Five Questions Concerning Managing Hepatitis C in the Justice System

Finding Practical Solutions for Hepatitis C Virus Elimination

Anne C. Spaulding, MD, MPH[a,b,*], Madeline G. Adee, cMPH[a], Robert T. Lawrence, MD, MEd[c], Jagpreet Chhatwal, PhD[d], William von Oehsen, JD[e]

KEYWORDS

• HCV elimination • Prison • Jail • Incarceration • Hepatitis C • Medicaid

KEY POINTS

- Most hepatitis C virus (HCV) in the United States is transmitted by injection drug use and most Americans who inject drugs are incarcerated at some point.
- HCV is concentrated in corrections; framework of population health compared with a focus on the individual may be necessary to address the epidemic.
- Surveillance data on HCV in correctional facilities is inconsistent and there are barriers to screening, but opt-out testing can work.
- Current direct-acting antiviral prices are prohibitively high for prison health care budgets; very few incarcerated persons receive treatment.
- There are options available for prison systems to overcome the gap between demand for and availability of treatment.

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[a] Department of Epidemiology, Rollins School of Public Health, Emory University, 1518 Clifton Road Room 3033, Atlanta, GA 30322, USA; [b] Department of Medicine, Morehouse School of Medicine, 720 Westview Dr SW, Atlanta, GA 30310, USA; [c] Alaska Department of Corrections, 550 West 7th Avenue, Suite 1860, Anchorage, AK 99501, USA; [d] Institute for Technology Assessment, Massachusetts General Hospital, Harvard University, 101 Merrimac Street, Floor 10, Boston, MA 02114, USA; [e] Powers Pyles Sutter & Verville PC, 1501 M Street Northwest, Seventh Floor, Washington, DC 20005-1700, USA

* Corresponding author. Department of Epidemiology, Rollins School of Public Health, Emory University, 1518 Clifton Road, Room 3033, Atlanta, GA 30322.
E-mail address: aspauld@emory.edu

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INTRODUCTION

Ignoring the portion of the United States' hepatitis C epidemic made up of persons with a history of incarceration leads to serious underestimations of hepatitis C virus (HCV) prevalence. At present in the United States, even among persons living in households, injection drug use is the most common route of infection with HCV.[1] As an illicit activity, parenteral drug use commonly results in incarceration; almost all people who inject drugs have a history of incarceration.[2,3] To eliminate HCV, the United States must engage the criminal justice system by increasing routine screening and making treatment with the new direct-acting antivirals (DAAs) against HCV accessible to persons who are imprisoned.[4]

The United States leads the world in the rate of incarceration.[5] In the United States, prisons house persons convicted of a crime and serving a sentence of a year or more. Jails detain persons awaiting trial or sentenced to shorter stays. The median length of a jail stay is 2 to 5 days.[6] Six states have unified jail/prison systems. All US correctional facilities have a high concentration of people who inject drugs (PWID) and thus a high prevalence of HCV. Recidivism is common in the US justice system and many persons, once incarcerated, tend to cycle in and out of facilities repeatedly[7] (**Fig. 1**). A 2014 article combined estimates of persons living with HCV who were homeless or institutionalized with those dwelling in households (NHANES [National Health and Nutrition Examination Survey] data). It estimated that 10 million Americans spent at least part of last year incarcerated and likely 30% of all Americans with hepatitis C pass through a prison or jail annually.[8] Among the 1.5 million Americans who are in prison at any given timepoint,[9] the authors estimate that 18%,[9] or 270,000, have antibodies to HCV. State prisons responding to a 2015 survey reported they are aware of about 106,000 (39%) persons so diagnosed.[10] Three-quarters of the 18% (13.5% or 1 in 7) are viremic[1] and thus candidates for HCV treatment once diagnosed.

Prisons, as opposed to jails, serve as particularly important sites to expand access to DAAs, because of the longer duration of sentences, which permits completion of a full course of treatment.[11] Directly observed medication administration helps ensure adherence. Those leaving prison typically have fewer connections to community health resources and so treatment while imprisoned is strategic. Rarely is a person in jail a candidate for starting DAAs, but jails occasionally initiate treatment of persons with advanced disease. Although prison can be a more strategic venue for treatment, few prisons aggressively seek to identify more persons to treat. Two-thirds of state prisons either offer no screening or only offer targeted testing of inmates reporting high-risk behavior, which significantly limits detection and potential treatment in this high-prevalence population.[8,12,13]

Beginning in 2012, more people died of HCV-related infections than of 60 other nationally notifiable infectious conditions, including human immunodeficiency virus (HIV), hepatitis B, and tuberculosis.[14] Nonetheless, hepatitis C has not generated the sense of urgency or diversion of funds associated with other infectious disease epidemics, perhaps because of its slow course, low prevalence in the general population, high cost of treatment, or spread outside the public's eye, primarily within groups that reside in the social shadows of poverty and drug use. As a result, a recent survey showed that the median proportion of people in state prisons with known HCV infection receiving treatment is only 0.49% (range, 0%–5.9%).[10] More and more prisons are being sued for denying treatment to those with hepatitis C, and at least 1 federal judge has declared that withholding medical treatment from a person incarcerated in a state prison constitutes cruel and unusual punishment.[15]

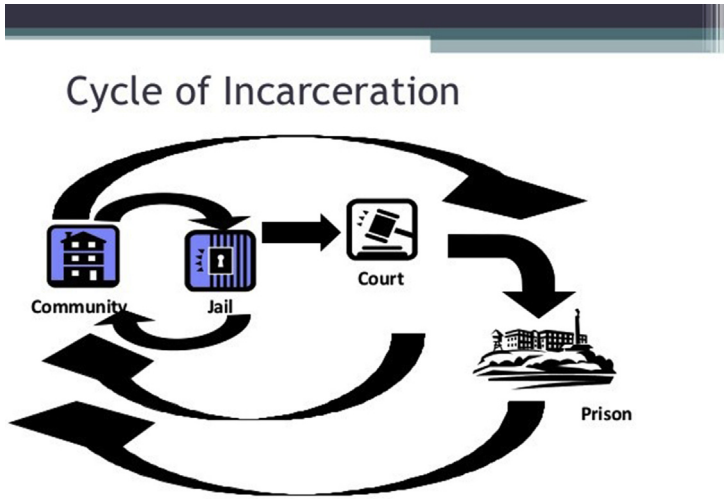

Fig. 1. Trajectories of persons caught in the criminal justice system. In the United States, after an alleged offense is committed, the individual may go to jail while awaiting trial. Those found guilty of a felony with a sentence greater than 1 year may be sent to prison. The arrows in this diagram illustrate the recurrent nature of confinement for those who have ever passed through a jail or prison; recidivism rates are high. (*Courtesy of* B. Zack, The Bridging Group, Oakland, CA; with permission.)

