Author's response to reviews

Title: An ecological comparison of diabetes in five black populations: Data from Modeling the Epidemiologic Transition Study (METS).

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Author's response to reviews: see over
Dear Dr. Marshall

Thank you for the initial review of our manuscript “4486119841601026- An ecological comparison of diabetes in five black populations: Data from Modeling the Epidemiologic Transition Study (METS).” We have altered our manuscript in line with the reviewers suggestions and comments and provide a point-by-point summary of these edits.

Thank you for your consideration.

Yours truly,

Lara Dugas, PhD, MPH
Title: As authors have examined individual data from five countries, suggest removing 'ecological' from the title (refer to aggregate estimates).

We have removed “ecological” from the title.

Abstract, background: This being a cross-sectional study, it is not appropriate to say 'examined the glucose regulation'; suggest mentioning the objective was to examine the factors associated with glucose or something like that. In this section, authors should provide a rationale for this study in addition to the objective of the study.

We have altered both the background and methods section of the manuscript to reflect the aim, as well as methods used in the current study.

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Authors should include multiple regression analyses to examine the association of physical activity, anthropometrics, and body composition with glucose levels at each site adjusting for age, sex, education and for each other. Similarly, for leptin, adiponectin and HOMA with glucose multiple regression analyses should be performed adjusting for these variables. All analyses should also account for 'site'.

Thank you for this suggestion. We ran the analyses for each site, as well as using dummy site variables and found the results to be similar. In our study MVPA did not have a significant association with plasma glucose, insulin, HOMA or adiponectin and therefore was not included in the final model. This result is similar to a paper we published recently using NHANES data (PeerJ. 2014 Aug 19 Farni et al.)

METS protocol included assessment of smoking, alcohol, diet, BP and medication history. It was not clear why these variables were not considered for the current study. As all these factors have earlier been shown to affect diabetes, these variables should also be included in the multivariable model.

In our analysis and stratifying for sex, we found among the men and women separately that plasma glucose was not correlated with smoking, alcohol, PA, or years of schooling, only with hypertension. However, for the regression model hypertension as well as smoking and sedentary time (1-min bouts) all contributed significantly to the final model and were therefore included. We did include years of education in the final model. For the multiple linear regression models for insulin and leptin, only age and BMI for insulin and for leptin age, sex and BMI were significant predictors. Similarly none of the diet variables, including % macro nutrient contribution, glycaemic index, or type of fats included in the diet had any significant relationship with glucose, insulin, HOMA or adiponectin.
Limitations should also mention the smaller sample size from each site."

We have added the limitation from small sample size.

**Additional Editorial Request:**

1.) Please provide a Competing Interest section heading.

We have now added the competing interest section heading.

**Reviewer 1**

1- Page 22, numbers for total Waist are wrong for both men and women. Please correct.

Thank you for this oversight, we have corrected the total values.

2- Multiple regressions should be added to the tables. Many hypotheses are being suggested by descriptive tables, but authors do not test them later in regression. For instance, role of education seems to be only important for women (Table 2a). This is EXTREMELY important!

In our analysis and stratifying for sex, we found among the men and women separately that plasma glucose was not correlated with smoking, alcohol, PA, or years of schooling, only with hypertension. However, for the regression model hypertension as well as smoking and sedentary time (1-min bouts) all contributed significantly to the final model and were therefore included. We did include years of education in the final model. For the multiple linear regression models for insulin and leptin, only age and BMI for insulin and for leptin age, sex and BMI were significant predictors. Similarly none of the diet variables, including % macro nutrient contribution, glycaemic index, or type of fats included in the diet had any significant relationship with glucose, insulin, HOMA or adiponectin.

3- Gender differences should be also discussed.

In the parent study, METS, men and women behave so differently with respect to body composition and other behavioral variables such as physical activity, and employed in manual occupations. As a result of this, we have published all of our research from METS as separate analyses for men and women. METS is not focusing on gender effects, instead of the effect of the epidemiologic transition.

4- The recent literature on cross-country differences in social and behavioral correlates of health in diabetes should be discussed. Some of these work include: PMID: 24393171 and PMID: 24559091.
Thank for mentioning these 2 studies we initially omitted, we have now added these works.

5- There are two major type of conclusions. One, comparing US and other countries. Two, comparison of countries within Africa. Discussion of US differs from other countries and African countries vary themselves should be clearly separated.

