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MAJOR ARTICLE

Cost-effectiveness of Direct Antiviral Agents for Hepatitis C Virus Infection and a Combined Intervention of Syringe Access and Medication-assisted Therapy for Opioid Use Disorders in an Injection Drug Use Population

Elizabeth R. Stevens,[1,2] Kimberly A. Nucifora,[1] Holly Hagan,[2,3] Ashly E. Jordan,[3,4] Jennifer Uyei,[1] Bilal Khan,[5] Kirk Dombrowski,[5] Don des Jarlais,[2] and R. Scott Braithwaite[1,3]

[1]Department of Population Health, New York University School of Medicine, New York, New York, USA; [2]New York University College of Global Public Health, New York, New York, USA; [3]Center for Drug Use and Human Immunodeficiency Virus Research, New York University College of Global Public Health, New York, New York, USA; [4]School of Public Health and Health Policy, City University of New York, New York, New York, USA; [5]Department of Sociology, University of Nebraska-Lincoln, Lincoln, Nebraska, USA

Background. There are too many plausible permutations and scale-up scenarios of combination hepatitis C virus (HCV) interventions for exhaustive testing in experimental trials. Therefore, we used a computer simulation to project the health and economic impacts of alternative combination intervention scenarios for people who inject drugs (PWID), focusing on direct antiviral agents (DAA) and medication-assisted treatment combined with syringe access programs (MAT+).

Methods. We performed an allocative efficiency study, using a mathematical model to simulate the progression of HCV in PWID and its related consequences. We combined 2 previously validated simulations to estimate the cost-effectiveness of intervention strategies that included a range of coverage levels. Analyses were performed from a health-sector and societal perspective, with a 15-year time horizon and a discount rate of 3%.

Results. From a health-sector perspective (excluding criminal justice system–related costs), 4 potential strategies fell on the cost-efficiency frontier. At 20% coverage, DAAs had an incremental cost-effectiveness ratio (ICER) of $27 251/quality-adjusted life-year (QALY). Combinations of DAA at 20% with MAT+ at 20%, 40%, and 80% coverage had ICERs of $165 985/QALY, $325 860/QALY, and $399 189/QALY, respectively. When analyzed from a societal perspective (including criminal justice system–related costs), DAA at 20% with MAT+ at 80% was the most effective intervention and was cost saving. While DAA at 20% with MAT+ at 80% was more expensive (eg, less cost saving) than MAT+ at 80% alone without DAA, it offered a favorable value compared to MAT+ at 80% alone ($23 932/QALY).

Conclusions. When considering health-sector costs alone, DAA alone was the most cost-effective intervention. However, with criminal justice system–related costs, DAA and MAT+ implemented together became the most cost-effective intervention.

Keywords. cost-effectiveness; HCV; PWID; combination intervention; DAA.

Hepatitis C virus (HCV) is a major cause of preventable morbidity and mortality worldwide [1]. Between 2010 and 2015, the number of new HCV infections in the United States nearly tripled [2], and HCV-related deaths in the United States exceeded deaths related to human immunodeficiency virus (HIV) and 60 other infectious diseases combined [3, 4].

In North America, there are an estimated 2.56 million people who inject drugs (PWID), and 1.41 million (55.2%) are estimated to be positive for HCV antibodies [5]. Combined, HCV infections and other consequences of drug injection contribute to billions of dollars of preventable expenses in health-care costs, as well as costs to society and individuals: in particular, costs associated with the criminalization of drug use [6–8]. The rise in HCV infections has been closely linked to the epidemic of misuse of prescription opioids in the United States, which has led to a resurgence of heroin use and injection in the United States [9, 10].

The risk of HCV acquisition can be reduced through effective PWID "harm reduction" strategies [11]. When syringe access programs (NSP) are combined with medication-assisted treatment (MAT) and provided simultaneously as a single intervention (ie, individuals on MAT also receive high NSP coverage [MAT+]), it is associated with a 76% reduction in the risk of HCV acquisition, compared to no MAT and low/no coverage with NSP [11]. This represents a significant improvement in efficacy, compared to implementing MAT and syringe access programs as separate interventions [11].

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Correspondence: E. R. Stevens, Department of Population Health, New York University School of Medicine, 227 E. 30th St., New York, NY 10016 (Elizabeth.stevens@nyulangone.org).

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Increasing the coverage of harm reduction in the form of MAT+ alone, however, may not be sufficient to address the rising rates of HCV infections [12, 13]. With new, highly effective antiviral medications becoming available, HCV treatment has the potential to transform the trajectory of HCV transmission and disease progression [14–17]. However, fewer than 13% of PWID who are living with HCV receive the current treatment regimen of direct antiviral agents (DAAs) [18], with nearly half of US states denying access to HCV treatment to those with current substance use disorders [19].

We are presently faced with a tremendous opportunity to achieve the World Health Organization's (WHO's) goal of HCV elimination [20]. New evidence suggests that only combination interventions addressing both prevention and treatment will reduce HCV in PWID to a significant degree [21]. Multicomponent interventions, however, can be too costly and/or too numerous to examine in randomized controlled trials. Therefore, we performed an allocative efficiency study, using a mathematical model that simulated the progression of HCV in PWID and the related consequences of HCV infection. We sought to determine the optimal scale-up strategy, in terms of cost-effectiveness, for various combinations of 2 intervention types that, together, address both HCV and opioid use disorder. The interventions included (1) a single intervention that combines MAT and 100% coverage of NSPs (ie, use of only sterile needles; the combination of which is henceforth referred to as the MAT+ intervention); and (2) DAA treatment to cure chronic HCV infection.

