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An Instrumental Variable Evaluation of Antidepressant Use on Employment Among HIV-Infected Women Using Highly-Active Antiretroviral Therapy in the United States: 1996-2004

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ABSTRACT

This paper examines the effect of antidepressant use on the likelihood of being employed among HIV-positive women receiving highly active antiretroviral therapy (HAART) in the United States from 1994 to 2004. We use instrumental variables to predict antidepressant use independently of outcomes; thus, addressing potential sources of bias -- more depressed women are more likely to receive antidepressant treatment, but they are also more likely to be unemployed. The results show that antidepressant use has a positive effect on the employment probability of women living with HIV. The proposed instrumental variables can be used to identify antidepressant use in the WIHS population. Among women receiving HAART, and controlling for individual and local area labor market characteristics, the use of antidepressants is associated with a higher probability of being employed.

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1. INTRODUCTION

Depression treatment has been shown to have an impact on the likelihood of being employed (Schoenbaum 2002) in the general population. Similarly, highly active antiretroviral therapy (HAART) has an important clinical effect, as well as an influence in terms of employment (Goldman and Bao 2004) among HIV infected individuals. However, there have been no studies so far evaluating the impact of antidepressant use on the employment for persons living with HIV and using HAART. Conducting this evaluation is important because depression is common, often under diagnosed and under treated in HIV-positive populations (Ciesla and Roberts 2001, Asch et al. 2003).

In an idealized randomized control trial, we would assign depressed HIV-positive patients on HAART to two groups: one group treated with antidepressants; and a control group that is not treated with antidepressants. Then, we would compare their employment outcomes after a suitable period of observation. This, of course, would be unethical: knowingly denying necessary medical treatment to patients who need it. The research question then may be best addressed with non-experimental methods but requires exercising considerable care, because simply comparing treated versus non-treated patients, in a setting where they themselves are in part responsible for seeking and complying with treatment, can result in biased estimates of the treatment effect.

This paper investigates the effect of antidepressant use on the patient's probability of employment using observational longitudinal data from a sample of women living with HIV, and who are using HAART. The analytical approaches explicitly take account of the fact that

observable and unobservable factors play a role in the relationship of interest. We use measures of the variability in Medicaid coverage for antidepressants over time and across States as instrumental variables for the use of antidepressants. This variability is directly related to the patient's likelihood of receiving antidepressant treatment, but we assume that it is not directly related to the participants' employment outcomes, except through the antidepressant treatment.

The next section provides a background of previous research, and a simple conceptual framework. Section 3 specifies the data sources and the population studied. Section 4 presents the analytical methods. Section 5 shows the results of the employment effect of antidepressant use for women living HIV and using HAART. The final section contains a discussion, and brief policy implications.

2. BACKGROUND

The impact of mental health on labor market outcomes has been documented in the literature. A study using nationally representative data (Ettner, Frank, and Kessler 1997) estimated the effect of several disorders, including major depression, on labor market outcomes. Women with depression were reported to be about eight percentage points less likely to be employed (a reduction in the probability of employment from 81.8 percent with no disorder, to 73.7 percent in the presence of major depression). A study at a regional level focusing on a low-income population (Alexandre and French 2001) examined the effect of depression on labor market outcomes in the Miami-Dade County, and found that depression decreased the probability of being employed by 19 percentage points.

In terms of treatment, data from a randomized controlled trial (Schoenbaum 2002) demonstrated that appropriate depression treatment has a positive effect on employment. The study found that 72 percent of patients exposed to the appropriate depression care were employed six months after treatment; compared to 53 percent of those who received no or inappropriate treatment.

Our conceptual framework is derived from the basic model of labor supply (Killingsworth 1983) where a person's decision to work is affected by a number of factors including: age, race, education, marital status, the market wage, non-earned income (or assets), and the general state of the economy. Particularly for women, the decision to work is also affected by the number of young children living at home, the partner's or spouse's employment status and wages (Killingsworth and Heckman 1986; Mroz 1987), as well as her physical and mental health (Ruhm 1992). Figure 1 illustrates the case of an HIV-positive person. At the end of an asymptomatic period: viral load increases, CD4 count decreases, symptoms of HIV disease appear, and HAART becomes necessary. In this scenario, employment decreases due to physical illness, treatment side effects, and possible depression. The basic hypothesis to be tested is that effective treatment for HIV disease and depression can reverse that trend.

HAART dramatically altered the natural course of HIV infection. Potent antiretroviral treatment effectively delays the occurrence of the acquired immunodeficiency syndrome (AIDS); and it extends the life expectancy of HIV-positive individuals (Cole et al. 2003; Detels et al. 1998; Palella et al. 1998). The literature confirms that HAART also affects labor market outcomes. Recent works document that HAART users are more likely to be employed, controlling for relevant covariates (Bernell and Shinogle 2005; Goldman and Bao 2004). Thus,

this study restricts the analysis to those individuals who are currently using HAART to avoid some of the confounding due to the high effectiveness of the potent antiretroviral treatment on employment outcomes.

The measure of the treatment effect is then one where exposures to HAART plus antidepressants are compared to HAART alone. The hypothesis is that HAART is effective in stabilizing current health; and that antidepressants have two additional effects in improving employment outcomes. First, a direct channel from antidepressant use to fewer and less severe depression symptoms to improved employment probabilities. Second, an indirect channel by which antidepressant use improves the probability of receipt and adherence to HAART (Cook et al. 2002; Cook et al. 2006; Kleeberger et al. 2004; Li et al. 2005), and thereby further improves health status, and employment probability. The overall objective of this paper is thus to examine whether the use of antidepressants has an impact on the employment of HIV-positive women who use HAART.

3. DATA

This paper uses data from the Women's Interagency HIV Study (WIHS) to test whether antidepressant use affects the likelihood of employment for women receiving HAART. Funded by the National Institutes of Health (NIH), WIHS is an on-going, multi-center, prospective cohort study started in 1994 to carry out comprehensive investigations of the impact of HIV infection in women. A total of 3,768 women have been enrolled; about 80 percent of them are from racial/ethnic minority groups. The sites are located in: Bronx, NY; Brooklyn, NY; Chicago, IL; Los Angeles, CA; San Francisco, CA; and Washington, DC. WIHS is one of the longest-running HIV cohort studies for women in the world. Visits are

scheduled twice per year. A detailed description of study methods and rationale for the cohort has been presented elsewhere (Barkan et al. 1998).

The present analysis uses WIHS data collected from April 1st, 1996 (when protease inhibitors (PIs) first became commercially available) through September 30th, 2004. Women eligible for this study were: HIV-positive, between the ages of 18 and 65 years, and for each observation analyzed they had been using HAART[1] since the previous calendar visit. A total of 1,838 women fulfilled all these eligibility criteria at baseline. They contributed a total of 12,727 person-visits and had a median follow-up time of 3.72 years.

4. ANALYTICAL METHODS

Estimating the employment effect of antidepressant use was complicated by endogeneity due to selection bias (or selection by indication) due to observable and unobservable variables. As individuals present more symptoms of depression (and as the CES-D score increases), the probability of receiving antidepressants was also likely to increase. However, at the same time, more depressed persons were also more likely to be jobless because of socio-economic, demographic, local area or other characteristics. The systematic but measurable differences that exist between treated and non-treated groups are often called "selection on observables." Other sources of bias that are due to unobservable factors can also affect both the outcome and the explanatory variable; for instance, some unmeasured factors, such as resilience or ability to cope, could enable participants to continue working and at the same time make them be less likely to be depressed.

To address these biases, we used an instrumental variables (IV) approach. The IV approach is a general method originally developed in the economics literature several decades ago (Angrist

and Krueger 2001), but more recently being applied in other fields as well (Angrist, Imbens, and Rubin 1996; Greenland 2000; Harris and Remler 1998; Moffitt 2005; Newhouse and McClellan 1998). Methods for correction of selection bias in the mental health literature have been applied in recent years also (Crown et al. 1998; Lu 1999; Salkever et al. 2004; Salkever, Slade, and Karakus 2006). The basic method involves two-stage least squares (2SLS). The first stage estimates the observed treatment choice based on the covariates and instruments, and the second stage predicts the outcome variable of interest. The instruments need to be highly correlated with the treatment choice; but cannot have direct effect on the outcome (Cameron and Trivedi 2005; Greene 2003; Wooldridge 2002).

