinical Research Consortium (CRC) on severe asthma and my travel is reimbursed. The ERS received funds from 5 industry partners to fund this CRC.
I am the independent European Federation for Allergy and Airways Diseases Patients' associations to the Chief Medical officer of Novartis on patient involvement in medicine innovations.
I am a patient advisor for the IMI PARADIGM project that is in part funded by EFPIA.
I am a volunteer at the Duthc Lung Foundation that receives funds from some industry partners.

Reviewer: 3

Comments:
This is an important issue for patients and for patient organisations in the light of concerns that have been raised in recent years about financial relationships between patient groups and industry and the threats these might pose to the integrity and reputation of patient groups. These are issues that, in my

own experience as a patient advocate, patient organisations are usually very much aware of and strive to conduct themselves ethically and transparently. However, despite a number of inherent limitations, the study findings made me aware of some less than ideal practices that need addressing by patient organisations.

As a general remark, I would like to see more effort made in the preamble to define the landscape and to define the role of patient advocates and growing importance of networking and umbrella organisations, and to describe the increasing number of educational programmes for patient advocates such as the European Patient Academy.

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

The paper addresses four questions that were also defined on PROSPERO International prospective register of systematic reviews:

. how prevalent is pharmaceutical or medical device industry funding of patient groups?

This is the first systematic review on the topic and confirms what is generally known, that pharmaceutical industry funding of patient groups is common in many higher income countries and disease areas. Sixteen studies looked at prevalence of industry funding of patient groups. More than half of the patient groups surveyed received some or all of their funding from industry. Some patient groups received funding from 6-7 industry donors.

What is lacking from these findings is the difficulty patient groups face in finding funding from alternative non-industry sources. Ensuring that they have funding from multiple sponsors can help patient organisations to maintain objectivity and ensure they are not dependent on a single source of income.

. how transparent are patient groups about industry funding?

Four studies reviewed by the authors analysed patient groups' websites and found that only one quarter to one third of the groups disclosed industry funding. The amount, use or the proportion of income derived from industry funding was rarely disclosed. This is a helpful finding and patient groups need to address this if this is so.

It would be helpful if the authors were to clarify the number of patient groups covered by these studies and their geographical location.

. does industry funding influence the positions of patient groups on specific issues?

The authors review four studies that analysed organisational positions versus industry funding, two of which included comparisons between industry-funded and non-funded groups. Two studies showed a low risk of bias and two showed a high risk of bias. Although in some cases the patient groups' positions were aligned with industry, no evidence was provided of overt industry influence, and the conclusion that these studies raised concerns about industry influence does therefore seem to be overstated.

The authors report that one study found that 5/8 of German patient groups had members of advisory boards with financial ties to industry. A more detailed analysis would be helpful, since industry draws its medical advisers from the same pool of expertise as patient groups, and it would be helpful to clarify if these advisors are solely funded by an industrial company or receive support from several companies, and what this consists of (speaking honoraria or more substantial support). Of more concern, a US study reported that 37/104 (35.6%) patient groups had at least one drug, device, or biotechnology company executive on the board.

.what do representatives of patient groups think about receiving industry funding?

This section is particularly disappointing. The authors review five studies on this question but provide only a short summary paragraph of their findings. Of particular note, a paper by Leto di Priolo S, et al (2012, ref 25) which conducted telephone interviews with 161 European policy makers, cancer

healthcare group representatives, and cancer patient group leaders is summarised in one sentence as reporting that 'industry was seen as a vital source of funding' (page 17, lines 21-22). This sentence appears to have been taken out of context and is not included in the Leto di Priolo study's results or conclusion 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.'

I would recommend a thorough reworking of this section of the paper.

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

I miss any mention of the way in which patient advocates are educated, for example, the European Patient Academy (EUPATI), the patient advocacy tracks at the ASCO, ECCO and ESMO congresses, the European School of Oncology patient advocacy masterclasses, and networking groups such as EURORDIS and WECAN.

It would also be relevant to reference the recent document released by WECAN on 'Guiding principles for reasonable legal agreements,' as an example of how patient organisations and industry interact. https://wecanadvocate.eu/rappnews/

• Is the treatment or intervention suggested or guidance given something which patients/carers can readily take up? or does it present challenges?
The authors recommend that patient groups should critically evaluate the role of industry funding on their operations and recommend a broader discussion around the role of industry funding in the patient group sector. These discussions are already taking place both in patient groups and in the umbrella patient organisations to which they belong. Patient organisations are generally aware of public concerns about industry funding and many are actively working on improving transparency and where possible reducing their dependence on industry sponsorship or diversifying their income.

The observation that 'Few patient groups have policies governing corporate sponsorship and transparency of funding arrangements on patient groups' websites is inadequate,' is helpful and one that patient groups should act on if not already doing so.

