BMJ - Decision on Manuscript ID BMJ-2019-050887

Body: 02-Aug-2019

Dear Dr. Frouard

Manuscript ID BMJ-2019-050887 entitled "Association between benefits paid by pharmaceutical companies to French general practitioners and their drug prescriptions in 2016: a retrospective study using the French Transparency in Healthcare and National Health Data System databases"

Thank you for sending us your paper. We sent it for external peer review and discussed it at our manuscript committee meeting. We recognise its potential importance and relevance to general medical readers, but I am afraid that we have not yet been able to reach a final decision on it because several important aspects of the work still need clarifying.

We hope very much 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.

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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.

Members of the committee were: Wim Weber (chair), Rafael Perera (chair), Elizabeth Loder, Tiago Villanueva, Timothy Feeney, José Merino

Decision: Put points

Detailed comments from the meeting:

First, please revise your paper to respond to all of the comments by the reviewers. Their reports are available at the end of this letter, below.

Please also respond to these additional comments by the committee:

- We liked the research question.

- Several editors commented that the choice of words for “benefits” and “acts” may not be ideal. By “benefits”, you mean payments of gifts. Why not use those words?

- Several editors also thought that the paper was hard to follow. Could you provide tables and boxes with some of the most relevant information, including the efficiency indicators?

- For proper assessment of the association that 'benefits' have biased behavior, we need a technical note (possibly as supplementary material) providing information on how the indicators used were created. In particular, we need to know:

a) What information was used in the creation of these indicators? Which methods were used (e.g. simple aggregation or based on some standardisation)? In particular, we need reassurance that these indicators are not just a reflection of workload by the GP which could then act as a critical confounder in the association.

and

b) if these indicators are indeed reflecting 'adequate' vs. 'inadequate' behavior as well as having a clear specification as the directionality of these indicators (e.g. higher levels = 'inadequate behavior' or the other way around).

- There are also some statistical issues that require addressing such as the use of a 0.001 as threshold. If there are a total of 12 X 5 comparisons made (indicators x groups compared) then a conservative p-value would be more like 0.0005. More information regarding stats methods used is also necessary.

- It is unclear if at least some of the observed associations are directly linked to volume (doctors' workload) and therefore this association could mainly be explained due to confounding. ‘The GPs performed 5 359 ± 2 510 acts for 1 681 ± 774 patients’, seems a very low number.

- One editor wondered “if use of these "prescription efficiency indicators" really is the best way to study this matter.” Can you please justify your choice of outcome? The outcomes are the 11 variables for financial incentives. They should tell us what the financial benefits exactly are, so we can interpret these accordingly. They speak of reimbursements, but how does that work ? This suggests that GPs can benefit from industry or the government, and they possible calculate the trade-offs.

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

Comments from Reviewers

Reviewer: 1

Summary:
This study evaluated the association between payments from pharmaceutical companies to general practitioner physicians in France and their prescribing practices by linking two French prescription databases. There was significant association between higher payments

by pharmaceutical companies and lower quality prescribing practices by General Practitioners (GPs).
Broad Comments:
The study's novelty lies in the first time evaluation of this association in France. The authors have interpreted the results appropriately and the conclusions are supported by the results. The authors have specified their underlying assumptions and have done a good job in listing the major limitations of the study. The primary outcomes studied were prescription efficiency indicators as continuous variables and authors employed ANOVA, Chi-square and multivariate linear regression (my interpretation – can authors please confirm this?) for studying the associations between independent and dependent variables. The primary independent variable evaluated is the amount of payment made by the pharmaceutical companies to the GPs. The authors categorized these for meaningful interpretations. The methods for study design and analysis are scientifically sound and are described in sufficient detail except specifically mentioning the statistical analyses employed (eg. Authors do not specify if linear regression was used). Overall, publishing this work will add to the literature on potential health and economic impacts of pharmaceutical promotions.
One major comment I have is how are the prescription efficiency indicators evaluated to be better or worse? Is there a reference that specifies this comparison?