This article poses 5 questions to illustrate dilemmas faced by correctional and public health administrators in the screening and treatment of hepatitis C in correctional populations. It explores how some strategies for reducing medication costs can be pursued by individual states and some by federal policy change alone, and discusses how treating persons who are incarcerated will be essential to bring the hepatitis C epidemic under control.[4]

QUESTION 1: IS HEPATITIS C VIRUS IN CORRECTIONS MORE EFFECTIVELY ADDRESSED USING THE FRAMEWORK OF POPULATION HEALTH COMPARED WITH A FOCUS ON THE INDIVIDUAL?

A paradigm shift, from an individual to population focus, usually occurs in the evaluation and management of infectious disease when a pathogen becomes widespread. When a disease threatens to affect wide portions of a population, the will and resources to address the epidemic must come from the broader society, often governing agencies. Under a population health–based paradigm, health planners use mechanisms for detection, contact investigation, and treatment of a widespread disease with the end goal of eradicating the disease. In the United States, the evaluation and management of HCV is currently in the transition between an individual-based and population-based approach.

Under an individual-based health care model, curative DAAs reach individuals who have meaningful access to health care and adequate resources to cover the cost of medications. This approach lowers HCV-related mortalities for some. Reaching most infected individuals, rectifying the current uneven access to treatment in the United States, and arresting the spread of HCV requires a shift toward a population-based process of evaluation and treatment. Like HIV or infectious

tuberculosis, treatment of HCV becomes prevention when communities target individuals at high risk for transmission for screening and treatment.

The US correctional system offers a model venue for elimination of hepatitis C among the highest-risk population, PWID.[16] Elimination of HCV among PWID, who are highly concentrated in correctional facilities, could be the most efficient way to reduce transmission of HCV in the community.[17] The inherent advantages that correctional departments have for making inroads into the HCV epidemic include having a health care delivery system already in place. If adequately funded, prisons could serve as strategic settings to contribute to a population-based model for elimination of HCV. High-risk individuals while confined are more likely to be sober and can focus on treatment. Furthermore, the highest risk for justice-involved individuals transmitting HCV within the community occurs during the period immediately after release.[18]

As an example of how financial constraints have been associated with correctional systems using an individual-based approach to treatment, there is the Federal Bureau of Prisons (FBOP). The FBOP publishes and frequently updates its clinical guidance on *Evaluation and Management of Chronic Hepatitis C Virus (HCV) Infection*.[19] These guidelines are accessible online and historically, when feasible, many states' prison systems have based their protocols on these guidelines. Whether following these guidelines will withstand legal and ethical scrutiny is being tested in federal courts. Access to treatment is not universal in the FBOP; patients with advanced stages of fibrosis are prioritized (**Box 1**). In 2015, this led to treating

Box 1
The Federal Bureau of Prisons aspartate transaminase to platelet ratio index method of prioritizing patients for treatment

- FBOP guidelines recommend universal anti-HCV antibody screening of all sentenced inmates, and for those who are anti-HCV positive, reflex HCV RNA viral load testing and reflex testing for HCV genotype.
- Certain comorbid medical conditions that are associated with HCV, or the necessity of immunosuppressant medication for a comorbid medical condition, may prioritize individuals for treatment.
- Treatment priority is usually based on degree of severity.[19] After diagnosis, the health providers look for signs of hepatic cirrhosis, with or without decompensation. Advanced disease prioritizes persons for treatment.
- As a predictor for advanced disease, an aspartate transaminase (AST) to platelet ratio index (APRI; [(AST/AST upper limit) $\times$ 100]/platelet count [10^9/L]) is calculated if no obvious cirrhosis is assessed. The APRI has been recommended as a screening tool where prevalence of HCV is high but resources for screening for fibrosis and cirrhosis are sparse.[24]
- Individuals with an increased APRI score are referred for liver imaging to confirm signs of cirrhosis or fibrosis, which, if present, qualify the patient for the highest priorities for treatment. For all patients with an APRI of 2.0 or greater, treatment is highest priority.
- If the APRI is greater than 1.0, fibrosis stage 2 or greater was found on a liver biopsy in the past, or certain comorbid conditions (eg, HIV, diabetes) are present, hepatitis treatment can still be prescribed, but priority is intermediate.
- The provider provides a pretreatment assessment. If priority criteria for treatment are met, a DAA can then be prescribed.
- Continuity of care for individuals who have already started DAAs before incarceration also creates a priority for treatment.

just 2.4% of infected persons.[20] Although the FBOP has recently relaxed its criteria of which stage of fibrosis will be prioritized for treatment, and lifestyle factors such as alcohol or illicit drug use are not categorically disqualifying, treatment of all incarcerated persons infected with HCV is far from available. A correctional health system usually examines the return on investment, both during the time frame of incarceration and over the lifetime of the individual, that an intervention will bring.[11] If HCV treatment costs decreased precipitously, the return on investing in DAAs for HCV would compare favorably with other health interventions in correctional medicine. Treatment of HCV would then decrease in line with the public health approach to other infectious disease epidemics.

Consider the population health–based approach taken by the US Department of Veterans' Affairs (VA). In 2016, supported by congressional funding and (an unpublished) negotiated reduction in pharmaceutical prices to approximately $15,000 (personal communication, Jules Levin, NATAP, 2018), the VA expanded treatment to all veterans with chronic HCV who do not have medical contraindications. The Veterans Health Administration follows screening guidelines endorsed by the US Centers for Disease Control and Prevention (CDC) and the US Preventive Services Task Force that recommend 1-time screening for all persons born between 1945 and 1965, and risk-factor screening for all those born outside this time frame.[21,22] The VA system follows joint treatment guidelines established by the American Association for the Study of Liver Diseases and the Infectious Disease Society of America (HCVguidelines.org). Treatment is no longer reserved for those with advanced liver disease or cirrhosis. Veterans with a chronic infection, even with no evidence of liver disease, qualify for treatment unless, ironically, the veteran happens to be incarcerated. Per VA policy, benefits for veterans infected with HCV are suspended when a veteran is in jail or prison under the assumption that the veteran's health care is covered by the corrections system.

Political will and, perhaps more important, favorable economics have allowed the VA to adopt population-based screening and treatment. Circumstances are not as favorable for correctional departments. Compounding the problems is the relative concentration of individuals infected with HCV within correctional institutions with rates more than 4-fold higher than the estimated 4% prevalence in the US veteran population[8,12,23] (**Table 1**).

The responsibility for funding prison health care depends on the jurisdiction. The federal government funds the FBOP; they can acquire drugs at a steep discount off a federal supply schedule (see Appendix 1). State governments alone are responsible for underwriting all state prison health care. Federal funds, including Medicaid and

Table 1
Comparison of population dynamics in the Veterans' Affairs Health System and in correctional systems

	VA Health System	Prison/Jails
HCV seroprevalence (%)	4	18
Point prevalence: number of patients with HCV in 1 d	170,000	386,000
Period prevalence: number of individual patients with HCV over 1 y	170,000	~2 million

The Veterans' Affairs Health System does not continuously add or subtract its population. Most incarcerated persons pass through only jail, and jails turn over their populations repeatedly over the course of 1 year.

