Author’s response to reviews

Title: Variation of polypharmacy in older primary care attenders occurs at prescriber level

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Author’s response to reviews:

Dear Editor-in-Chief,

Please find attached a revised version of our manuscript "Variation in polypharmacy in older primary care attenders occurs at prescriber level", which we would like to resubmit for publication as research article in BMC Geriatrics.

Your comments and those of the reviewers were highly insightful and enabled us to greatly improve the quality of our manuscript. In the following pages are our point-by-point responses to each of the comments.

Revisions in the text are shown using yellow highlights. We also discovered some typographical errors in Table 4(a) and (b). Corrections were made and highlighted. These corrections however did not affect the results or conclusions of the study.

We hope that the revisions in the manuscript and our accompanying responses will make our manuscript suitable for publication in BMC Geriatrics.
We shall look forward to hearing from you.

Point-by-point responses

Reviewer 1:

Comment:

1. This is a cross-sectional analysis in a cohort of older adults in primary care in Malaysia, aiming to analyse associations between polypharmacy (defined in a numerical way as 5 or more medicines prescribed during the encounter) on the one hand, and patients, practice, and prescriber characteristics on the other hand.

The observed differences between public and private sector could well be caused by difference in case-mix, with differences in precisely the patient variables relevant to polypharmacy (gender, educational level, multimorbidity) between the two sectors.

Response:

Thank you. Please allow us to clarify. Differences in polypharmacy rates between public and private sectors are still observed after adjusting for patient, prescriber and practice characteristics in the final model (Model 3). We do agree that these remaining differences may be further explained by other unmeasured patient, prescriber and practice characteristics and this may be answered in further studies investigating reasons behind the prescription of multiple drugs.

Comment:

2. I would have liked to see some more discussion about the possible bias in data capturing the medication use, either because of
(i) reimbursement issues, or

Are medications not recorded because not reimbursed (benzodiazepines)?

(ii) software issues

Are all prescriptions electronically recorded during encounters?

Response:

We thank the reviewer for his comments.

(i) Reimbursement issues

We have edited part of the introduction and discussion to explain the potential bias arising from reimbursement.

Introduction page 4, paragraph 1, line 82

"Healthcare in Malaysia is provided by a government-subsidised public sector where patients pay a minimal charge of US$0.30 per visit, and a private sector which operates through fees for services."

Discussion page 13, paragraph 4, line 319

"Studies on drug use may be biased in settings with medication reimbursement policies [23]. In the present study, all medications provided within public health facilities were subsidised by the government. On the other hand, payment for medications in private practice is predominantly borne out of pocket by patients, followed by employer or third-party payers. In the latter,
reimbursement is capped at a maximum cost rather than number of items. We acknowledge that whilst this may be a possible source of bias, we expect it to be minimal because neither number nor types of medications were restricted."

(ii) Software issues:

We believe software issues are not applicable in this study because data is collected through paper-based primary data collection rather than from pharmaceutical reimbursement data or electronic medical records.

We have also revised the following sections to provide more clarity on this issue.

Methods: page 5, paragraph 1, line 104

"The sampled practices were randomly assigned a data collection day when all the encounters of the day would be recorded. Data collection was done using self-administered written standardised questionnaire. At the end of each consultation, prescribers filled the questionnaire with information on patient demographics, diagnoses and medications prescribed. Information on individual providers and the facilities were also captured in a separate questionnaire."  

Discussion: page 14, paragraph 3, line 340

"Electronic prescription records would enable longitudinal analysis of drug use in patients. However, this was not a feasible option for data capture because it is available in only about 60% of public practices and in half of the private practices, each using different proprietary systems [20]. With self-administered questionnaires, the limitation of selective reporting could not be eliminated."
Comment:

3. Were the authors only looking at the prescriptions during the encounter and not at the full list of chronic medication?

If only the prescriptions issued during a cross-sectional encounter were recorded, it is not sure that this is a good indicator of the full medication list of the patients, with additional chronic medications for which in that encounter no refills were needed.

Response:

Yes, we only look at the prescriptions during the encounter and not at the full list of chronic medication. We agree that this is one of the limitations of this study. We have added the following statements on study limitations.

Discussion: Page 14, Paragraph 3, Line 337

"As the NMCS was a cross-sectional study, only the medications prescribed during the current visit were recorded. Information on patients' full list of chronic medications was not available as patients were not required to be registered with a single primary care provider. Future studies looking at the full list of concurrent medications for chronic conditions are warranted."

Comment:

4. It seemed odd to me that so little use of psychotropic use was recorded in the public health sector. The distribution over drug classes is not the pattern that is expected and comparable to other studies. Could the authors elaborate on that? I am afraid this impacts heavily on the comparability of the results of the study, and its validity.

Response:
Low rates of psychotropic medication usage have been reported by others in Malaysia.

We believe there are two reasons why these low rates are being observed. First, there is low awareness of mental illness from both patient and provider end and second, psychotropic agents including opioids and benzodiazepines are subject to strict control under the Dangerous Drugs Act and ongoing enforcement activities.

