

# Access to treatment for hepatitis C virus infection: time to put patients first



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Sound health policy puts patients first. Antiviral regimens approved in 2014 revolutionised treatment of hepatitis C virus (HCV) infection. Most patients can now be cured. These new regimens, however, were priced at US\$83 320–150 000 for a 3-month course. Public and private payers in the USA responded by limiting coverage to patients with advanced fibrosis or cirrhosis, keeping the drugs from being used to prevent those stages. These restrictions defy medical guidelines, lack scientific justification, and undermine public health efforts to stem transmission. Instead of reducing barriers to care, the system has erected new ones. As drug makers and payers battle over billions of dollars, the needs of patients have been cast aside. Physicians and governments have a duty to make sure health policy is driven by the needs of patients and public health. In this Personal View, I call upon these groups to lead the creation of a national consensus among all stakeholders that will allow the advances in therapeutics for HCV infection to be put to work to end the epidemic.

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## Introduction

2014 was a watershed year in the history of medicine. 70 years ago the discovery of penicillin heralded a new treatment era in which dreaded, often fatal, bacterial infections could readily be vanquished. Viral infections, however, remained incurable. Now, however, many lifelong and often fatal viral infections can be easily cured. Three highly effective oral regimens that clear hepatitis C virus (HCV) in nearly all patients were approved by the Food and Drug Administration for use in the USA in 2014.<sup>1</sup> HCV infection is the largest blood-borne viral epidemic in the USA, causes more deaths than HIV, and is the leading cause of cirrhosis, liver cancer, liver failure, and deaths from liver disease.<sup>1-3</sup> Treatment can prevent cirrhosis, liver failure, hepatocellular carcinoma, liver transplantation, and death, and can cure extrahepatic manifestations, relieve symptoms, and improve quality of life.<sup>4</sup> The ability to eradicate infection in nearly all infected people has made the prospect of eliminating HCV in high-income countries such as the USA plausible.<sup>5,6</sup>

As soon as these new therapies appeared, however, jubilation turned to frustration. Public and private payers restricted coverage to the sickest patients with advanced hepatic fibrosis or cirrhosis.<sup>7-10</sup> These restrictions closed off hope of using the drugs to prevent cirrhosis, stem transmission, and end the epidemic. The drugs' promise remained unfulfilled.

The rationing of curative medical treatment for an often fatal, communicable disease is a myopic policy and is counterproductive for patients and health systems. In this Personal View, I argue that physicians and governments have a responsibility to make sure that health policy is determined by the needs of the public, not the financial interests of rich organisations. These groups must lead the development of a national consensus—and enjoin the commitment of all stakeholders—to put the striking advances in therapeutics to work to end the hepatitis C epidemic. Drug makers and insurers must compromise to make this happen, but to do so neither need abandon their mission.

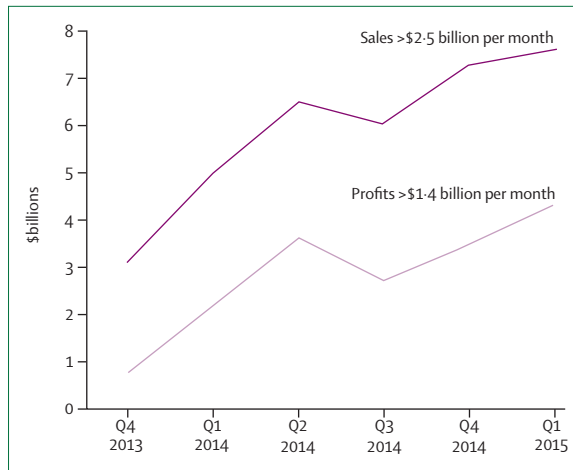
## A crisis of access

The impasse in access to new HCV treatments is the result of the system for financing drugs in the USA. The US Government grants patents to pharmaceutical companies to foster innovation in the development of drugs to benefit the public. The companies may charge whatever they please for new products, without interference from either government regulation or the free market. The list prices for 12-week regimens for HCV genotype 1 range from US\$83 320 to \$94 500, and even up to \$147 000 for daclatasvir plus sofosbuvir. At least a quarter of patients might need 24 weeks of treatment.<sup>11</sup>

