Brazil's strategy for eliminating HCV, like its response to HIV/AIDS, shows that it is possible for resource-limited countries to make modern, high-cost health care treatments available to all. Brazil continues to provide important lessons on using industrial policy to achieve health objectives, even in the presence of pharmaceutical patents.

Disclosure forms provided by the authors are available at NEJM.org.

From the Department of Public Administration, São Paulo Business School, São Paulo (E.M.F.), and the Oswaldo Cruz Foundation, Rio de Janeiro (F.I.B.) — both in Brazil; the Center for Latin American Studies, University of California, Berkeley, Berkeley (E.M.F.); and the Department of International Development, London School of Economics and Political Science, London (K.S.). Data collection for this article was funded under the auspices of the São Paulo Research Foundation.

1. Mesquita F, Santos ME, Benzaken A, et al. The Brazilian comprehensive response to hepatitis C: from strategic thinking to access to interferon-free therapy. BMC Public Health 2016;16:1132.
2. Parcerias para o desenvolvimento produtivo (PDP). Brasília: Ministério da Saúde, 2014.
3. Departamento de Vigilância, Prevenção e Controle das IST, do HIV/AIDS e das Hepatites Virais. Relato da reunião da comissão assessora para as hepatites virais. Brasília: Ministério da Saúde, 2018.
4. Decker S, Koons C. Gilead's patents on hepatitis C drug challenged by consumer group. Bloomberg. October 25, 2017.

DOI: 10.1056/NEJMp1812959
Copyright © 2019 Massachusetts Medical Society.

Universal Medicine Access through Lump-Sum Remuneration — Australia's Approach to Hepatitis C

Suerie Moon, M.P.A., Ph.D., and Elise Erickson, M.A.

High prices can restrict access to medicines in rich and poor countries alike. Australia's approach to providing direct-acting antivirals (DAAs) for patients with hepatitis C virus (HCV) suggests that, under certain conditions, innovative approaches to payment can remove price as a barrier to access. In Australia, medicines on the national formulary are largely paid for by the government. In 2015, the authorities negotiated an agreement to spend approximately 1 billion Australian dollars (U.S.$766 million) over 5 years in exchange for an unlimited volume of DAAs for HCV from suppliers. This approach has been called the "subscription" or "Netflix" model, and the state of Louisiana announced in January 2019 that it was pursuing a similar approach for HCV. The Australian agreement is confidential, though the basic information above has been publicly reported.[1]

Is this unconventional approach a good deal for Australians? We used publicly available data, including data from Medicare Australia, to find out. Seven DAA-containing HCV products were included in Australia's formulary as of August 2017 (see table). We compiled data on government spending per drug (excluding rebates) for 24 months from March 2016, when implementation began. We estimated the number of patients treated by dividing the total expenditure by published list price per treatment course, taking into account that some drugs are prescribed jointly with others. We assumed a standard treatment course of 12 weeks, recognizing that a small proportion of patients require 8 or 16 weeks. On the basis of patient-uptake trends, we projected the total number of patients over 5 years to calculate the effective per-patient price under lump-sum remuneration. We also estimated savings over traditional per-pack pricing, assuming that traditional prices would have been 23% lower than published list prices after confidential rebates (following the methods of Iyengar et al.[2]).

We found that in the program's first 2 years, 47,122 people were treated (see graph), with pent-up demand surging in the initial 12 months and stabilizing at an average of 1586 new patients per month over year 2. (Using different methods, others have estimated that 58,280 patients initiated treatment during this period, which suggests that our estimate is conservative.[3]) If utilization rates remained at year-2 levels, a total of 104,223 patients would be treated over 5 years, yielding a per-patient drug price of AU$9,595 (U.S.$7,352). Initially, the government had estimated that only 61,500 of the 230,000 people living with HCV in Australia would be treated during the term of the agreement, for a

The New England Journal of Medicine
Downloaded from nejm.org by KEVIN ROSTEING on March 20, 2019. For personal use only. No other uses without permission.
Copyright © 2019 Massachusetts Medical Society. All rights reserved.

