# Bridging Epidemiology and System Dynamics Modeling to Better Understand HCV Risk Among Young People Who Inject Drugs.

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# Abstract

### Background

Injection drug use is the leading risk factor for hepatitis C virus (HCV) transmission in the US. Despite the knowledge of the risk factors for HCV among people who inject drugs (PWID), there is a need to better understand how these multiple factors interact and impact young PWID.

### Methods

Data originated from a study of 539 New York City (NYC) residents ages 18-29 recruited via Respondent-Driven Sampling, who reported past-month nonmedical use of prescription opioids and/or heroin. Analyses are based on a subsample of 337 (62%) who reported injecting any drug 12 months prior to the interview. All variables were assessed via self-report, except HCV status, which was established via rapid antibody testing. Building on the statistical associations found we developed a qualitative system dynamics (SD) model to integrate into a single framework key risk and preventive factors for HCV.

### Results

HCV antibody prevalence is 31% with an overall incidence of 10 per 100 person-years. HCV status was independently correlated with sharing cookers with two or more people (AOR=2.17); injecting drugs 4-6 years (AOR=2.49) and 7 or more (AOR=4.95); lifetime homelessness (AOR=2.52); and being incarcerated two or more times (AOR=1.99). The SD model facilitates identifying non-linearities and feedback loop structures not included in the statistical model and high leverage points such as harm reduction and HCV treatment that could ameliorate the spread of HCV.

### Conclusion

The results may indicate an overall positive impact of harm reduction efforts in reducing HCV prevalence among young PWID in NYC while injection risks and structural factors remain areas of key concern. An SD approach contributes to a better understanding of how these risk factors interact and what policies could be effective in reducing HCV infections.

# Background

Injection drug use (IDU) is the leading risk factor for hepatitis C virus (HCV) transmission across urban, suburban, and rural settings in the US (1). Recent national surveillance data reveal an increase in reported cases of acute HCV infection every year from 2011 through 2018, with incidence nearly tripling (1,232 reported cases in 2011 vs 3,621 reported in 2018) (2). Despite the fact that urban areas such as New York City (NYC) generally have a wider availability of harm reduction resources to reduce incidence rates, the prevalence of HCV among young people who inject drugs (PWID) is similar to that of suburban and rural areas (3).

Now in its second decade, the opioid epidemic, with its intertwined use of pharmaceutical opioids (PO), heroin, and illicitly manufactured fentanyl, has led to an increase in injection drug use and continues to fuel an increase in HCV infections (4, 5). For many young people, sustained non-medical use of POs became a precursor to heroin use because heroin was more readily available and cheaper than POs (6-8). Data from the National Survey on Drug Abuse and Health (NSDUH) indicated that 4 out of 5 current heroin users started using POs beforehand (9). Many young people who experimented with medical opioids and heroin transitioned to drug injection, thus putting them at risk of HCV exposure (8, 10-12).

Other risk factors associated with HCV infection among PWID include needle sharing, sharing cookers and other injection paraphernalia (13), length of injection career (13-15), injecting in public spaces (14), and injecting prescription opioids (11, 16, 17). Beyond injection risk behaviors, several authors have reported on structural vulnerabilities that might contribute to the rapid spread of HCV among PWID including high rates of opioid misuse and drug overdose, unemployment, poverty (18, 19), incarceration (20-22), and homelessness (18, 23-25).

Despite the knowledge to date of the risk factors for HCV among young PWID, there is a need to better understand how the multiple factors that fuel the HCV epidemic interact. Since traditional statistical methods are limited in their ability to accurately capture complex structures, systems thinking and modeling are needed to expand our ability to learn from evidence and design policies to address complex challenges without resulting in unintended consequences such as an increase in drug use in response to the war on drugs policies (26). In this manuscript, we analyze our results from traditional statistical methods using a system dynamics (SD) modeling framework to uncover some of the complex structures and feedback loops underlying the HCV epidemic among young PWID. SD modeling is a systems science methodology that facilitates a better understanding of complex problems that change over time by determining feedback loop structures and identifying delays in the system (27). This approach is very useful to study the HCV epidemic and its growth among young PWID, which is influenced by several biological and behavioral factors and various domains (individual, interpersonal, community, and policy), and their interconnections (26).

In this paper, we investigate the prevalence of HCV and the incidence and risk factors associated with HCV antibody-positive status among a community sample of young PWID. Building on the statistical associations found, we then develop a qualitative SD model to integrate into a single framework key risk factors for HCV among young PWID. This model describes the non-linearities and feedback loop structures not included in the statistical model, as well as opioid use disorder (OUD) treatment, HCV treatment, and other policy factors that could ameliorate the spread of HCV among young PWID.