Specifically, we applied a linear probability model using a binary outcome and a binary treatment variable (Angrist 2001; Heckman 1978; Heckman and MaCurdy 1985). The empirical equations in this framework were:

$$Y_{it} = \alpha_i + \beta_i T_{it} + \gamma X_{it} + \varepsilon_{it} \qquad (1)$$

$$T_{it} = \delta_i + \theta X_{it} + \phi Z_{it} + \upsilon_{it} \qquad (2)$$

where for individual i at time t, Y is the outcome of interest (current employment), T is the treatment variable (antidepressant use since the previous visit), X is the covariates vector, Z are instrumental variables, and ε and υ are error terms. Under the random effects (RE) model, the individual term a_i is assumed to be uncorrelated to the covariates vector X, so that the conditional distribution $f(a|X)$ is not dependent on X. On the other hand, the fixed effects (FE) model leaves that distribution unrestricted, so that a and X may be correlated (Greene 2003). Under fixed effects, we estimated the following model:

$$\Delta Y_i = \beta_i \Delta T_i + \gamma \Delta X_i + \varepsilon_i \quad (3)$$

$$\Delta T_i = \theta \Delta X_i + \phi \Delta Z_i + \upsilon_i \quad (4)$$

where the symbol "∠" represents, the first difference, or a change in a variable from time *t* to time *t+1*. We assumed in the last model that equations (1) and (2) contain fixed effects for each individual, which can potentially be correlated with T_i but that cancel out in the first-differencing approach.

In the empirical estimation that follows, under fixed effects, the *X* covariates vector contains the following time-varying variables: CD4 cell count, detectable viral load (=1 if HIV RNA level is greater than 80 copies per ml; =0 otherwise), the depression symptoms score (CES-D), as well as a general quality of life index.[2] In addition, *X* contains local area labor market characteristics including the unemployment rate, and average real weekly earnings at the Metropolitan Statistical Area (MSA) level, and the adult employment ratio at the State level (see Appendix D). The hypothesized channels for the treatment effect should work through the CES-D, quality of life index, CD4 cell count and detectable viral load; thus, these variables were used at their previous calendar period levels to avoid endogeneity from antidepressant use since last visit into current-period health status measures.[3]

Under random effects, in addition to the time-varying control variables detailed above, *X* contains the following variables: age at visit; age squared; dummy variables for participants who are: high school graduate, African American, Hispanic, have a partner/spouse living at home; the number of children (age 18 or less) living with the participant; and dummy indicators for the participant's site. In addition, to control for specific thresholds marking either the probable presence of depression, or AIDS, we used dummy indicators for whether

the participants ever during the period of observation had a CES-D score above 22, a CD4 cell count below 200, or a viral load at or above one million copies of HIV RNA per ml. To control for AIDS-defining CD4 cell count was particularly important in the current context because such threshold may enable participants to obtain disability insurance.

We compared the results from "naïve" ordinary least squares (OLS), where antidepressant use was assumed to be exogenous, to the results we obtained using instrumental variables in a two-stage least squares (2SLS) model. Analyses were conducted using STATA ™ (Statistical Data Analysis, Special Edition, Version 9.1, College Station, Texas).

Instrumental Variables

To construct the instrumental variables for antidepressant use (listed in Appendix A), we used data on Medicaid drug reimbursement information for outpatient drugs. The data is available for drugs purchased on or after January 1, 1991, by State Medicaid agencies as reported to the Centers for Medicaid and Medicare Services (available on-line at: http://www.cms.hhs.gov/medicaid/drugs/drug5.asp). We downloaded the quarterly data files for the relevant States (California, District of Columbia, Illinois, Maryland, Pennsylvania, and New York) and the District of Columbia, for the relevant years (1996-2004). The data files contain prescription drugs claims and provide data on payments made to pharmacies and similar health care providers for drugs covered by Medicaid. Each claim contains an eleven-digit National Drug Code (NDC), brand or generic drug name, number of units of the prescription, and the date of the prescription was filled. We coded the reimbursements for antidepressants by antidepressant class: tricyclic antidepressants (TCAs), monoamine oxidase inhibitors (MAOIs), selective serotonin reuptake inhibitors (SSRIs), and other, using Food and Drug Administration (FDA) product registration name, and chemical compound for

classification (see list in Appendix C). To normalize some of the variables, we used the number of unique Medicaid beneficiaries who received at least one covered service during the year (derived from the Medicaid Statistical Information System (MSIS) State Summary Datamart, Centers for Medicare and Medicaid Services (available on line at: http://msis.cms.hhs.gov/).

We tested all the instruments for relevance (i.e., to see if they affected the probability of receiving antidepressant treatment). In particular, we ran first-stage regressions, to see if the coefficient estimates for the instruments were strongly significant and of the expected sign, controlling for all individual characteristics and local area labor market variables under both fixed effects and random effects. Also, model specifications with two or more instrumental variables were tested for validity (i.e., to see that the instruments were not directly correlated with the outcome variable). We conducted a Sargan exogeneity tests with null hypotheses that the instruments were valid (See Appendix E).

The rationale for using Medicaid-related instrumental variables was based on the premise that antidepressants in general, and serotonin reuptake inhibitors (SSRIs) in particular, became more widely used since the early 1990s (Tsuang and Tohen 2002). Modifying previous work in mental health treatment analyses, particularly for newer treatments for schizophrenia (Domino, Frank, and Rosenheck 2003; Salkever et al. 2004; Salkever, Slade, and Karakus 2006), we viewed these IVs as measures of the diffusion in pharmacological anti-depression treatment decisions State-wide.

We hypothesized that WIHS participants had a higher chance of receiving antidepressants in States with higher volume of antidepressant prescriptions per Medicaid beneficiary; or that

they were more likely to receive SSRIs in States where the percentage of SSRI prescriptions was higher. In other words, the treatment probability increased for WIHS participants as Medicaid reimbursement programs became more generous, and faster in adopting antidepressants, particularly SSRIs. Several reasons may explain this phenomenon. First, as physicians learned of wider coverage for antidepressants in general and SSRIs in particular, they may have started to prescribe them more. Second, peer effects exist in diffusion; thus, as some patients started receiving prescriptions for antidepressants, other patients learned about it and asked their own doctors in turn for prescriptions. Third, pharmaceutical companies might have also increased their advertisement, marketing efforts, and doctor's visits as the newer SSRIs and other antidepressants became available in the Medicaid reimbursement lists.

The variation across States and across time in terms of the coverage of antidepressants helped us to identify the treatment effect. Figure 2 shows the variation in the uptake of SSRIs in the relevant State Medicaid programs in terms of volume of SSRI prescriptions as percentage of the total volume of Medicaid prescriptions for the period 1996-2004. From a low of about 20 percent for the State of California in 1996, SSRI prescriptions as percentage of total antidepressant Medicaid prescriptions increase to a high of close to 60 percent for the District of Columbia in 2004. The percentages increase for all States in a slightly concave (downwards) function over time. The differences at the State level in the timing of uptake and diffusion of antidepressants, as well in the generosity of the different State Medicaid programs helped us to predict whether an individual was more likely to receive treatment, in conjunction with other site-specific and individual characteristics.

A priori the validity of the instruments (i.e., independence from the outcome of interest) was argued based on source, relative size, and degrees of separation between the study subjects and the State Medicaid policies. All the IVs were constructed from sources outside of the WIHS sample. The total WIHS study sample sizes at each site are small compared to the overall Medicaid State populations; hence, there was no reason to expect that State-wide Medicaid decisions should have been based on the specific needs of the (comparatively few) WIHS participants. In particular, there seemed to be no plausible reason to believe that Medicaid prescription coverage for antidepressants would affect the labor market outcomes of the individuals in the samples (once we controlled for antidepressant use).[4] Appendix B presents the total number of Medicaid beneficiaries for the relevant States for years 1996-2004. Note that the variation in Medicaid beneficiaries for these States is large, going from about 143,000 individuals in the District of Columbia in 1996, to about 9.3 million in the State of California in 2004. On the other hand, recall that the total number of participants for all sites for the WIHS cohort is a total of 3,768 and that we analyzed only a subset of those populations.

5. RESULTS

Table 1 shows the descriptive statistics for the WIHS sample. At baseline[5], 28.7 percent of the participants were employed and 13.7 percent of the participants were taking antidepressants. Although 62.7 percent of the participants had finished high school, only 7.6 percent completed four years of college. The predominant racial group of the sample was African American (53.2 percent), followed by Hispanic (28.7 percent), and Caucasian (15.2 percent). About 57 percent of participants lived on less than $12,000 per year; 58.6 had Medicaid (or Medi-Cal for California residents) insurance; and 8.3 had Medicare insurance. About 61 percent of participants had a detectable level of viral load (above 80 copies of HIV RNA per ml). WIHS

participants were distributed across the six study sites as follows: Bronx, NY (20.8 percent); Brooklyn, NY (15.7); Washington, DC (14.3); Los Angeles, CA (21.5); San Francisco, CA (13.9); and Chicago, IL (13.7 percent).

