Published in final edited form as:

J Viral Hepat. 2016 September ; 23(9): 664–666. doi:10.1111/jvh.12550.

Addressing reimbursement disparities for direct-acting antiviral therapies for hepatitis C virus infection is essential to ensure access for all

J. Grebely¹, A. Litwin², G. J. Dore¹

¹The Kirby Institute, UNSW Australia, Sydney, NSW, Australia;

²Division of General Internal Medicine, Department of Medicine, Albert Einstein College of Medicine and Montefiore Medical Center, Bronx, NY, USA

The development of well-tolerated, simple and highly efficacious interferon-free direct-acting antiviral (DAA) therapies for hepatitis C virus (HCV) infection is one of the greatest medical advances in recent decades [1], providing an opportunity to reverse the rising burden of advanced liver disease [2].

The high pricing and demand of direct-acting antiviral (DAA) regimens has led to many payers in the United States and other countries to restrict reimbursement access and reduce the impact on healthcare budgets [3]. In the United States, the majority of State Medicaid Committees require evidence of advanced fibrosis/cirrhosis (Stage F3–F4) and recent abstinence from illicit drugs, injecting drugs and alcohol (with the definitions of ‘use’ varying by jurisdiction) for reimbursement of DAA hepatitis C virus (HCV) therapies [3]. This is inconsistent with international clinical recommendations that treatment is indicated for people with HCV at all disease stages [4,5]. Further, rather than recommending exclusion of people who inject drugs (PWID), these recommendations in fact include PWID with earlier liver disease stages among a second-order priority group due to potential HCV treatment as prevention benefit [4,5].

In this issue of JVH, Younossi *et al.* [6] evaluated reasons for not starting sofosbuvir-based regimens among individuals prescribed HCV therapy between December 2013 and September 2014 in large network of specialty pharmacies and participating academic and community physicians in the United States (Trio Health Network). Among 3841 individuals prescribed a sofosbuvir-containing regimen, 8% ($n = 315$) did not start the prescribed therapy. Treatment initiation was lower among people receiving Medicaid insurance (65%) compared to those receiving commercial (94%) or Medicare (98%) coverage. Among those who did not start therapy, 81% of nonstarts were attributed to insurance-related processes and financial reasons, despite 27% of individuals having evidence of advanced liver disease (F3), a group which should be prioritized for therapy. Although individuals receiving Medicaid comprised only 10% of the total population, they accounted for 43% of people who did not start therapy. The major reasons for insurance denial in those receiving

Medicaid included missing/failed testing for illicit drugs (26%) and financial/insurance reasons (55%). It is also possible that those who were listed as being in the appeal process (18% in the Medicaid population) could have also being denied on the basis of illicit drugs. Further, some of the physician-directed non-starts may have been due to concerns around illicit drug use. As such, inappropriate restrictive reimbursement criteria could be having the effect of reinforcing or educating providers about incorrect practices. This study is important in highlighting the reimbursement barriers that are in place in the ‘real world’ among people seeking access to DAA HCV therapies. These findings are particularly concerning given that underserved populations with low socio-economic status, such as PWID, are most likely to require Medicaid, are disproportionately affected by HCV infection [7,8], have a rising burden of disease [9] and often have a number of other barriers to initiating therapy [10].

There are three explanations for the high proportion with insurance denial in this study, including (i) providers are unaware of the reimbursement restrictions and data submission requirements (given criteria vary widely between states); (ii) providers do not submit the complete data initially; (iii) providers disagree with the restrictions and submit the data knowing that the script is not likely to be authorized, but that there may be an opportunity for appeal based on further information (which is sometimes successful, but very time consuming). It would have been interesting if the authors had assessed the proportion of people with insurance denial due to missing/failed drug tests and financial/insurance reasons in those with advanced disease, who would have otherwise been eligible to receive therapy.

There are several factors that are required to address barriers related to the reimbursement of HCV therapies in other countries to enable access for all, including people who are highly marginalized (e.g., PWID).

