Prevalence of Neuropsychiatric Conditions in Patients Living With HIV-1 Treated With Antiretroviral Therapies – A Perspective From US Medicaid Data

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INTRODUCTION

- People living with human immunodeficiency virus (HIV)–1 are more likely than the general population to be affected by mental health disorders, such as anxiety, depression, and substance use disorder[1-4]; these disorders are also more common in the Medicaid population[5]
- Treatment adherence is a challenge for a substantial portion of people living with HIV-1 due, in part, to a higher prevalence of mental health disorders but also due to neuropsychiatric events (NPEs) that have been associated with antiretroviral therapy (ART) itself (eg, fatigue, headache, and insomnia)[6,7]
- Here we report the prevalence of mental health comorbidities and NPEs among Medicaid patients with HIV-1 infection and newly started on ART

OBJECTIVES

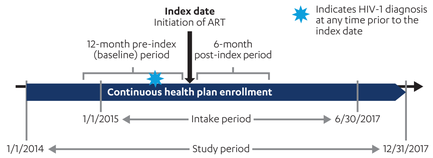
- To estimate and describe the prevalence of NPEs during the period following ART initiation in patients living with HIV-1 and newly treated with ART, relative to those without HIV, in a Medicaid population
- To describe the pretreatment comorbidities and demographic characteristics of patients living with HIV-1 and newly treated with ART

METHODS

Study Design

- This was a retrospective cohort study (**Figure 1**) using the IBM MarketScan® Multi-State Medicaid Database (MDCD) during the period between 1/1/2014 and 12/31/2017
  - The MDCD contains adjudicated US health insurance claims for Medicaid enrollees from multiple states. The data include hospital discharge diagnoses, outpatient diagnoses and procedures, and outpatient pharmacy claims
- The index date was defined as the first prescription fill date for any single- or multitablet ART regimen

Figure 1. Study design.

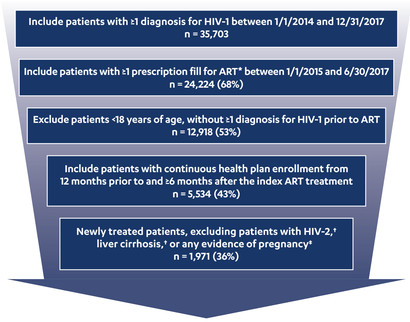


ART, antiretroviral therapy; HIV-1, human immunodeficiency virus–1.

Study Population

- The 2 patient cohorts were defined as follows:
  - **HIV-1–positive patients newly treated with ART**: Patients aged ≥18 years with HIV-1 and newly initiated on an ART regimen (**Figure 2**)
  - **Non-HIV cohort**: Exact attribute matching was performed to randomly select 1 patient from the non-HIV patient pool to match with an HIV patient based on age, gender, and diagnoses of hepatitis B virus and hepatitis C virus infection
- Patients were identified with ≥1 prescription fill for ART between 1/1/2015 and 6/30/2017 (intake period)
  - Patients were considered treatment naïve (or newly initiated on ART) if, prior to the index date, a 12-month ART-free period was observed
  - Any time prior to the index date, patients must have had ≥1 diagnosis of HIV-1
- A minimum baseline enrollment period of 12 months was required to measure clinical characteristics such as comorbidities and prior medication use
- Patients were followed for a minimum of 6 months (or 12 months for a sensitivity analysis) from the index date

Figure 2. Attrition of HIV-1 patients newly treated with ART.



HIV, human immunodeficiency virus; ART, antiretroviral therapy.
*ARTs observed with ≤3% frequency: Triumeq (30%), Genvoya (15%), Stribild (13%), Atripla (7%), Tivicay + Truvada (6%), Norvir + Prezista + Truvada (5%), Complera (3%), Descovy + Tivicay (3%), and Isentress + Truvada (3%).
†During the entire study period.
‡During the 12-month baseline period.