Medicare; private insurance; and pharmaceutical manufacturers' patient assistance programs do not cover state prison health care costs. The carve-out of correctional health care budgets from the rest of the US medical system poses the first challenge in treating persons in this sector of the epidemic.

QUESTION 2: WHAT ARE SOME ISSUES WITH TESTING FOR HEPATITIS C VIRUS IN PRISONS? DOES THE BENEFIT FOR POPULATION HEALTH OUTWEIGH THE INCREASING DEMAND FOR INDIVIDUAL HEALTH SERVICES?

Looking for Problems Whose Solutions Are Unfunded

The unaffordability of HCV treatment creates a disincentive for prisons to screen for HCV. Prisons have no legal mandate to screen for disease. However, once a disease such as hepatitis is diagnosed, deliberate indifference to health needs has been determined by the US Supreme Court to be a violation of the eighth amendment of the Constitution prohibiting cruel and unusual punishment.[11,15] Thus with screening, states may be obliged to incur greater medical costs for care and treatment.

National Survey on Surveillance in State Prisons Shows Reluctance to Screen

Routine, universal screening, without regard to purported risk factors, has occurred in either jails, prisons, or both in at least 28 of the 50 states. **Fig. 2** shows data collected in a recent survey of state prison medical directors, published literature on screening in jails, and an earlier survey of which state prison systems had conducted surveillance.[8,12] To these estimates, the authors have added data from recent surveillance

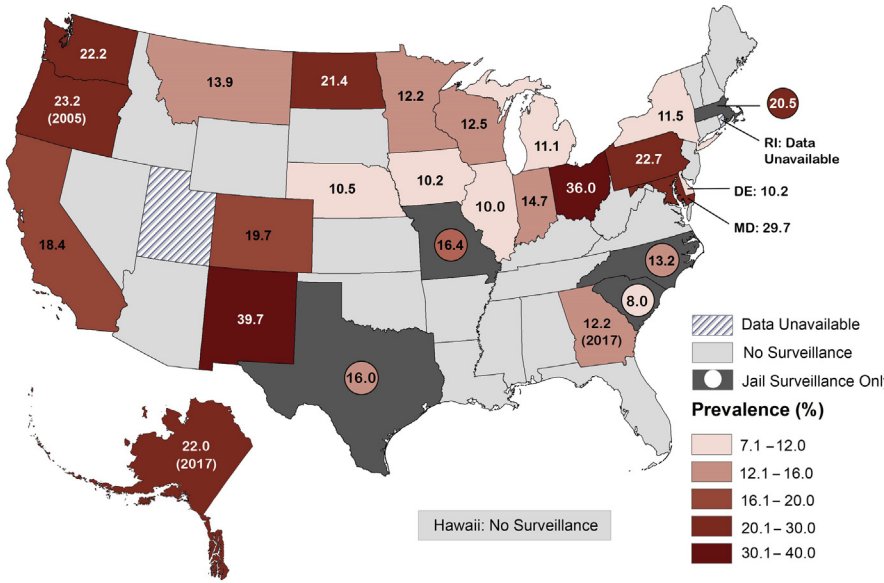

Fig. 2. Prevalence of antibodies to HCV in US state prison systems: estimates from 2016 National Survey of State Prison Systems unless date otherwise specified; with local jail data added. States that did not respond to survey, but where local jail data were available, are shaded in gray. The jail prevalence is provided in the circle within the state. (*Adapted from* Spaulding AC, Anderson EJ, Khan MA, et al. HIV and HCV in U.S. prisons and jails: the correctional facility as a bellwether over time for the community's infections. AIDS Rev 2017;19(3):142; with permission.)

in the Alaska and Georgia departments of corrections by this article's authors. The US Preventive Services Task Force's recommendations on whom to screen for HCV lists incarceration as a risk factor.[22] Studies show that limiting correctional screening to those with other risk factors excludes many persons infected with HCV.[25–27] Unlike screening for HCV, screening for HIV in prisons at intake is the norm, which shows that prison systems can systematically offer testing for blood-borne infections.[12] Screening reveals an HIV infection in an average of 1.3% of the prison population.[28] Many jails in areas of high HIV prevalence also perform routine screening for HIV.[6] Budgets are sufficient to treat the small proportion of persons with HIV.

Challenges with Comparing Data from the Reports of Multiple States' Hepatitis C Virus Screening Programs

Prison-provided surveillance data are not directly comparable because of inconsistencies in how data on HCV prevalence are collected; current data on HCV prevalence in prisons come from surveillance of entry, stock, and exit populations. Uncertainties that come from screening programs also arise when persons with unknown status and known positives are not addressed in a prespecified manner, as shown by a recent review of HCV screening in the unified jail/prison system of Rhode Island[29] (**Fig. 3**). Promotion by a professional society or government agency of a standard method to report prison prevalence of HCV would help states compare their data. Standardization would have a second effect: it would facilitate surveillance efforts for the United States as a whole, because the data could be added to nationwide estimates of HCV prevalence and geographic distribution.

First Case Study: Public Health Administrator Outside, Looking in on the Georgia Department of Corrections

Imagine yourself as a public health administrator in the state of Georgia. Historically, the Georgia State Department of Corrections (GDC) did not systematically perform HCV screening in its population of approximately 45,000, with 17,000 entrants and exits yearly. Beginning in 2016, a project team from Rollins School of Public Health, Emory University, sought to address hepatitis C case finding. With the backing of the Georgia Department of Public Health, the Emory team began a demonstration project of voluntary exit testing for antibodies to HCV with reflex testing for RNA. Funding came from industry. The offer of screening did not depend on prior testing, high

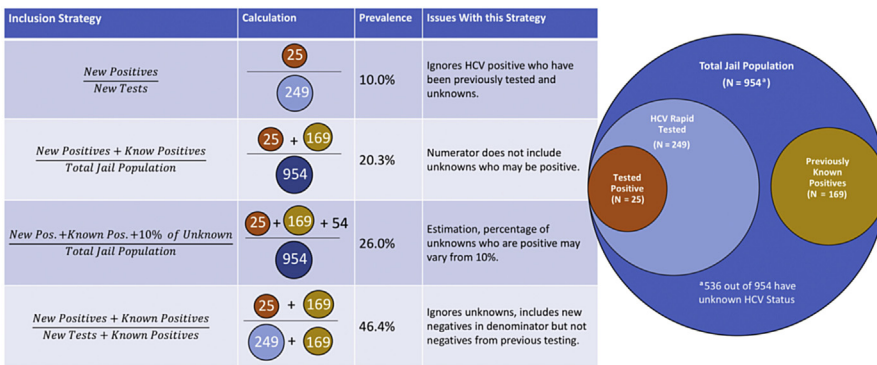

Fig. 3. Uncertainty over HCV prevalence, based on choice of numerator and denominator. (*Data from* Beckwith, et al. Journal of Public Health 2016, from modified analysis published in AIDS Review 2017.)

risk for HCV exposure, or HIV status. Emory staff provided periodic in-person information sessions on hepatitis for about-to-be-released persons; afterward, each attendee was given a chance to sign a testing consent form. Georgia has legally mandated screening for HIV on exit and HCV screening was added to this blood draw for those wanting testing. An Emory-employed social worker was engaged to provide help with discharge planning and linkage to community care for those diagnosed with HCV infection.

