Author’s response to reviews

Title: Cardiovascular Risk Factor Burden in Africa and the Middle East Across Country Income Categories: A post hoc analysis of the Cross-Sectional Africa Middle East Cardiovascular Epidemiological (ACE) study

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Author’s response to reviews:

23rd December 2017

Drs Herman Van Oyen and Olivier Bruyère,
Editors-in-Chief, Archives of Public Health
Re: Manuscript AOPH-D-17-00168 “Cardiovascular Risk Factor Burden in Africa and the Middle East Across Country Income Categories: A post hoc analysis of the cross-sectional Africa Middle East Cardiovascular Epidemiological (ACE) study”

Dear Drs. Van Oyen and Bruyère,

We thank your peer reviewers for their review of the above titled manuscript submitted for consideration for publication as an Original Article in Archives of Public Health.
We have addressed their feedback in the revised manuscript file, and outlined the responses in
the document, below. We have up-loaded a track-changes version and clean final draft of the
manuscript for your convenience.

We trust you now find our paper suitable for publication in your journal.

Yours sincerely,

Professor Frederick J. Raal, FRCP, FRCPC, FCP(SA), Cert Endo, MMED, PhD

Reviewer reports:

Reviewer #1: In this manuscript the prevalence rates of CVD risk factors are compared between
different countries from Africa and the Middle East and these prevalence rates are analysed on
the basis of the national incomes of the countries.

The study populations are adult stable outpatients from 94 clinics in 14 countries.

The crucial question regarding this manuscript relates to the external validity of the study; How
well do these patients represent ALL adult stable outpatients of these countries?

• Thank you for this important comment. We acknowledge the fact that the results of this
study do not represent a population-based estimate of cardiovascular risk factor prevalence.
Accordingly, this limitation is highlighted in the Discussion section of the manuscript on page
11, first paragraph.

• In the discussion section of the manuscript, it has been noted that the analysis is limited
by the fact that this was a cross sectional study with a one-time assessment of the modifiable CV
risk factors. Every fifth patient attending a primary care/outpatient clinic for any reason was
included in the study to minimize bias. It is possible that the patients attending the clinics were
the ones with more access and may be more affluent which may have caused a selection bias in
comparison with the general population in the countries analyzed. We feel that even though the
study does not represent a population based estimate of cardiovascular risk factor prevalence,
selection bias is reduced as a result of the patient inclusion/selection criteria and the large sample
size. However, we have modified the title in response to this point and to the Editor in Chief’s
point below to clarify that the original design of the ACE study was cross-sectional.

Are the barriers to consult in these clinics different between the countries? Could it be that in the
LI and LMI countries only affluent patients are seen in these clinics while in the HI countries
that social barrier is less existent?

• Thank you for the comment. It is possible that the patients attending the clinics were the
ones with more access to healthcare and may be more affluent which may have caused a
selection bias in comparison with the general population in the countries analyzed. We already note in the discussion that “given that this cohort had access to primary care, a selection bias may exist as these patients may be more affluent in comparison with the general population in the countries analyzed”. However, as both rural and urban sites were used this may partially mitigate the social class bias.

What were the participation rates in the different countries? The large samples by themselves do not reduce potential selection biases.

- Thank you for this point. Only 31 subjects (0.7%) did not agree to continue to participate in the study and some text has been added on page 6, first line under the baseline characteristics section. Given this low proportion, we do not feel this would have affected the study findings.

The CVD risk factors are well defined and an attempt was made to standardize the measurements; how well was this put into practice by the clinicians? How well were the labs standardized for measuring lipids and FPG?

- This was a cross sectional study and reflected the usual practice in the clinics. In addition, this study was not designed/powered to compare the income groups. This analysis across income groups is purely descriptive in nature. There were no standardized labs used in the study. None of the blood measurements were done in the doctor’s practice (point of care). All measurements were performed in a laboratory as per the clinic’s routine practice. We have included some additional text to clarify this in the statistical analysis section on Page 6.

Is the GNI per capita based on the number of ‘official citizens’, excluding expats and foreign workers who may represent the majority of the populations in some of the countries? Are these expats and foreign workers excluded from the study populations?

- The per capita income is based on the entire country population and is standard practice for income-based analysis. Every fifth patient, expat or citizen, attending the clinic for any reason was included in the study.

