PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Factors influencing the prescription pattern of essential medicines from the perspectives of general practitioners and patients: A qualitative study in China
AUTHORS	Chen, Xiaolei; Zhang, Tiancheng; Wang, Huanling; Feng, Zhengwen; Jin, Guanghui; Shao, Shuang; Du, Juan

VERSION 1 – REVIEW

REVIEWER	Joel Lexchin York University, School of Health Policy & Management
REVIEW RETURNED	15-Aug-2021

GENERAL COMMENTS	This manuscript examines attitudes and use of essential medicines by general practitioners and patients in urban Beijing. 1. I found sections of this manuscript to be very difficult to understand. The language in this manuscript needs to be thoroughly copy edited by someone who has English as a first language. 2. Line 42: What problem are the authors referring to? 3. Line 51: The authors mention that factors may be different in suburban districts but what about rural districts in the country? 4. Lines 63-64: What is the process for revising the NEML and choosing the drugs that are on the NEML? Are drugs removed from the NEML or just added to it? 5. Line 66: Is 18% the average amount of the health care budget spent on medications in OECD countries? 6. The authors need to provide a more detailed explanation about how medicines are paid for in China - is there public insurance, do people purchase private insurance, what percent of the population has any type of insurance? 7. Are the prices of medicines controlled in China and is so what types of price controls are in place? Are price controls different for generic and on-patent drugs? 8. Line 77: How does the National Essential Medicines Policy differ from the National Essential Medicines System? 9. Line 78: Does "domestic medicines" mean domestically produced medicines? 10. Line 79: Are the 417 chemicals and biologics just generic medicines or are some patented medicines? The authors also need to describe how generic medicines are regulated in China, e.g., do they need to be bioequivalent to the original brand-name medicine in order to be approved? Are generics tested for quality? 11. Line 114: Was the interview protocol pilot tested? 12. Line 127: How did the authors know beforehand which GPs would be able to answer questions clearly and logically? Also how did the authors define "logically"? 13. Line 129: How was "chronic disease" defined?

	14. Line 140: How are "understanding and presentation skills" defined? 15. Line 164: How were discrepancies in coding resolved? How is the data stored and how long will it be kept for? 16. Table 1: The authors need to explain the differences in the titles of the physicians, e.g., "attending doctor". The different types of insurance status need to be explained. Monthly income should also be given in an international currency, e.g., US $, Euros, Pounds. 17. Lines 192-193: I don't understand what "regulation for the proportion of medicines prescribed in CHSCs" means. 18. Line 199: Where do GPs acquire information about the efficacy and safety of medicines? Where do GPs get their information about EMs and non-EMs? 19. Lines 287-288: The authors need to explain what the "performance bonus" is. 20. Line 319: What do the authors mean by the term "difficult diseases", difficult to diagnose, difficult to treat, complex diseases such as pulmonary hypertension? 21. Line 347: What is the "deductible line"?

REVIEWER	Xin Li Nanjing Medical University, school of pharmacy
REVIEW RETURNED	04-Sep-2021

GENERAL COMMENTS	Overall, there are some minor suggestions. 1. The English writing is not precise, it would be great to revise the articles, with consultation from native speakers. 2. In the inclusion criteria of patients, how to define “visiting CHSCs for more than 6 months”? 3. The specific personnel task assignment does not need to be placed in the text, e.g. Line 151 “SS mainly responsible for the interviews, and XLC and TCZ played supportive roles and were responsible for the recordings.” 4. In a sentence, the expression of numbers needs to be consistent, e.g. Line 182 “Seventeen GPs and 22 patients with chronic diseases were interviewed….” 5. The policy advices provided in the section of discussion are very important. However, the authors could not provide any detailed policy suggestions in the section of Discussion, which may limit the practical value of the results and conclusions of this study. I suggest the authors to provide more specific and practical advices based on the context of China.

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

Dr. Joel Lexchin, York University

1. I found sections of this manuscript to be very difficult to understand. The language in this manuscript needs to be thoroughly copy edited by someone who has English as a first language.

Answer: Thanks for your suggestions. We have invited an English-speaking colleague to help us revise the manuscript.

2. Line 42: What problem are the authors referring to?

Answer: Thanks for your review comments. The problem refers to "the way about exploring the factors affecting the prescription pattern of essential medicines". The 'Strengths and limitations' section has been revised according to editor's suggestions, and this sentence was deleted.

