Author’s response to reviews

Title: Effectiveness of treatment of newly diagnosed hypertension in family medicine practices in South Croatia

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Author’s response to reviews:

Ms. Shlomo Vinker
Associate Editor
BMC Family Practice
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Re: Response to review of Manuscript FAMP-D-18-00254

Dear Editor,

We would like to thank you and the reviewers for the time and effort put into assessing our manuscript entitled “Treating newly diagnosed arterial hypertension: why primary care matters”.

We are very grateful for your valuable feedback and believe that the reviewers’ comments and remarks have identified important areas which required improvement for the overall clarity and presentation of the manuscript. We considered carefully all comments and suggestions and we revised our manuscript accordingly, marking all changes in red. Below, we provide a point by point description of how each reviewers’ comment was addressed in the manuscript.

Reviewer #1 (Christos Galanakis):

Please include all comments for the authors in this box rather than uploading your report as an attachment. Please only upload as attachments annotated versions of manuscripts, graphs, supporting materials or other aspects of your report which cannot be included in a text format.

Please overwrite this text when adding your comments to the authors.

Response:

Not applicable.

Reviewer #2 (D Toprak):

The manuscript is a good one as the issue and main aims. It has also a lot of data that can be used. However there are some main absent points those must be cleared:

- T test was used for bp changes which compairs the average of two groups. However we can not see how many of the patients were controlled and how many of them continued with high load pressure. I mean that also categorized data should be evaluated with chi-square test.

The blood pressure values should be classified as normotension and grouped high BP; and than cross tabs those show BP changes regarding living place, gender, age groups, education and economic status. Although antihypertensive drugs were listed, we can not see the results that show which one is the most effective after one year. Also although systolic bp was mentioned it
would be better to add a Table that shows affects of treatment on diastolic and systolic bp seperately (chi-square; to see how many patients continue with high bp or normal bp)

It would be better to write % and n together.

Response:

We appreciate the reviewer’s positive feedback on the manuscript. With respect to the advice, we performed the statistical analysis suggested. Our newly added three tables, Table A.1, A.2 and A.3 in the Additional File 1, reflect the comparison of general features and antihypertensive treatment between the patients who were normotensive one year after the initial diagnosis and the patients who did not achieve the targeted blood pressure. However, we did not find any significant difference considering living place, age, sex, employment, educational and marital status, or prescribed pharmacological subgroup or particular antihypertensive drug between hypertensive and normotensive patients after one year (all P-values >0.05). Accordingly, we addressed this issue in the Results section, by expanding the subsections entitled “Hypertension control” and “Drug prescriptions”. We highlighted antihypertensive drugs that were the most commonly prescribed among normotensive patients in the monotherapy group or in relation to overall prescriptions.

We also show in the revised manuscript that significantly lower proportion of patients continue with high blood pressure after one year, considering the definition of participants as hypertensive at the time of the study (mean systolic and/or diastolic pressure ≥140/90 mmHg). Regarding the reviewer's suggestion for writing percentage with n, we ensured this in the body text of the revised manuscript where applicable.

Reviewer #3 (Larry A. Green):

1) This historical cohort study exploits a nice natural distribution of patients and there care in different parts of Croatia and makes important contributions and is interesting to both public health and primary care clinicians/family physicians in particular.

Response:

We thank the reviewer for acknowledging the contribution of our manuscript and for providing comments which helped us strengthen the manuscript to its current form.

2) The title needs attention; it presently invites readers to learn about the importance of primary care and it is really about effects of treatment of newly diagnosed hypertension.

Response:
With respect to the reviewer’s advice, the title is now changed to “Effectiveness of treatment of newly diagnosed hypertension in family medicine practices in South Croatia” in the revised manuscript.

3) There is a good opportunity to enrich the introduction and discussion with data about the role of family physicians in Croatia and internationally recognized research about the importance of primary care. Indeed, the data presented set up a conclusion that primary care matters in Croatia and is capable of making important contributions to individual and population health. A very nice contribution indeed, if so developed.

Response:

We thank the reviewer for the suggestion; we have expanded the Introduction and Discussion section accordingly.

4) Methods: Early on and consistently throughout, declare that this paper measures and reports the cost of pharmacotherapy of newly diagnosed hypertension comparing the diverse settings of Croatia. This report is not about the cost of treating hypertension—as belatedly acknowledged near the end of the paper. There is nothing wrong with this limited focus; it just needs to be honored and sentences that make claims about "cost of tx" must stay within this definition.

