Author’s response to reviews

Title: Adherence to treatment and related factors among patients with chronic conditions in primary care: A cross-sectional study

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Version: 2 Date: 17 Aug 2019

Author’s response to reviews:

Shlomo Vinker, MD, MHA

Associate Editor

BMC Family Practice

August 18, 2019

Dear Dr. Vinker,

Please find enclosed an amended version of the manuscript entitled “Adherence to treatment and related factors among patients with chronic conditions in primary care: A cross-sectional study”, which we would like to resubmit for publication as a Research Article in BMC Family Practice.
We want to thank you and the reviewers for the thoughtful comments and constructive suggestions. They have been a great help to improve the quality of the manuscript. We have considered all the suggestions and modified the paper in response to the extensive and insightful reviewers’ comments. We have rewritten some paragraphs of the discussion and conclusion section to emphasize the importance of the role of the pharmacist in primary care and how the findings of the study contribute to the existing literature.

A point-by-point response to the reviewers’ comments has been enclosed as well as a tracked change version of the manuscript. We hope that the revisions in the manuscript and our accompanying responses will be sufficient to make our manuscript suitable for publication in BMC Family Practice.

We look forward to hearing from you at your earliest convenience.

Respectfully,

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Ref: FAMP-D-19-00153R1
Title: "Adherence to treatment and related factors among patients with chronic conditions in primary care: A cross-sectional study"
Journal: BMC Family Practice

TECHNICAL COMMENTS

Comment:
1) Please include email addresses of authors in title page.

Response:
We have now included email addresses of authors in the title page.
Comment:
2) Please include Figure Legends Headings.

Response:
To improve in clarity, we have now modified the figure legend as suggested.

REVIEWER COMMENTS

R Nascimento (Reviewer 1)

Comment:
1) I've revised the new manuscript and the authors' response. The main points have been addressed.

Response:
We want to thank the reviewer for the previous suggestions that helped to improve our manuscript.

Eric Kam Pui Lee (Reviewer 3):

Comments:
1) Thank you for this opportunity to review the manuscript. This is a cross-sectional study to determine the proportion of patients with chronic diseases who had good drug adherence and associated factors in primary care in Spain. It is generally well written, however,

Introduction

I think the knowledge gap needs to be highlighted more clearly. The authors are correct that the subject of drug adherence has been extensively studied, especially for individual chronic diseases; and these studies found different important factors. And then the author said that things may be different for people with multiple diseases and these diseases may interact together. And that Spain had highest prevalence of multimorbidity.

(i) If things are different for people with multiple diseases, then only people with multimorbidity should be included in this study. But this is not the case
If there is any pre-specified hypothesis or aim, this should be made clear in the introduction or objective section. No primary or secondary objectives were listed.

Response:

The reviewer stated that we “said that things may be different for people with multiple diseases and these diseases may interact together. And that Spain had highest prevalence of multimorbidity”. We want to clarify the reviewer our statement in lines 83-94. In these paragraphs we stated that “a series of factors, rather than a single one, determine patients’ ability to follow treatment recommendations correctly” and we stated that these factors, rather than multiple diseases as the reviewer suggested, “interact and potentiate each other’s influence in a framework determined by five dimensions” according to the WHO (1). The authors believe this statement is clear but are open to make any change if the reviewer thinks it needs improvement.

Furthermore, we believe the rationale of our study is strong because of the following arguments:

- The current rates of adherence to medication therapies remain low in developed countries (lines 78-82)

- Most of the existing research in adherence has focused on a single dimension-factor and has not taken into account the WHO framework (the social and economic, health-care team and system-related, condition-related, therapy-related, and patient-related factors) (lines 95-102).

- Many other studies have focused on a single-disease which limits the utility of the findings to the condition under study (lines 99-102).

- Primary care settings are ideal places to perform adherence studies because they offer more accurate results and minimize selection bias (lines 107-110).

- No studies, according to our knowledge, have used a multi-dimensional approach to evaluate factors associated with medication adherence in primary care settings in Spain (lines 285-287).

In summary, our study took into account the WHO framework and considered patients with one or more chronic condition in primary care settings, as multimorbidity is very common but not always occurs (3). A small percentage of the general population suffers from only one chronic condition (3–5) and that’s why the authors decided to include patients with one chronic condition. In our study 33 patients (11.04%) had one chronic conditions (information did not include in the manuscript), which is very approximate to the percentages found in previous research. Furthermore, we considered a significant number of chronic conditions in our study (Table s1) in a country with high prevalence of multimorbidity among adult population (4–6), which makes more accurate results.
We believe these arguments justify the rationale of our study and we also believe that our rationale is strong and the knowledge gap is clear.