# Methods

### *Study Design and Procedures*

This paper presents selected findings from a larger study that assessed the drug use practices and health risks of young adults (ages 18-29) in NYC who used opioids (including nonmedical use of POs and/or

heroin use). The current analyses focused on patterns and correlates of HCV infection among participants who injected drugs within the larger sample of young opioid users. Quantitative data were used to establish the prevalence of HCV antibody-positive status among the subset of participants who reported having injected drugs in the past twelve months. We also estimated HCV prevalence by duration of injection drug use (in years) and incidence per 100 person-years.

Study participants were recruited using Respondent-Driven Sampling (RDS), a form of chain-referral sampling designed to engage hard-to-reach populations by using participants' personal network connections to drive recruitment. This method, which can reach people who may not frequently be found in street settings, may yield a more representative sample than street recruitment. Using this method, an initial set of 20 "seeds" was directly recruited by research staff through referrals from harm reduction services, drug treatment programs, participants in the study's formative qualitative component, and other research projects. Each participant completed a structured assessment and was invited to refer up to three eligible peers from their opioid-using contacts to participate in the study.

This process was repeated with the seeds' recruits and for successive sample waves, leading to a total of 539 participants enrolled from August 2014 to April 2016. Eligibility criteria included nonmedical use of POs and/or heroin use 3 or more times in the past 30 days, current residence in NYC, 18–29 years old, English-speaking, and the ability to provide informed consent. Participants provided written informed consent and were compensated $60 USD for completing the assessment; an additional incentive was provided for each eligible participant they referred. Further details on the RDS methods used in this study are reported in Mateu-Gelabert et al. (2017). The study was approved by NDRI's Institutional Review Board, and all participants provided written informed consent.

Participants completed a computer-assisted, interviewer-administered structured assessment lasting 90–120 minutes and provided a fingerstick blood sample for on-site HCV antibody testing. The instrument included sociodemographic and behavioral questions (951 questions organized in 27 sections) related to the following domains: substance use and drug injection history and current practices; injection-related HIV/HCV risk behavior; opioid use and injection networks; and lifetime and recent overdose experiences, among other topics. The present analyses were based on the subset of the total sample (62%, n=337/539) who reported injecting any drug for nonmedical purposes at any point in the twelve months prior to the assessment. None of the participants who did not report injecting drugs tested HCV antibody positive (Ab+).

### *Measures*

In structured assessments and statistical analyses, nonmedical use of POs was defined as the use of POs "not prescribed for the respondent or use of these drugs only for the experience or feeling they caused" (28). The injection of POs was defined as injecting any opioid intended for oral intake. Two injection risk variables were assessed, sharing syringes and sharing cookers, both measured by the number of people with whom the sharing took place in the 12 months prior to the structured assessment. Sharing syringes was defined as using a syringe that had been previously used by someone else. Sharing

cookers was defined as using a cooker someone else had previously used or using it simultaneously with someone else.

Years of injection for each participant were determined by first calculating the number of days from the reported date of first injection to the date of the interview. For date of first injection, participants were asked to report the month and year of their first injection. The 15$^{th}$ of the reported month was used as the default for first day of injection. The number of days resulting from subtracting date of interview to date of first injection (the 15$^{th}$ of the month reported), was divided by 30.4375 and rounded to the closest integer to obtain the number of months each participant had injected drugs. The conversion from months to years of injection for 0 and 1 year was as follows: 0-11 months = 0 years; 12-18 months = 1 year. Additional years, from months of injection, were determined as follows: 19-30 months = 2 years; 31-42 months = 3 years; 43-54 months = 4 years; 55-66 months = 5 year; 67–78 months = 6 years; 79-90 months = 7 years; more than 91 months = 8 years or more.

Incarceration was measured by the number of times a participant was in jail or prison, independent of the duration of the detention or sentence. Homelessness was defined as staying on the street, in a shelter, in a Single Room Occupancy hotel (SRO), temporarily staying with friends or relatives, or living in a car. All variables were based on self-report data except for HCV antibody status, which was assessed with point-of-care rapid testing using the OraQuick Advance Rapid HCV Antibody Test (OraSure Technologies, Inc., Bethlehem, PA).

### *HCV Prevalence and Incidence by Years of Injection*

HCV prevalence was calculated by dividing the number of HCV Ab+ participants with a given year(s) of injection (i.e. 1 year, 2 years…) by the total number of participants with those given years of injection. Incidence calculations rely on several assumptions similar to those outlined by Jordan et al. 2015 in the study of HCV incidence in NYC between 2006-2013: a) all participants were HCV negative when they started injecting; b) HCV Ab+ participants had seroconverted at the midpoint between first injection and time of study interview; and c) those who reported injecting less than a year were assumed to have injected for 0.5 year (29). HCV incidence was calculated by a formula in which the numerator included the total number of HCV Ab+ participants with a given year(s) of injection period (i.e. 1 year, 2 years …). The denominator equaled the total number of injection years for HCV antibody-negative participants plus half the total years of injection for HCV Ab+ participants. The result was multiplied by 100 (and rounded to the nearest integer) to obtain HCV incidence per 100 person-years.

