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AIDS treatment and mental health: Evidence from Uganda

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ABSTRACT

Increased access to antiretroviral therapy (ART) in developing countries over the last decade is believed to have contributed to reductions in HIV transmission and improvements in life expectancy. While numerous studies document the effects of ART on physical health and functioning, comparatively less attention has been paid to the effects of ART on mental health outcomes. In this paper we study the impact of ART on depression in a cohort of patients in Uganda entering HIV care. We find that 12 months after beginning ART, the prevalence of major and minor depression in the treatment group had fallen by approximately 15 and 27 percentage points respectively relative to a comparison group of patients in HIV care but not receiving ART. We also find some evidence that ART helps to close the well-known gender gap in depression between men and women.

Introduction

The burden of disease associated with mental disorders in developing countries is attracting increasing attention (Patel et al., 2007a; Prince et al., 2007). Recent estimates suggest that mental disorders may account for as much as 10% of total disease burden as measured by disability adjusted life years or DALYs (Patel 2007), and depression is ranked as one of the top ten leading causes of disease burden measured by DALYs (Lopez, Mathers, Ezzati, Jamison, & Murray, 2006). Rates of mental illness have been shown to be particularly high among people living with HIV. A recent review estimates that the rate of mental disorders among HIV positive individuals is between 44 and 58% (Brandt, 2009). Depression appears to be the most common disorder. In sub-Saharan Africa, 10–20% of persons living with HIV have major depression and another 20–30% have elevated depressive symptoms or minor depression (Brandt, 2009; Collins, Homan, Freeman, & Patel, 2006; Myer et al., 2008). Other studies have also shown higher rates of anxiety, substance use, and posttraumatic stress in people living with HIV (Myer et al., 2008; Sebit et al., 2003).

While there is a clear association between mental illness and HIV, the direction of causality is less clear. Does being infected with HIV lead to worse mental health or does the causality run in the opposite direction? Both are plausible. There is a large literature showing that individuals with mental disorders engage in higher than average rates of risky behaviors ranging from unprotected sex, to sex with multiple partners, to drug use, making them much more likely to become HIV infected (Carey et al., 2004; Meade & Sikkema, 2005; Rosenberg et al., 2001). On the other hand, HIV infection may lead to worse mental health because of direct neurological effects of the virus (Freeman, Patel, Collins, & Bertolote, 2005), psychological stress induced by inability to provide for one's family because of ill health, and the social alienation associated with stigma and discrimination (Chandra, Ravi, Desai, & Subbakrishna, 1998; Tostes, Chalub, & Botega, 2004). Numerous studies have also documented a strong correlation between poor physical health and poor mental health (Das, Do, Friedman, & McKenzie, 2009; Mohanan & Maselko, 2010). Because causality is likely to run in both directions, separating one from the other is empirically challenging.

To shed some light on the question of whether HIV causes mental illness, we study the effect of antiretroviral therapy (ART) on depression. If HIV causes depression, for example through its effect on physical health, then treatment with ART should lead to a decrease in depression rates. If causality runs primarily in the other direction, then ART should have little or no effect on depression. It is also theoretically possible that ART may *worsen* mental health, for example because of the stress associated with adherence to a daily regimen of pill taking. Some antiretroviral drugs such as efavirenz have also been found to have psychiatric side effects (Kenedi & Goforth, 2011). The link between HIV and depression is of significant policy interest because depression has been linked to more rapid HIV disease progression (Antelman et al., 2007), lower adherence to HIV medication (Starace et al., 2002), and worse outcomes (Briongos-Figuero, Bachiller-Luque, Palacios-Martin, de Luis-Roman, & Eiros-Bouza, 2011; Cook et al., 2004).

The effects of ART on mental health, and in particular on depression have not been well studied. While there is no shortage of studies documenting the effects of ART on physical health and

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quality of life (Beard, Feeley, & Rosen, 2009; Jahn et al., 2008), and on economic wellbeing (Thirumurthy, Goldstein, & Graff Zivin, 2008), much less attention has been paid to the effects of ART on mental health. The available empirical evidence is mixed. While some studies have found beneficial effects (Bock et al., 2008; Jelsma, Maclean, Hughes, Tinise, & Darder, 2005), others have found no effect (Adewuya et al., 2007; Freeman, Nkomo, Kafaar, & Kelly, 2007), and at least one study has found a negative effect of ART on mental health (Pearson et al., 2009). The latter study, which was situated in Mozambique, found that depressive symptoms *increased* after 12 months on ART. A review by Brandt (2009) highlights some of the shortcomings of this literature that make it difficult to draw firm conclusions. Of the 23 studies that were reviewed, only 5 were longitudinal studies and of these, only 2 used a comparison group. This paper makes the following contributions: first we study the impact of ART on an important mental health disorder, depression, second, our panel study design with treatment and comparison groups allows for more robust identification, and third, we differentiate between impacts of ART on minor and major depression and explore whether there are heterogeneous effects by gender.

