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Regional and Rural-Urban Differences in the Use of Direct Acting Antiviral Agents for Hepatitis C Virus: The Veteran Birth Cohort

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Abstract

Background: Veterans with hepatitis C infection (HCV) may face geographic obstacles to obtaining treatment.

Objective: We studied the influence of region and rural versus urban residence on receipt of direct acting anti-viral medications (DAAs) for HCV.

Subjects: Veterans receiving care within Veterans Affairs Healthcare System born between 1945-65.

Research Design: Observational study using national electronic health record data.

Measures: Receipt of DAAs was defined as 1 filled prescription from 1/1/2014 to 12/31/2016. Region (South, Northeast, Midwest, and West) and residence (urban, rural-micropolitan, small rural towns, and isolated rural towns) variables were created using residential ZIP codes and rural urban commuting area (RUCA) codes. Multivariable models were adjusted for age, race, gender, severity of liver disease, comorbidities, and prior treatment experience.

Results: Among 166,353 eligible patients 64,854 received, DAAs. Variation by rural-urban residence depended on region. In unadjusted analyses, receipt varied by rural-urban designations within Midwest, and West regions ($p < 0.05$) but did not vary within the South ($p = 0.12$). Southern rural small town had the lowest incidence of DAA receipt (40.1%) whereas the incidence was 52.9% in Midwestern isolated rural towns. In adjusted logistic analyses, compared to southern urban residents (the largest single group), southern rural small town residents had the lowest odds, OR 0.85: 95% CI 0.75, 0.93, and Midwestern residents from isolated and small rural towns had the highest odds (ORs both 1.27) to receive treatment.

Conclusions: Substantial geographic variation exists in receipt of curative HCV treatment. Efforts are needed to provide more equitable access to DAAs.

Keywords

Hepatitis C; Direct Acting Antiretroviral; geographic variation; rural-urban variation and veterans

INTRODUCTION

Untreated **hepatitis C virus (HCV)** infection is associated with substantial resource utilization, morbidity and mortality.¹⁻³ In the United States, 2.7-3.9 million persons are estimated to be chronically infected with HCV and 75-80% of these individuals were born between 1945-1965.⁴⁻⁶ With cure rates greater than 90% and few reported side effects, second-generation (all oral) **direct acting anti-virals (DAAs)** make cure an attainable goal for nearly all patients.⁷⁻¹²

The Veterans Healthcare Administration System (VA) has made a major commitment to treating hepatitis C including provider training and unrestricted access to DAAs.¹³ However,

if experience with dissemination of antiretroviral treatment for **human immunodeficiency virus** (HIV) within VA is a guide,¹⁴ these steps may not be sufficient to overcome rural-urban and regional disparities in care. On a patient-level, such barriers likely include travel burden, access to transportation, rural/geography barriers and social isolation.¹⁵⁻²⁰ System level barriers may include limited availability of providers experienced in treating patients with HCV.^{18,19,21} For example, studies conducted within VA and other healthcare systems find that patients with HCV who have not received a gastroenterology (GI) or hepatology visit are less likely to receive HCV treatment.²² A study in the pre-DAA era found that rural patients had less access to HCV specialists.²²⁻²⁴ We previously documented higher HCV testing rates (54%) in urban VA centers compared to rural centers (47%) and modest regional variation in HCV testing based on Veteran Integrated Service Networks (VISNs).²⁵ However, our prior paper did not consider HCV treatment or interactions between region and rural-urban status.

From January 2014 until December 2016, over 60,000 individuals have been treated with DAAs in the VA.⁸ Despite prior evidence of geographic variation in dissemination of new treatments within VA, little is known about regional and rural-urban variation in provision of DAAs in VA. We hypothesized that DAA adoption would vary by region and rural-urban residence and that these two factors would interact.

METHODS

This analysis is focused on HCV treatment with DAAs in individuals with a positive HCV antibody or quantifiable HCV viral load.

