Cost-effectiveness and Budgetary Impact of Hepatitis C Virus Testing, Treatment, and Linkage to Care in US Prisons

Sabrina A. Assoumou,^{1,2} Abriana Tasillo,¹ Claudia Vellozzi,³ Golnaz Eftekhari Yazdi,¹ Jianing Wang,¹ Shayla Nolen,¹ Liesl Hagan,⁴ William Thompson,⁴ Liisa M. Randall,⁵ Lara Strick,^{6,7} Joshua A. Salomon,⁸ and Benjamin P. Linas^{1,2,9}

¹Section of Infectious Disease, Department of Medicine, Boston Medical Center, and ²Section of Infectious Disease, Department of Medicine, Boston University School of Medicine, Massachusetts; ³Grady Health System, and ⁴Prevention Branch, Division of Viral Hepatitis, Centers for Disease Control and Prevention, Atlanta, Georgia; ⁵Massachusetts Department of Public Health, Boston; ⁶Division of Allergy and Infectious Diseases, Department of Medicine, University of Washington, Seattle; ⁷Washington State Department of Corrections, Tumwater; ⁸Stanford University School of Medicine, California; and ⁹Department of Epidemiology, Boston University School of Public Health, Massachusetts

(See the Major Article by Gutkind et al on pages 1397–405.)

Background. Hepatitis C virus (HCV) testing and treatment uptake in prisons remains low. We aimed to estimate clinical outcomes, cost-effectiveness (CE), and budgetary impact (BI) of HCV testing and treatment in United States (US) prisons or linkage to care at release.

Methods. We used individual-based simulation modeling with healthcare and Department of Corrections (DOC) perspectives for CE and BI analyses, respectively. We simulated a US prison cohort at entry using published data and Washington State DOC individual-level data. We considered permutations of testing (risk factor based, routine at entry or at release, no testing), treatment (if liver fibrosis stage $\geq F3$, for all HCV infected or no treatment), and linkage to care (at release or no linkage). Outcomes included quality-adjusted life-years (QALY); cases identified, treated, and cured; cirrhosis cases avoided; incremental cost-effectiveness ratios; DOC costs (2016 US dollars); and BI (healthcare cost/prison entrant) to generalize to other states.

Results. Compared to “no testing, no treatment, and no linkage to care,” the “test all, treat all, and linkage to care at release” model increased the lifetime sustained virologic response by 23%, reduced cirrhosis cases by 54% at a DOC annual additional cost of \$1440 per prison entrant, and would be cost-effective. At current drug prices, targeted testing and liver fibrosis-based treatment provided worse outcomes at higher cost or worse outcomes at higher cost per QALY gained. In sensitivity analysis, fibrosis-based treatment restrictions were cost-effective at previous higher drug costs.

Conclusions. Although costly, widespread testing and treatment in prisons is considered to be of good value at current drug prices.

Keywords. hepatitis C; prisons; computer simulation model; cost-effectiveness; budgetary impact.

Approximately 30% of hepatitis C virus (HCV)-infected people in the United States (US) pass through the prison system annually [1, 2]. Previous studies demonstrate that HCV testing and treatment in prisons is likely cost-effective [3–5] and that it may reduce HCV transmission in the community [3]. A gap remains, however, between the value for money (cost-effectiveness) and the affordability of such strategies (budgetary impact). Real-world correctional systems often feel ill prepared and underfunded to lead the public health mission of HCV elimination. Providers and policy makers in correctional settings know that HCV treatment is important, but they need data to inform

the costs and outcomes they can expect to accrue from a variety of realistic and practical testing and treating algorithms. Our goal, therefore, was to evaluate the clinical benefit and budgetary impact of multiple, realistic and feasible HCV testing and treatment strategies in US state prisons.

METHODS

Analytic Overview

The Hepatitis C Cost-effectiveness model is an individual-level transition simulation model of HCV screening, treatment, and linkage to care (Supplementary Figure 1) [6–8]. We adapted the existing model to simulate the lifespan of incarcerated individuals aged ≥ 18 years, with or without HCV infection, and their transitions between prison and the community. We used individual-level data from the Washington State Department of Corrections (WADOC) to inform demographics and HCV epidemiology within a real-world prison population. We compared 15 strategies, each of which was a permutation of the following (Table 1):

Received 5 December 2018; editorial decision 28 March 2019; accepted 14 May 2019; published online May 16, 2019.

Correspondence: S. A. Assoumou, Department of Medicine, Section of Infectious Disease, Boston University School of Medicine, Boston Medical Center, 801 Massachusetts Ave, Crosstown Center, 2nd Floor, Boston, MA 02118 (sabrina.assoumou@bmc.org).

