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ORIGINAL PAPER

Antidepressant Treatment and Adherence to Antiretroviral Medications Among Privately Insured Persons with HIV/AIDS

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Abstract In order to examine relationships between depression treatments (antidepressant and/or psychotherapy utilization) and adherence to antiretroviral therapy (ART), we conducted a retrospective analysis of medical and pharmacy insurance claims for privately insured persons living with HIV/AIDS (PLWHA) diagnosed with depression ($n = 1{,}150$). Participants were enrolled in 80 insurance plans from all 50 states. Adherence was suboptimal. Depression treatment initiators were significantly more likely to be adherent to ART than the untreated. We did not observe an association between psychotherapy utilization and ART adherence, yet given the limitations of the data (e.g., there is no information on types of psychological treatment and its targets), the lack of association should not be interpreted as lack of efficacy.

Keywords Adherence · Depression · Antidepressant · Psychotherapy · Private insurance

Introduction

Care of chronic medical illnesses is frequently complicated by comorbid mental health conditions, particularly depression [1–4]. The self-care needed by persons with chronic conditions is often complex, involving frequent visits to providers, behavior modifications, and consistent medication adherence [5–7]. This in turn requires energy, motivation and strong cognitive functioning, such as planning, which may be undermined by depression [8–10]. Evidence for this negative impact can be found in a meta-analysis of studies comparing the adherence of patients with a chronic medical condition with accompanying depression to those without, which found that the odds of nonadherence were three times higher in those with depression [11].

The relationship between depression and HIV disease is particularly concerning, for two reasons. First, depression in persons with HIV is prevalent. Estimates of the prevalence of depression in HIV infected persons vary widely [12], depending on the population studied, stage of HIV infection, the prevalence of other complicating conditions such as substance abuse, and the assessment method. Bing et al. [13] found rates of 36% for major depression, 26% for dysthymia, and 22% for both ("double depression"). Second, any impact of depression on optimal adherence to antiretroviral therapy (ART) is consequential, because ART adherence is crucial to maximize the clinical benefits of treatment [14], delay

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disease progression [15], and to prevent the emergence and transmission of drug-resistant viruses [16]. Although recent data suggest that boosted protease inhibitors and non-nucleoside reverse-transcriptase inhibitors are more forgiving than nucleoside reverse transcriptase inhibitors and non-boosted protease inhibitors [17, 18], adherence at levels of 95% or greater has long been recommended [19]. Maintaining long-term adherence to ART is difficult due to complex regimens, unpleasant side effects and the fact that patients with HIV infection must take ART consistently for the duration of their lives [20–22]. Thus it is critical to identify modifiable factors—such as depression—that impede long-term adherence to ART.

Since 1996, a number of published studies have examined the relationship between depression and adherence to ART in HIV disease [14, 23–32]. Though they use many different study designs, and a wide variety of approaches to the measurement of adherence and depression, virtually all find associations with depression, including evidence that incident depression symptoms are associated with subsequent declines in optimal adherence [25]. There is also evidence that antidepressant medications are generally effective in treating HIV+ depressed patients [33–36]. While psychotherapy is a well-established and efficacious treatment for depression [37], research specifically on the efficacy of psychotherapy for depressed HIV+ patients is limited. Psychological interventions, while understudied, provide promising evidence that they can be specifically adapted to promote ART adherence [38, 39]. In summary, depression is often associated with ART nonadherence, although there is not yet sufficient prospective evidence that treatment of depression improves medication adherence.

In the United States, the HIV/AIDS epidemic has disproportionately affected traditionally disadvantaged and vulnerable populations [40], who are often uninsured or covered by public insurance programs [41]. Thus, this population has been the focus of most health services and adherence research. For example, Walkup et al. [32] used NJ Medicaid data to study the relationship between AD use and ART utilization in persons with HIV. They found that antidepressant use in 1 month was associated with a 28% increase in the odds of ART use in the subsequent month. One consequence of the emphasis in the literature on the publicly insured is a critical knowledge gap: population-level studies documenting adherence patterns among privately insured persons living with HIV/AIDS (PLWHA) are scarce or outdated.