The mean age of the participants at baseline was 37.4 years. Participants had an average of 0.5 minor children (ages 18 or younger) living with them (with a range from zero to 10). The mean CES-D (depression score) at baseline was 16 (which is also the cutoff for likely depression). The average quality of life index was 66; and the average CD4+ cell count of 397. In terms of constructed variables: at the metropolitan statistical area (MSA) level, the unemployment rate stood at 5.5 percent, and the mean earnings were $392 per week; at the State level, 62 percent of the non-institutionalized population (16 years and over) were employed. The main instrumental variable used in the WIHS analysis (z3: volume of SSRI prescriptions as percentage of total volume of Medicaid antidepressant prescriptions) had a mean of 42 (with a minimum of 20 and a maximum of 75).

We first analyzed the longitudinal data graphically. Figure 3 shows the percentage of participants who were employed at each visit; and the percentage of participants who were taking antidepressants at each visit. In general, there was an increasing pattern for both variables in the cohort over the follow-up time. The range for the percentage of women employed at each visit increased from 28.7 at baseline to a high of 42.9 at the 15th eligible (i.e., where at each observation HAART had been used since the previous calendar visit). The percentage of women using antidepressants over the follow-up period was lowest (13.7 and 13.3 percent) at the first two visits; and starting at the 8th visit, it fluctuated between 20 and 18 percent.

WIHS First Stage Regressions

Table 2 shows first stage regressions with FE assumptions for models with all the instrumental variables based on volume of Medicaid antidepressant prescription claims. All the coefficients on the instruments (2)-(4a) were positive and highly significant, with *t*-statistics well above three (and hence *F*-statistics above ten). Since z3 had the highest *t*-statistic (8.23), we now describe the results from that model to understand the determinants of antidepressant use. Note also that z4 had the second highest *t*-statistic (6.24), and so we will use this IV later as well. In column (3), the coefficient on the IV3 (z3) was positive and significant; for every 10-point increase in z3, the probability of using antidepressants increased by six percentage points. As expected, the CES-D in the previous period was a positively associated with the use of antidepressants since the last visit; for every 10-point increase in the previous visit CES-D, the probability of using antidepressants since the last visit increased by 1.2 percentage points. Moreover, for every percentage point increase in the unemployment rate, the likelihood of using antidepressants increased by 1.29 points; and for every 10-point increase in the adult employment ratio, the probability of antidepressant use increased by 10.81 percentage points.

Table 3 shows first stage models of the treatment (i.e., use of antidepressants) using RE assumptions. As before, note that the coefficients on the instrumental variables (2)-(4a) were positive and significant, with *t*-statistics well above three. Since the main result is the same as before, we do not further describe other results in Table 3.

Table 4 presents a linear probability model of employment showing the regression coefficients and their standard errors [in brackets]. The dependent variable was current employment. In the naïve OLS model, antidepressant use was assumed to be exogenous. In 2SLS IV models, use of antidepressants since last visit was instrumented using instrumental variables z3 and z4.

The first two columns of Table 4 show results from "naïve" random effects and fixed effects regressions under the exogeneity assumption. Under the naïve RE model, antidepressant use had a negative coefficient, which was not significant. Under FE model, the antidepressant use coefficient was slightly positive, but also not significant. On the other hand, in the last four columns, once we used the instrumental variables z3 and z4 to address the selection bias, the effect of antidepressants on employment was positive and significant under two models: IV3RE and IV4FE.

In column (3), in the two-stage least squares, random effects model (IV3RE), the employment probability was 43.96 percentage points higher for a participant who used antidepressants compared to one who did not. Five other factors in this model were associated with higher employment probabilities: high school graduation, husband or partner living with the participant, the quality of life index, CD4 cell count, and being a participant in the Washington, DC site (as compared to Chicago, IL, the reference site). Employment increased by 14.07 percentage points if the participant was a high school graduate; and it did so by 3.19 points if the participant lived with a husband or a partner. It also increased by 4.22 percentage points for each 10-point increase in the quality of index in the previous period; and it increased by 1.14 percentage points for each additional 100-cell increase in the CD4+ cell count at the previous calendar visit. When compared to Chicago (the reference site), participants in Washington DC had an 11.50 percentage-point higher employment probability.

On the other hand, four variables negatively associated with the employment probability were: age squared, CES-D at the previous visit, being a participant in the Bronx, NY, or in San Francisco, CA. For each 10-point increase in the CES-D score at the previous calendar visit,

the employment probability decreased by 2.5 percentage points. Compared to Chicago, participants in the Bronx had a 14.85-percentage-point lower employment probability; and those in San Francisco, CA had an 8.51-percentage-point lower probability of employment.

In column (6), under the IV4FE model, the employment probability was 44.89 percentage points higher for a participant who used antidepressants versus one who did not. The other significant factor in this model was the quality of life index at the previous calendar period. For each 10-point increase in the quality of index score, the employment probability of women living with HIV and using HAART increased by 1.61 percentage points.

Finally, note that non-linear and dynamic employment probability models produced qualitatively similar results; as it did a linear probability model where sample was restricted[6] to those participants who: a) had been taking HAART since the previous calendar visit, and b) had a CES-D above 22 at the previous calendar visit; thus, more directly addressing prior need. Further analyses are exhibited elsewhere (Galárraga 2006).

DISCUSSION

The findings suggest that the use of antidepressants improves the employment outcomes for the women in the Women's Interagency HIV Study (WIHS). This paper shows that instrumental variables (IV) based on the volume of the Medicaid prescriptions at the State level can be used to identify a positive effect of antidepressant use on the employment probability for a particular sample of participants.[7] In contrast, using the assumption that treatment is exogenous (in naïve regressions) results in coefficients that are significantly negative or slightly and insignificantly positive. Hence, for the WIHS data, there seems to be a large negative selection bias, which can be addressed using IVs. The main instrumental

variable (that capitalizes on the variation in Medicaid coverage for antidepressants across States and over time) is a strong predictor of treatment choice. As diffusion of antidepressants increases (particularly the relatively newer class of antidepressants called selective serotonin reuptake inhibitors or SSRIs), they become more popular in a particular State, and the likelihood of an individual person in the sample to use antidepressants also increases controlling for other relevant predictors of treatment.

The estimates of the treatment effect seem large in magnitude compared to previous results in the literature found for other interventions. Possible explanations for these findings are as follows. First, in the linear probability model when the R^2 of the first stage equation is not high, the variation of the predicted treatment probability of antidepressant use becomes very compressed, and small changes in that predicted probability translate into large changes in the predicted employment outcome probability. Second, the women in the WIHS sample are of low socio-economic and health status; thus HAART plus pharmacological depression treatment may have a stronger effect for this population. As general health status improves, and as individuals are more likely to be working, there may be a diminishing antidepressant effect on employment. Third, and perhaps more importantly, the effects found maybe larger than previous interventions because of the interactions between the direct effect (through mental health status), and the indirect effect (through HAART adherence); hence, resulting in important implications for clinical practice and policy

Increased and continued support for the inclusion of antidepressants in programs such as the AIDS Drugs Assistance Program (ADAP), Ryan White CARE Act, and Medicaid formularies

may be warranted for specific population groups, particularly low-income women, not only based on better medical outcomes, but also based on potential employment effects.

In terms of limitations, note that the current research does not make a distinction between labor force participation and employment: of participants who are jobless, WIHS questionnaires do not ask whether they looking for a job or not (that is, there is no possibility to know if the women participants are currently in the labor force or not). The current dichotomous variable of antidepressant use as a measure of anti-depression treatment is rudimentary: there is no data about how long participants have been taking the antidepressants (within visits), or the doses taken. Finally, the two hypothesized channels as to how the effect of antidepressant use works on employment need to be determined more specifically. Future research can test how much of the employment effect is working through mental health status, and how much of the effect is working through increased adherence to HAART, and hence better overall physical health.

