PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (**http://bmjopen.bmj.com/site/about/resources/checklist.pdf)** and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

ARTICLE DETAILS

TITLE (PROVISIONAL)	Do doctors in dispensing practices with a financial conflict of interest prescribe more expensive drugs? A cross-sectional analysis of English primary care prescribing data.
AUTHORS	Goldacre, Ben; Reynolds, Carl; Powell-Smith, Anna; Walker, Alex; Yates, Tom; Croker, Richard; Smeeth, Liam

VERSION 1 – REVIEW

REVIEWER	Jingjing Qian Auburn University, USA
REVIEW RETURNED	19-Oct-2018

GENERAL COMMENTS	Overall comment: the manuscript entitled “Do doctors in dispensing practices with a financial conflict of interest prescribe more expensive drugs? A cross-sectional analysis of English primary care prescribing data” used the national prescribing data for England to examine the association between dispensing practices with a financial conflict of interest and the likelihood of prescribing high-cost prescription options. The authors found that dispensing practices were more likely to prescribe high-cost drugs across all 4 classes compared to those practices without dispensing activities. The manuscript is well written in general. I have the following specific comments for editors and authors’ consideration regarding this manuscript: 1. Background: the authors mentioned dispensing practices in England “are generally found in rural areas that have fewer pharmacies, and help provide convenient access to medicines for patients”. Is there any difference in patient population, disease burden, socioeconomic factors between patient served by dispensing practices and those served by non-dispensing practice in England? Those factors can impact treatment selections and utilization. 2. Methods: the duration of dispensing data is not clear. The authors only mentioned January 2015 in Methods section, by how long did the national dispensing data cover for national Rx dispensing period? 3. Methods: as I mentioned above, there might be many confounders that could impact the association between higher cost prescription dispensing and dispensing practices. The authors did not adequately control for those potential confounders. 4. Methods: the definition of high vs low cost drugs can actually vary by time. Using a senior pharmacist to determine high vs low cost drugs can only work at the time of the study because cost of drugs will change by time when new product (brand or generic) comes to market or changes in drug supply. I appreciate the authors’ effort in determining high vs low cost drugs in this study,

BMJ Open: first published as 10.1136/bmjopen-2018-026886 on 5 February 2019. Downloaded from http://bmjopen.bmj.com/ on March 28, 2024 by guest. Protected by copyright.

	but the method (i.e. codes to determine high vs. low cost) actually is not reproducible. 5. Discussion: please address the limitation of the nature of cross-sectional analysis for this study. No causality should be indicated in study discussion and conclusion.

REVIEWER	Frank Moriarty Royal College of Surgeons in Ireland, Ireland
REVIEW RETURNED	25-Oct-2018

GENERAL COMMENTS	This manuscript reports a novel study of GP practice prescribing costs and dispensing status of the practice. This is a highly relevant study which explores this potential financial incentive for practitioners and contextualises the results in terms of national pharmaceutical spending for England. It makes excellent use of publicly available data to produce these important results. It is well designed and the authors have been highly transparent in sharing all relevant study materials to allow for replication or further related research (and this was very helpful in reviewing the manuscript). I have a few very minor comments/suggestions which I hope may help to improve this paper further. 1. In the Design section of the Abstract (page 2, line 20), perhaps the factors which were adjusted for in the multivariable logistic regression could be reported here. 2. In the Background section (page 4, line 32), the objectives refer to "more expensive branded drugs in place of cheaper and equally effective generic drugs". The reference here to branded and generic drugs runs slightly counter to the Methods where the authors provide the clear explanation that not all branded drugs are necessarily high cost and similarly generics are not necessarily low cost. Referring simply to expensive and lower cost drugs here may make the objectives more consistent with the Methods. 3. The Data preparation section of the Methods refers to total items dispensed and total quantity dispensed on page 5, line 28. These are referred to elsewhere as prescriptions and doses and I feel referring to these latter terms instead of or as well as items/quantity would provide more clarity, in particular for readers not familiar with these data files. 4. Given that items/quantity dispensed is referred to, it may be helpful to add a brief explanation in the Methods that the data covers prescribed medications which are dispensed. 5. On a related note, could the authors provide some extra context in the Background section on the degree of latitude for dispensers (be that in a pharmacy or a dispensing practice) to deviate from the product that has been prescribed? For instance if a prescription is for a branded product, can a generic product be substituted for this when dispensing, or if a product is prescribed based on the INN, is there latitude to dispense any product containing that drug? 6. The Results section (page 11, line 7) states "...dispensing practices are very significantly over-represented among the highest prescribers of high-cost drugs." It's clear from the percentages presented in Table 5 that this is the case however the reference to "significantly" begs the question of whether the authors conducted any null hypothesis statistical tests here?

BMJ Open: first published as 10.1136/bmjopen-2018-026886 on 5 February 2019. Downloaded from http://bmjopen.bmj.com/ on March 28, 2024 by guest. Protected by copyright.

VERSION 1 – AUTHOR RESPONSE

Reviewer(s)' Comments to Author: Reviewer: 1

Reviewer Name: Jingjing Qian Institution and

Country: Auburn University, USA

Overall comment:

the manuscript entitled “Do doctors in dispensing practices with a financial conflict of interest prescribe more expensive drugs? A cross-sectional analysis of English primary care prescribing data” used the national prescribing data for England to examine the association between dispensing practices with a financial conflict of interest and the likelihood of prescribing high-cost prescription options. The authors found that dispensing practices were more likely to prescribe high-cost drugs across all 4 classes compared to those practices without dispensing activities. The manuscript is well written in general.