• Are the outcomes described/measured in the study important to patients/carers? Are there others that should have been considered?

Patients are increasingly involved in medicines research and development and health technology assessment, as well as in reviewing grant proposals and manuscripts submitted for publication. There are scattered references to working with the EMA, FDA and NICE, but it would have been interesting to frame a separate research question on this subject and to draw these findings into an additional section of the paper.

In the section on implications for research, there is an oblique mention that 'Increased requirements of pharmaceutical companies for transparency about funding relationships may lead to more accurate estimates [about the association between industry funding and organisational policy]. (page 19 lines 22-24). It would be appropriate to provide a reference to legislation such as the Sunshine Act (USA). The associated reference is to EFPIA's Code of Practice on the relationships between the pharmaceutical industry and patient organisations. 2011. It omits mention of the more recent EFPIA document 'Working Together with Patient Groups (September 2017) which does not carry the weight of a code of practice but includes several sections on the principles of engagement. I suggest revising this section.

• Do you have any suggestions that might help the author(s) strengthen their paper and make it more useful for doctors to share and discuss with patients/ carers?

See above.

• Do you think the level of patient/carer involvement in the study could have been improved? If there was none do you have ideas on how they might have done so?

The investigators mention that no patients were involved in planning and conducting this review and that 'results will be disseminated to patient groups through publicly accessible conferences, workshops and the media'. I regret to say this implies to me that the authors are in an academic bubble, and fails to take account of the efforts that patient organisations are themselves putting into raising awareness of the need for transparency about their relations with industry and promoting best practice through networking with other patient groups and educational initiatives.

The study could have been enriched by consulting for example representatives of EUPATI (European Patients' Academy), WECAN (Workgroup of European Cancer Advocacy Networks) or one of the umbrella organisations of patient groups such as the ECPC (European Cancer Patients Consortium) or Eurordis (European Organisation for Rare Diseases) about the study design, to add supplementary questions, and to help to develop a picture of the study 'landscape'.

If this paper is accepted for publication I would encourage the journal to invite leaders of patient organisations and consortia to provide feedback and present the patient advocacy perspective as a letter(s) to the editor.

Additional Questions:
Please enter your name: Judith Taylor

Job Title: Secretary/Director

Institution: Thyroid Cancer Alliance (patient organisation)

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 <A HREF='http://www.bmj.com/about-bmj/resources-authors/forms-policies-and-checklists/declaration-competing-interests'target='_new'> (please see BMJ policy) please declare them here:

Reviewer: 4

Comments:
I was asked to review this paper, because I'm a patient advisor. As such, I found this study fascinating. Among patient advisors this is a very relevant and topical issue.

Perhaps I missed it, but I'm curious about the type of funding that organizations receive or that patients within the organizations receive. Is it only money or in-kind services, and what is the percentage of the organization's income, etc., which might be beyond the purview of this study, but interesting, nonetheless.

To make the article more accessible, especially to patients, I recommend using common and easy-to-understand words instead of verbiage that may not be known by readers. (e.g., "DerSimonian-Laird estimate of single proportions with Freeman-Tukey arcsine transformation was used.")

Since conflict of interest disclosure is mandated for all activities that have continuing medical education in the US, it seems that organizations should also reveal their funding sources, especially if they are influencing policy and healthcare decisions.

Thank you for all the work that went into this study. I appreciate your interest in examining this very important topic.

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?: No

Fees for consulting?:

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 <A HREF='http://www.bmj.com/about-bmj/resources-authors/forms-policies-and-checklists/declaration-competing-interests'target='_new'> (please see BMJ policy) please declare them here:

Reviewer: 5

Comments:
General comments
The authors report on a systematic review investigating industry funding of patient groups. To my knowledge no previous systematic reviews have covered this topic. The review is generally well conducted using appropriate methodology and is also clearly reported. However, I have some comments concerning the paper which I have addressed below.

Major compulsory revision

p8 para 8 The paragraph heading reads 'methodological quality'. However, in the text below and elsewhere in the manuscript the authors use the term 'risk of bias'. My main reservation regarding this manuscript, concerns the use of the 'Checklist for Prevalance Studies'. This checklist includes items related to statistical issues (e.g. item #8) and reporting quality (e.g. item #4). This is something different than bias/methodological quality. I am not aware of specific tools developed solely for addressing bias in prevalence studies, so this may be the best there is. However, I suggest to avoid the terms bias/methodological quality and instead just use 'quality'. Furthermore, using a tool based on different quality issues may impact on the tool's ability to measure what you want to measure (e.g. bias). In their analyses the authors found no difference in estimates based on 'low' and 'high' risk studies. This could be because the tools is not very good a measuring bias. Based on the cited tool reference (#9) I cannot find anything about how this tool was developed, validated or reliability tested. The authors should therefore also address the limitations of this tool in their discussion. Lastly, the authors use the term scale to describe the tool. The term scale is typically used when an overall summary score is derived based on 'scoring' of individual items, which is not the case (see The Cochrane Handbook).

