Author's response to reviews

Title: Prevalence of depression and associated risk factors among persons with type-2 diabetes mellitus without a prior psychiatric history: a cross-sectional study in clinical settings in urban Nepal

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Author's response to reviews: see over
AUTHORS’ RESPONSE: DEAR REVIEWERS, THANK YOU FOR THE VERY HELPFUL COMMENTS. WE HAVE MADE EVERY EFFORT TO ADDRESS THE POINTS RAISED BELOW. WE PROVIDE A DETAILED DESCRIPTION OF EACH CHANGE IN RESPONSE TO EACH ISSUE RAISED. WE FEEL THAT THE MANUSCRIPT HAS BEEN IMPROVED SIGNIFICANTLY BASED ON YOUR RECOMMENDATIONS.

Reviewer's report
Title: Prevalence of depression and associated risk factors among persons with type-2 diabetes mellitus without a prior psychiatric history: a cross-sectional study in clinical settings in urban Nepal
Version: 1 Date: 26 June 2013
Reviewer: Emily Mendenhall

Reviewer’s report:
This well-written paper with a good study design makes a significant contribution to the growing body of research on depression and diabetes in Nepal as well as South Asia. It also provides important insight into the research around the co-morbidity in low and middle income countries more generally. It is a timely paper and will be well-received in Nepal and South Asia more broadly by the growing number of researchers attending to issues of diabetes and its co-morbidity with depression. This paper should be published with a few modifications.

Major Compulsory Revisions
1. The study design excludes people who have had diabetes for less than three months. While this is a useful cut-off, particularly with regard to measuring A1c, it poses some unique challenges for this study. People with diabetes are most likely to present with depression during the first one to two years living with the disease, as they acclimate to the knowledge that they have the chronic illness and learn how to manage it appropriately through changes in lifestyle as well as medication adherence. Then, depressive symptoms generally decrease. It may be useful to redo these analyses with people who have had diabetes with no less than one year or two years. This should be considered in all analyses.

AUTHORS’ RESPONSE: THANK YOU FOR THIS SUGGESTION. WE DID A SENSITIVITY ANALYSIS OF ONLY PERSONS DIAGNOSED WITHIN TWO YEARS AND DID NOT FIND ANY ADDITIONAL SIGNIFICANT ASSOCIATIONS. IN TABLE 2B, WE HAVE THE FINDING THAT THE LONGER THE DURATION OF THE DIABETES THE LOWER THE DEPRESSION SCORES, WHICH IS CONSISENT WITH YOUR RECOMMENDATION. WE HAVE ADDED THIS TO THE DISCUSSION.

2. Qualitative researchers have found that some distress linked with chronic illness results from fear around what the disease means for his/her life. Therefore, could it be that less depression among people with a family history of diabetes could result from more familiarity with the disease, or having a “diabetes
prototype” wherein they understand that diabetes can be managed? (Referring to this sentence on page 14): “In this study family history of diabetes was associated with less depression suggesting that the current cases may be more lifestyle related and associated with other risk factors for depression.” While this comment attends to the issue of lifestyle, it also suggests that it is not only eating and activity patterns that affect depression; social support plays a major role.

AUTHORS’ RESPONSE: WE HAVE ADDED THIS EXPLANATION REGARDING REDUCED FEAR AS A POTENTIAL EXPLANATION FOR THIS FINDING.

3. On page 15 the authors mention the Weaver and Hadley (2011) paper in a way that indicates that it compares men and women; this paper looks exclusively at social roles among women. Modify this sentence to transition clearly into the final sentence/point in the paragraph around gender-role performance. An example from the Weaver-Hadley study would also be useful to juxtapose their findings to men’s erectile dysfunction (which is both biological and social).

AUTHORS’ RESPONSE: THANK YOU FOR POINTING OUT THIS OVERSIGHT. WE WERE AWARE THAT IT WAS WOMEN ONLY, BUT WE MISREPRESENTED IT IN THE TEXT. WE HAVE CORRECTED THIS.

4. Add a topic sentence to the paragraph that begins with “Age” on page 15.

AUTHORS’ RESPONSE: WE HAVE ADDED THE FOLLOWING TOPIC SENTENCES:

“Age is a strong predictor of depression in the general community in Nepal [32, 33, 35]. However, it was not a significant predictor in our Nepali clinical population with diabetes. Age has shown an inconsistent relationship with depression and in people with diabetes with depression in a number of studies:....”

