



# Shorter Duration Hepatitis C Virus Treatment is Associated with Better Persistence to Prescription Refills in People Who Inject Drugs: A Real-World Study

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## ABSTRACT

**Introduction:** Direct-acting antiviral (DAA) therapy is highly effective in curing hepatitis C virus (HCV) infection in people who inject drugs (PWID). Previous studies showed declining persistence to DAA therapy over the course of treatment. This study compares real-world medication persistence to prescription refills for 8- versus 12-week DAA in treatment-naïve PWID with chronic HCV with compensated cirrhosis or without cirrhosis.

**Methods:** Symphony Health's claims database was used to collect data from patients with chronic HCV aged  $\geq 12$  years who were prescribed 8- or 12-week DAA therapy between

August 2017 and November 2020 and had a diagnosis of addicted drug use within 6 months prior to index date. Eligible patients had medical/pharmacy claims in the 6 months before and 3 months after the first index medication fill date (i.e., index date). Patients completing all refills (8-week = 1 refill, 12-week = 2 refills) were deemed persistent. The percentage of persistent patients in each group, and at each refill step, was determined; outcomes were also assessed in a subgroup of Medicaid-insured patients.

**Results:** This study assessed 7203 PWID with chronic HCV (8-week, 4002; 12-week, 3201). Patients prescribed 8-week DAA treatment were younger ( $42.9 \pm 12.4$  vs  $47.5 \pm 13.2$ ,  $P < 0.001$ ) and had fewer comorbidities ( $P < 0.001$ ). Patients receiving 8- versus 12-week DAA had greater refill persistence (87.9% vs 64.4%,  $P < 0.001$ ). Similar percentages of patients missed their first refill (8-week, 12.1% vs 12-week, 10.8%); nearly 25% of patients receiving 12-week DAA missed their second refill. After baseline characteristics were controlled, patients prescribed 8- versus 12-week DAA were more likely to be persistent (odds ratio [95% confidence interval] 4.3 [3.8, 5.0]). Findings in the Medicaid-insured subgroup were consistent. **Conclusion:** Patients prescribed 8- vs 12-week DAA therapy had significantly greater prescription refill persistence. Most nonpersistence was due to missed second refills, highlighting the

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potential benefit of shorter treatment durations in this population.

**Keywords:** Compliance; Persistency; Hepatitis C virus; PWID; Real-world study

### Key Summary Points

#### *Why carry out this study?*

Direct acting antiviral (DAA) therapy is highly effective in curing chronic hepatitis C virus (HCV) infection in people who inject drugs (PWID), yet previous studies have consistently demonstrated that medication compliance declines over the course of treatment.

Shorter DAA treatment durations have the potential to greatly impact medication persistence among PWID, a population disproportionately affected by chronic HCV.

This study assessed whether shorter DAA treatment durations (8- vs 12-weeks) affect medication refill persistence in a population of treatment-naïve PWID with chronic HCV with compensated cirrhosis or without cirrhosis.

#### *What was learned from the study?*

Greater medication persistence was achieved with 8- versus 12-week DAA therapy and nonpersistence was primarily due to missed second refills.

Previous studies have shown that PWID are open to HCV therapy and these data suggest that 8- versus 12-week DAA therapy could help drive HCV elimination in this population.

## INTRODUCTION

Up to 40% of the global hepatitis C virus (HCV) disease burden is attributable to injection drug use and, in the USA, 67% of new HCV infections occur in people who inject drugs (PWID) [1, 2]. Despite the high proportion of PWID with HCV, healthcare providers' perceptions about their lack of treatment compliance and risk of reinfection introduce stigma for this population against extensive treatment efforts [3–5]. Likewise, many PWID also suffer from uncontrolled mental illness, housing instability, lack of social support, and poor access to healthcare [3, 6]. Yet, when questioned, many PWID stated they are willing to undergo treatment for HCV [3, 7]. Furthermore, the American Association for the Study of Liver Diseases (AASLD) and Infectious Diseases Society of America (IDSA) guidelines state that “active or recent drug use or a concern for reinfection is not a contraindication to HCV treatment” [1]. As a result of the high effectiveness of approved pangenotypic direct-acting antiviral (DAA) treatments and their relative simplicity in administration, the World Health Organization developed a strategy to eliminate HCV globally by 2030 [8, 9].