Data Source

We used electronic health record (**EHR**) data available through the VA national Corporate Data Warehouse (CDW). CDW is a data repository of over 8 million veterans in care starting on October 1, 1999, with at least one VA outpatient visit. It includes all laboratory test results as well as inpatient and outpatient utilization as indicated by procedure (Current Procedural Terminology codes) and diagnosis by International Classification of Diseases, Ninth Edition, Clinical Modification (ICD-9) codes. The database also includes patient demographics, vital status, and pharmacy utilization. To ensure complete identification of all relevant HCV tests, trends in completed HCV tests for each VA laboratory were reviewed. Test results were standardized by previously published methods.²⁶

Study Cohort

January 1, 2014 was chosen as the index date at which clinicians began prescribing all-oral combination DAA therapies.²⁷⁻²⁹ Patients with a positive HCV RNA and/or HCV antibody who had at least one VA visit from January 2014 forward were considered eligible. Patients with a negative **HCV** RNA prior to the index date, or patients with no urban/rural designation (see below) were excluded (Figure 1). VINCI (VA informatics and computing infrastructure) approval using DART (data access request tracker) was also obtained for access and use of CDW electronic data. Information extracted included baseline patient

characteristics, and factors that potentially predict or act as barriers to DAA HCV treatment for veterans born between 1945 and 1965.

Primary Measures

Outcome: Receipt of second-generation DAA was defined as 1 filled prescription of sofosbuvir, ledipasvir, simeprevir, daclatasvir or paritaprevir/ritonavir/ombitasvir plus dasabuvir (PrOD) from January 1, 2014 to December 31, 2016.

Primary Exposures: Residential status was determined by US Postal Service zone improvement plan (ZIP) codes. Two geographic exposures were considered—region and rural-urban status.

Region: Using state of residence as indicated by zip codes and standard regional groupings, residence was divided into census regions: Northeast (Connecticut, Maine, Massachusetts, New Hampshire, Rhode Island, Vermont, New Jersey, New York, Pennsylvania), Midwest (Illinois, Indiana, Michigan, Ohio, Wisconsin, Iowa, Kansas, Minnesota, Missouri, Nebraska, North Dakota, South Dakota), South (Delaware, Florida, Georgia, Maryland, North Carolina, South Carolina, Virginia, District of Columbia, West Virginia, Alabama, Kentucky, Mississippi, Tennessee, Arkansas, Louisiana, Oklahoma, Texas), and West (Arizona, Colorado, Idaho, Montana, Nevada, New Mexico, Utah, Wyoming, Alaska, California, Hawaii, Oregon, Washington).

Rural-Urban Status: ZIP codes were linked to rural urban commuting area (RUCA) codes using the ZIP code/RUCA code crosswalk file available from the University of Washington (<http://depts.washington.edu/uwruca/uses.html>). Briefly, RUCA codes are frequently used in studies of rural-urban variation in healthcare delivery and health behaviors. RUCA takes into account primary and secondary commuting patterns to Urbanized Areas, Urban Clusters, or smaller population centers to classify census tracts into 33 distinct categories, which typically are combined into fewer and larger categories for data analyses. We applied a commonly-used algorithm to collapse the 33 RUCA codes into a four level geographic residence variable.³⁰

- (1) **Urban:** have metropolitan cores (identified by the Census Bureau as having populations of at least 50,000, as well as adjacent counties that are economically and socially integrated with that core) and substantial primary or secondary commuting flow patterns to Urbanized Areas.³¹
- (2) **Rural-Micropolitan:** have micropolitan cores (urban clusters of 10,000–49,999 residents).
- (3) **Small Rural Towns:** have primary commuting flows to or within population centers of between 2,500 and 9,999 residents.
- (4) **Isolated Rural Towns:** less populated rural areas with no primary commuting flows to Urbanized Areas or Urban Clusters.

Secondary Variables

Other variables collected from the EHR and chosen a priori included age, gender, race, prescription fills for specific DAAs, body mass index (BMI), HCV genotype, **fibrosis-4** (FIB 4, a composite of aspartate transaminase, alanine transaminase, platelets and age), and **Alcohol Use Disorders Identification Test** (AUDIT-C, hazardous alcohol use defined as AUDIT-C \geq 4). ICD-9 administrative codes were used to determine cirrhosis, hepatocellular cancer, liver transplantation, diabetes, HIV, alcohol use disorder, substance use disorder, and severe mental health diagnoses (Appendix).

