Author’s response to reviews

Title: Assessment of utilization pattern of fixed dose drug combinations in primary, secondary and tertiary healthcare centers in Nepal: A cross-sectional study

Authors:

Arjun Poudel (a3.poudel@qut.edu.au)

Mohamed Izham Mohamed Ibrahim (mohamedizham@qu.edu.qa)

Mishra Pranaya (mishramp2002@yahoo.com)

Subish Palaian (subishpalaian@gmail.com)

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Editor

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Dear Dr. Sherwin,

Assessment of utilization pattern of fixed dose drug combinations in primary, secondary and tertiary healthcare centers in Nepal: A cross-sectional study

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Thank you for the comments on our manuscript from the reviewers and for considering this revised version. We really appreciate the opportunity given to clarify our introduction and to expand upon our methodology and results, which we feel has resulted in a more thorough and quality paper.

We have attached two versions of the manuscript: one with track changes and one “clean” version.

The following are our point-to-point responses with the original reviewer comments:

Reviewer 1

Comment 1.1
Please describe all abbreviations in the first instance when they first appear in the manuscript and thereon only use abbreviations.

Response 1.1

This has been amended throughout the manuscript.

Comment 1.2

In all sections (PHC, SHC and THC) of age distribution in the text, keep consistency while describing the percentage of patients/prescriptions in each age group. The current description is inconsistent.

Response 1.2

The following change has been incorporated in the manuscript:

(Results section; pg. 10) Part I: Primary health care center

Altogether, 100 prescriptions were encountered from the PHC center. The median (IQR) age of the patients was 36 (18-60) years, and majority were female (64%). A total of 206 drugs were prescribed, of which 20.4% (n=42) were FDCs. Analysis of the prescriptions was further carried out based on study objectives.

(Results section; pg. 12) Part II: Secondary health care center

A total of 100 prescriptions were derived from the SHC center. The median (IQR) age of the patients was 33 (28-45) years, and majority were female (60%). A total of 309 drugs were prescribed, of which 30% (n=93) were FDCs. The prescription analysis was further carried out based on the study objectives.

(Results section; pg. 13) Part III: Tertiary health care center

Altogether, 100 prescriptions were encountered from the THC center. The median (IQR) age of the patients was 32 (19-47) years, and majority were female (66%). A total of 270 drugs were prescribed, of which 33.5% (n=91) were FDCs. Further analysis was carried out based on the study objectives.

Comment 1.3

Mention 'EDL' for 'Essential Drug List' of Nepal … on page # 11.

Response 1.3

This has been corrected in the manuscript.
Comment 1.4

The results of the data analysis in this study are confined to tables. Providing results as figures will have much greater impact. Moreover, this will be very convenient for a reader to make direct visual comparison of prescription patterns, use/prescription of FDCs etc… Hence pictorial representation of results is suggested to improve the quality of the paper.

Response 1.4

We totally agree with the suggestion. The authors have prepared figures 1-8, instead of tables.

Comment 1.5

Some sections of manuscript need improvement of grammar, hence it is recommended to take a look of the entire manuscript for improvement.

Response 1.5

We have gone through and improve the grammar and language. You could see that major changes had been done on the ms.

Reviewer 2

Comment 2.1

Why you choose only 100 from each center as sample?

Response 2.1

A pilot study was conducted by our team to study the utilization pattern of FDCs in one of the PHC in Western Nepal. The PHC center had an average patient flow of 20 patients per day. However, we encountered that majority of patients returned empty handed because of the scarcity of medications and we were not able to generate information despite having multiple visit to the center. The PHC study site selected in this study had a similar scenario.

Considering the short timeframe of data collection and unavailability of required information in every alternate day visit, sample size was limited to be 100 prescriptions per settings. We could argue that the scenario might be different in SHC and THC that carter the health care need of large number of patients and hence sample size can be increased. However, we confined to a uniform sample size (n = 100) from each healthcare centres since our aim in this study was to analyse and compare the prescription pattern and costs differences between different levels of healthcare centres.
We are aware that this 100 prescriptions may not represent the overall scenario of the total population attending each healthcare centres. Hence, this was mentioned in the ‘study limitations’ section of the manuscript.