Regarding the prevalences of dyslipidemias the use of lipid lowering drugs (LLD) was very different between the four categories of GNI. This could have influenced the prevalences of certain lipid fractions. Assuming that the majority of these LLD are statins one could expect lower LDL-C values in the HI countries on the basis of the high use of LLD (32%). This could result in much higher LDL-C levels in patients not on LLD in HI countries compared to the LDL-C levels in patients not on LLD in LI or LMI countries.

- Thank you for this point. The definition of dyslipidemia in the study was based on those on lipid lowering drugs or those who had a fasting blood sample showing a high total cholesterol or high low-density lipoprotein (LDL)-cholesterol level a low high-density lipoprotein (HDL)-cholesterol level, a high triglyceride level, or a combination of these levels as per the (NCEP) (ATP) III guidelines as detailed on pages 4-5 of the manuscript. Therefore, in HI countries many of those categories as having dyslipidemia would have been placed in this group on the basis of receiving lipid-lowering treatment. Conversely, most of those categorized as having dyslipidemia
from LI countries would have been placed in this group due to having high TC or LDL-C levels (or low HDL-C levels) rather than receiving lipid-lowering treatment.

Reviewer #2: The article is nicely written with adequate references.

Some corrections are needed like in Page No. 5, line 20, instead of "BMI of ≥30 mg/m2", it will be "BMI of ≥30 Kg/m2".

• Thank you for pointing this out. It has been corrected on Page 5.

3. I have a query, in Page No. 7, line 16-17, you have written "....with slightly higher median SBP and DBP seen in patients from LI countries (Table 2). The prevalence of hypertension was notably lower in LI countries...", explain it.

• Thank you for highlighting this point. The differences in median blood pressure and prevalences of hypertension are merely descriptive as the study was not powered/designed to compare the various income groups. We have reworded the sentences on page 7 in the second paragraph to reflect this. We have also added on page 6, first paragraph, the fact that the differences seen across the income groups is merely descriptive and that the study was not powered to compare the differences/prevalences in CV risk factors across income groups.

References are adequate. Interpretation of the data is OK.

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Comments of the Editor-in-Chief

Title of manuscript should include information on period study

• Thank you for the comment. We have added the fact that this was a cross-sectional study in the title. The title now reads:

Cardiovascular Risk Factor Burden in Africa and the Middle East Across Country Income Categories: A post hoc analysis of the Cross-Sectional Africa Middle East Cardiovascular Epidemiological (ACE) study

Title of figures and tables should have information on study, time period

• Thank you for this comment. We have expanded the information in the legends for the figures and tables to include “… the cross-sectional Africa Middle East Cardiovascular Epidemiological (ACE) study conducted between July 2011 and April 2012, and stratified by national income group.” This has been added as above to the titles of the tables and figures.

As the study in a clinical trial, how representative is the study population
Thank you for the comment. As per reviewer one, we acknowledge the fact that the results of this study do not represent a population-based estimate of cardiovascular risk factor prevalence. However, we have highlighted this limitation in the Discussion section of the manuscript on page 11, first paragraph.

In the discussion section of the manuscript, it has been noted that the analysis is limited by the fact that this was a cross-sectional study with a one-time assessment of the modifiable CV risk factors. Every 5th patient attending a primary care/outpatient clinic for any reason was included in the study to minimize bias. It is possible that the patients attending the clinics were the ones with more access and may be more affluent which may have caused a selection bias in comparison with the general population in the countries analyzed. We feel that even though the study does not represent a population-based estimate of cardiovascular risk factor prevalence, selection bias is reduced as a result of the patient inclusion/selection criteria and the large sample size.

In the analysis, even descriptive, the survey weights should be used.

We describe the data using summary statistics, and when modeling was applied, i.e. logistic regressions, appropriate weights to the variables were applied due to the very nature of the analysis.

Conclusion: be more specific (e.g. give some suggestions) when indicating the public health measures to be taken.

Thank you for this comment. The following statement has been added in the conclusion.

“Some public health measures that could be considered require national strategies on CV risk management in the population, and ways for instituting protocols at primary care/outpatient clinics in order to identify CV risks early, and to manage them optimally by allocating adequate resources”.