Medication compliance (synonymous with adherence) refers to the extent of conformity to the provider's recommendations regarding day-to-day treatment timing, dosage, and frequency, whereas medication persistence refers to continuation of the treatment for the entirety of the prescribed duration [10]. Previous studies have demonstrated that compliance to DAA therapy declines over the course of treatment and would suggest that shorter treatment durations may mitigate this decline [11–15]. Moreover, several studies have demonstrated that, even with imperfect compliance, high sustained virologic response (SVR) rates were still achieved with shorter durations of DAA treatment [14–16]. While these data highlight the potential benefits of shorter treatment duration overall, it is especially important to assess how shorter durations may affect medication persistence in PWID, one of the populations with the heaviest HCV burden and in greatest need of treatment. Indeed,

active injection drug use was associated with greater nonadherence [12, 13].

The aim of this study was to compare real-world persistence to prescription refills for 8- versus 12-week DAA in treatment-naïve PWID with chronic HCV and compensated cirrhosis (CC) or without cirrhosis, which may inform treatment decisions for these patients.

## METHODS

### Study Design and Participants

This real-world study analyzed data from patients aged 12 years or older who were prescribed either 8- or 12-week DAA. Data were retrieved using the Symphony Health's administrative claims database (Symphony Health, an ICON plc Company, Blue Bell, PA, Patient-Source®, August 1, 2017 to November 30, 2020), which collects longitudinal, patient-level information on medical and pharmacy claims from a large set of commercial and government (Medicare and Medicaid) electronic claims processors across the USA. For this study, an 8-week DAA prescription was defined as an authorized DAA prescription written for one possible refill, with a total supply of 56 days; 12-week DAA prescriptions were written for two possible refills, with a total supply of 84 days. The index date was defined as the date for the first fill of 8- or 12-week DAA. Patients were required to have a diagnosis of chronic HCV with CC or without cirrhosis and a diagnosis of drug use addiction or drug abuse within 6 months prior to the index date. Eligible patients had medical and pharmacy claims in the Symphony Health database in the 6 months before (pre-index period) and 3 months after (post-index period) the first index medication fill date (i.e., index date). Patients were excluded if they were diagnosed with acute HCV (based on International Classification of Diseases, Tenth Revision [ICD-10] codes B17.10 and B17.11), diagnosed with hepatic failure or decompensation, received a kidney or liver transplant, or received other HCV treatment within the 6 months prior to their index date. Likewise, patients with prescriptions that report both 8- and 12-week DAA

were excluded. A subcohort of Medicaid-insured patients was identified. Data from this study were limited to claims made between August 2017 and November 2020.

This is a retrospective study with anonymous data from Symphony Health, a Health Insurance Portability and Accountability Act (HIPAA)-compliant deidentified claims database, and thus does not require institutional review board (IRB) approval. Likewise, patient consent was not required given that the data was deidentified.

### Outcomes

For this study, patients completing all refills (i.e., one refill in the 8-week group or two refills in the 12-week group) were deemed persistent. The percentage of persistent patients in each group for both matched and unmatched cohorts was determined; persistence at each refill step (i.e., 1st refill and 2nd refill) was determined between the unmatched 8- and 12-week groups. The likelihood of persistence in the matched 8-week group relative to the 12-week group was also determined. All outcomes were evaluated in a subgroup of Medicaid-insured patients.

### Statistical Analysis of Data

Baseline patient demographic and clinical characteristics were assessed descriptively. The percentage of patients with DAA refill persistence between unmatched groups, including the percentage of patients missing their first refill, was compared by chi-square test.