I have the following specific comments for editors and authors’ consideration regarding this manuscript:

Background: the authors mentioned dispensing practices in England “are generally found in rural areas that have fewer pharmacies, and help provide convenient access to medicines for patients”. Is there any difference in patient population, disease burden, socioeconomic factors between patient served by dispensing practices and those served by non-dispensing practice in England? Those factors can impact treatment selections and utilization.

As we described in the paper, we used proportions of high-cost drugs as our primary measure, with the total prescribing in each class of drugs as the denominator. This will inherently control for confounding by indication, by controlling for differences in case mix between practices. Consequently, there is no need to consider other factors, as there are no priori grounds that treatment failure or idiopathic response to the lower-cost treatment would be different in dispensing and non-dispensing practices. Our additional adjustment using deprivation scores, patient list size and number of GPs made no meaningful difference to our results (Table 2).

Methods: the duration of dispensing data is not clear. The authors only mentioned January 2015 in Methods section, by how long did the national dispensing data cover for national Rx dispensing period?

The data are for all prescriptions submitted for payment for January 2015, i.e. one month’s worth of data. We have amended the text to make this clearer.

Methods: as I mentioned above, there might be many confounders that could impact the association between higher cost prescription dispensing and dispensing practices. The authors did not adequately control for those potential confounders.

Please see our comment above. Consequently we do not agree that we did not adequately control for these confounders.

BMJ Open: first published as 10.1136/bmjopen-2018-026886 on 5 February 2019. Downloaded from http://bmjopen.bmj.com/ on March 28, 2024 by guest. Protected by copyright.

Methods: the definition of high vs low cost drugs can actually vary by time. Using a senior pharmacist to determine high vs low cost drugs can only work at the time of the study because cost of drugs will change by time when new product (brand or generic) comes to market or changes in drug supply. I appreciate the authors' effort in determining high vs low cost drugs in this study, but the method (i.e. codes to determine high vs. low cost) actually is not reproducible.

We agree that the list of high cost drugs is not applicable to different time frames, but for the purposes of the time frame used in this study, it is reproducible. Producing a method to consistently identify high and low cost drugs over different time frames is outside of the scope of this study

Discussion: please address the limitation of the nature of cross-sectional analysis for this study. No causality should be indicated in study discussion and conclusion.

We have added this into the manuscript.

Reviewer: 2 Reviewer Name: Frank Moriarty Institution and Country: Royal College of Surgeons in Ireland, Ireland

This manuscript reports a novel study of GP practice prescribing costs and dispensing status of the practice. This is a highly relevant study which explores this potential financial incentive for practitioners and contextualises the results in terms of national pharmaceutical spending for England. It makes excellent use of publicly available data to produce these important results. It is well designed and the authors have been highly transparent in sharing all relevant study materials to allow for replication or further related research (and this was very helpful in reviewing the manuscript).

I have a few very minor comments/suggestions which I hope may help to improve this paper further.

In the Design section of the Abstract (page 2, line 20), perhaps the factors which were adjusted for in the multivariable logistic regression could be reported here.

Thank you, we have added this into the abstract.

In the Background section (page 4, line 32), the objectives refer to "more expensive branded drugs in place of cheaper and equally effective generic drugs". The reference here to branded and generic drugs runs slightly counter to the Methods where the authors provide the clear explanation that not all branded drugs are necessarily high cost and similarly generics are not necessarily low cost. Referring simply to expensive and lower cost drugs here may make the objectives more consistent with the Methods.

Thank you, we have made this amendment.

The Data preparation section of the Methods refers to total items dispensed and total quantity dispensed on page 5, line 28. These are referred to elsewhere as prescriptions and doses and I feel

BMJ Open: first published as 10.1136/bmjopen-2018-026886 on 5 February 2019. Downloaded from http://bmjopen.bmj.com/ on March 28, 2024 by guest. Protected by copyright.

referring to these latter terms instead of or as well as items/quantity would provide more clarity, in particular for readers not familiar with these data files.

We believe we have already clarified this. In the section relating to data preparation, we state: “In this dataset, an “item” is a presentation appearing on a prescription, while “quantity” is the number of doses issued.”

Given that items/quantity dispensed is referred to, it may be helpful to add a brief explanation in the Methods that the data covers prescribed medications which are dispensed.

We have amended the section to reflect this.

On a related note, could the authors provide some extra context in the Background section on the degree of latitude for dispensers (be that in a pharmacy or a dispensing practice) to deviate from the product that has been prescribed? For instance if a prescription is for a branded product, can a generic product be substituted for this when dispensing, or if a product is prescribed based on the INN, is there latitude to dispense any product containing that drug?

Thank you, we have added a section to reflect this.

The Results section (page 11, line 7) states "...dispensing practices are very significantly over-represented among the highest prescribers of high-cost drugs." It's clear from the percentages presented in Table 5 that this is the case however the reference to "significantly" begs the question of whether the authors conducted any null hypothesis statistical tests here?

We have amended the text in this section.

VERSION 2 – REVIEW

REVIEWER	Jingjing Qian Auburn University, USA
REVIEW RETURNED	16-Nov-2018

GENERAL COMMENTS	Thanks for incorporating the comments into the revision.

REVIEWER	Frank Moriarty Royal College of Surgeons in Ireland, Ireland
REVIEW RETURNED	05-Nov-2018

GENERAL COMMENTS	I would like to thank the authors for addressing all of my previous comments, and I have no further revisions to suggest.

BMJ Open: first published as 10.1136/bmjopen-2018-026886 on 5 February 2019. Downloaded from http://bmjopen.bmj.com/ on March 28, 2024 by guest. Protected by copyright.