Estimates from the mid-1990s suggested that just under one-third (31%) of a national sample of PLWHA had private insurance [42], and it seems likely that the decline in the rate of work disability associated with improved antiretroviral care may have allowed more PLWHA to retain employer-based insurance, and increased this proportion [43]. Baseline (2000–2002) data from the multi-site HIV/AIDS Treatment Adherence, Health Outcomes, and Cost Study suggested that, among PLWHA with mental health visits who met criteria for both a psychiatric and substance abuse diagnosis, those with private insurance (but not those with Medicaid) had significantly more mental health visits per month [44]. Horberg et al. [24] conducted a retrospective study of a cohort of HMO patients who were either starting or switching ART, and found that depressed patients' adherence to SSRIs was associated with improved HIV drug adherence and improved laboratory parameters. However, they report only on SSRIs and they did not examine non-drug therapies (i.e., psychotherapy). Furthermore, the generalizability of these findings to those not in HMOs is questionable. In the current study, we conducted a retrospective analysis of medical claims to examine the relationship between depression treatments (antidepressant and/or psychotherapy), and ART adherence in a large commercially insured population. Specifically, we studied pharmacy refill data.

Methods

Participants and Data Sources

The study is a retrospective, observational secondary data analysis, using medical and pharmacy claims from the MarketScan Commercial Claims and Encounter Database, a large integrated data set for a commercially insured population. The database contains utilization information on privately insured enrollees employed by over 150 large firms and enrolled in 80 different health plans. Enrollees reside in all 50 states in the US. The data include information from insurance claims submitted by medical care providers or pharmacies to insurance companies for reimbursement, and enrollment information including age and gender. The current study examines claims for services provided between January 2003 and March 2007. Plans were excluded from the sample if the employer did not offer mental health benefits. The study population is limited to adult PLWHA who had initiated ART and were enrolled in a plan with prescription drug and mental health benefits for at least 12 months. Prior work has shown that claims-based data have high sensitivity in detecting PLWHA who utilize medical care [45]. PLWHA were identified by primary and secondary diagnosis codes reported on claims (ICD-9-CM diagnosis codes 042.xx, 043.xx, and 044.xx).

Measures

Pharmacy claims include data on dispense date, days supplied, and National Drug Code (NDC) for each prescription

filled. These data allowed us to construct a calendar for each person classifying each day of the observation period as covered or not covered by a protease inhibitor (PI, including amprenavir, atazanavir, fosamprenavir, indinavir, lopinavir/ritonavir, nelfinavir, ritonavir, saquinavir, tipranavir, tipranivir, and darunavir) or non-nucleoside reverse transcriptase inhibitor (NNRTI, including delavirdine, efavirenz, nevirapine, and etravirine). Days covered by a PI/NNRTI are considered as days on which a patient possessed the drugs for ART. In general, most recommended ART drug combinations include one PI/NNRTI [19]. Since persons with HIV generally take all of their ART medications or none of them [46], we believe this operationalization (days covered by a PI/NNRTI rather than days covered by a guideline recommended drug combination) is appropriate.

We measured treatment adherence (for ART and antidepressants) for the period between ART initiation and discontinuation (ART episode). ART discontinuation was flagged when there was a period longer than 60 days during which there was no evidence that a patient possessed ART (i.e., there was a 60 day period not covered by any PI/NNRTI). The discontinuation date was defined as the last day on which the patient possessed the drug, prior to the discontinuation flag. If there were multiple treatment episodes, we choose the longest one. The study population was limited to those with ART use for a period of at least 6 months, since the study aim is to examine adherence to therapy among established ART users. ART adherence, the study outcome, is operationalized as the medication possession ratio (MPR) for PI/NNRTI during the observation window for each patient. It is the ratio of the number of days for which the patient possessed a PI/NNRTI, to the total number of days in the observation window for that person. Since there are no pharmacy data for days spent in an inpatient facility, those days are excluded from both the numerator and the denominator of the MPR. Although recent data suggest that boosted protease inhibitors and non-nucleoside reverse-transcriptase inhibitors are more forgiving than nucleoside reverse transcriptase inhibitors and non-boosted protease inhibitors [17, 18], our observation period covers 2003–2007. Therefore we operationalized the binary indicator of ART adherence as possessing an ART drug for at least 90% of the treatment episode (i.e., MPR $\geq$ 90).