3. Line 51: The authors mention that factors may be different in suburban districts but what about rural districts in the country?

Answer: Thanks for your review comments. I wanted to express those factors may be different both in suburban and rural districts in the country. We have added the rural districts in the manuscript.

The contents revised are as follows:

The participants in our study were only selected from urban districts, and their understanding may be slightly different from those in suburban and rural districts. ('Conclusion' section, line 391-393, page 16, clean copy)

4. Lines 63-64: What is the process for revising the NEML and choosing the drugs that are on the NEML? Are drugs removed from the NEML or just added to it?

Answer: Thanks for your review comments.

Q1: The process for revising the NEML includes: (1) select evaluation experts randomly from a think-tank of experts on EMs; (2) establish a list of candidate medicines according to the evaluation results of evidence and pharmacoeconomic; (3) determine the NEML through voting by Experts; (4) release NEML approved by the National Essential Medicines Committee. ('Background' section, line 92-96, page 4, clean copy)

Q2: Drugs are allowed to be removed from and added to the NEML, within the changing pattern of drug usage. Taking the NEML 2018 for example, 22 kinds of medicines were removed from the NEML 2012, and 187 kinds of medicines were added into it.

('Background' section, line 99-100, page 4, clean copy)

5. Line 66: Is 18% the average amount of the health care budget spent on medications in OECD countries?

Answer: Thanks for your review comments. Yes, the average amount of the health care budget spent on medications in OECD countries is 18%. We have revised this sentence.

The contents revised are as follows:

Compared with an average of 18% in the Organization for Economic Co-operation and Development countries, medicines accounted for 20%-60% of health spending in developing countries. ('Background' section, line 56-58, page 3, clean copy)

6. The authors need to provide a more detailed explanation about how medicines are paid for in China - is there public insurance, do people purchase private insurance, what percent of the population has any type of insurance?

Answer: Thanks for your review comments.

Q1: The Chinese government has established a medical security system, including basic medical insurance system as backbone, medical aid system as safety net for the poor and commercial medical insurance system as supplementary. The basic medical insurance system includes Urban Employee Basic Medical Insurance (UEBMI, launched in 1998), New Rural Cooperative Medical Scheme (NRCMS, launched in 2003) and Urban Resident Basic Medical Insurance (URBMI, launched in 2007). And in 2016, NRCMS and URBMI were integrated as the Urban-Rural Resident Basic Medical Insurance Scheme (URRBMI). In China, medicines are mainly paid for by basic medical insurance. But medical insurance reimbursement only covers inpatient not outpatient medical expenses in most provinces, which lead to high out-of-pocket medical expenses. ('Background' section, line 64-81, page 3-4, clean copy)

Q2: In 2010, 92% of the Chinese population was covered by the basic medical insurance system, and the rate up to 97% in 2020. While only 6.9% population purchase private insurance in 2013 in China.

('Background' section, line 72-74, page 3-4, clean copy)

7. Are the prices of medicines controlled in China and is so what types of price controls are in place? Are price controls different for generic and on-patent drugs?

Answer: Thanks for your review comments.

Q1: Yes. A series of supporting policies targeting medicine price regulation and control were launched, e.g., establishing a province-based competitive-bidding system for medicines, implementing zero-markup drug policy for all chemicals medicines and the national centralized drug procurement policy.

Q2: The price controls are the same for generic and on-patent medicines.

('Background' section, line 105-108, page 5, clean copy)

8. Line 77: How does the National Essential Medicines Policy differ from the National Essential Medicines System?

Answer: Thanks for your suggestions. There were no differences between "National Essential Medicines Policy" and "National Essential Medicines System" in this manuscript. I have revised "National Essential Medicines Policy" into "National Essential Medicines System". ('Background' section, line 53, page 3, clean copy)

9. Line 78: Does "domestic medicines" mean domestically produced medicines?

Answer: Thanks for your review comments. Yes, the domestic medicines are medicines developed and produced by pharmaceutical companies in mainland China. According to the previous reference, all medicine are generic medicines in NEML 2009. We have revised this sentence.

The contents revised are as follows:

The State Council of China established the NEMS officially in 2009 and issued the National Essential Medicine List 2009 (NEML) containing 205 chemical generics and 102 traditional Chinese medicines ('Background' section, line 82-85, page 4, clean copy)

10. Line 79: Are the 417 chemicals and biologics just generic medicines or are some patented medicines? The authors also need to describe how generic medicines are regulated in China, e.g., do they need to be bioequivalent to the original brand-name medicine in order to be approved? Are generics tested for quality?