5. There are some issues with the paragraph (pp. 15-16) around income. Please refer to Leone et al.’s Globalization and Health 2012 paper entitled, “Diabetes and depression comorbidity and socioeconomic status in low and middle income countries (LMICs): a mapping of the evidence.” Those who are poor are less likely to know they have diabetes and/or seek medical care. With increasing rates of NCDs among the middle class and working poor in LMICs, and South Asia specifically (co-occurring with increased economic growth and affluence), the conclusion that the wealthy continue to have more problems around diabetes and other NCDs seems a bit overstated.

AUTHORS’ RESPONSE: THANK YOU FOR CLARIFYING THIS ISSUE FOR US. WE HAVE ADJUSTED THE TEXT ACCORDINGLY TO ADDRESS THIS ISSUE. FOR EXAMPLE, “Whereas obesity, metabolic syndrome, and diabetes are a greater risks among poor populations in high-income countries, affluence is associated with these poor health outcomes in some studies in South Asia [2]. However, the rapid economic transitions in India are demonstrating that high-income groups are able to mobilize behavioral and medical resources with an growing burden of chronic health problems falling upon the middle and lower class as is observed in high income countries [63-65]. Therefore, wealth may be a proxy for poor health habits, poor nutrition, limited exercise, excessive caloric intake, and smoking and drinking [66] at a specific moment in time in Nepal as the burden shifts
to other groups. Alternatively, our selection criteria may have confounded the association of wealth and depression, as we discuss in the limitations section below.”

6. A related issue is to the introduction’s statement: “In contrast to high-income countries, in South Asia, obesity, metabolic syndrome, and diabetes is a disease of wealthier members of the population [2].” It might be useful to indicate that in other South Asian countries a socioeconomic reversal of diabetes has been observed as the most affluent are becoming healthier and middle and lower classes are presenting high rates of NCDs (see Popkin et al 2012, Reddy et al 2007). What’s interesting about this point is that excluding those who have already had depression treatment may have played a role in why the affluent are more depressed in this sample. This is important because mental health and depression are strongly correlated and may play a role in why other studies have found lower income people with diabetes present with more depression. This is a topic worth considering for this paper.

AUTHORS’ RESPONSE: THANK YOU FOR RAISING THIS POINT. IT IS NOT SOMETHING WE HAD ORIGINALLY CONSIDERED. WE HAVE ADDED THIS TO THE DISCUSSION. SEE SAMPLE INSERTED TEXT FOR #5 ABOVE.

7. Social problems, such as gender inequality, may be discussed as causes for women’s higher rates of depression when compared to men. However, these findings are not varied from the general population, so, as other studies have indicated, they may reflect the greater population trends for depression (underscoring the impact of social problems on depression among people with diabetes as opposed to only disease-related problems).

AUTHORS’ RESPONSE: WE HAVE ADDED THIS HELPFUL POINT TO THE DISCUSSION AS WELL, IN PARTICULAR POINTING OUT THAT DIABETES MAY HAVE COMPARABLE FUNCTIONAL CONSEQUENCES FOR BOTH SEXES, WHEREAS WOMEN ARE MORE VULNERABLE Socially EVEN IN THE ABSENCE OF PHYSICAL DISEASE.

Minor Revisions
1. The authors use the term “diabetics” throughout; there is some hesitation to use this term across the diabetes literature. “People with diabetes” is preferred.

AUTHORS’ RESPONSE: THIS HAS BEEN CORRECTED THROUGHOUT TO READ “PERSONS LIVING WITH DIABETES.”

2. Several typos (missing or misplaced words, commas out of place, extra spaces) should be corrected. These are minor and can be corrected with a close read of the final manuscript once other revisions are complete.
   a. An example of where edits should be made are to this sentence (p. 15): “This contrasts with community studies of depression that show a consistently show greater prevalence among Nepali women compared to men.”
b. And this one (p. 16): “Integration of mental health services in primary care will be important combat prevent development of depression among diabetes patients.”