Payers denounced the prices, declaring them patently unaffordable and refused to cover the drugs except for patients with the most advanced disease. For instance, the nation's two largest private insurers restricted payments to patients with advanced fibrosis (Metavir stage F3) or cirrhosis (stage F4), among other restrictions.<sup>7,8</sup> While these actions protected the insurers' bottom lines, it inflicted no pain on the drug companies. Prices did not change and record profits were reaped in 2014 (figure).<sup>12</sup> Rather, patients were caught in the crossfire and denied treatments that are cheap to manufacture<sup>13</sup> and deliver a safe, quick, easy cure.<sup>1</sup>

State Medicaid programmes have been especially aggressive at erecting barriers to treatment.<sup>9,10</sup> Most restrict coverage to patients who already have extensive liver damage, many require patients to submit urine samples to prove they do not use illicit drugs or alcohol, and some deny antiviral therapy to patients who have previously received a diagnosis of or treatment for substance misuse.<sup>9</sup> Six states require patients to undergo liver biopsy as a condition of treatment,<sup>9</sup> which is medically unnecessary and not for the patient's benefit.

None of these policies has medical justification. Evidence clearly supports treatment in nearly all people with HCV infection, irrespective of fibrosis<sup>1</sup> or substance misuse.<sup>1,14-17</sup> Treating all patients is cost-effective, even at full price, compared with treating only the sickest patients.<sup>18</sup> Selective denial of medically necessary care for



**Figure: Sales and profits for new hepatitis C virus drugs<sup>12</sup>**

Companies' pricing decisions served their own financial interests at the expense of patients' wellbeing.

high-cost conditions is discriminatory,<sup>19</sup> illegal under the Affordable Care Act,<sup>20</sup> and a violation of Federal Medicaid law (42 U.S.C. § 1396r-8[d]).<sup>21</sup> The Obama administration has said that it will investigate insurance companies that discriminate in this way.<sup>19,20</sup> Yet, there will be little appetite for forcing financially strapped Medicaid programmes to pay billions more to pharmaceutical companies already making large profits.<sup>12</sup>

Competition between pharmaceutical companies has brought prices down to some degree, but they are unlikely to fall to the supply-demand nexus. If the market operated freely, prices would fall by several orders of magnitude: one study found that a drug priced at \$1000 per pill could be produced for \$1–20.<sup>13</sup> AbbVie's decision to price its new regimen just 12% below Gilead's illustrates how small an effect competition can have on pricing in oligopoly markets. Pricing in such markets reflects an arrangement that has been called a gentleman's agreement<sup>22</sup> or, more technically, mutual forbearance.<sup>23</sup> In vying for market share, the two manufacturers have offered discounts and rebates. Gilead said they would give an average discount of 46% in 2015,<sup>24</sup> although how far prices actually fell is unknown because all negotiations are secret. Merck's new regimen, though, which was approved on Jan 28, 2016, had a list price 48% lower than that of Gilead's, and is widely believed to match the discounted Gilead and AbbVie prices. These reductions will certainly allow more patients to be treated, but even 50% reductions of the original very high prices will not make the drugs available to all who need them. The availability of a new regimen at the price already being paid for older regimens will not alter the fiscal landscape unless further discounts are offered.

### Rationing of treatment

The pricing and payer restrictions effectively mean that the US health-care system has, for the first time, widely

adopted a policy of rationing curative medical treatment for a life-threatening communicable disease. By following this policy, drugs are being withheld from millions of people in the USA. Most patients who previously could have been treated no longer can. Onerous preauthorisation processes, requiring extensive documentation, multiple appeals, and ever-increasing hours of provider time, along with the knowledge that many patients will ultimately be denied anyway, dissuade many doctors and patients from trying to obtain treatment for HCV infection or even from screening for it. When coverage is approved, the copay (the charge to the customer) is often prohibitive. Thus, for most patients, HCV infection is now only hypothetically curable.

