

PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Prevalence, awareness, treatment and control of hypertension in a self-selected sub-Saharan African urban population: A cross-sectional study
AUTHORS	Kengne, Andre Pascal ; Dzudie, Anastase; Muna, Walinjom; Ba, Hamadou; Menanga, Alain; Kouam Kouam, Charles; Abah, Joseph; Monkam, Yves; Biholong, Christian; Mintom, Pierre; Kamdem, Felicite; Djomou, Arnel; Ndjebet, Jules; Ouambo, Cyrille; Luma, Henry; Ngu, Kathleen; Kingue, Samuel

VERSION 1 - REVIEW

REVIEWER	Dr Juliet Addo Lecturer, London School of Hygiene and Tropical Medicine, UK
REVIEW RETURNED	03-May-2012

THE STUDY	The participants included in the study are not representative of the general Cameroon population as they were self-selected. The authors have however acknowledged this as a limitation of the study.
GENERAL COMMENTS	<p>This paper addresses an important health problem in sub Saharan Africa (SSA) where previous studies have highlighted the high prevalence of hypertension particularly in urban areas. It is well written and adds to the available evidence from the sub region. There are however a few issues that require addressing or clarification.</p> <p>The authors state the aims clearly including assessing the variability of the prevalence and determinants by region and gender which is clearly an interesting aspect of this paper particularly if there are significant differences between these regions in terms of perhaps level of urbanisation or occupation. This information is not clearly given and the prevalence, awareness, control etc is not reported by the regions except for the graph showing the mean blood pressure readings. I am also not certain why there were such differences in the number reporting from each of the cities sampled.</p> <p>The method of recruitment which was by self-selection could potentially have biased the participation and over-estimated the prevalence of hypertension as was discussed by the authors. Could this have affected the response to the survey from particular cities more than others?</p> <p>The authors do state the measurement of blood pressure on one visit only as a limitation. This is clearly important. In most similar</p>

	<p>studies several readings of blood pressure have been taken on the same day where it was not possible to arrange for a repeat visit and the average of two or three readings determined. There is however no reporting of this being done in this study where it appears only one measurement was taken.</p> <p>Was there a measure of socioeconomic status such as level of education or wealth and could this be a predictor of hypertension prevalence and control?</p> <p>The authors did not state that they aimed to determine the level of hypertension control according to the number of risk factors and so I am uncertain what Figure 2 adds to the study. Was the plan to study total cardiovascular risk as well? Table 2 also reporting on blood pressure categories in participants could also be presented by a few sentences in the results section.</p> <p>The manuscript could therefore be shortened considerably. Minor comment is to stick to the term participants instead of subjects.</p> <p>Overall, this paper adds to the literature that reflects the lack of awareness, treatment and control of hypertension in SSA and highlights the need for addressing these effectively.</p>
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REVIEWER	<p>Dr Niklaus Daniel Labhardt, MD MIH SolidarMed Seboche Hospital Botha-Bothe Lesotho</p> <p>I have no conflicts of interest to be declared</p>
REVIEW RETURNED	20-May-2012

THE STUDY	<p>Overall Study Design: The authors state, the objective is to "quantify the burden ... of hypertension, treatment and control rates among adults in major cities in Cameroon". These objectives can not be answered by the study design applied in this paper for two reasons:</p> <ol style="list-style-type: none"> 1. To assess the burden, treatment and control rates among adults in urban Cameroon, one should use another sampling method than the one used in the study. This study used persons who attended by their own motivation a screening campaign. The study sample can therefore not be considered as being representative and therefore not provides information about the overall burden and control-rates in urban Cameroon. 2. A single BP-measurement per individual is not reliable. It may lead to a substantial overestimation of the prevalence. (see: Bovet, P., Gervasoni, J.P., Ross, A.G., Mkamba, M., Mtasiwa, D.M., Lengeler, C., Burnier, M. & Paccaud, F., 2003, Assessing the prevalence of hypertension in populations: are we doing it right? Journal of hypertension, 21(3), pp. 509-17.) <p>The two limitations are acknowledged under limitations. However, the first one is not a limitation. In my view it is a recruitment bias.</p> <p>Overall English is good. However, some of the wording may be checked again.</p>
RESULTS & CONCLUSIONS	DISCUSSION:

	<p>The subsection on prevalence of hypertension should be reviewed. I think the present study cannot add any evidence to prevalence in the Cameroon population (see above).</p> <p>The subsection on awareness should equally be reviewed based on the same problem of self-selection.</p> <p>CONCLUSION:</p> <p>The conclusion "In conclusion, our study confirms the high prevalence of hypertension previously reported in urban settings in Africa. Detection, treatment and control efforts are still well below optimal." cannot be made based on this study (see above).</p>
GENERAL COMMENTS	<p>In general the paper is very well written, statistical methods are appropriate and the results are well presented. However, I think due to the selection bias, the study does not answer its major objective. The subsequent detailed analyses about predictors of hypertension in this specific population are indeed correct. However, it is nothing new and as a considerable number of the individuals diagnosed being hypertensive in this study may in reality be normotensive, the usefulness of these analyses are questionable to me.</p> <p>I fully acknowledge the importance of hypertension in sub-Saharan Africa and basically any publication about this topic is welcome. However, I doubt if the findings of this study really contribute to our knowledge due to the selection bias and the one single-reading procedure. I would recommend to shorten the manuscript considerably and to resubmit it as a brief report or short communication, summarizing the findings from screening campaigns in 3 different urban settings in Cameroon.</p>

REVIEWER	<p>Albertino Damasceno Professor of Cardiology, Eduardo Mondlane University Maputo, Mozambique</p> <p>I have no conflict of interests.</p>
REVIEW RETURNED	28-May-2012

THE STUDY	<p>This interesting study that evaluated hypertension and other cardiovascular risk factors in a large population and in 4 different cities has in our opinion two major problems.</p> <p>The sample used to evaluate the prevalence of hypertension was based on a group of self selected adults that voluntary came to be evaluated. Although some recent papers have been published using the same methodology, this should be not accepted as a standard epidemiological methodology. With this sample it is not possible to generalize the results neither to the urban population of Cameroon nor to the national population.</p> <p>This can be clearly seen in the large differences of people that was observed in the 4 different cities – a very small group of people observed in 2 regions in the West and North West regions (304 - 14.3%) compared with a large group that came in the littoral (1167 - 54.1%). This turns any comparison among regions very unlikely.</p> <p>Another way to see that the sample is not a representative one is the division of the participants by age groups. While in the Center city the younger group in the largest and the older the smaller as expected in the other 3 regions the sample shows the contrary with the older being more common than the younger denoting a non representative sample of the population.</p> <p>Big differences between the mean systolic and diastolic blood pressures of the center city and the other ones are shown as well as very big differences in the prevalence of self reported diabetes in</p>
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	<p>men between the Center city (about 4%) and the West and North west cities (about 16%). In our opinion, if not explained, this reflects the bias in the selection of the participants.</p> <p>The second problem that is not clear in the methodology is how was the blood pressure measured? The value of the blood pressure used to classify these adults as hypertensive/normotensive patients is the result of a single measurement or the mean of several measurements? The measurement during a single encounter was already used in several epidemiological studies and is the methodology proposed by WHO in the STEP wise approach but this value should be the mean of 3 consecutive measurements. The authors do not specify how many measurements have done in each participant. If only one measurement was done, like is understandable in the methodology of the paper, the discriminative power of this single measurement is very poor and this should be clearly stress in the methodology and the discussion.</p>
GENERAL COMMENTS	<p>Just three other small remarks:</p> <p>Line 18 on page 8 >94 in men and >80 in women</p> <p>Alcohol consumption was done using just beer or wine consumption. Was the consumption of traditional alcoholic beverages or whisky and other distillates also evaluated?</p> <p>The classification of a current smoker as someone who stop smoking for less than 3 years is a very particular one and probably result in a over estimation of smokers.</p>

VERSION 1 – AUTHOR RESPONSE

Reviewer(s)' Comments to Author:

Reviewer: Dr Juliet Addo
Lecturer, London School of Hygiene and Tropical Medicine, UK

The participants included in the study are not representative of the general Cameroon population as they were self-selected. The authors have however acknowledged this as a limitation of the study.

This paper addresses an important health problem in sub Saharan Africa (SSA) where previous studies have highlighted the high prevalence of hypertension particularly in urban areas. It is well written and adds to the available evidence from the sub region. There are however a few issues that require addressing or clarification.