Propensity-score matching was used to adjust for differences in baseline patient characteristics between treatment groups (i.e., age at index, sex, ethnicity, insurance type, liver fibrosis or cirrhosis, extrahepatic manifestations [diabetes, cardiovascular disease, chronic kidney disease, non-Hodgkin's lymphoma, cognitive impairment, Parkinson's, mixed cryoglobulinemia, insulin resistance, thyroid cancer, head and neck cancers, nephritis], and mental disorders [alcohol-related disorder, physiological mental disorders, mood disorders,

anxiety/nonpsychotic mental disorders, and other mental disorders]). A propensity score demonstrates the likelihood of a patient being prescribed a particular treatment option (i.e., 8- or 12-week DAA) based on a set of observed baseline characteristics. A logistic regression model, with index treatment as the dependent variable and observed baseline characteristics as the independent variables, was used to calculate propensity scores. Patients from the 8-week DAA group were matched 1:1 with 12-week DAA patients, with replacement based on the logit of the propensity score with a maximum allowable absolute difference between propensity scores of 0.001 to optimize the closeness of matches. Patient characteristics were considered balanced if the standardized difference between matched treatment groups was less than 0.1 [17–19].

The percentage of patients with DAA refill persistence between matched groups was compared by chi-square test. The likelihood of DAA persistence between matched 8- and 12-week groups was estimated by logistic regression analysis in the propensity-score-matched cohorts. Odds ratios (OR) and corresponding 95% confidence intervals (CI) are reported. All analyses were replicated in the subgroup of Medicaid-insured patients including both matched and unmatched populations.

## RESULTS

### Patient Demographics

In total, 7203 PWID were assessed in the study (8-week,  $n = 4002$ ; 12-week,  $n = 3201$ ). Patient demographics and clinical characteristics prior to matching are in the Supplementary Materials (Tables S1 and S2).

After propensity-score matching, there were 2653 patients in each group (8- vs 12-week DAA therapy) and baseline patient and clinical characteristics were similar (Table 1). Briefly, the mean age was approximately 45 years and fewer than half of patients were female (42–43%). Nearly three-quarters of patients were insured by Medicaid and baseline comorbidities were similar between groups. Approximately 40% of

patients in both groups had mood affective disorders and nonpsychotic mental disorders, such as anxiety or dissociative mental disorders.

Subanalyses were also conducted among Medicaid-insured patients. Prior to matching, baseline patient demographics and characteristics were similar between the overall- and Medicaid-insured cohorts (Tables S1 and S2). After matching, there were 1828 Medicaid-insured patients in each group; baseline characteristics were similar between 8- and 12-week groups (Table 2). The mean age was approximately 44 years, fewer than half were female, and baseline comorbidities were similar between groups. Similar to the overall-matched cohort (Table 1), 40–44% of patients had mood affective or nonpsychotic mental disorders.

### Refill Persistence Between 8- and 12-Week DAA Treatment Groups

Among the propensity-score-matched population, patients receiving 8- versus 12-week DAA therapy had significantly greater overall persistence (87.9% vs 62.5%;  $P < 0.001$ ; Fig. 1). Findings were similar in the unmatched population (87.9% vs 64.4%,  $P < 0.001$ ; Fig. S1a in the supplementary material). When further broken down, the rate for patients missing their first refill was 12.1% in those prescribed 8-week treatment and 10.8% in those prescribed 12-week treatment; nearly 25% of patients receiving 12-week DAA missed their second refill (Fig. S1a).

### Refill Persistence Between 8- and 12-Week DAA Treatment Groups Insured by Medicaid

Findings in the Medicaid-insured specific, propensity-score-matched populations were similar to the overall cohort; patients receiving 8- versus 12-week treatment had significantly higher persistence (8-week, 89.0%; 12-week, 61.1%;  $P < 0.001$ ; Fig. 1). Findings were similar among the unmatched Medicaid-insured population (8-week, 88.7% vs 12-week, 61.9%,  $P < 0.001$ ; Fig. S1b). Similar proportions of patients in both groups (11.2%;  $P = 0.855$ )

