Author's response to reviews

Title: A price and use comparison of generic versus originator cardiovascular medicines: a hospital study in Chongqing, China

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Author's response to reviews: see over
Author’s response to reviewers’ comments

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Author’s responses to reviewers’ comments:

Dear Ms Calumpita,

Thank you very much for your letter of August 21 recommending that I revise my manuscript entitled “Impact of price regulation on the utilization of generic cardiovascular medicines” (MS: 2609671699323380). I have followed the reviewers’ comments and revised the manuscript accordingly. Below I respond point-by-point to the comments of the reviewers. Changes in the text are underlined. I hope my revisions address your concerns. Thank you very much for reviewing my manuscript.

Sincerely yours,

Wenjie Zeng
Section Editor’s Comments

1. Figure cropping

*It is important for the final layout of the manuscript that the figures are cropped as closely as possible to minimise white space around the image. For more information, see the instructions for authors: [http://www.biomedcentral.com/info/ifora/figures](http://www.biomedcentral.com/info/ifora/figures).*

Answer: Following this comment I have revised the figures in the new version of my manuscript. Thank you.
Reviewer 1:

1. About the Background. *The context of the study should be explained more detailed.* The author writes about health care reform, but does not illustrate the existing health care system including pharmaceutical supply. In some of the references (16-18) these topics are explained, but the health care system should be shortly described also in this paper.

Answer: Thank you for your comment. I have added some information about the evolution of China’s health care system and pharmaceutical supply chain for generic drugs. I hope this will provide some reference for potential readers.

2. About the Background. *The separation of drug prescription and dispensing (SPD) may also be unfamiliar to readers.* It has been quite common in Asian countries that physicians and pharmacists are allowed to both prescribe and dispense drugs. The author writes: “In China, the separation of drug prescription and dispensing (SPD) has attracted much discussion, but no common agreement has been achieved.” What does this mean? Can hospital pharmacies also sell drugs to public?

Answer: I have provided further details about SPD in the revised version. In most Asian countries, the phenomenon of physicians prescribing and dispensing medicines is common based on historical reasons; these are a barrier to SPD. However, in some countries or districts like Japan, South Korea, and Taiwan, the implementation of SPD is underway. China is paying close attention to the implementation of SPD in these countries, but has not yet achieved common agreement on whether follow this reform. Furthermore, hospital pharmacies now sell drugs to patients according to a doctor’s prescription.

3. About the Background. *In the paper the researcher writes that current reimbursement system used in pharmaceutical expenditure in Chinese hospital includes doctors to overprescribe drugs to patients and to prescribe drugs that produce the greatest profit. Profit to whom?*
The current reimbursement system used in pharmaceutical expenditure in Chinese hospitals induces dispensing doctors (DDs) to overprescribe drugs to patients and to prescribe drugs that produce the greatest profit for themselves. This has added in the new version.

4. About the Background. The context needs also some figures about total drug costs in China, if these are available.

Answer: In 2010 the pharmaceutical revenue of Chinese public hospitals amounted to 405.39 billion CNY (approximately US$62.37 billion), representing 45.80% of business total revenue. I was unable to obtain official data on the total drug costs in China, but I have added a table to illustrate the evolution of average per capita pharmaceutical expenditure for inpatients and outpatients.

5. About the Method. The data was obtained from the magazine company of China Pharmacy. Could the author describe the source material more? How the drug utilization data is collated from hospitals? The researcher used hospital’s procurement price in comparison. Is this also the price that the patient pays for an individual drug?

Answer: Drug utilization data are actually collated from the hospital’s procurement records, which are easy to obtain and are regarded as the same as the actual utilization by patients. I have included this in the revised manuscript.

The price that the patient pays for an individual drug is called retail price in this paper, which is 15–50% higher than the procurement price. This was illustrated in the first paragraph of “Price calculation, comparison”.

6. About the Method. How much are drug expenditures from the total budget of the study hospital?

Answer: According to official data, in 2010 the pharmaceutical revenue of Chinese public hospitals represented 45.80% of total business revenue (above 4). These data were not from my target hospital, but can be regarded as being representative average data.
7. About the Discussion. *The discussion is a bit hard to understand, because of the lacking context of the study.*

Answer: I have added some background material and rewritten the section to improve the understanding of the discussion.

8. About the Conclusions. *I think that the conclusions are not based on the results of the study. The author writes: “For China’s comprehensive healthcare policy makers, the decline of drug prices alone couldn’t cut the pharmaceutical expenditures; on the contrary, it may exert a negative influence on the supply side and demand side of generic drugs.” This conclusion cannot be drawn based on this paper.*

Answer: I have rewritten the conclusions section and it is now based on the findings of my study.

9. *Quality of written English: Not suitable for publication unless extensively edited*

Answer: I have engaged the services of an English-language editing company, Edanz, to edit my manuscript again.

I appreciate your useful comments and suggestions. Thank you very much.

