Annals of Internal Medicine

MEDICINE AND PUBLIC ISSUES

Restrictions for Medicaid Reimbursement of Sofosbuvir for the Treatment of Hepatitis C Virus Infection in the United States

Soumitri Barua; Robert Greenwald, JD; Jason Grebely, PhD; Gregory J. Dore, MBBS, PhD; Tracy Swan; and Lynn E. Taylor, MD

The aim of this study was to systematically evaluate state Medicaid policies for the treatment of hepatitis C virus (HCV) infection with sofosbuvir in the United States. Medicaid reimbursement criteria for sofosbuvir were evaluated in all 50 states and the District of Columbia. The authors searched state Medicaid Web sites between 23 June and 7 December 2014 and extracted data in duplicate. Any differences were resolved by consensus. Data extracted were whether sofosbuvir was covered and criteria for coverage based on the following categories: liver disease stage, HIV co-infection, prescriber type, and drug or alcohol use. Of the 42 states with known Medicaid reimbursement criteria for sofosbuvir, 74% limit sofosbuvir access to persons with advanced fibrosis (Meta-Analysis of Histologic Data in Viral Hepatitis [METAVIR] fibrosis stage F3) or cirrhosis (F4). One quarter of states require persons co-infected with HCV and HIV to be receiving antiretroviral therapy or to have suppressed HIV RNA levels. Two thirds of states have restrictions based on prescriber type, and 88% include drug or alcohol use in their sofosbuvir eligibility criteria, with 50% requiring a period of abstinence and 64% requiring urine drug screening. Heterogeneity is present in Medicaid reimbursement criteria for sofosbuvir with respect to liver disease staging, HIV co-infection, prescriber type, and drug or alcohol use across the United States. Restrictions do not seem to conform with recommendations from professional organizations, such as the Infectious Diseases Society of America and the American Association for the Study of Liver Diseases. Current restrictions seem to violate federal Medicaid law, which requires states to cover drugs consistent with their U.S. Food and Drug Administration labels.

Ann Intern Med. doi:10.7326/M15-0406 **www.annals.org**

For author affiliations, see end of text.

This article was published online first at www.annals.org on 30 June 2015.

Highly effective (cure rate >90%), once-daily, oral interferon-free treatments with minimal adverse effects are now available for hepatitis C virus (HCV) infection. Worldwide, an estimated 80 to 150 million persons have chronic HCV (1, 2). If left untreated, chronic HCV can lead to cirrhosis, liver failure, and hepatocellular carcinoma (HCC) (3, 4). Rates of advanced liver disease complications, associated health care costs, and liver disease–related mortality are rising worldwide (3, 4). Regimens for treating HCV seem to be curative and reduce liver-related and all-cause mortality (5). Uptake of HCV treatment has been low in many settings (6–8) in part because of the poor tolerability of interferon-based regimens. Widespread access to interferon-free regimens has the potential to greatly affect HCV morbidity and mortality.

Sofosbuvir, a pan-genotypic nucleotide analogue NS5B polymerase inhibitor indicated for treatment of chronic HCV in combination with other direct-acting antivirals (DAAs), was approved by the U.S. Food and Drug Administration (FDA) on 6 December 2013. Sofosbuvir is the first DAA indicated for use as part of an interferon-free regimen. Compared with interferon-based therapy, sofosbuvir-based interferon-free regimens show response rates greater than 90%, shortened treatment duration (8 to 12 weeks), and improved tolerability and safety (although with some combinations, lower responses are seen in persons with more advanced disease and certain HCV genotypes) (9–14).

The wholesale acquisition cost of sofosbuvir is $1000 per day (equating to $84 000 for a 12-week course) and must be used with 1 or more medications at additional cost. A fixed-dose, single-tablet combination of sofosbuvir and ledipasvir (an NS5A inhibitor) is now available at a wholesale acquisition cost of $1125 per day ($63 000, $94 500, and $189 000 for an 8-, 12-, and 24-week course, respectively). The high price of these regimens and high demand (actual or anticipated) for them has led payers to institute restrictions on their access, although by law, Medicaid programs are entitled to a rebate of at least 23% (15, 16). Although some payers have negotiated ample rebates, they have not altered their reimbursement restrictions.

Further complicating matters is the fact that different federal standards apply depending on whether a beneficiary is eligible under "traditional" Medicaid or is "newly eligible" for Medicaid in 1 of the 28 states that have implemented the Patient Protection and Affordable Care Act Medicaid expansion provision (16). Within the 51 fee-for-service Medicaid programs, there are also different programs and requirements for different populations and different models of care financing and delivery (for example, fee-for-service and managed care organizations). For the purposes of this article, we have focused on state fee-for-service programs and not managed care. Because our focus here is on clinical factors, detailed legal analysis of the many complex Medicaid program rules is beyond the scope of this article.

In the United States, a disproportionate number of persons living with HCV have low income (17). For purposes of this article, "low income" means having income at or below the highest state Medicaid eligibility limit for parents of dependent children. Currently, the state with the highest Medicaid income eligibility limit is Connecticut at 201% of the federal poverty level. Further, the 2015 federal poverty level for a single person in all states except Alaska and Hawaii is $11 770; 201% equals $23 658 (18). Most persons are eligible for reimbursement of HCV therapy through Medicaid, which is the jointly funded federal and state partnership that

provides health insurance for low-income persons meeting the program's eligibility criteria. Each state has wide discretion in administering its own Medicaid program. Although this creates unique Medicaid programs in each state, states must follow some federal standards (16). These include covering all FDA-approved drugs, consistent with FDA labeling, whose manufacturers participate in Medicaid's prescription drug rebate program (19), and not discriminating in drug coverage—thus a state "may not arbitrarily deny or reduce the amount, duration, or scope of a required service . . . to an otherwise eligible beneficiary solely because of the diagnosis, type of illness, or condition" (20).

In 2014, the American Association for the Study of Liver Disease and the Infectious Diseases Society of America (AASLD/IDSA) issued recommendations (21) for testing, managing, and treating HCV (which are updated regularly). Little is known about the consistency in applying these guidelines by state Medicaid committees to reimbursement criteria for sofosbuvir. The aim of this study was to systematically evaluate state Medicaid policies for the reimbursement of sofosbuvir for HCV treatment in the United States.

METHODS

We evaluated Medicaid reimbursement criteria for sofosbuvir for all 50 states and the District of Columbia. We searched state Medicaid Web sites between 23 June and 7 December 2014. Locating criteria for coverage was difficult. Each state has different means of organizing Medicaid information online, no consistent word search was able to locate each policy, and each state required a different process to find the appropriate policies or forms. As such, this search was confined to online information. When state policy was unclear, and when states did not operate a fee-for-service pharmacy program, we indicated that the state criteria and policies were unknown. Only states with fee-for-service programs were included.

