Author's response to reviews

**Title:** Epidemiology of multimorbidity and implications for healthcare: Cross-sectional survey among 162,464 community household residents in southern China

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**Version:** 2

**Date:** 28 August 2014

**Author's response to reviews:** see over
Re: Manuscript "Epidemiology of multimorbidity in China and implications for the healthcare system: Cross-sectional survey among 162,464 community household residents in southern China"

Dear Editor,

Thank you very much for the comments on the above paper and for giving us the opportunity to revise our manuscript for reconsideration by *BMC Medicine*. The comments raised by external reviewers have been addressed point-by-point, and the discussion has revised in order to strengthen it. The revisions to the paper are detailed below. We very much hope our responses are sufficiently comprehensive to convince the editorial team of the suitability of our paper for publication in *BMC Medicine*. We look forward to hearing from you in due course.

Yours sincerely,
On behalf of all authors

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Reviewer's report - Referee 1

Title: Epidemiology of multimorbidity and implications for healthcare: Cross-sectional survey among 162,464 community household residents in southern China

Version: 1 Date: 21 July 2014

Reviewer: Alexandra prados-Torres

Reviewer's report:

The innovativeness of this article is mainly due to the population studied, China, where epidemiology of multimorbidity is not described yet. The paper is well written and methodologically correct.

Our response: We are very grateful for your positive comments on the significance of the study topic and the methodology used in the study.

However, I strongly suggest the authors consider the following:

Minor revisions:

1) Methods. The authors mention that the study used self-report data from a large cross-sectional community household health survey. Those items from the National Health Services Survey (NHSS) 2008 included and analysed of this study should be clearly stated and provided as an annex, to ensure replicability. In fact it should be clarified if the information is directly gathered from the original questionnaire, or an “ad hoc” survey was conducted for this study.

Our response: We have now revised this section as "We directly used the questions in the original NHSS to collect information on demographics, socio-economics, lifestyle behaviours, and healthcare characteristics. The original close-ended question (consisting of fourteen chronic conditions) was modified into an open-ended question (‘Do you have any chronic conditions that have been diagnosed or treated by any healthcare providers within the past six months?’). The NHSS captured fourteen chronic conditions including: malignant neoplasm (cancer), diabetes mellitus, chronic rheumatic heart disease, angina pectoris, other forms of ischemic heart disease, pulmonary heart disease, hypertension, cerebrovascular disease, emphysema, chronic obstructive pulmonary disease (COPD), other forms of COPD, asthma, chronic liver disease and liver cirrhosis, and rheumatoid arthritis and disc disease. As per your instruction, we have provided additional information in Additional Table S1 where we listed the items from the NHSS and others, as well as those analysed in this study. Please see lines 99-103 and
2) Methods. The authors explain that “the selection of included morbidities was based on the methodology adopted in a previous UK study [3] and another systematic review [28] in which morbidities recommended as a core for international multimorbidity studies were listed. To take into consideration China’s healthcare context, major morbidities captured in the National Health Services Survey in China [25] were also included”. It is suggested that, in order to increase comparability among studies, Table S1 shows clearly those coincident/non coincident chronic conditions included in the multimorbidity count.

Our response: Thanks for your advice. We have now used superscripts in Additional Table S1 to indicate those chronic conditions listed in the UK study [Barnett K, Mercer SW, Norbury M et al. Lancet 2012, 380:37-43], the systematic review study [Diederichs C, Bergeret K, Bartels DB. J Gerontol a-Biol 2011, 66:301-311], and the National Health Services Survey in China [Center for Health Statistics and Information, Ministry of Health, P.R.China]. Please see Additional Table S1 for the revision.

Discretionary revisions:

3) Discussion. The authors say in the section about comparison with other studies that: “This is the first large scale study to examine the epidemiological pattern of multimorbidity…”. The term “pattern of multimorbidity” is commonly used among the scientific community to describe a specific aspect of multimorbidity, the presence of systematic associations among diseases. If this aspect of multimorbidity is not going to be addressed in the study, we recommend avoiding it the term this paper.

Our response: Thanks for your advice. We have deleted the item in the paper. Please see line 280 for the revision.

4) Discussion. In the limitations section, the authors mention that “health care use is only measured by usual source of healthcare.”, but no further discussion is made about the potential misclassification of individuals, neither about its impacts on the occurrence of multimorbidity. Further development and clarification regarding the findings related to this variable would be appreciated. Moreover, this limitation of the study should make the authors be very cautious when interpreting the results, especially
if, as stated in the paper, “the primary care-orientated healthcare reform is ongoing in China”.