Study Outcomes

- **Primary outcome**: prevalence of NPEs during the post-index period, relative to a non-HIV population
  - NPEs of interest are presented as both individual NPEs and categorized as chronic or acute, based on input from a clinical expert (see **Tables 2** and **3** for groupings)
  - The prevalence of NPEs of interest was calculated by dividing the number of patients having NPEs (chronic or acute) by the total cohort (ie, HIV-1 patients newly treated with ART or non-HIV)
- For patients with continuous enrollment for 12 months after the index date, a sensitivity analysis of NPE prevalence, relative to the non-HIV cohort, was performed
- NPE prevalence was also assessed during the 12-month *baseline* period, relative to the non-HIV cohort

Statistical Analysis

- Descriptive statistics are reported, including means and standard deviations (SDs) for continuous variables and frequencies and proportions for categorical variables

RESULTS

Baseline Period

- The study included 1,971 treatment-naïve, HIV-1–infected patients (**Figure 2**)
- Among these HIV-1 patients newly treated with ART, the mean (SD) age was 38.5 (12.7) years, 14.0% were ≥55 years of age, and 41.4% were female (**Table 1**)
  - The mean (SD) Quan-Charlson comorbidity index (QCI) score was 4.2 (2.2); QCI is a measure of comorbidity burden to which HIV/acquired immunodeficiency syndrome contributes 4 points
  - The comorbidities during the baseline period that were observed most commonly included hypertension (32.1%), hyperlipidemia (13.4%), and obesity (10.9%; see complete list in **Table 1**)

Table 1. Demographic and Baseline Clinical Characteristics Among HIV-1 Patients Newly Treated With ART

	HIV-1 patients newly treated with ART (n = 1,971)
Demographics	
Age, mean (SD), years	**38.5 (12.7)**
Age group, n (%), years	
18-24	320 (16.2)
25-34	521 (26.4)
35-44	436 (22.1)
45-54	418 (21.2)
55-64	274 (13.9)
≥65	2 (0.1)
Female, n (%)	**816 (41.4)**
Women of childbearing potential,* n (%)	**606 (30.7)**
Race, n (%)	
White	331 (16.8)
Black	1,177 (59.7)
Hispanic	31 (1.6)
Other	315 (16.0)
Unknown	117 (5.9)
Plan type, n (%)	
HMO	1,042 (52.9)
Other†	929 (47.1)
Index year, n (%)	
2015	709 (36.0)
2016	799 (40.5)
2017	463 (23.5)
12-month baseline comorbid conditions‡	
QCI score, mean (SD)	**4.2 (2.2)**
Comorbid conditions, n (%)	
Substance use disorder	1,005 (51.0)
Drug abuse	985 (50.0)
Alcohol abuse	154 (7.8)
Hypertension	632 (32.1)
Depression	557 (28.3)
Anxiety	359 (18.2)
Hyperlipidemia	265 (13.4)
Obesity	214 (10.9)
Diabetes	195 (9.9)
COPD	176 (8.9)
Hepatitis C virus	161 (8.2)
Cardiovascular disease	150 (7.6)
Opportunistic infection	136 (6.9)
12-month baseline procedures and medication use	
Medication use, n (%)	**1,358 (68.9)**
Narcotics/opioids	986 (50.0)
Antidepressants	492 (25.0)
Antianxiety agents	401 (20.3)
Antihypertensives	296 (15.0)
Antipsychotic agents	248 (12.6)
Antihyperlipidemics	148 (7.5)
Antidiabetics	117 (5.9)
HIV-1–related procedures,§ n (%)	**1,474 (74.8)**
Other general procedures, n (%)	**1,760 (89.3)**
Complete blood count	1,580 (80.2)
Comprehensive metabolic panel	1,522 (77.2)
Infectious agent detection by nucleic acid	1,099 (55.8)
Syphilis test, nontreponemal antibody	933 (47.3)
Hepatitis B surface antibody	689 (35.0)
Hepatitis C antibody	99 (5.0)

HIV-1, human immunodeficiency virus–1; ART, antiretroviral therapy; SD, standard deviation; HMO, health maintenance organization; QCI, Quan-Charlson comorbidity index; COPD, chronic obstructive pulmonary disease.
*Women of childbearing potential: age ranged from 18 to 49 years.
†Other plan type includes preferred provider organization.
‡Only comorbidities included in the QCI are presented.
§HIV-1–related procedures were CD4+ count, HIV-1 antibody test, HIV-1 viral load test, HIV-1 antigen test, and HIV-1 genotypic resistance test.

