Rapid Initiation of Antiretroviral Treatment Following Diagnosis of Human Immunodeficiency Virus Among Medicaid-covered Patients: A Real-world Evaluation

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BACKGROUND

- In 2013, 55 million individuals had healthcare coverage through Medicaid in the United States (US)[1]; within that population, it was estimated that 284,500 individuals were living with human immunodeficiency virus (HIV),[2] making Medicaid the insurance provider for 25% of all individuals living with HIV in the US[3]
- With the success of highly active antiretroviral therapy (ART) in decreasing mortality and morbidity, HIV is now a manageable chronic condition[4]
- New guidelines for the treatment of HIV suggest that morbidity and mortality could be further reduced if ART is initiated immediately after diagnosis (i.e., rapid initiation), regardless of CD4 lymphocyte cell count[5-8]
- Since Medicaid insurance payments per patient with HIV were 7 times higher than those made for the average adult,[2,9] describing characteristics of newly diagnosed HIV-1 patients based on timeliness of receipt of ART could help identify ways of reducing Medicaid costs and improving the overall health of these patients

OBJECTIVE

- To assess the real-world time to ART initiation and describe clinical and economic outcomes in Medicaid patients based on timeliness of ART initiation

METHODS

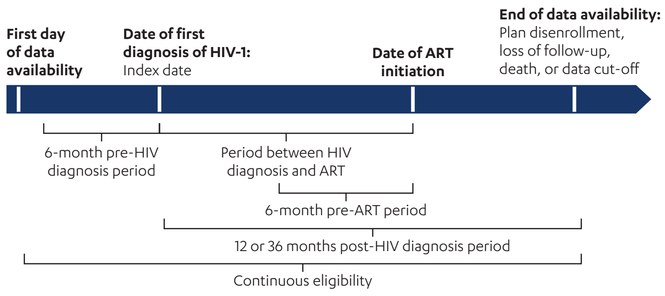
Data Sources

- Pharmacy and medical claims from Medicaid databases from 6 states (Iowa [1998:Q1 – 2017:Q1], Kansas [2001:Q1 – 2017:Q1], New Jersey [1997:Q1 – 2014:Q1], Missouri [1997:Q1 – 2017:Q1], Mississippi [2006:Q1 – 2017:Q1], and Wisconsin [2004:Q1 – 2013:Q4]) were analyzed
- Medicaid databases contain information on patient eligibility (e.g., age, gender, enrollment start/end dates, and date/year of death, if applicable), medical claims (e.g., type of service, dates of service, International Classification of Diseases, 9th/10th revision, Clinical Modification [ICD-9-CM/ICD-10-CM] diagnoses, and Current Procedural Terminology [CPT] procedure codes), and prescription drug claims (e.g., name, dosage, formulation, days supplied, and National Drug Codes [NDCs])
- All data collected were de-identified in compliance with the patient confidentiality requirements of the Health Insurance Portability and Accountability Act (HIPAA)

Study Design and Patient Selection

- A retrospective longitudinal study was conducted
- The index date was defined as the date of the first HIV-1 diagnosis (**Figure 1**)
- Outcomes were observed during 2 periods (**Figure 1**):
  - During the 6-month pre-ART initiation period for all clinical characteristics
  - During a fixed time period following the first HIV-1 diagnosis (i.e., 12 and 36 months) for the evaluation of healthcare costs

Figure 1. Study design scheme.



Inclusion Criteria

- ≥1 claim with a diagnosis of HIV-1 (ICD-9-CM codes: 042, 795.71, and V08; ICD-10-CM codes: B20, R75, and Z21)
- Both pharmacy and medical claims records available
- ≥6 months of continuous insurance eligibility before the date of the first HIV-1 diagnosis
- ≥18 years old as of the first observed HIV-1 diagnosis
- ≥1 claim for any antiretroviral agent after the first HIV-1 diagnosis, in 2012 or after
- Receive the antiretroviral agent as part of an ART regimen
  - "ART regimen" is defined as having a claim for a protease inhibitor (PI), an integrase strand transfer inhibitor (INSTI), or a non-nucleoside reverse transcriptase inhibitor (NNRTI) in combination with ≥2 nucleoside reverse transcriptase inhibitors (NRTIs); all agents had to be claimed within 14 days of each other
  - Boosting agents were not taken into account when defining an ART regimen
- Initiate an ART regimen within 360 days of the first HIV-1 diagnosis