AUTHORS’ RESPONSE: THE MANUSCRIPT HAS BEEN EDITED FOR GRAMMAR AND STYLE.

Level of interest: An article of importance in its field
Quality of written English: Acceptable
Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.
Declaration of competing interests:
Dr. Brandon Kohrt is a colleague with whom I work with on anthropological projects unrelated to the current paper.

Reviewer's report
Title: Prevalence of depression and associated risk factors among persons with type-2 diabetes mellitus without a prior psychiatric history: a cross-sectional study in clinical settings in urban Nepal
Version: 1 Date: 21 July 2013
Reviewer: Lesley Jo Weaver
Reviewer's report:
This clinic-based study assesses the prevalence of depression among people with diabetes in Kathmandu, Nepal—a timely and important topic that has received little, if any, coverage in Nepal. The study is well designed, with rigorous methods of psychiatric assessment and inclusion/exclusion criteria that eliminate individuals who might be predisposed toward depression for reasons other than their diabetes. This fact lends credibility to the paper’s claim to provide evidence of a directional association leading from diabetes to depression, despite its cross-sectional nature. The results are presented in a straight-forward and clear manner, but I found that in some cases, the simple presentation was too simplified. In several places, the authors failed to fully address potential reasons for their findings, and implications. Most of the comments below are intended to encourage a more nuanced analysis of the statistical results in their sociocultural context.
Discretionary Revisions
1. In the introduction, the authors mention the bidirectionality of the relationship between diabetes and depression. Later in the paper (perhaps in the discussion/limitations section), they should address the fact that they only explored one half of the relationship. The manuscript would be further strengthened by briefly mentioning possible future steps for addressing the other half of the relationship.

AUTHORS’ RESPONSE: WE HAVE ADDED DISCUSSION ON THIS IN THE LIMITATIONS SECTION BEFORE CONCLUDING THE PAPER.
Minor Essential Revisions
1. Minor grammatical and punctuation errors need to be corrected throughout the manuscript to reflect standard English styles. Also in several places, words are repeated or omitted.

AUTHORS’ RESPONSE: THE MANUSCRIPT HAS BEEN EDITED FOR GRAMMAR AND STYLE.

2. In the introduction, the first three paragraphs could be condensed into a shorter and more integrated conversation of diabetes/depression, instead of addressing them in separate paragraphs. For instance, the first and third paragraphs (beginning with "Diabetes is a growing public health concern in Asia” and “The association between depression and diabetes has been reported in South Asia...” respectively) could be combined and edited down somewhat.

AUTHORS’ RESPONSE: THE FIRST THREE PARAGRAPHS HAVE BEEN COMBINED AS RECOMMENDED.

3. The introduction needs a stand-alone paragraph that clearly states the objectives and justification of the study. The last two sentences of the introduction address objectives in a clear manner, but this section should also refer back to the literature reviewed in previous paragraphs to provide clear justification of the study.

AUTHORS’ RESPONSE: THANK YOU FOR THIS SUGGESTION. WE HAVE DONE THIS.

4. The word “syndemic” at the top of page 16 is not used correctly. See Singer’s 2009 book.

AUTHORS’ RESPONSE: THANK YOU FOR POINTING THIS OUT. WE HAVE REMOVED THE MENTION OF SYNDEMIC IN THIS PAPER.

Major Compulsory Revisions
1. In the Settings section, the authors observe that community based studies of depression in Nepal have reported prevalences ranging from 28-41%. If this is accurate, the prevalence of 40% reported in this study might not be significantly higher than a general population-based level. Ideally, the authors would assess depression in a non-diabetic control group. If this is not possible, the similarity between prevalences in community-based studies and in this study needs to be addressed directly in the first paragraph of the Discussion section, where the authors compare their observed prevalence to prevalences in previous studies.
AUTHORS’ RESPONSE: THANK YOU FOR POINTING THIS OUT. WE HAVE NOW ADDED TEXT THAT THE RATE OF DEPRESSION AMONG THIS SAMPLE WITH DIABETES IS SIMILAR TO RATES OBSERVED AMONG OTHER HIGH RISK GROUPS (E.G. LOW CASTE DALIT GROUPS) AND IN AREAS WITH HIGH STRUCTURAL VIOLENCE CHARACTERIZED BY POVERTY, LACK OF SOCIAL SERVICES, LACK OF HEALTH CARE, LACK OF EDUCATION, AND EXPOSURE TO INTERPERSONAL VIOLENCE: “It is important to note that the prevalence of depression in this sample of persons living with diabetes (40%) is comparable to rates of depression observed among other risk groups in Nepal such as low caste Dalit groups (BDI-based depression prevalence, 50%) [35], populations with high political violence exposure including both adults civilians (Dang district, BDI-based depression prevalence, 43%) [32] and child soldiers (depression prevalence, 53%) [59], and populations with high rates of structural violence including poverty, lack of education, lack of health care, and high rates of gender discrimination (Jumla district, BDI-based depression prevalence, 41%) [33].”.