Data were extracted by 2 coauthors in duplicate and entered into a standardized spreadsheet; 2 different coauthors crosschecked the extracted data. Any differences were resolved by consensus. Each entry was double-checked by another coauthor to ascertain accuracy. For each state, the following data were extracted from Medicaid reimbursement criteria: whether sofosbuvir was covered (paid for by Medicaid) and the criteria for coverage. Most Medicaid programs require preapproval of certain medications before a patient may receive them, and providers must complete this prior authorization. For each state, Medicaid prior authorization criteria for sofosbuvir were also extracted, where available. The date of the state Medicaid reimbursement publication and uniform resource locators of the prior authorization and the preferred drug list were recorded and entered into a database (Microsoft Excel, version 14.4.4 [Microsoft]).

Criteria for sofosbuvir coverage based on the following categories were recorded: liver disease stage, HIV co-infection, prescriber type, and drug or alcohol use. For criteria about liver disease staging, data were collected on the level of fibrosis required for reimbursement (either none indicated, Meta-Analysis of Histologic Data in Viral Hepatitis [METAVIR] fibrosis stage F2 or higher, or F3 or F4), eligibility for persons with decompensated cirrhosis, and whether a liver biopsy was mandatory to provide evidence of advanced fibrosis. For criteria about HIV co-infection, data were collected on whether HIV status needed to be documented, and if positive, whether the patient had to be receiving antiretroviral therapy (ART) or have suppressed HIV RNA levels. For prescriber type, data were collected on whether the prescriber had to be a specialist (gastroenterology, hepatology, infectious diseases, or liver transplantation) or whether treatment decisions needed to be made in consultation with a specialist. For criteria about drug or alcohol use, data were collected on whether there were any substance-related access criteria, and if so, whether drug or alcohol counseling was required, whether patients had to be evaluated for drug and/or alcohol dependence, whether a period of abstinence was required (1, 3, 6, or 12 months) before sofosbuvir therapy, and whether drug or alcohol testing and/or treatment was required before sofosbuvir therapy.

RESULTS

Overall, 42 states (82%), including the District of Columbia, had publicly available information about Medicaid reimbursement criteria for sofosbuvir (**Tables 1** and **2** and **Figures 1** and **2**). Nevada is the only state that does not require prior authorization for sofosbuvir. Nine states have unknown criteria, with neither the prior authorization nor eligibility information publicly available.

Of the 42 states, including the District of Columbia, with known Medicaid reimbursement criteria for sofosbuvir, 81% (n = 34) restrict sofosbuvir reimbursement on the basis of liver disease stage (**Table 1**). In 4 states (10%), reimbursement is restricted to only persons with cirrhosis (F4). In two thirds of states (n = 27), sofosbuvir reimbursement is restricted to persons with advanced fibrosis (F3) or cirrhosis (F4). In 2 states (5%) and 1 state (2%), reimbursement is also provided for those with moderate (F2) and mild (F1) fibrosis, respectively. In the remaining states, no reimbursement criteria are based on disease stage (n = 8 [19%]). Sofosbuvir use is restricted in persons with decompensated cirrhosis in 7 states (17%). Colorado is the only state that explicitly includes persons with decompensated cirrhosis. Liver biopsy staging is required for demonstrating cirrhosis in 5 states (12%), although Arkansas also requires a liver biopsy for evidence of bridging fibrosis (F3). In Tennessee, a liver biopsy or transient elastography are the only options allowed to demonstrate cirrhosis.

Nineteen states (45%) require information about HIV status. Ten (24%) require that patients be receiving ART or have evidence of HIV virologic suppression.

Twenty-nine states (69%) have restrictions based on prescriber type. In 14 states (33%), the prescriber

Table 1. U.S. State Eligibility/Ineligibility Criteria for Sofosbuvir Approval*

Requirement	States, *n*	States
Fibrosis†		
None indicated	8	Alabama, Massachusetts, Minnesota, Mississippi, North Carolina, Nevada, Utah, and Wyoming
Minimum stage F2	3	Maryland, Maine‡, and Oklahoma
Minimum stage F3–F4	31	Alaska; Arkansas; Arizona; California; Colorado; Connecticut§; Washington, DC; Delaware§; Florida; Iowa; Idaho; Illinois§; Indiana; Kentucky; Louisiana; Missouri; Montana; Nebraska; New Hampshire; New York; Ohio; Oregon§; Pennsylvania; Rhode Island; South Dakota; Tennessee; Virginia; Vermont; Washington; Wisconsin; and West Virginia
Decompensated cirrhosis‖		
Ineligible	7	Alaska; Washington, DC¶; Idaho; Kentucky; Oklahoma; Tennessee; and Washington
Eligible	1	Colorado
Mandatory liver biopsy to prove cirrhosis		
Liver biopsy	5	Alaska**, Arkansas, Iowa, Louisiana††, and Nebraska
Liver biopsy or elastography	1	Tennessee‡‡
HIV co-infection		
Requests documentation of HIV status	19	Alaska; Alabama; Arizona; California; Washington, DC; Delaware; Florida; Louisiana; Massachusetts; Maryland; Nebraska; New Hampshire; New York; Ohio; Oregon; South Carolina; Vermont; Wisconsin; and West Virginia
If HIV co-infection, the patient must be receiving ART or have a controlled viral load	10	Alaska§§; Alabama§§; Arizona§§; California§§; Washington, DC; Delaware§§; Florida§§; Maryland§§; New York; and West Virginia§§
Prescriber limitations		
Must be a hepatologist, gastroenterologist, or infectious diseases or liver transplantation physician	14	Florida, Iowa, Indiana, Louisiana, Maryland, Maine, New Hampshire, New York, Ohio, Pennsylvania, Rhode Island‖‖, Tennessee¶¶, Wisconsin, and Washington***
By or in consultation with one of these physicians	15	Arizona; California; Colorado; Connecticut; Washington, DC; Idaho; Illinois†††; Kentucky; Mississippi; Montana; Oklahoma; Oregon; South Dakota; Virginia; and West Virginia
None indicated	13	Alabama, Alaska, Arkansas, Delaware, Iowa, Massachusetts, Missouri, Nebraska, Nevada, North Carolina, Minnesota, Utah, and Wyoming
Prior authorization		
Unknown information on prior authorization	9	Georgia, Hawaii, Kansas, Michigan, New Jersey, North Dakota, New Mexico, South Carolina, and Texas
State without this requirement	1	Nevada

ART = antiretroviral therapy.
* When states are not included in a category, it is not certain whether they are providing or denying access to sofosbuvir on the basis of that limitation, only that there is not a written rule in their publicly reported policy.
† Meta-analysis of Histologic Data in Viral Hepatitis (METAVIR) fibrosis stage (F0–F4).
‡ F1.
§ Must be F4.
‖ Defined as a Child-Pugh score >6 (class B or C).
¶ If HIV co-infection.
** For F3.
†† For genotypes 2 and 3.
‡‡ Only 2 options given for proving cirrhosis.
§§ Requires either HIV viral load (copies/mL) or $CD4^+$ cell count ($\times 10^9$ cells/L).
‖‖ Other prescribers may request designation as an approved prescriber upon submission of a written request supporting this capability.
¶¶ Must have state Medicaid provider identification.
*** State Medicaid provider identification or prescriber is participating in and/or consults with Project Extension for Community Healthcare Outcomes (22).
††† Only first prescription needs consultation.

has to be a specialist (gastroenterology, hepatology, infectious diseases, or liver transplantation), whereas in 15 states (36%), treatment decisions can be made by a nonspecialist after consultation with a specialist.