Since our goal is to examine the relationship between depression treatment and ART adherence, our analyses focused on patients who were diagnosed with depression during an ART treatment episode ($n = 1{,}150$). Patients were classified as having depression if, during the ART treatment episode, they had one or more of the following ICD-9 codes: 296.2-MDD single episode, 296.3-MDD recurrent episode, 311-depressive disorder NOS, 300.4-dysthymia, 293.83 mood disorder due to medical condition, 296.90-mood disorder NOS, 309.1-prolonged depressive reaction and 296.99-other specified affective disorders. Among these patients, we defined independent variables that capture treatment patterns for depression. For antidepressant users, using methods similar to those described above, we calculated the medication possession ratio for antidepressants. We defined the start date of the antidepressant treatment episode as the date of the first antidepressant fill during the person's observation period; we defined the end date as either the date of antidepressant discontinuation (not possessing an antidepressant for 60 days or more) or as the end of the observation window (i.e., the end of the ART treatment episode). We then created several depression treatment measures. For the first depression treatment measure, depressed patients were categorized as having no antidepressant treatment, treatment with very poor antidepressant refill persistence (MPR between 1 and 50%), treatment with relatively poor antidepressant refill persistence (MPR between 51 and 80%), and treatment with full antidepressant refill persistence (MPR greater than 80%). For psychotherapy, a meta-analysis of the effects of various types of psychotherapy (cognitive behavioural interventions) guided our operationalization. It found reductions in depression in response to psychotherapy, particularly in trials that provided 11 or more sessions [47]. Consequently, utilization of psychotherapy was categorized as receipt of: no sessions, 1–10 sessions, or 11 or more sessions, during the ART treatment episode. Psychotherapy sessions were identified from procedure codes submitted with claims, and included individual and group therapy [33, 48].

Control variables (Table 1) included gender and age (identified from the enrollment files), and whether the patient received treatment for substance abuse (alcohol or drug) during the enrollment period (identified using diagnosis codes recorded on insurance claims). Unlike data from public insurance systems (e.g., Medicare, Medicaid), no data on race were provided in the claims or enrollment files. Diagnosis codes used to define substance abuse and procedure codes used to define psychotherapy are available from the corresponding author.

Analyses

First, we cross tabulated the depression treatments (antidepressants and psychotherapy) for the population that was diagnosed with depression, to describe the patterns of depression treatment (Table 2). Second, we described ART adherence during the ART use period, stratified by depression treatments (Table 3). For each of the various levels and types of depression treatment, we calculated the

Table 1 Patient Characteristics

	(%)
Gender (% female)	13.0
Age (%)	
18–34	8.2
35–49	69.3
50–64	22.4
Substance abuse treatment (% yes)	10.5
ART adherence (MPR)	
90–100%	47.8
80–89%	31.7
70–79%	12.2
60–69%	7.3
0–59%	1.0

$N = 1{,}150$

MPR Medication possession ratio during persistent period

proportion of the population that achieved a medication possession ratio for ART greater than 90%. We also presented 95% confidence intervals for those proportions.