Statistical Analysis

Urban and rural residents (by RUCA definition) were characterized using descriptive statistics (frequencies and percentages or mean and standard deviation (SD)). We determined associations between region and rural-urban residence and DAA adoption using three logistic regression analyses: 1) unadjusted models; 2) models adjusted for demographics (age, gender, race) only; and 3) models adjusted for demographics, severity of liver disease (FIB4 $>$ 3.25, cirrhosis, hepatocellular carcinoma, and liver transplantation), and relevant comorbid disease (diabetes, obesity, HIV infection, hazardous alcohol use, alcohol use disorder, substance use disorder, and severe mental illness). Cumulative incidence rates were estimated using Gray's method for accounting for competing risk (i.e. death).³² Analyses were done using SAS 9.4 (Cary, NC) and R version 3.4.2. Missing data were imputed using multiple imputation (10 imputations) under the missing at random assumption.

RESULTS

Cohort Characteristics

From January 2014 to December 2016, we identified 166,353 eligible persons. The mean age of patients was 60.8 years (SD=4.9 years), 55.4% were white, and 96.7% were men. Overall, 24.8% had FIB-4 $>$ 3.25, 16.6% of patients had a diagnosis of cirrhosis, 1.5% had hepatocellular cancer, and 0.8% had undergone liver transplant. The majority of patients lived in the south (Table 1, n=76,851 or 46.2%) and/or in an urban setting (n= 148,159 or 89.1%). Only 10.9% (n=18,194) lived in any rural setting. The largest proportion of patients living in a rural setting in any region was in the Midwest (15.6%, data not otherwise shown). During our observation period, 64,854 (39.0% of eligible patients) received at least one prescription of DAA therapy.

Rural persons were more likely than urban to be white (76.5% vs. 52.8%, $P < 0.01$ for overall race comparison) and less likely to have a substance or alcohol use diagnosis (31.9% vs. 42.2%, $p < 0.01$ and 34.0% vs. 40.1%, $p < 0.01$ respectively).

Predictors of DAA Receipt

Urban-rural variation in incident DAA prescription depended upon region (Figure 2 a-d). Midwestern and Northeastern veterans experienced the greatest variation in receipt of DAAs by rural-urban residence (Figure 2a-2b). Given the results of Figure 2 and the pairwise comparisons within region (Figure 2 table), we created a 16 level variable that addresses the interaction between region and urban/rural status.

Before and after adjustment (Table 2) DAA receipt varied by region and rural-urban status. Compared to southern urban dwellers, those living in southern small towns had 0.85 times the odds (95% CI 0.77, 0.93) of receiving DAAs and those living in all areas of the Midwest (OR range from 1.11 to 1.27) had greater odds of receiving DAAs. Other independent positive predictors of DAA receipt included: being male, severe liver disease, a diagnosis of cirrhosis, receipt of a liver transplant, prior treatment for HCV, being obese, having a diagnosis of HIV, and having a diagnosis of severe mental illness. Presence of Hepatocellular Cancer, a diagnosis of substance use, or a diagnosis of alcohol use disorder were associated with lower odds of treatment.

DISCUSSION

Second-generation DAA therapies have ushered in an era of safer, better-tolerated treatments for HCV. Our analyses suggest that substantial geographic disparities exist within the first 3 years of approval of second-generation DAAs, and those disparities differ by urban/rural status (i.e. interaction between urban/rural status and region), with the incidence of DAA treatment receipt ranging from 40.1% to 52.9% (Figure 2). After adjustment, in models examining the odds of receiving a DAA, and compared to the largest group (southern residents living in an urban setting), Midwestern residents in any setting had greater odds of receiving DAAs. Residents of the rural south had lower odds of receiving DAAs compared to their urban southern counterparts.

It is not surprising that variation in utilization by rural settings is influenced by region³³. Not all rural environments are the same across the United States. For example, rural communities in Vermont, Alabama, Iowa, and Alaska are likely to vary substantially in their physical environments, access to healthcare, and cultural contexts. This was apparent in our study, which found significant variation in DAA use in rural compared to urban communities, depending on the geographic region examined. The variations in DAA use between rural and urban residence observed in the Northeast and Midwest were much less pronounced in the South.

