Depression and All-Cause Mortality in an HIV Treatment Cohort in Rural Uganda

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Abstract

Objective: To determine the extent to which depression is associated with mortality among persons living with HIV (PLHIV) initiating antiretroviral therapy (ART).

Methods: 694 treatment-naïve PLHIV in rural Uganda were followed from initiation of ART. Each participant provided quarterly data through blood draws and structured interviews. Baseline depression symptom severity and mental health status were measured using locally adapted versions of the Hopkins Symptom Checklist and MOS-HIV mental health summary. Vital status was ascertained through participant tracing after missed study visits. We fit Cox proportional hazards regression models, adjusting our estimates for baseline age, sex, marital status, educational attainment, household asset wealth, CD4+ T-lymphocyte cell count, body mass index, and MOS-HIV physical health summary.

Results: Over 4.3 median years of follow-up, only 48 participants (7%) were lost to follow-up and there were 44 deaths. After multivariable adjustment, probable depression was associated with increased mortality (AHR=2.24; 95% CI, 1.08-4.62), while mental health-related quality of life was not (AHR=0.98; 95% CI, 0.94-1.03).

Conclusions: Depressed mood is associated with increased mortality among HIV+ persons initiating ART. Screening for depression may be a relatively low-cost method of identifying HIV+ persons at high risk for mortality. Whether pre-ART depression reflects underlying immune activation or poor overall health status should be addressed in future studies.

Background

- Depression has been associated with systemic immune activation **[1]**, which in turn has been implicated in increased mortality among persons living with HIV (PLHIV) **[2]**
- The only study in sub-Saharan Africa to examine the depression-mortality relationship was conducted among HIV-positive women who lacked access to HIV antiretroviral therapy (ART) **[3]**
  - The extent to which the depression-mortality relationship holds among PLHIV initiating ART is unclear

The UARTO Study

- Data were drawn from the Uganda AIDS Rural Treatment Outcomes (UARTO) study, a prospective cohort of PLHIV initiating ART in Mbarara, a rural region of southwest Uganda
- Initiated in 2005, with active participants followed through 2014
- Participants seen every 3-4 months for blood draws and structured interviews conducted in the local language (Runyankore)
- Ethical approval for all study procedures obtained through UCSF, Partners/MGH, and Mbarara University of Science & Technology

Primary Measures

- Outcome of interest was all-cause mortality, confirmed through contact tracing in the event of missed study visits
- 15-item Hopkins Symptom Checklist for Depression (HSCL), modified for the local context with the addition of a 16th item
  - Conventional threshold of >1.75 applied to indicate probable depression / clinically significant symptoms of depression
- Medical Outcomes Study-HIV Health Survey (MOS-HIV) Mental Health Summary score, widely used to assess mental health-related quality of life among PLHIV in a variety of cultural contexts
  - MOS-HIV has good reliability and validity among PLHIV in Uganda

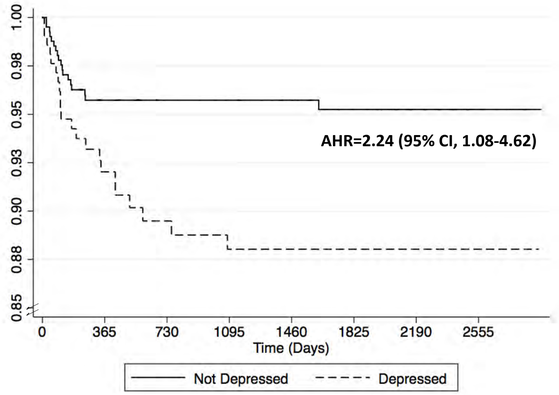
Statistical Analysis

- We fitted 2 Cox proportional hazards regression models to the data, with baseline depression and mental health-related quality of life specified as the primary explanatory variables of interest
- Adjusted for the following baseline covariates: age, sex, marital status, educational attainment, household asset wealth, CD4+ T-lymphocyte cell count, body mass index, and MOS-HIV Physical Health Summary score
- *Sensitivity Analysis:* the regression models were re-fitted to the data after restricting estimation to the subset of participants who had achieved initial viral suppression
  - Avoids confounding by health status and removes early mortality from consideration

Results

- Of 694 participants, 480 were women (69%); baseline median values were: age, 34 years (IQR, 28-40); CD4 count, 162 (IQR, 91-249); HSCL depression score, 1.4 (IQR, 1.2-2.0); and MOS-HIV mental health summary score, 53 (IQR, 47-59).
- 216 (31%) met screening criteria for probable depression.
- Over 4.3 median years of follow-up, 48 participants (7%) were lost to follow-up and there were 44 deaths.

Figure 1. Cumulative Survival, by Baseline Depression and Adjusted for Covariates



- In multivariable-adjusted Cox proportional hazards regression models, probable depression was associated with increased mortality (adjusted hazard ratio [AHR]=2.24; 95% CI, 1.08-4.62)
- Mental health-related quality of life was not (AHR=0.98; 95% CI, 0.94-1.03).
- When estimation was restricted to the subset of participants who had achieved initial viral suppression, the association with depression increased in magnitude but was less precisely estimated (AHR=6.32; 95% CI, 1.56-25.7)

Conclusions

- Among PLHIV initiating ART in rural Uganda, clinically significant symptoms of depression were associated with an increased risk of all-cause mortality
- This finding is consistent with another study, initiated prior to the advent of effective HIV treatment and completed prior to HIV treatment scale-up, involving HIV-positive women in Tanzania **[3]**
- Prior work showing that depression is associated with greater rates of tryptophan catabolism through the kynurenine pathway and lower plasma tryptophan levels **[1]** may explain these observations
- Sensitivity analysis suggests that this finding is unlikely to be explained by confounding by health status

References

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