Clinical Infectious Diseases® 2020;70(7):1388–96

© The Author(s) 2019. Published by Oxford University Press for the Infectious Diseases Society of America. All rights reserved. For permissions, e-mail: journals.permissions@oup.com.
DOI: 10.1093/cid/ciz383

1. Testing in prisons: (a) no testing at intake, (b) targeted testing of people who inject drugs and individuals born between 1945 and 1965 at intake, (c) routine testing of all inmates at intake, or (d) routine testing at prison release.
2. Treatment in prisons: (a) no treatment in prison, (b) treatment only for individuals with Metavir liver fibrosis stage F3 or higher ($\geq F3$), or (c) treatment for all individuals diagnosed with HCV infection at intake. For options “b” and “c,” only individuals with at least 12 months remaining in their sentence were eligible for treatment in prison.
3. Linkage to care intervention at prison release for individuals diagnosed with HCV infection, but not treated in prison: The simulated linkage to care intervention was based on the Antiretroviral Treatment and Access Services case management program for human immunodeficiency virus (HIV). The intervention included up to 5 visits with a case manager. It focused on addressing barriers to healthcare and building a relationship promoting linkage to care [9].

Primary outcomes from the model included life expectancy; quality-adjusted life-years (QALY); proportion of HCV infections identified, treated, and cured; undiscounted healthcare cost per prison entrant from the Department of Corrections (DOC) budgetary perspective; lifetime discounted costs from the healthcare sector perspective; and incremental cost-effectiveness ratios (ICERs).

Model Structure

Cohort Characteristics

WADOC offers routine, opt-out HCV testing to all incoming incarcerated persons (details below). We simulate a cohort including all prison entrants, each of whom is characterized by the age, sex, expected sentence duration, identified drug use history, HCV status, and liver fibrosis stage of an individual in the WADOC data set. An individual is characterized as having identified drug use history if he/she was arrested for a drug use-related offense, or self-reported a history of drug use at intake.

Movement Into and Out of Prison

Individuals start the simulation in prison and transfer to the community at the end of their sentences. After release, individuals are subject to a monthly probability of reincarceration. When simulated individuals return to prison, they are retested for HCV infection in prison as indicated by the simulated strategy.

HCV Natural History

At the start of the simulation, each HCV-infected individual is assigned a Metavir liver fibrosis stage based on an aspartate aminotransferase-to-platelet ratio index value at intake [10]. Throughout the simulation, infected individuals are exposed to a monthly probability of progressing to the next fibrosis stage. HCV infection at every fibrosis stage is associated with decreased quality of life and increased healthcare costs. When

Table 1. Strategies Considered

1. No testing in prison, no treatment in prison, no linkage intervention
2. Testing by risk factors at prison intake, no treatment in prison, no testing at release, linkage intervention
3. Testing by risk factors at prison intake, no treatment in prison, no testing at release, no linkage intervention
4. No testing at prison intake, no treatment, testing at release, no linkage intervention
5. No testing at prison intake, no treatment, testing at release, linkage intervention
6. Testing by risk factors at prison intake, treatment in prison if liver fibrosis stage $\geq F3$, no testing at release, linkage intervention
7. Testing by risk factors at prison intake, treatment in prison if liver fibrosis stage $\geq F3$, no testing at release, no linkage intervention
8. Testing by risk factors at prison intake, treatment for all in prison, no testing at release, linkage intervention
9. Testing by risk factors at prison intake, treatment for all in prison, no testing at release, no linkage intervention
10. Testing all at prison intake, no treatment in prison, no testing at release, linkage intervention
11. Test all at prison intake, no treatment in prison, no testing at release, no linkage intervention
12. Test all at prison intake, treatment in prison if liver fibrosis stage $\geq F3$, no testing at release, linkage intervention
13. Test all at prison intake, treatment in prison if liver fibrosis stage $\geq F3$, no testing at release, no linkage intervention
14. Test all at prison intake, treatment for all in prison, no testing at release, linkage intervention
15. Test all at prison intake, treatment for all in prison, no testing at release, no linkage intervention

individuals reach F4 liver fibrosis, they face a risk of HCV-attributable mortality. Fibrosis progression is interrupted by cure, but resumes on reinfection.

HCV Risk Behaviors

All individuals are categorized as either “drug users” (any type of drug use) or “non-drug users.” Identified drug use status affects risk of death from causes other than HCV, healthcare costs and quality of life, and incidence of HCV reinfection. Because the data source did not contain a marker for injection drug use vs noninjection use, we assume that the rate of HCV reinfection for all current drug users is the same as for current injection drug users, which tends to bias the simulation away from cost-effectiveness findings. HCV reinfection incidence is a fixed input.

Testing, Treatment, and Linkage to Care

For targeted testing, only individuals born between 1945 and 1965, and those with an identified history of any type of drug use (either self-reported at prison intake or assumed from their offense) are offered testing. In routine testing, everyone is tested, regardless of age or identified risk. Those identified with HCV infection must then link to HCV treatment in the prison. A proportion of those eligible for treatment then initiate treatment. All testing strategies assume a rate of HCV testing and treatment in the community, in addition to testing in prisons. Thus, if a person is not tested in a correctional setting, he or she may

still be identified and cured in the future. Patients not tested or treated in prison and individuals who become reinfected with HCV maintain future opportunities to be identified, linked to care, and cured [11].