**Our response:** We have now re-written this part as “The variable on health care use in the current study was based on the usual source of health care classified as either primary care or secondary care provider only. Given the ongoing primary care-oriented healthcare reform in place, the examination of aspects such as the use of different models of primary care providers, total healthcare cost, drug prescriptions, and missed healthcare use due to cost to the patient would be useful in future research”. Please see lines 306-310 for the revision.

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

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests

**Our response:** We have made efforts in language corrections throughout the manuscript, and thank you for your positive comments on the statistical methodology used in our paper.
**Reviewer's report - Referee 2**

**Title:** Epidemiology of multimorbidity and implications for healthcare: Cross-sectional survey among 162,464 community household residents in southern China

**Version:** 1  
**Date:** 4 August 2014  
**Reviewer:** Matthew M. Boulton

**Reviewer's report:**

Comments to the authors:

1. Thank you for asking me to review this paper. Multi-morbidity in the Chinese population is an important public health and medical issue. I provide general and specific comments to the authors as follows:

   **Our response:** Thank you for your positive comments on the significance and implications of the study topic.

2. Line 31-33: It would be helpful if the authors could relate chronic diseases to the overall causes of death in China while also providing some specific comparative prevalence figures for more common chronic diseases to provide a better context for the readership. Can you say more specific about the age structure of the Chinese population rather than just a generic statement about it aging?

   **Our response:** Thanks for your advice. We have now revised as "As the largest developing country in transition, chronic diseases have already become China’s most challenging health threat, accounting for 79% of all deaths, among which, cardiovascular diseases, cancer, chronic respiratory disease, and diabetes contributed to approximate 33%, 20%, 17%, and 1%, respectively [Source: Preventing chronic diseases: a vital investment: World Health Organization; 2005]. The demographic transformation in the aging structure is happening apace in China, where the proportion of the elderly aged 60 and above (12%) will exceed that of people aged 0–14 years by 2019, and is expected to grow to approximately 34% of its total population by 2050 [Source: Kowal P, Williams S, Jiang Y et al. Aging in Asia: findings from new and emerging data initiatives. Washington, D.C.: National Academies Press 2012, pp 415-437]. This will likely translate into substantial increases in the burden on health systems". Please see lines 31-34 and 46-49 for the revision.
3. Line 38: How are multi-morbidities unique in terms of the treatment burden relative to those with just one major condition and why is this important for China particularly?

**Our response:** We have elaborated that "however, most guidelines are planned and implemented using a single disease approach in which diseases are treated in isolation [Source: Fam Pract 2010, 27:1-2]. Multimorbid patients are often treated by a range of different healthcare specialists (for each chronic disease) especially in China where specialist care is dominant [Source: Health Affair 2008, 27:460-468]. This very often results in numerous different hospital visits, polypharmacy, repeated investigations and substantial treatment burden [Source: Lancet 2012, 380:7-9]". Please see lines 38-42 for the revision.

4. Line 48-51: This small bit of information on the CHCs is not really helpful (or necessary) unless it is further developed and you can say more about them to provide better context or just eliminate altogether

**Our response:** Thanks for your advice. We have eliminated this part of information to avoid redundancy.

5. Line 52: You need to elaborate on what you mean by gate keeper function as that could be interpreted several different ways

**Our response:** We have elaborated that "China’s primary care providers do not have a gate-keeper function, i.e., referral from primary care doctors to hospital specialists (secondary care providers) are not mandatory. Patients can directly consult a doctor in primary care or secondary care”. Please see lines 53-56 for the revision.

6. Line 54: This is the first mention of a secondary care facility, please explain/

**Our response:** Secondary care facilities refer to hospitals where physicians can see a patient directly without referral from primary care doctors. Please see line 54 for the revision.