METHODS

We combined 2 previously validated simulations, including an agent-based simulation of HCV and HIV transmission among a PWID population [22] and a Markov model of HCV-related liver disease progression [23], to estimate the cost-effectiveness of intervention strategies that included a range of coverage levels of MAT+ and DAA in New York City (NYC). The agent-based model determined the HCV incidence and prevalence rates for a cohort of PWID with varying intervention coverage levels of MAT+ and DAA. The Markov model was then used to generate health-care costs and clinical outcomes related to the treatment of HCV and HCV-related health care for each intervention strategy. Select input parameters specific to this analysis can be found in Table 1, and a complete summary of inputs for the 2 component simulations can be found in prior publications [22, 23].

Intervention Strategies

We simulated 25 intervention scenarios, representing combinations of 2 intervention types at varying degrees of scale-up coverage. Intervention scenarios included MAT+, where MAT would be linked to NSPs, as a single intervention [11], and DAAs to cure HCV. These interventions were simulated under various combinations of annual intervention coverage levels for MAT+ (20%, 40%, 60%, and 80%) and DAA (5%, 10%, 15%, and 20%). In the case of MAT+, the term 20% MAT+ means 20% of PWID would receive MAT and there would be 100% NSP coverage for those receiving MAT. The standard of care (SC) in NYC includes some levels of MAT (43%), NSP (16% PWID receiving, on average, 246 syringes per PWID), and DAA (22%) coverage [34–36], which were represented in the baseline HCV transmission rates of the model. The intervention coverage levels represent a percent of coverage on top of the coverage already present in SC.

Agent-based Network Simulation of Hepatitis C Virus Transmission

HCV transmission was modeled by an agent-based network simulation of PWID that was developed by Dombrowski and Khan [22, 37, 38]. This agent-based simulation has been described previously [22, 37, 38]. The simulation creates a population of agents who are assigned behavioral and demographic states, disease statuses, risk propensities, and risk network connections, derived from data from the Centers for Disease Control [39, 40] and validated against recent meta-analyses [41] and NYC incidence and prevalence estimates [39, 42]. Risk network connections represent drug co-use relationships with regular co-injectors, with whom risk events are likely to happen. In the simulation, agents act independently to perform risk acts within social networks, based on their risk propensities. They also change social networks through a process that periodically removes 1 of their links and replaces it with a new link. Over time, individuals may become infected with HCV.

Following the approach of Khan and colleagues [43], the model was calibrated using a per-risk-act infection probability for HCV as a tuning parameter. The final setting (0.009 chance of infection per risk act) produced current HCV infection prevalence levels (60–70%) that matched then-current HCV levels in the NYC PWID population (and among US PWID more generally) [39, 44, 45].

Interventions were applied in the simulation as follows: (1) SC, meaning no change in prevention or treatment activities beyond those currently implemented in NYC; (2) MAT+, which would reduce the transmission risk; and (3) treatment with DAA to chronically infected agents. In each scenario, an individual can be reinfected with HCV if the infection is cleared or successfully treated. The simulation was used to generate HCV incidence and prevalence trajectories for each intervention scenario (Figure 1). These HCV incidence trajectories were then used as input parameters for the Markov model.

Markov Liver Disease Model

We utilized a previously validated decision analytic Markov model [23], simulating HCV treatments; the development

Table 1. Key Model Inputs

Variable	Value	Reference
Disease progression		
HCV incidence	Varied	From agent-based simulation; Figure 1
MAT+ intervention effect on HCV acquisition risk	RR 0.26	[11]
Probability of spontaneous HCV clearance by 12 months	0.243	[13]
Annual rate of developing compensated cirrhosis, given HCV positivity	0.0197	[24]
HCC screening frequency	6 months	[25, 26]
Healthcare costs, 2016 $		
Ultrasound for HCC	135	[27]
Biopsy	762	[28]
Computerized tomography	282	[28]
Magnetic resonance imaging	496	CMS Medicare
HCV screening	111.58	CMS Medicare
HCV antiviral	61 020	CMS Medicare
Liver transplant	85 570	CMS Medicare
Liver transplant complications	65 010	CMS Medicare
Radiofrequency ablation	4130	[28]
Radiofrequency ablation complications	316	CMS Medicare
Sorafenib, annual	11 778	CMS Medicare
Sorafenib complications	99	CMS Medicare
Surgical resection	45 694	CMS Medicare
Surgical resection complications	3155	CMS Medicare
TACE, annual	9001	[28]
TACE complications	397	CMS Medicare
Terminal care, death related to surgery	35 783	[29]
Terminal care, related to HCC or liver disease	33 688	[30]
Intervention costs		
Direct-acting antivirals, per regimen	50 580	[31]
Methadone treatment, annual per person, including medication and integrated psychosocial and medical support services, assuming daily visits	6552	[32]
Buprenorphine treatment, annual per person, for stable patient, provided in a certified OTP, including medication and twice-weekly visits	5980	[32]
Needle and syringe programs, annual per person	183	CT Department of Health
Injection drug use-related crime costs, annual per person	35 494	[33]

Abbreviations: CMS, Centers for Medicare & Medicaid Services; CT, Connecticut; HCC, hepatocellular cancer; HCV, hepatitis C virus; MAT+, medication-assisted treatment with syringe access programs; OTP, opioid therapy provider; RR, relative risk; TACE, transarterial chemoembolization.

and progression of HCV-related cirrhosis; liver failure; HCC; and their treatment to generate the quality-adjusted life-years (QALYs) and costs associated with each intervention strategy. The model was developed by Uyei et al [23] to evaluate the optimal surveillance frequency for patients with HCV-related compensated cirrhosis, and was validated against data from the Veterans Outcomes and Costs Associated with Liver Disease study. The model was then modified to take the incidence rate data generated by the agent-based simulation as input (see Table 2 and Figure 1) [22]. Figure 2 illustrates the interactions of the 2 simulations, including model stages and available treatment at each stage.