Of the 42 states, including the District of Columbia, with known Medicaid reimbursement criteria for sofosbuvir, 88% of states (*n* = 37) include drug or alcohol use in their eligibility criteria for sofosbuvir reimbursement. Eight states (19%) require that all patients be evaluated for substance use disorder or alcohol dependence, and 50% of states (*n* = 21) require a period of abstinence from drugs or alcohol use or abuse for all patients (**Table 2**). An additional 9 states (21%) require abstinence only for patients with a history of substance abuse. Most states require that all patients, regardless of history, abstain from drug and alcohol use for 6 months (*n* = 11), whereas others require abstinence periods of 1 month (*n* = 2), 3 months (*n* = 5), or 12 months (*n* = 2). Most states (*n* = 27 [64%]) require urine drug screening before treatment to assess drug or alcohol use, with

Table 2. U.S. State Substance Use–Related Requirements for Sofosbuvir Approval*

Requirements Related to Substance Use	States, *n*	States
Unknown†	9	Georgia, Hawaii, Kansas, Michigan, New Jersey, North Dakota, New Mexico, South Carolina, and Texas
Inquires or has criteria related to substance use or abuse‡	37	All except Connecticut, Indiana, Nevada, Minnesota, and Utah
Requires counseling about abstention or effects of alcohol or drugs	6	Colorado; Maine; Mississippi; West Virginia; Washington, DC; and Montana
Requires all patients to be evaluated for a substance use disorder and/or alcohol dependence	8	California, Nebraska, Tennessee, Kentucky, New York, Vermont, Virginia, and Ohio
Requires a period of abstinence from drugs and/or alcohol use or abuse before treatment for all patients, regardless of history		
Time unknown	1	Ohio§
1 mo	2	Florida and Wyoming
3 mo	5	Alaska; Washington, DC; Delaware; Iowa; and Missouri
6 mo	11	Kentucky, Mississippi, Pennsylvania, South Dakota, West Virginia, Oregon, Alabama, Colorado, Wisconsin, Montana, and Oklahoma
12 mo	2	Louisiana‖ and Illinois
Requires a period of abstinence from drug and/or alcohol use or abuse only for persons with any history of abuse (past or recent) before HCV treatment		
3 mo	1	Washington¶
6 mo	8	Arizona**, California, Idaho, Washington**, Maryland, Nebraska, Tennessee, and Rhode Island
"Commitment to abstinence"	1	North Carolina††
Asks about or requires substance or alcohol use disorder treatment for persons with a history of abuse	17	Arkansas, California, Florida, Kentucky, Maryland, New Hampshire, Nebraska, North Carolina††, Pennsylvania, Rhode Island, Tennessee, Virginia, Washington, Montana, Wisconsin, Massachusetts, and Vermont
Allows persons to bypass abstinence or recent abuse if in treatment	6	California, Florida, Maryland, Nebraska, Rhode Island, and Washington‡‡
Requires persons with a history to be in, or have completed, treatment	3	Tennessee, Kentucky, and Virginia
Requires drug or alcohol testing before treatment		
For everyone	21	Alaska; California; Colorado; Washington, DC; Delaware; Florida; Hawaii; Illinois; Iowa; Kentucky; Louisiana; Missouri§§; Nebraska; New Hampshire; New York; Tennessee; Virginia; West Virginia; Wyoming; Oklahoma; and Vermont
Only for those with a history of abuse	6	Pennsylvania, Mississippi‖‖, Arizona¶¶, Idaho***, Louisiana***, and Colorado†††
Prior authorization form inquires about alcohol or substance use or abuse, but no particular requirements are apparent	4	Massachusetts, New York, New Hampshire, and Arkansas