The authors state the aims clearly including assessing the variability of the prevalence and determinants by region and gender which is clearly an interesting aspect of this paper particularly if there are significant differences between these regions in terms of perhaps level of urbanisation or occupation. This information is not clearly given and the prevalence, awareness, control etc is not reported by the regions except for the graph showing the mean blood pressure readings. I am also not certain why there were such differences in the number reporting from each of the cities sampled.

Our response: Thank you for raising this point. We have addressed the issue by updating the former Table 3 (now Table 2) to introduce region-specific data, in addition to those on gender. The result section has also been updated to reflect this change.

Differences in the number of participants across regions likely reflect differences in the sizes of the

background population of the participating cities. For instance Yaounde (Centre region) and Douala (Littoral region) have got population sizes in the region of 1.3 to 1.5 million, while Bafoussam (West region) and Bamenda (North-West region) have less than 0.5 million population each.

The method of recruitment which was by self-selection could potentially have biased the participation and over-estimated the prevalence of hypertension as was discussed by the authors. Could this have affected the response to the survey from particular cities more than others?

Our response: Analyses stratified by region (Table 2 and 3) suggest that participants from regions other than Centre and Littoral likely included relatively more participants who were aware of their status for hypertension, and likely receiving treatment. However, the relatively small number of participants from those regions would not significantly affect the overall results.

The authors do state the measurement of blood pressure on one visit only as a limitation. This is clearly important. In most similar studies several readings of blood pressure have been taken on the same day where it was not possible to arrange for a repeat visit and the average of two or three readings determined. There is however no reporting of this being done in this study where it appears only one measurement was taken.

Our response: Based on the predefined protocol of the survey and to limit the workload for the staff (given the limited staff number) and waiting time for participants, only those participants with an abnormal first reading were requested to have a second BP measurement. Even on such a protocol, some participants with raised BP left without having their second BP measured, and few other second measurements failed to be reported in some participants. Overall, of the 688 participants not known to suffer from hypertension and who had a raised BP (SBP/DBP \geq 140/90) based on the first measurement, a second valid measurement was available for 537 (78%). We have now repeated the analysis and found that among the 537, 85.8% (462 participants) had raised BP based on the average of the two measurements. This at the population level will translate into about 5% point overestimation of the prevalence of new hypertension based on a single measurement. We have added this new information as a sensitivity analysis indicated both in the methods, results and discussion chapters. The relevant sections read:

In the method section:

“Sensitivity analysis

The main analyses were based on a single blood pressure measurement. To assess the potential effects of ‘regression to the mean’ phenomenon on the prevalence of hypertension, a sensitivity analysis was conducted among participants with a raised initial blood pressure (SBP/DBP \geq 140/80 mmHg) and who had their blood pressure taken a second time on the same day. This analysis was based on the average of the first and second measurements.”

In the result section

“Sensitivity analysis

Among participants with newly diagnosed hypertension based on the first blood pressure measurement (688 participants), 537 (78.0%) had a valid second measurement. Their mean blood pressure (SD) was 159.4 (19.0) for systolic and 94.4 (14.2) mmHg for diastolic based on the first measurement. Equivalent values were 154.5 (19.0) and 93.0 (13.1) mmHg based on the average of the two measurements. Of the 537 participants 461 (85.8%) had hypertension (systolic/diastolic blood pressure \geq 140/90 mmHg) using the average of the two blood pressure measurements.”

In the discussion, under the limitation section

“Diagnosis of hypertension among those with no history of hypertension in our study was based on a single blood pressure measurement. Our sensitivity analysis suggests that this approach could inflated the crude prevalence by about 5.4% and 4.6% among those not known to have hypertension prior to the survey and at the total population level respectively. Nevertheless, even after accounting for this possible effect, our estimates would still be within sampling variation of the figures previously reported in this setting. It is also of note that no participant received a definitive diagnosis of hypertension as the result of taking part in this study. Those with elevated blood pressure levels were instead referred to health care facilities for further evaluation.”

Was there a measure of socioeconomic status such as level of education or wealth and could this be a predictor of hypertension prevalence and control?

Our response: Unfortunately, we did not collect data on these important predictors.