Cost-effectiveness Analysis

We conducted simulations where the intervention combination strategies were activated 1 at a time, and calculated the health benefits, costs, and cost-effectiveness ratios of each over a 15-year time horizon. These simulations were compared to a reference case, SC, where no additional coverage of intervention strategies was implemented beyond the coverage already present in NYC. A 5-year lead-in period was used prior to activating intervention strategies to arrive at stochastic stability and to avoid transient effects from the initial population network starting point [46–48]. Outcomes measured include total QALYs gained, cost per QALY gained, HCV incidence and prevalence rates, and incremental cost-effectiveness ratios (ICERs).

The analysis was performed using 2 perspectives: a health sector perspective and a limited societal perspective. Both analysis scenarios incorporated intervention costs and health-care costs; however, the societal perspective analyses also included the costs associated with the criminalization of substance use, composed of the costs of policing, court, corrections, and criminal victimization [33]. Criminal justice system costs were used

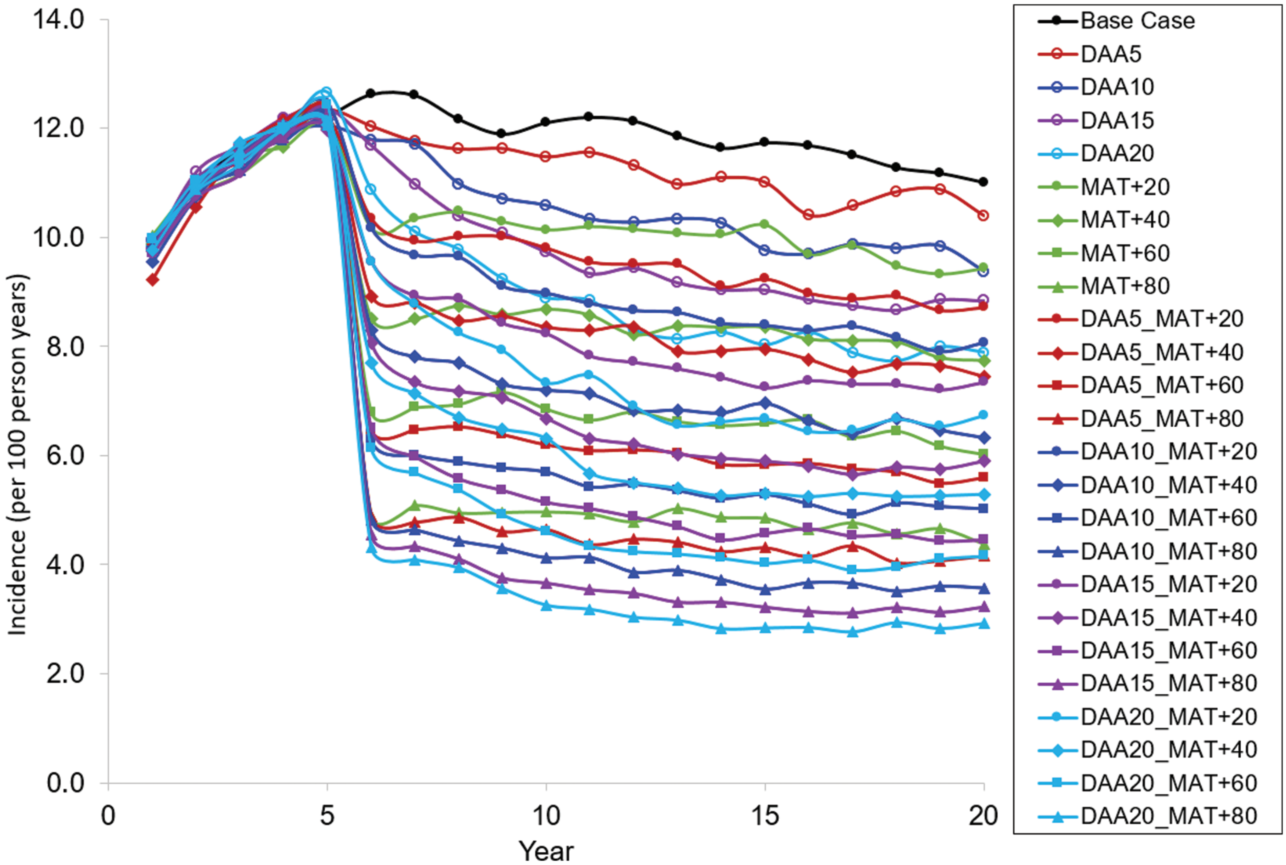

Figure 1. Hepatitis C virus incidence by intervention strategy. Numbers indicate percentage extent of coverage. Abbreviations: DAA, direct antiviral agents; MAT+, m–edication-assisted therapy and needle syringe intervention.

as a surrogate for societal costs, as they represent a large proportion of the direct costs of opioid use disorder (OUD) [49]. The analyses did not include costs related to opioid overdoses or HIV screening and treatment, and did not examine the impact of living with HCV on employment or income. Base case analyses used a MAT cost for buprenorphine, and a sensitivity analysis was performed using methadone costs. Costs of HCV treatments and interventions were assessed within the Markov model and reflect 2016 United States dollars. Cost inputs can be found in Table 1.