- The most common (≥10%) NPE claims during the 12-month baseline period for HIV-1 patients newly treated with ART were diagnosed depression (28.2%), headache (19.0%), anxiety (18.4%), fatigue (16.0%), diagnosed and treated depression (15.3%), and bipolar/manic depression (11.2%). In the non-HIV cohort, the most common (≥10%) NPEs were anxiety (15.2%), diagnosed depression (15.0%), and diagnosed and treated depression (11.2%; **Table 2**)

Table 2. Prevalence of Individual NPEs of Interest During the 12-month Baseline Period

Prevalence of NPEs, n (%)	Non-HIV cohort (n = 1,971)	HIV-1 patients newly treated with ART (n = 1,971)
Chronic	**518 (26.3)**	**815 (41.3)**
Anxiety	300 (15.2)	363 (18.4)
Depression, diagnosed	296 (15.0)	556 (28.2)
Depression, diagnosed and treated	221 (11.2)	301 (15.3)
Bipolar/manic depression	122 (6.2)	221 (11.2)
Trauma- and stressor-related disorders	94 (4.8)	179 (9.1)
Cognitive impairment/poor concentration	6 (0.3)	7 (0.4)
Acute	**399 (20.2)**	**738 (37.4)**
Dizziness	77 (3.9)	141 (7.2)
Fatigue	147 (7.5)	316 (16.0)
Headache	172 (8.7)	374 (19.0)
Insomnia/sleep disorder	108 (5.5)	119 (6.0)
Suicidal ideation	34 (1.7)	99 (5.0)

NPE, neuropsychiatric event; HIV, human immunodeficiency virus; ART, antiretroviral therapy.

Post-index Period

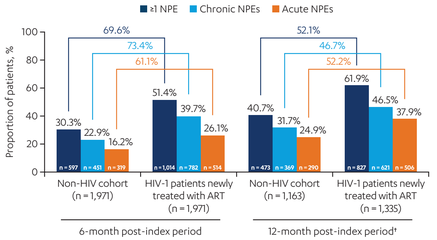
- During the 6-month post-index period, 51.4% of HIV-1 patients newly treated with ART had a claim for ≥1 NPE relative to 30.3% of patients in the non-HIV cohort (**Table 3**)
- Over 12 months, among HIV-1 patients newly treated with ART, 61.9% had ≥1 distinct NPE claim, 36.6% had ≥2 distinct NPE claims, 19.3% had ≥3 unique NPE claims, and 10.4% had ≥4 distinct NPE claims; these proportions were lower in the non-HIV cohort (40.7%, 24.4%, 14.0%, and 6.5%, respectively; **Table 3** and **Figure 3**)
- The prevalence of individual NPEs of interest during the 6- and 12-month post-index periods are shown in **Table 3**

Table 3. Prevalence of Overall and Individual NPEs of Interest During the Post-index Periods