We model HCV treatment with a pangenotypic regimen—8 weeks of glecaprevir/pibrentasvir for individuals without cirrhosis, and 12 weeks of sofosbuvir/velpatasvir for those with cirrhosis. When individuals achieve sustained virologic response (SVR), we assume that HCV-attributable costs decrease by 50% and quality of life increases, although it never returns to that of an age- and sex-matched individual without history of infection (Table 2). Liver-attributable mortality decreases by 94% among individuals who have cirrhosis and attain HCV cure [12]. The linkage to care program increases the probability of therapy in the community after release and accrues linkage-related costs to the DOC budget.

Base Case Inputs

Clinical Data

Table 2 provides descriptive statistics of cohort demographics, HCV infection prevalence, and fibrosis stages as sampled from the WADOC data set. Transitions into and out of active drug use were informed by the AIDS Link to Intravenous Experience (ALIVE) cohort [14]. Information on the natural history of HCV infection, mortality, and cascade of care inputs was obtained from cohort studies [12, 15–20]. Data regarding the cascade of care among incarcerated HCV-infected individuals were limited; therefore, we used publications on incarcerated HIV-infected individuals [9, 19, 30]. Diagnostic test characteristics were obtained from prospective studies while treatment effectiveness was derived from randomized controlled trials [22, 31].

Health-related Quality of Life and Cost

Health state utilities were informed by the literature and were computed using a multiplicative function of utilities related to current age and sex, liver fibrosis stage, drug use status, and incarceration status [28]. Since DOCs typically do not receive the same degree of HCV drug discounted pricing [32], we estimated treatment costs using the wholesale acquisition cost (WAC) [26]. We used the Medicare fee schedule to determine laboratory tests costs, and all costs were expressed in 2016 US dollars [27].

ANALYSES

We simulated the lifetime progression of the cohort from prison intake until death. We projected lifetime clinical outcomes, cost-effectiveness, and budgetary impact for each strategy. First, we performed cost-effectiveness analyses (CEAs) to identify and eliminate dominated strategies—strategies costing more than a competing strategy while providing less clinical benefit (strong dominance), or costing more on a cost per QALY basis

than another option while providing greater benefit (extended dominance). For CEAs, we discounted all costs and benefits 3% annually, and assumed a healthcare sector cost perspective and a lifetime time horizon. We expressed ICERs as the cost per QALY gained and interpreted cost-effectiveness conclusions using a willingness-to-pay threshold of \$100 000 per QALY [33].

Next, we estimated the budgetary impact of nondominated strategies using a DOC perspective, a 1-year time horizon, and no cost discounting. We expressed the total 12-month budgetary impact as the additional cost per person entering the prison compared to current practice. Finally, we conducted broad, deterministic sensitivity analyses to identify factors influencing either cost-effectiveness or budgetary impact conclusions, and to explore the stability of the findings.

Ethical Considerations

This study was approved by the Boston University Medical Center Institutional Review Board and the Washington State Department of Corrections Review Board.

RESULTS

Base Case

Clinical Outcomes

As expected, increased testing and treatment improved health outcomes. Moving from “no testing, no treatment in prison, and no linkage to care” to the most extensive policy of “test all, treat all, and linkage to care at release” substantially reduced liver fibrosis severity (Supplementary Figure 2) and increased the proportion of lifetime SVR (37% to 60%). There was also a 54% reduction in the lifetime cumulative prevalence of cirrhosis (Table 3).

Expanding testing had little impact on health outcomes unless there was also an increase in treatment access in prison, or linkage to care in the community (Table 3). When treatment in prisons was limited to only those patients with $\geq$ F3 liver fibrosis, expanding from risk-based to routine testing improved lifetime SVR by only 3% (39% vs 42%), and decreased the lifetime cumulative prevalence of cirrhosis by 13% (Table 3). In comparison, maintaining risk-based testing, but expanding treatment to all individuals with identified HCV infection, increased the proportion attaining SVR by 8% and reduced prevalence of cirrhosis by 7%. Adding linkage to care after release also improved outcomes. For example, “test all, treat all, and linkage to care at release” provided a higher proportion of lifetime SVR compared with “testing all, treat all, no linkage to care” (60% vs 54%).

Cost-effectiveness

Individuals in the simulated cohort composed of HCV-infected and HCV-uninfected individuals died on average at age 67 years, and accumulated \$176 310 in discounted lifetime medical costs. For HCV-infected individuals, comparing the “test all, treat all,