We calculated the ICERs of each intervention strategy. ICERs measure the additive benefits and costs of each strategy, compared with its next best alternative. A cost per QALY gained value of less than $100k was considered cost-effective [50].

RESULTS

Hepatitis C Virus Incidence

The strategies that most reduced the HCV incidence were a combination of MAT+ at 80% with a DAA coverage of 10%, 15%, and 20%, reducing incidences to 3.57, 3.23, and 2.93 cases per 100 person-years, respectively, from the base case of 11.00 cases per 100 person-years (Figure 1). Similarly, a combination of MAT+ at 80% with a DAA coverage of 10%, 15% and 20%

Table 2. Incidence Rate of Hepatitis C Virus Among Uninfected Agents in 100 Person Years

Intervention	Standard Care	DAA 5%	DAA 10%	DAA 15%	DAA 20%
Standard Care	11.00 (0.25)	10.40 (0.35)	9.37 (0.39)	8.84 (0.28)	7.89 (0.33)
MAT+ 20%	9.43 (0.68)	8.72 (0.30)	8.07 (0.28)	7.35 (0.16)	6.74 (0.32)
MAT+ 40%	7.74 (0.37)	7.44 (0.67)	6.33 (0.33)	5.90 (0.21)	5.29 (0.26)
MAT+ 60%	6.02 (0.38)	5.58 (0.41)	5.02 (0.32)	4.46 (0.28)	4.16 (0.28)
MAT+ 80%	4.38 (0.29)	4.16 (0.30)	3.57 (0.28)	3.23 (0.20)	2.93 (0.15)

Data are from [22]. Measures were after the completion of 15-year simulations that followed a 5-year burn-in period. Results show the mean and standard deviation for each state from 15 independent simulations of networked populations of 10 000 actors. Abbreviations: DAA, direct antiviral agents; MAT+, medication-assisted treatment with syringe access programs.

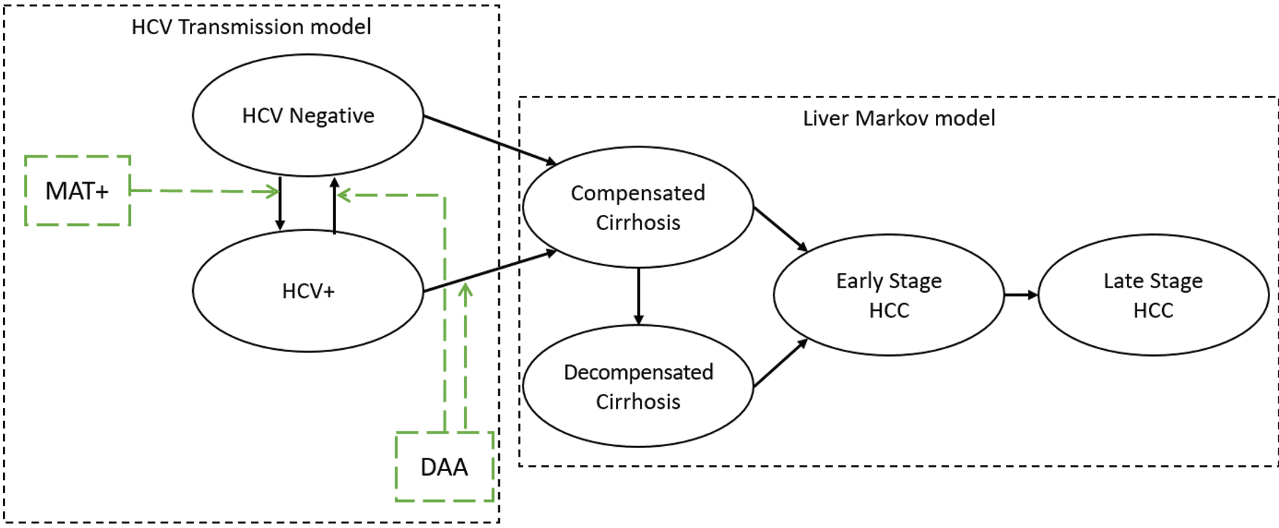

Figure 2. Transmission and progression of hepatitis C virus-related compensated cirrhosis and stage-specific treatments. Abbreviations: DAA, direct antiviral agents; HCC, hep–atocellular cancer; HCV, hepatitis C virus; MAT+, medication-assisted therapy and needle syringe intervention.

decreased the HCV prevalences to 43.6%, 39.8%, and 36.2%, respectively, from the base case of 61.6%.

