Author's response to reviews

Title: Outpatient Prescription Practices in Rural Township Health Centers in Sichuan Province, China

Authors:

Qian Jiang (johnsoncat@126.com)
Bo Nancy Yu (yubn@cc.umanitoba.ca)
Guiying Ying (yingguiying@163.com)
Jiaqiang Liao (ljq19861023@163.com)
Huaping Gan (ganhuaping120@163.com)
James Blanchard (james_blanchard@umanitoba.ca)
Juying Zhang (juying109@163.com)

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Author's response to reviews: see over
Dear Editors,

Thank you for the interest in our manuscript entitled “Outpatient Prescription Practices in Rural Township Health Centers in Sichuan Province, China”. According to the comments of the four reviewers, we have revised the previous version of the manuscript. We hereby respond to the comments point-by-point as following.

We deeply appreciate your consideration of our manuscript, and we look forward to hearing from you soon. If you have any queries, please don’t hesitate to contact us at the address below.

Thank you and best regards.

Yours sincerely,

Qian Jiang, Bo Nancy Yu, Guiying Ying, Jiaqiang Liao, Huaping Gan, James Blanchard, Juying Zhang

Corresponding author:
Name: Juying Zhang
E-mail: juying109@163.com

Reviewer’s report 1 (No. 1969168580659325)
Reviewer: P Ravi Shankar

- Major compulsory revisions:
Comment 1. Page 3, background section, paragraph 1, kindly explain what is a township health center and its role in the Chinese healthcare system.

Response 1: We revised ‘Background’ in blue according to the reviewer’s suggestion. Moreover, we also added some information about the 4th National Health Services Survey (NHSS).

Revised part:

Since the founding of the People’s Republic of China in 1949, public health prevention and health care services have been organized around a three-tier health care delivery system. In urban areas, the three-tier network is composed of street clinics, district hospitals, and city hospitals. In rural areas, it consists of village clinics, township health centers (THCs), and county hospitals. The
basic features of this system remain the same up to date [2]. The THCs are at the central position of the rural three-tire network. Their missions are to provide basic medical and public health services for the locals, train health technical workers, and guide the village clinics and other health care facilities in rural areas. In 2001, a new policy, titled “The Guidelines on Rural Health Sector Reform and Development” and promulgated by the central government (State Council 2001), emphasized that each township should have the ownership of one health center which is supported by the local government. This policy gives the THCs the government-owned status with responsibility of providing basic health services for hundred millions of rural residents. The THCs play an important role in the national health service system for controlling infection diseases, improving the quality of health services and guaranteeing people’s health in rural areas of China, and were regard as one of the “three magic weapons (cooperative medical schemes, barefoot doctors and township health centers)” of the rural health services of China by WHO[3].

The Fourth National Health Services Survey (NHSS, 2008) was conducted when a new round of medical and health system reform was launched. In this regard, the main purpose of this survey is to provide basic information for the implementation and assessment of the new round of medical and health system reform, and to provide proofs for "Healthy China 2020" in its planning of objectives, targets and major action plans [4]. The second purpose of the survey is to evaluate the performance of health reform and development of the previous five years. In order to know the outpatient medication utilization in the primary health care institutions, to guide the rational use of medications, to reduce the cost of the prescriptions and to provide reference and information to support the health care reform for both local and central governments, the Ministry of Health of China (MoH) conducted the Outpatient Prescription Survey, as an additional part to the 4th NHSS in 2008.

Comment 2. Paragraph 3 and elsewhere money should also be stated in an international currency like US dollars for the benefit of international readers. The conversion rate of Yuan and US Dollars should also be stated.

Response 2: Revised as in the text and tables.

Comment 3. In the Background section, information about how primary healthcare is delivered in China is required. Are the township health centers run by the government and is consultation and medicines free for patients?

Response 3: We revised ‘Background’ with a brief introduction about the health care delivery system in China (see ‘Response 1’).

In 2001 the State Council promulgated a new policy, “Guidelines on Rural Health Sector Reform
This new policy emphasized that each township government is mandated to run one health centre. A township health centre provides basic health care services to rural residents. These services are partially covered by Rural New Cooperative Medical Scheme (NCMS), which is a government-run voluntary insurance program, combining household contributions with central and local government subsidies. Households covered by NCMS could receive reimbursement, and the cost coverage depends on the local government policy.