Table 2. Model Input Parameters

Variable	Base Case Value	Range Evaluated	Source
Cohort characteristics			
Mean age, y	36	33–39	WADOC (unpublished)
Proportion male, %	88	84–92	WADOC (unpublished)
Mean remaining sentence duration, mo	32	29–35	WADOC (unpublished)
Median rearrest incarceration duration, mo	12	10–14	WADOC (unpublished)
Baseline proportion PWID, %	40	35–45	WADOC (unpublished)
SMR, active PWID	6.1	5.2–7.0	[13]
Monthly probability of recovery from drug use	0.0139	0.0104–0.0174	[14]
Monthly probability of relapse to drug use	0.032	0.024–0.04	[14]
Baseline prevalence of chronic hepatitis C, %	14	7–21	WADOC (unpublished)
HCV infection in PWIDs (cases/100 PY)	12.3	2.7–17.1	[15]
Probability of clearing acute infection	0.26	0.19–0.32	[16]
HCV testing and other cascade of care parameters			
Background testing (tests per 100 PY)			
Community, general	2.73	1.37–4.10	MarketScan (unpublished)
Community, PWID	40	20–60	[17]
Linkage to care in the community			
Age ≤30 y, %	17.9	9.0–26.9	[18]
Age ≥30 y, %	28.9	14.5–43.4	[18]
Proportion of individuals identified with HCV in prison who initiate HCV-related care during prison time, % ^a	96	90–99	[19]
Proportion of individuals identified with HCV in prison and are linked to care at prison release, %	65	30–90	[9]
Probability of reengaging with care after being lost to follow-up, % ^b	15	10–20	Assumption (see foot-note)
HCV disease progression			
Monthly liver fibrosis progression rate			
F0–F1	0.0107	0.00535–0.01605	[20]
F1–F2	0.00492	0.00246–0.00738	[20]
F2–F3	0.00650	0.00325–0.00975	[20]
F3–F4	0.00967	0.00484–0.01451	[20]
F4–decompensated cirrhosis	0.00975	0.00488–0.01463	[20]
Liver mortality (deaths/100 PY)			
F4 (cirrhosis)	3	2–3	[12]
Decompensated cirrhosis	21	16–27	[12]
Therapy			
Therapy initiation in prison, %	67	34–99	[19]
Therapy initiation in the community, %	92	75–99	[21]
Treatment completion, %	97	94–100	[22]
Hepatotoxicity, %	0.36–1.18	(0.18–0.59)–(0.54–1.77)	[22]
SVR ^c after treatment, noncirrhotic, %	99	95–100	[22]
SVR after treatment, cirrhotic, %	93	90–96	[22]
Costs			
Routine medical costs per month with HCV, F0–F2, \$	296	148–444	[23, 24]
Routine medical costs per month with HCV, F3–F4 ^d , \$	528	264–792	[23, 24]
Routine medical costs per month with HCV, decompensated cirrhosis ^d , \$	1001	500–1500	[23, 24]
HCV therapy costs per month			
Complete course per month, no cirrhosis, glecaprevir/pibrentasvir ^e (8-wk course), \$	13 200	6600–19 800	[25]
Complete course per month, cirrhosis, sofosbuvir/velpatasvir (12-wk course), \$	22 920	15 940–29 900	[26]
Managing hepatotoxicity, \$	239	200–280	[27]
Intervention for linkage to care at prison release, \$	2250	1688–2813	[9]
Quality of life			
Without history of IDU or HCV infection (age specific) ^f	0.763–0.922	(0.685–0.844)–(0.841–1.00)	[28]
With history of active IDU	0.68	0.55–0.75	[28]
With history of past IDU	0.82	0.70–0.90	[28]

Table 2. Continued

Variable	Base Case Value	Range Evaluated	Source
With history of HCV, by fibrosis stage			
F0–F3	0.94	0.84–1.00	
F4	0.75	0.60–0.90	[29]
Decompensated	0.60	0.45–0.75	
After treatment, by fibrosis stage			
F0–F3	0.97	0.94–1.00	Expert opinion
F4	0.94	0.91–0.97	
Decompensated	0.75	0.60–0.90	

Costs are in 2016 US dollars. A range is reported for quality of life because this input was stratified by age. A range is reported for hepatotoxicity because treatment regimens were associated with different rates of liver toxicity.

Abbreviations: HCV, hepatitis C virus; IDU, injection drug use; PWID, person who injects drugs; PY, person-years; SMR, standardized mortality ratio; SVR, sustained virologic response; WADOC, Washington State Department of Corrections.

^aHCV-related care is defined testing or workup related to HCV treatment (HCV RNA testing, fibrosis staging).

^bTwenty-year probability of reengaging with care assumed to be half of original linkage probability (15% probability over 20 years).

^cProbability of SVR given reaching end of treatment.

^dCosts varied as a function of age and sex.

^eAt the time of this analysis, the cost of glecaprevir/pibrentasvir was not available on RedBook, and we made some assumptions using available reported cost.

^fThe <1.0 utility for those living without HCV infection reflects lower quality of life for individuals with HCV risk factors such as substance use.

and linkage to care at release” strategy to “no testing, no treatment, and no linkage to care,” life expectancy was greater by approximately 2 years (66 vs 64 years), and discounted lifetime costs increased by \$21 640 (\$220 510 vs \$198 870).

Risk-based testing and testing only at release (current practices in some prisons) were both dominated—meaning that they are an inefficient allocation of resources (Table 3). Similarly, restricting treatment to individuals with ≥F3 liver fibrosis staging was a dominated strategy regardless of testing strategy.

