Author's response to reviews

Title: Blood pressure control and antihypertensive pharmacotherapy patterns in a hypertensive population of Eastern Central Region of Portugal

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Author's response to reviews: see over
Cover Letter

Dear Sirs,

We are submitting the revision of the our paper entitled, "Blood pressure control and antihypertensive pharmacotherapy patterns in a hypertensive population of Eastern Central Region of Portugal", for consideration for possible publication in the “Research article” section of the BMC Health Services Research.

Please, see bellow how the suggestions of the reviewers were addressed. All changes made when revising the manuscript are underlined. Please let us know if further corrections are needed.

There is no conflict of interest to disclose.

Sincerely,

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Reviewers’ remarks

Reviewer #1 (Alice Ong)

1. Clear objective in text, but separating this into a new paragraph in both the abstract and main article background would make it visually more obvious. [Comment 1 -discretionary]

Done.

2. Method used is appropriate but difficult to ascertain how the duration of hypertension was chosen. Assume this was from hospital records? or did some people have diagnosis prior to attending hospital clinic? [Comment 2 -minor essential revision if data available]

Yes, it was from hospital records. Available information from the hospital electronic medical records includes patient demographics, medical problems (including the date on which each medical problem was first diagnosed), various measures of physiological status, and medications prescribed.

Data extraction was, thus, rewritten to include the underlined information.

Some people may have diagnosis (or suspected diagnosis) of arterial hypertension prior to attending hospital clinic. Some patients were diagnosed with hypertension when they lived in another region of the country; when they changed residency to our region they were referred to the hypertension / dyslipidemia clinic in the university teaching hospital of Cova da Beira Hospital Centre, Covilhã.

It should be emphasized that due to a decreased supply of primary care practitioners in this Region of Portugal that has led to a shortage in primary care delivery, this outpatient clinic provides follow-up care to hypertensive patients by a health care team
composed of internal medicine physicians and nurses and virtually all patients managed and monitored in this clinic have essential arterial hypertension.

**This is now stated in the same paragraph (the underlined).**

7. unclear if group is planning to do further work in this area. are they planning to prospectively collect data? perhaps collaborate with other geographical areas? [Comment 3 -discretionary - clarification]

This is an interesting question, not fully developed in our manuscript to comply with the “Instructions for authors”. Actually, we are now prospectively collecting data from our hypertensive patients in order to identify, by logistic regression, significant predictors of uncontrolled hypertension. We are also planning a multidisciplinary health care intervention to address some possible underlying causes of uncontrolled hypertension aimed to improve BP control. We would like to evaluate the benefits of this intervention in a randomised controlled trial.

These later studies had as its starting point the retrospective study described in this manuscript.

9. Writing of background in abstract and main body could perhaps be revised to make it a little clearer. [Comment 4 -minor essential revisions]

In the abstract perhaps something like "Interventions to improve blood pressure control in hypertension have had limited success in clinical practice despite the evidence of cardiovascular disease prevention in randomised controlled trials"

Done.

In conclusion of abstract consider removing "Although", and inserting "however" before "many hypertensive patients prescribed....".

Done.

The following part of the conclusion has an unclear meaning "being this control worse among patients at high risk...."
This is a pertinent remark. That sentence was substituted as follows:

“this control being worse among patients with diabetes or chronic kidney disease.”

In main article text background section.

Substitute "heart attack and stroke and one of the most important...." with "with myocardial infarction and stroke being one of the most important health problems in Portugal causing excess morbidity and mortality."[insert a reference]

Done. The reference was also inserted (important remark).

Half way down page 4 (background section) needs revision. "One of the major.....
This definition does not take.."
Perhaps something like "The definition of controlled hypertension in this Portuguese survey was considered.....and did not take into account those with diabetes mellitus or chronic kidney disease. Then a new sentence starting with "The seventh report of....(JNC7), set a lower BP target of 130/80 for those with diabetes or chronic kidney disease."

Done.

End of page 4.
Perhaps instead of "The Eastern...." start with something like "Cova de...is a university teaching hospital and a ??regional tertiary referral centre"

This hospital is not considered a tertiary referral centre in the true sense of the word, although it has an almost complete range of services including pediatrics, general medicine, various branches of surgery and psychiatry.
More rigorously, this hospital is classified as a “secondary care” hospital. However, in Portugal, some primary care facilities (notably the emergency department) are located within hospitals.
More importantly, due to a decreased supply of primary care practitioners in this Region of Portugal that has led to a shortage in primary care delivery, this hypertension/dyslipidemia outpatient clinic provides follow-up care to hypertensive patients by a health care team composed of internal medicine physicians and nurses and virtually all patients managed and monitored in this clinic have essential arterial hypertension.
This is now stated in the text (the underlined).