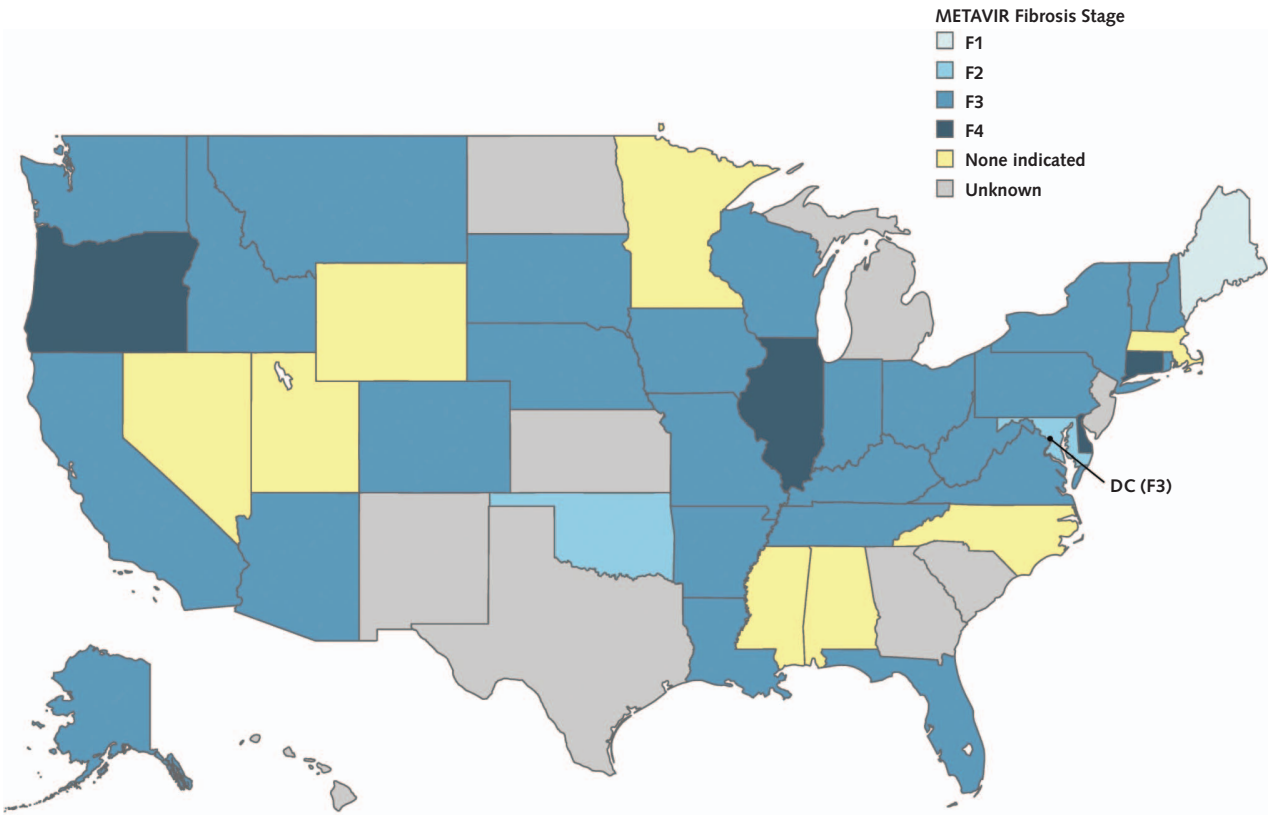
HCV = hepatitis C virus.
* When states are not included in a category, it is not certain whether they are providing or denying access to sofosbuvir on the basis of that limitation, only that there is not a written rule in their publicly reported policy.
† No prior authorization or criteria available.
‡ Some states in their abstention policies (either generally or for persons with past or current substance use) explicitly state that persons must refrain from alcohol or drug *abuse*, whereas others are more broad in requiring that persons abstain from alcohol or drug *use*.
§ Requires screening for and maintenance of sobriety before and during treatment.
‖ Illinois does not specifically reference a period of abstinence but instead broadly requires that a person "not have evidence of substance abuse diagnosis or treatment" in the past 12 mo. It is also the only state to include a long list of data sources that will be used for verification, including but not limited to medical record entries, the state's narcotic prescription registry database, reports from a hospital, and/or records of an emergency department visit.
¶ If in treatment, must have been in remission for 3 mo.
** Must have been in remission for 6 mo.
†† Alcohol only.
‡‡ If participating in treatment, abstinence requirement decreases to 3 mo.
§§ Within each of 3 previous mo.
‖‖ Injection drug use only.
¶¶ Random drug screens during treatment.
*** Monthly during treatment.
††† Routine during treatment.

only 6 (14%) requiring testing specifically for persons with previous drug or alcohol abuse. Six states permit persons enrolled in addiction treatment to bypass abstinence requirements. Further, 6 states require drug and alcohol counseling. Overall, 69% of states (*n* = 29) had restrictions based on advanced liver disease and drug or alcohol use criteria, 5% (*n* = 2) had restrictions based only on advanced liver disease, 19% (*n* = 8) had restrictions based only on drug or alcohol use criteria, and 7% (*n* = 3) had no restrictions on advanced liver disease nor drug or alcohol use criteria.

DISCUSSION

Considerable heterogeneity is present in Medicaid reimbursement criteria for sofosbuvir across the United States. Restrictions based on liver disease severity are common, with three quarters of states restricting sofos-

Figure 1. Medicaid reimbursement criteria for sofosbuvir based on documented level of liver fibrosis stage required for reimbursement.



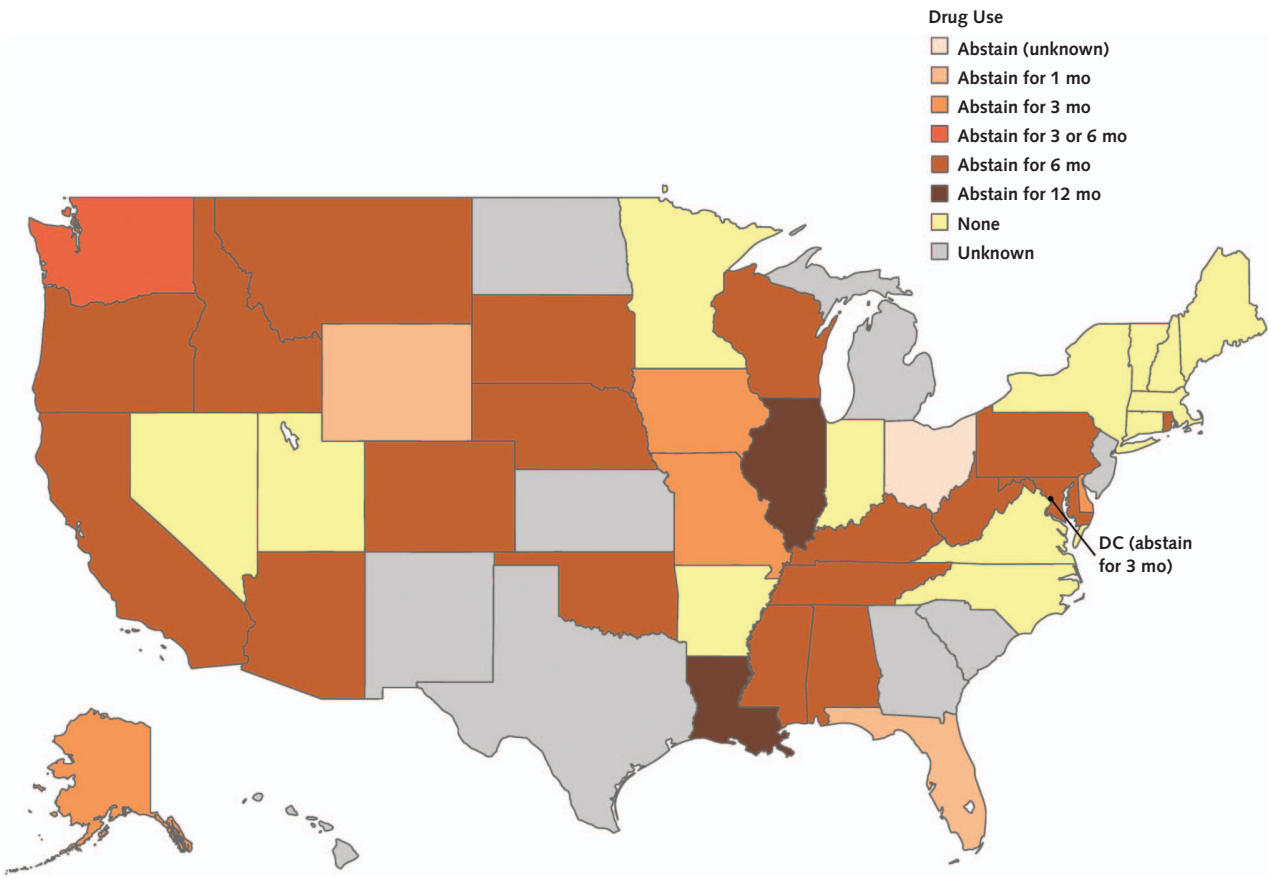
METAVIR = Meta-Analysis of Histologic Data in Viral Hepatitis.

buvir to persons with advanced fibrosis (F3) or cirrhosis (F4). One quarter of states require that persons living with HIV be receiving ART or have suppressed HIV RNA levels, whereas two thirds restrict sofosbuvir on the basis of prescriber type. Drug or alcohol use is included in the eligibility criteria of 88% of state Medicaid committees, with half requiring a period of abstinence and two thirds requiring urine drug screening. The restrictions are not consistent with the FDA-approved labeling for sofosbuvir or evidence-based recommendations and should be reconsidered (23).