A previous study in the pre-DAA era found that although rural patients had less access to HCV specialists, this did not translate to lower HCV treatment rates.²²⁻²⁴ The lack of difference in treatment rates for urban and rural veterans in prior studies during the interferon-era may reflect the very small number of treated patients overall in that era. Treatment rates have increased by over 12-fold with the wide availability of all-oral DAA's, enhancing statistical power to detect a significant difference between treatment subgroups.⁸

While the VA is one of the few healthcare systems that has treated enough patients with DAAs to support a study addressing this question, it is important to keep in mind that the VA differs in important ways from US non-Veteran health care. VA patients have few insurance-associated barriers to care, many of which are inherent to privatized, insurance-based health systems. Non-VA rural populations possess more elderly patients and children, higher unemployment and underemployment, as well as higher percentages of poor, uninsured, and underinsured residents, less affected by government-operated medical care through the VA.^{34,35} Health literacy and education is also not directly assessed which may impact important

decisions to treat and may lead to differences in DAA adoption. Therefore, our results may not be generalizable to a system where cost and insurance are paramount determinants of healthcare utilization.^{36,37}

Furthermore, due to the low percentage of women in our study, as well as the VA caring for a largely male population, examinations of gender disparities or gaps in practice patterns cannot be fully assessed. Disparities in health care can also be influenced by physician availability, clinical judgment and patient-level factors such as knowledge and willingness to seek treatment and travel burden. We did not have the data to evaluate these factors.

Despite these limitations, our study has several strengths. Most importantly, our analyses use a national database summarizing all veterans' prescribed DAA therapy from 2014 to December 2016. The VA health system is America's largest integrated health care system providing comprehensive services to over 8 million Veterans each year via over 1,700 sites of care. Since VA funding for HCV is centralized nationally¹³, it seems unlikely that variations in funding support within VA would act as a confounder for analyses of geographic disparities. Additionally, although most patients included were from an urban setting, this study illustrates a substantial number of patients are DAA adopters that live in rural settings, suggesting a potential to expand treatment efforts directed at this population. Additional strengths include the ability to track multiple DAA therapies over time including newer DAA treatments such as daclatasvir or PrOD.

In conclusion, Midwestern and Northeastern veterans are more likely to be early adopters of second-generation DAA treatments for HCV. The south census region had the lowest national treatment rates. Urban-rural differences in DAA treatment varied by region. Within the south, rural veterans were the least likely to receive treatment. In contrast, within the Midwest and Northeast, rural residence was associated with an increased likelihood of treatment. Future studies are needed to explore provider specific characteristics and prescribing habits within these settings in addition to patient knowledge assessments to explain these disparities. With these data, dedicated, government-sponsored interventions should target Southern-dwelling veterans in an effort to improve overall adoption of HCV treatment.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations:

DAA	direct acting anti-viral
HCV	hepatitis C virus

VA	Veterans Administration
HIV	human immunodeficiency virus
SD	standard deviation
AUDIT-C	Alcohol Use Disorders Identification Test

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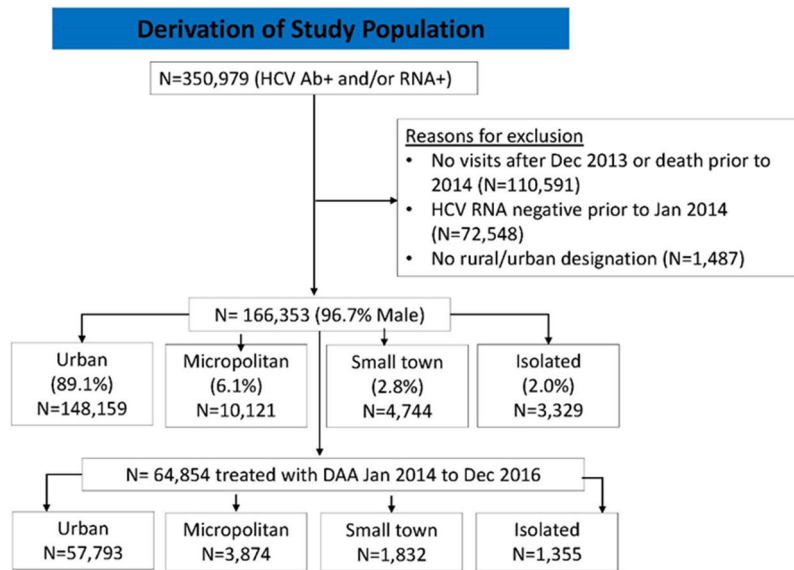