We used multivariate logistic regressions to address the main study questions (Table 4). First, we examined whether depression treatment (with antidepressant medications, psychotherapy, or both) among those with a claims-based depression diagnosis was associated with better ART adherence, when compared to those who did not receive any depression treatment. Second, we examined, among those treated for depression, whether ART adherence varied with the type of depression treatment used (antidepressant medications, psychotherapy, or both). Third, among depressed persons, we examined whether better adherence to depression treatment was associated with better ART adherence. In addressing this third issue, we included independent variables measuring the extent of antidepressant adherence (classified as MPR 0-50%, MPR 51-80%, and MPR 81-100%) and number of psychotherapy visits (none, 1–10 sessions/year, and 11 or more sessions/year). Because we suspected that those treated with antidepressant medications, psychotherapy, or both might differ, we estimated three different models: one for the subpopulation who used antidepressant medications (± psychotherapy), one for the subpopulation who used psychotherapy (± antidepressant medications), and one for the subpopulation using either treatment type. Psychotherapy combined with antidepressant use has the largest evidence base supporting its efficacy for various populations, including PLWHA [49–51]. Therefore, the third of these models (i.e., model for the subpopulation using either treatment type) included an interaction term for antidepressant use and psychotherapy use. All multivariable models controlled for gender, age, receipt of substance abuse treatment, and the duration of observation (i.e., the length of the ATR treatment episode). Analyses were performed with Stata v.10.

Table 2 Depression treatment patterns for PLWHA diagnosed with depression

Antidepressant treatment		Psychotherapy sessions		
		None ($n = 426$, 37.0%)	1–10 ($n = 219$, 19.0%)	11+ ($n = 505$, 44.0%)
No antidepressant use	($n = 272$, 23.7%)	63	61	148
		5.5	5.3	13
		23.2	22.4	54.4
0% < ADP MPR ≤ 50%	($n = 210$, 18.3%)	79	58	73
		9.9	5.4	6.4
		37.6	27.6	34.8
50% < ADP MPR ≤ 80%	($n = 273$, 23.7%)	133	51	89
		11.6	4.4	7.7
		48.7	18.7	32.6
80% < ADP MPR	($n = 395$, 34.4%)	151	49	195
		13.1	4.3	17.0
		38.2	12.4	49.4

Within the cells, the first figure represents cell size, second figure represents cell percentage, and the third figure represents row percentages

Percentages may not add up to 100 due to rounding

Spearman's rho = −0.0618. Probability of statistic testing independence of psychotherapy sessions and antidepressant treatment: prob > |t| = 0.036

MPR Medication possession ratio during persistent ART use period

Table 3 ART adherence by depression treatment

Antidepressant treatment	Psychotherapy sessions (%)			
	None	1–10	11+	All
No antidepressant use	28.6 (17.3–39.8)	32.8 (20.9–44.7)	28.4 (21.1–35.7)	29.4 (24.0–34.8)
0% < ADP MPR ≤ 50%	49.4 (38.2–60.5)	24.1 (13.0–35.3)	50.7 (39.1–62.2)	42.9 (36.1–49.6)
50% < ADP MPR ≤ 80%	23.3 (16.1–30.5)	68.6 (55.8–81.5)	41.6 (31.3–51.9)	37.7 (32.9–43.5)
80% < ADP MPR	74.8 (67.8–81.8)	65.3 (51.8–78.8)	67.7 (61.1–74.3)	70.1 (65.6–74.7)
All	47.2 (42.4–51.9)	46.1 (39.5–52.7)	49.1 (44.7–53.5)	47.8 (44.9–50.7)

Figures represent the rate that achieved >90% medication possession ratio for ART, during persistent ART use period. Figures in parenthesis are 95% confidence intervals

Results

Patient Characteristics

Thirteen percent of the population was female (Table 1); 69% were between the age of 35 and 49, and 22% were between the age of 50 and 64. Average age was 43.3 years in 2003. Eleven percent received a diagnosis code from a medical care provider indicative of substance abuse.