**Table 1** Propensity-score-matched baseline patient demographic and clinical characteristics

	8-Week DAA <i>N</i> = 2653	12-Week DAA <i>N</i> = 2653	Standardized difference
Baseline patient characteristics			
Age (years), mean ± SD	45.5 ± 12.6	45.4 ± 12.7	0.012
Age group (years), <i>N</i> (%)			0.032
12–17	0 (0.0)	0 (0.0)	–
18–35	710 (26.8)	717 (27.0)	–
36–55	1244 (46.9)	1217 (45.9)	–
> 55	699 (26.3)	719 (27.1)	–
Female gender, <i>N</i> (%)	1141 (43.0)	1119 (42.2)	– 0.009
Race/ethnicity, <i>N</i> (%)			0.006
White	1334 (50.3)	1321 (49.8)	–
Black	334 (12.6)	341 (12.9)	–
Hispanic or Latino <sup>a</sup>	181 (6.8)	184 (6.9)	–
Other	24 (0.9)	26 (1.0)	–
Unspecified	780 (29.4)	781 (29.4)	–
Insurance type at treatment initiation, <i>N</i> (%)			0.025
Commercial	288 (10.9)	282 (10.6)	–
Medicare	452 (17.0)	465 (17.5)	–
Medicaid	1900 (71.6)	1889 (71.2)	–
Other	13 (0.5)	17 (0.6)	–
Baseline comorbidities <sup>b</sup>			
Liver fibrosis or cirrhosis, <i>N</i> (%)	204 (7.7)	200 (7.5)	0.003
Extrahepatic manifestations <sup>c</sup> , <i>N</i> (%)			
Type 2 diabetes	289 (10.9)	282 (10.6)	– 0.006
Cardiovascular disease	251 (9.5)	258 (9.7)	–
Chronic kidney disease	171 (6.4)	171 (6.4)	0.003
Non-Hodgkin lymphoma	2 (0.1)	3 (0.1)	– 0.012
Cognitive impairment	6 (0.2)	7 (0.3)	– 0.007
Parkinson's disease	3 (0.1)	4 (0.2)	–
Mixed cryoglobulinemia	3 (0.1)	2 (0.1)	0.022
Insulin resistance	7 (0.3)	5 (0.2)	0.016
Esophageal cancer	0 (0.0)	0 (0.0)	–

**Table 1** continued

	8-Week DAA <i>N</i> = 2653	12-Week DAA <i>N</i> = 2653	Standardized difference
Prostate cancer	0 (0.0)	0 (0.0)	–
Thyroid cancer	0 (0.0)	0 (0.0)	–
Head and neck cancers	2 (0.1)	3 (0.1)	–
Nephritis/nephrotic syndrome/nephrosis	5 (0.2)	6 (0.2)	–
Mental disorders, <i>N</i> (%)			
Alcohol related disorder	495 (18.7)	498 (18.8)	– 0.002
Mental disorders due to known physiological conditions	28 (1.1)	30 (1.1)	– 0.007
Mood (affective) disorders	1112 (41.9)	1134 (42.7)	– 0.021
Nonpsychotic mental disorders <sup>d</sup>	1032 (38.9)	1061 (40.0)	– 0.029
Other mental disorders <sup>e</sup>	442 (16.7)	451 (17.0)	– 0.012

*DAA* direct acting antiviral, *ICD-10-CM* International Classification of Diseases, Tenth Revision, Clinical Modification, and *SD* standard deviation

<sup>a</sup>Hispanic and/or Latino ethnicity is not a mutually exclusive distinction

<sup>b</sup>Baseline comorbidities based on ICD-10-CM codes

<sup>c</sup>Category includes additional low frequency comorbidities (< 10 observations): non-Hodgkin lymphoma, cognitive impairment, Parkinson's disease, mixed cryoglobulinemia, insulin resistance, thyroid cancer, head and neck cancers, and nephritis

<sup>d</sup>Includes anxiety, dissociative, stress-related, somatoform, or other nonpsychotic mental disorders

<sup>e</sup>This includes disorders of adult personality/behavior, intellectual disabilities, pervasive/specific developmental disorders, behavioral/emotional disorders with onset usually occurring in childhood/adolescence, and unspecified mental disorders

missed their first refill and 26.4% of patients prescribed 12-week treatment missed their second refill (Fig. S1b).

### Likelihood of Persistence Between Matched 8- and 12-Week DAA Treatment Groups

In the matched populations, patients prescribed 8-week DAA had greater odds of persistence compared to 12-week DAA (OR [95% CI] 4.3 [3.8, 5.0]; Fig. 1). Similarly, in the matched Medicaid-insured population, likelihood of refill persistence was significantly higher in patients prescribed 8- versus 12-week DAA treatment (OR [95% CI] 5.2 [4.3, 6.1]).