Analysis of Australia's HCV-Treatment Agreement.*

Variable	Value
Estimated no. of patients, March 2016–February 2018	47,112
Projected no. of patients to be treated, March 2018–February 2021	57,101
Projected no. of patients over 5 yr, March 2016–February 2021	104,223
Per-patient price under AU$1 billion (U.S.$766 million) lump-sum remuneration	AU$9,595 (U.S.$7,352)
Total cost with traditional pricing	AU$7,424,121,699 (U.S.$5,688,982,145)
Total cost with lump-sum pricing	AU$1,000,000,000 (U.S.$766,000,000)
Estimated savings to Australian government	AU$6,424,121,699 (U.S.$4,922,698,620)
Estimated additional no. of people treated during the agreement	93,413
Per-patient price under AU$1 billion (U.S.$766 million) agreement under original government projections (61,500 people)	AU$16,260 (U.S.$12,460)
Per-patient price if monthly patient volumes decline from March 2018 (sensitivity analysis 1)	AU$14,011 (U.S.$10,736)
Per-patient price if budget cap increase by 50% (sensitivity analysis 2)	AU$14,392 (U.S.$11,028)

* Drugs included in Australia's Pharmaceutical Benefits Schedule (as of August 1, 2017) are sofosbuvir–velpatasvir (Gilead), ledipasvir–sofosbuvir (Gilead), sofosbuvir (Gilead), paritaprevir–ritonavir–ombitasvir and dasabuvir (AbbVie), elbasvir–grazoprevir (Merck), daclatasvir (BMS), and paritaprevir–ritonavir–ombitasvir, dasabuvir, and ribavirin (AbbVie).

price per patient of AU$16,260 (U.S.$12,460).[4] Both the government's initial estimate and our updated prices fall far below those paid in other countries with a per capita gross national income similar to Australia's — for example, U.S.$72,765 (AU$94,958) in the United States and U.S.$55,284 (AU$72,146) in Iceland for ledipasvir–sofosbuvir.[2]

With traditional per-pack pricing, in contrast, the government would have to spend AU$6.42 billion (U.S.$4.92 billion) more to treat the same number of people; or it could treat 93,400 fewer patients with a fixed budget of AU$1 billion (U.S.$766 million). Put another way, a minimum of 14,038 people would need to be treated to achieve equivalence between lump-sum and traditional pricing at an expenditure level of AU$1 billion; this number of patients was exceeded in the first 6 months of the program.

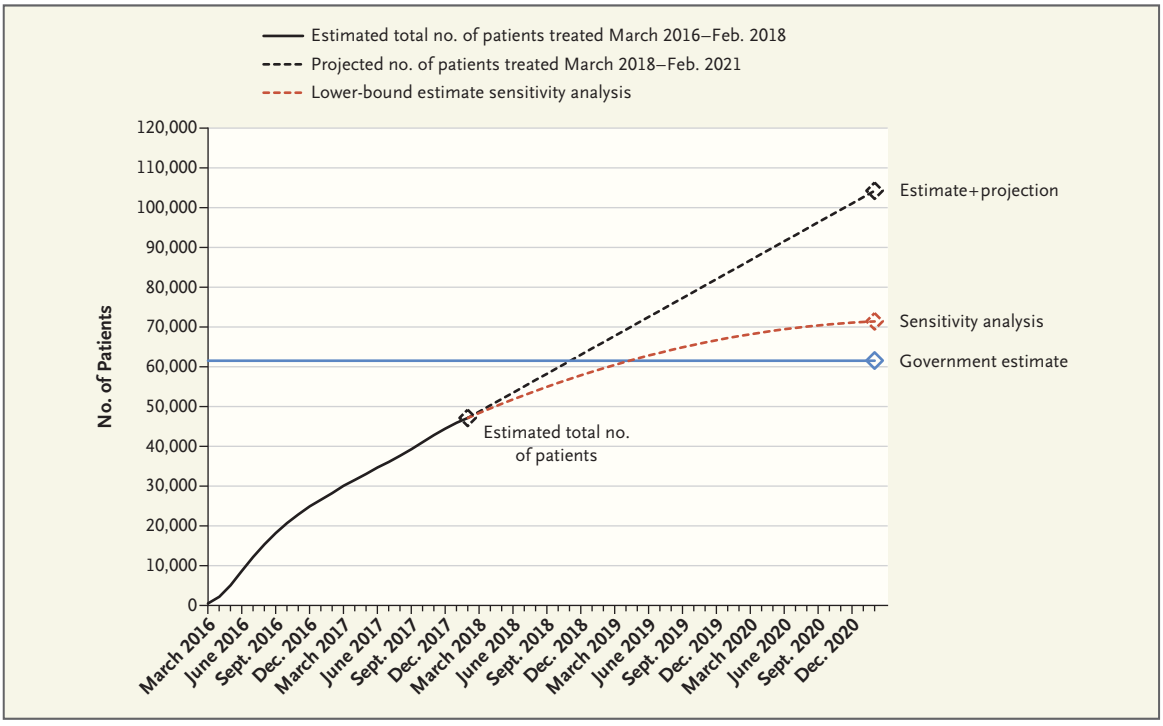
For a more pessimistic estimate, we assumed that monthly patient numbers decrease monotonically at the average rate of decline observed in year 2, yielding 71,372 treated at AU$14,011 (U.S.$10,736). This assumption is reasonable if hard-to-reach populations are precisely those who have yet to present for treatment. Furthermore, since the agreement is confidential, we do not know whether there is some flexibility in the budget cap — for example, if volumes exceed initial estimates. If we increase the budget cap by 50%, assuming steady demand, the average price will be AU$14,392 (U.S.$11,028). Both these higher prices still fall far below those paid in similar countries.