Exclusion Criteria

- First HIV-1 diagnosis was recorded during an inpatient stay that lasted ≥10 days
  - This exclusion was added to take into account that all services received in an inpatient setting may not be recorded; as such, patients may have initiated an ART regimen during a long stay, but that information could be missing from the data
- ≥1 claim with a diagnosis of HIV-2 at any time
- ≥1 claim for an antiretroviral agent at any time before the first HIV-1 diagnosis
  - Patients who received oral pre-exposure prophylaxis (PrEP) at any time before the first HIV-1 diagnosis were not excluded from the study

Study Cohorts

- Patients were classified into mutually exclusive groups based on timeliness of receipt of ART after HIV-1 diagnosis (treated within 14 days, >14 to ≤60 days, >60 to ≤180 days, and >180 to ≤360 days)

Study Measures

- Demographic characteristics were assessed at the time of HIV-1 diagnosis and included age, gender, and race
- Clinical characteristics were assessed during the 6-month period pre-ART initiation to ensure similar observation periods for all cohorts, and included diagnosis of opportunistic infections, most common laboratory tests, and presence of mental health comorbidities
  - Mental health comorbidities that affected ≥10% of patients (i.e., anxiety disorders, depressive disorders, and substance-related and addictive disorders[10]) were reported to explore the possible relationship between mental health issues and time to treatment initiation
- The type of ART regimen initiated was assessed at the time of ART initiation
- All-cause healthcare costs were evaluated during the 12- and 36-month periods following the first HIV-1 diagnosis; healthcare costs included costs related to pharmacy and medical services
  - Medical services included emergency room visits, inpatient visits, outpatient visits, and other services (including, but not limited to, mental health institute admissions, long-term care admissions, and home care)

Statistical Analysis

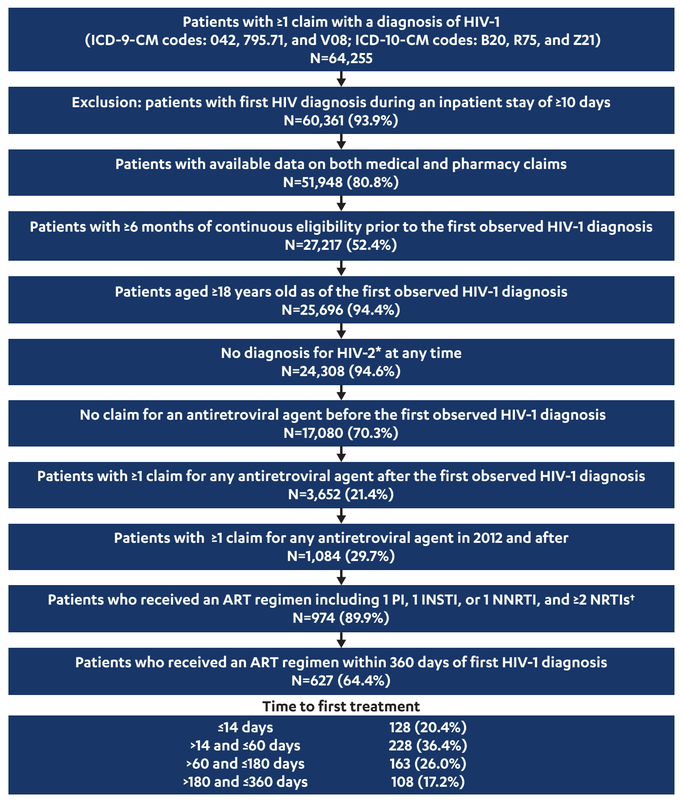
- Descriptive statistics were generated to summarize demographics, clinical characteristics, and healthcare costs; percentages were used to summarize categorical variables while means and standard deviations (SDs) were used for continuous variables
- Healthcare costs were adjusted to 2017 US dollars (USD)