Answer: Thanks for your review comments.

Q1: After reviewing the relevant literatures, the 417 chemicals and biologics are generic medicines.

The contents revised are as follows:

To date, the NEML has been revised for 8 times, and the latest version came into effect in 2018, including 417 kinds of chemical generics and 268 kinds of traditional Chinese medicines. ('Background' section, line 96-100, page 4)

Q2: A series of measures were proposed by the government to improve the quality of EMs, e.g., assessing the consistency of quality and efficacy between generic medicines and original medicine, optimizing the manufacturing process, improving the quality of excipient and packaging material, and establishing strict drug-approval procedure (they need to be bioequivalent to the original medicine in order to be approved). ('Background' section, line 85-90, page 4, clean copy)

11. Line 114: Was the interview protocol pilot tested?

Answer: Thanks for your suggestions. Yes, it is the interview protocol pilot tested.

The contents revised are as follows:

A pilot test of 5 experts was conducted to assess the readability, reasonableness and understandability of the interview guide. ('Study design' section, line 133-134, page 6, clean copy)

12. Line 127: How did the authors know beforehand which GPs would be able to answer questions clearly and logically? Also how did the authors define "logically"?

Answer: Thanks for your suggestions.

Q1: With the recommendation of managers in selected CHSCs, interviewees who met the inclusion criteria were invited to participate in this research. ('Participants and recruitment' section, line 144-145, page 6, clean copy)

Q2: The "logically" means "good verbal expression skills".

The contents revised are as follows:

could answer the interviewer's questions clearly and have good verbal expression skills. ('Participants and recruitment' section, line 147, page 6, clean copy)

13. Line 129: How was "chronic disease" defined?

Answer: Thanks for your suggestions. The "chronic disease" in our study refers to the noncommunicable diseases with the characteristics of long duration and multiple causation.

The contents revised are as follows:

And we selected and interviewed a total of 22 patients with noncommunicable diseases (NCD: the disease with the characteristics of long duration and multiple causations). ('Participants and recruitment' section, line 148-150, page 6, clean copy)

14. Line 140: How are "understanding and presentation skills" defined?

Answer: Thanks for your suggestions. "Understanding skills" means "could understand the q uestions" and "presentation skills" means "good verbal expression skills".

The contents revised are as follows:

could understand the questions and have good verbal expression skills. (‘Participants and rec ruitment’ section, line 162-163, page 7, clean copy)

15. Line 164: How were discrepancies in coding resolved? How is the data stored and how long will it be kept for?

Answer: Thanks for your suggestions.

Q1: If there was ambiguity in coding and category creation, the researchers discussed and resolved disagreement till consensus was reached. (‘Data analysis’ section, line 192-194, page 8, clean copy)

Q2: We manage our data through NVivo software, for example by helping to store, annotate texts, to locate words, phrases and segments of data, to name and label. And we have kept the audio-taped data and word data in a folder. When data analysis is completed, the data will be retained permanently.

The contents revised are as follows:

Data management and coding was supported through NVivo software. (‘Data analysis’ section, line 184-185, page 8, clean copy)

16. Table 1: The authors need to explain the differences in the titles of the physicians, e.g., "attending doctor". The different types of insurance status need to be explained. Monthly income should also be given in an international currency, e.g., US $, Euros, Pounds.

Answer: Thanks for your suggestions.

Q1: These titles include resident physician, attending physician, associate chief physician and chief physician, which were sorted in an ascending order. Primary professional position refers to residents, intermediate position refers to attending physicians and senior position refers to associate chief physicians and chief physicians. (‘Result’ section, line 204-205, page 9, clean copy)

Q2: Urban-Rural Resident Basic Medical Insurance Scheme (URRBMI) covers urban and rural residents without formal employment, including children, students, elderly people without previous employment and migrants; Urban Employee Basic Medical Insurance (UEBMI) covers employees and retirees who have work units or are engaged in the individual economy; Government-funded insurance refers to a social security system implemented by China to

cover civil servant and has the characteristics of no deductibles and visiting at designated hospital. ('Result' section, line 206-211, page 9, clean copy)

Q3: Personal monthly income has been given in US dollars. ('Result' section, table 1, page 9, clean copy)

17. Lines 192-193: I don't understand what "regulation for the proportion of medicines prescribed in CHSCs" means.

Answer: Thanks for your suggestions. We have replaced the "regulation for the proportion of medicines prescribed in CHSCs" with "the minimum requirement for the prescription proportion of EMs". ('Result' section, line 217-218, page 10, clean copy)

18. Line 199: Where do GPs acquire information about the efficacy and safety of medicines? Where do GPs get their information about EMs and non-EMs?