Quality-adjusted Life-years Gained

All intervention strategies including 20% DAA coverage resulted in the highest number of QALYs gained; a combination of 20% DAA coverage and MAT+ at 20%, 40%, 60%, and 80% coverage resulted in 0.99, 1.04, 1.07, 1.09, and 1.12 QALYs gained per capita, respectively. Intervention strategies containing MAT+ alone had the lowest QALYs gained per capita, with 80% MAT+ coverage resulting in 0.12 QALYs gained per capita. (Figure 3A)

Costs Per Capita

When implemented using a health-sector perspective, intervention strategies—including MAT+ at 80% coverage—resulted in the greatest change in per capita costs. A combination of 80% MAT+ coverage and DAA coverage of 10%, 15%, and 20% increased costs by $49 964, $55 138, and $60 266 per capita, respectively, compared to SC, wich was at $3298 per capita. The lowest costs were seen in strategies with MAT+ alone at 20% coverage and with DAA alone at 5% or 10% coverage, increasing costs by $10 306, $9762, and $15 903 per capita, respectively. (Figure 3B)

When including criminal justice system–related costs, all interventions containing MAT+ reduced costs. Costs were reduced most by MAT+ with 80% coverage and by MAT+ with 80% coverage, combined with DAA coverage of 5% and 10%, which reduced costs by $196 276, $187 126, and $181 672 per capita, respectively. DAA with 20% coverage increased costs the most, by $27 601 per capita (Figure 3C).

In sensitivity analyses, when comparing changes in costs for the use of methadone versus the baseline of buprenorphine in the MAT+ strategies, methadone increased the costs for all strategies, with strategies containing MAT+ with 20%, 40%, 60%, and 80% coverage increasing by $958, $1916, $2875, and $3835 per capita, respectively.

Cost-effectiveness

When implemented from a health-sector perspective (Table 3), 4 potential strategies fell on the cost-efficiency frontier. DAA alone at 20% coverage, and combinations of DAA 20% and MAT+ at 20%, 40%, and 80% coverage, had ICERs of $22 470/QALY, $172 091/QALY, $332 205/QALY, and $385 824/QALY, respectively (Figure 4A). Note that MAT+ coverage of 60% fell very close to the efficiency frontier, likely as a result of stochastic variation. When implemented from a societal perspective, all strategies were cost-saving, excluding the noncombination DAA strategies. Of these cost-saving strategies, 2 fell on the cost-efficiency frontier: MAT+ at 80% coverage and the combination of DAA at 20% and MAT+ at 80% coverage (ICER of $20 049/QALY; Figure 4B). In sensitivity analyses, when assuming a lower cost of DAA ($26 400), the strategies falling on the efficiency frontier remained the same in both the health-sector and modified societal perspectives; however, strategies with DAA alone had more favorable ICERs.

DISCUSSION

Our analyses suggested that from a health-sector perspective, a scale-up of DAA to 20% coverage was the most cost-effective strategy, with an ICER of $22 471/QALY. The next most cost-effective strategy was DAA at 20% coverage, combined with MAT+ at 20% coverage, with an ICER of $172 091/QALY. However, when considering criminal justice system–related societal costs, a strategy of MAT+ with 80% coverage became