Depression Treatment Patterns

Less than a quarter (23.7%) of those with a depression diagnosis did not have pharmacy claims for antidepressants

Table 4 Logistic regression models predicting antiretroviral therapy medication adherence during persistent period

Sub-sample	Model 1 Diagnoses in claims history (n = 1,150)	Model 2 Diagnoses in claims history + any treatment (n = 1,087)	Model 3 Diagnoses in claims history + ADP use (n = 878)	Model 4 Diagnoses in claims history + psychotherapy (n = 724)	Model 5 Diagnoses in claims history + any treatment (n = 1,087)
Covariates					
Any treatment[a]					
No	Ref.	–	–	–	–
Yes	2.52* (1.40, 4.53)	–	–	–	–
Treatment type					
None	–	–	–	–	–
Antidepressant alone	–	2.24* (1.53, 3.28)	–	–	–
Psychotherapy alone	–	Ref.	–	–	–
Both	–	2.75* (1.90, 3.99)	–	–	–
Antidepressant use					
None	–	–	–	Ref.	Ref.
0% < ADP MPR ≤ 50%	–	–	Ref.	1.50 (0.90, 2.49)	1.99* (1.25, 3.17)
50% < ADP MPR ≤ 80%	–	–	0.64* (0.43, 0.96)	1.82* (1.13, 2.92)	1.45* (0.94, 2.26)
80% < ADP MPR	–	–	2.68* (1.82, 3.94)	4.98* (3.16, 7.82)	6.63* (3.84, 11.4)
Psychotherapy utilization					
None	–	–	Ref.	–	Ref.
1–10 sessions per year	–	–	1.14 (0.75, 1.74)	Ref.	1.22 (0.82, 1.82)
11+ sessions per year	–	–	1.24 (0.89, 1.74)	0.94 (0.65, 1.37)	1.27 (0.85, 1.92)
Dummy indicating interaction of (80+ % ADP MPR) and (11+ sessions of psychotherapy)	–	–	–	–	0.80 (0.44, 1.43)

Coefficients represent odds ratios. All models control for gender, age, receipt of any substance abuse treatment and observations length

Medication adherence is operationalized as binary outcome indicating 90% or more antiretroviral therapy MPR. * $p < 0.05$

ADP antidepressant, *MPR* medication possession ratio

[a] Antidepressant use or psychotherapy

(Table 2). Just over a third (34.4%) of those with depression were using antidepressant medications and were in the highest adherence group (>80% MPR). Thirty-seven percent had no claims for psychotherapy during the observation period; whereas almost half of the population (44%) received 11 or more sessions of psychotherapy. Psychotherapy claims were more common among those with no antidepressant use than among those who used antidepressants (Pearson $\chi^2(3) = 41.04$, $Pr < 0.001$). Among depressed patients who took antidepressants ($n = 878$), those with better adherence to antidepressant medications tended to have more psychotherapy visits than those with worse adherence (Spearman's rho $= -0.0618$, $Pr > |t| = 0.036$).

ART Adherence

Adherent patients were defined as those with a MPR of ≥90% during the ART treatment episode. Adherence was suboptimal. Forty-eight percent had a medication possession ratio (MPR) of ≥90%, 32% had an MPR between 80 and 89%, and the remaining 20% had an MPR below 80% (Table 1). ART adherence rates were strongly associated with antidepressant adherence rates (column labelled All, Table 3). Among those who did not use any antidepressant, 30% were adherent to ART (95% CI 24.0–34.8). Among those who had the best adherence to antidepressants, 70% were adherent to ART (95% CI 65.6–74.7). Those with suboptimal adherence to antidepressant use had better ART adherence than those who did not use any antidepressants, but worse ART adherence than those with better adherence to antidepressants. Confidence intervals for ART adherence, for the group with an antidepressant MPR of 0–50% and the group with an antidepressant MPR of 51–80%, were overlapping. Rates of ART adherence did not vary with psychotherapy use; it ranged from 46% to 49%, with confidence intervals overlapping (row labelled All, Table 3).

In Table 3, we observed that the relationship of ART adherence to antidepressant use remained after the study population was stratified by psychotherapy utilization; ART adherence remained lowest among those who did not use antidepressants and highest among those with the best adherence to antidepressants. Rates of ART adherence did not vary with psychotherapy use, even after the study population was stratified by antidepressant use.