The project began in 1 prison, but as of January 2018, exit testing is occurring in 5 of 33 state prison facilities. To date, just 12.5% of persons who have undergone the full information session have opted out of exit testing. A total of 299 persons have been tested for anti-HCV antibodies; reflex polymerase chain reaction (PCR) testing is performed when antibodies are found. Seroprevalence was 10.7% and 56% of those who were anti-HCV positive (6.0% of all tested persons) were viremic. About 6.3% of tests were done in patients in the 1945 to 1965 birth cohort, and 26.3% of persons tested were anti-HCV positive; among those younger than the baby boomer generation, 6% were HCV seropositive. Two patients with viremia volunteered that they already knew about their infection; questions about prior diagnosis were not systematically asked.

After the demonstration project period, there are 3 possible options for HCV screening:

Cease testing

This option would not promote access to cure for infected people. However, without continued allocation of resources, and support from the Department of Public Health, correctional administrators may consider this the only feasible strategy going forward.

Continue opt-in exit testing

The benefits are that non-targeted HCV screening at exit situates testing in an existing infrastructure for health care. For Georgia, testing occurs at a time when phlebotomy is already mandated, so no additional health workers are needed. Persons found to be viremic on exit can access treatment in the community, where patients may qualify for federally funded programs (eg, Medicaid/Medicare/Veterans' Health Administration/ Indian Health Service); patient assistance programs established by pharmaceutical companies; and, for a minority of persons leaving the prison who secure employment with health benefits, private insurance. These 3 funding options are not available for prisons while persons are incarcerated. Furthermore, by routine, nontargeted testing, the state of Georgia can determine the prevalence of HCV, which will help with future program planning.

The risks are that many, if not most, of those exiting the prison system in Georgia do not have access to health care. Persons found to have infection learn of their potential need for vaccination, cancer screening, and treatment just as they are exiting a setting in which comprehensive treatment is available.

Shift testing from exit to entry

The benefits are that patients can learn of their HCV diagnosis while in a setting in which the prison cannot be deliberately indifferent to health care needs. Increased awareness of infection will likely increase the demand for treatment. Treat in a setting of enforced sobriety. Additional care, such as vaccinations and cancer screening, can be provided. The prevalence of HCV viremia is lower in Georgia than in many other states. If the number of cases found is less than the number originally perceived to

exist, setting up a screening and treatment program may be feasible, especially if the cost of medications is decreasing.

The risk is that persons may not finish treatment before release. Although prisons may commence treatment only for those with greater than 3 months left on their sentence, some may leave early; treatment models for continuity of care after release would be required.[30] The heart of a treatment program is identifying persons to treat, but finding cases may be perceived as obligating a system to underfunded programs.

QUESTION 3: WHAT ARE OPPORTUNITIES AND CHALLENGES FACING HEALTH ADMINISTRATORS FOR TREATING HEPATITIS C IN A STATE PRISON SYSTEM?

In managing hepatitis C once diagnosed, when funds are insufficient to cure all, US prison systems, in addition to low commitment to screening, have adopted a combined approach of prioritizing the most urgent cases and negotiating lower prices for medications.

Second Case Study: Alaska, Navigating the Complexities of Screening for and Treating Hepatitis C Virus from the Inside

Imagine yourself as a medical director for the Department of Corrections in Alaska, one of 6 states whose justice system combines both jail and prison services. Alaska has 12 correctional facilities spread over a geographic area more than twice the size of Texas. Although Alaska averages 30,000 criminal remands (pretrial commitments) per year, because of recidivism these intakes do not represent unique individuals. For example, in 2017 a total of 17,565 individuals were remanded to an Alaskan facility. Approximately 45% of these entrants stay in the system greater than 1 year.

Alaska makes treatment decisions without reference to sentence, but, for the sake of determining the feasibility of a population-health approach, consider a hypothetical scenario in which a state such as Alaska treats the population of individuals with a sentence greater than 1 year. Because about 45% of entrants remain in the system beyond 1 year, the authors estimate that $17{,}565 \times 0.45$, or 7900 individuals, would be screened and considered for treatment if infected.

Case finding

Routine testing for HCV antibody is performed by the Alaska State Virology Laboratory for any person in the system as part of an opt-in testing model (on request by the patient or initiated by the provider). Beginning in 2016, seropositive results were reflexively tested for genotype. Although PCR is not performed by the state virology laboratory for screening purposes, a positive genotype is considered a surrogate for the presence of virus. The patient is presumed to be virus free when genotype cannot be determined. A quantitative test for viral load is drawn for individuals being considered for treatment.

Prevalence

A chart audit at 2 facilities, Spring Creek Correctional Center in Seward, Alaska, a male facility housing up to 551 sentenced persons, and the Highland Mountain Correctional Center in Eagle River, Alaska, a female facility housing up to 404 sentenced and unsentenced women, revealed that approximately 22% of persons in the correctional population are anti-HCV antibody positive.

Applying these findings to the entire system, if 22% of 7900 entrants whose stay exceeds 1 year are infected, then 1738 persons may be antibody positive, and 1300 are HCV viremic.

Budget

Not including behavioral health, the Alaska Department of Corrections Division of Health and Rehabilitation Services spends approximately $30 million per year on its health care services for all confined persons. At the initial prices for DAAs, the cost of treating all viremic persons would have been greater than this entire budget.

Converting to a population-health approach is feasible, but only if the cost of treatment is proportionate to the prevalence of a disease in the population being treated (Fig. 4). Consider a comparison between the proportionate costs of HCV treatment and HIV treatment. HIV prevalence is approximately 1%; each treated patient costs $40,000 per year, or $4 million if 100 are treated a year. With discounts, the cost of treating each patient with HCV is $40,000, the same price as a year's worth of HIV treatment, but more than 20 times more persons in prisons and jails are infected than with HIV.

There are several options a state prison system can pursue to maximize the number of cures:

Note that these are not mutually exclusive options. The more persons discovered to have infection, the greater the need for a way to pay for more treatment. If the overall budget for health care does not increase, the price per cure must decrease.

1. Increase in-prison HCV screening: with such high prevalence of hepatitis C, if testing were more aggressive (eg, opt-out rather than opt-in), more persons would know their antibody status. This approach is promoted by the FBOP.