Specific comments:
1. Page 7, line 43: "Drug prescriptions per act": What does this mean? Does it mean prescriptions prescribed on a single patient visit?
2. Page 8, line 49-50: "on Internet since 2013": the use of term 'on Internet' is not clear. Can authors clarify what this statement means?
3. Page 10, line 23: "We recruited GPs…." seems incorrect terminology, since it's a retrospective study, authors can say, "We included GPs…"
4. Page 10, line 32-33: Its unclear why second matching could not be performed for 6.2% of all listed GPs?
5. Page 10, line 42-54: The reference for the 11 indicators is missing here.
6. Page 11, line 8-9: "number of acts performed per year": its not clear what this means? (Similar to comment#1)
7. Page 12, line 50-51: "they performed 5359…" Is it an average (mean and SD) reported? Please specify.
8. Figure 2: It's not clear what is being reported in the figure 2? Is the legend missing for the figure?
9. In limitations, are any of the drugs evaluated available as over-the-counter (OTC) ie without prescription in France? Eg Aspirin and PPIs are available without prescription in US and may other countries. If these are available as OTC, how does this limit the interpretations for the prescription efficiency indicators using these two drug classes?
10. Page 16, line 55-56: "…suggest a possible gradual association..." what does gradual mean here?

Additional Questions:
Please enter your name: Manvi Sharma

Job Title: Assistant Professor

Institution: University of Mississippi

Reimbursement for attending a symposium?: No

A fee for speaking?: No

A fee for organising education?: No

Funds for research?: No

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Reviewer: 2

“Association between benefits paid by pharmaceutical companies to French general practitioners and their drug prescriptions in 2016: a retrospective study using the French Transparency in Healthcare and National Health Data System databases”

The researchers have used administrative data for research purposes to draw associations between GPs prescribing patterns and payment from pharmaceutical companies. This is an area of research that needs more data and I applaud them for their use of these data to bring further attention to this area.

However, I cannot recommend this paper for publication. To draw these conclusions, the researchers either need to determine the drugs the company sells that contributed to each physician, or the frequency with which the physician prescribed the drugs of that company. The link is strong enough in this case. Rather, this paper demonstrates how prescribing patterns differ across physicians. One factor may be payments, but the link in this paper is not strong enough to enter the peer reviewed literature. I also had other questions the researchers need to address if it was to be considered for publication:

Questions:

1. What is the “the health scandal concerning benfluorex (Mediator®)” elaborate for international readers.

2. Are the data for drug dispensing or prescription? In the data description it is unclear as both types of datasets are mentioned. Are the researchers able to analyse drug prescription and drug reimbursed data? If so, it would be interesting to see if there are any discrepancies in the two datasets. Prescription data would be better data to answer this question as dispensed data have the inherent bias of relying on patients to fill the prescription.

3. The meaning of this phrase is unclear. “i) GPs who worked with a particular mode of exercise.” Does it mean physicians with a particular specialty? Please reword.

4. The meaning of this phrase is unclear. “postal code of the commune of exercise”. Please reword.

5. Was database linkage only performed on GPs meeting the inclusion criteria, or all GPs listed in the National Council of the College of Physicians? I.e. was the 6.2% of all GPs or of those we met the inclusion criteria? Please clarify.

6. The meaning of this phrase is unclear. "Number of acts performed per year". Does it mean number of prescriptions written, number of prescriptions filled, number of patients seen? Replace acts with a clearer word for what this represents.

7. The term "best prescribing behaviours" is problematic. The researchers are examining 11 indicators of prescription efficiency. Relabelling the behaviour as 'most efficient prescribing patterns' is more accurate.

8. In the flow chart, the monetary breakdown for each step of the inclusion and exclusion are not required. If they are deemed as required, then include in a table in the appendix, one column per cohort inclusion criteria. Also, use absolute numbers and proportions to clearly demonstrate if there was one GP reimbursement group that was affected by an of the inclusion criteria.

9. In line with my overall comments above, is there any way to link the types of drugs physicians prescribe and the drug company that paid them? If a hypertension drug company contributed, but the physician prescribes benzodiazepines, then this is not evidence that the contribution affected their prescribing pattern, rather this demonstrate the variability in physician prescribing patterns.

Additional Questions:
Please enter your name: Bianca Blanch

Job Title: Research Manager

Institution: Hello Sunday Morning

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

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