As a consequence, health systems and community and public health organisations have been deterred from embarking on initiatives to screen for HCV infection. Marginalised populations, such as ethnic minorities, socioeconomically disadvantaged groups, and people with histories of incarceration, mental health disorders, homelessness, or substance misuse, are already disproportionately affected by HCV infection.<sup>25</sup> Compounding this issue, a study of 2321 patients in four states showed that 46% were denied Medicaid payments for HCV therapy, even after appeal, compared with 10% of patients who had private insurance.<sup>26</sup> The net effect—as morbidity and mortality fall among patients with better coverage and access to high-quality care, while the indigent and those with poor access to health care go without treatment—will be sharply widening inequities in morbidity and mortality from HCV.

A policy of rationing demands rigorous examination of its ethical and budgetary underpinnings, but in the case of HCV treatment, these remain to be produced for public scrutiny. It is not sufficient, as some have done,<sup>27,28</sup> to multiply the estimated number of people with HCV infection by the list price of the drugs, and to compare the result with annual pharmacy budgets, for five reasons. First, treatment for HCV infection is a one-time expenditure, not an annual one. If the whole cost were incurred in 1 year, it would fall to zero the following year. Second, the expenditure is likely to be spread out over at least 5–10 years. Most people are unaware they are infected with HCV and will not find out within 1 year's time because many people do not see a doctor every year and because many physicians are unaware of the screening guidelines<sup>29,30</sup> or do not follow them. Third, most patients, once they test positive, do not complete the process from diagnosis to referral to specialty care to starting treatment to achieving cure.<sup>31</sup> Fourth, the groups disproportionately affected by HCV infection have substantial barriers to accessing health care. And, fifth, drug prices have been discounted substantially. One analysis that assumed an average drug discount of only 11% estimated the cost of treating all patients identified by risk-based and birth-cohort screening at \$136 billion over 5 years.<sup>32</sup> This amount is similar to the US health-care

expenditures for HIV care, and is less than 1% of the total US health-care expenditure, which now exceeds \$3 trillion annually. After this amount had been spent, the bulk of the epidemic would have been eliminated, meaning that disease burden and expense would fall off sharply. Additionally, use of drugs to interrupt transmission now would reduce the disease burden and costs associated with infections that would be prevented. Thus, payer rationing is as indefensible as predatory pricing.

### Price versus cost

Triage of patients by physicians is also not a solution. As stewards of health-care resources, physicians must limit expenditure on costly interventions of low or uncertain value. In the case of HCV infection, it has been argued that physicians have a duty to select which patients will receive treatment.<sup>33</sup> But, the value of HCV treatments is not low or uncertain. Additionally, while cost and price are often conflated, they are not the same. Cost is a characteristic of an intervention that cannot be changed much without new methods or technologies. It requires sacrifice by society because the resources spent cannot be used for anything else. By contrast, price is a decision made independently of the costs of developing or manufacturing a drug<sup>34</sup> and can be changed at will. It does not represent any sacrifice by society. Rather, it is a mechanism for determining how much money will be transferred from one sector of society to another; in the case of drugs, this is from patients, insurers, and the public to pharmaceutical manufacturers. HCV treatment is pricey, not costly. Production costs are almost negligible.<sup>35</sup> The value to patients and society, however, is substantial.<sup>34</sup> Withholding treatment from patients harms them in order to accommodate the financial stand-off between pharmaceutical companies and payers.

### Non-voluntary licensing

Payers and drug makers could negotiate prices that would allow everyone infected to be treated, assuring the largest possible market for the drugs and freeing doctors and public health programmes to initiate efforts to end the epidemic. With drug manufacturers making more than \$1 billion per month and insurers protecting their exposure by restricting access, however, neither group has much incentive to change the status quo or has shown any great interest in doing so. Both sides have been willing to sacrifice patients' wellbeing to achieve financial benefit for themselves.