Comment 4. Page 4, Methods section: Kindly clarify whether the data the authors used came from the national survey. Did the authors carry out any survey of their own? Do the authors’ have to take any permission to use the national survey data for publication purposes?

Response 4: As revised in the text. We have clarified the data we used came from the 4th NHSS (see the first paragraph of ‘Methods’). The data used in the study was collected by Sichuan Health Information Center and West China School of Public Health of Sichuan University, which were responsible for data collection and analysis as contract units of the 4th NHSS. Juying Zhang, the corresponding author of this paper, worked as a statistic expert of the 4th NHSS, and most of the Chinese authors (Qian Jiang, Guiying Ying, Huaping Gan and Juying Zhang) participated in the implementation or data analysis of the 4th NHSS in Sichuan province. The authors have got the permission from the Center for Statistics Information, MoH of China to use the data for publication purposes.

Revised part:

The data used in this study came from the Outpatient Prescription Survey of the THCs in Sichuan Province, which was a part of the 4th National Health Services Survey (NHSS) of China in 2008.

Comment 5. Why were the particular dates of sampling chosen? The authors have to explain whether sampling from just four days will give a representative data and information about prescribing patterns. Were the prescribers aware that they were being monitored? What about ethical approval and ethical considerations of the study?

Response 5: As revised in the text. We have added a paragraph to ‘Method’ to explain the sampling method according to the reviewer’s suggestion.

Revised part:

Designed by an expert panel from the Center for Statistics Information, Ministry of Health (MoH) of China with Household Survey, Health Institution Survey, Prescription Survey and Medical
Staff Survey all packed in the 4th NHSS, the four sub-surveys were implemented in the same city/town/district at the same time. The three-stage probability proportion to size sampling method was adopted to ensure that about 1% of the population in each sampling province was included in the household survey, and a sufficient sample size obtained in the Health Institution Survey and the Prescription Survey. Prior to the formal survey, a pilot study was conducted by MoH of China. Results of the pilot study showed that the average number of daily outpatient prescriptions among THCs was about 25 per day. Statistical experts from the Center for Statistics Information, MoH estimated that 100 prescriptions sampled from each THC would be sufficient to represent the basic annual prescription practice of the THC. In short, the sampling method could both ensure adequate sample size and the representativeness of the sample. The selected four days in the Prescription Survey represented the four seasons: spring, summer, autumn and winter respectively on one hand. On the other hand, they also represented one day of a week, excluding weekends, statutory holidays and other special days.

Since the NHSS is a national survey organized by the MoH, all health institutions and individuals involved had responsibilities and obligations to cooperate with the investigators. The 4th NHSS was approved by the ethics committees of Center for Statistics Information, MoH. The Contract units, such as Sichuan University and Sichuan Health Information Centre, were only responsible for data collection and analysis. In addition, the Prescription Survey was completely anonymous, and fully took human rights and ethical issues into consideration when it was designed, so the prescribers would not care whether they were being monitored at all.

**Comment 6.** Page 4, disease distribution: It is true that the authors have taken samples from all seasons. However, one day is too short a period according to the reviewer and this may have affected the diseases observed in the study. How can the authors justify that these are the common diseases in the region’s population given their limited sampling period?

**Response 6: Please see ‘Response 5’.** This is one of the major limitations of this Prescription Survey. We have added this point to the last paragraph of ‘Limitations’.

**Revised part:**

In the process of the Prescription Survey of the 4th NHSS, MoH of China and provincial health bureaus took a series of measures to control the quality of the survey strictly. However, due to thousands of prescriptions were collected and only a small portion of questionnaires (5% of the total) were checked and reviewed, the misstatements or omissions, which we could not predict and avoid, might exist. **Further more, we could not collect prescriptions of the whole year.**
This may have affected the disease distribution observed in study because of the limited sampling period. All of aforementioned limitations may impact the results of the survey and our study.

Comment 7. Page 4, the cost should also be in US dollars for international readers.

Response 7: Revised as in the text and tables.

Comment 8. Page 5: What is Chinese patent medicine and why was it studied in the drug utilization survey?