Lastly, we believe the aims of the study are well-describe and do not need any change.

Comment:

2) Population and sampling

Despite the author said "we accepted an expected proportion of the participants not adhering to prescribed medications of 75% [23,24]", this is not consistent with the hypothesis the authors are having. In the introduction, they have said that "only half of patients with chronic conditions, however, take their medications as prescribed" and in the discussion from line 292 to 302, most of the previous studies found that the proportion of good adherence is around 39-50%.

The choice of using 75% with a confidence interval of 5% (rather wide), and that the results of proportion of good adherence in this study of around 50% has made this study underpowered. As this cannot be changed, this must be discussed as one of the weakness of this study.

Response:

We chose a 75% of prevalence of medication non-adherence based on the findings of previous studies (7,8) that had similar methodology and population to our study. These studies were conducted in Spain and Italy (country with a similar healthcare system to Spain), among people with multiple chronic conditions, and used the same instrument to measure adherence (the Morisky-Green-Levine Questionnaire). However, we agree with reviewer that our results might be "underpowered" due to the difference between the reference level of non-adherence used to calculate the sample size and the final findings. We have now incorporated this matter in the limitations section as the author suggested: “Lastly, the reference proportion of participants not adhering to prescribed medications proposed to calculate the sample size of the study differs from the final findings, which may somewhat underpowered our results.” (lines: 385-387).

Comment:

3) Outcome measurements

As the primary outcome is drug adherence (I suppose), the author rather need to justify strongly why other drug compliance detection method is not used, e.g. detection in blood stream/urine, automatic detection bottle etc.
Response:

We have now justified the use of the Morisky, Green, and Levine Self-Reported Medication Questionnaire in the methods section as follows: “This method is simple, easy to implement, and has the ability to identify reasons underlying the medication adherence behavior. Furthermore, it has been widely used in a large amount of studies and clinical settings.” (lines: 165-168).

Comment:

4) Specificity of around 40% should not be considered as GOOD psychometric properties as said in discussion section.

Response:

We appreciate reviewer’s concern and we have now modified this matter in the discussion section as follows: “Nonetheless, the Morisky-Green-Levine questionnaire has yielded good fair psychometric properties (sensitivity = 0.81, specificity = 0.44), and provided a useful tool to evaluate medication adherence in numerous chronic disease studies” (lines: 376-378).

Comment:

5) Discussion

The authors need to highlight what new knowledge has been generated. The proportion of good adherence is similar to previous study and it is not surprising that good knowledge leads to good adherence.

Response:

We thank the reviewer for the suggestion. We have now amended the discussion section to emphasize the importance of the role of pharmacists in the context of medication adherence and we have highlighted how the findings of our study contributes to the existing literature.
Comment:

6) Minor comments, some sentences need clarification

- on line 134, "after screening, research assistants randomly approached potential participants presenting...", what's the screening about?

Response:

We thank the reviewer for the suggestion. The screening refers to “candidates’ screening” as it is explained in the previous sentence: “The investigators screened potential candidates for participation at each center. After screening, research assistants randomly approached potential participants presenting at the centers for follow-up consultations....” (lines: 137-140). To improve in clarity, we have address this matter as follow: “The investigators screened potential candidates for participation at each center. After candidates’ screening, research assistants randomly....”

Comment:

7) - on line 254, "the level of high adherence to treatment according to.... was 55.5%. This is not easy to be understood. Perhaps, may consider use the word "the proportion of patients with high adherence...."

Response:

We totally agree with reviewer and have modified the sentence as suggested: “The proportion of adherent patients to treatment according to the Morisky-Green-Levine questionnaire was 55.5% (lines: 258-259).

Michal Shani, MD MPH (Reviewer 4):

Comment:

Treatment adherence is an important issue in chronic care and this study adds information about factors associated with medication adherence.

The authors addressed most of the issues.
The results indicated that the number of pharmacies used for refilling prescriptions treatment adherence decreased. It seems more accurate to address the role of pharmacist in the primary care team than the pharmacy itself or the computerized system that should be used.

Response:

We thank reviewer for the suggestions. The computerized system approach was suggested by reviewer #1 in the previous review. We agree with reviewer that addressing the role of pharmacist in the primary care team may more approachable. Based on this, we have now modified the discussion section and focused on the importance that the pharmacist may have in the primary care team.