The lower per-patient prices are a central benefit of the Australian approach, but they are not the only ones. Payers benefit because Australia can offer universal access to DAAs with certainty about the cost to the public purse. The cost of treating each additional patient is zero to marginal.

Suppliers benefit as well: the arrangement was economically feasible because the manufacturing costs of DAAs are small relative to their price. For example, production costs for a 12-week course of sofosbuvir have been estimated at U.S.$68 to U.S.$136 (AU$89 to AU$177).[5] Companies receive a considerable financial reward for innovation and face reduced risk thanks to guaranteed revenue over 5 years. Gilead, Australia's largest DAA supplier, was the first company to bring a DAA to market in 2013, and its global DAA revenues and market share eroded substantially after other firms introduced competing products.

Would firms have earned higher revenues through traditional pricing? Possibly, but that was not guaranteed. As many other countries are doing, the government could have restricted patient eligibility in order to control total costs, capping firms' total revenue. Firms also benefit because a lump-sum arrangement does not pinpoint a price; other countries that negotiate prices with reference to Australia's (a common practice) cannot use it as leverage. Finally, the agreement was not compulsory. If the lump-sum amount was too low, firms could

The New England Journal of Medicine
Downloaded from nejm.org by KEVIN ROSTEING on March 20, 2019. For personal use only. No other uses without permission.
Copyright © 2019 Massachusetts Medical Society. All rights reserved.



Estimated 5-Year Patient Volumes in Australia and Corresponding Per-Patient Prices of DAA-Containing HCV Treatments.

The estimated total no. of patients in February 2018 was 47,122. Estimate+projection includes 104,223 people and yields a price per patient of AU$9,595 (U.S.$7,352). Sensitivity analysis includes 71,372 people and yields a price per patient of AU$14,011 (U.S.$10,736). Government estimate includes 61,500 people and yields a price per patient of AU$16,260 (U.S.$12,460).

simply have refused to supply the Australian market. The agreement's existence suggests that firms found it more attractive than the best alternative.

The benefit to patients and the public is that all who need the medicines can receive them. Australia has avoided the rationing (e.g., according to severity of disease) that other countries have adopted for DAAs. The government also has the incentive to encourage at-risk persons to present for treatment earlier: each additional person treated reduces the per-patient drug price and the number who will be left to receive treatment after the agreement ends. Curing patients may reduce HCV transmission in the population as well.

The arrangement is arguably the largest real-world implementation of "delinkage," in which pharmaceutical innovation is rewarded separately from drug prices, a principle that has been widely endorsed as a way to support both innovation and access. The overall approach is analogous to patent buyouts, in which patent holders are paid to concede their monopoly rights, clearing the path for lower-cost generics to immediately reach the market. Such arrangements have not yet been widely implemented to address high drug prices, however.

Can this approach be extended to other medicines? Three key conditions are required. The payer must be able to reasonably predict volumes in order to identify a lump sum that will yield adequate benefits over the traditional approach. The manufacturing cost must be a relatively small proportion of the price. And suppliers must be willing to take this nontraditional approach and able to meet growing volumes of demand. Such agreements may therefore be less suitable, for example, for low-priced biologics when manufacturing costs represent a large proportion of the price, or for rare-disease products for which volumes and production capacities are limited.