**Reviewer 2:**

1. General (essential minor revisions). *Better to use ‘patented’ rather than ‘branded’ to avoid any confusion as there are branded generics available in a number of countries. This can be added to the definitions use (page 4)*

Answer: Thank you for your comment. I agree that it was not appropriate to use “branded” products. I suggest then that the use of the term “originator” might be more appropriate in China’s pharmaceutical market, because in China we usually use “originator medicines” to describe foreign-invested products. These products are typically characterized as having higher prices. I have used the term “originator” in the revised version and have amended the definition.
2. General (essential minor revisions). Also good to expand in various sections whether dealing with generics vs. originators (ATC Level 5) or versus patented products in a class (ATC Level 4). I believe the author is mainly referring to ATC Level 5 but good to confirm this

Answer: I confirm that this paper is mainly referring to ATC Level 5.

3. General (essential minor revisions). Regulations for the marketing authorisation of generics in China, i.e. similar to FDA regulations? This is because concerns with the quality of generics may be one reason for their generally low utilisation as seen in some European and other countries. In addition, at the top of page 10 - the author suggests that a potential future measure could be ‘further evaluation of quality consistency between generic and branded drugs should be performed’

Answer: For the market licensing of a drug, the corresponding information to be provided to the department in charge is almost the same in China as required by the FDA, but this is not enough for the public to recognize the quality of the generic medicine. Therefore, the government has tried to further evaluate the quality consistency between generic and branded drugs.

4. About the Background. a) Page 1 – First paragraph – add further references to enhance the content.

Answer: Thank you very much for providing me with these further references. I have used this material in the newer version.

5. About the Background. b) Page 1 – second paragraph. Better to say ‘INN name’ rather than ‘generic’ name – Line 5 – as in line with academic publications

Answer: I changed the sentence to “generic or INN name”, because for older products physicians are asked to prescribe using generic names, and for new products using INN names.

6. About the Background. b) Page 1 – second paragraph. Line 5/6 – why has INN prescribing not been followed up by the Chinese government (and also address this in
the discussion – later)? Now see compulsory INN prescribing increasing in some countries, e.g. Lithuania - Garuoliene K et al. European countries with small populations can obtain low prices for drugs: Lithuania as a case history. Expert Rev. Pharmacoeconomics Outcomes Res 2011; 11: 343-9, with trends in INN prescribing likely to continue to help conserve costs as well as reduce potential patient confusion especially if patients are dispensed a different branded generic on each occasion with slightly different names

Answer: In the newer version, I have rewritten the sentence to state that it is not that the stipulation was not implemented, but this policy has done little for generic utilization where physicians both prescribe and dispense drugs. A more detailed explanation can be found in the manuscript.

7. About the Background. b) Page 1 – second paragraph. Line 8 – Do you mean ‘In China, the potential separation of drug prescription ....’ as you go on to state that the proposal has attracted much discussion but not implementation as in Japan, Korea or Taiwan. In addition on Page 3 under data sources state ‘under the current situation of no SPD’

Answer: Yes, I mean that China has not yet introduced SPD, but that it has been frequently discussed. I have made this clear in the new version under the heading “--Physicians”.

8. About the Background. c) Top of page 2 – It would be good to have more details of the inducements for doctors to overprescribe drugs as well as prescribe those with the highest profit margin (Ref 17) to give more substance to the rest of the paper and interesting information for the readers of this paper

Answer: I have done so in the new version under the heading “--Physicians”.

9. About the Methods. Top of page 4 – second line – you refer to ‘we’ – do you mean ‘I’ as only one author?

Answer: I am sorry for this mistake and I have edited that sentence accordingly.
10. About the Methods. Start of second paragraph under ‘Selection of generics’ – not sure what is meant by ‘two specifications with one product’ – I suggest this needs further explanation

Answer: This is a policy included with the generic prescription in the “Prescription Management Ordinance” implemented in 2007. For a generic drug, not more than two dosage forms are allowed into a hospital; for injection and oral dosage forms, not more than two preparations for each dosage form are allowed (with the exception of other dosage forms and drug dose specifications required for special situations). I have deleted this description as it is complex and its removal does not affect the value of the manuscript.

11. About the Methods. Reference to support the use of DDDs (which I agree with) need to be added and the year of the DDDs.

Answer: I have added references regarding my data collection.

12. About the Discussion. Page 8 – lines 4 and 5. Does the author mean ‘volume index of branded drugs to generics was 1.63’ rather than ‘volume price index’. In addition, possibly ‘the volume of branded drugs was 63% higher than generics’ rather than discussing price and then volumes?

Answer: In that paragraph I discuss the price comparison. “Volume price index” is used because the price index was calculated according to the weighted volume rather than value of the procurement.

13. About the Discussion. Page 9 – Agree that a number of factors are needed for a sustainable generics market. Some of these are outlined in Dylst P et al.

Page 10 - Additional supply side measures could include greater transparency in the pricing of generics. Demand-side measures could be ensuring INN prescribing is monitored/ enforced (see earlier), implement strategies to limit corruption/abuse of rebates as seen recently in Korea; and potentially prescribing restrictions for patented drugs in a class vs. generics where these are seen as similar in all/ nearly all patients, e.g. statins and others as well as ARBs
Answer: I have included this material in my manuscript.

14. *Quality of written English: Needs some language corrections before being published*

Answer: I have engaged the services of an English-language editing company, Edanz, to edit my manuscript again.

I appreciate your useful comments and suggestions. Thank you very much.