We have clearly indicated which comparisons are comparing US to other sites and comparisons between African countries.

6- Cross-country comparisons in correlates of manual labor should also reported.

We have performed a chi squared analysis to examine manual labor differences by site.

7- in a series of new tables, authors should compare cross country comparisons with laboratory outcomes. How countries are different in effect of education, BMI, etc on glucose, insulin, and other lab data?

Table 1 presents side-by-side country comparisons for all demographic and laboratory data. We chose US as the reference for the comparisons and statistical significance was set at an alpha p-level of <0.05.

8- Finally, the interactions between place and factors on BMI are also important. Is sex * U.S significant in table 3? What about income * US?

We did not use income in our study.

Reviewer 2.

1. Abstract: The aim of the study is missing. Please restructure last paragraph of abstract and mention aim. The last paragraph can be moved to the introduction part of discussion section, or can also mention it as a strength of this study.

We have altered the background of the abstract and introduced an aim.

2. Statistical methods section needs improvement. The authors should present the statistical analysis performed; such as correlation (pearson?, spearmen?), multivariate linear regression( which determinants were included in the analysis), etc., the p value and which statistical software used is missing. Kernel density graph was presented but not mentioned in results but also in methods. All readers are not familiar with these graphs.

We have significantly altered the methods section, adding the statistical package, the p-value at which significance was denoted as well as more detailed information regarding the analyses performed.
3. Results: In Table 1, descriptive statistics were presented and it is obvious that some differences exist between countries. However we can not interpret whether these differences were statistically significant or not. For example, row 226; “Ghanian women were the most physically active, while those from USA and Jamaica appeared to be the least physically active and most sedentary”. I believe if you can make comparison between groups using ANOVA or Kruskall-Wallis followed by Mann-Whitney-U test depending on distribution characteristics of your data, it will enrich results section.

By design, this population-based study has very different environments, allowing us to understand the associations between different environments and health. However, the reviewer is correct that adding p-values to table 1 enhances the reader’s interpretations. We have now added these.

5. Results: correlations; While presenting correlations, the strength of correlation is more important than significance level. Hence, please add magnitude and direction of correlation coefficients (r value) to your results and mention whether the correlation is strong, medium or weak, and positive-negatively associated. The nature of the correlation (i.e. strength as well as direction) was already indicated in the table, the p-value was denoted using a symbol below the table.

6. Results: regressions; I believe the authors made a multivariate linear regression, so the country variables should be entered as dummy variables; such as (Jamaica;yes:1, no:0) etc. If so, one country should be omitted from the analysis, because of high correlation. The name of Table 3 can be like; The association between fasting glucose level and determining factors according to multivariate regression. Table 3; BMI 95% CI is presented as (0.672-0.442), the low number should come first; (0.442-0.672)

The reviewer is correct regarding both the co-linearity with the dummy variables and and we have now corrected our regression table and changed the title of the table.

7. The relationship between figures and results is missing. The figures should be mentioned at results. Thank you for commenting on the figures, we have determined that Figures 1a/1b and 2a/2b add no additional value to the manuscript because the data is already contained in the tables. As such, Figure 3a/b has now become figure 1a and 1b and we have added a short description to both the methods and results sections.

8. Discussion: It would be beneficial if you can mention some of the limitations of the study. We have now added a limitations section to the discussion.
9. The conclusion sentence is missing. At row 350; the authors mention: “to summarize, this study examined......, this sentence can be moved to first paragraph of discussion. A conclusion sentence like the one in your abstract should be added here.

We have added a conclusion section and moved the sentence to the first paragraph of the discussion.

10. Figure 2: Mean values of anthropometric measurements were given by countries, but country names are missing in the graph.

We have removed figure 2, which adds no additional value/information to the manuscript.

Minor Essential revision

1. Abstract; Abbreviations should be explained at their first use; such as CVD, PA, SES. Same goes all through the manuscript.

We have now explained abbreviations prior to their first use.

2. Number of decimals used while presenting mean values should be the same in all tables. In table 1 all values except HOMA-IR have 1 decimal.

We have changed the table to be consistent and include only 1 decimal place for all values.

3. Row 124: weight and height was measured as previously described-add reference here again.

We have added the reference.