	6-month post-index period		12-month post-index period*	
	Non-HIV cohort (n = 1,971)	HIV-1 patients newly treated with ART (n = 1,971)	Non-HIV cohort (n = 1,163)	HIV-1 patients newly treated with ART (n = 1,335)
Patients with ≥1 NPE, n (%)	**597 (30.3)**	**1,014 (51.4)**	**473 (40.7)**	**827 (61.9)**
With ≥2	297 (15.1)	495 (25.1)	284 (24.4)	488 (36.6)
With ≥3	137 (7.0)	231 (11.7)	163 (14.0)	257 (19.3)
With ≥4	49 (2.5)	102 (5.2)	76 (6.5)	139 (10.4)
Prevalence of NPEs, n (%)				
Chronic	**451 (22.9)**	**782 (39.7)**	**369 (31.7)**	**621 (46.5)**
Anxiety	252 (12.8)	311 (15.8)	231 (19.9)	263 (19.7)
Depression, diagnosed	244 (12.4)	514 (26.1)	228 (19.6)	457 (34.2)
Depression, diagnosed and treated	175 (8.9)	317 (16.1)	168 (14.4)	305 (22.8)
Bipolar/manic depression	103 (5.2)	200 (10.1)	79 (6.8)	176 (13.2)
Trauma- and stressor-related disorders	94 (4.8)	168 (8.5)	80 (6.9)	146 (10.9)
Cognitive impairment/ poor concentration	1 (0.1)	3 (0.2)	2 (0.2)	4 (0.3)
Acute	**319 (16.2)**	**514 (26.1)**	**290 (24.9)**	**506 (37.9)**
Dizziness	65 (3.3)	93 (4.7)	57 (4.9)	107 (8.0)
Fatigue	120 (6.1)	192 (9.7)	134 (11.5)	205 (15.4)
Headache	113 (5.7)	234 (11.9)	121 (10.4)	271 (20.3)
Insomnia/sleep disorder	71 (3.6)	90 (4.6)	75 (6.4)	92 (6.9)
Suicidal ideation	29 (1.5)	62 (3.1)	26 (2.2)	69 (5.2)
Suicide attempt	–	–	9 (0.8)	16 (1.2)

NPE, neuropsychiatric event; HIV, human immunodeficiency virus; ART, antiretroviral therapy.
*Includes only patients with a minimum 12-month post-index period.

Figure 3. Prevalence of NPEs of interest during the post-index periods.*



NPE, neuropsychiatric event; HIV, human immunodeficiency virus; ART, antiretroviral therapy.
*Percentages above the brackets indicate percentage change (ie, increase) from the proportion of patients in the non-HIV cohort to the proportion of HIV-1 patients newly treated with ART.
†Includes only patients with a minimum 12-month post-index period.

LIMITATIONS

- Misclassification bias may have been introduced through several sources (eg, erroneous or missing claims codes)
- Data for this study are from insurance claims, which may underestimate the prevalence of NPEs among HIV-1 patients newly treated with ART (eg, underreporting from patients or underdiagnosis from providers)
- The frequency of newly emerging NPEs following ART initiation is still unknown, as this study only assessed the prevalence, not the incidence, of NPEs
- Classification of NPEs as chronic or acute was not determined by the duration of the NPE; rather, it was based on input from a clinical expert

CONCLUSIONS

- **In the Medicaid population, HIV-1–positive patients newly treated with ART experienced a higher prevalence of NPEs during the 6 months immediately following initiation relative to a control cohort without HIV; moreover, among patients newly treated with ART, NPEs were more common over the 12-month post-index period**
  - These findings highlight the importance of individualizing ART; for HIV-1 patients with pre-existing neuropsychiatric disorders, there is a need to consider selecting an initial ART regimen that does not have a propensity to worsen NPEs
  - Among patients with HIV-1, the presence of NPEs may potentially impact treatment adherence and lead to regimen switching/discontinuation and/or the development of resistance; an ideal regimen for these patients would have a high genetic barrier to resistance and be a single-tablet regimen
  - Future studies should investigate factors that influence the frequency of NPEs
- **During the 12-month *baseline* period, patients with HIV-1 and newly initiated on ART had a higher NPE burden relative to those without HIV**
  - Further research should be done to explore how the presence of NPEs and neuropsychiatric disorders or conditions may impact adherence and the risk for HIV acquisition

REFERENCES

1. Fettipace A, et al. *J Acquir Immune Defic Syndr*. 2017;74(4):423-431.
2. Lowther K, et al. *Int J Nurs Stud*. 2014;51(8):1171-1189.
3. Rabkin JG. *Curr HIV/AIDS Rep*. 2008;5(4):163-171.
4. Reid S, Dwyer J. *Psychosom Med*. 2005;67(2):260-269.
5. Gibson TB, et al. *MM Med*. 2009;174(9):936-943.
6. Hoffmann C, Libre JM. *AIDS Rev*. 2019;21(1):4-10.
7. Paolillo EW, et al. *Alcohol Clin Exp Res*. 2017;41(8):1518-1525.

DISCLOSURES

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