RESULTS

Timeliness of Receipt and Type of ART Regimen Initiated

- A total of 64,255 patients had ≥1 claim with an HIV-1 diagnosis; 627 (1.0%) individuals were included in the analysis based on inclusion/exclusion criteria (**Figure 2**); of note, 347 out of 974 treated patients (35.6%) initiated an ART regimen >360 days after HIV-1 diagnosis and were excluded from the study
- Among patients treated within 360 days (N=627), 128 (20.4%) were treated within 14 days, 228 (36.4%) between >14 and ≤60 days, 163 (26.0%) between >60 and ≤180 days, and 108 (17.2%) between >180 and ≤360 days (**Figure 2**)
- The average time to ART initiation was 88.8 days (SD=94.8, median=46.0)

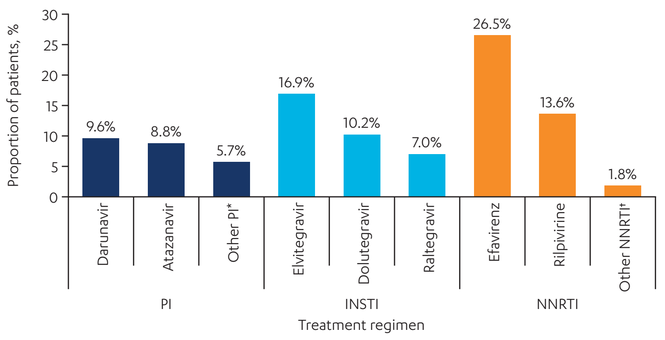
Figure 2. Identification of the study population.



*HIV-2 diagnosis was identified using ICD-9-CM code 079.53 and ICD-10-CM code B97.35.
†An ART regimen was defined based on claims filled within 14 days of each other.

- In total, 24.1%, 34.1%, and 41.8% of patients were initiated on a PI-, INSTI-, or NNRTI-based regimen, respectively; the proportion of patients who initiated each regimen type was similar across all cohorts
- Darunavir (9.6%) and atazanavir (8.8%) were the most commonly used PIs; elvitegravir (16.9%) and dolutegravir (10.2%) were the most commonly used INSTIs; efavirenz (26.5%) and rilpivirine (13.6%) were the most commonly used NNRTIs (**Figure 3**)

Figure 3. Proportion of patients who received each ART class per treatment regimen.



*Other PI includes: lopinavir (4.9%), nelfinavir (0.6%), indinavir (0.0%), fosamprenavir (0.2%), saquinavir (0.0%), amprenavir (0.0%), and tipranavir (0.0%).
†Other NNRTI includes: nevirapine (1.4%), etravirine (0.3%), and delavirdine (0.0%).

Demographic and Clinical Characteristics

- Age, gender, and race were similar across all cohorts; mean age was 40.1 (SD=12.3) years, 42.7% of the selected patients were females, and more than half (53.9%) were black
- Overall, more than 50% of patients were initiated on a single-tablet regimen; the highest proportion (63.3%) was observed in patients treated within 14 days (**Table 1**)
- 4.6% of patients treated within 180 days had ≥1 diagnosis of an opportunistic infection in the 6-month period pre-ART initiation; this proportion reached 5.6% for patients treated between >180 and ≤360 days (**Table 1**)

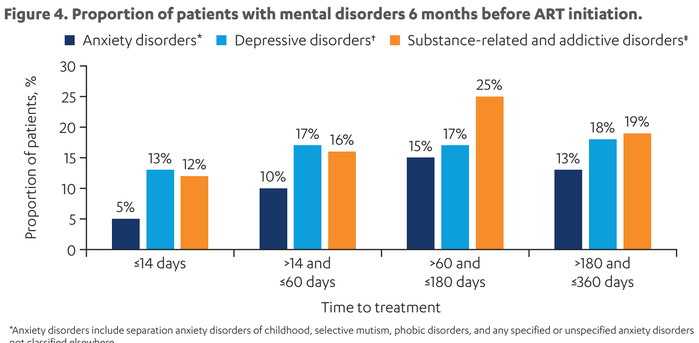
Table 1. Demographic and Clinical Characteristics

