

Clinical Characteristics and Treatment Patterns Among US Patients With HIV

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HIV is a chronic viral infection that attacks CD4 T lymphocytes (T cells) and weakens the ability of infected patients to fight other infections and diseases. HIV represents a significant healthcare burden in the United States. As of 2016, more than 1 million Americans had received an HIV diagnosis and were living with HIV, and there were 15,807 deaths among people with HIV due to any cause that year.¹ Although the rate of new HIV diagnoses has been declining since 2012, the number of Americans with newly diagnosed HIV was 38,739 in 2017.²

If left untreated, HIV can develop into AIDS.³ However, due to advances in antiretroviral therapy (ART), people living with HIV can achieve prolonged disease-free survival, sustained virologic suppression, CD4 cell repletion, and reduced rates of hospitalization if they maintain high adherence to their ART regimen.⁴⁻⁶ As a result, rates of HIV-related morbidity and mortality have been dramatically reduced, and HIV is now a largely manageable chronic disease.^{4,7,8} At the time of this study, an ART regimen consisted of a 3-drug combination of 2 nucleoside reverse transcriptase inhibitors (NRTIs) with either an integrase strand transfer inhibitor (INSTI), a nonnucleoside reverse transcriptase inhibitor (NNRTI), or a boosted protease inhibitor (PI).⁹

Although people living with HIV are now less likely to experience acute, life-threatening complications of HIV, there are still challenges to consider when managing a chronic disease that persists for decades. For example, people living with HIV have an increased risk of developing a range of comorbidities such as cardiovascular disease (CVD), cancer, kidney disease, liver disease, neurocognitive disease, and osteoporosis.¹⁰⁻¹² Many of these comorbidities are associated with increasing age^{10,13} but may also result from an increased life span and resultant cumulative exposure to ART.^{10,14} The complex challenge of managing HIV with ART for life involves maintaining long-term control of HIV viral replication while simultaneously managing tolerability, toxicity, and drug-drug interactions, which can lead to reduced adherence.

The aim of the present study was to examine the demographics, clinical characteristics, and treatment patterns of people living with HIV using ART in the United States.

ABSTRACT

OBJECTIVES: Describe the clinical characteristics and treatment patterns of patients with HIV-1 who have commercial or Medicare health insurance in the United States.

STUDY DESIGN: Retrospective cohort study.

METHODS: Administrative claims for adult commercial and Medicare health plan enrollees with evidence of HIV-1 and antiretroviral therapy (ART) between January 1, 2007, and March 31, 2017, were assessed. Current and previous complete ART regimens were identified using a claims-based algorithm. Results were stratified by treatment status and insurance type.

RESULTS: Of 18,699 eligible patients, 5027 (27%) had no previous ART regimens; 15,275 (82%) had commercial insurance. Mean age was 47.5 years. Common comorbidities included hyperlipidemia, cardiovascular disease, hypertension, depression, and anxiety. The mean number of ART regimens was 1.43, with 31% of patients having 2 or more regimens. Mean (SD) daily pill burden was higher in patients with more than 1 ART regimen over time (5.7 [6.0] pills) or with Medicare insurance (9.2 [8.0] pills) than in patients with no previous ART (1.9 [4.4] pills) or with commercial insurance (3.7 [4.7] pills). Overall, 60% of patients achieved 90% or greater adherence to their ART regimen and 16% had a prescription filled for any contraindicated medication to an ART during their regimen.

CONCLUSIONS: This descriptive study demonstrated that people living with HIV enrolled in Medicare have a significant amount of comorbidities and total pill burden. Although advancements in ART have significantly improved life expectancy and quality of life for people living with HIV, it is important to take into account individual complexities such as comorbidities and pill burden when selecting ART regimens.

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METHODS

Study Overview

This was a retrospective cohort study using administrative claims data for commercial and Medicare Advantage (herein referred to as Medicare) health plan enrollees with evidence of HIV in the Optum Research Database (ORD) between January 1, 2007, and March 31, 2017 (study period) (Figure 1). Informed consent and institutional review board approval were not needed because of the deidentified nature of the retrospective claims data source.