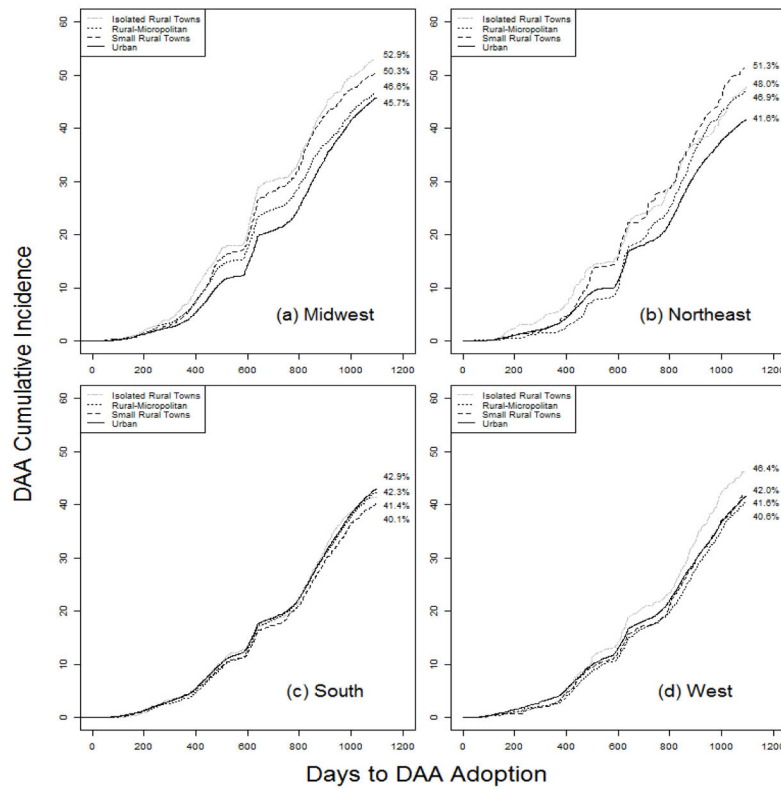
Figure 1:
Study Flow Chart

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Unadjusted p-values for pairwise comparisons of urban-rural designation within region

Comparisons	Midwest	Northeast	South	West
Urban vs. Isolated	<0.01	0.22	0.38	0.08
Urban vs. Rural-Micropolitan	0.36	0.06	0.83	0.34
Urban vs. Small	0.15	<0.01	0.08	0.18
Isolated vs. Rural-Micropolitan	<0.01	0.84	0.76	0.02
Isolated vs. Small	0.03	0.26	0.69	0.50
Rural-Micropolitan vs. Small	<0.01	0.15	0.14	0.16

Figure 2 a-d: Cumulative Incidence of Adoption of Direct Acting Antiretroviral (DAA) Treatment by Region and Rurality from index date (1/1/2014) to cohort end (12/31/2016) accounting for competing risk of death. Values in the table represent unadjusted p-values for pairwise comparisons of urban-rural designation within region (i.e. comparison of the curves within a region) demonstrating the interaction between region and rural-urban designation.

Table 1:

Characteristics of 166,353 Direct Acting Antiretroviral (DAA) Eligible Patients, By Rural-Urban Residence