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TABLES AND FIGURES

Table 1: WIHS Sample Descriptive Statistics

At Baseline	Obs	Percentage
Participant currently employed	1817	28.7
Use of antidepressant since last visit	1837	13.7
Participant is a high school graduate	1818	62.7
Completed 4 years of college	1818	7.6
Race Caucasian	1821	15.2
Race African American	1821	53.2
Race Hispanic	1821	28.7
Income is less than $12,000 per year	1722	56.8
Married or living with partner	1811	34.6
Currently has Medicaid or Medi-Cal insurance	1804	58.6
Currently has Medicare insurance	1804	8.3
HIV RNA > 80(cp/ml)	1732	60.6
Bronx, NY	1838	20.8
Brooklyn, NY	1838	15.7
Washington, DC	1838	14.3
Los Angeles, CA	1838	21.5
San Francisco, CA	1838	13.9
Chicago, IL	1838	13.7

	Obs	Mean	Median	Std.Dev.	Min	Max
Visit date (decimal year)	1838	1999.63	1998.86	2.47	1996.25	2004.75
Total number of eligible subsequent visits	1838	6.9	6	4.6	1	18
Age at Visit (in years)	1838	37.4	37	8.1	18	65
Minors living w/participant (age<=18)	1818	0.5		1.1	0	10
Overall depression score, CES-D (60=worst)	1649	16	14	12	0	60
Quality of life scale (100=best)	1641	66	67	20	4	100
Number of CD4 positive cells (helpers)	1764	397	354	276	0	3838
Unemployment rate (MSA)	1838	5.5	5.7	1.3	2.4	7.4
Real weekly earnings at MSA level (in Jan'94$)	1838	392	395	22	334	461
Adult employment ratio (State)	1838	62	61	2	58	71
IV1: Antidep Rx / total Medicaid Rx	1838	5	5	1	3	6
IV2: Antidep Rx per Medicaid beneficiary (x100)	1838	14	11	7	3	55
IV2a: Antidep Rx per adult Medicaid bene (x100)	1838	33	28	17	7	142
IV3: SSRI Rx / total Medicaid antidep Rx	1838	42	41	9	20	75
IV4: SSRI Rx per Medicaid beneficiary (x100)	1838	6	5	4	1	30
IV4a: SSRI Rx per adult Medicaid bene (x100)	1838	15	11	10	3	77

Table 2: WIHS Probability of Antidepressant Use FE

Fixed Effects(FE) First Stage Regression

	(1)	(2)	(2a)	(3)	(4)	(4a)
IV1: AntidepRx/tot MedicaidRx	-0.0152					
	[0.0133]					
IV2: AntidepRx/Medicaid bene(x100)		0.0057				
		[0.0012]**				
IV2a: AntidepRx/adult Medicaid bene(x100)			0.0019			
			[0.0005]**			
IV3: SSRI Rx/tot Medicaid antidepRx				0.006		
				[0.0007]**		
IV4: SSRI Rx/Medicaid bene(x100)					0.0119	
					[0.0019]**	
IV4a: SSRI Rx/adult Medicaid bene(x100)						0.0045
						[0.0008]**
Overall depression score at *t-1*	0.0011	0.0011	0.0011	0.0012	0.0011	0.0011
	[0.0006]*	[0.0006]*	[0.0006]*	[0.0006]*	[0.0006]*	[0.0006]*
Qual.of life index(x10) at *t-1*	-0.0048	-0.0044	-0.0044	-0.004	-0.0043	-0.0043
	[0.0038]	[0.0038]	[0.0038]	[0.0037]	[0.0038]	[0.0038]
CD4(x100)cells at *t-1*	0.0058	0.0043	0.0047	0.0017	0.0033	0.0038
	[0.0026]*	[0.0027]	[0.0026]	[0.0027]	[0.0027]	[0.0027]
Detectable viral load at *t-1*	-0.0123	-0.0123	-0.0129	-0.005	-0.011	-0.0118
	[0.0106]	[0.0106]	[0.0106]	[0.0105]	[0.0105]	[0.0105]
Unemployment rate (MSA)	0.0231	0.0282	0.0282	0.0129	0.0243	0.0253
	[0.0061]**	[0.0061]**	[0.0062]**	[0.0062]*	[0.0061]**	[0.0061]**
Wk. earnings MSA ($100s)	0.002	-0.0162	-0.0156	0.0191	-0.0167	-0.0179
	[0.0251]	[0.0251]	[0.0252]	[0.0249]	[0.0250]	[0.0251]
Adult emp.ratio, State(x10)	0.0677	0.0564	0.0583	0.1081	0.0742	0.0738
	[0.0285]*	[0.0266]*	[0.0266]*	[0.0272]**	[0.0267]**	[0.0267]**
Constant	-0.3301	-0.3767	-0.3744	-0.9461	-0.4614	-0.4514
	[0.2034]	[0.2031]	[0.2033]	[0.2155]**	[0.2037]*	[0.2038]*
Observations	6399	6399	6399	6399	6399	6399
Number of WIHS IDs	1542	1542	1542	1542	1542	1542
R^2	0.01	0.01	0.01	0.02	0.01	0.01
R^2 within	0.01	0.01	0.01	0.02	0.01	0.01
R^2 between	0.03	0.00	0.00	0.01	0.00	0.00
R^2 overall	0.02	0.01	0.01	0.02	0.01	0.01
t-statistic on IV coefficients	-1.14	4.92	4.13	8.23	6.24	5.73

Standard errors in brackets

* Significant at 5%; ** Significant at 1%

Notes:

MSA = Metropolitan Statistical Area

Adult employment ratio= total employed/non-institutionalized civilian population age 16 and over.

Table 3: WIHS Probability of Antidepressant Use RE

Random Effects(RE) First Stage Regression

	(1)	(2)	(2a)	(3)	(4)	(4a)
IV1: Antidep Rx/tot.Medicaid Rx	-0.0117					
	[0.0124]					
IV2: Antidep Rx/Medicaid bene(x100)		0.0052				
		[0.0011]**				
IV2a: AntidepRx/adult Medicaid bene(x100)			0.0017			
			[0.0004]**			
IV3: SSRI Rx/tot.Medicaid antidepRx				0.005		
				[0.0007]**		
IV4: SSRI Rx/Medicaid bene(x100)					0.0104	
					[0.0018]**	
IV4a: SSRI Rx/adult Medicaid bene(x100)						0.0039
						[0.0007]**
Age at visit (x10)	0.0558	0.0629	0.0618	0.0465	0.0628	0.0626
	[0.0543]	[0.0542]	[0.0542]	[0.0541]	[0.0541]	[0.0542]
Age at visit (x10) squared	-0.0015	-0.0028	-0.0025	-0.0022	-0.0032	-0.003
	[0.0066]	[0.0066]	[0.0066]	[0.0066]	[0.0066]	[0.0066]
High school graduate (=1)	0.0002	0.0028	0.0022	0.004	0.004	0.0035
	[0.0143]	[0.0143]	[0.0143]	[0.0142]	[0.0142]	[0.0142]
African American (=1)	-0.1066	-0.1089	-0.1087	-0.1124	-0.1103	-0.1102
	[0.0184]**	[0.0183]**	[0.0183]**	[0.0183]**	[0.0183]**	[0.0183]**
Hispanic (=1)	-0.0901	-0.0911	-0.0904	-0.0991	-0.0926	-0.0918
	[0.0209]**	[0.0208]**	[0.0208]**	[0.0208]**	[0.0208]**	[0.0208]**
Married/partner (=1)	-0.0126	-0.0125	-0.0126	-0.0141	-0.0121	-0.0123
	[0.0100]	[0.0100]	[0.0100]	[0.0099]	[0.0100]	[0.0100]
Minors (ages<=18)	-0.0005	-0.0032	-0.0025	-0.0083	-0.0051	-0.0044
	[0.0040]	[0.0040]	[0.0040]	[0.0041]*	[0.0040]	[0.0040]
CES-D at *t-1*	0.0011	0.0011	0.0011	0.001	0.001	0.0011
	[0.0005]*	[0.0005]*	[0.0005]*	[0.0005]*	[0.0005]*	[0.0005]*
Qual.of life index(x10) at *t-1*	-0.014	-0.0142	-0.0141	-0.0147	-0.0144	-0.0143
	[0.0031]**	[0.0031]**	[0.0031]**	[0.0031]**	[0.0031]**	[0.0031]**
CD4(x100)cells at *t-1*	0.0054	0.0045	0.0048	0.0035	0.0041	0.0043
	[0.0021]*	[0.0021]*	[0.0021]*	[0.0021]	[0.0021]	[0.0021]*
Detectable viral load at *t-1*	-0.0022	-0.0027	-0.0031	0.0035	-0.0017	-0.0023
	[0.0094]	[0.0094]	[0.0094]	[0.0094]	[0.0094]	[0.0094]
Ever CES-D>22 (=1)	0.0748	0.0765	0.0759	0.0798	0.0777	0.0771
	[0.0149]**	[0.0149]**	[0.0149]**	[0.0149]**	[0.0148]**	[0.0149]**
Ever CD4<200 (=1)	-0.0197	-0.0204	-0.0202	-0.0173	-0.0199	-0.0198
	[0.0151]	[0.0151]	[0.0151]	[0.0151]	[0.0151]	[0.0151]
Ever viral load>=1m (=1)	-0.0448	-0.0465	-0.045	-0.0535	-0.0474	-0.0461
	[0.0933]	[0.0930]	[0.0931]	[0.0929]	[0.0929]	[0.0929]
Unemployment rate (MSA)	0.0162	0.0204	0.0205	0.0069	0.0166	0.0175
	[0.0057]**	[0.0057]**	[0.0058]**	[0.0058]	[0.0057]**	[0.0057]**
Wk.earnings MSA($100s)	-0.018	-0.0328	-0.0328	-0.0001	-0.0324	-0.0336