We have added the following statements to elaborate on the rates of psychotropic drug use.

Discussion: page 13, paragraph 2, line 303

"Studies had shown that older persons were highly susceptible to inappropriate prescribing of psychotropic substances [42, 43], but this was not observed in this study. It is known that overall use of psychotropic drugs is very low in Malaysia compared to other countries [44]. There are two possible reasons why low rates of psychotropic drug use were observed. First, mental illness is under-recognised from both patient and provider perspectives in the local setting [45]. Second, psychotropic agents including opioids and benzodiazepines are subject to strict control under the Dangerous Drugs Act and ongoing enforcement activities [44]."

Comment:

5.

(i) Some mention could be made of recent studies linking polypharmacy to outcomes such as hospitalisations and mortality.

(ii) Some mention could be made of the attempts not only to quantify polypharmacy but also to appraise the quality of prescribing by using explicit criteria of (in)appropriate prescribing, and quantifying "misuse" and "underuse".
Thank you. We agree with the reviewer’s comments and the following statements have been added

Response:

(i) Introduction: page 3, paragraph 3, Line 71

"Polypharmacy was also shown to be associated with higher all-cause mortality rate [13] and increased unplanned hospitalisation [14] in older person."

(ii) Discussion: page 13, paragraph 3, line 313

"This underlines the need to look into the appropriateness of prescribing in this study population. Currently, there are ongoing efforts to quantify inappropriate prescribing of medication in primary care practices in Malaysia, especially looking at the usage of NSAIDS. A study by Khoo et al found that medication errors rates of up to 50% in Malaysian public clinics [47]. Therefore, further assessment on prescribing quality based on predefined criteria is necessary to determine areas for practice improvement."

Comment:

6. A small remark: in the introduction, It would be good to focus on demographical data of 65+ (not 60+) only and to give some examples of much greyer populations in Western Europe (e.g. with 17% of 65+ in 2016 in Belgium).

Response:

We agree with the reviewer and removed the part on older persons aged 60+ years.

It now reads:
Introduction: page 4, paragraph 1, line 78

"The global population of people aged 65 years and above will constitute about 17% in 2050 with nearly two-thirds residing in Asia [18]."

Reviewer 2:

Comment:

1. This study analysed the associated factors of polypharmacy in public and primary care clinics in Malaysia. However, most of the factors in the study have been known to be associated with polypharmacy

Response:

Thank you. We agree with reviewer#2 that patient factors are known to be associated with polypharmacy. However, its associations with prescriber and practice characteristics are less frequently assessed and medication prescribing is a process measure that is directly controlled by individual prescribers. We also determined the level at which variation in polypharmacy is greatest (patient, prescriber or practice). This will enable us to tease out the relevant level for targeting interventions.

We have revised the rationale of this study in the introduction.

Introduction page 4, paragraph 2, line 88

"Further, medication prescribing is likely to be influenced at patient, prescriber and practice levels. Determining the level at which variations in polypharmacy is greatest is important for targeting interventions. Two studies in Europe [25, 26] had studied the effect of higher levels on polypharmacy but such a study has not been done in a developing country. Identifying associated
factors at various levels would enable a targeted intervention to be developed to reduce polypharmacy. Hence this study aimed to determine the rate of polypharmacy among older primary care attenders in a developing country like Malaysia and examine its association with patient, prescriber and practice characteristics. We also intend to determine whether variation in polypharmacy is the greatest at the patient, prescriber or practice level.”

Comment:

2.

(i) There are no specifications regarding the multimorbidity in Table 1 and 2 and in

(ii) figure 1 the group of medication most frequently prescribed are just generally reported (only the five most prescribed are documented in the text).

Response:

(i) We thank the reviewer for pointing this out. We added footnote on definition of multimorbidity for Table 1 and 2, which have been relabelled as Table 1 and 3 respectively.

Results: pages 22 & 25

For Tables 1 and 3, the following footnote has been added

"Multimorbidity refers to having 2 or more chronic conditions;"

(ii) We acknowledge that listing the top 5 prescribed medications in the text may not be sufficient to describe the medications most frequently involved in polypharmacy. We have added
a table (Table 2, page 23) listing the top 20 medications by public and private sectors to give further details to the therapeutic groups listed in Figure 1.

Comment:

3 The readers would benefit from a more detailed description of methods used to collect data on diseases and drugs prescribed.

Response:

We have added further details on the methods to collect data on drugs and disease in the following sections:

Methods: page 5, paragraph 1, line 104

"The sampled practices were randomly assigned a data collection day when all the encounters of the day would be recorded. Data collection was done using self-administered written standardised questionnaire. At the end of each consultation, prescribers filled the questionnaire with information on patient demographics, diagnoses and medications prescribed. Information on individual providers and the facility were also captured in a separate questionnaire."

Discussion: page 14, paragraph 3, line 340

"Electronic prescription records would enable longitudinal analysis of drug use in patients. However, this was not a feasible option for data capture because it is available in only about 60% of public practices and in half of the private practices, each using different proprietary systems [20]. With self-administered questionnaires, the limitation of selective reporting could not be eliminated."