Response 8: Chinese patent medicine, we called Zhongcheng Yao in Chinese, is a kind of traditional Chinese medicine. They are standardized herbal formulas. "patent" refers to the standardization of the formula. Specifically, Chinese patent medicine use traditional medicine and herb drugs as raw materials under the guide of pharmaceutical theory and is progressing into certain dose form according to the prescription book and confined method. Patents may come in the forms such as teapills, dripping pills, liquids, syrups, powders, granules, instant teas, and capsules. In China, all Chinese patent medicines of the same name will have the same proportions of ingredients, and manufactured in accordance with the PRC Pharmacopoeia, which is mandated by law.

Chinese patent medicine has a long history, and covers a wide variety of kinds and applications. The development of Chinese patent medicine has been based on clinical pharmacology and therapeutics. This development is one of the important components of Chinese medicine and pharmacy.

In China, Many of the Chinese patent medicines have been well-known and habitually and widely used, due to their features of curative effect, convenience and inexpensiveness. They are often used when a patient's condition is not severe and the medicine can be taken as a long-term treatment. So the utilization of CPM was included in the outpatient prescription survey of the 4th NHSS.

Revised part (in the first paragraph of ‘Utilization of Chinese patent medicine’):

Chinese patent medicine (CPM), we called Zhongcheng Yao in Chinese, is a kind of traditional Chinese medicine. "Patent" refers to the standardization of the formula. Specifically, CPM use traditional medicine and herb drugs as raw materials under the guide of pharmaceutical theory and is progressing into certain dose form according to the prescription book and confined method. Patents may come in the forms such as teapills, dripping pills, liquids, syrups, powders, granules,
instant teas, and capsules, just like western medicines. In China, Many of the CPMs have been well-known and habitually and widely used, due to their features of curative effect, convenience and inexpensiveness. They are often used when a patient's condition is not severe and the medicine can be taken as a long-term treatment. So the utilization of CPM was included in the Prescription Survey of the 4th NHSS.

Comment 9. Page 5: Why did the authors study the utilization of hormones? Which hormone preparations are the authors referring to?

Response 9: ‘Hormone’ was a mistranslation in the original manuscript. It should be translated as ‘glucocorticoids’. We found that there was irrational use or over-use of glucocorticoids in THCs in Sichuan indeed when analyzing the prescription data, so we believe ‘utilization of glucocorticoids’ should be a focus of our study.

The definition of ‘antibiotics’, ‘glucocorticoids’ and ‘injections’ in this article are consistent with the standard definition of the 4th NHSS. We have added a paragraph to the end of ‘Method’ to explain the definition.

Revised part:

The definitions of ‘antibiotic’, ‘glucocorticoid’ and ‘injection’ in this article are consistent with the standard definitions of the 4th NHSS. ‘Antibiotic’ refers to synthetic antibacterial medications and antimicrobial agents of non-plant components covering penicillin, medications of other anti-bacterial, anti-skin infection, anti-ophthalmic infection and anti-diarrhoeal that contain gentamicin, quinolones or other compound. Medications of anti-filariasis, anti-leprosy, anti-TB, anti-fungal and anti-malarial were not defined as ‘antibiotics’. Glucocorticoids’ refers to systemic glucocorticoid, excluding local glucocorticoid, such as some glucocorticoid applying topically. ‘Injections’ are exclusive of vaccination,. solvent, systemic or local anesthesia,. subconjunctival and retrobulbar injections.

Comment 10. Page 6, why has the national prescription system of China recommended an average of six drugs per prescription which is nearly three times the WHO recommended value?

Response 10: The WHO recommended value was an ‘optimal’ or a ‘theoretical’ standard. As many developing country with backward medical services, MoH of China developed ‘the Prescription Administrative Policy of China (2007)’ according to the practice and reality of China, which specified that the average number of medication per encounter must be no more than 5.
However, the average number of medication per encounter in China is gradually declining year by year. We believe that the MoH of China would modify and adjust the national standard after the 5th NHSS in 2013, and the new standard should be much closer to the WHO standard.

**Comment 11.** Page 7, are the authors able to suggest any possible reasons why prescribers use hormones and antibiotics together?

**Response 11:** As we stated in the ‘Limitations’ section, “The study is descriptive without in depth analysis of medications by name and dosage of specific medicines, and by physical condition of the patients. This is due to the fact that the Prescription Survey of the 4th NHSS didn’t collect such information.”, so the reasons for rural doctors prescribing both antibiotics and glucocorticoids together for certain infections which were not suitable for such intense treatment could not be explored in the survey. However, we believe there are several potential reasons behind the irrational use of medications (of course, including unnecessary and irrational co-prescribing of antibiotics and glucocorticoids in THC prescription practice) in rural clinic settings, and we have explained these reasons in ‘Results’ section.