2. The manuscript needs to more specifically address why high income might be associated with depression in Nepal but not in other South Asian countries, such as India. If income serves as a proxy for increased health-harming behaviors in Nepal, as the authors suggest, one would expect to see similar trends in India, where the growing middle and upper classes experience increasing sedentization, rich diets, and also currently experience the highest rates of chronic diseases like diabetes.

AUTHORS’ RESPONSE: AS PER THE RECOMMENDATIONS OF REVIEWER #1 WHO WAS ALSO CONCERNED ABOUT THIS ISSUE, WE HAVE ADDED ADDITIONAL CONFOUNDING FACTORS THAT MAY HAVE LED TO THIS ASSOCIATION. IN PARTICULAR, THERE IS A STRONG ASSOCIATION BETWEEN POVERTY AND DEPRESSION IN NEPAL AS ELSEWHERE IN THE WORLD. THE ASSOCIATION OF DEPRESSION AND HIGHER INCOME MAY RESULT FROM OUR EXCLUSION CRITERIA ELIMINATING PERSONS WITH PRE-EXISTING DEPRESSION, WHO MAY BE MORE LIKELY TO BE LOW SES. WE HAVE ADDED TEXT TO THE DISCUSSION AND LIMITATIONS SECTION REGARDING THIS POINT.

3. It is noteworthy that behavioral and socially mediated predictor variables, such as socioeconomic status, erectile dysfunction, living in a nuclear family, injecting insulin, and monthly income, were among the strongest predictors of depression, as opposed to biological measures of health such as HbA1c and hypertension (here, WHR is an obvious exception, although WHR does have important social valences as well). This trend deserves some mention in the discussion and would enrich the stated conclusion that “Depression is associated with indicators of more severe diabetic disease status.” These indicators convey more complex information than simply diabetes status. Why, in this cultural context, might social/behavioral predictors be more strongly associated with mental health than biomarkers? What are the implications for diabetes/depression management?
AUTHORS’ RESPONSE: WE HAVE RAISED THIS ISSUE IN THE DISCUSSION. WHILE WE DO NOT FEEL THAT THE DATA LENDS ITSELF TO WEIGHTING BIOMARKERS VS. SOCIAL-BEHAVIORAL FACTORS, WE DO EMPHASIZE THAT SOCIAL-BEHAVIORAL FACTORS MAY BE AS IMPORTANT AS DISEASE CONTROL IN MENTAL HEALTH AMONG PERSONS WITH DIABETES. DIABETES IS ONLY ASPECT OF THESE VULNERABILITY FACTORS THAT CAN CONTRIBUTE DIRECTLY TO DEPRESSION INDEPENDENT OF DIABETIC STATUS. WE SUGGEST THAT A STUDY DIRECT AND INDIRECT EFFECTS OF DIABETES ON DEPRESSION WOULD BE HELPFUL WAY TO FRAME FUTURE STUDIES.

4. There is currently no discussion of the study's limitations. This should be addressed, even if briefly, in the Discussion section.

AUTHORS’ RESPONSE: WE HAVE ADDED A LIMITATIONS SECTION.

Level of interest: An article of importance in its field
Quality of written English: Needs some language corrections before being Published

AUTHORS’ RESPONSE: ADDITIONAL ENGLISH LANGUAGE EDITING WAS COMPLETED.

Statistical review: No, the manuscript does not need to be seen by a statistician.
Declaration of competing interests:
I declare that I have no competing interests.