Data Source

Data sourced from the ORD included medical claims, pharmacy claims, socioeconomic status, and enrollment data. Medical claims or encounter data were collected for all types of provided services, including specialty, preventive, and office-based treatments, and complied with insurance industry standards. Pharmacy claims covered all outpatient prescriptions filled and covered by the health plan. Socioeconomic data came from various individual- and population-level databases.

Study Population

Study participants were required to have 1 or more nondiagnostic medical claims (defined as claims that were not affiliated with diagnostic radiology, pathology, or laboratory venues to exclude rule-out diagnoses) with a diagnosis code for HIV-1 (*International Classification of Diseases, Ninth Revision, Clinical Modification [ICD-9-CM]*: 042, v08; *International Classification of Diseases, Tenth Revision, Clinical Modification [ICD-10-CM]*: B20, Z21) in any position during the study period; have 1 or more pharmacy claims for an ART between January 1, 2012, and March 31, 2017 (identification period); and be continuously enrolled in a health plan with medical and pharmacy benefits for at least 12 months prior to the start of the most recent complete ART regimen. The index date was defined as the start date of the most recent complete ART regimen (index regimen) during the identification period, and the fixed 12-month period immediately preceding the index date was defined as the preindex period. Participants had to be 18 years or older as of the index date and were excluded from the study if they had 1 or more nondiagnostic medical claims with a diagnosis code for HIV-2 (*ICD-9-CM*: 079.53; *ICD-10-CM*: B9735) in any position during the study period.

ART Regimen Algorithm

The most recent ART regimen (index regimen) and all previous ART regimens during the study period were defined using a claims-based algorithm. The index regimen included all ART prescriptions (core, backbone, and booster) filled within the first 15 days after the index date. The end of each regimen was defined as the earliest date of

TAKEAWAY POINTS

Although advancements in antiretroviral therapy (ART) over the past few decades have significantly improved life expectancy and quality of life in patients with HIV, this retrospective cohort study:

- ▶ Identified that people in the United States living with HIV, particularly those living longer with HIV and who are enrolled in Medicare, experience a high level of comorbidities and total medication burden
- ▶ Demonstrated the complexity of people living with HIV in terms of overall disease burden and the need for individualized considerations for healthcare providers to select the most appropriate ART regimen to ensure long-term treatment success

discontinuing the core or backbone agent (60-day gap after run-out) or starting of a new core or backbone agent. Regimens that ended due to disenrollment or study cutoff were considered censored. Patients with just 1 ART regimen during the preindex period were considered newly diagnosed (treatment naïve) and patients with more than 1 ART regimens were defined as treatment experienced.

