Reviewer's report

Title: Effects of ethnicity and CD4 count on glucose metabolism among HIV patients on highly-active antiretroviral therapy (HAART)

Version: 1 Date: 9 November 2012

Reviewer: dominic reeds

Reviewer's report:

This paper seeks to explore the relationship between ethnicity, CD4 count and metabolic risk. The methods used appear to be appropriate for the outcome measures.

Major compulsory revisions

The title of this paper and the goal according to the introduction is to assess the effect of ethnicity... This study design only allows for assessment of the relationship between or association of, and as a cross sectional study is not designed to formally test the effect of any variable on another. I strongly suggest amending the title and stated goal of the study to reflect this.

The patients selected, by design, had hypertriglyceridemia (spelled wrong in the abstract). Hypertriglyceridemia is clearly associated with insulin resistance, according to the metabolic syndrome model of Reaven, and has been shown to be associated with insulin resistance in people with HIV receiving HAART (reeds et al, 2004). Indeed, the HOMA was ~3 which is suggestive of insulin resistance in each group. Given this, it is reasonable to view the subjects as a distinct population from a randomly selected cohort of people with HIV, many of whom will not have high triglyceride levels and lack insulin resistance. This is clearly a design limitation and should be noted as such in the discussion. Further, the findings of this study should be considered to be limited only to patients with high triglycerides. Again as noted in the discussion, the insulin secretory response relative to the change in glucose, was abnormal irrespective of CD4 strata suggesting that both groups were well on their way to developing diabetes.

A major finding of this study was that in the moderate CD group hispanics had the highest glycemic excursions whereas in the low group, AA had the worst glycemic changes. This is all predicated on the cut-off of 300. While the authors provide a rationale for this cut-off I would like to know if cut-offs of 350 or 200 are do these change the findings?

It is hard to know what to make of the findings of an interaction of ethnicity with glycemic excursion. Is it possible that this is a fluke finding or was this a pre-specified goal of the study? If CD4 level was not associated with dysglycemia, the authors should explain why they then sought to determine if this was affected by ethnicity. It is hard to believe that whole-body glucose concentration is dramatically affected by differences in CD4 glucose uptake. I agree that systemic inflammation could be involved but the hsCRP values were if
anything lower in the low CD4 group.

As noted above, the discussion should not that the findings of this study cannot be extrapolated to the HIV population as a whole, but only those with high triglycerides or other signs of insulin resistance.

Minor

As noted by the authors, it is not surprising that A1C was higher in AA as most studies have shown about a 0.2-0.3 point higher A1C for any given glucose in AA than Caucasians and were actually about that expected. Indeed the mean A1c for AA was almost in the prediabetic range. What proportion of each group met A1C criteria for diabetes and/or prediabetes. As A1c covaried with ethnicity, I believe that the statistical methods employed would tend to favor showing that there was an interaction between ethnicity, A1C and fasting glucose, so I think it is hard to know what to make of this finding (bottom of page 9-10).

The table is too long. I would delete height, weight, hip and leave BMI, adiposity, waist and waist:hip ratio and perhaps fat-free mass. Consider deleting the 30-90 minute time-points in the OGTT in the table to make it more readable, could just such incremental or absolute AUC.

The association of PI use with lower fasting glucose is interesting as several studies have suggested that efavirenz increases fasting glucose (Levitt NS. Effect of nonnucleoside reverse transcriptase inhibitor-based antiretroviral therapy on dysglycemia and insulin sensitivity in South African HIV-infected patients, JAIDS). Is it possible to determine if efavirenz was associated with elevated fasting BG in the database?

Lines 4-6 page 10, are grammatically incorrect

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Acceptable

**Statistical review:** Yes, but I do not feel adequately qualified to assess the statistics.

**Declaration of competing interests:**

I declare that I have no competing interests