7. Line 62-64: Although the authors allude to studies in other countries in terms of chronic conditions and healthcare utilization, this paper really doesn’t seem to address that. Rather it is a largely descriptive piece on multi-morbidity and the socio demographic associations with that but says relatively little specific about health care utilization across these different factors and has very little discussion devoted to that topic.
**Our response:** Thanks for your advice. Our study aimed to describe the epidemiology of multimorbidity in a large, nationally representative sample in southern China, and explores factors associated with multimorbidity and its association with the usual source of healthcare. We agree that it is largely descriptive, as was previous work from the UK published by our group in the Lancet (Barnett et al 2012). Given the fact that research into multimorbidity is at an early stage internationally, we feel that such descriptive work is important, especially in countries such as China which has a largely single-disease, episodic, and specialist-based approach to chronic disease management. We have now made reference in the discussion to a recently published study from Brazil, which showed that the implementation of nation-wide primary care approach substantially reduced morbidity and mortality relating to chronic diseases [Source: BMJ 2014, 349:g4014]. Another recent study showed that better continuity of care for those with chronic diseases may ultimately lead to lower episode-based costs, fewer hospitalisations and emergency department visits, and fewer complications [Source: JAMA Intern Med 2014, 174:742-748]. A generalist primary care-based approach is considered to be the most appropriate way to manage multimorbid patients as it provides a holistic approach with continuity and coordination of care [Source: Lancet 2012, 380:37-43]. Nevertheless, fragmentation of health care in China is common, and continuity of primary care is often lacking [Source: Health Affair 2008, 27:460-468]. The growth of the hospital specialist care during the past twenty years has widened the divide between primary care and secondary care [Source: Routledge Handbook of Global Public Health in Asia. Oxford, UK: Routledge publisher; 2014 April: 584-600]. Although China is encouraging the utilisation of primary care by giving insured patients preferential rates, those uninsured or with higher income, as shown in our study, appear to preferentially seek services directly at secondary care. This might reflect the fact that healthcare delivery in China is still dominated by secondary care [Source: Malaysian Family Physician 2013, 8:2-10], and specialists are often considered more trustworthy and skilful than general practitioners [Source: Brit Med J 2010, 341]. However, in other countries it has been found that multimorbid patients who rely on specialist services in secondary care have more difficulties with fragmentation of care [Source: Health Affair 2011, 30:2437-2448]. Thus we argue therefore in the discussion that developing a high quality primary care-based approach built on continuity, coordination and whole person care should be a top priority in China, especially in light of the growing issue of multimorbidity. Please see lines 253-267 for the revision.

8. **Line 76-78:** Who or what entity sponsored and/or paid for this survey….the Chinese government?
Our response: Yes, the survey was sponsored by the Department of Health, Guangdong province. Please see lines 78-79 for the revision.

9. Line 79-83: What was the relative contribution of each of these factors in terms of the actual selection the prefectures. The selection criteria need to be more fully explained including hospital ownership of the CHCs. The CHCs are governmental, are they not? No explanation was provided for the different operating models for CHCs so it is impossible to understand the implication of these being hospital run or owned.

Our response: Thanks for your advice. We conducted a large cross-sectional community household survey (sponsored by the Department of Health, Guangdong province) among approximately 5% of the general resident population of all ages in three prefectures in Guangdong province, southern China in 2011. The prefecture setting in this study are medium-to-small scale cities or towns consisting of fifteen-to-thirty districts with total household population size of around one-to-two million. These prefectures have characteristics similar to the national average in terms of population demographics [The Sixth National Population Census. National Bureau of Statistics of China, 2011], urbanisation rate (40.11 versus 34.71) [Source: China Urbanisation Rate Investigation Report: China International Urbanization Development Strategy Research Committee, 2011] and CHCs per unit population ratio (6.97 versus 5.74) [Source: China Health Statistics Yearbook: Ministry of Health. P.R.China, 2011]. CHCs that are government-owned and hospital-managed serve as the major primary care provider, which are regarded as a department within the hospital and typically functions as an outreach clinic”.

Please see lines 78-86 for the revision.

10. Line 83-90: So, was the unit of randomization the neighborhoods? How does the Neighborhood authority relates to the residential communities, does the former oversee the latter?

Our response: Yes. We used a multistage, stratified random sampling methodology for the selection of neighbourhood residential communities. In the first stage, all districts where community health centres (CHCs) were in place as primary care providers were selected as Primary Sampling Units (PSU). In the second stage, sub-districts within each PSU were randomly selected as Secondary Sampling Units (SSU). In the third stage, neighbourhood residential communities within each SSU were randomly selected as Tertiary Sampling Units (TSU). Households within residential communities were then
randomly selected from the household lists obtained from Community Neighbourhood Authority (a grass-roots administrative agency). This Authority oversees the residential communities for household registration. Please see lines 86-90 for the revision. The details of sampling were also shown in Additional Figure S1.

