



The Effect of Antidepressant Medication on Antiretroviral Adherence and HIV-1 RNA Viral Load

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Abstract

Background: Depression is known to worsen the course of HIV, but it is unknown whether and/or how treatment with antidepressant medication improves HIV outcomes.

Subjects: Participants were selected from a cohort of HIV+ homeless and marginally housed adults living in San Francisco if they had been started on HAART.

Primary Outcome: log₁₀ HIV-1 RNA viral load

Statistical Analysis: A marginal structural model was fitted using ordinary least squares (OLS) and weighted by inverse probability of treatment and censoring (IPTC) weights. The treatment estimate was adjusted for numerous confounders.

Primary Finding: OLS regression showed a -0.56 log₁₀ effect of antidepressants on viral load (95% CI, -1.04 to -0.08; P=0.02), compared to no treatment. IPTC-weighting showed a -0.83 log₁₀ difference (95% CI, -1.62 to -0.04; P=0.04). When 7-day self-reported adherence was added to the model, the treatment estimate was reduced to -0.11 (P=0.79).

Conclusions: Antidepressant medication treatment results in a statistically significant reduction in viral load. This effect is mediated largely through improved adherence to HAART.

Background

- Depression is known to worsen the course of HIV illness
- Multiple potential mechanisms may account for this observed relationship, including:
 - Worsened adherence to HAART, or
 - Disturbances in HPA axis directly affecting immune function
- Unknown whether treatment with antidepressant medication can improve HIV outcomes, either through:
 - Improved adherence to HAART, or
 - Enhanced natural killer cell function and other improved immune responses

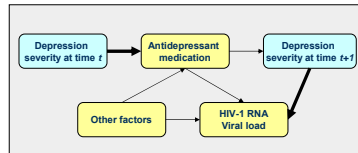
The REACH Cohort

Research on Access to Care in the Homeless

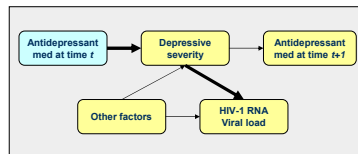
- HIV-infected homeless and marginally housed persons on highly active antiretroviral therapy (HAART)
- Systematically recruited from homeless shelters, free-meal programs, and single-room occupancy hotels in San Francisco
- Structured questionnaires and blood collections administered at baseline and on a quarterly basis: socio-demographics, alcohol and drug use, health services utilization, health status
- 418 participants, 1330 person-years of follow-up
- Only 2% loss to follow-up annually
- Written consent obtained from all participants; study procedures approved by the Committee on Human Research

Analytic Conundrum

- Time-dependent confounding exists when a covariate (in this case, depressive severity) predicts treatment *and* outcome



- Control for time-dependent confounding by depressive severity gives biased estimates because it lies in the causal pathway from antidepressant medication to viral load



Statistical Analysis

- Conventional methods will give biased results
 - Crude estimate with no control for confounding ignores the fact that depressive severity increases the probability of antidepressant medication treatment
 - Control for baseline depressive severity ignores the fact that subsequent worsening of depression increases the probability of antidepressant medication treatment
 - Control for time-updated values of depressive severity ignores the fact that antidepressant medication acts partly by lowering depressive severity
- Marginal structural model (MSM) fit to data using ordinary least squares (OLS) regression and/or logistic regression, with inverse probability-of-treatment weights (IPTW)
 - Analogous to conducting a randomized, controlled trial each month, among participants still not taking antidepressant medication
 - IPTW controls for confounding by modeling the probability of treatment given covariates
 - Weights are inversely proportional to the probability of a subject receiving the observed treatment
- Dependent variable: HIV-1 RNA viral load (OLS model), probability of viral suppression (logistic model)
- Independent variable: any antidepressant medication use
- Treatment estimate adjusted for demographic characteristics, alcohol and drug use, depression severity, and diagnosis of major depression
- To determine whether antidepressant effect was mediated by adherence to HAART, 7-day self-reported adherence was entered into the MSM and the change in the treatment coefficient was reassessed
 - Pill count adherence data were available for only a subset of participants (258 person-years of follow-up), thus used in a sensitivity analysis

Results

	Effect of antidepressant on log ₁₀ HIV-1 RNA viral load	Effect of antidepressant on probability of viral suppression
	β (95% CI)	OR (95% CI)
Unweighted	-0.56 (-1.04, -0.08)	1.29 (0.96, 1.74)
IPTW	-0.83 (-1.62, -0.04)	1.44 (0.86, 2.39)
IPTW, with self-report adherence	-0.11 (-0.92, 0.71)	1.02 (0.58, 1.80)
IPTW, with pill count adherence	-0.15 (-1.07, 0.77)	1.15 (0.53, 2.49)

Conclusions

- Antidepressant medication treatment resulted in a statistically significant reduction in viral load
- The effect was mediated largely through improved adherence to HAART

Funding

- This study was funded by NIMH 54907. HIV RNA kits were donated by Roche. Dr. Tsai received additional support from NIH/NCRR UCSF-CTSI UL1 RR024131. Dr. Bangsberg received additional funding from NIAAA 015287. Dr. Weiser received additional funding from NIMH 79713-01.