	Timeliness of receipt of ART			
	≤14 days	>14 and ≤60 days	>60 and ≤180 days	>180 and ≤360 days
Time to treatment, days, mean ± SD	5.3 ± 5.2	32.8 ± 12.5	115.5 ± 36.0	265.8 ± 49.8
Age at HIV diagnosis, years, mean ± SD	40.6 ± 11.6	39.0 ± 12.9	41.1 ± 12.4	40.5 ± 11.5
Female, %	44.5	42.5	41.7	42.6
Race, %				
White	25.8	27.6	17.8	31.5
Black	54.7	50.9	63.2	45.4
Other*	19.5	21.5	19.0	23.1
Patients who initiated a single-tablet regimen, %	63.3	57.5	57.7	56.5
Patients with ≥1 diagnosis of an opportunistic infection† in the 6-month period pre-ART, %	4.7	4.8	4.3	5.6
Location of first HIV diagnosis, %				
Emergency room	2.3	3.5	3.1	2.8
Inpatient	7.0	13.2	11.0	12.0
Pathology and laboratory procedures and services received in the 6-month period pre-ART, %				
Infectious agent detection by nucleic acid	43.8	64.9	69.9	37.0
Complete blood count	42.2	56.6	54.0	42.6
Comprehensive metabolic panel	36.7	57.0	58.3	35.2
T-cells: absolute CD4 and CD8 count	34.4	46.9	52.8	25.0
Syphilis test, nontreponemal antibody	28.1	44.7	50.9	13.0
Lipid panel	25.0	37.7	36.2	18.5
Hepatitis B surface antibody	20.3	38.2	24.5	9.3
Hepatitis C antibody	20.3	38.6	28.2	8.3
Infectious agent antigen detection by immunoassay technique	18.0	34.2	22.7	6.5
Urinalysis	14.1	26.3	27.6	17.6

*Includes: Hispanic and patients for whom race was unknown.
†The opportunistic infections considered were: pneumocystis pneumonia, toxoplasma gondii encephalitis, mycobacterium tuberculosis infection, disseminated mycobacterium avium complex disease, histoplasma capsulatum infection, coccidioidomycosis, cryptococcosis, and cytomegalovirus disease.

- During the 6-month pre-ART period, the proportion of patients with mental disorders was generally higher with delay of ART initiation (**Figure 4**)
  - Anxiety disorders: proportion of patients statistically higher among those treated between >60 and ≤180 days and >180 and ≤360 days of diagnosis versus those treated within 14 days
  - Depressive disorders: proportion of patients not statistically different between cohorts
  - Substance-related and addictive disorders: proportion of patients statistically higher among those treated between >60 and ≤180 days of diagnosis versus those treated within 14 days

Figure 4. Proportion of patients with mental disorders 6 months before ART initiation.



*Anxiety disorders include separation anxiety disorders of childhood, selective mutism, phobic disorders, and any specified or unspecified anxiety disorders not classified elsewhere.
†Depressive disorders include major depressive disorders, mood disorders, dysthymic disorders, premenstrual tension syndrome, and other depressive episodes.
‡Substance-related and addictive disorders include alcohol, cannabis, hallucinogen, opioid, sedative, hypnotic, anxiolytic, cocaine, nicotine, inhalant, any other stimulant, and any other psychoactive substance abuse or dependence, as well as tobacco use and gambling.

Healthcare Costs

- Total medical costs (i.e., costs related to emergency room visits, inpatient visits, outpatient visits, and other services) increased with delayed ART initiation during the 12-month post–HIV-1 diagnosis period (**Figure 5A**)
- All-cause total healthcare costs, which include medical and pharmacy costs, generally decreased with delayed ART initiation over the same period (**Figure 5B**); this reduction was driven by lower pharmacy costs for those who initiated ART between >60 and ≤360 days
- However, the long-term benefits of rapid ART initiation appeared over the 36-month post–HIV-1 diagnosis period, as both total medical costs and total healthcare costs increased with delayed ART initiation (**Figures 5A** and **5B**)
- During the 12-month post–HIV-1 diagnosis period, cumulated inpatient and emergency room visit costs ranged from $3,342 for patients treated within 14 days to $6,904 for those treated between >60 and ≤180 days; in the 36-month post–HIV-1 diagnosis period, these costs ranged from $5,958 for patients treated between >14 and ≤60 days to $12,745 for those treated between >60 and ≤180 days
- Similar results were observed for medical costs and healthcare costs per-patient-per-month; in the 12-month post–HIV-1 diagnosis period, medical costs increased while pharmacy costs decreased with delay of ART initiation, resulting in generally decreasing total costs per-patient-per-month, while in the 36-month post–HIV-1 diagnosis period, both medical and healthcare costs increased with delay of ART initiation, highlighting the long-term benefits of rapid initiation (**Figures 5C** and **5D**)