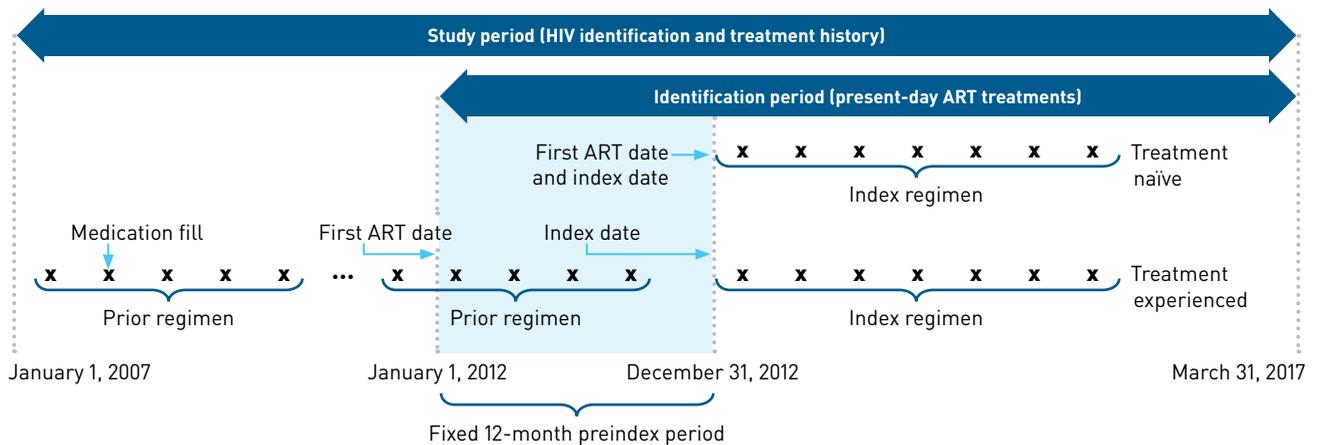
Measures

Demographics and clinical characteristics, including comorbidities and treatment patterns, were assessed during the fixed 12-month preindex period. Select comorbidities of interest were reported, and a modified Quan-Charlson (QC) comorbidity index score^{15,16} was calculated based on the presence of diagnosis codes on medical claims excluding HIV/AIDS. AIDS-defining conditions included Burkitt lymphoma, candidiasis, coccidioidomycosis, coccidiosis, cryptosporidiosis, cytomegalovirus, encephalopathy, herpes, histoplasma, Kaposi sarcoma, large cell lymphoma, malignant neoplasm of cervix, mycobacteria, pneumocystis pneumonia, pneumonia, primary central nervous system lymphoma, progressive multifocal leukoencephalopathy, salmonella septicemia, and toxoplasma meningoencephalitis. Renal dysfunction, another comorbidity of interest, included renal insufficiency (mild, moderate, and severe), acute renal failure, and end-stage renal disease, as well as conditions that were unknown or mixed types. Prescription fills for specific concomitant medications were recorded, and the average daily pill burden for all medications during the fixed 12-month preindex period was calculated using the number of prescriptions filled and days' supply for each medication. In addition, average daily pill burden for ART medications only and non-ART medications only were calculated.

Adherence to ART was assessed using the proportion of days covered¹⁷ (PDC) measure, which was calculated by dividing the total number of days covered by an ART by the total number of days continuously enrolled from the first ART filled through the study cutoff date, March 31, 2017. The average PDC to ART and the proportion of patients meeting 90% or greater PDC were reported.

Contraindicated medicines filled during each identified regimen during the fixed 12-month preindex period were identified for each ART class (ie, INSTI, NNRTI, NRTI) using HHS 2016 guidelines and supplemented with information from medication package inserts.¹⁸ Contraindicated medications were then reviewed by a pharmacist

FIGURE 1. Study Design



ART indicates antiretroviral therapy.

with infectious disease expertise. Contraindicated medications for multiclass ART combinations were separated by the type of core agent with and without a booster medication. Contraindicated medications during the index regimen were measured only for patients who were uncensored.

Statistical Analysis

All variables were summarized descriptively. Frequencies and percentages were reported for categorical variables, and means, medians, and SDs were reported for continuous variables. Results were stratified by patients' treatment status (treatment naïve or treatment experienced) and insurance type (commercial or Medicare).

RESULTS

Demographics and Clinical Characteristics

Overall, 18,699 patients met the selection criteria; of these, 15,275 (82%) had commercial insurance and 3424 (18%) had Medicare insurance. A total of 5027 (27%) were treatment naïve and 13,672 (73%) were treatment experienced (Figure 2). Baseline demographics for the study population are presented in Table 1. The mean age of patients was 47.5 years, 84% were men, and more than half (56%) resided in the South. Patients with commercial insurance were generally younger (mean = 45.0 years) and more often male (87%) compared with patients with Medicare insurance (58.6 years and 73%, respectively) (Table 1). The age and gender of patients stratified by treatment status were generally similar to those of the overall population (Table 1).