The authors did not state that they aimed to determine the level of hypertension control according to the number of risk factors and so I am uncertain what Figure 2 adds to the study. Was the plan to study total cardiovascular risk as well? Table 2 also reporting on blood pressure categories in participants could also be presented by a few sentences in the results section.

The manuscript could therefore be shortened considerably.

Our response: We have now removed the table 2 and kept only the narrative summary in the results section. We have also removed the Figure 2 and all reference to that figure as well.

Minor comment is to stick to the term participants instead of subjects.

Our response: We now use ‘participants’ throughout

Overall, this paper adds to the literature that reflects the lack of awareness, treatment and control of hypertension in SSA and highlights the need for addressing these effectively.

Our response: Thank you for the appreciation

Reviewer: Dr Niklaus Daniel Labhardt, MD MIH SolidarMed Seboche Hospital Botha-Bothe Lesotho

I have no conflicts of interest to be declared

Overall Study Design:

The authors state, the objective is to "quantify the burden ... of hypertension, treatment and control rates among adults in major cities in Cameroon". These objectives can not be answered by the study design applied in this paper for two reasons:

1. To assess the burden, treatment and control rates among adults in urban Cameroon, one should use another sampling method than the one used in the study. This study used persons who attended by their own motivation a screening campaign. The study sample can therefore not be considered as being representative and therefore not provides information about the overall burden and control-rates in urban Cameroon.
2. A single BP-measurement per individual is not reliable. It may lead to a substantial overestimation of the prevalence. (see: Bovet, P., Gervasoni, J.P., Ross, A.G., Mkamba, M., Mtasiwa, D.M.,

Lengeler, C., Burnier, M. & Paccaud, F., 2003, Assessing the prevalence of hypertension in populations: are we doing it right? *Journal of hypertension*, 21(3), pp. 509-17.)

The two limitations are acknowledged under limitations. However, the first one is not a limitation. In my view it is a recruitment bias.

Our answer: Thank you for raising these points, which as recognised by the reviewer have been highlighted in the limitation section of the manuscript. We feel that both are potential sources of biases ('selection bias' for the 1st and 'regression to the mean' for the second). We feel that the 'limitation section' of the article is the place where all issues from the study conception through to data analysis and reporting, that can potentially affect the internal and or external validity of the study are acknowledged.

With regard to point 1, we have made no claim that our sample was representative of the background Cameroonian population in participating cities, and would refrain from doing so. We have rather discussed extensively on those factors that could potentially make our sample to be different from the background population. The most we could do was to attempt to control some of the possible biases that could result from our sampling approach; through reporting of the age and standardised estimates for instance. We now even provide those standardised estimates by participating city. We also have to acknowledge the challenges of conducting a representative population-based survey in a country where no household numbering has been implemented, and with virtually no funding as done for the current study. In such a context, previous studies have been conducted by selecting for instance a suburb in a given city (supposedly representative of the population of the city), then enumerating the household to allow a random sample. That our results are in major ways similar to those from those studies perhaps suggests that the two approaches have possibly captured the same characteristics in the population. Therefore, our results have utility in the context of those available.

With regard to point 2, please see our answer to reviewer #1 on the further steps we have undertaken to quantify the possible magnitude of the overestimation induced by our reliance on a single BP measurement. Our sensitivity analyses suggest that the approach could have inflated the crude prevalence by about 5% point. Even accounting for such an effect the prevalence would still be high, reflecting the background high prevalence reported in previous studies. We do however recognised that this may not be the more appropriate approach for assessing BP levels in surveys and have again emphasized it in the limitation section.

Overall English is good. However, some of the wording may be checked again.

Our answer: We have checked the manuscript again and fixed those wording issues identified.

DISCUSSION:

The subsection on prevalence of hypertension should be reviewed. I think the present study cannot add any evidence to prevalence in the Cameroon population (see above).

The subsection on awareness should equally be reviewed based on the same problem of self-selection.

Our answer: Thank you for raising this point. We have now removed the claim that our study updates the prevalence of hypertension in country. We however feel that it is still important to cautiously discuss our findings in the context of available data, as this provide of opportunity of speculating on the possible biases introduced by the methodological limitations discussed above.

CONCLUSION:

The conclusion "In conclusion, our study confirms the high prevalence of hypertension previously reported in urban settings in Africa. Detection, treatment and control efforts are still well below optimal." cannot be made based on this study (see above).