Can you provide numbers for the initial sample from the records in the practices and then how many were excluded, and then showing the resulting study population? The tables showing demography of the patients are good; can you provide fuller description of the practices from whence the study population came—how big, how many doctors/staff, long-standing or newly established, perhaps taking an approach similar to published standards for reporting implementation studies in primary care practices (sometimes called "Dissemination and Implementation" research). Illuminate the nature of the National Insurance Fund for unfamiliar readers and further explain the importance of the difference between fully covered and partially covered drugs.

Response:

a) We thank the reviewer for the discerning comment related to the cost of hypertension treatment. It was already emphasized at the end of the Discussion section that our definition of the annual cost of treating one newly diagnosed hypertensive patient should not be interpreted as the cost to healthcare systems and society within a classical pharmacoeconomic evaluation. To avoid any possible confusion, we completely deleted the phrases “economic cost” and “economic analysis” in the revised manuscript. We agree with the reviewer that this calculated
cost of drug treatment should be reported and perceived as the secondary outcome measure; we hope we now clearly express this point in the revised manuscript.

b) Since this is a historical cohort study, family medicine physicians included in the study selected and extracted data from their family medicine offices files only for patients that were eligible for inclusion according to the established criteria, disregarding all other data.

c) We expanded the subsection Study participants and data collection of the Methods section in the revised manuscript to highlight the way included primary care practices function in Croatia.

d) Regarding the reviewer’s constructive remark to ensure general information on the Croatian Health Insurance Fund and further explain its role in the Croatian healthcare system, we introduced a new paragraph in subsection Main outcome measures of the Methods section and added a new sentence in the Discussion section. We believe these all changes improved the readability of the manuscript, so we thank the reviewer for the valuable suggestions.

5) The bias introduced concerning thiazides--only available in combinations—is quite important and if possible, you might explain/comment on how this may have distorted your findings and whether or not you think it is important in drawing your conclusions. It seems to me that by definition, a clinician prescribing a thiazide is deciding to use a two-drug regimen, perhaps to initiate treatment, whereas a clinician starting with an ACE inhibitor only is deciding to commence treatment with a one drug regimen--an important clinical decision that is subject to guideline recommendations.

Response:

We thank the reviewer for identifying this area of potential ambiguity. Abiding with this suggestion, we introduced a new sentence in the Discussion section of the revised manuscript.

6) Back to the importance of primary care, given what your study shows: Don't you have evidence that supports confirming that Croatia's family physicians in the countries diverse settings are capable--of diagnosing and managing hypertension, and already are succeeding in establishing control for more than half of their diagnosed patients; AND at the same time calling out the gap in treatment of recognized hypertensive patients that can be closed to good effect???? How good could this get? And what steps might be taken to help family physicians detect more of their patients with hypertension and get a larger proportion under control? Here lies important implications worthy of publication.
Response:

We thank the reviewer for the remark. One of the most important implications of our study is definitely the key role family medicine physicians have in hypertension management in Croatia. In the Discussion section we aimed to compare the prescribing pattern with recommendations from current clinical practice guidelines, without diminishing achieved success of physicians in AH control. We agree with the reviewer that the detection of high blood pressure is the area for possible improvement. However, in this research, with focus put just on the treatment and control of already diagnosed hypertensive patients, we did not evaluate that first step, and these issues definitely present the basis for our planned further studies. Nonetheless, we introduced a new paragraph in the Discussion section, notifying that the prevalence of arterial hypertension in family medicine practices in Croatia is lower than the population prevalence.

7) If readily available, might you compare the costs of drug treatment that you define in Croatia to reported costs in other countries? This is an opportunity to comment on whether these costs are small or big, comparatively. This comparison would be similar to the comparisons of control numbers you cite in references 14, 33, 34, 35, 36, 37. A nice package of relevant published numbers that position your research and show its importance.

Response:

We thank the reviewer for the insightful comment; we agree that the comparison of costs would place our findings in an appropriate context. However, as we already stated in the response to the reviewer's #4 comment, our definition of the annual cost of prescribed treatment was not equal to pharmacoeconomic outcomes evaluation reported in several other researchers, and therefore not comparable. Nonetheless, we already found and cited in the Discussion section one European study which estimated the cost of antihypertensive drugs in general practice in the equal way as we did (price of box times number of boxes prescribed).

8) The paper is well written and easy to understand. There are a few minor edits related to English that can readily be addressed and at least a couple that are probably substantive, e.g. in methods "input data" probably means "demographic data" and in the conclusion "convergence" probably means "association."

Response:

This is now changed as indicated by the reviewer. The revised manuscript was checked by Shelly Pranić, PhD, who is a native English speaker.
We hope that the revised manuscript is now suitable for publication in the BMC Family Practice. We are, of course, ready to make further changes if necessary. Thank you for your consideration.

Sincerely,

Diana Jurić

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