Most states restrict sofosbuvir reimbursement to persons with advanced fibrosis (F3) or cirrhosis (F4), which is inconsistent with recent AASLD/IDSA recommendations (20). These recommendations state that HCV treatment is indicated for all patients with chronic HCV (regardless of disease stage) because HCV therapy is curative; improves quality of life; slows liver disease progression; and reduces the risk for cirrhosis, end-stage liver disease, HCC, and all-cause mortality (21). The recommendations state that patients at highest priority for immediate treatment include those with advanced fibrosis (F3) or compensated cirrhosis (F4) because of the higher risk for severe complications (for example, hepatic decompensation or HCC). Patients with fibrosis (F2) are listed in the next priority group for treatment because of their high risk for complications (21). However, most states do not include persons with fibrosis (F2) in their Medicaid reimbursement criteria. Note that persons with advanced fibrosis remain at risk for HCC even after achieving sustained virologic response (SVR) and must have long-term surveillance (24). In contrast, once HCV is cured in persons with mild to moderate liver disease, liver disease progression is rare. Requiring liver biopsy may pose the highest risk for death in HCV care with all-oral regimens.

The requirement that HIV-infected persons be receiving ART or have suppressed HIV RNA levels is also inconsistent with AASLD/IDSA recommendations indicating that persons co-infected with HIV and HCV are also at high priority for treatment because of their high risk for complications (21). HIV accelerates the HCV disease course, with faster progression to cirrhosis, liver failure, and increased HCV-related mortality (25–27). The safety and efficacy of sofosbuvir-based, interferon-free combination therapy for co-infected persons is similar to results among those with HCV monoinfection (21, 28, 29). Reasons are varied about why co-infected persons may not be receiving ART (for example, normal $CD4^+$ T-cell counts and low HIV RNA levels) or have suppressed HIV RNA levels (for example, drug-resistant HIV). Physicians who treat such co-infected persons

Figure 2. Medicaid reimbursement criteria for sofosbuvir based on the required period of abstinence from drug and alcohol use.



may prefer to commence and complete HCV treatment first, before ART initiation, because HCV therapy is brief; further, DAA therapy often limits what antiretrovirals can be used concomitantly because of drug–drug interactions.

Two thirds of states have restrictions based on physician type, which is inconsistent with current practice whereby internists, other primary care physicians, HIV physicians not trained as infectious diseases specialists, nurse practitioners, and physician assistants treat HCV with pegylated interferon and ribavirin. The availability of sofosbuvir-based, interferon-free regimens simplifies therapy and reduces treatment-associated toxicities, which offers an opportunity for an expanded provider base for HCV treatment in patients without advanced cirrhosis (30).

The overwhelming majority of states restrict access to sofosbuvir for persons who inject drugs (PWID), those receiving treatment for drug dependency (for example, opioid substitution therapy), and those drinking alcohol. Most new and existing cases of HCV in the United States exist among current or former PWID (31). Since 2002, the National Institutes of Health HCV guidelines support HCV treatment regardless of injection drug use (32), and the AASLD/IDSA, European Association for the Study of the Liver, International Network on Hepatitis in Substance Users, and World Health Organization all advocate for inclusion of persons who use drugs in HCV treatment (21, 33–35). A growing body of evidence shows that there is no justification for systematically withholding HCV treatment from PWID (21, 33, 36). The SVR rates are similar in PWID with or without opiate replacement therapy (21, 33, 36–39). Drug use in the 6 months preceding HCV therapy initiation is not necessarily associated with poorer response to HCV therapy (40–42). Reported rates of reinfection after SVR among PWID are low—generally a 1% to 5% risk per year, although concerns about reinfection rates in other subpopulations, such as surgeons, do not garner similar attention (33, 43). Rather than recommending the exclusion of PWID, AASLD/IDSA guidelines include PWID with earlier liver disease stages among a second-order priority group because of the prevention benefit of potential treatment; HCV treatment among PWID may decrease HCV transmission (21). In addition, evidence shows that HCV treatment of current and former PWID is cost-effective, particularly when the prevention benefits are consid-

ered (44). Further, Medicaid does not similarly deny medications for other diseases to persons who use or have used drugs or alcohol.

Alcohol misuse and HCV infection frequently coexist (45–48). Hepatitis C virus and alcohol act synergistically in causing more severe liver injury than seen with either disease alone (4, 48, 49). Persons with coexisting alcohol disorders are at a higher risk for HCV-related complications (4, 48, 49). Curing HCV is easier than curing alcohol disorders because pharmacotherapy for alcohol misuse is limited, and behavioral interventions are not always successful. The SVR rates are similar in drinkers and nondrinkers (49, 50).Further, the AASLD/IDSA recommendations have no HCV treatment restrictions regarding alcohol use.

This study examined criteria in Medicaid fee-for-service programs only—not in Medicaid managed care organizations. Results therefore reflect a subset of overall state Medicaid reimbursement criteria for sofosbuvir rather than a comprehensive catalog of all restrictions in state Medicaid programs. Future research on reimbursement criteria in Medicaid managed care organizations will be important to develop a more thorough understanding of Medicaid enrollees' access to sofosbuvir.

Current restrictions may violate federal Medicaid law, which requires states to cover drugs consistent with their FDA labels. Under the federal Medicaid statute, virtually all drugs from pharmaceutical manufacturers that have rebate agreements with the Secretary of Health and Human Services (which includes the manufacturer of sofosbuvir) must be available under state Medicaid programs, with only limited methods of restricting coverage (19). None of the restrictions on sofosbuvir coverage detailed here seem to meet the criteria for permissible restrictions. Although the price of new therapies creates financial challenges for federal and state Medicaid budgets, decisions for prioritizing patients for more immediate therapy should be based on clinical criteria and medical evidence. It is recommended that the restrictions be removed; apart from potentially being a human rights violation, they do not make (economic) sense in terms of clinical, public, and long-term health. In setting restrictions as a concession to economic constraints, the significant longer-term public health and economic benefits of curing HCV should be considered and weighed against the upfront treatment costs.