Multivariate Models of ART Adherence

Multivariate models were specified, controlling for gender, age, receipt of any substance abuse treatment and duration of observation. In these models, among those diagnosed with depression (Model 1), those who initiated depression treatment (antidepressants and/or psychotherapy use) were significantly more likely to be adherent to ART (AOR = 2.52, 95% CI 1.40, 4.53) than those with no treatment.

In the subpopulation that initiated depression treatment (Model 2), those receiving psychotherapy alone were significantly less likely to be adherent to ART than those receiving antidepressants alone (AOR = 2.24, 95% CI 1.53–3.28) or those receiving both antidepressants and psychotherapy (AOR = 2.75, 95% CI 1.90–3.99).

The final three models investigated the dose response relationship between depression treatment and ART adherence, for the subpopulation that was diagnosed with depression and initiated depression treatment. In Model 3, we investigated whether adherence to antidepressant treatment was associated with better ART adherence, among the subpopulation who initiated antidepressant therapy, and controlling for psychotherapy utilization and other covariates. The antidepressant MPR predicted adherence to ART in a nonlinear fashion. The odds of ART adherence among those with relatively poor (50–80% MPR) antidepressant adherence were lower than the odds of ART adherence among those with poor antidepressant adherence (≤50% MPR) (AOR = 0.64, 95% CI 0.43, 0.96). However those with an antidepressant MPR of ≥80% were significantly more likely to be adherent to ART (≥90% MPR) than those with poor antidepressant adherence (AOR = 2.68, 95% CI 1.82, 3.94). Model 4 examined whether more psychotherapy sessions were associated with better ART adherence, among those that received psychotherapy, after controlling for antidepressant utilization and other covariates. Having 11 or more psychotherapy sessions, instead of 10 or fewer, was not associated with better ART adherence (AOR = 0.94, 95% CI 0.65, 1.37).

In the final model (Model 5), we investigated the dose response to both treatment modalities, allowing for interactions, for the subpopulation that utilized any treatment. All levels of antidepressant medication use were significantly associated with better ART adherence. The OR for ART adherence was 6.63 (95% CI 3.84, 11.4) for those with an MPR of ≥80% compared to those with no antidepressant use. The interaction between antidepressant use and psychotherapy use was not significant (AOR = 0.80, 95% CI 0.44, 1.43). Psychotherapy was not significantly associated with better ART adherence.

For other covariates, the findings were robust regardless of subpopulation or model specification (data not shown). Consistent with earlier findings [52–54], adherence improved with age; females were less likely to be adherent to ART than males; and those who received a diagnosis of substance abuse were significantly less likely to be adherent than those with no diagnosis.

Discussion

We found support for our hypothesis that depression treatment patterns are associated with ART adherence. For patients with a depression diagnosis, the odds of being adherent with ART are greater for treated than untreated patients, and the odds of being adherent with ART are significantly greater for drug therapy alone than psychotherapy alone.

In Models 3, 4 and 5, we examined, simultaneously, adherence to antidepressant treatment and number of psychotherapy visits attended, with consistent findings. In the model limited to antidepressant users (Model 3), the model limited to psychotherapy users (Model 4), and the model that included those receiving either one or both treatments (Model 5), antidepressant adherence of $\geq$80% was significantly and strongly associated with greater odds of ART adherence. Number of psychotherapy visits attended was not associated with ART adherence in any of the models.

Our findings concord with those of previous research; among persons with HIV and depression, treating depression symptoms with pharmacotherapy is associated with improvements in ART adherence [24, 32, 55]. However, the current literature, including this study, is limited to retrospective observational studies establishing associations. The current study is not a controlled study comparing antidepressant treatment to a placebo in relation to ART adherence. Difficulties in establishing the nature of the association (i.e., whether treating depression symptoms would increase ART adherence) with observational data have been noted [56]. Future research should be designed to both investigate whether better antidepressant adherence would improve ART adherence, and to quantify the gains from antidepressant treatment.