But we need not accept the status quo. Doctors can, and have, influenced drug prices. When three leading oncologists publicly decried the price of a new cancer drug,<sup>35</sup> the manufacturer dropped the price by half.<sup>36</sup> Large price hikes for pyrimethamine and cycloserine were reversed after physicians and others protested.<sup>37,38</sup> And when monopoly or oligopoly pricing harms the public's health, the government, acting in the public

interest, can remedy the situation by exercising options such as non-voluntary licensing. Mandatory licensing is authorised in the USA under Federal law (28 U.S.C. § 1498[a]), which allows the government to use patented inventions without permission, so long as reasonable compensation is paid to the patent owner.<sup>39,40</sup> Even with generous royalties, the government could authorise generic manufacturers to make and sell drugs for distribution to patients under its care at a tiny fraction of the current cost. On the basis of the principles that access to medicines is a universal human right and that governments have a duty to protect their citizens' rights, non-voluntary licensing is well founded in international law.<sup>41–46</sup> Mandatory licences, or the threat of issuing them, along with pressure from the US Government, were crucial to creating the arrangements that brought antiretroviral and other medications to millions in poor countries, and made ciprofloxacin available to the US Government during an anthrax scare.<sup>47–50</sup>

Non-voluntary licensing could be a tough sell in the US political climate, but one senator has already proposed this approach.<sup>51</sup> Challenges to patent monopoly pricing are in wide use in Europe and elsewhere.<sup>52–57</sup> In fact, virtually every other country in the world regulates drug prices, and all pay less for drugs than the USA. Drug makers argue that regulating prices will stifle innovation, but no reliable formula exists for calculating how much profit is needed for innovation. The USA's unregulated system does a poor job of incentivising innovations useful to society.<sup>58,59</sup> The US Government grants drug makers monopoly pricing power to incentivise them to develop drugs that meet public needs. When they use that power to price the drugs out of reach of the public, the rationale for monopoly pricing rights falters. Governments need to consider how much preventable morbidity and mortality they are willing to accept for the sake of preserving corporate monopolies.

### Momentum for change

Rising public frustration about ever-increasing drug prices has created momentum for change and the potential for action. Three-quarters of the US public believe that pharmaceutical prices are unreasonable and that the Government should limit them.<sup>60</sup> Two leading US presidential candidates announced plans to limit runaway drug prices and patients' out-of-pocket expenses.<sup>61</sup> An increasing number of policy experts are calling for government action to reduce the prices of HCV drugs and have proposed various mechanisms for such action.<sup>62–65</sup> At least 11 class action lawsuits have been filed in six states challenging pricing, payer restrictions, and denial of care. Some state Medicaid programmes seem to be responding to the demand, evidence, falling prices, and the possible threat of litigation. The state of Connecticut has agreed to cover HCV treatment for all Medicaid recipients without restriction<sup>66</sup>—belying assertions that universal access is unaffordable—as has

**Panel: Actions needed to end the HCV epidemic in the USA**

**Pharmaceutical manufacturers**

- Reduce prices and make discounts contingent on removal of all restrictions to patients' access
- Guarantee access to antiviral drugs to uninsured or underinsured patients, including people who are incarcerated or use illicit drugs, free of charge if necessary

**Public and private insurers**

- Remove all barriers to HCV drug access

**Pharmaceutical manufacturers and the federal and state governments**

- Fund programmes for outreach to people who use illicit drugs and incarcerated people to provide harm reduction services, including overdose prevention and access to sterile injection equipment and education, prevention services, testing, and treatment for HCV infection

**Federal government**

- Enable collective negotiation of drug prices by public and even private insurers, as other countries have, so they may exert downward pressure on drug prices