The mean baseline QC comorbidity score for the overall population was 0.74, after excluding HIV/AIDS (Table 2). For patients stratified by insurance type, the mean QC scores were 0.55 and 1.58 for patients with commercial insurance and Medicare insurance, respectively. For patients stratified by treatment status, the mean QC scores were

0.53 and 0.82 for treatment-naïve and treatment-experienced patients, respectively. Common comorbidities in the overall population included hyperlipidemia (41%), CVD (41%), hypertension (34%), depression (17%), anxiety (14%), any AIDS-defining condition (13%), any cancer (10%), any renal dysfunction (9%), dementia (2%), and osteoporosis (1%) (Table 2). These comorbidities were generally more common in treatment-experienced patients and patients with Medicare insurance compared with treatment-naïve patients and patients with commercial insurance, respectively (Table 2). The most common preindex concomitant medications for treatment-naïve and treatment-experienced patients were antihypertensives (21% and 36%, respectively), antihyperlipidemics (12% and 29%), anticancer medications including systemic steroids (23% and 24%), psychotherapeutic agents (17% and 29%), gastroesophageal reflux disease medications (11% and 18%), and antidiabetic medications (5% and 9%).

Treatment Patterns

Most common ART regimens. The index regimen in the overall population included 53% of patients on INSTIs, 94% on NRTIs, 36% on NNRTIs, 24% on PIs, and 40% on booster medications.

The mean numbers of regimens were 1.38 and 1.61 for patients with commercial insurance and Medicare insurance, respectively, with 72% and 60% of patients having 1 regimen, 20% and 27% having 2 regimens, and 7% and 13% having 3 or more regimens.

Pill burden. The distribution of patients' pill burden of both ART and non-ART medications is shown in Figure 3. A higher proportion of patients with Medicare insurance had a total pill burden of 5 or more pills per day (73%) compared with patients with commercial insurance (31%; Figure 3 [A]). In addition, more treatment-experienced patients had a total pill burden of 5 or more pills per day compared with treatment-naïve patients (48% vs 13%, respectively; Figure 3 [B]). The mean daily pill burden for the overall patient population

was 4.69 pills for ART and non-ART medications combined: 1.54 pills for ART medications only and 3.15 pills for non-ART medications only. Patients with Medicare insurance had a higher overall pill burden (mean = 9.23 pills) than those with commercial insurance (mean = 3.68 pills). This trend was maintained for both ART medications only (Medicare insurance vs commercial insurance, 2.32 pills vs 1.37 pills) and non-ART medications only (6.91 pills vs 2.31 pills). Treatment-naïve patients had a lower total daily pill burden compared with treatment-experienced patients (mean = 1.87 pills vs 5.73 pills). This trend was also maintained for ART medications only (treatment naïve vs treatment experienced, 0.05 pills vs 2.09 pills) and for non-ART medications only (1.82 pills vs 3.64 pills).