Minor compulsory revision

p5 para 2 One of the primary aim is to describe the prevalence of industry funding. However, the concern related to industry funding of patient groups may differ depending on the degree of funding. For example, if 90% of all income is from industry it may be a cause for greater concern than if it is only 5%. While the authors report on this I think this should receive more attention in the manuscript here and in general and since they report on it I think it also needs to be described in the aims. E.g. How prevalent and to which degree is ……

p6 para The authors searched Web of Science, Scopus and Google Scholar using search strings. However, these databases (Web of Science in particular) are also citation databases and I wonder why they searched them using the same strategy as MEDLINE and Embase. Typically citation databases are searched based on included studies in order to identify other recent studies citing them.

p6 para 3 I am unsure whether 'outcome' is the appropriate term her. I would not use outcome to describe prevalence and for #3 the actual outcome is 'position on health and policy issues' whereas the text describes an association between comparison and outcome.

p7 para 2 The authors should please define what is meant by pharmaceutical and device industry. I.e. were companies producing vaccines, vitamins and nutritional supplements considered as part of the pharmaceutical industry? Were companies producing diagnostic tools/equipment considered to belong to the device industry? What about companies producing software/apps?

p7 para 4 line 7 I am unsure what is meant by 'primary outcome'. No primary or secondary outcomes are defined in this systematic review as far as I can see. Do the authors mean primary outcome according to the publication of the included studies? I assume that they included all relevant data despite the data being reported as a primary or secondary outcome in study publications.

p7 para 4 According to the headings of the results section the authors estimated 7 measures (e.g. 'prevalence of industry funding of patient groups'). Four of these are described under 'outcome measures' in 'Study selection' and all are mentioned in the paragraph below concerning GRADE. However, mentioning them under GRADE without introducing them before is somewhat confusing. I suggest that the authors report all 7 in a separate section to give the reader a better overview.

p12 para 1 line 2-3 See comment above. Reporting of baseline data is a reporting quality, not a bias issue.

p12 para 2 line 3-4 As previously described I think the degree of industry funding should be described and discussed in more detail as it is an important result.

p12 para 3 line 3-5 The authors compare the results of the low risk with the high risk group. So this is essentially a subgroup analysis and not a sensitivity analysis. Sensitivity analysis is typically done in order to test the robustness of findings on the basis on review decision e.g. eligibility criteria or publication status. So in a sensitivity analysis the results would be compared against the primary analysis and not each other. I suggest reporting it as a subgroup analysis as this is typically what is done in relation to study quality (see Cochrane Handbook).

p12 para 3 I suggest describing which post-hoc subgroup analyses were done in the appendix and just describing that various analyses were done and none explained the heterogeneity.

p13 para 3 In the results section the groups 'consultation' and 'website analysis' are reported separately, but in Figure 4 an overall estimate is provided. I think pooling these very heterogeneous sources should be avoided so I suggest not reporting the overall estimate in Figure 4. Also one can question pooling the data from the two studies of 'consultation' since the results are very heterogeneous likely due to difference in sources used.

p14 para 3-4 p15 para 1-3 The reporting of these four studies is in my mind too detailed and it is unclear to me why they should receive more attention than the 23 other studies. I suggest reporting them in a more overall manner and the report these details in the appendix. Also some of the results are available in Figure 5 so no need to describe it in detail here.

p18 para 1 As described above I think more emphasis should be put on reporting degree of industry funding in patient groups. Also I think the authors should discuss whether a summary prevalence estimate makes sense across such a heterogeneous group of organisations from different countries.

p18 para 1 line16 I suggest focusing on the uncertainty of the estimate instead of the sample size.

p18 para 2 line 7 I suggest writing 'may not be generalisable'. Generalisability is only a problem if the estimates should differ in other populations and we do not know this.

p19 I think a section putting the study in 'context' seems to be missing. Both in relation to discussing the differences in estimates across included studies, but also discussing the findings in relation to industry influence on other issues (e.g. research, clinical practice etc). Also I suggest the authors discuss ponetial 'double counting' in the review. Was there a chance that some of the included studies sampled the same patient organisations and if so how could this influence the findings. Lastly, some studies seems to be 'investigative journalism' and not 'scientific studies' which have undergone peer review. The authors should please discuss whether they believe this could have influenced the findings.

p28 The Jorgensen 2004 study is described as multiple for 'disease focus'. As far as I can see the topic is breast cancer screening (i.e. a single disease). If this is the case, then the authors should please correct this and any impact it has on the subgroup analyses.

p31-2 I suggest using appropriate GRADE terminology in the 'comments' i.e. imprecision instead of small sample size and inconsistency instead of heterogeneity. Also it should be described for each comment whether it leads to up- or downgrading. Lastly I suggest organisational instead of institutional.