**Revised Part:**

In summary, these results discussed above indicate that the irrational use of medications is a big problem for the rural THCs in Sichuan. In China, health centres in rural areas in general have poorer resources than district or city health facilities, and hence less likely to attract doctors with higher degrees or better experiences [1]. This evidence speculates some possible causes of irrational use of medications: (a) the rural medical institutions’ pursuit of maximizing the economic benefits, (b) the lack of medical skills and knowledge of rational medication use among rural doctors, and (c) the lack of basic medical devices and guidelines for diagnosis in primary health care institutions. The average cost in median per encounter in THCs of Sichuan was 16.30 Yuan ($2.59) in 2008, significantly lower than that of the national average 24.84 Yuan ($3.94) in the same period [18]. This suggests that the main reason for the irrational prescription practice in Sichuan province is not pursuing economic benefits, but the non-competency (lack of medical skills and knowledge) of doctors and shortages of the basic medical devices for diagnosis. According to the data from the Facilities Survey of the 4th NHSS of China (2008), in Sichuan Province, a large proportion of the health professionals in rural areas had relatively low education and low professional quality. Almost half (49.4%) of them in THCs had only technical secondary school education [32]. The average number of medical practitioners in THCs was lower than the national average (4 vs. 6), and the average number of assistant medical practitioners in THCs was
also lower than the national average (3 vs. 4) [18, 32]. Meanwhile, a considerable amount of the rural THCs in Sichuan still lacked basic diagnostic equipment. Only 24.1% of THCs were equipped with automatic biochemical analyzers, and 27.6% of them had spectrophotometers [32]. Furthermore, we analyzed the median number of CPM and western medicines prescribed per encounter among the 30 sampled THCs. The results showed more or less evenly distributed median number of CPM per encounter among the THCs, but an unevenly distribution of the numbers of western medicines prescribed per encounter (see Figure 1). This means the prescription practice for western medicine was not administered in the same pattern among these THCs. Thus, we speculate that the irrational prescription practice may also be related to the quality control on prescription practice in certain THCs. These data suggest that apart from taking some measures to advance the administration system and the regulations for the rational use of medications, the provincial government must take some effective and practical actions at the same time, such as providing further education and training programs (especially on the rational use of medication) for the rural doctors; improving hardware facilities of rural THCs to reduce the irrational medication use caused by lacking of diagnostic equipment. In addition, some Chinese scholars have suggested establishing a public reporting system to supervise the prescription practices of the doctors [33].

Comment 12. Who are the prescribers in the health centers studied? Are they doctors or paramedical personnel?

Response 12: In the rural township health centers of China, only medical doctors can prescribe medications.

Comment 13. Page 8, the use of the term ‘drug abuse’ is confusing. Internationally the term has a different meaning. Do the authors mean ‘irrational use of drugs’?

Response 13: Yes, it should be ‘irrational use of medications’, we revised it in the text. Thanks.

Comment 14. The Discussion section in many areas is rambling and not well focused. There are abrupt transitions from one sentence to the other and in many cases the authors’ writing is difficult to understand.

Response 14: Revised.

Comment 15. The authors have not stated their conclusions clearly in the manuscript though they have done so in the Abstract.
Response 15: Both conclusions in the manuscript and abstract have been revised.

Comment 16. The number of tables at seven I feel is too large. I feel four tables would be ideal and data from some of the tables can be mentioned in the text.

Response 16: Revised. We have merged some tables, and now there are only four tables and one figure.

Comment 17. In conclusion I feel the authors' have good data in their study but the data has not been well presented. The language needs significant improvement throughout the manuscript and the authors should take the help of a native English speaker to copyedit the manuscript. The presentation of the manuscript should be improved.

Response 17: Revised.

Comment 18. As the authors’ are considering an international journal as an outlet for their work they should compare their results with those found in health facilities in other developing countries. At present the references are mainly from China and in many cases the international reader is not provided enough background material to understand the significance of the results.

Response 16: Thanks for your suggestions. We have added a few reports and reference from other developing countries, such Cambodia, India and Pakistan in the ‘Discussion’ section. Further more, we have provided more information in both ‘Background’ and ‘Methods’ to help the readers to understand the results of our study.