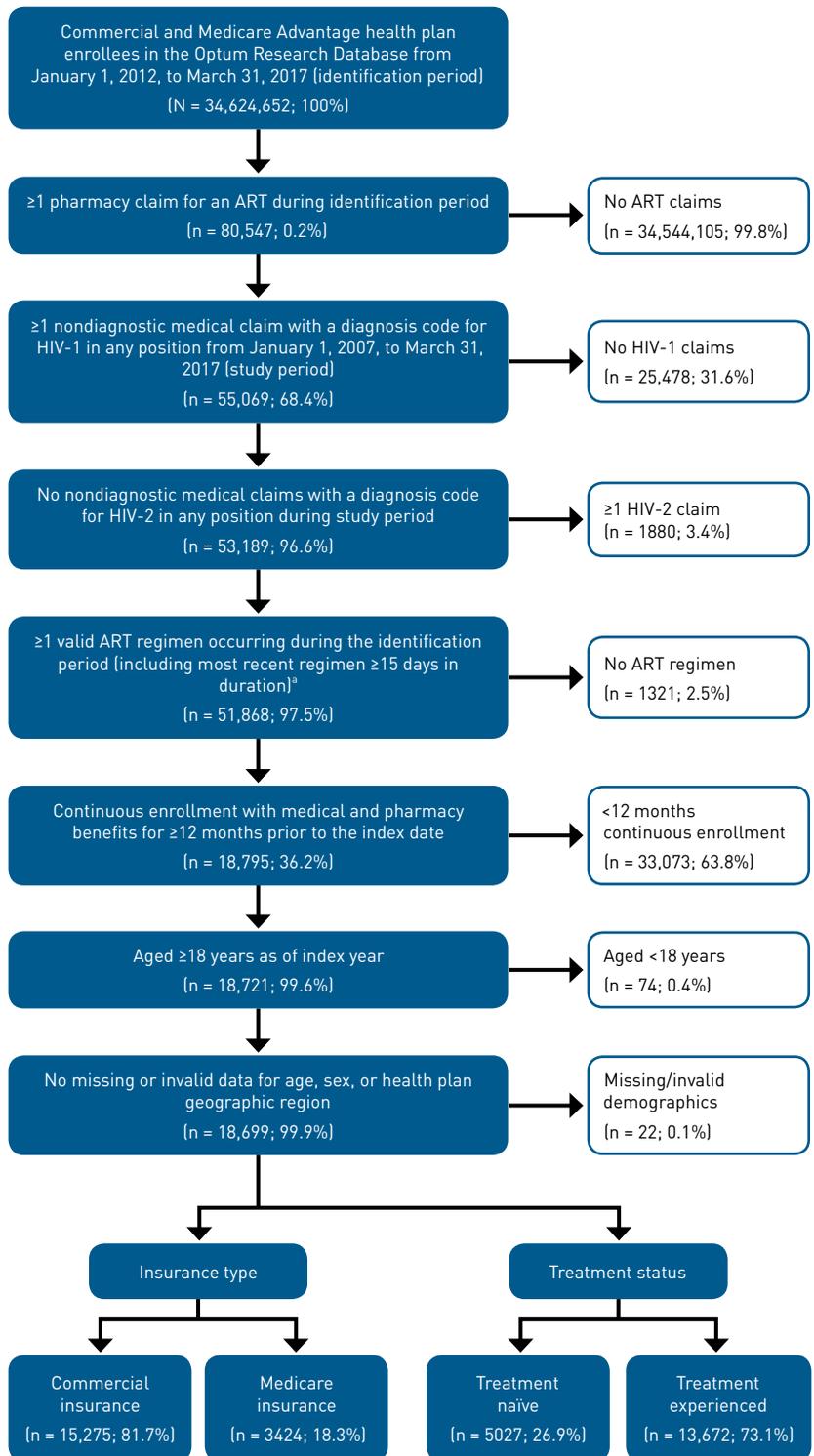
A total of 60% of patients in the overall population achieved 90% or greater adherence to their ART regimen (PDC ≥90%), whereas the proportion of patients stratified by insurance type with PDC ≥90% was higher in those with Medicare insurance (66%) compared with those with commercial insurance (59%).

Contraindicated medications. Overall, 16% of patients had a prescription filled for any contraindicated medication to an ART during the index regimen. Potentially contraindicated medication fills were higher in treatment-experienced patients (18%) and patients with Medicare insurance (25%) compared with treatment-naïve patients (13%) and patients with commercial insurance (15%). Similar results were observed for contraindicated medication use during previous regimens.

DISCUSSION

This descriptive retrospective cohort study of a US healthcare claims database showed that people living with HIV experience a variety of comorbidities and take a number of medications outside of HIV medications. This trend seemed to grow in the treatment-experienced and Medicare populations. This analysis showed that Medicare patients and those who were treatment experienced had high rates of comorbidities such as depression (28% and 18%, respectively), CVD (70% and 44%), and any renal dysfunction (22% and 11%). These groups also had high percentages

FIGURE 2. Sample Attrition by Insurance Type and Treatment Status



ART indicates antiretroviral therapy.

*Index date defined as the start of the most recent ART regimen. Index date may differ from the date of the first ART claim if more than 1 ART regimen was observed during the identification period. Regimens occurring during the identification period could have begun as early as January 1, 2008.