Comment 2.2

Please add new relevant references to your discussion?

Response 2.2

The following sentences and new references are added in the ‘introduction’ section (pg. 4) of the manuscript.

“Several interventions have however, been initiated such as the banning of irrational combinations, market withdrawing and ceasing the manufacturing of IFDCs [10, 11]. Despite these interventions, IFDCs are still available in the market and are used extensively. The interventions are not successful due to several reasons. One such reason relates to exporting of FDCs that are banned in a particular country to the neighboring countries [12]. Such exports hinder the interventional process of government or individuals trying to weed out irrational combinations from their country. “

New references added:


Comment 2.3

There are references as old as more than 20 years back? Please re look into this thoroughly

Response 2.3

The older references are updated with newer ones throughout the manuscript. This has also been addressed in reviewer’s comment 2.2.

Comment 2.4

Please clearly highlight future strategies and recommendations.
Response 2.4

The following section has been added in the manuscript (pg. 20)

“Recommendations: Educational interventions to improve prescribing at different levels may be required. There is a need to strengthen the mechanism for continuing professional development of practitioners to ensure that they possess the necessary skills and knowledge to prescribe rationally. Government agencies and non-government health organizations should take a lead in this initiative. The medical and pharmacy schools must take the responsibility to train their students and young practitioners the way to access new combinations more logically and should be based on evidence. There is also need for adequate awareness program for the consumers to be aware of the hazards of irrational FDCs with careful monitoring and censoring the misleading claims by pharmaceutical industries. Further studies over a long period of time are required to provide a baseline data of utilization of FDCs which will be beneficial for future longitudinal studies. Extensive studies on comparison between the private and government healthcare centers are urgently required.”

Reviewer 3

Comment 3.1

It is unclear to non-specialized readers the reason why FDCs are considered inappropriate a priori. Likewise, a low use of essential drugs does not necessary mean lack of appropriateness, especially in developing Countries. This should be justified and discussed by the authors. In other words, is there a proof (from previous studies) that FDCs are actually unnecessary? In this context, to claim inappropriateness, a clinical diagnosis is needed. I notice that the authors do have this information from the encounter form, but no data are presented. Presentation and discussion of these data would strongly increase the impact of the paper and I encourage the authors to provide and discuss them.

Response 3.1

The categorization of rational and irrational FDCs is now mentioned in the ‘introduction section’ (pg. 4) of the manuscript.

We agree with the reviewer’s comment that- low use of essential drugs does not always relate to inappropriateness. To highlight this issue in the manuscript we have added following sentence in ‘discussion’ section (pg. 19)

“Although a low usage of FDCs from essential drug lists does not always suggest the inappropriate use, the low prevalence of prescribed FDCs from the established guidelines and formularies in this study (despite being available free or at low cost by governments), indicate that their use was poor leading to the irrational use of other FDCs that has no any established therapeutic justification.”
Comment 3.2

The study is based on a limited sample of patients interviewed 8 years ago (2009). The authors should comment on this aspect, because it is plausible that current situation is different from the setting data were obtained. This should be considered at least as a limitation and discussed accordingly.

Response 3.2

We agree with the reviewer’s comment. The following sentence has been added in the ‘study limitation’ section (pg.20) of manuscript.

“All, this study was conducted few years back in 2009; the current trends on medication use, their prevalence and availability might differ now as several interventions might have been initiated to minimize the use of FDCs.”

Comment 3.3

A number of tables are presented. However, I believe that many of them can be re-arranged or, alternatively, provided as supplementary material to avoid duplication of the information with the text. Accordingly, the results section can be modified by removing some of the headings.

Response 3.3

This has been modified as suggested- part of which are responded in reviewer’s comment 1.4.

Comment 3.4

Minor Aspects

Response 3.4

All the suggested changes are incorporated in the manuscript.