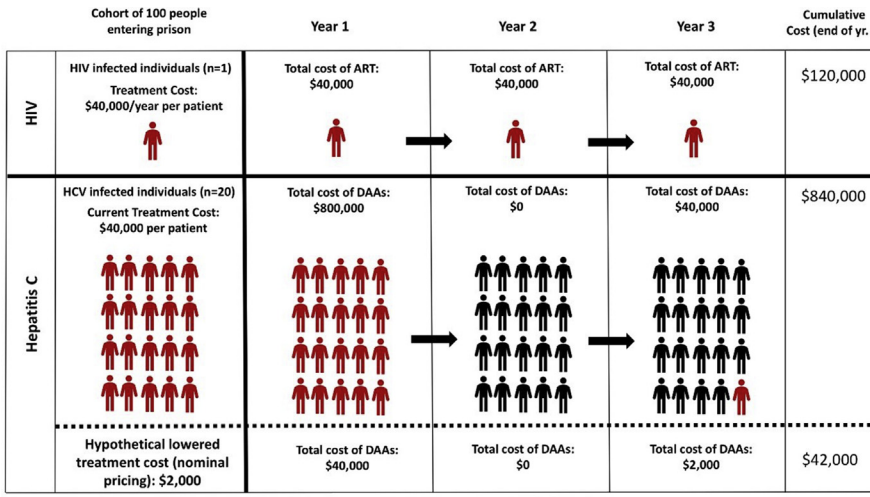

Fig. 4. Hypothetical treatment cost for a cohort of 100 people, entering the Alaska Department of Corrections, incarcerated for 3 years (upper limit of typical length of stay for persons with felony conviction), with HIV treatment cost for comparison. Assuming HIV prevalence of 1% and HCV prevalence of 20%, this shows that, with such a high prevalence of HCV in correctional populations, the burden of drug costs is incurred up-front when cases are identified, then annual expenditures decline for these entrants as individuals are cured. This expenditure is compared with the cost of HIV treatment, which is spread over the length of time an individual is incarcerated. The initial cost is $40,000 per treatment course. At a reduced price of $2,000, an estimated nominal price per regimen (explained later), the Alaska Department of Corrections could much more easily afford treatment of individuals with hepatitis C. ART, antiretroviral therapy.

Benefits: More persons will learn whether they are infected. Recommendations for persons with viremia could be followed: immunize against hepatitis A, hepatitis B, and pneumococcus. For those with advanced liver disease, perform upper endoscopy to rule out esophageal varices and image the liver to rule out masses suggestive of hepatocellular carcinoma. Refer persons for treatment.

Risks: If opt-out testing is offered too aggressively, those with inadequate understanding of a right to refuse may feel coerced to undergo testing. With more testing, demand for medical services, including treatment of hepatitis C, could outstrip the budget.

2. Negotiate acquisition cost for treatment: state prison systems and local jails have a limited number of options to reduce the price of treatment. Although they are scarce, vehicles do exist to obtain lower-priced medications to treat their correctional populations. The Medicaid drug rebate provisions require that the manufacturers give their best price to the Medicaid program, but there are ways for state prison systems to work around this best-price requirement, as outlined in question 5.

Benefits: Prices for DAAs can be reduced and more patients can therefore be treated.

Risks: Most options require cooperation on the part of at least 1 pharmaceutical company, and careful navigation of federal drug pricing laws.

3. Prioritize persons for treatment based on severity or comorbid conditions. See response to question 1 for the approach recommended by the FBOP guidelines.

Benefits: Patients are assessed system wide in an equitable way. Resources are used to treat persons for whom treatment is most urgent. Patients who will experience little disease progression if treatment is postponed for a year or two may be treated later, when the price of treatment decreases.

Risks: Although the APRI (aspartate transaminase to platelet ratio index) score has a high specificity for detecting cirrhosis, it has a low sensitivity (**Box 2**, **Table 2**). Reliance

Box 2
Applying the Federal Bureau of Prisons guidelines to state systems: Georgia and Alaska

Adapting the HCV management guidelines of the FBOP to a state program could be a feasible first step toward the eventual goal of having hepatitis C treatment follow the American Association for the Study of Liver Diseases guidelines. The number of cases of HCV needing treatment that the Georgia prison system would find if opt-out testing were initiated for entrants could be estimated, in keeping with the FBOP guidelines. The number of cases found could then be compared with the number the system has the capacity to treat per year. In GDC in financial year 2017, 219 persons were treated.

Parameters: it was necessary to determine what percentage of patients with HCV viremia would have an APRI more than 1.0. In the Alaska Department of Corrections, 13% had APRI greater than 1.0. Evaluation, management, and follow-up may be difficult to conduct if the time the individual is the correctional system is less than 1 year, so only patients with an expected length of stay greater than 1 year are considered for treatment in this example. In addition, experience shows that about 91% of patients offered treatment in prison accept it.[32] Approximately 23% of persons with HCV viremia were treated in GDC. This percentage is strikingly similar to the percentage of persons with HCV viremia in the Washington Department of Corrections: they estimated that 23% of their population with HCV viremia had an APRI greater than 1.0.[33]

Summary: note that testing entrants to the Georgia prisons system would identify roughly the number of new patients that the prison infrastructure has the capacity to treat. The number treated in Alaska would be about 155 patients a year.

Table 2
Comparing treatment projections: Alaska and Georgia prison systems, 2018

	Alaska Department of Corrections	Georgia DC
Number of unique entrants per year	17,565	17,000
Number viremic if prevalence similar to pilot study	2900	1020
Number with stay (jail + prison) >1 y	1305	1020
Number with APRI>1.0	170 (13%)	240 (23.5%)
Number consenting to treatment (91%)	155	219

on the APRI score may be misleading. One systematic review found that more than 50% of negative APRI results, using a cutoff of 2.0 as recommended by the FBOP, could be falsely negative, thereby providing a false sense of reassurance regarding the patient's liver status.[31]

QUESTION 4: WHAT ARE CURRENT DIRECT-ACTING ANTIVIRAL PRICES, AND WHAT BARRIERS EXIST FOR PRISONS TO REDUCE THESE PRICES?

State prisons typically buy medications on the open market through wholesalers at prices that represent the highest markups in the US drug market.[10,34] As of the start of 2018, the listed price, or average wholesale price (AWP), of new DAA regimens ranges between $26,400 and $96,000 per treatment course in the United States. Although several studies have shown that these drugs are cost-effective in the general population at the given price,[35,36] they remain unaffordable for many payers, especially prison health services, even after accounting for existing discounts.[10] Because of budget constraints, state corrections cannot purchase the amount of medication needed to meet the demand.

How Price Is Derived

A good benchmark for comparing drug prices is the average manufacturer price (AMP), which is defined in federal law and generally represents the manufacturer's average price nationwide for a drug within the retail class of trade.[37,38] Not all prices, such as AMP, are published, but, because they are derivatives of other prices, these unpublished numbers can be estimated. Using financial year 2018 pricing data supplied by the GDC for their AWP for DAAs ($69,773) and the 340B price when their patients with hepatitis C use a safety-net hospital ($38,186), the authors estimated AMP for an 84-day course of treatment.

The AWP represents a markup of approximately 17% over wholesale acquisition cost (WAC). Hence, WAC is $57,912. If the 340B price represents 23.1% less than the AMP, then AMP is $49,657 (ie, 38,186/0.769). If Medicaid pricing represents a 24% discount off AMP, then the Medicaid rebate price is $37,399. Although the VA price is unpublished, multiple providers have informally disclosed that it is in the $10,000 to $11,000 range. The nominal price must be less than 10% of the AMP. An 84-day course of treatment costs $400 or less to manufacture[39,40] (**Fig. 5**, **Table 3**). Additional details on pricing and calculations are in Appendix 1.