CLINICAL

TABLE 1. Patient Demographics

Demographics	Total (N = 18,699)	Insurance Type		Treatment Status	
		Commercial (n = 15,275)	Medicare (n = 3424)	Treatment Naïve (n = 5027)	Treatment Experienced (n = 13,672)
Total observation time in years, ^a mean (SD)	5.1 (2.7)	5.3 (2.8)	4.2 (2.3)	5.2 (2.7)	5.1 (2.7)
Age in years, mean (SD)	47.5 (12.1)	45.0 (10.9)	58.6 (10.7)	42.3 (12.0)	49.4 (11.5)
18-34, n (%)	3044 (16.3)	2990 (19.6)	54 (1.6)	1452 (28.9)	1592 (11.6)
35-49, n (%)	7131 (38.1)	6546 (42.9)	585 (17.1)	2150 (42.8)	4981 (36.4)
50-64, n (%)	7168 (38.3)	5453 (35.7)	1715 (50.1)	1237 (24.6)	5931 (43.4)
≥65, n (%)	1356 (7.3)	286 (1.9)	1070 (31.3)	188 (3.7)	1168 (8.5)
Male sex, n (%)	15,718 (84.1)	13,213 (86.5)	2505 (73.2)	4307 (85.7)	11,411 (83.5)
Race/ethnicity, n (%)					
White	9594 (51.3)	8151 (53.4)	1443 (42.1)	2556 (50.9)	7038 (51.5)
African American/black	4898 (26.2)	3685 (24.1)	1213 (35.4)	1325 (26.4)	3573 (26.1)
Hispanic	2731 (14.6)	2342 (15.3)	389 (11.4)	747 (14.9)	1984 (14.5)
Other ^b	414 (2.2)	373 (2.4)	41 (1.2)	132 (2.6)	282 (2.1)
Unknown/missing	1062 (5.7)	724 (4.7)	338 (9.9)	267 (5.3)	795 (5.8)
Geographic region, n (%)					
South	10,435 (55.8)	8496 (55.6)	1939 (56.6)	2917 (58.0)	7518 (55.0)
Midwest	3082 (16.5)	2542 (16.6)	540 (15.8)	860 (17.1)	2222 (16.3)
West	2657 (14.2)	2421 (15.9)	236 (6.9)	627 (12.5)	2030 (14.9)
Northeast	2519 (13.5)	1810 (11.9)	709 (20.7)	621 (12.4)	1898 (13.9)
Other	6 (0.0)	6 (0.0)	0 (0.0)	2 (0.0)	4 (0.0)

^aNumber of years from health plan enrollment until the earliest date of disenrollment or study end (March 31, 2017).

^bIncludes other, less commonly reported races/ethnicities.

TABLE 2. Select Comorbidities Among All Patients and Patients Stratified by Insurance Type and Treatment Status

	Total (N = 18,699)	Insurance Type		Treatment Status	
		Commercial (n = 15,275)	Medicare (n = 3424)	Treatment Naïve (n = 5027)	Treatment Experienced (n = 13,672)
QC comorbidity score, ^a mean (SD)	0.74 (1.40)	0.55 (1.18)	1.58 (1.91)	0.53 (1.16)	0.82 (1.47)
Select comorbidities, ^b %					
Hyperlipidemia	40.8	37.4	56.2	27.1	45.9
CVD	40.6	34.1	69.6	31.5	43.9
Hypertension	33.7	27.7	60.2	24.8	36.9
Depression	16.5	14.0	27.6	12.1	18.2
Anxiety	13.5	12.3	19.2	11.1	14.4
Any AIDS-defining condition	12.8	12.0	16.1	14.5	12.1
Any cancer	10.0	8.1	18.2	7.2	11.0
Any renal dysfunction	9.0	6.3	21.5	5.2	10.5
Dementia	1.6	0.7	5.6	1.0	1.9
Osteoporosis	1.4	0.8	3.8	0.6	1.7

CVD indicates cardiovascular disease; QC, Quan-Chartson.

^aHIV/AIDS excluded in calculation of QC comorbidity score.

^bCommon/select comorbidities during the 12-month preindex period.