We did not observe an association between psychotherapy utilization and ART adherence. Yet, there are empirically supported therapies that have been shown to be effective in other studies (for example, specially adapted protocols that combine cognitive behavioral therapy with adherence promoting components—"Cognitive Behavioral Therapy for Adherence and Depression" or CBT-AD) [39]. Many factors (that we were not able to measure) may be responsible for the lack of an association. First, patients who are not inclined to take medications (regardless of their class) may be more likely to seek psychotherapy as the treatment of choice for depression. Second, our claims data did not include information on the types of psychological treatment provided (e.g., cognitive-behavior therapy, nondirective supportive treatment, behavioral activation treatment, or interpersonal psychotherapy), the problems it targets, or the specific interventions used. It may be that adherence benefits require therapy adaptations of the interventions included in CBT-AD. Perhaps, some therapists emphasize adherence to ART as an important goal of psychotherapy, and engage patients in a discussion of barriers to and problem solving around adherence while other therapists may emphasize more traditional psychotherapy goals (e.g., improved mood, improved interpersonal relationships, or emotional resilience) that may have a less direct impact on ART adherence. Future research should include more detailed data on the psychotherapy provided (e.g., type, frequency, targets, emphasis, and interventions) and its association with ART adherence. PLWHA would be better served by mental health providers who try to motivate them to adhere to appropriate treatments for their conditions. Mental health practitioners serving the needs of people living with HIV should be trained with workforce development efforts, such as post graduate certificate programs and continuing education courses that emphasize the skills (e.g., motivational interviewing, behavior change) and knowledge (e.g., disease progression, medication side effects) needed to increase ART adherence.

We found that more than three-fourths of those with depression filled a prescription for an antidepressant during the observation period, a rate higher than we had anticipated. Analyses of HCSUS data from 1996 indicated that 43% of those with a mood disorder diagnosis, based on a structured interview, reported antidepressant use in the prior 6 months [57]. This may reflect the fact that we studied a commercially insured population, with better access to both mental health providers and medications than patients studied in the HCSUS data. It may also reflect increased treatment rates over the decade [58].

The contributions of the current study include: a geographically diverse sample residing in all 50 states, the inclusion of both antidepressant treatment and psychotherapy, and a large sample size that enables us to investigate dose–response relationships, and provides us with the ability to quantify the association between various depression treatments and ART adherence. ART adherence was measured during an ART treatment episode, with discontinuations longer that 60 days viewed as conceptually different from other lapses in adherence.

There are several study limitations. First, because this is an observational study, we cannot attribute causation to the relationships found. That is, we cannot conclude that better antidepressant adherence was responsible for or caused improved ART adherence. Demonstration of causation would ideally require an experimental study design, but can be time consuming and relatively difficult to implement. It is possible that there are third variables that are responsible for the association we found. For example, certain patients may just be more willing to take pills, irrespective of pill type (antidepressants or ART medications). Such variables cannot be captured with the current design. If experimental

designs are not possible, future research should try to measure potential confounders, such as willingness to take pills, irrespective of the type of pill (antidepressant or ART).

Second, although the dataset is large, it is nonetheless a convenience sample of privately insured beneficiaries. Information on race, education level, income, depression severity and previous depression treatment outcomes are not available in these claims data; their inclusion would provide further insights. Third, our adherence measures are based on pharmacy refills and do not guarantee ingestion of the medications. High concordance between claims based pharmacy measures and pills counts have been found [59], and among HIV patients, pharmacy-based adherence measures have predicted survival [60]. However, a recent study suggests poor correlation between pharmacy-based claims and electronic drug monitoring [61]. Future research should investigate other definitions of adherence.

Conclusions

In conclusion, we found a strong, statistically significant association between adherence to antidepressant medications and adherence to ART. Depression comorbidity and treatment patterns in this large, national population of patients with HIV, whose care is financed by employment-based insurance, largely replicate findings from more disadvantaged populations in the public insurance systems. While these observational data cannot support causal inference, they do add to accumulating evidence that depression treatment may improve ART adherence. PLWHA may gain additional benefits from the diffusion of evidence supported psychotherapies (e.g., CBT-AD) for ART adherence, to the mental health providers that serve them.

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