Barriers to Reducing Price

Because of the market impact of certain federal laws, pharmaceutical companies cannot simply discount their medications to a level that would permit prisons to purchase sufficient supplies of drug to meet correctional population demands. In particular, the

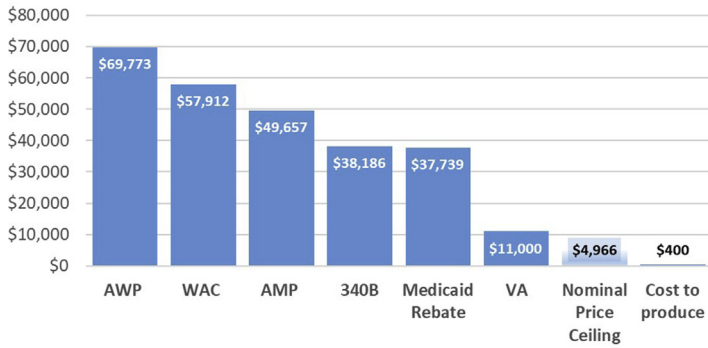

Fig. 5. Estimated price per course of treatment, for most commonly used DAAs. Length of treatment used in this calculation is a 12-week, or an 84-day, supply of drugs. See appendix for an expanded explanation of each pricing level. (*Data from* Georgia Department of Corrections, November 2017. Cascade format introduced at online site for "340B University." Available at: www.HRSA.gov. Accessed March 19, 2018.)

manufacturers cite the adverse financial consequences of discounting their medications as a result of the federal laws underlying (1) the Medicaid drug rebate program (MDRP), (2) the 340B drug pricing program (340B program), (3) the federal ceiling price (FCP) to which the federal government's 4 largest drug purchasers (the VA, Department of Defense, Public Health Service, and Coast Guard) are entitled, and (4) the average sales price (ASP) formula used by the Medicare Part B program to reimburse hospitals and clinicians for physician-administered drugs[41–44] (see Appendix 1 for more details.) The most significant threat to manufacturer pricing arises out of a unique requirement in the MDRP that a manufacturer extend its best price on brand-name drugs to the entire Medicaid and 340B programs, with only a few exceptions.[45] The result is that if a correctional facility were successful in negotiating deep discounts, those discounts would likely reduce the prices at which manufacturers could legally sell their drugs within federal programs. Industry clearly has an incentive to overstate the impact of these federal programs when negotiating with potential purchasers, but the barriers are nonetheless real.

Table 3
Summary of prices in the hepatitis C therapeutics market

Term	Abbreviation	Meaning	Georgia Price ($)
Average wholesale price	AWP	Sticker price	69,773
Wholesale acquisition price	WAC	What wholesalers pay	57,912
Average manufacturer's price	AMP	What it costs the manufacturer	49, 657
Price paid by a 340B covered entity	340B	Maximum price that can be paid by a safety-net entity (340B program of HRSA)	38,186
Nominal price	—	≤10% of AMP (see response to question 5)	4000 (hypothetical)

Abbreviation: HRSA, Health Resource and Service Administration.
All prices are authors' estimates of actual prices, unless otherwise stated.

Net Result

The net result of the current pricing structure is that high-risk persons are not being treated, and companies cannot sell their product to meet the demand. There is a gap between demand and what can be purchased under existing market conditions. Of note, this is similar to the so-called deadweight-loss concept: why existing regulations and patent law surrounding DAA pricing leads to a market situation "enjoyed by neither the patent holder or the public"[46] when prices are too high. This situation leaves an untapped market (Fig. 6).

QUESTION 5: HOW CAN PRISON SYSTEMS OVERCOME THE GAP BETWEEN DEMAND FOR AND AVAILABILITY OF TREATMENT? WHAT ARE THE PROS AND CONS OF CORRECTIONAL FACILITIES ADOPTING VARIOUS STRATEGIES TO ACCESS DIRECT-ACTING ANTIVIRALS AND MANAGE HEPATITIS C?

Given the complex web of federal drug pricing laws and the financial pressures they exert on manufacturers not to discount their prices in the nonfederal market, state and local correctional systems currently have limited options for reducing the prices they pay for DAAs (see Appendix 1). It is therefore essential that state or local correctional departments pursue a purchasing strategy that is exempt from best price. After that, they can consider more refined methods for reducing their DAA acquisition costs.

State or Local Departments of Corrections Can Potentially Use the Following Strategies to Purchase Drugs at a Lower Price than they Currently Pay, Without Violating the Best-price Rule

1. Contracts with entities eligible for discounts under the 340B Drug Pricing Program: the 340B program enables safety-net providers to qualify for reduced prescription drug prices. Pharmaceutical companies participating in Medicaid must offer drug discounts to 340B-covered entities, which include disproportionate share hospitals and federally qualified health centers serving lower-income communities. State prisons are not eligible for coverage under 340B, but they may enter a contract with a covered entity to treat an incarcerated person as a patient of the covered facility.[11]

Benefits: Moderate discounts are possible with these mechanisms.

Risks: Discounts are inadequate to substantially increase the number of persons infected with HCV that the justice system can treat.

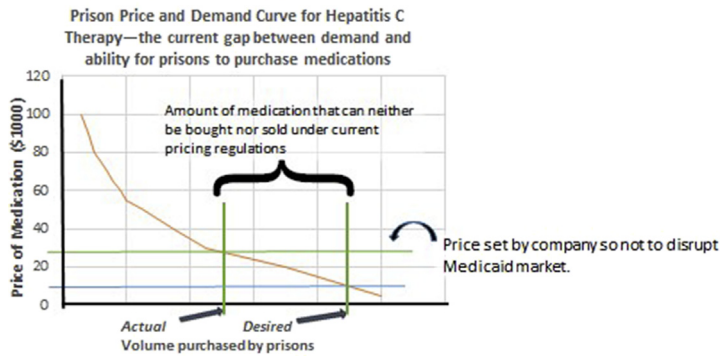

Fig. 6. The untapped DAA market. The lower horizontal line represents a price that permits prisons to purchase the volume needed to adequately address hepatitis C.

2. Pooled procurement: another potential strategy is known as pooled procurement, by which states, counties, and municipalities band together and buy medications in bulk from the manufacturer. By purchasing in bulk, states may obtain lower prices for medications. Some states also participate in the Minnesota Multistate Contracting Alliance for Pharmacy (www.mmcap.org), a group-purchasing organization for government facilities to negotiate reduced prices. The depth of the discounts that states are able to obtain are unknown because the contracts are kept confidential. The drug prices that state prison systems reported to a *Wall Street Journal* reporter in 2016 showed that discounts are often just slightly less than full list price.[47] In order to obtain more substantial discounts with pooled procurement, that are less than best price, this strategy would need to be combined with a Section 1115 waiver (detailed later).

Benefits: Moderate discounts are possible with these mechanisms.