Characteristic	Total		DAA ^a Receipt (col %)	Urban ^b (col %)	Rural (col %)			p-value ^g	p-value ^h
	n	col %			Micro- politan	Small Town	Isolated		
n	166,353	100.0%	64,854	148,159	10,121	4,744	3,329		
Gender								0.03	<0.01
Female	5,473	3.3%	37.7%	3.3%	3.0%	2.8%	2.9%		
Male	160,880	96.7%	39.0%	96.7%	97.0%	97.2%	97.1%		
Mean Age^c in years (SD)	60.7 (4.5)	NA	60.8 (4.4)	60.7 (4.5)	60.6 (4.6)	60.7 (4.6)	61.0 (4.6)		
Race								<0.01	<0.01
White	92,210	55.4%	38.8%	52.8%	73.9%	77.6%	82.9%		
Black	64,041	38.5%	40.3%	41.2%	19.5%	15.4%	9.6%		
Native Hawaiian/Pacific Isl.	660	0.4%	36.1%	0.4%	0.4%	0.3%	0.5%		
American Indian/AK Native	1,343	0.8%	37.6%	0.7%	1.2%	1.3%	1.9%		
Asian	332	0.2%	34.6%	0.2%	0.2%	0.1%	0.1%		
Mixed Race	1,034	0.6%	40.5%	0.6%	0.6%	0.7%	0.6%		
Unknown/Other	6,733	4.1%	29.5%	4.0%	4.3%	4.6%	4.4%		
Census Region								<0.01	<0.01
South	76,851	46.2%	38.8%	46.7%	43.7%	44.7%	33.3%		
West	37,306	22.4%	37.7%	22.2%	25.2%	22.6%	24.5%		
Midwest	30,646	18.4%	41.7%	17.5%	24.5%	25.4%	32.4%		
Northeast	21,550	13.0%	38.1%	13.6%	6.6%	7.3%	9.8%		
HCV Genotype								<0.01	<0.01
1	104,453	62.8%	51.8%	63.5%	58.1%	57.0%	55.4%		
2	11,688	7.0%	47.8%	6.8%	8.5%	8.8%	10.5%		
3	7,423	4.5%	43.2%	4.3%	5.8%	5.9%	5.4%		
4	1,180	0.7%	46.5%	0.7%	0.6%	0.5%	0.5%		
5 or 6	25	0.0%	60.0%	0.01%	0.01%	0%	0%		
Multiple Genotypes	458	0.3%	56.6%	0.3%	0.3%	0.3%	0.2%		
Unknown	41,126	24.7%	2.9%	24.4%	26.7%	27.5%	28.2%		
HCV Complications									
FIB4>3.25 ^d	26,656	24.8%	45.8%	24.8%	24.7%	25.4%	22.8%	<0.01	<0.01
Cirrhosis	27,568	16.6%	44.4%	16.7%	15.4%	15.9%	13.5%	<0.01	<0.01
Hepatocellular Carcinoma	2,523	1.5%	30.1%	1.5%	1.4%	1.4%	1.5%	0.65	0.25
Liver Transplant	1,325	0.8%	56.3%	0.8%	0.9%	0.8%	1.0%	0.32	0.13
Treatment Experience	10,156	6.1%	60.1%	6.1%	6.1%	6.2%	5.9%	0.94	0.97
Prior Interferon	9,127	5.5%	58.7%	5.5%	5.5%	5.7%	5.3%		
Prior Boceprevir	839	0.5%	73.1%	0.5%	0.5%	0.5%	0.4%		

Characteristic	Total		DAA ^a Receipt (col %)	Urban ^b (col %)	Rural (col %)			p-value ^g	p-value ^h
	n	col %			Micro- politan	Small Town	Isolated		
Prior Telaprevir	190	0.1%	73.2%	0.1%	0.1%	0.04%	0.2%		
Specialist Clinic Visit									
Gastroenterology	103,159	62.0%	45.3%	62.4%	59.6%	59.0%	57.1%	<0.01	<0.01
Infectious Disease	36,803	22.1%	46.3%	22.4%	17.5%	16.4%	16.9%	<0.01	<0.01
Comorbid Disease									
Diabetes	48,627	29.2%	40.8%	29.6%	26.7%	27.2%	24.2%	<0.01	<0.01
BMI>30 kg/m ² ^d	37,787	30.1%	46.1%	29.9%	31.1%	30.8%	33.1%	<0.01	<0.01
HIV	4,481	2.7%	46.8%	2.9%	1.1%	0.8%	0.7%	<0.01	<0.01
AUDIT C ≥4 ^d	18,114	16.7%	35.3%	16.6%	17.6%	17.7%	18.3%	<0.01	<0.01
Alcohol Use Disorder	65,635	39.4%	37.0%	40.1%	35.0%	35.5%	28.8%	<0.01	<0.01
Substance Use Disorder	68,364	41.1%	36.9%	42.2%	33.1%	32.4%	27.5%	<0.01	<0.01
Severe Mental Illness ^e	66,021	39.7%	39.8%	40.0%	38.1%	37.8%	35.3%	<0.01	<0.01
Mortality^f									
After Treatment	1,697	1.0%	NA	1.0%	1.2%	1.1%	1.0%	0.56	0.23

^aRaw percentages of the individuals with the given characteristic

^bCategorize rural vs. urban Veteran residence by RUCA (Rural-urban commuting area) codes linked to residential ZIP.

