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, ¹² 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}

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

Clinical Infectious Diseases® 2020;70(12):2652–62

© 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/ciz726

Received 18 March 2019; editorial decision 9 July 2019; accepted 29 July 2019; published online August 11, 2019.

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).

- 38. Dombrowski K, Khan B, Habecker P, Hagan H, Friedman SR, Saad M. The interaction of risk network structures and virus natural history in the non-spreading of HIV among people who inject drugs in the early stages of the epidemic. AIDS Behav 2017; 21:1004–15.
- Neaigus A, Reilly KH, Jenness SM, et al. Trends in HIV and HCV risk behaviors and prevalent infection among people who inject drugs in New York City, 2005–2012. J Acquir Immune Defic Syndr 2017; 75(Suppl 3):S325–32.
- Centers for Disease Control and Prevention. HIV infection, risk, prevention, and testing behaviors among persons who inject drugs—national HIV behavioral surveillance: injection drug use, 20 US cities, 2012. HIV Surveillance Special Report 2015; 11.
- Smith DJ, Combellick J, Jordan AE, Hagan H. Hepatitis C virus (HCV) disease progression in people who inject drugs (PWID): a systematic review and metaanalysis. Int J Drug Policy 2015; 26:911–21.
- Jordan AE, Des Jarlais DC, Arasteh K, McKnight C, Nash D, Perlman DC. Incidence and prevalence of hepatitis C virus infection among persons who inject drugs in New York City: 2006–2013. Drug Alcohol Depend 2015; 152:194–200.
- Khan B, Dombrowski K, Saad M, McLean K, Friedman S. Network firewall dynamics and the subsaturation stabilization of HIV. Discrete Dyn Nat Soc 2013; 2013:1–16.
- Boelen L, Teutsch S, Wilson DP, et al; Hepatitis C Incidence and Transmission Study (HITS) investigators. Per-event probability of hepatitis C infection during sharing of injecting equipment. PLOS One 2014; 9:e100749.
- Martin NK, Foster GR, Vilar J, et al. HCV treatment rates and sustained viral response among people who inject drugs in seven UK sites: real world results and modelling of treatment impact. J Viral Hepat 2015; 22:399–408.
- Hamra G, MacLehose R, Richardson D. Markov chain Monte Carlo: an introduction for epidemiologists. Int J Epidemiol 2013; 42:627–34.
- 47. Block HW, Savits TH. Burn-in. Stat Sci 1997; 12:1-19.
- Meyn SP, Tweedie RL. Markov chains and stochastic stability. London, United Kingdom: Springer-Verlag, 1993.
- Florence CS, Zhou C, Luo F, Xu L. The economic burden of prescription opioid overdose, abuse, and dependence in the United States, 2013. Med Care 2016; 54:901–6.
- Neumann PJ, Cohen JT, Weinstein MC. Updating cost-effectiveness-the curious resilience of the \$50 000-per-QALY threshold. N Engl J Med 2014; 371:796-7.
- Iversen J, Dore GJ, Catlett B, Cunningham P, Grebely J, Maher L. Association between rapid utilisation of direct hepatitis C antivirals and decline in the prevalence of viremia among people who inject drugs in Australia. J Hepatol 2019; 70:33–9
- Russolillo A, Moniruzzaman A, McCandless LC, Patterson M, Somers JM.
 Associations between methadone maintenance treatment and crime: a 17-year

- longitudinal cohort study of Canadian provincial offenders. Addiction 2018; 113:656-67.
- King JB, Sainski-Nguyen AM, Bellows BK. Office-based buprenorphine versus clinic-based methadone: a cost-effectiveness analysis. J Pain Palliat Care Pharmacother 2016; 30:55–65.
- Gryczynski J, Jaffe JH, Schwartz RP, et al. Patient perspectives on choosing buprenorphine over methadone in an urban, equal-access system. Am J Addict 2013: 22:285–91.
- 55. Schuckit MA. Treatment of opioid-use disorders. N Engl J Med 2016; 375:357-68.
- Carrieri MP, Amass L, Lucas GM, Vlahov D, Wodak A, Woody GE. Buprenorphine use: the international experience. Clin Infect Dis 2006; 43(Suppl 4):S197–215.
- Larney S, Peacock A, Leung J, et al. Global, regional, and country-level coverage
 of interventions to prevent and manage HIV and hepatitis C among people who
 inject drugs: a systematic review. Lancet Glob Health 2017; 5:e1208–20.
- Smyth BP, O'Connor JJ, Barry J, Keenan E. Retrospective cohort study examining incidence of HIV and hepatitis C infection among injecting drug users in Dublin. J Epidemiol Community Health 2003; 57:310–1.
- Maher L, Jalaludin B, Chant KG, et al. Incidence and risk factors for hepatitis C seroconversion in injecting drug users in Australia. Addiction 2006; 101:1499–508.
- Martin NK, Vickerman P, Grebely J, et al. Hepatitis C virus treatment for prevention among people who inject drugs: modeling treatment scale-up in the age of direct-acting antivirals. Hepatology 2013; 58:1598–609.
- 61. Turner KM, Hutchinson S, Vickerman P, et al. The impact of needle and syringe provision and opiate substitution therapy on the incidence of hepatitis C virus in injecting drug users: pooling of UK evidence. Addiction 2011; 106:1978–88.
- 62. Martin NK, Hickman M, Hutchinson SJ, Goldberg DJ, Vickerman P. Combination interventions to prevent HCV transmission among people who inject drugs: modeling the impact of antiviral treatment, needle and syringe programs, and opiate substitution therapy. Clin Infect Dis 2013; 57(Suppl 2):S39–45.
- Nguyen TQ, Weir BW, Des Jarlais DC, Pinkerton SD, Holtgrave DR. Syringe exchange in the United States: a national level economic evaluation of hypothetical increases in investment. AIDS Behav 2014; 18:2144–55.
- Kwon JA, Anderson J, Kerr CC, et al. Estimating the cost-effectiveness of needlesyringe programs in Australia. AIDS 2012; 26:2201–10.
- Krebs E, Enns B, Evans E, et al. Cost-effectiveness of publicly funded treatment of opioid use disorder in California. Ann Intern Med 2018; 168:10–9.
- Westbrook RH, Dusheiko G. Natural history of hepatitis C. J Hepatol 2014;
 61:S58-68
- Razavi H, Elkhoury AC, Elbasha E, et al. Chronic hepatitis C virus (HCV) disease burden and cost in the United States. Hepatology 2013; 57:2164–70.