Risks: Discounts are inadequate to increase the number the system can treat substantially.

3. Nominal pricing: state correctional systems, or group purchasing organizations of which they are a part, could request nominal pricing from the manufacturer. A nominal price is defined as a price less than 10% of AMP[48] and paid by any facility identified in Section 1927(c) (1) (D) (i) of the Social Security Act, or any determined to be a safety-net provider by the Secretary of Department of Health and Human Services (DHHS).[49] The DHHS Secretary can approve of nominal pricing based on the type of facility, services provided, population served, and the number of other nominal price eligible facilities in the same service area.[50] Although the exact AMP is confidential, this would make the price substantially less.

Benefits: Prisons and jails are clearly within the realm of public institutions deemed appropriate for nominal pricing consideration. Given that a complete course of DAAs costs between $200 and $400 to produce, this would still be more than the production cost for the pharmaceutical company. Importantly, using nominal pricing would not affect the manufacturers' Medicaid market or best price. Transactions could be proposed to Centers for Medicare & Medicaid Services (CMS) in advance to confirm that the manufacturer is not incurring any risk by extending nominal pricing to correctional facilities. Nominal pricing would create the most substantial discount.

Risks: Agreement to nominal pricing is entirely at the discretion of the pharmaceutical company.

State Departments of Corrections Can Also Team with the State Medicaid Program in Order to Use the Following Strategy

A. Section 1115 waiver: states may act individually to request exemption from the best-price rule via a waiver permitted under Section 1115 of the Social Security Act. If approved by the federal government, the waiver could allow the state Medicaid agency to negotiate supplemental rebates from manufacturers on behalf of itself and other state agencies (eg, the Department of Corrections) that were exempt from best-price calculations. By negotiating on behalf of other state agencies that are willing to use the state Medicaid's preferred drug list, the Medicaid agency would presumably have greater leverage in negotiating supplemental rebates from manufacturers. This strategy would require state agencies to collaborate to win approval of the waiver from the federal government. The companies could then pursue either a new lower price or charge a fee by month for whatever amount of drug would be demanded by state entities, a sort of subscription plan.

As summarized earlier, vehicles do exist for states to obtain lower-priced medications to treat their prison populations. Because these options require states to invest significant resources for limited benefits, some stakeholders have questioned whether legislative change may be necessary to empower states to negotiate lower prices.

Legislative Change That Would Allow Departments of Corrections to Purchase Drugs at a Lower Price Without Violating the Best-Price Rule

1. Change the best price rule statutorily: one proposal is to amend federal regulations that stipulate which entities are excluded from Medicaid's best-price rule. There are currently 19 exceptions to the best-price rule, and through legislation a 20th exception could be created. If state prisons were added as an excluded or exempt entity, they could negotiate prices lower than Medicaid and receive discounts like those available to the VA and Indian Health Service. This possibility has the benefit of applying to state prisons in all states if changed.

Other Solutions Require Examining Patent Law for the New Direct-Acting Agents

1. Purchasing a patent: The National Academies of Medicine in their phase II report on the elimination of hepatitis B and C recommended that the DHHS should purchase the patent or licensing rights to a DAA that could then be used to treat patients left uncovered at present. This recommendation would require voluntary cooperation from at least 1 pharmaceutical company. Furthermore, the company willing to grant patent rights to a drug may be selling a product that would not do well under current marketplace conditions, such as a DAA with activity against only a limited number of genotypes or associated with a cure rate less than the 99% seen with the most recently developed agents. To the best of our knowledge, since the report was published in April 2017, no company has volunteered to sell their patent.
2. Evoking eminent domain: in April of 2017, a group of experts in law, economics, and public health met at Johns Hopkins University to provide advice, specifically to the state of Louisiana, on purchasing treatment of Medicaid beneficiaries and prisons. The group then wrote an open letter to Louisiana's Secretary of Health, which advocated the state invoke a little-used provision in the US Code: 28 U.S.C §1498, which authorizes the government to make use of patented inventions, including medication.[51] This strategy would essentially evoke eminent domain over use of the patented medication. The company holding the patent can obtain compensation for use of the patented invention but cannot prevent the government from the action.[46] This power was used particularly frequently in the 1960s for procuring drugs, such as antibiotics, by the Department of Defense and the Veterans Health Administration.[46] In more recent times, the US government threatened to invoke §1498 to obtain ciprofloxacin in bulk at the time of the anthrax attacks in 2001. This threat was never carried out because, in response, Bayer reduced the cost of the medication by more than 70% during negotiations with the federal government.[46]

DISCUSSION

Society benefits by more aggressively screening for and treating hepatitis C in incarcerated populations. Screening and treatment of incarcerated persons is cost-effective for society as a whole, and would reduce hepatitis C burden in the overall US population. Several modeling studies have evaluated the long-term benefits and costs of providing HCV screening and treatment in corrections. He and colleagues[16]

showed that universal opt-out screening of inmates for HCV in United States prisons would reduce ongoing HCV transmission, the incidence of advanced liver diseases, and liver-related deaths. Universal HCV screening followed by treatment with DAAs had an incremental cost-effectiveness ratio (ICER) of $19,800 per additional quality-adjusted life year (QALY), which is lower than that of the birth-cohort screening in the general population ($35,700–$65,700 per QALY).[52–55]

An interesting finding of the modeling study by He and colleagues[16] was that most of the benefits of interventions in prisons would accrue in the community, because a larger proportion of releasees to the community would have been cured of the disease. Compared with no screening, universal screening for up to 10 years would diagnose 123,000 new HCV cases, and 71,000 of those would be diagnosed among inmates currently incarcerated. Furthermore, such interventions would prevent 12,500 new HCV infections in the next 30 years. Of the averted infections (ie, incidence), around 90% of them would have occurred in the general population; that is, outside the prisons. Furthermore, HCV screening in prisons would prevent a total of 12,500 liver-related deaths, 1200 liver transplants, 9000 cases of hepatocellular carcinoma, and 7500 cases of decompensated cirrhosis, and most of them would be prevented outside prisons.

A study by Martin and colleagues[56] showed that doubling prison testing rates (such as through opt-out testing) with oral DAAs would be cost-effective in United Kingdom prisons (ICER £15,090 [approximately US$20,059] per QALY gained). In addition, if greater than 10% of referred PWID are treated in prison (2.5% base case), HCV treatment would be highly cost-effective (ICER<£13,000 [approximately US$17,280]). Another study by Martin and colleagues[57] showed that increasing case finding can be cost-effective in prisons if continuity of treatment and care is ensured after release.

Evidence for the value of HCV screening and treatment in corrections available from modeling studies can guide policy makers in establishing evidence-based guidelines that can restrict disease spread and improve outcomes in those already infected. The prioritization of cases in treating hepatitis C with curative DAAs has been called into question by data from a recent study that showed DAA treatment is important for reducing mortality at all stages of fibrosis.[58] HCV prevention efforts focusing on corrections not only will reduce HCV burden but will provide a good value for care. From a societal perspective, investing in prison health care to increase access to screening and treatment would be money well spent.