Reviewer's report 2 (No. 1505566370661022)
Reviewer: Samir Malhotra

- Major Compulsory Revisions

Comment 1. Please give more information about township health center and rural preventive health care network in China.

Response 1: We revised ‘Background’ in blue according to the reviewer’s suggestion. Moreover, we also added some information about the 4th National Health Services Survey (NHSS).

Revised part:

Since the founding of the People’s Republic of China in 1949, public health prevention and health care services have been organized around a three-tier health care delivery system. In urban areas, the three-tier network is composed of street clinics, district hospitals, and city hospitals. In rural
areas, it consists of village clinics, township health centers (THCs), and county hospitals. The basic features of this system remain the same up to date [2]. The THCs are at the central position of the rural three-tire network. Their missions are to provide basic medical and public health services for the locals, train health technical workers, and guide the village clinics and other health care facilities in rural areas. In 2001, a new policy, titled “The Guidelines on Rural Health Sector Reform and Development” and promulgated by the central government (State Council 2001), emphasized that each township should have the ownership of one health center which is supported by the local government. This policy gives the THCs the government-owned status with responsibility of providing basic health services for hundred millions of rural residents. The THCs play an important role in the national health service system for controlling infection diseases, improving the quality of health services and guaranteeing people’s health in rural areas of China, and were regard as one of the “three magic weapons (cooperative medical schemes, barefoot doctors and township health centers)” of the rural health services of China by WHO[3].

The Fourth National Health Services Survey (NHSS, 2008) was conducted when a new round of medical and health system reform was launched. In this regard, the main purpose of this survey is to provide basic information for the implementation and assessment of the new round of medical and health system reform, and to provide proofs for "Healthy China 2020" in its planning of objectives, targets and major action plans [4]. The second purpose of the survey is to evaluate the performance of health reform and development of the previous five years. In order to know the outpatient medication utilization in the primary health care institutions, to guide the rational use of medications, to reduce the cost of the prescriptions and to provide reference and information to support the health care reform for both local and central governments, the Ministry of Health of China (MoH) conducted the Outpatient Prescription Survey, as an additional part to the 4th NHSS in 2008.

Comment 2. Provide information on costs in $ or any other international currency (as well) The indicators used are WHO indicators - this should be mentioned.

Response 2: Revised as in the text and tables.

Revised part (about WHO indicators, in ‘Methods’ section):

Topics of the outpatient prescription survey included: the number of the prescriptions, the distribution of the diseases, the utilization practice of different drugs and the cost. Seven indicators were described in this study: (1) diseases distribution (the top 10 common diseases); (2) average cost per encounter; (3) average number of drugs per encounter; (4) percentage of encounters with
antibiotic prescribed; (5) percentage of encounters with hormone prescribed; (6) percentage of encounters with hormone & antibiotic prescribed; (7) percentage of encounters with injection prescribed. Among the above indicators, (2)(3)(4)(5)(7) were WHO standard indicators [27].

Comment 3. What is meant by “The utilization of hormone”? Probably something else is what authors are trying to say (steroids?). For e.g. "COPD and pneumonia prescriptions with hormones were the highest" is not at all clear.

Response 3: Revised. ‘Hormone’ was a mistranslation in the original manuscript. It should be translated as ‘glucocorticoids’.

The definition of ‘antibiotics’, ‘glucocorticoids’ and ‘injections’ in this article are consistent with the standard definition of the 4th NHSS. We have added a paragraph to the end of ‘Method’ to explain the definition.

Revised part:

The definitions of ‘antibiotic’, ‘glucocorticoid’ and ‘injection’ in this article are consistent with the standard definitions of the 4th NHSS. ‘Antibiotic’ refers to synthetic antibacterial medications and antimicrobial agents of non-plant components covering penicillin, medications of other anti-bacterial, anti-skin infection, anti-ophthalmic infection and anti-diarrhoeal that contain gentamicin, quinolones or other compound. Medications of anti-filariasis, anti-leprosy, anti-TB, anti-fungal and anti-malarial were not defined as ‘antibiotics’. Glucocorticoids’ refers to systemic glucocorticoid, excluding local glucocorticoid, such as some glucocorticoid applying topically. ‘Injections’ are exclusive of vaccination, solvent, systemic or local anesthesia, subconjunctival and retrobulbar injections.