Answer: Thanks for your review comments

Q1: GPs acquire information about the efficacy and safety of medicines from training and feedbacks of patients. ('Result' section, line 226-228, page 10, clean copy)

Q2: GPs get their information about EMs and non-EMs from community health service information system.

19. Lines 287-288: The authors need to explain what the "performance bonus" is.

Answer: Thanks for your suggestions. Performance bonus refers to economic incentives upon completion of performance indicator.

The contents revised are as follows:

If I can't reach the standard, the payment for performance will be influenced. ('Result' section, line 320-321, page 14, clean copy)

20. Line 319: What do the authors mean by the term "difficult diseases", difficult to diagnose, difficult to treat, complex diseases such as pulmonary hypertension?

Answer: Thanks for your suggestions. Yes, "difficult diseases" refers to a type of diseases with complex etiology, difficult to diagnose, and difficult to treat such as pulmonary hypertension, brain atrophy, Raynaud's disease. We think "complex diseases" is more

appropriate. We have revised the “difficult diseases” into “complex diseases” in the manuscript. (‘Discussion’ section, line 347, page 15, clean copy.)

21. Line 347: What is the "deductible line"?

Answer: Thanks for your suggestions. We replaced "deductible line" with " deductibles ". Deductible refers the amount you pay for covered health care services before your insurance plan starts to pay. With a $2,000 deductible, for example, you pay the first $2,000 of covered services yourself. (‘Background’ section, line 77-79, page 4, clean copy)

Reviewer: 2
Dr. Xin Li, Nanjing Medical University
Comments to the Author:
Overall, there are some minor suggestions.
1. The English writing is not precise, it would be great to revise the articles, with consultation from native speakers.
Answer: Thanks for your suggestions. We have invited an English-speaking colleague to help us revise the manuscript.

2. In the inclusion criteria of patients, how to define “visiting CHSCs for more than 6 months”?

Answer: Thanks for your review comments. The patients with chronic noncommunicable diseases are required to lifelong medication. Considering patients visited in CHSCs frequently could be familiar with the NEMs. So, we selected the patients with NCDs, who need to consecutive visit CHSCs more than 6 months, and at least once a month.

The contents revised are as follows:

consecutively visiting CHSCs more than 6 months, and at least once a month. (‘Participants and recruitment’ section, line161-162, page 7, clean copy)

3. The specific personnel task assignment does not need to be placed in the text, e.g. Line 151 “SS mainly responsible for the interviews, and XLC and TCZ played supportive roles and were responsible for the recordings.”

Answer: Thanks for your suggestions. I have deleted the contents in the manuscript.

4. In a sentence, the expression of numbers needs to be consistent, e.g., Line 182 "Seventeen GPs and 22 patients with chronic diseases were interviewed…."

Answer: Thanks for your suggestions. I have revised the expression of numbers in the manuscript as follows: "A total of 17 GPs and 22 patients". ('Result' section, line 201, page 8, clean copy)

5. The policy advices provided in the section of discussion are very important. However, the authors could not provide any detailed policy suggestions in the section of Discussion, which may limit the practical value of the results and conclusions of this study. I suggest the authors to provide more specific and practical advices based on the context of China.

Answer: The practical advices has been provided in the manuscript.

The contents revised are as follows:

It is suggested that the government should continue to strengthen oversight on the quality and safety of EMs, e.g., entrust third-party agencies to complete the consistency evaluation of EMs, encourage enterprises to carry out post-marketing evaluation of EMs, improve adverse drug reaction monitoring and reporting systems. Additionally, effectiveness and clinical quality measurement on EMs by the government should be openly accessible to increase public confidence. ('Discussion' section, line 335-340, page 14, clean copy)

It suggests to increase the proportion of EMs prescribed in secondary and tertiary hospitals appropriately and encourage doctors in secondary and tertiary hospitals to give priority to EMs. Meanwhile, financial incentives for physicians could help increase the proportion of EMs prescribed. For GPs, it is necessary to improve their ability to make better diagnosis and treatment decisions, further to increase patients' trust in them. ('Discussion section', line 356-361, page 15, clean copy)