Our answer: We have changed the wording. It now reads:

"In conclusion, our study provides findings suggesting the high prevalence of hypertension previously reported in urban settings in Africa. Detection, treatment and control efforts are likely still well below optimal."

In general the paper is very well written, statistical methods are appropriate and the results are well presented. However, I think due to the selection bias, the study does not answer its major objective.

The subsequent detailed analyses about predictors of hypertension in this specific population are indeed correct. However, it is nothing new and as a considerable number of the individuals diagnosed being hypertensive in this study may in reality be normotensive, the usefulness of these analyses are questionable to me.

I fully acknowledge the importance of hypertension in sub-Saharan Africa and basically any publication about this topic is welcome. However, I doubt if the findings of this study really contribute to our knowledge due to the selection bias and the one single-reading procedure. I would recommend to shorten the manuscript considerably and to resubmit it as a brief report or short communication, summarizing the findings from screening campaigns in 3 different urban settings in Cameroon. (MANAGING EDITOR'S NOTE - please note BMJ Open does not publish short reports; if you wish to do this you will need to submit elsewhere)

Our answer: We thank the reviewer for his appreciation. We are well aware of the potential effects of the issues raised on our findings and have discussed them at length in the manuscript. We remain however of those who believe that 'the perfect' shouldn't be the enemy of 'the possible' and would prefer to strive with the little means available to us, to generate any evidence that can potentially inform health service and policy solutions. We also believe that keeping a full paper aid the provision of detailed information with potential utility locally and even beyond.

Reviewer: Albertino Damasceno
Professor of Cardiology, Eduardo Mondlane University Maputo, Mozambique

I have no conflict of interests.

This interesting study that evaluated hypertension and other cardiovascular risk factors in a large population and in 4 different cities has in our opinion two major problems.

The sample used to evaluate the prevalence of hypertension was based on a group of self-selected adults that voluntary came to be evaluated. Although some recent papers have been published using the same methodology, this should be not accepted as a standard epidemiological methodology. With this sample it is not possible to generalize the results neither to the urban population of Cameroon nor to the national population.

This can be clearly seen in the large differences of people that was observed in the 4 different cities – a very small group of people observed in 2 regions in the West and North West regions (304 - 14.3%) compared with a large group that came in the littoral (1167 - 54.1%). This turns any comparison among regions very unlikely.

Our response: Thank you for the appreciation and for raising this point which we have addressed already above (see our answer to reviewer #1). There are true differences in the population size of the participating cities, with Douala and Yaounde being much larger than Bafoussam and Bamenda.

Everything else being equal, one would expect fewer participants from the latter, which is been reflected in the turn out numbers by city in our study.

Another way to see that the sample is not a representative one is the division of the participants by age groups. While in the Center city the younger group is the largest and the older the smaller as expected in the other 3 regions the sample shows the contrary with the older being more common than the younger denoting a non-representative sample of the population.

Our response: We have attempted to address this point now by providing age standardised prevalence by participating city. Please see the new table 2 in the main manuscript. Big differences between the mean systolic and diastolic blood pressures of the center city and the other ones are shown as well as very big differences in the prevalence of self-reported diabetes in men between the Center city (about 4%) and the West and North west cities (about 16%). In our opinion, if not explained, this reflects the bias in the selection of the participants.

Our response: We now report the age-standardised prevalence by participating centres, which suggest differences by city in prevalence, awareness and treatment. In the absence of specific data on the background access to hypertension diagnosis and care by city, it is very difficult to speculate on the likely direction of the effect of possible bias if any. We have however provided the following points in the discussion.

“It is also possible that many participants already diagnosed with hypertension, and perhaps on treatment and controlled on such treatment, did not feel the need to attend the screening campaign again. This would have the undesirable effect of biasing our estimates by providing much lower than the true figures. It is also possible that those with known and treated condition instead turned out in higher number to use the campaign as an opportunity for their health checkup free of charge. Our stratified analyses suggest that this mix could vary substantially by participating centers.”

The second problem that is not clear in the methodology is how was the blood pressure measured? The value of the blood pressure used to classify these adults as hypertensive/normotensive patients is the result of a single measurement or the mean of several measurements? The measurement during a single encounter was already used in several epidemiological studies and is the methodology proposed by WHO in the STEP wise approach but this value should be the mean of 3 consecutive measurements. The authors do not specify how many measurements have done in each participant.