SUMMARY

- The opioid epidemic may be contributing to the plateau in prison HCV prevalence. The previously seen decline in prevalence has stalled. Greater access to HCV treatment in prison settings could help re-ignite a decline in prevalence of the disease.
- Access to prison-based treatment requires knowledge of whom to treat. At current levels of funding for HCV management, prisons are not aggressively seeking cases.
- In order to make screening acceptable in a system focused on avoiding deliberate indifference to known health problems, a policy to treat only the most urgent cases may be the lesser of 2 evils. The alternative is to continue not to screen, although the ideal solution is to reduce prices.
- Within current laws and regulations, use of nominal pricing seems to be the most viable option for substantially reducing prices. If this is not approved by the Secretary of Health and Human Services or if no pharmaceutical company is willing to sell medications at this price, other strategies are necessary. Some negotiating

power can be realized by individual corrections departments. However, changes in laws and policy at the federal level may be needed to help prisons contribute to efforts to make hepatitis C a rare disease for everyone.

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APPENDIX 1: PRICING LEVELS OF DRUGS IN THE US MARKET

- AWP is a drug-specific published price that was originally intended to represent the average price paid to wholesalers by pharmacies, doctors, and other customers (including correctional pharmacies) but that is now considered more like a sticker or list price than an actual market price.[37,38]
- WAC is the estimated manufacturer's list price to wholesalers, before any rebates or discounts are applied.
- AMP is the average price paid to a manufacturer by wholesalers for the manufacturer's drugs distributed to retail community pharmacies and by retail community pharmacies that purchase the drug directly from the manufacturers, subject to certain exceptions.[37] Pharmaceutical companies are required to report this price quarterly to the federal government.
- MDRP.

Background and Additional Information on the Medicaid Drug Rebate Program

The Omnibus Budget Reconciliation Act of 1990 is the enabling legislation for the MDRP, which results in savings for the Medicaid program. The MDRP is administered by the CMS, an agency within the DHHS.[59] Congress's goal in creating the rebate program was to ensure that federal and state taxpayers, who fund the Medicaid program,

are not paying more for pharmaceuticals than any other US purchaser. It achieves this goal by contractually obligating each pharmaceutical manufacturer to pay state Medicaid programs a quarterly rebate for each covered outpatient drug reimbursed by Medicaid. Although participation in the drug rebate program is optional for manufacturers, they have a strong incentive to enter into rebate agreements with the government because both Medicaid and Medicare are prohibited from reimbursing any drug manufactured by a company that refuses to execute a rebate agreement.[44]

For brand-name drugs, the rebate is based on the greater of either (1) a 23.1% discount off the drug's AMP or (2) the difference between the AMP and the manufacturer's best price for that drug.[60] In either case, an additional rebate is due if the drug's AMP increases more than the consumer price index, a measure of inflation.[59] The Medicaid rebate net price is the net price paid to a manufacturer after deducting the statutory rebate amount from the original price of the drug.[61] Because the Medicaid net price for a brand-name drug is at least as good as the best price for that drug, the Medicaid net price should generally be better than any price available in the private sector. With respect to generic and over-the-counter drugs, the rebate is 13% of the drug's AMP.[59,62]

The MDRP statute defines many of the key terms contained in the law's language. For example, based on the statute's definition of "manufacturer," the rebate obligations extend to not only traditional producers of pharmaceuticals but also to drug repackagers and relabelers.[63] Under the statute's definition of "covered outpatient drug," the class of drugs subject to rebates includes both prescription and nonprescription drugs and prescription biologic products, depending on the setting in which they are used.[63]

Could Prisons Qualify for Best Price?

Under 42 C.F.R. 447.505, which sets forth rules under Section 1927(c) (1) (C) of the Social Security Act, state prisons are not currently listed as exempt from the rule and are thus unable to buy medications at costs lower than the best price that drug companies offer to Medicaid, other than with certain exceptions listed earlier.

Some have advocated legislation to permit prisons to access drugs under the best-price agreement. One risk to proposing this strategy is that the Congressional Budget Office (CBO) may need to rate this proposal before congress votes on it. The CBO may assume that, if new discounts are proposed, the manufacturers would cut rebates elsewhere, including the price for medications purchased by the US government. With this assumption, the price for drugs purchased by Medicaid would increase. However, the assumption does not follow edicts encoded in federal law or regulation. Given that the state prison market is virtually untapped, industry would not need to increase prices elsewhere to offset the new discount; instead, their markets would be expanding. If Medicaid agencies lobby against extending an exception to prisons, prisons can ask their state Medicaid to cooperate with them to reduce prices.

- 340B: maximum price that can be charged to a 340B covered entity. The 340B ceiling price is calculated quarterly by the drug's manufacturer by subtracting the MDRP rebate amount from AMP. The minimum MDRP rebate for brand name drugs is AMP $\times$ 23.1%.[60]
- The Federal Supply Schedule. Under the Veterans Health Care Act of 1992,[64] the VA negotiates drug prices on behalf of many government agencies. Deepest discounts are for 4 entities (known as the Big 4) that are on the Federal Supply Schedule: the VA, Department of Defense, Public Health Service, and the US Coast Guard. Their price for medications is the FCP, which must represent at

least 24% off the AWP. Lesser discounts may be given to other federal agencies, such as the FBOP,[10] but the federal prison system still enjoys discounts not shared by state governments.[20]

The nominal price is the price that is less than 10% of AMP.[48] Five categories of purchasers and a sixth category of safety-net providers approved by the DHHS Secretary are allowed to negotiate and pay a nominal price, without establishing a new best price for purposes of the MDRP and 340B programs.[49,50,65]

- Cost to produce: $400 or less.[39,40]

Although the precise impact of the MDRP, 340B, FCP, and ASP laws on the prices paid by state and local correctional institutions can vary significantly by program,[66] they all disincentivize manufacturers from discounting their prices, including those charged for the new DAAs. That is because, if a state or local correctional facility is successful in negotiating deep discounts, those discounts would likely lower the prices at which the drugs' manufacturers could legally sell their drugs within those federal programs. All 4 programs rely on an averaging mechanism for calculating pricing so that, if a manufacturer agrees to sell 1 or more of its drugs at a low price within the nonfederal correctional market, those sales will have the effect of reducing the drugs' average price, which, in turn, will reduce program payment for those drugs. Sales to nonfederal correctional institutions are a small share of the total US pharmaceutical market so their impact on these average federal prices will be incremental and therefore modest. The more significant threat to manufacturer pricing arises out of a unique requirement in the MDRP that a manufacturer extend its best price on brand name drugs to the entire Medicaid and 340B programs. The impact of the Medicaid best-price requirement is more dramatic because, rather than reducing pricing incrementally, it can lead to a sharp decline in pricing that is sudden and triggered by a single transaction. In calculating best price, a manufacturer must, among other things, include cash discounts, volume discounts, rebates, and free goods (when contingent on any purchase requirement) but not take into account prices that are merely nominal in amount.[65]