	[0.0238]	[0.0239]	[0.0240]	[0.0238]	[0.0238]	[0.0239]
Adult emp.ratio, State(x10)	0.056	0.0474	0.0492	0.0906	0.0627	0.0625
	[0.0265]*	[0.0246]	[0.0246]*	[0.0253]**	[0.0247]*	[0.0247]*
Bronx,NY (=1)	0.0615	0.0682	0.0792	0.0658	0.0704	0.0839
	[0.0267]*	[0.0260]**	[0.0265]**	[0.0258]*	[0.0259]**	[0.0263]**
Brooklyn,NY(=1)	0.0213	0.0248	0.0369	0.0183	0.0249	0.0395
	[0.0269]	[0.0262]	[0.0266]	[0.0261]	[0.0261]	[0.0265]
Washington,DC(=1)	0.0327	0.1417	0.1332	0.0183	0.13	0.1323
	[0.0312]	[0.0339]**	[0.0347]**	[0.0278]	[0.0310]**	[0.0318]**
Los Angeles,CA(=1)	0.0021	0.0784	0.0712	0.0294	0.0815	0.0817
	[0.0245]	[0.0289]**	[0.0294]*	[0.0246]	[0.0277]**	[0.0283]**
San Francisco,CA(=1)	0.1055	0.1856	0.1791	0.1134	0.1836	0.1854
	[0.0281]**	[0.0324]**	[0.0331]**	[0.0279]**	[0.0309]**	[0.0315]**
Constant	-0.2817	-0.3764	-0.3755	-0.7563	-0.4386	-0.4382
	[0.2248]	[0.2253]	[0.2257]	[0.2340]**	[0.2258]	[0.2262]
Observations	6292	6292	6292	6292	6292	6292
Number of WIHS IDs	1521	1521	1521	1521	1521	1521
R^2 within	0.01	0.01	0.01	0.02	0.01	0.01
R^2 between	0.12	0.12	0.12	0.13	0.13	0.13
R^2 overall	0.08	0.09	0.09	0.09	0.09	0.09
t-statistic on IV coefficients	-0.94	4.81	4.12	7.04	5.86	5.41

Standard errors in brackets

* Significant at 5%; ** Significant at 1%

Notes:

MSA = Metropolitan Statistical Area

Adult employment ratio= total employed/non-institutionalized civilian population age 16 and over.

Table 4: WIHS Linear Probability Model of Employment

	Naive OLS		Instrumental Variables (IV)			
	OLS RE	OLS FE	IV3RE	IV4RE	IV3FE	IV4FE
	(1)	(2)	(3)	(4)	(5)	(6)
Used antidep since *t-1*(=1)	-0.0144	0.0047	0.4396	0.3819	0.1630	0.4489
	[0.0146]	[0.0158]	[0.1927]*	[0.2213]	[0.1416]	[0.1923]*
Age(10yrs)	0.1603		0.1169	0.1388		
	[0.0707]*		[0.0678]	[0.0761]		
Age(10yrs)squared	-0.0206		-0.0175	-0.0208		
	[0.0086]*		[0.0081]*	[0.0091]*		
High school(=1)	0.1411		0.1407	0.1446		
	[0.0198]**		[0.0174]**	[0.0212]**		
African American(=1)	-0.1029		-0.0560	-0.0601		
	[0.0257]**		[0.0306]	[0.0363]		
Hispanic(=1)	-0.0757		-0.0416	-0.0404		
	[0.0292]**		[0.0305]	[0.0367]		
Married/partner(=1)	0.0215		0.0319	0.0261		
	[0.0118]		[0.0129]*	[0.0127]*		
Minors(ages<=18)	0.0013		-0.0018	0.0014		
	[0.0047]		[0.0050]	[0.0049]		
CES-D at *t-1*	-0.0013	-0.0003	-0.0025	-0.0019	-0.0005	-0.0007
	[0.0006]*	[0.0006]	[0.0007]**	[0.0007]**	[0.0006]	[0.0007]
Qual.life index(x10)at *t-1*	0.0281	0.0139	0.0422	0.0329	0.0147	0.0161
	[0.0036]**	[0.0041]**	[0.0051]**	[0.0048]**	[0.0042]**	[0.0046]**
CD4(x100)at *t-1*	0.0126	0.0077	0.0114	0.0103	0.0068	0.0052
	[0.0023]**	[0.0029]**	[0.0027]**	[0.0028]**	[0.0031]*	[0.0033]
Viral load>80 at *t-1*(=1)	0.0010	0.0102	-0.0017	0.0025	0.0117	0.0145
	[0.0108]	[0.0116]	[0.0120]	[0.0115]	[0.0118]	[0.0127]
Unemployment rate(MSA)	0.0010	-0.0034	-0.0058	-0.0055	-0.0068	-0.0129
	[0.0064]	[0.0067]	[0.0079]	[0.0077]	[0.0074]	[0.0083]
Wk.earnings,MSA($100s)	0.0166	0.0208	0.0287	0.0220	0.0216	0.0229
	[0.0268]	[0.0276]	[0.0308]	[0.0284]	[0.0278]	[0.0298]
Adult emp.ratio,State(x10)	0.0335	0.0451	0.0061	0.0119	0.0366	0.0212
	[0.0280]	[0.0292]	[0.0328]	[0.0320]	[0.0305]	[0.0332]
Bronx,NY(=1)	-0.1105		-0.1485	-0.1313		
	[0.0349]**		[0.0335]**	[0.0390]**		
Brooklyn,NY(=1)	-0.0379		-0.0613	-0.0417		
	[0.0354]		[0.0323]	[0.0377]		
Washington,DC(=1)	0.1498		0.1150	0.1344		
	[0.0372]**		[0.0350]**	[0.0405]**		
Los Angeles,CA(=1)	-0.0264		-0.0408	-0.0284		
	[0.0335]		[0.0299]	[0.0357]		
San Francisco,CA(=1)	-0.0353		-0.0851	-0.0776		
	[0.0379]		[0.0399]*	[0.0467]		
Constant	-0.4754	-0.1339	-0.3389	-0.3371	-0.0889	-0.0076
	[0.2649]	[0.2229]	[0.2897]	[0.2909]	[0.2287]	[0.2466]
Observations	6285	6305	6285	6285	6305	6305

Number of WIHS IDs	1521	1524	1521	1521	1524	1524
R^2 within	0.01	0.01	0.00	0.00	.	.
R^2 between	0.20	0.13	0.11	0.11	0.03	0.0003
R^2 overall	0.16	0.11	0.08	0.08	0.03	0.001

Standard errors in brackets

* Significant at 5%; ** Significant at 1%

Notes:

Table reports the coefficients and standard errors [in brackets] for linear probability models where the outcome variable is current employment. In the naive OLS model, antidepressant use was assumed to be exogenous. In the IV, 2SLS, use of antidepressants since last visit has been instrumented using instrumental variables: z3 (quarterly volume of selective serotonin reuptake inhibitor (SSRI) prescriptions as percentage of total Medicaid antidepressant prescriptions, at the State level) and z4 (SSRI prescriptions per Medicaid beneficiary (x100).

MSA = Metropolitan Statistical Area.

Adult employment ratio= total employed/non-institutionalized civilian population age 16 and over.