## DISCUSSION

This study demonstrated that shorter treatment duration (8 vs 12 weeks) was associated with significantly greater likelihood of refill persistence in an HCV-infected population of PWID. While refill persistence statistics were comparable between groups for the first refill, nearly a quarter of patients prescribed 12-week DAA therapy missed their second refill. The finding of greater refill persistence in the 8- versus 12-week group was maintained when data were stratified to analyze Medicaid-insured patients only.

Medication possession ratio (MPR) and proportional days covered (PDC) are two common methods used to calculate compliance for maintenance medication from pharmacy

**Table 2** Propensity-score-matched baseline patient demographic and clinical characteristics among Medicaid-insured patients

	<b>8-week DAA</b> <i>N</i> = 1828	<b>12-week DAA</b> <i>N</i> = 1828	<b>Standardized difference</b>
Baseline characteristics			
Age (years), mean ± SD	43.5 ± 11.4	43.6 ± 11.4	– 0.006
Age group (years), <i>N</i> (%)			0.021
12–17	0 (0.0)	0 (0.0)	–
18–35	548 (30.0)	531 (29.0)	–
36–55	920 (50.3)	923 (50.5)	–
56–75	360 (19.7)	374 (20.5)	–
Female gender, <i>N</i> (%)	849 (46.4)	801 (43.8)	0.018
Race/ethnicity, <i>N</i> (%)			0.031
White	910 (49.8)	901 (49.3)	–
Black	220 (12.0)	213 (11.7)	–
Hispanic or Latino <sup>a</sup>	126 (6.9)	134 (7.3)	–
Other	18 (1.0)	18 (1.0)	–
Unspecified	554 (30.3)	562 (30.7)	–
Baseline comorbidities <sup>b</sup>			
Liver fibrosis or cirrhosis, <i>N</i> (%)	126 (6.9)	121 (6.6)	0.009
Extrahepatic manifestations <sup>c</sup> , <i>N</i> (%)			
Type 2 diabetes	182 (10.0)	190 (10.4)	– 0.018
Cardiovascular disease	147 (8.0)	156 (8.5)	– 0.008
Chronic kidney disease	90 (4.9)	94 (5.1)	– 0.008
Non-Hodgkin lymphoma	1 (0.1)	1 (0.1)	–
Cognitive impairment	5 (0.3)	5 (0.3)	–
Parkinson's disease	0 (0.0)	1 (0.1)	– 0.033
Mixed cryoglobulinemia	0 (0.0)	0 (0.0)	–
Insulin resistance	4 (0.2)	2 (0.1)	0.044
Esophageal cancer	0 (0.0)	0 (0.0)	–
Prostate cancer	0 (0.0)	0 (0.0)	–
Thyroid cancer	0 (0.0)	0 (0.0)	–
Head and neck cancers	0 (0.0)	2 (0.1)	– 0.047
Nephritis/nephrotic syndrome/nephrosis	2 (0.1)	4 (0.2)	– 0.027

**Table 2** continued

	8-week DAA <i>N</i> = 1828	12-week DAA <i>N</i> = 1828	Standardized difference
Mental disorders, <i>N</i> (%)			
Alcohol related disorder	342 (18.7)	360 (19.7)	− 0.029
Mental disorders due to known physiological conditions	14 (0.8)	17 (0.9)	− 0.018
Mood (affective) disorders	795 (43.5)	794 (43.4)	0.008
Nonpsychotic mental disorders <sup>d</sup>	725 (39.7)	743 (40.6)	− 0.013
Other mental disorders <sup>e</sup>	275 (15.0)	312 (17.1)	− 0.049

*DAA* direct acting antiviral, *ICD-10-CM* International Classification of Diseases, Tenth Revision, Clinical Modification, and *SD* standard deviation

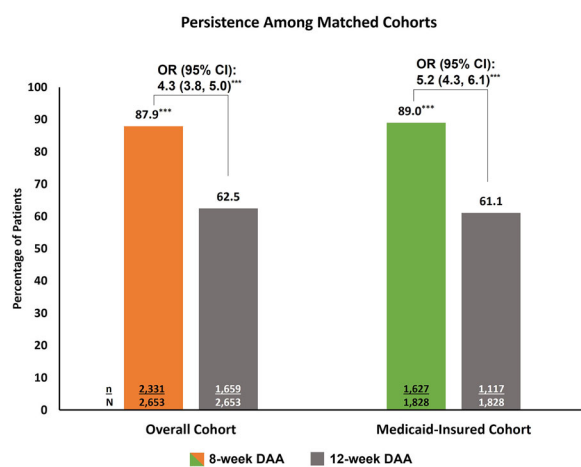
<sup>a</sup>Hispanic and/or Latino ethnicity is not a mutually exclusive distinction