### *Data Analysis*

### *Statistical Approach*

All statistical analyses were conducted in the program R, versions 3.2.2 and 3.2.4 (R Core team, 2015) and IBM SPSS v.25 (Chicago, IL). First, binary associations of the variable of interest (HCV antibody positive status) were computed with a series of sociodemographic (gender, race/ethnicity, household

income growing up, lifetime homelessness) and injection risk variables (syringe- and cooker-sharing in the past 12 months, as well as number of incarcerations, years of injection, and knowing one or more opioid users older than 29 years old). Log ratios and p-values were computed for all binary associations using a Wald chi-squared test, with a 95% confidence interval (30). Following the strategy described in Hosmer et al., variables with $p < 0.25$ in bivariable analyses were then included in a multivariable model (31). The multivariable model was run using a generalized linear model (R version 3.2.4, glm 4.13-19), and adjusted odds ratios were computed using the model estimate. Results were verified with logistic regression in SPSS.

### *System Dynamics Approach*

Although our traditional inferential statistical analyses identified significant linear associations with HCV infection, they lack a description of how the variables interact with each other and impact PWID during their injection trajectories to increase the odds of HCV infection. Building on the statistical results, we developed an operational model using SD methodology (32) that depicted a hypothesized dynamic structure and sequence of actions that impacted and led to changes in the number of HCV infections among young PWID. Our SD model attempted to integrate key structural, behavioral, and biological factors into a single framework that demonstrates the underlying causal feedback loop structures.

## Results

The study sample consisted of 337 opioid injectors, 65% men and 34% women. The mean age of the sample was 25 (SD = 3; range 18–29). Thirty-nine percent of the sample had completed high school or received their GED and 37% attended some college. The majority of the sample was White (74%), followed by Latinx (18%), and 8% other. Thirty-nine percent reported an annual household income while growing up of $50,000 or less; 35% from $51,000 - $100,000 and 26% reported incomes while growing up of $101,000 or more. Sixty-nine percent had experienced homelessness during their lifetime.

Thirty-nine percent reported receptive syringe sharing in the 12 months before participating in the study: 26% with one person and 13% with 2 or more people. Sixty percent reported sharing cookers in the past 12 months: 21% shared cookers with one person and 39% shared with 2 or more people.

# HCV Prevalence and Incidence

Prevalence and incidence data are based on 332 of the 337 PWID for whom we could ascertain years of injection. Thirty percent (n = 101) of PWID tested HCV antibody-positive. The sample HCV antibody-positive prevalence and incidence per years of injection (from less than a year to 8 years or more) are presented in Table 1. The prevalence of HCV among those who had injected for less than one year was 2.9%; this increased to 12.5% among those who had injected for one year, 20.9% among those who had injected for two years, and 28.9% among those who had injected for three years. Prevalence was between 40%-48% for those who had injected for 5 to 7 years. The highest prevalence was among those who injected for 8 years or more (59.7%). The incidence per 100 person-years of injection (PYI) was 6 for those

who had injected less than a year and more than doubled to 13/100 PYI for those who had injected for one year. Incidence remained near 10/100 PYI (range 7–12) for the subsequent 2–7 years of injection.

# Data Analysis

# Bivariate and Multivariate Associations

Key variables were chosen to test their association with HCV status. Bivariate and multivariate results are displayed in Table 2. In the adjusted model, there were significantly higher odds of HCV positive status among those who: had experienced lifetime homelessness (adjusted odds ratio [AOR]: 2.52, CI: 1.19–5.36); shared cookers with two or more people in the past 12 months (AOR: 2.15, 95% CI: 1.05–4.37); had been incarcerated 2 or more times (AOR: 1.99, 95% CI: 1.06–3.73); and had injected drugs for 4 to 6 years (AOR: 2.49, 95% CI: 1.22–5.09) or 7 or more years (AOR: 4.95, 95% CI: 2.35–10.46).

# System Dynamics (SD) Model

As a first step in building an HCV SD model, we depicted the Table 2 results within a diagram shown in Fig. 1. We drew arrows that graphically represented significant associations with HCV antibody-positive status: homelessness, PO injection, sharing syringes and cookers with 2 or more people, injecting drugs for 4 or more years, being incarcerated 2 or more times, and knowing any opioid users older than 29 years of age (Fig. 1). Each link (arrow) corresponded to a significant association that was identified in the bivariate analysis (dashed lines) and the multivariate analysis (solid lines). The arrows were accompanied by a polarity sign, with the positive sign (+) indicating that two variables changed in the same direction. For example, an increase in “years of drug injection” was associated with an increase in the number of “young PWID who are HCV Ab+.” Negative signs indicated that two variables changed in opposite directions. The diagram presented in Fig. 1 only consists of arrows representing positive links because no negative associations were identified in the statistical analysis.