"COPD and pneumonia prescriptions with hormones were the highest" have been revised.

Revised part:

Among the top 10 common diseases, the highest proportions of prescriptions with glucocorticoids were for rheumatoid arthritis (42.86%), COPD (32.61%) and pneumonia (30.86%), which were much higher than other diseases (see Table 4).

Comment 4. Please provide more information on "national prescription system of China" - is it a National Formulary? (page 6)

Response 4: Revised. ‘National prescription system of China’ was a mistranslation in the original
manuscript. It should be translated as ‘the Prescription Administrative Policy of China’, Which was promulgated by the Ministry of Health (MoH of China) and implemented from May 1, 2007. We have revised it in the text.

**Comment 5.** "Otherwise, unnecessary use of antibiotics will give rise to side effects, high cost and other problems” (page 6). Add drug resistance.

**Response 5:** We have added ‘drug resistance’ to the sentence you mentioned in the second paragraph of ‘Discussions’ as your suggestion.

**Revised part:**

Otherwise, any unnecessary usage of multiple antibiotics will give rise to side effects, drug resistance, high cost and other problems [13-15].

**Comment 6.** I am not aware of the term "Chinese patent medicine" (I am sure other readers may feel the same); how is it different from Chinese traditional medicine? Please explain.

**Response 6:** Chinese patent medicine, we called Zhongcheng Yao in Chinese, is a kind of traditional Chinese medicine. They are standardized herbal formulas. “patent” refers to the standardization of the formula. Specifically, Chinese patent medicine use traditional medicine and herb drugs as raw materials under the guide of pharmaceutical theory and is progressing into certain dose form according to the prescription book and confined method. Patents may come in the forms such as teapills, dripping pills, liquids, syrups, powders, granules, instant teas, and capsules. In China, all Chinese patent medicines of the same name will have the same proportions of ingredients, and manufactured in accordance with the PRC Pharmacopoeia, which is mandated by law.

Chinese patent medicine has a long history, and covers a wide variety of kinds and applications. The development of Chinese patent medicine has been based on clinical pharmacology and therapeutics. This development is one of the important components of Chinese medicine and pharmacy.

In China, Many of the Chinese patent medicines have been well-known and habitually and widely used, due to their features of curative effect, convenience and inexpensiveness. They are often used when a patient's condition is not severe and the medicine can be taken as a long-term treatment. So the utilization of CPM was included in the outpatient prescription survey of the 4th NHSS.
Revised part (in the first paragraph of ‘Utilization of Chinese patent medicine’):

Chinese patent medicine (CPM), we called Zhongcheng Yao in Chinese, is a kind of traditional Chinese medicine. "Patent" refers to the standardization of the formula. Specifically, CPM use traditional medicine and herb drugs as raw materials under the guide of pharmaceutical theory and is progressing into certain dose form according to the prescription book and confined method. Patents may come in the forms such as teapills, dripping pills, liquids, syrups, powders, granules, instant teas, and capsules, just like western medicines. In China, Many of the CPMs have been well-known and habitually and widely used, due to their features of curative effect, convenience and inexpensiveness. They are often used when a patient's condition is not severe and the medicine can be taken as a long-term treatment. So the utilization of CPM was included in the Prescription Survey of the 4th NHSS.

Comment 7. Disease should be classified as per ATC or any other standard classification. For e.g. "female genital diseases" is not standard.
Response 7: The Classification of Diseases in this study comes from the “Classification table of Diseases” of the 4th NHSS of China, which classifies all the diseases into 132 categories.

Comment 8. More data on drug use should be given : which drugs, doses, DDDs, etc
Response 8: The Outpatient Prescription Survey of the 4th NHSS did not collect the information about the names and doses, DDDs, etc of the drugs, so more data on drug use could not be given in our study. We have revised this in the ‘Limitations’.

Revised part:

There are a number of limitations of the study. The study is descriptive without in depth analysis of medications by name and dosage of specific medicines, and by physical condition of the patients. This is due to the fact that the Prescription Survey of the 4th NHSS didn't collect such information.

- Minor Essential Revisions.
Comment: Grammatical errors at several places
Response: Revised.
Reviewer: Rashmi Kumar

- Major changes:

Comment 1. The investigators have mentioned that sampling was according to Probability proportionate to size, but the description is like 3 stage cluster sampling. More description is needed about the sampling method.