<sup>b</sup>Baseline comorbidities based on ICD-10-CM codes

<sup>c</sup>Category includes additional low frequency comorbidities (< 10 observations): non-Hodgkin lymphoma, cognitive impairment, Parkinson's disease, mixed cryoglobulinemia, insulin resistance, thyroid cancer, head and neck cancers, and nephritis

<sup>d</sup>Includes anxiety, dissociative, stress-related, somatoform, or other nonpsychotic mental disorders

<sup>e</sup>This includes disorders of adult personality/behavior, intellectual disabilities, pervasive/specific developmental disorders, behavioral/emotional disorders with onset usually occurring in childhood/adolescence, and unspecified mental disorders



**Fig. 1** Overall refill persistence among propensity-score-matched patients with HCV receiving 8- vs 12-week DAA therapy. *CI* confidence interval, *DAA* direct-acting antiviral, *HCV* hepatitis C virus, *OR* odds ratio. \**P* < 0.05; \*\**P* < 0.01; \*\*\**P* < 0.001

dispensing records [20]. These methodologies, however, may not be appropriate for short-term treatment of HCV, as medication therapy is

primarily limited to 8 or 12 weeks, with the majority of the patients requiring only one or two refills to complete treatment. MPR and PDC assessments require at least two prescription fills; excluding prescriptions that only require one fill would underestimate the compliance for an 8-week treatment duration [20], thus MPR and PDC methodologies were not used in this study. Instead, we assessed the number of patients completing all refills (i.e., one refill in the 8-week group or two refills in the 12-week group) and whether trends were similar among Medicaid-insured patients. Patients completing all refills were deemed persistent.

This study's findings highlight the impact that shorter durations have on refill persistence as shown by a greater than 20% difference in the proportion of persistent patients between the 8- and 12-week treatment groups, regardless of insurance type. These rates of treatment incompleteness are comparable to those presented in the ANCHOR study. Among 100 PWID who were dispensed 12-week sofosbuvir/velpatasvir in that study, 84% completed all



three bottles and just 66% within the study window. While imperfect adherence, which contributed to 37% of patients completing treatment more than 7 days after their anticipated end date, did not significantly impact SVR rates, completion of two or more bottles (persistence) was significantly associated with achieving SVR [16]. Glecaprevir/pibrentasvir (G/P) is the first 8-week pangenotypic treatment approved for treatment-naïve patients with chronic HCV, both without cirrhosis and with CC [21]. Ten phase 3 clinical trials compared the compliance to G/P for 8 or 12 weeks in treatment-naïve patients with HCV and demonstrated a modest, but statistically significant decline in compliance with longer treatment duration; SVR rates remained high with either 8- or 12-week therapy [15]. Studies across a range of different DAA regimens have shown that with longer treatment duration, patients become less compliant [11–15, 22–24].

While DAA treatment persistence data is limited in the literature, there are several real-world analyses that have shown varying lost-to-follow-up rates that may include patients who never completed their refills altogether [25–27]. Therefore, an understanding of the impact of not completing treatment on SVR would be useful and may be extrapolated from published data on cure rates from when DAAs were used for shorter durations than their approved labels. Phase 2 studies of sofosbuvir/velpatasvir (400/100 mg) ± ribavirin examined 8-week treatment in HCV genotypes 1 and 2. The virologic failure rates observed were 12–19%, thus this shorter treatment duration was not pursued in phase 3 trials [28]. Six-week treatment of recently acquired HCV infection with sofosbuvir/velpatasvir was also found to be inferior to 12-week treatment as a result of higher rates of relapse [29]. Glecaprevir/pibrentasvir, which is approved for 8-week treatment for most patients, was similarly tested with a 6-week duration in patients with acute HCV infection and achieved a 96% SVR rate. If one assesses the possible impact of only 1 month of treatment (missing 1st refill), SVR rates reported to date are 59% with G/P and 40% with ledipasvir/sofosbuvir [30, 31]. While most of these studies are limited by small numbers of patients, it may be

generally concluded that poor DAA persistence will not achieve optimal cure rates and may result in the development of antiviral resistance complicating re-treatment [30].