Concerns include that full coverage for HCV treatment could, in the short term, mean less coverage for other conditions. It is unrealistic, however, to expect that all potential candidates will immediately seek HCV treatment. One example of this is Massachusetts. Despite relatively unrestricted sofosbuvir access in its Medicaid fee-for-service program, recent data indicate that only 14% of Massachusetts Medicaid enrollees known to be diagnosed with HCV are engaged in treatment (22, 51).

Transparent, easily accessible, consistent, and evidence-based Medicaid criteria will permit greater and more equitable access to DAAs. As the HCV standard of care changes over time, it will be inefficient and costly to have differing treatment access protocols in the 51 fee-for-service programs and many more Medicaid managed care plans, with all of them being revised over time. More consistency is needed across the system so that where a Medicaid patient lives does not dictate what treatment she or he receives. Although this study examined sofosbuvir in particular, the first FDA-approved DAA as part of an interferon-free regimen, Medicaid may be setting a precedent as new DAAs are approved. Medicaid policies should be responsive to changes in standards of care and new treatment developments. State Medicaid pharmacy and therapeutics committees (or their equivalent) are generally responsible for implementing these policy changes and should be expected to act as expeditiously as possible to ensure that significant clinical changes are addressed in state Medicaid programs. These data suggest that state Medicaid policies for access to new DAAs should be reviewed and revised in line with national clinical recommendations.

From Brown University and The Miriam Hospital, Providence, Rhode Island; Harvard Law School, Cambridge, Massachusetts; University of New South Wales, Sydney, Australia; and Treatment Action Group, New York, New York.

Note: Dr. Taylor and Mr. Greenwald had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Dr. Taylor affirms that she has listed everyone who contributed significantly to the work. There was no involvement of any pharmaceutical company or commercial entity in the preparation of this work.

Disclaimer: The views expressed in this publication do not necessarily represent the position of the Australian government. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institute of Allergy and Infectious Diseases or the National Institutes of Health.

Acknowledgment: The authors thank Evan Cunningham (The Kirby Institute, University of New South Wales, Sydney, Australia) for his assistance with preparing the figures for this manuscript; Amy Rosenberg (Center for Health Law and Policy Innovation, Harvard Law School, Cambridge, Massachusetts) for her suggested edits; and Kellen Wittkop and Sam Hammond (Center for Health Law and Policy Innovation, Harvard Law School, Cambridge, Massachusetts) for assistance with data collection.

Financial Support: The Kirby Institute is funded by the Australian Government Department of Health and Ageing. Dr. Grebely is supported by a National Health and Medical Research Council Career Development Fellowship. Mr. Greenwald is supported by Harvard Law School. Dr. Taylor is supported by a Rhode Island Innovation Fellowship from the Rhode Island Foundation for her "Rhode Island Defeats Hep C" project and the Lifespan/Tufts/Brown Center for AIDS Research (grant P30AI042853 from the National Institute of Allergy and Infectious Diseases). Ms. Barua was supported by the Lifespan/Tufts/Brown Center for AIDS Research Summer Student Internship program (grant P30AI042853).

Disclosures: Disclosures can be viewed at www.acponline.org/authors/icmje/ConflictOfInterestForms.do?msNum=M15-0406.

Requests for Single Reprints: Lynn E. Taylor, MD, Department of Medicine, Division of Infection Diseases, The Warren Alpert Medical School of Brown University, The Miriam Hospital, 164 Summit Avenue, Center for AIDS Research Building, Room 156, Providence, RI; e-mail, LTaylor@Lifespan.org.

Current author addresses and author contributions are available at www.annals.org.