Methods

The study setting

Uganda is often held up as a HIV/AIDS success story in Africa. Initially one of the highest HIV prevalence countries in the region, the 1990s saw a dramatic decline in HIV prevalence rates from a high of 18.5% in 1992 to about 5% in 2000 (Kirungi, Musinguzi, Opio, & Madraa, 2002). This decline in prevalence has been attributed to strong proactive government leadership, an effective grassroots prevention campaign, and an open approach to managing the epidemic that helped to reduce the stigma associated with the disease (Schoepf, 2003; Slutkin et al., 2006). Currently, there are an estimated 1.2 million people in Uganda living with HIV/AIDS, about 57% of whom are female, and 12.5% of whom are children under 15 (Uganda AIDS Commission 2012). Heterosexual transmission accounts for the vast majority (80%) of HIV infections in Uganda, with mother to child transmission accounting for about 20% of cases. There is some indication that HIV infections may be on the rise (Shafer et al., 2008) with recent estimates showing an 11% increase in HIV incidence from 115,775 new cases in 2007/2008 to 128,980 new cases in 2009/2010.

Study design

This study was carried out between July 2008 and October 2010 at two HIV clinics in Kampala, Uganda. Between June 2008 and April 2009, 482 eligible patients were enrolled into the study. Although statistics on study refusal were not recorded, the study interviewers indicate that nearly all clients who were eligible agreed to enroll in the study. Eligibility criteria for participation included patient type (patients new to HIV care), age (adults 18 and older), completion of an evaluation for ART eligibility, and a CD4 count $<$400 cells/mm^3. The latter restriction was to increase the similarity between patients in the treatment (ART) group, and patients in the comparison (non-ART) groups, since randomization was not ethical as ART was widely available at the study sites and in most of Uganda.

257 patients were eligible for ART and assigned to the treatment group, while 225 patients met study participation criteria but were not eligible for ART and were assigned to the comparison group. ART eligibility was defined based on clinical criteria (CD4 count $<$200 cells/mm^3 or WHO Stage III/IV disease), and adherence readiness as assessed through clinic attendance and having a 'treatment supporter'. This is typically a relative or friend who will help the patient access and adhere to treatment. Individuals are only required to identify someone who can play this role; the 'treatment supporter' otherwise does not play a formal role in the patient's treatment. We also note that it is rare for patients to be refused ART because of the inability of the patient to identify a 'treatment supporter'.

All study participants received standard HIV care, which included monitoring and treatment of infections, and prescription of appropriate prophylactic medications. Psychiatric care was not available at the study clinics during the study period, and antidepressants were not used to treat depression; however, counseling services were available to clients when requested or recommended by the provider, and generally consisted of pre- and post-HIV test counseling, ART adherence counseling, and counseling related to HIV disclosure and sexual and reproductive health issues.

Study subjects were assessed at baseline, at 6 months, and again at 12 months. Assessment consisted of a clinical assessment (opportunistic infections, medications, CD4 count), and an interviewer-administered survey. The survey collected information about patient characteristics including economic outcomes; attitudes toward treatment; adherence to medication; sexual behavior, and physical and mental health. All participants also received compensation of approximately $2.50 (6000 Uganda Shillings) after each study assessment (this is roughly equivalent to a day's wages). The protocol was approved by the Institutional Review Board of Makerere University, College of Health Sciences and the Uganda National Council of Science and Technology.

Empirical strategy

Our objective is to estimate the impact of ART on depression. Our basic regression model is a difference-in-difference (D-in-D) linear probability model that compares the *change* in depression for the treatment group (individuals in the ART group) to the *change* in depression for the comparison group. All models are estimated on an intent-to-treat basis. The basic model takes the following form:

$$\begin{aligned}\text{Depression}_{it} = {} & \beta_0 + \beta_1 \text{Treated}_i + \beta_2 \text{Treated}_i{*}6\text{ months} \\ & + \beta_3 \text{Treated}_i{*}12\text{ months} + \boldsymbol{X}_i'\boldsymbol{\delta} + \nu_t + \varepsilon_{it}\end{aligned}$$

where Depression_{it} is a binary indicator for whether an individual has major depression (or minor depression in alternative specifications) at time t. Depression was assessed using the nine-item Patient Health Questionnaire (PHQ-9). The PHQ-9 is commonly used to screen for depression in primary health care settings. It has 9 questions, each measuring the frequency of a symptom over the last two weeks using a rating scale from 0 'not at all' to 3 'nearly every day', and scores are summed (the maximum possible score is therefore 27). A score of 5–9 indicates minor depression, while 10 or higher indicates major depression; within the classification of major depression is three levels of severity: moderate (scores of 10–14), moderate to severe (15–19) and severe (20 and greater) (Kroenke, Spitzer, & Williams, 2001). Treated_i is an indicator for whether the individual was assigned to the ART group at baseline. Treated_i * 6 months and Treated_i * 12 months are the explanatory variables of interest. β_2 and β_3 represent the impact of ART on depression at 6 and 12 months respectively. $\boldsymbol{X_i}'$ is a vector of baseline characteristics that include age, sex, education, marital status, health status, employment status, number of children, household size, and household wealth quintiles. We include these variables to control for baseline differences between individuals in the treatment and comparison groups. ν_t are the time (survey wave) dummies included to control for common time trends.