First, reductions in prices for HCV regimens will be required to enable broadened access. As the initial introduction of HCV therapies in clinical practice, there have been substantial discounts to the list prices for available DAA HCV therapies which have been negotiated with payers. It is likely that further drug discounting, particularly in the context of a competitive pharmaceuticals market, should facilitate the loosening of reimbursement restrictions over the next decade. However, in the United States, Medicare cannot negotiate directly with pharmaceutical companies, making discounting in this setting problematic. As such, changes in government legislation may be required to ensure that people receiving Medicare, who are often the poorest and socially marginalized, are able to access therapies through loosened restrictions.

Second, greater advocacy is needed to convince policy makers to change reimbursement guidelines to remove restrictions based on drug- and alcohol-use criteria. As has previously been highlighted, it is unethical to withhold HCV treatment from people who use drugs [11]. Justifications for these restrictions that have been given are that people who use or inject drugs and those with alcohol misuse cannot adhere to the treatment regime; that they have worse outcomes than other patients at comparable disease stages; a higher likelihood of HCV re-infection; and that there is a lack of data on treatment outcomes with the new interferon-free HCV therapies in this population. However, these reasons are not based on evidence and are unjust [11]. Interferon-based HCV therapy [12–14] and interferon-free

DAA therapy [15–19] are effective in people with a history of injecting drug use, people receiving OST and people with recent or ongoing injecting drug use. Among participants receiving the once-daily DAA therapy of grazoprevir/elbasvir in the C-EDGE CO-STAR study ($n = 201$), 91.5% achieved an SVR and 95.5% had >95% adherence to therapy, despite almost half of people having ongoing drug use at baseline and during therapy [18]. Ongoing drug use at baseline or during therapy had no impact on response to therapy or adherence [18]. As highlighted in the AASLD/IDSA guidelines, ‘there is no data to support the utility of pretreatment screening for illicit drug or alcohol use to identify a population more likely to successfully complete HCV therapy. These requirements should be abandoned, because they create barriers to treatment, and unnecessary cost and effort, and potentially exclude populations that are likely to obtain substantial benefits from therapy. Scale up of HCV treatment in persons who inject drugs is necessary to positively impact the HCV epidemic in the United States and globally’.

Third, a strong commitment and leadership from government and policy makers is required to continue to ensure that viral hepatitis is part of a broader public health strategy towards the elimination of viral hepatitis. In Australia, in what has been coined a ‘watershed moment’ in Australian medical history, on 1 March 2016, Australia became the first country in the world to make new DAA HCV therapies available to all patients, without restrictions based on disease stage or recent drug use and involving general practitioners in prescribing. The broad availability of DAA therapies enables Australia to be a global leader in addressing the public health impact of HCV and serves as a model for other settings. A similar commitment from other countries internationally is urgently needed.

Addressing disparities based on reimbursement for DAA therapies will require partnerships between pharmaceutical companies, providers, governments, researchers and the community to ensure access for all to address the burden of HCV and work towards global HCV elimination.

FINANCIAL SUPPORT

The Kirby Institute is funded by the Australian Government Department of Health and Ageing. The views expressed in this publication do not necessarily represent the position of the Australian Government. JG is supported by a National Health and Medical Research Council Career Development Fellowship. GD is supported by a National Health and Medical Research Council Practitioner Research Fellowships.

DISCLOSURES

JG is a consultant/advisor and has received research grants from AbbVie, Bristol Myers Squibb, Gilead Sciences and Merck. GD is a consultant/advisor and has received research grants from Abbvie, Bristol Myers Squibb, Gilead, Merck, Janssen and Roche. AL is a consultant/advisor and has received research grants from Gilead Sciences, Merck, Janssen and Bristol Myers Squibb.

Abbreviations:

DAA	direct-acting antiviral
HCV	hepatitis C virus
PWID	people who inject drugs

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