^cAge on January 1, 2014

^dPercentages of missing data: 35.3% (N=58,790) missing FIB-4; 24.5% (N=40,741) missing BMI; 34.9% (N=57,975) missing AUDIT-C

^eIncludes major depression, bipolar disorder, post-traumatic stress disorder, and schizophrenia

^fBetween January 1, 2014 and December 31, 2016

^gComparison of 4 categories of Region using Chi-square test of association

^hComparisons of Urban and Rural using Chi-square test of association

Abbreviations: DAA, direct acting anti-retroviral; HCV, hepatitis C virus; HIV, human immunodeficiency virus; SD, standard deviation; BMI, body mass index; AUDIT-C, alcohol use disorders identification test; FIB4, Fibrosis 4

* Baseline Laboratory data and AUDIT-C score: Closest to January 2014, and restricted to within one year prior to baseline. FIB-4 score = [age × aspartate aminotransferase] / [platelets × alanine aminotransferase^{1/2}]

Table 2: Association of Patient Characteristics with Direct Acting Antiretroviral (DAA) Adoption

Characteristic	Unadjusted			Adjusted for Demographics			Fully Adjusted		
	OR	95% CI	p-value	OR	95% CI	p-value	OR	95% CI	p-value
Region			<0.01			<0.01			<0.01
South-Urban	Ref			Ref			Ref		
Isolated Rural Towns	0.92	0.82	1.04	0.94	0.83	1.06	0.94	0.83	1.06
Rural Metropolitan	0.95	0.89	1.01	0.95	0.90	1.02	0.95	0.89	1.01
Small Rural Towns	0.85	0.78	0.93	0.87	0.79	0.95	0.85	0.77	0.93
Midwest-Urban	1.12	1.08	1.15	1.12	1.08	1.15	1.15	1.12	1.19
Isolated Rural Towns	1.24	1.10	1.40	1.28	1.13	1.44	1.27	1.12	1.44
Rural Metropolitan	1.07	0.98	1.16	1.10	1.01	1.19	1.11	1.02	1.19
Small Rural Towns	1.22	1.09	1.37	1.26	1.13	1.42	1.27	1.13	1.43
Northeast-Urban	0.96	0.92	0.99	0.95	0.92	0.98	0.93	0.90	0.96
Isolated Rural Towns	1.04	0.83	1.30	1.06	0.85	1.32	1.00	0.79	1.25
Rural Metropolitan	1.10	0.94	1.28	1.12	0.96	1.31	1.07	0.91	1.25
Small Rural Towns	1.22	0.99	1.52	1.26	1.01	1.55	1.24	1.00	1.54
West-Urban	0.95	0.92	0.97	0.93	0.86	1.01	1.00	0.97	1.03
Isolated Rural Towns	1.10	0.96	1.27	1.15	1.00	1.33	1.21	1.05	1.40
Rural Metropolitan	0.89	0.82	0.97	0.93	0.86	1.01	0.94	0.87	1.03
Small Rural Towns	0.94	0.83	1.07	0.98	0.87	1.12	1.02	0.90	1.16
Age				1.005	1.00	1.01	0.999	0.997	1.001
Female				0.97	0.92	1.03	0.91	0.86	0.96
Race									
White				Ref			Ref		
Black				1.07	1.04	1.09	1.09	1.07	1.12
Native Hawaiian/Pacific Isl.				0.90	0.77	1.05	0.87	0.74	1.03
American Indian/AK Native				0.95	0.85	1.07	0.96	0.86	1.08
Asian				0.85	0.68	1.07	0.82	0.65	1.03
Mixed Race				1.08	0.95	1.22	1.08	0.95	1.22

Characteristic	Unadjusted			Adjusted for Demographics			Fully Adjusted		
	OR	95% CI	p-value	OR	95% CI	p-value	OR	95% CI	p-value
Unknown/Other				0.66	0.63	0.70	0.66	0.62	0.70
HCV Complications									
FIB4>3.25							1.16	1.13	1.20
Cirrhosis							1.18	1.15	1.22
Hepatocellular Carcinoma							0.46	0.42	0.50
Liver Transplant							1.70	1.52	1.92
Prior Treatment Experience							2.29	2.20	2.39
Comorbid Disease									
Diabetes							0.99	0.97	1.02
BMI>30 kg/m ²							1.15	1.12	1.18
HIV							1.37	1.29	1.46
AUDIT C >=4							0.72	0.70	0.74
Alcohol Use Dependence							0.95	0.92	0.97
Substance Use Dependence							0.83	0.81	0.85
Severe Mental Illness							1.08	1.05	1.10