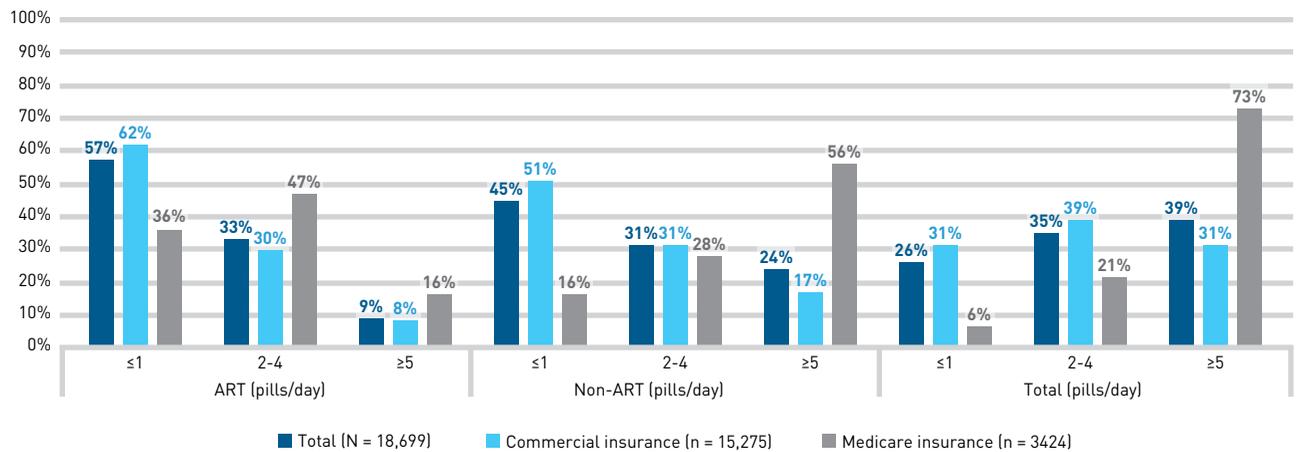
of patients taking 5 or more pills per day (ART and non-ART combined), at 73% of those enrolled in Medicare and 48% of the treatment-experienced patients.

These data highlight the need for individualized treatment approaches for HIV to support long-term treatment success. The HHS

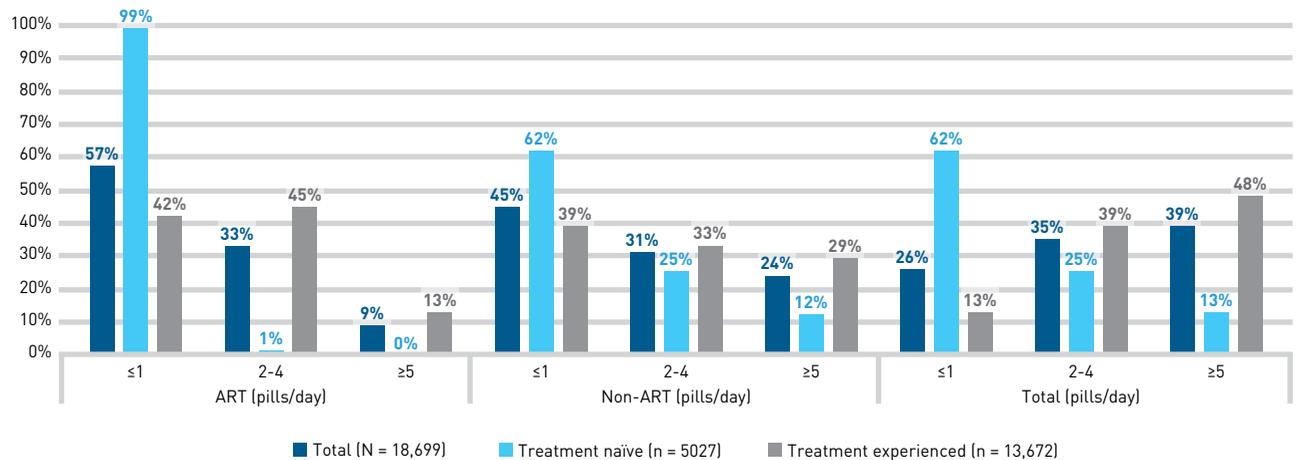
guidelines recommend considering many factors when selecting a patient-specific regimen, including potential adverse effects, patient comorbidities, possible interactions with concomitant medications, results of pretreatment genotypic drug-resistance testing, and regimen convenience.⁹ Therefore, it is essential that healthcare

FIGURE 3. Proportion of Daily Pill Burden in Patients Stratified by (A) Insurance Type and (B) Treatment Status

A. Insurance Type



B. Treatment Status



ART indicates antiretroviral therapy.

providers have a diversity of treatment options available to address the complex needs of patients with HIV, particularly as they age.