Discretionary revision

Abstract - review methods I suggest reporting study quality assessment before data analysis.

Abstract – results The sentence "Transparency of industry…." Does not read clearly in relation to the estimate of 27%. Suggest something like…"Among patient organisations having received industry funding 27% (95% CI: 24-31%) disclosed this information on their websites.

Abstract conclusion While 'majority' is correct I would suggest 'around half'. Also the term 'rate' is used to describe a prevalence, which is incorrect. I suggest instead 'with prevalence estimates ranging from 20% to 88% among the included studies'.

p4 para 1 The authors may also consider to describe that some patient groups are included in guideline development.

p4 para2 Line 3-5 I suggest providing a reference for this statement.

p6 para 1 I suggest reporting the PROSPERO record ID here. No need to report it as a citation.

p6 para 2 Line 1 I suggest reporting the exact date (i.e. January 20th 2018).

p6 para 3 line 17 I am unsure what is meant by 'secondary outcomes based on survey data'.

p7 para 3 line 4 Does this refer to the pair of investigators (i.e. two) or should all eight be involved in cases of disagreement?

p9 para 2 line 7 I suggest describing the cut-off for proportion of industry funding. It is not clear from this paragraph nor the data extraction section how 'service provision' and 'advocacy only' was coded.

p11 para 1 line 5 I suggest 'not research' instead of 'not empirical'. Also it is not clear to me why editorials and commentaries were not excluded at abstract stage since this should have been apparent.

p11 para 2 The authors use 1 decimal on their estimates in many cases. However, many of these estimates are based on only 20 to 30 groups. I therefore suggest writing percentages without decimals. Also I suggest writing 8 to 1215 (27,36). 8 (36) to 1215 (27) looks like it is the SD in parenthesis and not the study reference.

p11 para 3 line 1-6 Most of this paragraph seems redundant as it is implicit from the methods that meta-analysis was only done if data were available.

p11 para 3 line 6-8 I suggest moving this to the methods section.

p12 para 2 line 2-3 This sentence seems redundant as the next paragraph provides the meta-analysis estimate.

p13 para 1 The word donor, sponsor and funder seems to be used synonymously here and elsewhere in the manuscript. To avoid confusion I suggest using only one term.

p13 para 2 line 1 I suggest reported instead of discussed.

p13 para 3 It is not always clear that the results relates to groups which received industry funding and who disclosed this information.

p14 para 1 I think the word 'versus' is used in a confusing sense here since the analysis is actually whether there is an 'association'. Also the quality assessment is previously described so no need to repeat it here.

p14 para 2 I suggest association instead of links.

p15 para 4 line 1-4 I suggest reporting this in the methods section.

p16 para 3 This does not seem to be part of study aims though in some sense it can be viewed as a sort of transparency about industry affiliation and it would maybe be more appropriate to describe it in that section.

p18 para 1 line 8 Since there are only two studies I would not describe this as a range.

p19 para 2 line 4-5 Triangulate is used here and elsewhere. This is a term typically used in qualitative research and I would just suggest deleting it. I.e…..should use multiple sources. Also I suggest avoiding 'true prevalence' and instead write better estimate. The truth may not be possible to find.

p21 para 2 line 4 Were the two authors also prohibited from assessing study quality of their own studies?

p21 para 3 line 4 It is unclear what #5690 refers to.

p33 I am unsure what 23/59 is? Also I suggest just reporting the mean amount for Kopp 2018 and not the total. Otherwise the authors should report the total for the 2 other studies by multiplying the mean with the number of groups.

p34 Table 4 I suggest that the authors describe that this relates to groups having received industry funding (see previous comment).

p36 Instead of describing that 17 additional records were identified I suggest reporting how many additional studies were actually included based on other sources. This gives some sense of the sensitivity of the database search.

p37 I suggest yellow is unclear (between red and green) and the blank is NA. Similar to Cochrane RoB colours.

Additional Questions:
Please enter your name: Andreas Lundh

Job Title: Senior Researcher

Institution: Centre for Evidence-Based Medicine Odense (CEBMO)

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 <A
HREF='http://www.bmj.com/about-bmj/resources-authors/forms-policies-and-checklists/declaration-competing-interests'target='_new'> (please see BMJ policy) please declare them here: I have previously collaborated with one of the authors (BM) on two papers, but we have no current collaboration and we have never met in person.

Date Sent:
18-Apr-2019