A variety of methods could be utilized to educate patients about EMs, involving taking regular lectures, and disseminating correct knowledge on EMs through television and the Internet. ('Discussion section', line 373-375, page 15-16, clean copy)

Therefore, to stimulate patients to choose EMs, it is necessary to adjust the reimbursement ratio of medicines, e.g., making the reimbursement ratio of EMs much higher than that of non-EMs. ('Discussion section', line 383-385, page 16, clean copy)

VERSION 2 – REVIEW

REVIEWER	Joel Lexchin York University, School of Health Policy & Management
REVIEW RETURNED	30-Nov-2021

GENERAL COMMENTS	The revisions that the authors have made have significantly improved the manuscript but there are still further changes that need to be made. 1. The English has been improved but is still awkward in certain places and further copy editing is necessary by someone who has English as a first language. 2. In the Discussion the authors need to put their findings in the context of other research that has examined the same topic in other jurisdictions. 3. Page 4, line 49: The concept of essential medicines may be more widely applied in developing countries, but it was never meant exclusively for them. 4. Page 4, line 51: When the authors say "adequate amounts" do they mean a large enough amount of the particular medicine to satisfy the needs of the population? 5. Page 4, lines 58-59: "And up to 90%..." is not a sentence. 6. Page 4, lines 66-67: What does the medical aid system cover? What additional items are covered by the commercial medical system? 7. Page 5, lines 78-79: I don't understand what the authors mean when they say that deductibles are set for each type of medical insurance. 8. Page 5, line 81: When the authors say "private insurance" are they referring to "commercial medical insurance" that they mentioned on the previous page? 9. Page 7, line 143: Did any of the invited GPs decline to be interviewed? If so, what percent declined? 10. Page 7, lines 148-149: Was there a separate interview guide for patients? If so, how was the guide developed and was it pilot tested? 11. Page 7, lines 153-155: Monetary amounts should also be expressed in a widely used international currency, e.g., US dollars, Euros. 12. Page 8, lines 157-159: Did any of the invited patients decline to be interviewed? If so, what percent declined? 13. Page 11, line 214: When the authors say the "interview transcriptions" are they referring to the interviews of both the GPs and the patients? Were there differences between the GPs and the patients in the factors that they identified? 14. Page 11, line 224: What is the difference between evidence-based effectiveness and definite efficacy? 15. Page 15, line 329: "While, the NEMLs..." is not a sentence. 16. Page 15, line 337: What do the authors mean by "enterprises"? 17. Page 16, line 354: I don't understand what the authors mean by the phrase "they usually refill medicines rather than seek a doctor". 18. Page 16, line 369: There needs to be a reference for the statement that doctor-patient relationships in China are deteriorating.

REVIEWER	Xin Li Nanjing Medical University, school of pharmacy
REVIEW RETURNED	21-Dec-2021

GENERAL COMMENTS	I think this manuscript is yet in a publishable form and I recommend that the paper be published in BMJ open.

VERSION 2 – AUTHOR RESPONSE

Reviewer: 1

Dr. Joel Lexchin, York University

1. The English has been improved but is still awkward in certain places and further copy editing is necessary by someone who has English as a first language.

Answer: Thanks for your suggestions. We have invited editage corporation to help us revise the manuscript and our manuscript was assigned to Vikas Narang.

2. In the Discussion the authors need to put their findings in the context of other research that has examined the same topic in other jurisdictions.

Answer: Thanks for your suggestions.

We have cited the results of other studies in our discussion.

The contents revised are as follows:

(1) In the interviews, the efficacy and safety of medicines were considered important determinants of EM use by both GPs and patients, which was consistent with reports of previous studies in Chengdu and Xinjiang provinces. ('Discussion' section, line 352-354, clean copy)

(2) In an Australian study, GPs thought specialists had a strong influence on their judgment when prescribing medicines in some clinical areas. In our study, the prescription recommendations from physicians in tertiary or secondary hospitals were considered another important factor affecting the prescription pattern of EMs in CHSCs. ('Discussion' section, line 363-366, clean copy)

(3) It cannot be denied that patients have strong autonomy and preference in selecting medicines, and that the demands of patients significantly affect the prescription behaviors of physicians. ('Discussion' section, line 388-390, clean copy)

(4) One study indicated that higher burdens on patients are associated with higher numbers of selected EMs. ('Discussion' section, line 405-406, clean copy)

3. Page 4, line 49: The concept of essential medicines may be more widely applied in developing countries, but it was never meant exclusively for them.