Ultimately, all the parameters of this approach could be adjusted — the lump-sum amount, duration (e.g., depending on patent terms or better technologies on the horizon), and payment structure to account for nonnegligible production costs. The key idea to be retained — the core principle

The New England Journal of Medicine
Downloaded from nejm.org by KEVIN ROSTEING on March 20, 2019. For personal use only. No other uses without permission.
Copyright © 2019 Massachusetts Medical Society. All rights reserved.

of delinkage — is that each additional patient does not represent a high cost to the payer, so the payer need not unduly restrict access. Overall, when production costs represent a small proportion of a medicine's price — as is the case for most patented small-molecule drugs and high-priced biologics — lump-sum remuneration for innovation may be an effective, underused strategy for achieving universal access.

Disclosure forms provided by the authors are available at NEJM.org.

From the Graduate Institute of International and Development Studies, Geneva (S.M., E.E.); and the Harvard T.H. Chan School of Public Health, Boston (S.M.).

1. Hepatitis Australia. The benefits and costs of new hepatitis C treatments in Australia: information sheet. March 8, 2017 (https://static1.squarespace.com/static/50ff0804e4b007d5a9abe0a5/t/58bf63e4d2b8578f5301e3ef/1488937960565/Benefits+and+Costs+of+Hepatitis+C+Treatments+in+Australia+20170308+%28formated%29.pdf).
2. Iyengar S, Tay-Teo K, Vogler S, et al. Prices, costs, and affordability of new medicines for hepatitis C in 30 countries: an economic analysis. PLoS Med 2016;13(5):e1002032.
3. Monitoring hepatitis C treatment uptake in Australia. Sydney: The Kirby Institute, July 2018 (https://kirby.unsw.edu.au/report/monitoring-hepatitis-c-treatment-uptake-australia-issue-9-july-2018).
4. Public summary document — March 2015 PBAC meeting: Sofosbuvir 400 mg, tablet; Sovaldi; Gilead Sciences Pty Ltd. March 2015 (http://www.pbs.gov.au/industry/listing/elements/pbac-meetings/psd/2015-03/Files/sofosbuvir-psd-march-2015.pdf).
5. Hill A, Khoo S, Fortunak J, Simmons B, Ford N. Minimum costs for producing hepatitis C direct-acting antivirals for use in large-scale treatment access programs in developing countries. Clin Infect Dis 2014;58:928-36.

DOI: 10.1056/NEJMp1813728
Copyright © 2019 Massachusetts Medical Society.

Reducing Unfair Out-of-Network Billing — Integrated Approaches to Protecting Patients

Mark A. Hall, J.D., Loren Adler, B.A., Paul B. Ginsburg, Ph.D., and Erin Trish, Ph.D.

The emergence of health plans with narrower provider networks has been hailed by some observers as a positive development arising in part from more competitive market conditions brought about by the Affordable Care Act (ACA).[1] As long envisioned by health policy analysts, competition among insurers is beginning to drive meaningful value-based competition among providers.

Others, however, are concerned about the implications of narrower networks for consumers. The inclusion of fewer contracted providers makes out-of-network treatment more common, which exposes patients to substantially higher out-of-pocket costs. A health plan might offer either no coverage outside its contracted network or coverage that is subject to higher deductibles and for only those charges that the plan deems reasonable.[2] The ACA-mandated caps on out-of-pocket spending don't apply to out-of-network charges, so the resulting costs for patients can be financially ruinous.

When patients are able to receive adequate care within their health plan's network, restrictions on provider choice are a tolerable trade-off for lower premiums. However, high charges for out-of-network care are demonstrably unfair in two circumstances: when plans have inadequate networks and when patients are treated by providers they don't choose. In some cases, inadequate networks may force patients to seek out-of-network providers in order to receive appropriate care. For instance, a network might not have enough surgeons with appropriate experience for a patient with cancer who needs complex surgery. In other cases, patients may be subject to "surprise" billing when they unknowingly receive out-of-network care or have no opportunity to stay in their health plan's network, even if the network is otherwise adequate — such as if they receive emergency care at out-of-network facilities[3] or are treated by out-of-network specialists practicing at in-network facilities.

There is widespread agreement that patients deserve protection from out-of-network billing in these circumstances. But state and federal regulators and private accreditation groups that set network-adequacy requirements have found it challenging to protect patients without squelching desirable market dynamics. For example, declaring that an adequate network requires a certain number of physicians in a given specialty within a specified distance can give those specialists extraordinary market power to demand virtually any price to join a plan's network. But with too lit-

The New England Journal of Medicine
Downloaded from nejm.org by KEVIN ROSTEING on March 20, 2019. For personal use only. No other uses without permission.
Copyright © 2019 Massachusetts Medical Society. All rights reserved.