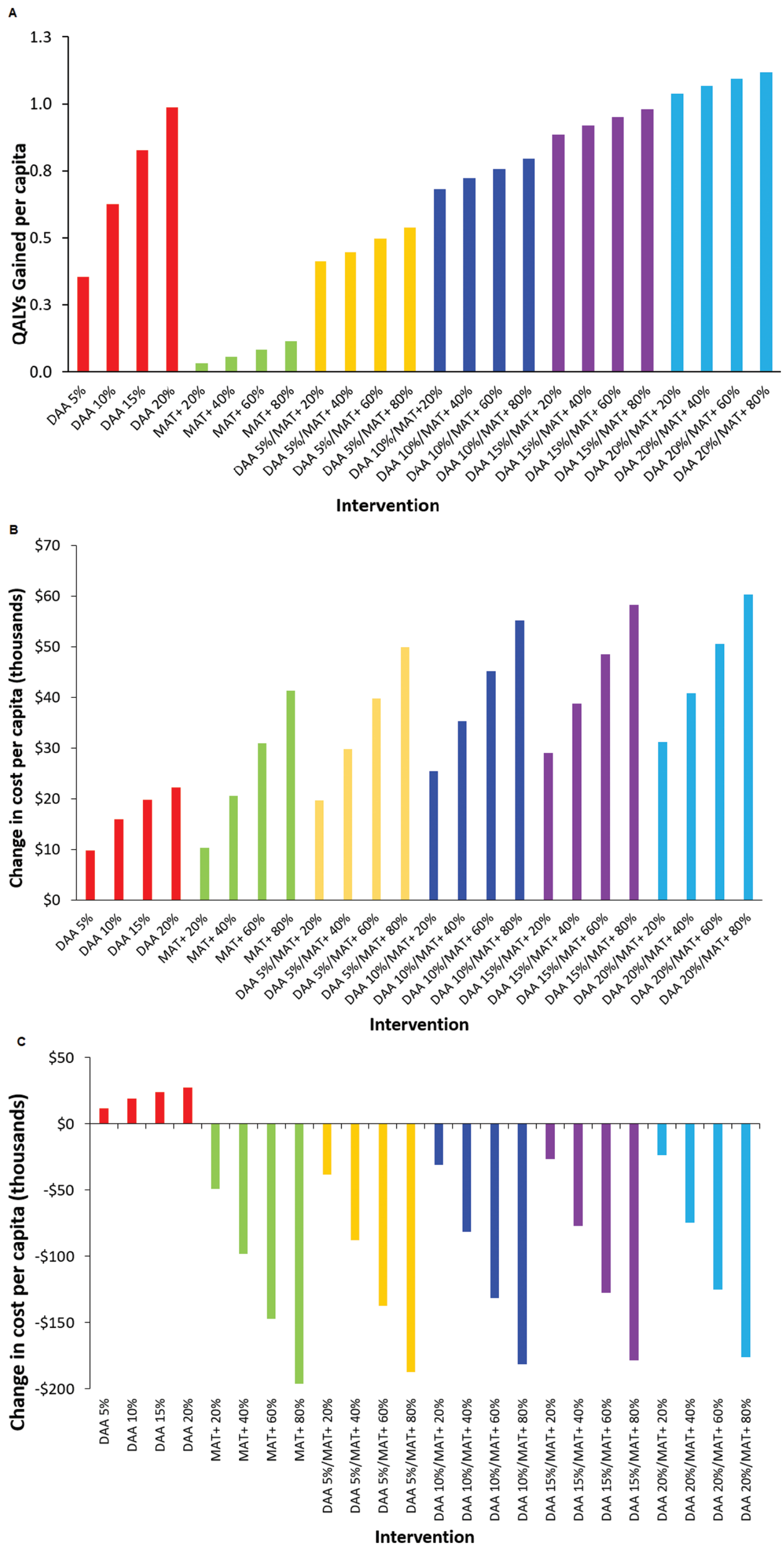

Figure 3. *A*, Quality-adjusted life-years (QALYs) gained per capita over 20 years. *B*, Change in costs per capita over 20 years, from the health sector perspective. *C*, Change in costs per capita over 20 years, including crime costs. Percentages indicate extent of coverage. The colors only signify the different combination groups, (ie, DAA% vs MAT+% vs DAA 5%/MAT+% vs DAA10%/MAT+% vs DAA15%/MAT+% vs DAA20%/MAT+%) The colors can be anything, including all one color if necessary; we were just trying to visually separate the different combination groupings. Abbreviations: DAA, direct antiviral agents; MAT+, medication-assisted therapy and needle syringe intervention.

Table 3. Intervention Incremental Cost-effectiveness

Intervention	Total Costs, Discounted $	Incremental Cost, Discounted $	Total QALYs, Discounted	Incremental Effect, QALYs	ICER, $/QALY
Health sector perspective					
Standard care	3928	-	6.853	-	-
DAA 5%	13 690	9762	7.208	0.356	Ext. dominated
MAT 20%	14 233	10 306	6.885	0.032	Dominated
DAA 10%	19 831	15 903	7.478	0.625	Ext. dominated
DAA 5%/MAT 20%	23 613	19 685	7.267	0.414	Dominated
DAA 15%	23 724	19 797	7.680	0.828	Ext. dominated
MAT 40%	24 551	20 623	6.910	0.058	Dominated
DAA 20%	26 117	22 189	7.840	0.987	22 470
DAA 10%/MAT+ 20%	29 398	3281	7.534	−0.306	Dominated
DAA 15%/MAT 20%	32 888	6772	7.739	−0.101	Dominated
DAA 5%/MAT+ 40%	33 752	7635	7.301	−0.539	Dominated
MAT 60%	34 874	8757	6.935	−0.905	Dominated
DAA 20%/MAT+ 20%	35 064	8948	7.892	0.052	172 090
DAA 10%/MAT+ 40%	39 211	4147	7.576	−0.316	Dominated
DAA 15%/MAT 40%	42 640	7576	7.771	−0.121	Dominated
DAA 5%/MAT+ 60%	43 779	8715	7.351	−0.541	Dominated
DAA 20%/MAT 40%	44 687	9622	7.921	0.029	332 204
MAT 80%	45 203	517	6.967	−0.954	Dominated
DAA 1−0%/MAT+ 60%	49 154	4467	7.610	−0.311	Dominated
DAA 15%/MAT 60%	52 401	7714	7.803	−0.118	Dominated
DAA 5%/MAT 80%	53 892	9205	7.392	−0.529	Dominated
−DAA 20%/MAT+ 60%	54 471	9785	7.945	0.024	Ext. dominated
DAA 10%/MAT+ 80%	59 065	14 379	7.647	−0.274	Dominated
DAA 15%/MAT+ 80%	62 227	17 541	7.833	−0.088	Dominated
DAA 20%/MAT+ 80%	64 194	19 507	7.972	0.051	385 824
Including crime costs					
Standard care	300 968	-	6.853	-	-
−MAT+ 80%	104 692	−196 276	6.967	0.115	Cost saving
DAA 5%/MAT+ 80%	113 842	9150	7.392	0.425	Ext. dominated
DAA 10%/MAT+ 80%	119 296	14 604	7.647	0.680	Ext. dominated
DAA 15%/MAT+ 80%	122 681	17 989	7.833	0.865	Ext. dominated
DAA 20%/MAT+ 80%	124 828	20 137	7.972	1.004	20 049
MAT+ 60%	153 808	28 980	6.935	−1.036	Dominated
DAA 5%/MAT+ 60%	163 594	38 766	7.351	−0.621	Dominated
DAA 10%/MAT+ 60%	169 541	44 713	7.610	−0.361	Dominated
DAA 15%/MAT+ 60%	173 245	48 417	7.803	−0.169	Dominated
DAA 20%/MAT+ 60%	175 684	50 856	7.945	−0.026	Dominated
MAT+ 40%	202 905	78 077	6.910	−1.061	Dominated
DAA 5%/MAT+ 40%	213 320	88 492	7.301	−0.671	Dominated
DAA 10%/MAT+ 40%	219 683	94 855	7.576	−0.396	Dominated
DAA 15%/MAT+ 40%	223 811	98 983	7.771	−0.201	Dominated
DAA 20%/MAT+ 40%	226 431	101 603	7.921	−0.051	Dominated
MAT+ 20%	251 976	127 147	6.885	−1.087	Dominated
DAA 5%/MAT+ 20%	262 892	138 064	7.267	−0.705	Dominated
DAA 10%/MAT+ 20%	269 852	145 024	7.534	−0.438	Dominated
DAA 15%/MAT+ 20%	274 321	149 492	7.739	−0.233	Dominated
−DAA 20%/MAT+ 20%	277 273	152 445	7.892	−0.080	Dominated
DAA 5%	312 526	187 697	7.208	−0.763	Dominated
DAA 10%	320 125	195 297	7.478	−0.494	Dominated
DAA 15%	325 188	200 360	7.680	−0.291	Dominated
DAA 20%	328 569	203 740	7.840	−0.132	Dominated