Figure 1: Conceptual Framework

The Effect of Antidepressant Use on Employment

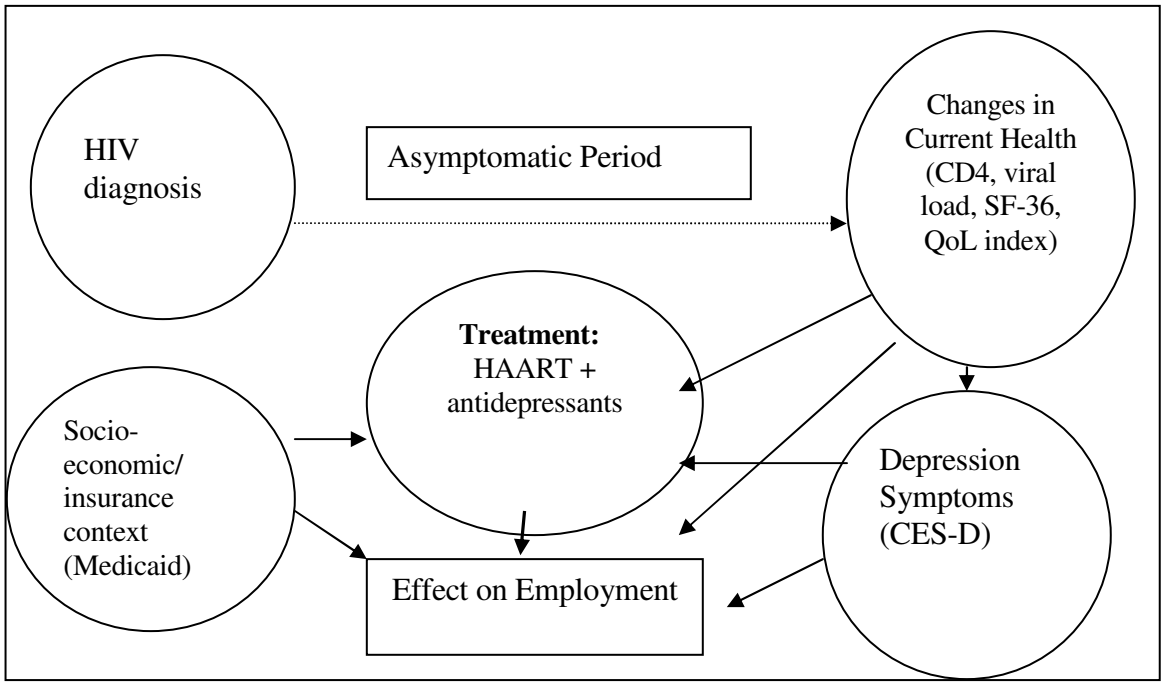
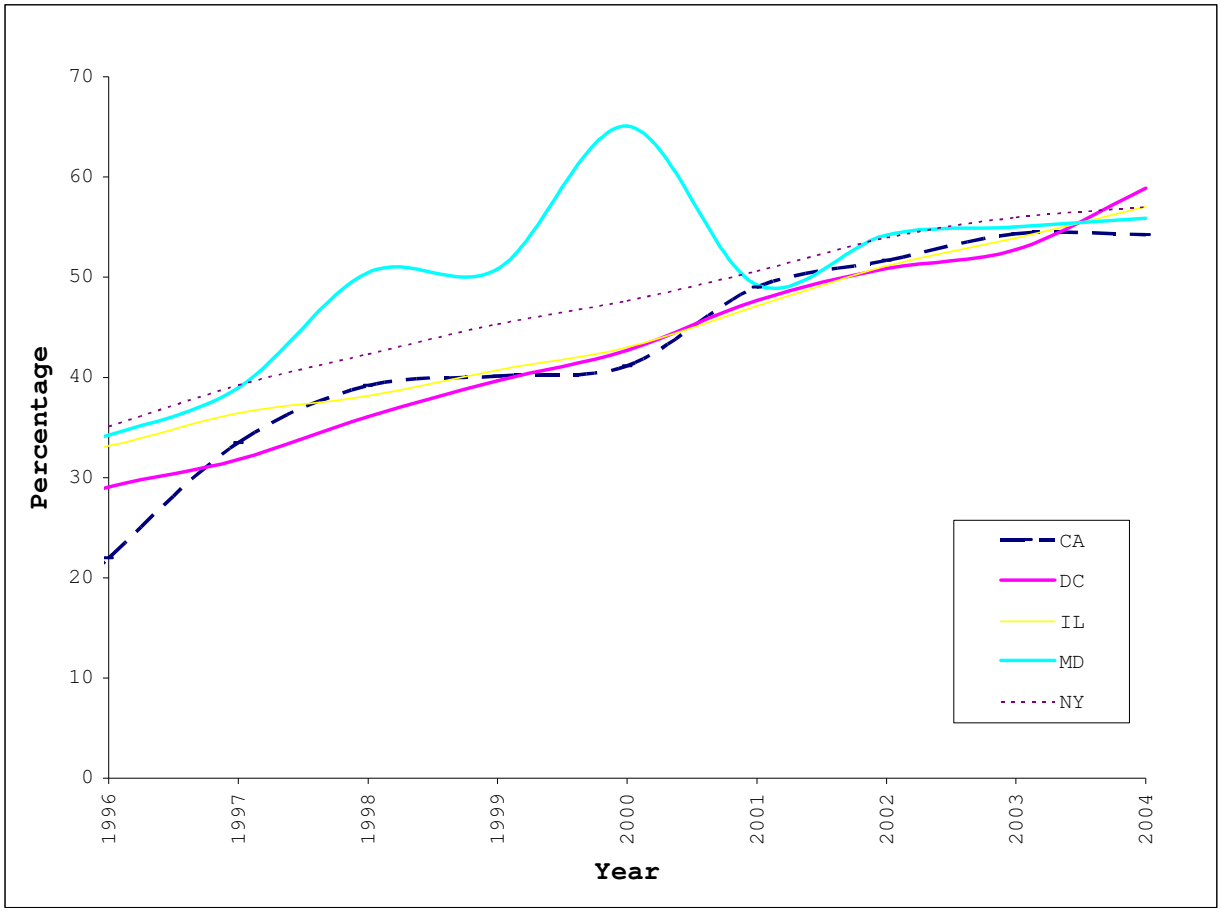
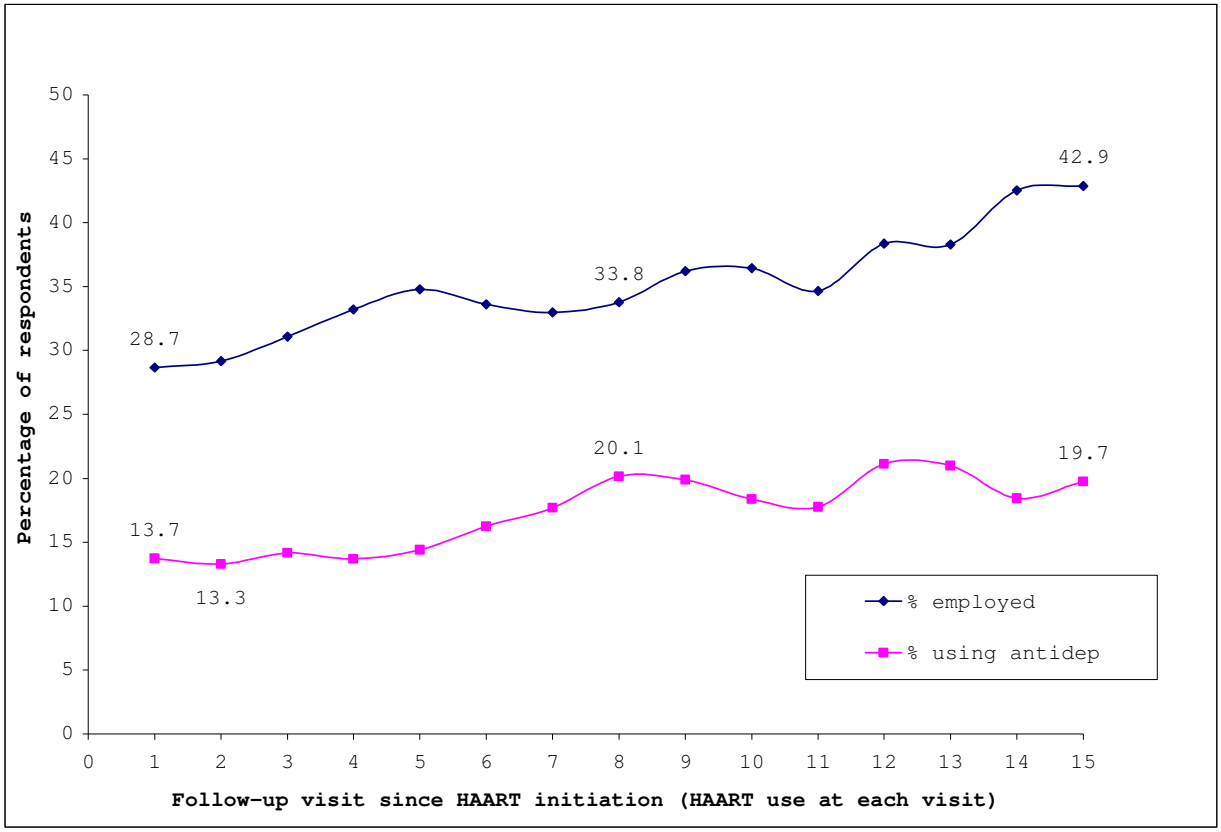


Figure 2: SSRI Rx as Percentage of Antidepressant Medicaid Rx



Source: Medicaid drug utilization information for outpatient drugs purchased on or after January 1, 1991, by State Medicaid agencies according to reimbursement data reported to the Centers for Medicaid and Medicare Services; available on-line at: http://www.cms.hhs.gov/medicaid/drugs/drug5.asp [Accessed on 14 May 2005].

Figure 3: WIHS Employment and Antidepressant Use over Follow-up Time



Source: Women's Interagency HIV Study (WIHS) data with selection criteria as follows: HIV-positive women, ages 18-65, using HAART since April 1, 1996; HAART user since previous calendar visit. Number of eligible participants at baseline: 1,838.