Answer: Thanks for your suggestions. I have revised the manuscript as follows. By 2017, at least 137 countries worldwide, including developed and developing countries, had established their own national essential medicines systems (NEMS). ('Background' section, line 54-56, clean copy)

4. Page 4, line 51: When the authors say "adequate amounts" do they mean a large enough amount of the particular medicine to satisfy the needs of the population?

Answer: Thanks for your suggestions.

The "adequate amounts" means enough amount of the medicine to satisfy the priority healthcare needs and public health of the population. We have replaced "adequate amounts" with "sufficient supply".

The contents revised are as follows:

EMs are those that satisfy the priority healthcare needs of the population and have sufficient supply, show efficacy and safety, and comparative cost-effectiveness. ('Background' section, line 52-54, clean copy)

5. Page 4, lines 58-59: "And up to 90%..." is not a sentence.

Thanks for your suggestion. I have revised this sentence.

The contents revised are as follows:

Compared with an average of 18% in the Organization for Economic Co-operation and Development countries, medications accounted for 20%–60% of health spending in developing countries, and up to 90% of people purchase medicine through out-of-pocket payments in developing countries. ('Background' section, line 60-63, clean copy)

6. Page 4, lines 66-67: What does the medical aid system cover? What additional items are covered by the commercial medical system?

Answer: Thanks for your suggestion.

The medical aid system provides double benefits to the poor; this includes subsidizing their enrollment in basic medical insurance and providing cash assistance to reimburse their medical expenditures [15]. As a supplement to the basic medical insurance system, commercial medical insurance covers out-of-pocket medical expenses after reimbursement by the basic medical insurance, as well as various insurance products beyond the coverage of basic medical insurance, such as the medical second option, advanced registration, and VIP ward reimbursement ('Background' section, line 77-84, clean copy)

7. Page 5, lines 78-79: I don't understand what the authors mean when they say that deductibles are set for each type of medical insurance.

Answer: Thanks for your suggestion.

A health insurance deductible is a set amount of money that insured person pay out of pocket before the medical insurance starts to pay any benefits. With a $2,000 deductible, for example, you should pay the first $2,000 of covered services yourself. Each type of health insurance has its own deductible. The amount of the deductible depends on the type of medical health insurance plan you own.

The contents revised are as follows:

Second, health insurance deductibles (i.e., an amount of money that an insured person pays out of pocket before the medical insurance begins paying the covered medical services) have been set up for each type of medical insurance, including UEBMI, URRBMI, and commercial medical insurance. ('Background' section, line 89-93, clean copy)

8. Page 5, line 81: When the authors say "private insurance" are they referring to "commercial medical insurance" that they mentioned on the previous page?

Answer: Thanks for your suggestions. "Private insurance" and "commercial medical insurance" carry the same meaning. We have revised this sentence.
The contents revised are as follows:
only 6.9% of people purchased commercial medical insurance in China in 2013. ('Background' section, line 95-96, clean copy)

9. Page 7, line 143: Did any of the invited GPs decline to be interviewed? If so, what percent declined?

Answer: Thanks for your suggestions. All the GPs selected by purposive sampling method in our study were interested and willing to participate in the interviews,
and the response rate was 100%.
The contents revised are as follows:
All GPs invited to participate in our study were included in the interviews, and the response rate was 100%. ('Method' section, line 160-161, clean copy)

10. Page 7, lines 148-149: Was there a separate interview guide for patients? If so, how was the guide developed and was it pilot tested?

Answer: Thanks for your suggestions.
(1) Yes. The interview guide for patients was written in 'Method' section, line 197-200.
The contents revised are as follows:
Topics included (1) the standard for selecting medicine to treat NCD(s), (2) properties of medicines that patients were concerned about, (3) attitudes toward EMs, and (4) reasons for accepting or rejecting GPs' suggestions to change the types of medicines (EMs or not). ('Method' section, line 197-200, clean copy)
(2) The qualitative semi-structured interview guide of patients was developed based on existing literature, research objectives.
The contents revised are as follows:
The qualitative semi-structured interview guidelines for GPs and patients were developed based on the existing literature and research objectives. ('Method' section, line 148-149, clean copy)
(3) A pilot test conducted by five patients to assess the readability, reasonableness, and understandability of the interview guideline.
The contents revised are as follows:
Pilot tests were separately conducted by five GPs with five patients to assess the readability, reasonableness, and understandability of the interview guidelines.
('Method' section, line 150-151, clean copy)

11. Page 7, lines 153-155: Monetary amounts should also be expressed in a widely used international currency, e.g., US dollars, Euros.