The only 2 strategies that emerged as nondominated and therefore an efficient use of limited resources were “test all, treat all, no linkage to care” and “test all, treat all, and linkage to care at release” (Figure 1). Compared to “no testing, no treatment, and no linkage to care,” the “test all, treat all, no linkage” strategy provided an additional 0.1374 discounted QALY, at an incremental discounted cost of \$2670, resulting in an ICER of \$19 000 per QALY gained (Table 3). Compared to “test all, treat all, no linkage,” the “test all, treat all, and linkage to care at release” strategy resulted in an additional 0.0673 QALY at an incremental cost of \$1590, resulting in ICER of \$24 000 per QALY gained.

Budgetary Impact Analysis

The 1-year budgetary impact to the DOC, expressed as the additional cost per individual entering the prison, was \$1300 per person for “test all, treat all, no linkage to care” and \$1440 per person for “test all, treat all, and linkage to care at release” compared with current practice.

Sensitivity Analyses

Recent reductions in the price of HCV medications have changed the economic context and impacted both cost-effectiveness

and budgetary impact conclusions. When using the WAC for sofosbuvir-velpatasvir (\$22 920 per month for a 3-month course), the “test all, treat ≥F3 with linkage to care” was no longer dominated and had an ICER of \$64 200 per QALY compared with “test all, treat ≥F3 without linkage to care at exit” (the next best strategy) (Supplementary Figure 3). The budgetary impact of “treat all” strategies was also sensitive to cost assumptions. When we assumed the WAC for sofosbuvir-velpatasvir, the 1-year additional cost per person for the “test all, treat all, and linkage to care at release” strategy was \$3030 per person, compared to \$1440 per person for the base case (Figure 2).

The finding that “test all, treat all, with linkage at release” was cost-effective was robust to all realistic estimates of HCV prevalence in corrections. Indeed, “test all, treat all, with linkage at release” was cost-effective unless the total prevalence of HCV was <0.1% and there were no incident HCV infections. Looking more broadly across all model parameters, within reasonable variations in our base case assumptions “test all, treat all, and linkage to care at release” had an ICER <\$100 000 per QALY gained (Supplementary Table 1). Testing and treating remained cost-effective even with HCV reinfection rates as high as 17.1 cases per 100 person-years (base case 12.3 cases/100 person-years), though high reinfection rates influenced the budgetary impact [15, 34].

DISCUSSION

Several key findings emerge from this work. First, recent drug price reductions have altered conclusions about the best approach for HCV testing and treatment in prisons. At higher costs observed when direct-acting antivirals were approved in 2013, prioritizing individuals with more advanced liver disease was an appropriate use of limited resources to control cost.

Table 3. Base Case Cost-effectiveness Analysis Results

Strategies	Undiscounted Remaining Life Expectancy, y	Total Discounted Cost/Person, \$	Discounted Remaining QALY/ Person	ICER (\$/QALY)	Lifetime SVR, %	Reduction in Cirrhosis Cases When Compared to Current Practice, %
1. No testing in prison, no treatment in prison, no linkage intervention (reference)	31.41	176 310	14.3672	...	37	...
3. Testing by risk factors at prison intake, no treatment in prison, no testing at release, no linkage intervention	31.42	176 430	14.3692	Extended dominated ^a	37	1
11. Test all at prison intake, no treatment in prison, no testing at release, no linkage intervention	31.45	176 640	14.3787	Extended dominated	38	4
4. No testing at prison intake, no treatment, testing at release, no linkage intervention	31.45	176 640	14.3791	Extended dominated	38	4
7. Testing by risk factors at prison intake, treatment in prison if liver fibrosis $\geq$ F3, no testing at release, no linkage intervention	31.46	177 050	14.3864	Extended dominated	39	5
9. Testing by risk factors at prison intake, treatment for all in prison, no testing at release, no linkage intervention	31.47	177 720	14.4000	Extended dominated	47	12
2. Testing by risk factors at prison intake, no treatment in prison, no testing at release, linkage intervention	31.49	178 310	14.4109	Extended dominated	47	15
13. Test all at prison intake, treatment in prison if liver fibrosis $\geq$ F3, no testing at release, no linkage intervention	31.65	178 460	14.4591	Extended dominated	42	18
6. Testing by risk factors at prison intake, treatment in prison if liver fibrosis $\geq$ F3, no testing at release, linkage intervention	31.51	178 590	14.4193	Dominated ^b	48	17
8. Testing by risk factors at prison intake, treatment for all in prison, no testing at release, linkage intervention	31.52	178 850	14.4251	Dominated	52	19
15. Test all at prison intake, treatment for all in prison, no testing at release, no linkage intervention	31.73	178 980	14.5046	19 000	54	39
10. Testing all at prison intake, no treatment in prison, no testing at release, linkage intervention	31.78	179 880	14.5289	Extended dominated	55	44
5. No testing at prison intake, no treatment, testing at release, linkage intervention	31.79	180 280	14.5336	Extended dominated	57	46
12. Test all at prison intake, treatment in prison if liver fibrosis $\geq$ F3, no testing at release, linkage intervention	31.85	180 500	14.5589	Extended dominated	56	49
14. Test all at prison intake, treatment for all in prison, no testing at release, linkage intervention ^c	31.87	180 570	14.5719	24 000	60	54

Costs are rounded to nearest \$10, QALYs to nearest 0.0001, ICERs to nearest \$1000/QALY. Small inconsistencies may be present due to rounding.