It should also be mentioned that in Portugal specialists may take patients without a referral from another physician and it is up to the patient to determine whether self-referral is allowed by the insurance company. Self-referral to a specialist is frequent as prior referral from another physician is not considered necessary.

Other Minor essential revisions
(Comment 5) Table 1 and Methods "Study population" on page 5 and end of page 8 "age-group <35" is there a lower age limit?? age 16 ?18, assume it was adults?

This is an important and quite pertinent remark. The lower age limit for attending the hypertension/dyslipidemia clinic is 18 years.

"Study population" on page 5 was rewritten as follows: Patients, all adults aged 18 or over, were included if they had an established diagnosis of arterial hypertension…

end of page 8 "age-group <35" was rewritten as:
“age-group ≥18 - <35”

Table 1 and Table 2 “<35" was rewritten as:
“≥18 - <35”

(Comment 6) end of page 8 "and most patients" what proportion or percentage??

Pertinent remark. The sentence "and most patients" was rewritten as follows:

“and 59.2% patients”

(Comment 7) page 11 on antihypertensive therapy - were the 9 who were counselled younger?? would be useful to give an indication of age
This is an insightful and interesting remark.
It is worth noting that these 9 patients were significantly younger than the average population, with an overall mean age of 44 ± 13 years (P < 0.001).

This is now mentioned in the same paragraph (the underlined).

(Comment 8) although mentioned in results section there was an absence of discussion of findings reported in figure 1 and at the bottom of page 11 in the discussion section.

Pertinent remark.

The percentage of patients taking a higher number of antihypertensive drugs were higher in patients with a lower target BP (≤130/80 mmHg) (Figure 1), suggesting that an effort is being made to further lower BP in hypertensives with diabetes or CKD.

This is now mentioned in the discussion (the underlined, end of page 14).

Reviewer #2 (Deepak Subramanian)

Major Compulsory Revisions:
1) Methods, paragraph 2: The study population in this study consists of outpatients at a hypertension / dyslipidaemia clinic at a university teaching hospital. Since the vast majority of hypertensive patients are managed and monitored in the primary care sector, it may be that this group of patients are being monitored at a hospital clinic due to their blood pressure being too difficult to control in the community.

This is a quite pertinent remark.

We should have emphasized that due to a decreased supply of primary care practitioners in this Region of Portugal that has led to a shortage in primary care delivery, this outpatient clinic provides follow-up care to hypertensive patients by a health care team composed of internal medicine physicians and nurses and virtually all patients managed and monitored in this clinic have essential arterial hypertension.

This is now stated in the same paragraph (the underlined).
It should also be mentioned that in Portugal specialists may take patients without a referral from another physician and it is up to the patient to determine whether self-referral is allowed by the insurance company. Self-referral to a specialist is frequent as prior referral from another physician is not considered necessary. Furthermore, some primary care facilities (notably the emergency department) are located within hospitals.

1) (cont.) There were also a large proportion of patients in the study (65%) who had had a high BP for more than five years. This might explain why the proportion of adequately controlled patients was low in this study.

This remark as well as remark 3) of “Discretionary Revisions” (regarding medication adherence) are important and quite pertinent remarks that prompted us to review and discuss our data related to medication adherence. Indeed, a closer analysis of the data related to medication adherence (physician observations about medication adherence, written on the medical chart) has led us to conclude that those data were biased and unreliable. In discussing this mater with all physicians involved, we find out that not all physicians write (on the medical chart) observations about medication nonadherence. Moreover, in the same discussion, all physicians and nurses expressed their belief that medication nonadherence is a major factor for uncontrolled BP.

Furthermore, based on this pertinent remark, we have carried out a literature review that also led us to the conclusion that patient persistence with prescribed therapy for any chronic disease typically declines over time, and hypertension is no exception.[1-3]

These conclusions led us to introduce some alterations in our revised manuscript, in order to include medication nonadherence as a possible reason for the low success in blood pressure control.

2) Discussion, paragraph 1: The authors need to expand upon the possible reasons for the low success in adequate hypertensive control in their patient population, given that the other cited studies demonstrated much greater success in achieving adequate blood pressure control.
Other possible underlying causes of poor BP control are guidelines unawareness and therapeutic inertia on the part of providers and poor adherence and persistence with prescribed medications and lifestyle modifications by patients. Results of studies suggest that antihypertensive medications are frequently not intensified when BP remains uncontrolled, termed clinical inertia [4-6]. In the recent Harris Survey [7], more than 30% of hypertensive patients reported that their medication was not changed or increased despite the fact that their BP was still >140/90 mmHg. Antihypertensive medication nonadherence is another major factor that must be thought about when considering the possible reasons for the inadequate BP control. Indeed, there is a large proportion of patients in our study (65%) who had hypertension for over five years and patient persistence with prescribed therapy for any chronic disease typically declines over time, and hypertension is no exception [1-3].