References

1. **Gower E, Estes C, Blach S, Razavi-Shearer K, Razavi H.** Global epidemiology and genotype distribution of the hepatitis C virus infection. J Hepatol. 2014;61:S45-57. [PMID: 25086286] doi:10.1016/j.jhep.2014.07.027
2. **Mohd Hanafiah K, Groeger J, Flaxman AD, Wiersma ST.** Global epidemiology of hepatitis C virus infection: new estimates of age-specific antibody to HCV seroprevalence. Hepatology. 2013;57:1333-42. [PMID: 23172780] doi:10.1002/hep.26141
3. **Grebely J, Dore GJ.** What is killing people with hepatitis C virus infection? Semin Liver Dis. 2011;31:331-9. [PMID: 22189973] doi:10.1055/s-0031-1297922
4. **Hajarizadeh B, Grebely J, Dore GJ.** Epidemiology and natural history of HCV infection. Nat Rev Gastroenterol Hepatol. 2013;10:553-62. [PMID: 23817321] doi:10.1038/nrgastro.2013.107
5. **van der Meer AJ, Veldt BJ, Feld JJ, Wedemeyer H, Dufour JF, Lammert F, et al.** Association between sustained virological response and all-cause mortality among patients with chronic hepatitis C and advanced hepatic fibrosis. JAMA. 2012;308:2584-93. [PMID: 23268517] doi:10.1001/jama.2012.144878
6. **Volk ML, Tocco R, Saini S, Lok AS.** Public health impact of antiviral therapy for hepatitis C in the United States. Hepatology. 2009;50:1750-5. [PMID: 19824079] doi:10.1002/hep.23220
7. **Lettmeier B, Mühlberger N, Schwarzer R, Sroczynski G, Wright D, Zeuzem S, et al.** Market uptake of new antiviral drugs for the treatment of hepatitis C. J Hepatol. 2008;49:528-36. [PMID: 18682313] doi:10.1016/j.jhep.2008.04.021
8. **Butt AA, Justice AC, Skanderson M, Rigsby MO, Good CB, Kwoh CK.** Rate and predictors of treatment prescription for hepatitis C. Gut. 2007;56:385-9. [PMID: 17005764]
9. **Lawitz E, Sulkowski MS, Ghalib R, Rodriguez-Torres M, Younossi ZM, Corregidor A, et al.** Simeprevir plus sofosbuvir, with or without ribavirin, to treat chronic infection with hepatitis C virus genotype 1 in non-responders to pegylated interferon and ribavirin and treatment-naive patients: the COSMOS randomised study. Lancet. 2014;384:1756-65. [PMID: 25078309] doi:10.1016/S0140-6736(14)61036-9
10. **Nelson DR, Cooper JN, Lalezari JP, Lawitz E, Pockros PJ, Gitlin N, et al; ALLY-3 Study Team.** All-oral 12-week treatment with daclatasvir plus sofosbuvir in patients with hepatitis C virus genotype 3 infection: ALLY-3 phase III study. Hepatology. 2015;61:1127-35. [PMID: 25614962] doi:10.1002/hep.27726
11. **Afdhal N, Reddy KR, Nelson DR, Lawitz E, Gordon SC, Schiff E, et al; ION-2 Investigators.** Ledipasvir and sofosbuvir for previously treated HCV genotype 1 infection. N Engl J Med. 2014;370:1483-93. [PMID: 24725238] doi:10.1056/NEJMoa1316366
12. **Jacobson IM, Gordon SC, Kowdley KV, Yoshida EM, Rodriguez-Torres M, Sulkowski MS, et al; POSITRON Study.** Sofosbuvir for hepatitis C genotype 2 or 3 in patients without treatment options. N Engl J Med. 2013;368:1867-77. [PMID: 23607593] doi:10.1056/NEJMoa1214854
13. **Kowdley KV, Gordon SC, Reddy KR, Rossaro L, Bernstein DE, Lawitz E, et al; ION-3 Investigators.** Ledipasvir and sofosbuvir for 8 or 12 weeks for chronic HCV without cirrhosis. N Engl J Med. 2014;370:1879-88. [PMID: 24720702] doi:10.1056/NEJMoa1402355
14. **Lawitz E, Mangia A, Wyles D, Rodriguez-Torres M, Hassanein T, Gordon SC, et al.** Sofosbuvir for previously untreated chronic hepatitis C infection. N Engl J Med. 2013;368:1878-87. [PMID: 23607594] doi:10.1056/NEJMoa1214853
15. **Reau NS, Jensen DM.** Sticker shock and the price of new therapies for hepatitis C: is it worth it? [Editorial]. Hepatology. 2014;59:1246-9. [PMID: 24493069] doi:10.1002/hep.27039
16. **Centers for Medicare & Medicaid Services.** Medicaid drug rebate program. Accessed at www.medicaid.gov/medicaid-chip-program-information/by-topics/benefits/prescription-drugs/medicaid-drug-rebate-program.html on 10 February 2015.
17. **Henry J. Kaiser Family Foundation.** State health facts: Medicaid income eligibility limits for adults as a percent of the federal poverty level. Menlo Park, CA: Henry J. Kaiser Family Foundation; 2015. Accessed at kff.org/health-reform/state-indicator/medicaid-income-eligibility-limits-for-adults-as-a-percent-of-the-federal-poverty-level on 8 April 2015.
18. **Office of the Assistant Secretary for Planning and Evaluation; U.S. Department of Health and Human Services.** 2015 poverty guidelines. Accessed at aspe.hhs.gov/poverty/15poverty.cfm on 8 April 2015.
19. 42 U.S.C. § 1396r–8. Payment for covered outpatient drugs: requirements for formularies. Accessed at www.law.cornell.edu/uscode/text/42/1396r-8 on 9 June 2015.
20. 42 C.F.R. § 440.230. Sufficiency of amount, duration, and scope. Accessed at www.law.cornell.edu/cfr/text/42/440.230 on 9 June 2015.
21. **American Association for the Study of Liver Diseases; Infectious Diseases Society of America.** Recommendations for testing, managing, and treating hepatitis C. Accessed at www.hcvguidelines.org on 18 January 2015.
22. **Arora S, Thornton K, Murata G, Deming P, Kalishman S, Dion D, et al.** Outcomes of treatment for hepatitis C virus infection by primary care providers. N Engl J Med. 2011;364:2199-207. [PMID: 21631316] doi:10.1056/NEJMoa1009370
23. **Gilead Sciences.** Sovaldi [package insert]. Foster City, CA: Gilead Sciences; 2014. Accessed at www.gilead.com/~/media/Files/pdfs/medicines/liver-disease/sovaldi/sovaldi_pi.pdf on 14 April 2015.
24. **Aleman S, Rahbin N, Weiland O, Davidsdottir L, Hedenstierna M, Rose N, et al.** A risk for hepatocellular carcinoma persists long-term after sustained virologic response in patients with hepatitis C-associated liver cirrhosis. Clin Infect Dis. 2013;57:230-6. [PMID: 23616492] doi:10.1093/cid/cit234
25. **Lo Re V 3rd, Kallan MJ, Tate JP, Localio AR, Lim JK, Goetz MB, et al.** Hepatic decompensation in antiretroviral-treated patients co-infected with HIV and hepatitis C virus compared with hepatitis C virus-monoinfected patients: a cohort study. Ann Intern Med. 2014;160:369-79. [PMID: 24723077] doi:10.7326/M13-1829
26. **Chen TY, Ding EL, Seage Iii GR, Kim AY.** Meta-analysis: increased mortality associated with hepatitis C in HIV-infected persons is unrelated to HIV disease progression. Clin Infect Dis. 2009;49:1605-15. [PMID: 19842982] doi:10.1086/644771
27. **Weber R, Sabin CA, Friis-Møller N, Reiss P, El-Sadr WM, Kirk O, et al.** Liver-related deaths in persons infected with the human immunodeficiency virus: the D:A:D study. Arch Intern Med. 2006;166:1632-41. [PMID: 16908797]
28. **European Association for the Study of the Liver.** EASL Clinical Practice Guidelines: management of hepatitis C virus infection. J Hepatol.2014;60:392-420.[PMID:24331294]doi:10.1016/j.jhep.2013.11.003
29. **Sulkowski MS, Naggie S, Lalezari J, Fessel WJ, Mounzer K, Shuhart M, et al; PHOTON-1 Investigators.** Sofosbuvir and ribavirin for hepatitis C in patients with HIV coinfection. JAMA. 2014;312:353-61. [PMID: 25038354] doi:10.1001/jama.2014.7734
30. **Kottilil S, Wright M, Polis MA, Masur H.** Treatment of hepatitis C virus infection: is it time for the internist to take the reins? Ann Intern Med. 2014;161:443-4. [PMID: 25222390] doi:10.7326/M14-0741