Abbreviations: ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life-year; SVR, sustained virologic response.

^aExtended dominance: strategies costing more on a cost per QALY basis than another option providing greater benefit.

^bStrong dominance: strategies costing more than a competing strategy while providing less clinical benefit.

^cTest all at prison entry, treat all individuals with at least 12 months in their sentence duration and linkage to care for those who are not treated in prison.

Although even at previous prices “test all, treat all” had an appealing ICER, it was unaffordable to many prisons. At today’s lower treatment costs, however, systems treating only patients with advanced fibrosis could use their available funds to attain better population-level outcomes, without increase in total spending, by moving to a “treat all” approach.

Second, current targeted testing approaches, which are an intuitively appealing strategy for many prisons, are a dominated strategy and should not be employed. Because many HCV cases occur among individuals who were born after 1965 and who have no identified history of drug use, targeting testing among those deemed to be at highest risk misses too many cases [32].

Above all, this analysis demonstrates that dialogue about HCV treatment in prisons needs to evolve to reflect the dynamic market for curative medications and avoid the historical conversation about treatment costing “one thousand dollars per pill [26].” Lower drug costs reduce the budgetary impact for treating all HCV-infected patients in prisons by >50%, but whether the new price point is “affordable” remains a question. In WADOC, with approximately 8000 intakes every year, the budgetary impact of “test all, treat all, and linkage to care at release” would be approximately \$11.5 million in the first year of the program compared with “no testing, no treatment, and no linkage to care.” This corresponds to

Figure 1. Cost-effectiveness frontier for hepatitis C virus infection testing and treatment in prisons. The figure illustrates the effectiveness, cost, and incremental cost-effectiveness of all 15 strategies considered. The color of each shape represents alternative testing approaches (no testing, testing by risk factors, testing all at entry, and testing all at release). Shapes (circles vs triangles) represent whether linkage to care is included in the strategy. The size of the shape represents alternative treatment approaches (no treatment, treatment if liver fibrosis stage $\geq$ F3, and treatment for all). Strategies located to the right of the efficiency frontier result in either lower quality-adjusted life expectancy at higher cost than an alternative strategy or a higher cost per quality-adjusted life-year gained. Strategies testing all at entry to prison provide better clinical outcomes than other testing approaches. “Test all, treat all, and linkage to care at release” also improves outcomes. The 2 strategies located on the cost-effectiveness frontier are “test and treat all with or without linkage to care.”

Figure 2. Sensitivity analysis for per-person 1-year budgetary impact from the prison perspective. The figure shows the influence of decreased drug price on the cost per person admitted to the prison. The green shape represents the “test all, treat all, and linkage to care at release” strategy. The blue shape shows the “test all, treat $\geq$ F3, and linkage to care at release” strategy. For “test all, treat all, and linkage to care at release,” the per-person additional cost compared to current practice fell from \$3030/person to \$1440/person when drug prices were decreased. For “test all, treat $\geq$ F3, and linkage to care at release,” there was only a modest change from \$630/person to \$550/person.

approximately 89% of the total pharmaceutical budget in 2016 [35]. The quandary in which prison systems find themselves is clear. Efforts to control cost result in inefficient spending and wasted resources with poor outcomes. Testing and treating all provided the best “value for money,” but because HCV is so prevalent in prisons, testing and treating all

remains an expensive undertaking. Implementing routine testing and treatment strategies will necessitate additional resources and outside partnerships.

One innovative model for financing HCV therapy is the “Netflix model” [36], so called because it involves payers committing to a fixed monthly fee in exchange for securing

unlimited supply of HCV treatment. Currently, in many states, however, the Department of Corrections is excluded from group negotiations between pharmaceutical manufacturers and public payers such as Medicaid. That silo effect is one contributor to the high cost of HCV treatments in correctional settings. Thus, the Netflix model, while attractive, may be difficult to implement in the real world.

There were some notable limitations to our study. First, we chose not to include HCV transmission in our simulation. Previous work demonstrates that HCV screening and treatment in correctional settings may decrease HCV incidence in the community [3]. At this time, however, most correctional systems have inadequate infrastructure and funding to support that public health effort. Rather than duplicate the finding about transmission dynamics, our goal was to generate cost and benefit data that assume the perspective of the corrections system and can therefore inform real-world decision making.

Our model was populated using data from the WADOC and we performed extensive sensitivity analyses to determine the generalizability to other US state prisons. Our findings were robust within reasonable variations in our base case estimates. We also provide an estimate of budgetary impact per new individual entering the prison system. Armed with a known population size and a known cost of testing and treatment, systems should be able to estimate that cost.