This is now stated in the same paragraph (the underlined).

3) Discussion, paragraph 2: The authors need to expand upon why there was no statistically significant difference in BP control between obese and non-obese individuals, and between males and females, in their study, given that these might be important factors in resistant hypertension.

We re-analysed data related to obese and nonobese hypertensive patients and the following paragraph were judged more appropriate:

Obesity is identified as one cause of resistant hypertension and there was a trend, albeit not significant, toward higher BP control between nonobese hypertensive patients (40% vs 28%, 0.127). The nonsignificant difference in BP control rate between obese and nonobese in our analysis could be because of the limited sample size, because >75% of the patients with diagnosed arterial hypertension were nonobese (body mass index < 30).

(It is possible that greater sample sizes would produce statistically significant differences between obese and nonobese hypertensive patients, provided that other factors, including medication adherence, remain nonsignificantly different.)

This is now stated in the same paragraph (the underlined).
The differences in rates of BP control between males and females were not significant in the <140/90 mmHg and in the <130/80 mmHg BP targeted population. Our results are in accordance with a recent study assessing gender difference in BP control that used the same cut points of uncontrolled BP defined by the JNC 7 [8].

The underlined sentence was added.

Minor Essential Revisions:
1) Background, paragraph 1: Citation for JNC 7 guidelines needs to be given and included in the References.

This remark is absolutely correct.
Done.

3) Methods, paragraph 2: It is unclear from the sentence, ‘Patients with both compelling indications and special indications were classified into the former group’ as to which group they are classified in; this section needs to be rewritten to clarify this.

This section was rewritten in the following manner (underlined):

Compelling indications for antihypertensive drugs are based on benefits from outcome studies or existing clinical guidelines; the compelling indication is managed in parallel with the BP [9]. Patients with both compelling indications and special indications were classified into the “compelling indications” group.

4) Methods, paragraph 2: The time period for data collection has not been specified [was mentioned in the Abstract]; needs to be included here.

Again, a quite pertinent remark. The following underlined was added:
Patients were included if they had an established diagnosis of arterial hypertension (BP measurements in the clinic of $\geq 140/90$ mmHg) and had attended at least two medical appointments over a one and a half year period (from January 2008 to June 2009).

5) Methods, paragraph 4: Last phrase beginning ‘and a P-value of less than....’ is superfluous and can be removed.

We think this phrase is important to mention. Many authors also focus this question in the statistical analysis section.

6) Results, paragraph 1: Last sentence (beginning ‘It should be noted that the first months....’) is discussion and should be moved to a more appropriate place in the Discussion section.

We think that this sentence here explains immediately why 6 hypertensive patients, which have been admitted to the hypertension clinic recently, were excluded from our study.

We are trying to better explain the last sentence: “…and their antihypertensive medication was probably not yet fully titrated.”

Discretionary Revisions:
1) Methods: The authors may wish to consider combining Tables 2 and 4 for clarity and ease of comparison.

We agree absolutely.
Done.

2) Discussion, paragraph 1: The authors imply that the main reason for failure to adequately control BP in those with DM and CKD is due to prescribers not adequately following the JNC 7 guidelines. Whilst this is an acceptable interpretation, the authors may wish to consider other possible reasons for this, given that this is a finding common to almost all the cited studies in this paragraph.
We agree entirely with this remark and we think that this issue is now more developed in the discussion (final part of paragraph 1).

Other possible underlying causes of poor BP control are guidelines unawareness and therapeutic inertia on the part of providers and poor adherence and persistence with prescribed medications and lifestyle modifications by patients.

This is now stated in the final part of paragraph 1 (the underlined).

3) Discussion, paragraph 6: The authors may wish to consider including the collected data regarding medication adherence, since that would obviously have a huge bearing on the proportion of patients with adequate hypertensive control.

This remark has already been addressed when answering to item 1 of Major Compulsory Revisions.

Minor issues not for publication:
1) There are many grammatical and typographical mistakes throughout the paper, which are too numerous to list here. The authors may wish to consider having their article professionally edited to eliminate these from the submitted version prior to publication.

Done.
We have now to agree with this remark.
References