Extended dominance indicates that the intervention is more costly and yields more benefit, but not as great a benefit, as the next most costly intervention.
Abbreviations: DAA, direct antiviral agents; Ext., extended; ICER, incremental cost-effectiveness ratio; MAT, medication-assisted treatment; MAT+, medication-assisted treatment with syringe access programs; QALY, quality-adjusted life-year.

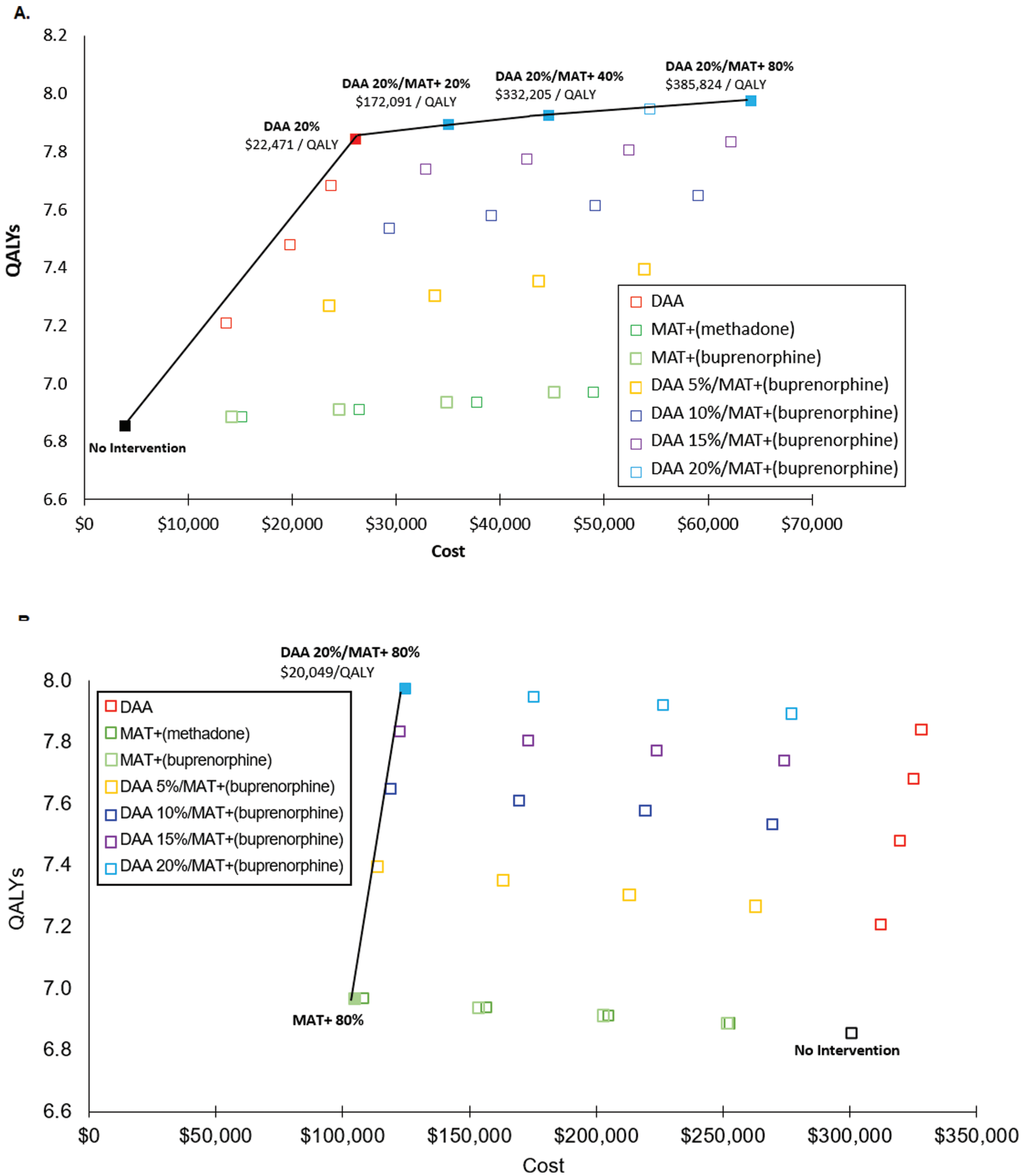

Figure 4. Cost-effectiveness frontier (*A*) from a health sector perspective and (*B*) including crime-related costs. Solid points are on the cost-effectiveness frontier. Percentages indicate extent of coverage. Abbreviations: DAA, direct antiviral agents; MAT+, medication-assisted therapy and needle syringe intervention; QALY, quality-adjusted life-year.

the most cost saving. In addition to being highly cost-effective, the combination of DAA with 20% coverage and MAT+ with 80% coverage would greatly reduce the HCV incidence (73%; from 11 to 2.93/100PY) within 15 years. These intervention coverage levels, however, still fall short of the WHO HCV elimination goal of reducing incidences by 90% by 2030 [20]. To achieve the WHO elimination goals, an aggressive approach—with high coverage of both DAA and MAT+—is likely necessary. Increasing the coverage of DAA may be particularly effective, as it directly reduces the prevalence of HCV in the population, also reducing the transmission risk. Additionally, identifying PWID who have the highest risk of onward transmission may further help achieve the WHO HCV elimination goal [51].