Another limitation is that because the WADOC database does not contain an indicator of injection vs noninjection drug use, we could not simulate the details of injection (vs noninjection) drug use. In the base case, we assumed that any individual entering prison whose intake nurse documented “chemical dependency” carried a risk of HCV reinfection after cure equivalent to active injection drug users. This assumption tended to bias the conclusions away from cost-effectiveness, because it likely overestimated the number of patients who would be reinfected after HCV cure.

In addition, we used information on HIV linkage to care rates, as we did not have comparable information for HCV. Correctional systems are experimenting with postrelease linkage to care interventions, and they will be evaluated in time. While we wait for such data, however, a decision must be made about what to do today. A strength of a simulation modeling approach is that it allows the investigator to integrate best available data at the time of the analysis and then to use sensitivity analyses to test the robustness of results to those assumptions.

In conclusion, given the decrease in HCV drug costs, commonly used and intuitive cost-control strategies—targeted testing and/or treatment restrictions to individuals with advanced disease—may not lead to the best allocation of limited resources, or to the best population health outcomes. Nevertheless, even with recent decreases in drug costs, “test all, treat all, and linkage to care at release” would consume the

majority of a state prison system’s pharmaceutical budget in most states. Addressing HCV in prisons will require investment in correctional health and partnerships, including with public health departments.

Supplementary Data

Supplementary materials are available at *Clinical Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Note

Disclaimer. The findings and conclusions of this study are those of the authors and do not necessarily represent the official position of the US Centers for Disease Control and Prevention (CDC) or the National Institutes of Health (NIH).

Financial support. This work was supported by the CDC and National Center for HIV, Viral Hepatitis, STD, and TB Prevention Epidemiologic and Economic Modeling Agreement (grant number 5NU38PS004644), which contributed to the conception, design, and analysis and the decision to submit the manuscript for publication. Support was also obtained from the National Institute on Drug Abuse (grant numbers K23 DA044085-01, R01DA046527, and P30 DA040500) and the National Institute of Allergy and Infectious Diseases (5P30AI042853-18) of the NIH.

Potential conflicts of interest. The authors: No reported conflicts of interest. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

References

1. Spaulding AS, Kim AY, Harzke AJ, et al. Impact of new therapeutics for hepatitis C virus infection in incarcerated populations. *Top Antivir Med* 2013; 21:27–35.
2. Varan AK, Mercer DW, Stein MS, Spaulding AC. Hepatitis C seroprevalence among prison inmates since 2001: still high but declining. *Public Health Rep* 2014; 129:187–95.
3. He T, Li K, Roberts MS, et al. Prevention of hepatitis C by screening and treatment in U.S. prisons. *Ann Intern Med* 2016; 164:84–92.
4. Tan JA, Joseph TA, Saab S. Treating hepatitis C in the prison population is cost-saving. *Hepatology* 2008; 48:1387–95.
5. Liu S, Watcha D, Holodniy M, Goldhaber-Fiebert JD. Sofosbuvir-based treatment regimens for chronic, genotype 1 hepatitis C virus infection in U.S. incarcerated populations: a cost-effectiveness analysis. *Ann Intern Med* 2014; 161:546–53.
6. Assoumou SA, Tasillo A, Leff JA, et al. The cost-effectiveness of one-time hepatitis C screening strategies among adolescents and young adults in primary care settings. *Clin Infect Dis* 2018; 66:376–84.
7. Linas BP, Barter DM, Leff JA, et al. The cost-effectiveness of improved hepatitis C virus therapies in HIV/hepatitis C virus coinfecting patients. *AIDS* 2014; 28:365–76.
8. Linas BP, Barter DM, Morgan JR, et al. The cost-effectiveness of sofosbuvir-based regimens for treatment of hepatitis C virus genotype 2 or 3 infection. *Ann Intern Med* 2015; 162:619–29.
9. Linas BP, Barter DM, Leff JA, et al. The hepatitis C cascade of care: identifying priorities to improve clinical outcomes. *PLoS One* 2014; 9:e97317.
10. Lin ZH, Xin YN, Dong QJ, et al. Performance of the aspartate aminotransferase-to-platelet ratio index for the staging of hepatitis C-related fibrosis: an updated meta-analysis. *Hepatology* 2011; 53:726–36.
11. Evans E, Li L, Min J, et al. Mortality among individuals accessing pharmacological treatment for opioid dependence in California, 2006–10. *Addiction* 2015; 110:996–1005.
12. Bruno S, Zuin M, Crosignani A, et al. Predicting mortality risk in patients with compensated HCV-induced cirrhosis: a long-term prospective study. *Am J Gastroenterol* 2009; 104:1147–58.
13. Mathers Bradley M, Degenhardt L, Bucello C, Lemon J, Wiessing L, Hickman M. Mortality among people who inject drugs: a systematic review and meta-analysis. *Bull World Health Organ* 2013; 91:102–23.
14. Galai N, Safaiean M, Vlahov D, Bolotin A, Celentano DD. Longitudinal patterns of drug injection behavior in the ALIVE study cohort, 1988–2000: description and determinants. *Am J Epidemiol* 2003; 158:695–704.