Figure 5. Healthcare costs during the 12- and 36-month post–HIV-1 diagnosis periods.*,†,‡,§

*Total cumulated medical costs correspond to the sum of costs for outpatient visits, inpatient visits, emergency room visits, and other services (including, but not limited to, mental health institute admissions, long-term care admissions, and home care) incurred over the 12- or 36-month period post HIV-1 diagnosis.
†Total cumulated healthcare costs correspond to the sum of pharmacy and medical costs incurred over the 12- or 36-month period post HIV-1 diagnosis. Medical costs include costs related to outpatient visits, inpatient visits, emergency room visits, and other services (including, but not limited to, mental health institute admissions, long-term care admissions, and home care).
‡Medical costs per-patient-per-month correspond to total cumulated medical costs per patient presented in panel A divided by 12 or 36 months, depending on the period over which costs were evaluated.
§Healthcare costs per-patient-per-month correspond to total cumulated healthcare costs per patient presented in panel B divided by 12 or 36 months, depending on the period over which costs were evaluated.

LIMITATIONS

- Claims databases may contain inaccuracies or omissions in diagnoses and other variables, although this is not expected to be different between cohorts
- The Medicaid data used in the study came from 6 states and may not be generalizable to the overall Medicaid population, other states, non-Medicaid patients, or non-insured patients; furthermore, Medicaid patients with HIV-1 may be different and could receive different types of ART compared to non-Medicaid patients with HIV-1
- An antiretroviral claim was assumed to indicate its use; however, patients might not have adhered to the treatment regimen as prescribed
- Although patients were excluded if they had an antiretroviral claim prior to the first HIV-1 diagnosis, it is possible that some patients received an antiretroviral agent from another source, such as the Ryan White HIV/AIDS Program[11]; such drug utilization is not recorded in the Medicaid data
- Patients who initiated an ART regimen >360 days after the first HIV-1 diagnosis were excluded from the study; therefore, a smaller proportion of patients treated within 14 days and a longer time to ART initiation would have been observed if all treated patients had been included in the study
- Given the descriptive nature of the study, no adjustments were made for differences in characteristics between cohorts

CONCLUSIONS

- **This study revealed that only 20.4% of Medicaid patients initiated ART within 14 days of HIV-1 diagnosis and average time to ART initiation was 88.8 days (median=46.0)**
- **Approximately one third of patients (347 out of 974) were excluded from this study because they initiated an ART >360 days after their first HIV-1 diagnosis, suggesting that a large proportion of patients could be engaged in care more rapidly**
- **Although the proportion of patients initiated on a single-tablet regimen was highest among patients initiated on ART within 14 days of diagnosis (63.3%), an opportunity remains to initiate more patients on this type of regimen**
- **During the 6-month pre-ART period, the proportion of patients with mental comorbidities was generally higher with delay of ART initiation**
  - **As treatment nonadherence is more likely in patients with mental health issues[12] and may be associated with development of drug-resistance mutations,[13] single-tablet regimens that have a low risk of neuropsychological adverse events and high genetic barrier to resistance should be considered for these patients to rapidly initiate treatment**
- **Over 36 months post HIV-1 diagnosis, patients with delayed ART initiation accumulated more healthcare costs than those with rapid initiation, highlighting the long-term benefits of rapid ART initiation following diagnosis**

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DISCLOSURES

All authors participated in the design of the study, interpretation of the results, and preparation of the poster. BE, HR, PL, and AS conducted the statistical analyses. CB, NT, and KD are full-time employees of Janssen and may be Johnson & Johnson stockholders. BE, HR, PL, and AS are employees of Analysis Group, Inc., which is contracted to provide services for Janssen Scientific Affairs, LLC. This study was supported by Janssen Scientific Affairs, LLC. Editorial assistance was provided by Michael Iannucci, of MedErgy, and was funded by Janssen Scientific Affairs, LLC.

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