Models with 80% MAT+ coverage provided the most favorable cost-effectiveness. However, even if MAT+ coverage were only 40–60%, these strategies remained cost-effective compared to SC. The number of people in need of OUD treatment is much higher than what is available system-wide, and these analyses emphasize the potentially potent role a scale-up of MAT+ could have among PWID. Indeed, when considering criminal justice costs averted, all strategies including a MAT+ component were cost saving when compared to SC. With a large share of direct costs of the OUD being costs to society, attributable to nearly $8 billion within the criminal justice system [49], the cost-effectiveness of strategies that include MAT+ can be attributed to the effect of MAT-type interventions on reducing criminal justice system costs among PWID [33, 52].

In spite of their effectiveness for treating OUDs, strategies with the highest coverage of MAT+ were not the most cost-effective when viewed exclusively from a health-sector perspective, due to the costs associated with MAT [32]. The costs associated with MAT+ and the probability of its successful implementation may be improved by prioritizing the expansion of MAT+ programs focusing on the use of buprenorphine. While medication costs are higher, overall, buprenorphine is less costly than methadone to implement, due to the way the medications are administered [32, 53]. Unlike methadone, buprenorphine can be provided as an office-based therapy [54–56], reducing the costs associated with maintaining specialized clinics, along with increasing access to providers and reducing the burden on patients [54]. An alternative and complementary strategy would be to focus efforts on administering both buprenorphine and methadone in similar ways (eg, changing regulations so that both medications be office-based).

In spite of their effectiveness for decreasing the risk of HCV infections [11], the United States in general has been unsuccessful in providing HCV prevention interventions, including NSPs and MATs, to address the needs of those currently eligible for treatment. With only 19% of PWID receiving MAT and 30 sterile needles distributed per PWID per year on average, the United States lags far behind other developed countries, including Australia, which has provided access to MAT for 52% of PWID and distributes nearly 400 sterile needles per PWID per year [57]. This suggests an important fraction of the deficits in HCV prevention may reside in structural factors (eg, specific policies and components of the US health-care system) rather than being entirely attributable to patient-level factors (eg, nonadherence). Given the significant adverse public health consequences of the opioid epidemic [58, 59], the expansion of MAT+ services also offers an avenue to increase access to engagement in both the treatment and prevention of the consequences of OUD.

Our study results are consistent with previous studies that examined the economic impact of the individual components of the intervention strategies examined in this study [60–64], which have suggested that treating OUD would likely be cost saving from a societal perspective [65].

Limitations

Our study has several notable limitations. First, the societal perspective analyses were limited in scope, as they did not include all societal costs stemming from PWID. However, given US drug policies, criminal justice system costs represents the largest direct contributor to societal costs associated with PWID [6, 8]; therefore, the analyses likely represent a conservative estimate of cost-effectiveness. Similarly, by using wholesale DAA acquisition costs, estimates of the cost-effectiveness of DAA coverage likely represent conservative estimates as, in practice, DAA may be less expensive.

Second, chronic HCV is typically asymptomatic; however, up to 20% of individuals with a chronic HCV infection will develop cirrhosis in an average of 20 years [66]. As a result of the 15-year time horizon, which was selected to avoid assumptions about changing medical technology over a lifetime, the long-term reduction in medical costs associated with the reduction in cases of chronic HCV were not fully captured. The lifetime cost of an individual with a chronic HCV infection has been estimated at $68 010 [67]. Therefore, our cost-effectiveness estimates are likely to represent a lower bound for the true cost effectiveness of the interventions.

Third, the number of interventions investigated were limited and additional scale-up scenarios, such as higher levels of DAA coverage, may be even more cost effective than those options evaluated. Similarly, the impact of the various interventions on other health outcomes not modeled, such as those related to overdose prevention and HIV, may improve the cost-effectiveness of these intervention combinations further.

Fourth, given the highly complex nature of HCV progression to liver disease, as well as the intricacies of the health-care delivery system, we made a number of simplifying assumptions in order to contain the size of the Markov model. For example, we did not model comorbidities, such as alcohol use disorder or nonalcoholic steatohepatitis, which could potentially have altered the rate of disease progression for a proportion of patients. Despite these simplifications, we believe the Markov model used incorporates the most relevant characteristics of disease progression and health-care utilization in this population.

Finally, these particular analyses do not yet consider uncertainty around model parameters or costs. However, both the agent-based network simulation of HCV transmission and the Markov liver disease model used to perform these analyses have been placed through rigorous sensitivity analyses [23].

CONCLUSIONS

Among the 25 intervention scenarios considered, when considering health-sector costs alone, DAA with 20% coverage was the most cost-effective intervention. However, when considering criminal justice system–related costs, MAT+ with increasing levels of coverage become the most cost-effective interventions.

Notes

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