Numerous advances in ART have resulted in an increased life span and quality of life for people living with HIV, with predicted life spans now close to those of the general population.⁵ Nonetheless, HIV still represents a significant and underrecognized healthcare burden in the United States. Although people living with HIV are now benefiting from prolonged survival, they also experience an increased level of complications, many of which increase with age.^{11,12} These complexities include a high medication burden, increased risk of drug toxicity as a consequence of the lifelong requirement of ART, the management of comorbidities, and the potential for drug-drug interactions.^{10-12,14,19,20} The combination of ART and concomitant medications required to manage comorbidities increases total medication burden and may result in poor treatment adherence in people with HIV²⁰; in turn, this may negatively affect clinical outcomes such as sustained virologic suppression, maintenance

of immunity, and prevention of disease progression. For instance, a meta-analysis of 19 randomized controlled trials in patients with HIV found that higher pill burdens were associated with lower treatment adherence and reduced virologic suppression for both once-daily and twice-daily regimens.²¹ As our analysis did, previous studies have also found high average daily pill burdens in people living with HIV.^{19,22} These results suggest a need for consideration of pill burden for people living with HIV, particularly those in the older population, who may be experiencing multiple comorbid conditions and have a higher risk of drug-drug interactions, to ensure continued positive clinical outcomes.^{19,23}

Limitations

This study is not without limitations. For instance, administrative claims data may be subject to coding or input errors. In addition, the presence of diagnosis codes on medical claims does not prove the presence of actual disease. For example, it is possible that this study

included patients with HIV-1 diagnosis codes without the actual disease; however, to minimize this risk, patients were selected using diagnosis codes on nondiagnostic medical claims only (to not select individuals being tested for HIV) and patients were required to have filled pharmacy claims for ART. Moreover, the pharmacy claims for filled prescriptions do not indicate whether the medication was correctly consumed. In this study, treatment-naïve patients were defined as those having no prior ART fills during the fixed 12-month preindex period and were assumed to be newly diagnosed with HIV; however, these patients may have received an ART prior to this time period and may have had an extended gap in treatment. Furthermore, medication timings were not taken into account; therefore, prescriptions filled for contraindicated medications during each complete regimen period did not necessarily overlap with the prescriptions filled during the regimen. Because patients were required to be filling ART medications to treat their HIV as an inclusion criterion, this study is not generalizable to people living with HIV who are not receiving medical care. Finally, because this study included only commercial insurance or Medicare health plan enrollees who had a minimum of a year of continuous enrollment, the findings cannot be generalized to other insured or uninsured populations, those who may have changed coverage, or those who may have died due to more advanced disease.

CONCLUSIONS

This descriptive retrospective study demonstrated that people living longer with HIV or those enrolled in Medicare have a significant amount of comorbidities and total pill burden. Although advances in ART have significantly improved life expectancy for people living with HIV, the overall management of individual comorbidities and medication burden has become increasingly complex. When choosing an ART regimen, it is important to take into account the full list of comorbidities, potential drug-drug interactions due to concomitant medications, and total pill burden to improve the overall disease burden for patients living with HIV. ■

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Authorship Information: Concept and design (JLP, TB, CB-P, KA, AO); acquisition of data (TB, CB-P, KA); analysis and interpretation of data (JLP, CB-P, KA, AO); drafting of the manuscript (JLP, TB, AO); critical revision of the manuscript for important intellectual content (JLP, TB, CB-P, KA); statistical analysis (CB-P, KA); obtaining funding (JLP); and administrative, technical, or logistic support (JLP).

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