Answer: Thanks for your suggestions.

GDP per capita has been given in US dollars.

The contents revised are as follows:

In stage one, six districts were divided into three types of regions based on the GDP per capita, including regions with a GDP per capita of over USD 46,000 (*Dongcheng and Xicheng* districts), a GDP per capita between USD 31,000 and USD 46,000 (*Haidian and Chaoyang* districts), and a GDP per capita below USD 31,000 (*Fengtai and Shijingshan* districts) ('Method' section, line 169-173, clean copy)

12. Page 8, lines 157-159: Did any of the invited patients decline to be interviewed? If so, what percent declined?

Answer: Thanks for your suggestions.

Three patients declined to be interviewed and the percentage was 12.0%.

The contents revised are as follows:

however, three out of 25 patients (12.0%) refused to be interviewed. ('Method' section, line 177-178, clean copy)

13. Page 11, line 214: When the authors say the "interview transcriptions" are they referring to the interviews of both the GPs and the patients? Were there differences between the GPs and the patients in the factors that they identified?

Answer: Thanks for your suggestions.

(1) Yes, they are the interviews of both the GPs and the patients.

(2) Yes. We identified five main themes from GPs and four main themes from patients, respectively. There are four common themes and one theme was specific only to GPs.

The contents revised are as follows:

Overall, GPs and patients had surprisingly similar views on the factors affecting EM prescription patterns during interviews. Analysis of the interview transcriptions of both GPs and patients yielded five themes related to the factors affecting the prescription pattern of EMs, including four common themes: (1) efficacy and safety of medicines, (2) prescription recommendations from physicians in tertiary or secondary hospitals, (3) patients' medication preference, (4) financial status of patients; and one theme specific only to GPs: (5) minimum requirement for the prescription of EMs. ('Result' section, line 233-239, clean copy)

14. Page 11, line 224: What is the difference between evidence-based effectiveness and definite efficacy?

Answer: Thanks for your suggestions.

There are not difference between evidence-based effectiveness and definite efficacy. We have revised this sentence.

The contents revised are as follows:

The interviews showed that GPs were willing to prescribe medications with evidence-based effectiveness. ('Result' section, line 244-245, clean copy)

15. Page 15, line 329: "While, the NEMLs..." is not a sentence.

Answer: Thanks for your suggestion.

I have revised this sentence.

The contents revised are as follows:

The WHO recommended that EMs should be selected according to their evidence of efficacy and safety, while the NEMLs were formulated and modified by expert opinions and clinical experience ('Discussion' section, line 349-351, clean copy)

16. Page 15, line 337: What do the authors mean by "enterprises"?

Answer: Thanks for your suggestion.

It refers to pharmaceutical enterprises. We have revised this sentence.

The contents revised are as follows:

encourage pharmaceutical enterprises to carry out post-marketing evaluation of EMs. ('Discussion' section, line 358-359, clean copy)

17. Page 16, line 354: I don't understand what the authors mean by the phrase "they usually refill medicines rather than seek a doctor".

Answer: Thanks for your suggestion.

Patients in China usually associate large and prominent hospitals with high quality and professional medical care, and prefer to visit these hospitals for all spectrums of diseases. Most patients' first choice would still be the tertiary or secondary hospitals, when real health problems (e.g. fluctuant blood pressure) emerge. The biggest attractiveness of CHSCs for the patients seemed to be prescription renewal, and only small of the patients had a real problem to consult. Patients just want to refill their prescription rather than have a real problem to consult.

We have revised this sentence to express clearly. The contents revised are as follows:

Second, under the hierarchical medical system, although an increasing number of patients will visit CHSCs as their primary option, many simply want to refill their medications rather than consult a physician, as they do not have a real or urgent problem. ('Discussion' section, line 377-380, clean copy)

18. Page 16, line 369: There needs to be a reference for the statement that doctor-patient relationships in China are deteriorating.

Answer: Thanks for your suggestion.

We have added a reference for the statement that doctor-patient relationships in China are deteriorating. (Reference 54, clean copy)