If only one measurement was done, like is understandable in the methodology of the paper, the discriminative power of this single measurement is very poor and this should be clearly stress in the methodology and the discussion.

Our response: Please refer to our answer to reviewer 1 on this point above.

Just three other small remarks:

Line 18 on page 8 >94 in men and >80 in women

Our response: This was based on the IDF definition of metabolic syndrome.

Alcohol consumption was done using just beer or wine consumption. Was the consumption of traditional alcoholic beverages or whisky and other distillates also evaluated?

Our response: We thank the reviewer for this remark. Alcohol consumption was based on self-reported beer, wine and whisky consumption. Traditional alcoholic beverage was not evaluated in this study.

The classification of a current smoker as someone who stop smoking for less than 3 years is a very particular one and probably result in an over estimation of smokers.

Our response: We do agree that the wording is somehow inaccurate and misleading. Please read: "Participants who smoked at least one cigarette per day at the time of the study were classified as current smokers, and those who have smoked for at least 3 years in the past, but had stopped by the time of the study were classified as former smokers."

VERSION 2 – REVIEW

REVIEWER	Addo, Juliet Kings College London
REVIEW RETURNED	19-Jul-2012

GENERAL COMMENTS	<p>The previous review have been addressed considerably. There are a few points that need attention.</p> <p>Firstly, the aims in the abstract have not been rephrased as done in the main text. They do mention that they will quantify the burden of hypertension.</p> <p>In the results section on page 10, there is the mention of optimal BP. This needs to be defined.</p> <p>Results: The reporting of regression analyses from Tables 4 and 5 should focus on the adjusted values as these are the interesting bits not the unadjusted.</p> <p>Conclusions: Please rephrase the first two sentences of the conclusion as they are currently unclear.</p>
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REVIEWER	Albertino Damasceno, Professor of Cardiology, Eduardo Mondlane University, Maputo, Mozambique
REVIEW RETURNED	11-Jul-2012

THE STUDY	Although the methodology used was not the most appropriate, now the manuscript explains clearly the limitations of this methodology.
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VERSION 2 – AUTHOR RESPONSE

Reviewer(s)' Comments to Author:

Reviewer: Dr Juliet Addo
King College London

There is no competing interests.

The authors have addressed the concerns raised in the previous review to a large extent. The points which cannot be addressed have been acknowledged. I am making a few points for modification below but do not need to see this again.

Our response: We thank you for the appreciation

The previous review have been addressed considerably. There are a few points that need attention. Firstly, the aims in the abstract have not been rephrased as done in the main text. They do mention

that they will quantify the burden of hypertension.

Our response: We have changed the wording. The sentence now reads:

“We report the prevalence and determinants of hypertension, detection, treatment and control rates among adults in major cities in Cameroon.”

In the results section on page 10, there is the mention of optimal BP. This needs to be defined.

Our response: This is based on the ESC 2007 guideline definition. We have now provided the definition. The relevant sentence reads:

“An optimal BP (systolic BP<120 and diastolic BP<80 mmHg) was observed in 21.6% of men and 29.6% of women.”

Results: The reporting of regression analyses from Tables 4 and 5 should focus on the adjusted values as these are the interesting bits not the unadjusted.

Our response: we have modified the section which now reads:

“Unadjusted and adjusted odd ratios and 95% confidence intervals for the association of prevalent hypertension with potential predictors are shown in Table 3. In multivariable logistic regression models adjusted for age, sex, parental history of hypertension, body mass index and region, the significant predictors of prevalent hypertension were male sex, increasing age, Region, parental history of hypertension, personal history of diabetes, high BMI and high waist circumference (Table 3) . In multivariable models with similar level of adjustment (Table 4), male sex, high BMI and physical inactivity were associated with poor control of hypertension, while being from Regions other than Centre or Littoral was associated with good control among treated patients (Table 4).”

Conclusions: Please rephrase the first two sentences of the conclusion as they are currently unclear.

Our response: The two sentences have been modified and now read:

“In conclusion, our study has provided findings that are in line with the high prevalence of hypertension previously reported in urban settings in Africa. The study further suggests that efforts to detect and treat to the targets those with the disease are still below optimal.”