11. Line 93: Who oversees the NHSS, please provide more detail since this was a source of many of your survey questions.

Our response: The National Health Services Survey (NHSS) has been conducted every five years since 1993 and is overseen by the Center for Health Statistics and Information, Ministry of Health) [Source: Center for Health Statistics and Information, Ministry of Health, P.R.China, 2008, ISBN 9787811362619]. Please see lines 97-99 for the revision.

12. Line 116” It was not clear if “those unable to respond” were persons who were not home at the time or were persons who were unable to physically or cognitively unable to respond, please clarify and provide more detail since a fairly large percentage of your survey respondents were persons answering for the person of interest which introduces a number of other recall and related issues.

Our response: Thank you for your comments. We previously reported in the results section that "14.46% of total surveys were answered by householders/guardians on behalf of household members". We acknowledge that this is a fairly large percentage, and indeed it is particularly time- and resource-consuming to do repeated visits for more than three times to look for respondents who were absent from home at the time of visit, given the relatively large number of sample size (N=163,959) and the existing resources to complete this survey study which was cross-sectional in nature. We have now clarified as "for those who were absent from home at the time of visit (after two unsuccessful attempts) or those with cognitive difficulties, information was gathered from the householder or the guardian, whoever was most familiar with him/her". Please see lines 123-126 for the revision.

13. Line 199-120: How were medical records used to corroborate the survey and it would be important to quantify how often you were able to do this since you cite it as a methodology for reducing recall bias? It obviously important to know whether that was 10%, 25%, 50%, or 75% (etc) of the time because of the potential impact of doing what it was intended to do? How did the health care staff reconcile the two when there was disagreement between them, please provide some detail?
Our response: We have now clarified as "All respondents who self-reported the presence of chronic conditions were invited to examine their paper-based medical reports obtained from previous healthcare visits and annual check-ups to reduce recall bias. Conditions that were not reported by the respondents were reviewed by onsite-healthcare staff to supplement the information provided". Please see lines 126-129 for the revision.

14. Discussion section: I feel as if there isn’t too much surprising in your findings? The fact that persons have more multi-morbidities with age and unhealthy lifestyle choices is hardly new. Is there more you can say about your findings in terms its trajectory now that China has reversed the one child policy and the resultant long term changes that might occur with the age pyramid and in the context of the current age pyramid? How does the huge float (internal migrants) play into all of this since they tend to have worse health outcomes and less access to public health and health care services than the remainder of the population? Overall, the discussion feels underdeveloped given the richness of your data.

Our response: Thank you for your positive comments on the richness of our data. It is indeed well established from many studies around the world that multimorbidity is significantly associated with increasing age. With regard to the discussion from the one-child policy angel, China has an especially rapidly ageing population, as a result of not only improved longevity but also due to the one-child policy introduced in 1979 [Source: Kaneda T. Chinas concern over population aging and health. Washington, DC: Population Reference Bureau; 2006]. A drastic decline in the elderly-support ratio has been predicted, from 9 working-age adults (aged 15 to 64) per elderly (aged 65 and above) to only 2.5 by 2050 [Source: World Population Prospects. Sex and age distribution of the world population], i.e., there will be far fewer working-age adults to support a rapidly ageing population. As multimorbidity increases substantially with age, this is likely to further endanger the affordability of care in China where health care still largely relies on out-of-pocket payments, particularly for elderly people who likely have higher healthcare needs yet less affordability. The recent relaxation in the one-child policy may allow the health care of the elderly to be shared among more siblings and thus alleviate the burden on individuals in the long term. However, the high prevalence of multimorbidity in the elderly found in the present study is likely to challenge this, especially given the current preference for secondary care which is likely to be costly and duplicative.
The relationship between lifestyle factors and chronic conditions is of course well established, but the relationship with the co-occurrence of multiple long-term conditions has yet to be fully explored [Source: a Research Protocol by Ryan A, Galvin R, Fortin M, Smith SM (2014) Lifestyle risk factors and multimorbidity risk: a systematic review. PROSPERO 2014:CRD42014009593]. A recent Canadian study found a bivariate effect of smoking on multimorbidity, but there was a lack of association with physical activity or alcohol consumption [Source: BMC Public Health 14: 686]. In contrast, our study supported that the presence of unhealthy lifestyle factors including smoking, alcohol drinking, salty diet and physical inactivity significantly increased the likelihood of multimorbidity among the Chinese population. The between-study variance might due to the measurement of multimorbidity which only included fourteen frequent conditions in the Canadian study [Source: BMC Public Health 14: 686]. Nevertheless, both studies implied the need for a holistic and person-centred approach promoting healthy lifestyles as a prevention and intervention strategies to the management of multimorbidity.

