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How to eliminate hepatitis C virus among PWID in the United States

Harel Dahari[1] and **Basmattee Boodram**[2]

[1]The Program for Experimental & Theoretical Modeling, Division of Hepatology, Loyola University Medical Center, Maywood, Illinois, 60153, United States

[2]Division of Epidemiology and Biostatistics, School of Public Health, University of Illinois at Chicago, Chicago, IL, United States

Hepatitis C (HCV) is a leading cause of chronic liver disease and mortality worldwide. The World Health Assembly and World Health Organization (WHO) have recognized the need to prevent and control HCV infection, and the WHO proposed that HCV elimination was feasible by 2030 through reducing new chronic infections by 90% and HCV-related mortality by 65%. In the USA, as many as 3 million people are chronically infected with HCV, with more than 30,000 new infections occurring annually[1]. Elimination strategies are urgently needed that focus on the estimated 1.3 million people who inject drugs in the USA, the group at highest risk for acquiring and transmitting HCV infection. The development of oral direct-acting antiviral therapies help to make HCV elimination achievable, with reported cure rates >90%, which can prevent liver disease progression and HCV transmission. However, barriers to the use of direct-acting antiviral therapies for HCV in people who inject drugs persists, including cost of DAAs, poor linkage to care and adherence, possible reinfection and PWID lifestyle. A better understanding of the factors that would promote HCV elimination in people who inject drugs is imperative to inform policy development and strategic planning (eg, efforts to shorten the duration of direct-acting antiviral therapy to lower its cost and increase adherence[2, 3]).

Previous in-silico modelling efforts in people who inject drugs in the USA[4, 5] which projected a decline of HCV incidence and prevalence as a result of enhanced screening or scale-up of direct-acting antiviral therapy, did not include data on networks of people who inject drugs. In a modelling study reported in The Lancet Infectious Diseases, Alexei Zelenev and colleagues[6] generated synthetic networks using data from 1574 people who inject drugs in Hartford, CT, USA, and developed a network-based mathematical model to simulate HCV and HIV transmission. The investigators simulated seven treatment-as-prevention strategies (assigning treatment randomly to people who inject drugs vs targeting those with injection partners, with varying proportions of network peers also receiving treatment) at various levels of treatment coverage to reduce or eliminate chronic HCV prevalence in people who inject drugs over 10-year or 20-year periods. Their results suggest

Correspondence to: Harel Dahari.

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that, on average, random-based strategies are the most effective approach to reduce HCV prevalence, a finding that is in agreement with a network-based analysis outside the USA.[7] In places with HCV prevalence of less than 60% in people who inject drugs (eg, Chicago, IL, and Washington, DC), treatment scale-up of 12% per year over a 10-year period is projected to eliminate HCV infection. However, in places with high (>70%) HCV prevalence in people who inject drugs (eg, Atlanta, GA, and Newark, NJ), anything but huge treatment scale-up will have little effect on reducing HCV prevalence over 10 years.

Zelenev and colleagues' findings provide an important advance in our understanding of HCV transmission in urban populations of people who inject drugs and how treatment-as-prevention strategies with direct-acting antivirals can affect HCV incidence and prevalence within these networks. Further studies with even more robust models are needed to build on this work. Elimination of HCV in people who inject drugs in the USA requires reductions in HCV transmission and improvements in the low rates of treatment initiation and completion. To this end, future models must simulate both harm reduction strategies (eg, access to clean syringes, engagement in opioid substitution therapy, behavioural counselling) and treatment-as prevention strategies. Moreover, the contributions of specific subpopulations that drive transmission and incidence (such as young people who inject drugs) and mortality trends (eg, older people who inject drugs) should inform the specific types and combinations of strategies modelled.

Previous models, many based on populations outside the USA, have not addressed how differences between subpopulations of people who inject drugs could alter the effectiveness of HCV elimination strategies. The role of geographical differences among populations of people who inject drugs also requires attention. Fuelled by the prescription opioid misuse epidemic, injection drug use is increasing predominantly in young, non- Hispanic white people in non-urban areas, which is where most of the HCV outbreaks in the past 5 years have been reported.[8, 9] Substantial regional variation also exists. For example, in young, non-Hispanic white people who inject drugs, HCV prevalence was found to be significantly higher in those from Baltimore than those from Chicago, which is partially explained by individual-level factors and close proximity to an urban area.[10] Unlike other countries (eg, Australia), US populations of people who inject drugs are highly heterogeneous, and most people who inject drugs are not linked to health services (eg, drug treatment, clinical care), with many lacking insurance and having highly unstable residences.[11, 12] The prospect of HCV vaccines provides a further modelling consideration. Since direct-acting antivirals do not prevent re-infection, the development of HCV vaccines could provide another important intervention. However, only one vaccine candidate has reached a phase 2 efficacy trial (NCT01436357).

Computational models are needed that address the dynamic and complex interplay of the many factors that contribute to the high incidence and prevalence of HCV in people who inject drugs at the individual level (eg, risk behaviours), the social level (eg, injection networks), the structural level (eg, access to clean syringes), and the geographical level (eg, non-urban residence) to inform the intervention strategies that are most effective.

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