**Federal and state governments**

- Require insurers to provide HCV treatment as an essential health benefit under the Affordable Care Act

- Ensure sufficient funding for HCV treatment for all who need it, including people who are uninsured, indigent, or incarcerated
- Remove legal barriers to syringe access programmes and pharmacy sales of sterile syringes
- Fully implement syringe access programmes sufficient to meet the needs of their populations

**Physicians, health systems, academic medical centres, medical societies, patients, and advocates**

- Organise local, regional, and national partnerships between clinicians who treat patients with HCV and those who care for people who use illicit drugs to provide screening, prevention services, and treatment
- Advocate vigorously for universal access to HCV medications
- Screen of populations at risk, especially communities affected by pharmaceutical opioid and heroin use<sup>78</sup>

**All stakeholders**

- Organise local, state, and national coalitions devoted to stopping spread of HCV, through education, prevention services, testing, and treatment, by building communication and collaboration
- Render it unacceptable to engage in practices that keep HCV drugs out of the hands of those who need them

HCV=hepatitis C virus.

the Department of Veterans Affairs.<sup>67</sup> Several commercial insurers have also begun to loosen restrictions.

In November, 2015, the Centers for Medicare and Medicaid Services informed states that Federal law requires them to provide HCV treatment to Medicaid recipients.<sup>68</sup> In December, 2015, the Senate Finance Committee issued a scathing bipartisan report censuring Gilead's pricing of its new HCV drugs.<sup>34</sup> In January, 2016, the Governor of New York and the Massachusetts Attorney General took steps toward government action to reduce drug prices. Against this backdrop, Merck chose to list its regimen at half the price of Gilead's rather than simply to match the discounts the other companies were offering. This decision illustrates that drug prices are sensitive to political pressure.<sup>69,70</sup> All these developments suggest a climate that is receptive to change.

Yet, for now, solid roadblocks still face most patients in the USA who seek treatment. On July 1, 2015, Gilead closed its assistance programme to HCV patients whose insurers would not cover their medications, deliberately amplifying patients' distress for the express purpose of increasing the pressure on insurers to cover those drugs.<sup>71,72</sup>

**A way forward**

Sound health policy puts patients first. Our health-care system should be reducing barriers to care, not erecting

new ones. The new drug treatments for HCV could help us to bring the epidemic under control, but only if drug makers lower prices and insurers cover the drugs without restrictions.<sup>5</sup> Pharmaceutical companies have responsibilities not just to shareholders, but also to society<sup>73-75</sup>—and many do make substantial efforts to meet them<sup>76</sup>—while insurers have a fiduciary responsibility to cover safe and effective treatments for life-threatening conditions.

Two stakeholder groups have the authority and the mandate to guide health-care policy to benefit patients and the public: physicians have a duty to advocate for the best interests of patients, while controlling threats to public health is the purview of governments. Physicians and governments must take control of health policy and not let it be convulsed by power struggles between multibillion dollar entities. Instead, together with patients and advocates,<sup>77</sup> they must insist that the needs of patients and public health be restored to the centre of health-care policy. A consensus must be forged by all stakeholders to act in concert against the HCV epidemic, rather than as adversaries, each pursuing its own self-interest (panel). Physicians and government can, and must, exercise the leadership to enjoin this consensus, articulate its importance, and drive the process forward.

No one would dream of withholding penicillin until syphilis progressed to end-organ damage and patients could prove they were abstinent from drugs, alcohol, and

possible re-exposure to the spirochete. This policy is no more rational when applied to HCV. With drugs now able to cure nearly 100% of patients, with minimum side-effects, there is no justification for perpetuating a system that withholds readily available treatment from millions who need it. Once we unite behind a resolve to put patients and public health first, we can put the remarkable new advances in therapeutics to work, moving towards the common goal of ending the HCV epidemic.

2014 should have been a year of celebration. If we act now, 2016 can be.

#### Declaration of interests

I declare that I have no competing interests.

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