We agree with your comments that migrant population might have worse health outcomes and poor access to health care due to the absence of social medical insurance coverage which was already captured in our study. We did not specifically look into the multimorbidity of the migrant groups who tend to have irregular source of care which is difficult to measure in an accurate manner. Also, such migrant groups only account for a limited proportion among the entire population in our study sites. We adopted the methodology that was similar to the National Health Services Survey (NHSS) to include only residents with household registry (a.k.a., "hukou", an official identification of a person as a regular resident of an area), such that a more accurate measure of usual source of care was available.

Overall, we have substantially re-written the Discussion section. Please see lines 203-211, 213-231, 233-242, and 254-268 for the revision.

15. Line 196-206: Much of this is just a recapitulation of your study design and is probably unnecessary. With careful editing, I think this paper could be easily edited down to a Brief Report format especially given the relative paucity of new findings.

Our response: We have re-written this section - "Relationship with other studies". However, we do not agree that a largely shorted paper in Brief Report format would be sufficient enough to provide readers of BMC Medicine with our study findings on the epidemiology of multimorbidity and implications for
healthcare given the richness of our data. From a global perspective, multimorbidity is the biggest
challenge facing healthcare systems around the world, and thus estimates of prevalence (despite the
inherent limitations) are required in different countries especially in China where there is limited
information on this among people who accounts for one fifth of the world’s total population. A very
recent systematic review synthesised the evidence on prevalence, determinants and patterns of
multimorbidity in 12 developed countries [Source: PLoS One 2014, 9:e102149], and pointed out that
knowledge on multimorbidity in other developing countries remains largely unknown. Moreover, in the
past five years, the published research literature has mainly focused on the prevalence and the impact of
single chronic diseases in China. China has and continues to experience an epidemiological transition of
chronic diseases which pose enormous challenges to the healthcare system and the government. Thus to
publish a large study (as far as we know the first) on a sample that appears to be nationally
representative across several demographic variables seems to us to be very important – for China and
for the international community. Following all your above comments, we have substantially re-written
the Discussion section and please see lines 203-211, 213-231, 233-242, and 254-268 for the revision.

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

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests

**Our response:** We have made efforts in language corrections throughout the manuscript, and thank you
for your positive comments on the statistical methodology used in our paper.
Reviewer's report - Referee 3

Title: Epidemiology of multimorbidity and implications for healthcare: Cross-sectional survey among 162,464 community household residents in southern China

Version: Date: 5 August 2014

Reviewer: Anne Taylor

Reviewer's report:

Thank you for the opportunity to review this paper. I found the paper interesting, well written and comprehensive and as such suitable for publication.

Our response: Thank you for your very positive comments on our paper.

Minor edits required include:

1. Abstract – conclusion – 1st sentence is clumsy; 2nd sentence – resources (plural). I also don’t think ‘lead’ is the right word. ‘Further resources to lead the management of multimorbidity’ is not a thoughtful conclusion. Everybody needs more resources! Resources won’t lead!

Our response: We have revised the conclusion section as "Multimorbidity is now common in China. The reported preferential use of secondary care over primary care by patients with multimorbidity has many major implications. There is an urgent need to further develop a strong and equitable primary care system." Please see the abstract section for the revision.

2. Background – Page 4 – last paragraph. Australasia is not a country (it is a region).

Our response: This is a typo - should be Australia rather than Australasia. We have corrected it accordingly. Please see line 63 for the correction.

3. Study design – Page 5 – line 89 – change survey to surveys

Our response: We have changed the word accordingly. Please see line 93 for the revision.


Our response: We have revised accordingly. Please see line 99 for the revision.
5. References – need capitals on Journal titles – eg Bmc should be BMC; JAMA: the journal – should be JAMA: The Journal.

**Our response:** We have updated the capitals on Journal titles as instructed. Please see the reference section for the revision. Thank you.

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests

**Our response:** Thank you for your positive comments on the quality of written English and statistical methodology in our paper.