APPENDICES

Appendix A: Instrumental Variables (IV)

IV	Description	Rationale for Relevance
z1	Volume of antidepressant prescription claims as percentage of total volume of Medicaid prescription claims.	Those living in States where more antidepressants are prescribed as percentage of total Medicaid claims are more likely to receive antidepressants.
z2	Volume of antidepressant prescription claims per Medicaid beneficiary (x100).	As number of antidepressant prescriptions per Medicaid beneficiary increases, the likelihood that sample beneficiaries receive treatment also increases.
z2a	Volume of antidepressant prescription claims per adult Medicaid beneficiary (x100).	As number of antidepressant prescriptions per Medicaid adult beneficiary increases, the likelihood that sample beneficiaries receive treatment also increases.
z3	Volume of Medicaid prescriptions claims for selective serotonin reuptake inhibitors (SSRIs) as percentage of total volume of Medicaid antidepressant prescriptions.	Participants have a higher chance of receiving antidepressants in States where SSRI diffusion has been more rapid, and where State programs are more generous.
z4	Volume of SSRI prescription claims per Medicaid beneficiary (x100).	As SSRI prescriptions per Medicaid beneficiary increase, the likelihood that the participants receive treatment also increases.
z4a	Volume of SSRI prescription claims per total adult Medicaid beneficiary (x100).	As SSRI prescriptions per adult Medicaid beneficiary increase, the likelihood that the participants receive treatment also increases.

Notes: All of the instrumental variables were constructed on a quarterly basis for the years 1996-2004 at the State level; and then assigned to each individual's visit observation for participants in WIHS according to the relevant State and visit date. CMS defines number of prescriptions in each State data file as "The number of prescriptions reimbursed to pharmacists for the drug for the quarter covered".

Sources: Data on claims refers to Medicaid drug utilization information for outpatient drugs purchased on or after January 1, 1991, by State Medicaid agencies according to reimbursement data reported to the Centers for Medicaid and Medicare Services; available on-line at: http://www.cms.hhs.gov/medicaid/drugs/drug5.asp [Accessed on 14 May 2005]. Data on Medicaid beneficiaries are from the Medicaid Statistical Information System (MSIS) State Summary Datamart (SSD); available on-line at: http://bizapps.cms.hhs.gov/msis/ [Accessed on 7 June 2005].

Appendix B: Medicaid beneficiaries (in thousands) by State, 1996-2004

Year/State	CA	DC	IL	MD	NY
1996	5,107	143	1,454	399	3,281
1997	4,855	128	1,400	402	3,152
1998	7,082	166	1,364	561	3,073
1999	6,801	133	1,455	586	3,234
2000	7,918	139	1,519	626	3,420
2001	8,583	141	1,658	656	3,591
2002	9,301	144	1,731	693	3,921
2003	9,319	158	1,830	729*	4,450
2004*	9,337	172	1,929	765	4,979

*Preliminary estimates

Sources:
MSIS State Summary, for years 1996-1998. Medicaid Statistical Information System (MSIS), Centers for Medicare and Medicaid Services. Available on line at: http://www.cms.hhs.gov/medicaid/msis/mstats.asp [Accessed on 17 June 2005]; CMS DataMart for years 1999-2003. Medicaid Statistical Information System (MSIS) State Summary Datamart), Centers for Medicare and Medicaid Services. Available on line at: http://msis.cms.hhs.gov/ [Accessed 21 August 2005].

Appendix C: List of Antidepressants by Class

	SSRIs	**Proprietary Names**
1	Citalopram Hydrobromide	Celexa
2	Escitalopram oxalate	Lexapro
3	Fluvoxamine	Luvox
4	Paroxetine	Paxil, Pexeva
5	Fluoxetine	Prozac, Sarafem
6	Sertraline	Zoloft
7	Olanzapine/fluoxetine	Symbyax
	TCAs	
8	Amitriptyline	Elavil, Endep
9	Amitriptyline/Chlordiazepoxide	Limbitrol
10	Amoxapine	Amoxapine, Asendin, Asendis, Defanyl, Demolox
11	Clomipramine	Anafranil
12	Desipramine	Norpramin
13	Desipramine	Pertofrane
14	Doxepin	Adapin, Sinequan, Zonalon
15	Imipramine	Tofranil
16	Maprotiline	Ludiomil
17	Nortryptyline	Aventyl HCl, Pamelor
18	Protriptyline	Vivactil
19	Trimipramine	Surmontil
	MAOIs	
20	Phenelzine	Nardil, Triavil
21	Tranylcypromine	Parnate
22	Isocarboxazid	Marplan
	Others	
23	Bupropion	Wellbutrin, Zyban
24	Buspirone	Buspar
25	Duloxetine	Cymbalta
26	Liothyronine	Cytomel, Triostat
27	Lithium	Eskalith, Lithane, Lithobid, Lithotabs
28	Methylphenidate	Ritalin, Ritalin-SR
29	Mirtazapine	Remeron
30	Nefazodone	Serzone
31	Reboxetine	Edronax, Vestra
32	Thioridazine	Mellaril, Mellaril-S
33	Trazodone	Desyrel
34	Venlafaxine	Effexor
35	Perphenazine/Amitriptyline	Etrafon
36	Chlordiazepoxide / Amitriptyline	Limbitrol
37	Phenelzine sulfate	Nardil, Nardelzine

Classes: Tricyclic antidepressants (TCAs), selective serotonin reuptake inhibitors (SSRIs), monoamine oxidase inhibitors (MAOIs). **Sources:** Food and Drug Administration, Center for Drug Evaluation and Research, on-line at: http://www.fda.gov/cder/drug/antidepressants/MDD_alldruglist.pdf [Accessed 6 June 2005]; eMedicine Drug Search Database from the eMedicine Clinical Knowledge Database by Johns Hopkins Medicine, on-line at: http://www.imedicine.com [accessed June 6, 2005]; and the complete drug reference database, MARTINDALE by Thomson MICROMEDEX, available on-line at: http://healthcare.thomsonhc.com/hcs/librarian [Accessed on 7 December 2004].

Appendix D: Local Area Earnings, Employment and Unemployment

Earnings

We constructed average earnings for the relevant Metropolitan Statistical Areas (MSAs) using data from the Current Population Survey (CPS), a monthly household survey conducted by the Bureau of the Census for the Bureau of Labor Statistics.

The CPS provides comprehensive information on the employment and unemployment experience of the U.S. population. The Bureau of Labor Statistics (BLS) conducts the Earner Study (Outgoing Rotation) that includes basic questions for each of the twelve months and also a special set of earners questions, including weekly earnings. The survey asks these questions to the portion of the population that corresponds to wage and salaried workers (self-employed persons in incorporated businesses are excluded). These data are collected in the two outgoing rotation groups as a part of the basic CPS labor force interview. We used the following variables from the survey: month of interview, educational attainment, weekly earnings before deductions, total hours worked last week, and the earnings weight. We estimated weighted average weekly earnings for each month for every year between 1996 and 2004 for the following consolidated MSAs: Chicago-Gary-Kenosha, IL-IN-WI; Los Angeles-Riverside-Orange County, CA; New York-Northern New Jersey-Long Island, NY-NJ-CT-PA; San Francisco-Oakland-San Jose, CA; Pittsburgh-Beaver Valley, PA; and Washington-Baltimore, DC-MD-VA-WV.

The questionnaire responses are given in current dollars. To express these earnings in constant terms, we used the monthly CPI for the respective MSA. Hence, the average weekly earnings are expressed in constant dollars of January 1994.

Since the CPS Earners Study allows estimation of earnings based on the educational characteristics of the sample, we constructed a low estimate of earnings based on educational achievement. Low earnings estimates correspond to the average earnings for educational attainment equal to or below high school graduate level. High earnings estimates correspond to the average earnings for educational attainment for four-year college graduates.

Sources:

Bureau of Labor Statistics. 2005. *Current Population Survey*. Available on-line at: http://www.bls.gov/cps/home.htm [Accessed on 17 August 2005].

Unicon Research Corporation, Data Utilities for Population Research. Available on-line at: http://www.unicon.com/ [Accessed on 7 September 2005].

Unemployment Rate

We used the data for unemployment from the Local Area Unemployment Statistics (LAUS) program which produces monthly and annual employment, unemployment, and labor force data for Census regions and divisions, States, counties, metropolitan areas, and many cities, by place of residence.

The basic concepts involved in identifying the employed and unemployed are as follows: Persons who have jobs are employed; persons who are jobless, looking for jobs, and available for work are unemployed; and persons who are neither employed nor unemployed are not in the labor force. The unemployment rate is defined as the number of unemployed persons as a percent of the labor force (Ehrenberg and Smith 2003).