15. Sacks-Davis R, Grebely J, Dore GJ, et al; InC3 Study Group. Hepatitis C virus reinfection and spontaneous clearance of reinfection—the InC3 study. *J Infect Dis* **2015**; 212:1407–19.
16. Micallef JM, Kaldor JM, Dore GJ. Spontaneous viral clearance following acute hepatitis C infection: a systematic review of longitudinal studies. *J Viral Hepat* **2006**; 13:34–41.
17. Coffin PO, Jin H, Huriaux E, Mirzazadeh A, Raymond HF. Trends in use of health care and HIV prevention services for persons who inject drugs in San Francisco: results from National HIV Behavioral Surveillance 2005–2012. *Drug Alcohol Depend* **2015**; 146:45–51.
18. Viner K, Kuncio D, Newbern EC, Johnson CC. The continuum of hepatitis C testing and care. *Hepatology* **2015**; 61:783–9.
19. Iroh PA, Mayo H, Nijhawan AE. The HIV care cascade before, during, and after incarceration: a systematic review and data synthesis. *Am J Public Health* **2015**; 105:e5–16.
20. Smith DJ, Combellick J, Jordan AE, Hagan H. Hepatitis C virus (HCV) disease progression in people who inject drugs (PWID): a systematic review and meta-analysis. *Int J Drug Policy* **2015**; 26:911–21.
21. Younossi ZM, Bacon BR, Dieterich DT, et al. Disparate access to treatment regimens in chronic hepatitis C patients: data from the TRIO network. *J Viral Hepat* **2016**; 23:447–54.
22. Feld JJ, Jacobson IM, Hezode C, et al. Sofosbuvir and velpatasvir for HCV genotype 1, 2, 4, 5, and 6 infection. *N Engl J Med* **2015**; 373:2599–607.
23. Agency for Healthcare Research and Quality. Total health services-mean and median expenses per person with expense and distribution of expenses by source of payment: medical expenditure panel survey household component data [generated interactively]. Available at: <http://meps.ahrq.gov/mepsweb/>. Accessed 12 July 2017.
24. Davis KL, Mitra D, Medjedovic J, Beam C, Rustgi V. Direct economic burden of chronic hepatitis C virus in a United States managed care population. *J Clin Gastroenterol* **2011**; 45:e17–24.
25. Nisen M. AbbVie wages HCV drug-price war. *BloombergGadfly*, **2017**. Available at: https://www.bloomberg.com/gadfly/amp/articles/2017-08-07/abbvie-mavyret-price-threatens-gilead-hepatitis-dominance?utm_source=STAT+Newsletters&utm_campaign=6155ad6ce1-EMAIL_CAMPAIGN_2017_08_07&utm_medium=email&utm_term=0_8cab1d7961-6155ad6ce1-149726369. Accessed 4 August 2017.
26. Solutions M. Drug topics red book online, **2017**. Available at: <http://www.micromedexsolutions.com/>. Accessed 13 September 2017.
27. United States Department of Health and Human Services Center for Medicare Services. Physician Fee Schedule. Available at: <http://www.cms.gov/Medicare/Medicare-Fee-for-Service-Payment/PhysicianFeeSched/index.html?redirect=/PhysicianFeeSched>. Accessed 3 August 2017.
28. Sullivan PW, Ghushchyan V. Preference-based EQ-5D index scores for chronic conditions in the United States. *Med Decis Making* **2006**; 26:410–20.
29. McLernon DJ, Dillon J, Donnan PT. Health-state utilities in liver disease: a systematic review. *Med Decis Making* **2008**; 28:582–92.
30. Afdhal NH, Zeuzem S, Schooley RT, et al; New Paradigm of HCV Therapy Meeting Participants. The new paradigm of hepatitis C therapy: integration of oral therapies into best practices. *J Viral Hepat* **2013**; 20:745–60.
31. Freiman JM, Tran TM, Schumacher SG, et al. Hepatitis C core antigen testing for diagnosis of hepatitis C virus infection: a systematic review and meta-analysis. *Ann Intern Med* **2016**; 165:345–55.
32. Beckman AL, Bilinski A, Boyko R, et al. New hepatitis C drugs are very costly and unavailable to many state prisoners. *Health Aff (Millwood)* **2016**; 35:1893–901.
33. Neumann PJ, Russell LB, Sanders GD, Siegel JE, Ganiats TG. Cost effectiveness in health and medicine. 2nd ed. New York, NY: Oxford University Press, **2017**.
34. Astell-Burt T, Flowerdew R, Boyle P, Dillon J. Is travel-time to a specialist centre a risk factor for non-referral, non-attendance and loss to follow-up among patients with hepatitis C (HCV) infection? *Soc Sci Med* **2012**; 75:240–7.
35. Department of Corrections Washington State. Operating Budget Request 2017–2019 Biennium. Available at: <http://www.doc.wa.gov/about/agency/docs/2017-19-operating-budget.pdf>. Accessed 4 November 2017.
36. Trusheim MR, Cassidy WM, Bach PB. Alternative state-level financing for hepatitis C treatment—the “Netflix model.” *JAMA* **2018**; 320:1977–8.