Response 1: We have added a paragraph to ‘Methods’ to explain the sampling method according to the reviewer's suggestion.

Revised part:

Designed by an expert panel from the Center for Statistics Information, Ministry of Health (MoH) of China with Household Survey, Health Institution Survey, Prescription Survey and Medical Staff Survey all packed in the 4th NHSS, the four sub-surveys were implemented in the same city/town/district at the same time. The three-stage probability proportion to size sampling method was adopted to ensure that about 1% of the population in each sampling province was included in the household survey, and a sufficient sample size obtained in the Health Institution Survey and the Prescription Survey. Prior to the formal survey, a pilot study was conducted by MoH of China. Results of the pilot study showed that the average number of daily outpatient prescriptions among THCs was about 25 per day. Statistical experts from the Center for Statistics Information, MoH estimated that 100 prescriptions sampled from each THC would be sufficient to represent the basic annual prescription practice of the THC. In short, the sampling method could both ensure adequate sample size and the representativeness of the sample. The selected four days in the Prescription Survey represented the four seasons: spring, summer, autumn and winter respectively on one hand. On the other hand, they also represented one day of a week, excluding weekends, statutory holidays and other special days.

Comment 2. Sample size calculation is not mentioned.

Response 2: Revised. Please see ‘Response 1’

- Minor changes:

1. English grammar and writing style need much improvement.
   Response: Revised.

2. The investigators have not studied the prescriptions all through the year. This should be pointed out in limitations.
   Response: Revised. We have pointed out this in ‘Limitations’.

3. There are too many tables.
   Response: Revised. We have merged some tables, and now there are only four tables and one
Reviewer's report 4 (No. 2111283688669512)
Reviewer: Adrian Sleigh
- Major Compulsory Revisions

Comment 1. We need more information in Methods on the NHSS prescription survey instrument. Who collected and reported the data, on what form, and with what training and supervision? Was the data collection form pre-tested and shown to be accurate? In particular, did the survey respondents have clear definitions of the various drug categories - especially 'antibiotics' and 'hormones'? Did 'antibiotics' include all antimicrobials? Did 'injection' include intravenous infusion? Can the authors define 'hormones' more specifically - do they mean 'corticosteroids'? If so that specific term should replace 'hormones' throughout the text.

Response1: We have added some information to ‘Methods’ according to the review’s suggestions. Before start the formal Prescription Survey, the MoH of China conducted a pilot study in the sampling provinces, and the results indicated that the data collection form was practical and accurate.

Revised part:

Designed by an expert panel from the Center for Statistics Information, Ministry of Health (MoH) of China with Household Survey, Health Institution Survey, Prescription Survey and Medical Staff Survey all packed in the 4th NHSS, the four sub-surveys were implemented in the same city/town/district at the same time. The three-stage probability proportion to size sampling method was adopted to ensure that about 1% of the population in each sampling province was included in the household survey, and a sufficient sample size obtained in the Health Institution Survey and the Prescription Survey. Prior to the formal survey, a pilot study was conducted by MoH of China. Results of the pilot study showed that the average number of daily outpatient prescriptions among THCs was about 25 per day. Statistical experts from the Center for Statistics Information, MoH estimated that 100 prescriptions sampled from each THC would be sufficient to represent the basic annual prescription practice of the THC. In short, the sampling method could both ensure adequate sample size and the representativeness of the sample. The selected four days in the Prescription Survey represented the four seasons: spring, summer, autumn and winter respectively on one hand. On the other hand, they also represented one day of a week, excluding weekends, statutory holidays and other special days.

‘Hormone’ was a mistranslation in the original manuscript. It should be translated as ‘glucocorticoids’. The definition of ‘antibiotics’, ‘glucocorticoids’ and ‘injections’ in this article
are consistent with the standard definition of the 4th NHSS. We have added a paragraph to the end of ‘Method’ to explain the definition.