We retrieved monthly data for the unemployment rate for every year between 1996 and 2004 for the following MSAs: Baltimore-Towson, MD; Chicago-Naperville-Joliet, IL-IN-WI; Los Angeles-Long Beach-Santa Ana, CA; New York-Northern New Jersey-Long Island, NY-NJ-PA; Pittsburgh, PA; San Francisco-Oakland-Fremont, CA; Washington-Arlington-Alexandria, DC-VA-MD-WV. Then, we calculated quarterly averages to assign to each individual observation in WIHS depending on visit date and site.

LAUS is a cooperative effort between federal and State agencies to prepare monthly estimates of total employment and unemployment for approximately 7,200 areas including Census regions and divisions, States, and Metropolitan Statistical Areas.

These employment and unemployment estimates are key indicators of the economic conditions at the local level. The concepts and definitions underlying LAUS data are derived from the Current Population Survey (CPS), the household survey that is the official measure of the labor force for the nation. The models at the State level are controlled to aggregate to the monthly labor force estimates from the CPS at national level in "real time". The models use current and historical data from the CPS, the Current Employment Statistics (CES) program, and State unemployment insurance (UI) systems.

Source: Bureau of Labor Statistics. 2005. *Local Area Unemployment*. Available on-line at: http://www.bls.gov/lau/home.htm [Accessed on September 7th, 2005]

Adult Employment Ratio at the State Level

To control for discouraged workers (i.e., those who are no longer in the labor force because they are not working and they are not looking for a job), we constructed a measure of adult employment at the State level. This measure is the ratio of the employed over the total non-institutionalized civilian population aged 16 and over (NCP16+) (regardless of whether they are in the labor force or not). The BLS does not produce time series with the NCP16+ for the MSA level; thus, we used The Geographical Profile of Employment and Unemployment series that reports the NCP16+ at the State level on a yearly basis.

More specifically, discouraged workers are persons who are not in the labor force, but who want and are available for a job, and who have looked for work sometime in the past 12 months (or since the end of their last job if they held one within the past 12 months). However, they are not currently looking for a job because they believe there are no jobs available or there are none for which they would qualify.

Sources: Bureau of Labor Statistics (various years). *Geographical Profile of Employment and Unemployment, 1996-2004*. Washington, D.C.: Bureau of Labor Statistics.

Bureau of Labor Statistics. 2005. *Local Area Unemployment*. Available on-line at: http://www.bls.gov/lau/home.htm [Accessed on September 7th, 2005].

Appendix E: Instrumental Variables Tests

Validity Tests

To test for IV validity (i.e., that the instruments should not have any direct influence on the outcome), we performed exclusion restrictions tests by including the instrumental variables z4 and z4a (in quadratic form) directly in the outcome regression, and computing relevant likelihood ratio tests. We carried out a test for Sargan overidentification tests (Cameron and Trivedi 2005) with a joint null hypothesis that the instruments were valid (i.e., uncorrelated with the error term in the outcome regression), and that the excluded instruments are correctly excluded from the estimated equation. Under the null, the test statistic is distributed as $\chi 2$ in the number of overidentifying restrictions. A rejection casts doubt on the validity of the instruments.

The Sargan statistic (overidentification test of all instruments) for the WIHS was 3.072 with a *p*-value of 0.0796, thus we accepted the null of instrument validity.

Relevance Tests

In addition to reporting the t-statistics of the first stage IV regression coefficients, we conducted tests to check that the IVs were relevant (i.e., that they were strong predictors of treatment). We first conducted likelihood ratio tests for z3 and z4 (in quadratic form) for WIHS. These tests rejected the hypotheses that the IVs were equal to zero in the treatment equation.

In addition, we performed an Anderson canonical correlations likelihood-ratio test to see if the first-stage equation was identified (i.e., that the excluded instruments were relevant). The null hypothesis was that the matrix of reduced form coefficients had rank $K-1$, where K is number of regressors (i.e, Ho: equation is underidentified). Under the null of underidentification, the statistic is distributed as $\chi 2$ with degrees of freedom equal to $L-K+1$, where L is the number of instruments (included and excluded). This statistic provides a measure of instrument relevance; rejection of the null indicates that the model is identified.

For the WIHS, the $\chi 2$ was 61.46 with a *p*-value of 0.000; thus, rejecting the null of underidentification.

Weak IV Tests

It is important to test that the instrumental variables be strong predictors of treatment choice so to avoid the problem of weak instruments (Bound, Jaeger, and Baker 1995).

To test whether the instrumental variables were weak, we checked the Cragg-Donald statistic as suggested by Stock and Yogo (Stock and Yogo 2002). The null hypothesis is presence of weak instruments (i.e., that the IVs are only weakly identified; or that they only weakly help to predict treatment).

For the WIHS model, the critical value for 2SLS, for one endogenous regressor, and seven exogenous regressors is 19.86 [see pg. 58 in (Stock and Yogo 2002)]., and the Cragg-Donald statistic was 30.87; thus rejecting the null hypothesis of weak identification.

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NOTES

[1] The definition of HAART in the WIHS was guided by the DHHS/Kaiser Panel (DHHS/KFF 2005) guidelines and defined as: (a) two or more nucleoside or nucleotide reverse transcriptase inhibitor (NRTIs) in combination with at least one protease inhibitor (PI) or one non-nucleoside reverse transcriptase inhibitor (NNRTI) (88% of WIHS observations classified as HAART); (b) one NRTI in combination with at least one PI and at least one NNRTI (5%); (c) a regimen containing ritonavir and saquinavir in combination with one NRTI and no NNRTIs (1%); and (d) an abacavir or tenofovir containing regimen of three or more NRTIs in the absence of both PIs and NNRTIs (6%), except for the three-NRTI regimens consisting of: abacavir + tenofovir + lamivudine OR didanosine + tenofovir + lamivudine. Combinations of zidovudine (AZT) and stavudine (d4T) with either a PI or NNRTI were not considered HAART. The most frequent case of monotherapy was of one NRTI (92%). Of the other monotherapy cases, taking only PIs accounted for 6%; while taking only NNRTIs accounted for 2%. All other ART regimens were classified as combination therapy. The three most frequent cases of combination therapy were: (a) only two NRTIs (67%); (b) three or more NRTIs without abacavir or tenofovir and in the absence of PIs and NNRTIs (11%); and (c) at least one PI and at least one NNRTI in the absence of NRTI (4%).

[2] This investigation uses the Center for Epidemiologic Studies-Depression scale (CES-D) to assess depression symptoms (Radloff 1977). The scale ranges from zero to 60. A cutoff at or above 16 indicates "probable cases of depression"; a cutoff above 22 is a more stringent measure of likely depression. In addition, to complement clinical indicators of disease progression (CD4 and viral load), we use a multi-item scale as a proxy for productivity-related measures: the quality of life index (Bozzette et al. 1995).

[3] For all the analyses presented the covariate vector for the individual characteristics (CD4, viral load, CES-D, and quality of life index) is lagged for one period to correct for the likely contemporaneous endogeneity from antidepressant treatment. However, results using the covariate vector at time t (instead of time $t-1$) produced similar positive results of the same magnitude (results not shown). Similarly, all the IV random effects models presented here use the first lag of time-varying covariates, and additional binary indicators of whether: participants had ever had CES-D scores above 22, ever had CD4 cell counts below 200, or ever had viral load at or above one million HIV RNA copies per ml. Results (not presented here) obtained when the worst-ever indicators are not included generate qualitatively similar results as well. Also, including dummy

variables for insurance status (Medicare, Medicaid) produced results quite similar to the main analysis. We did not include insurance status in the final specification because it is likely to be endogenous in the employment equation.

[4] Unobservable respondent characteristics may be only weakly correlated with the overall State-level Medicaid program statistics since the number of people in the Medicaid program is so large relative to the number of respondents in the study. It seemed unlikely also that respondents' unobserved proclivities to seek depression treatment would have induced them to relocate to States where there were relatively more Medicaid beneficiaries receiving antidepressants.

[5] Baseline was defined as the first visit for which a participant was: a) on HAART since the last calendar visit; and b) had any CES-D score at the previous calendar visit.

[6] Additional analyses that limit the study group to participants with probable depression, CES-D>22 in the previous calendar period, produce similar positive results, of higher magnitude. This alternative study design, however, excludes the women with lower CES-D whose depression score stays low because of antidepressant use; while it over accounts for the effects of those for whom the antidepressants fail to reduce CES-D. These results, thus, would ignore the benefits of "maintenance" treatment, and over-emphasize the effects of possible "drug failure" or ineffectiveness at the individual level. The restricted analysis observes only the discrete changes at the beginning of the treatment, and neglects any other effects if later the antidepressants work properly and CES-D scores decrease below 22.

[7] The positive effect on employment is present even though, in general, due to program income limits, being on Medicaid actually reduces the likelihood that a female household head will work (Moffitt and Wolfe 1992).