31. **Williams I.** Epidemiology of hepatitis C in the United States. Am J Med. 1999;107:2S-9S. [PMID: 10653448]
32. **U.S. Department of Health and Human Services; National Institutes of Health; NIH Consensus Development Program; Office of Disease Prevention.** Management of Hepatitis C: 2002: National Institutes of Health consensus conference statement, 10–12 June 2002. Accessed at consensus.nih.gov/2002/2002hepatitisc2002116html.htm on 19 December 2014.
33. **Robaeys G, Grebely J, Mauss S, Bruggmann P, Moussalli J, De Gottardi A, et al; International Network on Hepatitis in Substance Users.** Recommendations for the management of hepatitis C virus infection among people who inject drugs. Clin Infect Dis. 2013;57 Suppl 2:S129-37. [PMID: 23884061] doi:10.1093/cid/cit302
34. **European Association for the Study of the Liver.** EASL recommendations on treatment of hepatitis C 2014. J Hepatol. 2014;61:373-95. [PMID: 24818984] doi:10.1016/j.jhep.2014.05.001
35. **World Health Organization.** Guidelines for the screening, care and treatment of persons with hepatitis C infection: April 2014. Accessed at apps.who.int/iris/bitstream/10665/111747/1/9789241548755_eng.pdf on 18 December 2014.
36. **European Association for the Study of the Liver.** EASL Clinical Practice Guidelines: management of hepatitis C virus infection. J Hepatol. 2011;55:245-64. [PMID: 21371579] doi:10.1016/j.jhep.2011.02.023
37. **Hellard M, Sacks-Davis R, Gold J.** Hepatitis C treatment for injection drug users: a review of the available evidence. Clin Infect Dis. 2009;49:561-73. [PMID: 19589081] doi:10.1086/600304
38. **Mauss S, Berger F, Goelz J, Jacob B, Schmutz G.** A prospective controlled study of interferon-based therapy of chronic hepatitis C in patients on methadone maintenance. Hepatology. 2004;40:120-4. [PMID: 15239094]
39. **Matthews G, Kronborg IJ, Dore GJ.** Treatment for hepatitis C virus infection among current injection drug users in Australia. Clin Infect Dis. 2005;40 Suppl 5:S325-9. [PMID: 15768342]
40. **Sylvestre DL, Litwin AH, Clements BJ, Gourevitch MN.** The impact of barriers to hepatitis C virus treatment in recovering heroin users maintained on methadone. J Subst Abuse Treat. 2005;29:159-65. [PMID: 16183464]
41. **Grebely J, Raffa JD, Meagher C, Duncan F, Genoway KA, Khara M, et al.** Directly observed therapy for the treatment of hepatitis C virus infection in current and former injection drug users. J Gastroenterol Hepatol. 2007;22:1519-25. [PMID: 17645460]
42. **Dore GJ, Hellard M, Matthews GV, Grebely J, Haber PS, Petoumenos K, et al; Australian Trial In Acute Hepatitis C Study Group.** Effective treatment of injecting drug users with recently acquired hepatitis C virus infection. Gastroenterology. 2010;138:123-35.e1-2. [PMID: 19782085] doi:10.1053/j.gastro.2009.09.019
43. **Aspinall EJ, Corson S, Doyle JS, Grebely J, Hutchinson SJ, Dore GJ, et al.** Treatment of hepatitis C virus infection among people who are actively injecting drugs: a systematic review and meta-analysis. Clin Infect Dis. 2013;57 Suppl 2:S80-9. [PMID: 23884071] doi:10.1093/cid/cit306
44. **Martin NK, Vickerman P, Miners A, Foster GR, Hutchinson SJ, Goldberg DJ, et al.** Cost-effectiveness of hepatitis C virus antiviral treatment for injection drug user populations. Hepatology. 2012;55:49-57. [PMID: 21898506] doi:10.1002/hep.24656
45. **Singal AK, Anand BS.** Mechanisms of synergy between alcohol and hepatitis C virus. J Clin Gastroenterol. 2007;41:761-72. [PMID: 17700425]
46. **Rosman AS, Waraich A, Galvin K, Casiano J, Paronetto F, Lieber CS.** Alcoholism is associated with hepatitis C but not hepatitis B in an urban population. Am J Gastroenterol. 1996;91:498-505. [PMID: 8633498]
47. **Hutchinson SJ, Bird SM, Goldberg DJ.** Influence of alcohol on the progression of hepatitis C virus infection: a meta-analysis. Clin Gastroenterol Hepatol. 2005;3:1150-9. [PMID: 16271348]
48. **Corrao G, Aricò S.** Independent and combined action of hepatitis C virus infection and alcohol consumption on the risk of symptomatic liver cirrhosis. Hepatology. 1998;27:914-9. [PMID: 9537428]
49. **Anand BS, Currie S, Dieperink E, Bini EJ, Shen H, Ho SB, et al; VA-HCV-001 Study Group.** Alcohol use and treatment of hepatitis C virus: results of a national multicenter study. Gastroenterology. 2006;130:1607-16. [PMID: 16697724]
50. **Le Lan C, Guillygomarc'h A, Danielou H, Le Dréau G, Lainé F, Védeilhié C, et al.** A multi-disciplinary approach to treating hepatitis C with interferon and ribavirin in alcohol-dependent patients with ongoing abuse. J Hepatol. 2012;56:334-40. [PMID: 21756854] doi:10.1016/j.jhep.2011.05.021
51. **Graham CS, Greenwald R, Lenz K.** Understanding the reimbursement environment in hepatitis C. Presented at Massachusetts Department of Public Health, Boston, Massachusetts, 6 April 2015. Accessed at www.chlpi.org/wp-content/uploads/2014/01/HCV_DPH_Payer_4_5_15_combined_final.pdf on 8 June 2015.

Current Author Addresses: Ms. Barua: Brown University, 69 Brown Street, Box 2222, Providence, RI 02912.
Mr. Greenwald: Center for Health Law and Policy Innovation, Harvard Law School, 122 Boylston Street, Jamaica Plain, MA 02130.
Drs. Grebely and Dore: The Kirby Institute, University of New South Wales, Wallace Wurth Building, Sydney New South Wales 2052, Australia.
Ms. Swan: Treatment Action Group, 611 Broadway, Suite 308, New York, NY 10012.
Dr. Taylor: Department of Medicine, Division of Infectious Diseases, The Warren Alpert Medical School of Brown University, The Miriam Hospital, 164 Summit Avenue, Center for AIDS Research Building, Room 156, Providence, RI 02906.

Author Contributions: Conception and design: J. Grebely, L.E. Taylor.
Analysis and interpretation of the data: S. Barua, R. Greenwald, J. Grebely, G.J. Dore, T. Swan, L.E. Taylor.
Drafting of the article: S. Barua, R. Greenwald, J. Grebely, T. Swan, L.E. Taylor.
Critical revision of the article for important intellectual content: J. Grebely, G.J. Dore, Swan T, L.E. Taylor.
Final approval of the article: S. Barua, R. Greenwald, J. Grebely, G.J. Dore, T. Swan, L.E. Taylor.
Statistical expertise: S. Barua, J. Grebely.
Obtaining of funding: S. Barua, L.E. Taylor.
Administrative, technical, or logistic support: S. Barua, J. Grebely, L.E. Taylor.
Collection and assembly of data: S. Barua, R. Greenwald, J. Grebely, L.E. Taylor.