PWID with chronic HCV infection often face several challenges to accessing, adhering to, and persisting on treatment. Social factors, such as stigma associated with drug use or HCV infection, homelessness, mental health disorders, lack of social support, or mistrust of the healthcare system can play roles in medication persistence in PWID with HCV [32]. PWID currently engaged in addiction recovery or those managing ongoing drug use may see HCV treatment as a secondary priority [33]. However, HCV treatment and medication persistence are especially important in this phase because, despite ongoing drug use, PWID who completed HCV treatment still demonstrated high rates of SVR achievement [1, 34]. Peer support programs for PWID geared toward increasing education on harm reduction strategies, disease education, and treatment options have been effective in several settings, most commonly opioid addiction treatment centers [35]. PWID are often referred to secondary centers to receive testing and/or treatment. This may be difficult for a population with a high rate of transportation, housing, and financial instability and often results in patients missing appointments or being lost to follow-up [33]. Moreover, Frankova et al. determined stable housing to be the greatest positive predictor of HCV medication persistence among PWID [36]. It is important to note that, in this study, we assessed patients receiving 28-day supplies of DAA therapy with each refill. Depending on where patients received their treatment (i.e., addiction or mental health clinics, primary care, etc.) the quantity of medication received with each refill may vary. Indeed, patients in addiction clinics may receive daily or weekly supplies (e.g., “take home” supplies [37]) which may require them to return several times to complete a full round of curative treatment, whereas patients in primary care may receive monthly supplies. More research is needed to understand how persistence may be impacted by these differences in supply per refill; however, this study suggests that providing the complete treatment course

to patients at the start of treatment may benefit patients. Healthcare provider perceptions regarding medication persistence in PWID are also a major factor in their receiving treatment for HCV [38, 39]. In a survey of 103 doctors, providers indicated they were 32% less likely to treat veteran patients currently using other drugs, such as cocaine or heroin [38]. However, according to AASLD/IDSA guidelines, active or recent drug use or a concern for reinfection is not a contraindication to HCV treatment and healthcare providers should be offering treatment to PWID [1].

To our knowledge, this is the first study using a large medical/pharmacy claims data set to assess the effect of shorter duration HCV treatment on medication refill persistence in PWID. This analysis excluded patients with acute HCV, prior HCV treatment, or those with hepatic failure or decompensation, which allowed us to assess a more general HCV population. Limitations of this study are that, while patients may have adhered to their prescription refills, these data cannot confirm that the patient was compliant with the treatment regimen. Likewise, database studies do not provide socioeconomic status or behavioral information, which may confound persistence findings. However, a secondary analysis of Medicaid patients may shed light on this topic. Although the probability is low given therapy durations, patients who did not complete the necessary prescription refills may have refilled their prescriptions in other systems that were not covered by Symphony Health. This study used administrative claims data that did not include laboratory results, thus SVR rates could not be assessed. As a result, it could not be determined whether patients who did not complete their refills achieved SVR at 12 weeks post-treatment; further study is needed to assess this. This analysis was limited to those who completed therapy. These data may not be generalizable to other populations, or even all PWID, not covered by the database used in the analysis.

## CONCLUSION

In this study, patients prescribed 8-week DAA therapy had significantly greater refill persistence than patients prescribed 12-week DAA therapy. Importantly, first refill statistics were similar between groups; however, the majority of nonpersistence was due to missed second refills, thus highlighting the benefit of shorter treatment durations in this population. The data presented here demonstrated that high medication persistence is possible in the PWID population. This supports the AASLD/IDSA recommendation that all PWID with HCV receive curative treatment, regardless of active, recent, or past drug use [1].

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**Compliance with Ethics Guidelines.** This is a retrospective study with anonymous data from Symphony Health, a HIPAA-compliant de-identified claims database, and thus does not require IRB approval. Likewise, patient consent was not required given that the data was deidentified.

**Data Availability.** The data sets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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