**Revised part:**

The definitions of ‘antibiotic’, ‘glucocorticoid’ and ‘injection’ in this article are consistent with the standard definitions of the 4th NHSS. ‘Antibiotic’ refers to synthetic antibacterial medications and antimicrobial agents of non-plant components covering penicillin, medications of other anti-bacterial, anti-skin infection, anti-ophthalmic infection and anti-diarrhoeal that contain gentamicin, quinolones or other compound. Medications of anti-filarias, anti-leprosy, anti-TB, anti-fungal and anti-malarial were not defined as ‘antibiotics’. Glucocorticoids’ refers to systemic glucocorticoid, excluding local glucocorticoid, such as some glucocorticoid applying topically. ‘Injections’ are exclusive of vaccination., solvent, systemic or local anesthesia., subconjunctival and retrobulbar injections.

**Comment 2.** In the Limitations section there is no mention of possible measurement error. This possible error needs to be considered in the Limitations section and if it occurred some comment is needed on the impact of the error on study results.

**Response 2:** We have revised it in ‘Limitations’.

**Revised part:**

In the process of the Prescription Survey of the 4th NHSS, MoH of China and provincial health bureaus took a series of measures to control the quality of the survey strictly. However, due to thousands of prescriptions were collected and only a small portion of questionnaires (5% of the total) were checked and reviewed, the misstatements or omissions, which we could not predict and avoid, might exist. Further more, we could not collect prescriptions of the whole year. This may have affected the disease distribution observed in study because of the limited sampling period. All of aforementioned limitations may impact the results of the survey and our study.

**Comment 3.** 3. The locus of the survey needs to be clarified using standard Chinese terminology. I am not familiar with the term “Township Health Centre”? Where do they fit into the Chinese health system? Could the authors mean Village Health Centre. (staffed by village doctors) or perhaps Township (former commune) Hospital (outpatient care) staffed by Township Hospital Doctors? It may help to create a diagram showing at what level in the health care system hierarchy the survey took place.

**Response 3:** We revised ‘Background’ in blue according to the reviewer’s suggestion. Moreover,
Revised part:

Since the founding of the People’s Republic of China in 1949, public health prevention and health care services have been organized around a three-tier health care delivery system. In urban areas, the three-tier network is composed of street clinics, district hospitals, and city hospitals. In rural areas, it consists of village clinics, township health centers (THCs), and county hospitals. The basic features of this system remain the same up to date [2]. The THCs are at the central position of the rural three-tier network. Their missions are to provide basic medical and public health services for the locals, train health technical workers, and guide the village clinics and other health care facilities in rural areas. In 2001, a new policy, titled “The Guidelines on Rural Health Sector Reform and Development” and promulgated by the central government (State Council 2001), emphasized that each township should have the ownership of one health center which is supported by the local government. This policy gives the THCs the government-owned status with responsibility of providing basic health services for hundred millions of rural residents. The THCs play an important role in the national health service system for controlling infection diseases, improving the quality of health services and guaranteeing people’s health in rural areas of China, and were regard as one of the “three magic weapons (cooperative medical schemes, barefoot doctors and township health centers)” of the rural health services of China by WHO[3].

The Fourth National Health Services Survey (NHSS, 2008) was conducted when a new round of medical and health system reform was launched. In this regard, the main purpose of this survey is to provide basic information for the implementation and assessment of the new round of medical and health system reform, and to provide proofs for "Healthy China 2020" in its planning of objectives, targets and major action plans [4]. The second purpose of the survey is to evaluate the performance of health reform and development of the previous five years. In order to know the outpatient medication utilization in the primary health care institutions, to guide the rational use of medications, to reduce the cost of the prescriptions and to provide reference and information to support the health care reform for both local and central governments, the Ministry of Health of China (MoH) conducted the Outpatient Prescription Survey, as an additional part to the 4th NHSS in 2008.

Comment 4. Some relevant literature is missing from this paper (eg a paper by Sun X et al that I coauthored - ‘Prescribing behaviour of village doctors under China’s New Cooperative Medical Scheme’, Social Science & Medicine, Volume 68, Issue 10, May
2009, Pages 1775-1779; Some literature referred to by this SSM paper also is not mentioned), The authors need to check again for relevant Chinese literature on this important topic.

Response 4: Thanks for the review’s suggestion and advice. ‘Prescribing behaviour of village doctors under China's New Cooperative Medical Scheme’ is an excellent article and a valuable reference for our next study about the prescribing practice in village clinics in Sichuan Province. However, the research objects of that study are village clinics, and the research object of our study are THCs, they are not comparable since they are different primary health care facilities in rural medical services system of China (We have added a brief introduction about THC to ‘Background’ section in our paper, please see ‘Response 3’).