This type of diagram (Fig. 1), referred to as a “correlational model,” lacks operational thinking (32). It is solely constructed from data analysis and captures essentially the exogenous perspective on HCV exposure among young PWID. Although these links can provide some initial insight into the complexity of how HCV is spread, the model represents linear thinking; the links are independent of each other, it does not indicate differences in degree among relationships. The depiction of actual decision-making processes of actors within the system is also omitted (32, 33). In order to study complex problems such as the HCV epidemic, we needed to expand the model to include how the structure of the system and interactions among its elements determine HCV outcomes. In SD modeling, we identify the structure of the system by depicting different feedback loops (33).

In extending the structure from Fig. 1, and building upon the statistical inferences from Table 2, we transitioned to an SD model by developing a stock-and-flow diagram that captured the physics and operations of the system impacting HCV outcomes among young PWID (See Fig. 2). We developed the SD model using the Stella® Architect modeling software during a series of sessions with our co-authors,

drawing on previously published findings from this study (16, 34–41) and current literature on HCV transmission among young PWID (13–15). In this stock-and-flow diagram, we defined different stock (or state) variables as represented by boxes to capture a significant dynamic at the individual level, a vulnerability to HCV infection corresponding to years of injection (Fig. 2). This model presents different stages in the drug injection trajectory and HCV infection status of young PWID represented by the following stocks: '*HCV Susceptible – Young PWID with ≤ 1 Year of drug injection (IDU)*', '*HCV Infected – Young PWID with ≤ 1 Year of drug injection*', '*HCV Susceptible – Young PWID with > 1 Year of drug injection*', and '*HCV Infected – Young PWID with > 1 Year of drug injection*'. Each stock connects to inflow and outflow arrows that represent the flow of individuals coming in and out of the system or transitioning from one state to another. For example, when '*HCV Susceptible – Young PWID with ≤ 1 Year of drug injection (IDU)*' become HCV infected during 1st year IDU, they flow to the stock at the lower left-hand corner of 'HCV Infected – Young PWID with ≤ 1 Year of drug injection'. Similarly, as young PWID continue injecting over multiple years, they become more vulnerable to HCV as the risk of HCV infection increases per years of injection (also indicated in Table 1). Thus, they move to the stock of '*HCV Susceptible – Young PWID with > 1 Year of drug injection*'.

The specific cutoff point of 1 year is based on the incidence findings presented earlier, which show that HCV incidence among Young PWID with > 1 year IDU is approximately double the incidence among Young PWID with multiple years of injection drug use. As years of injection increase, PWID are more likely to know (and to inject drugs with) older PWID who are more likely to be HCV infected, leading to a higher risk of infection (29, 38). Similarly, continued drug injection among PWID over multiple years leads to an increased likelihood of sharing syringes and other injection paraphernalia with HCV-infected PWID. The greater the frequency of sharing events, the higher the likelihood of HCV infection for young PWID and their transition to the stock of '*HCV Infected – Young PWID with ≥ 1 Year of drug injection*'.

We also represent the hypothesized causal relationships over time between variables in Fig. 2 using arrows with a polarity sign and the resulting feedback loops relevant to the outcome of HCV exposure. A closed sequence of arrows (i.e., complete circles) forms a feedback loop. In the model, we have identified two major reinforcing (R) feedback loops as highlighted by bold arrows. A reinforcing loop has zero or an even number of negative links and can create virtuous or vicious cycles, leading to exponential growth or exponential decline, where a problem becomes better or worse over time, often at an increasing rate.

The reinforcing loops illustrated in Fig. 2 provided some initial insights in regard to the acceleration or slowdown of the number of young PWID that become infected with HCV. The reinforcing loops R1 – *HCV Spread among Young PWID with ≤ 1 Year of drug injection* and R2 – *HCV Spread among Young PWID with > 1 Year of drug injection*, referred to the growth of HCV infections among young PWID who came in contact with young PWID already infected through repeated sharing of needles and cookers with two or more PWID. This structure represents an adaptation of the classic contagion structure referred to as the *SIR: Susceptible-Infected-Recovered* model (42). The underlying key assumption is that the number of individuals who become exposed to HCV is a function of the number of persons who already have hepatitis C. Therefore, if more young opioid users transition to drug injection, it is likely that they will

come into contact with young PWID who have HCV and will also become infected, making this loop vicious. The qualitative model in Fig. 2 graphically represents interactions over time among key variables and describes feedback structures that govern the dynamics of injection drug use (IDU), HCV risk, and HCV prevalence among young PWID.

# Discussion

In this paper, we report an overall HCV antibody prevalence of 31% for a sample of young people ages 18–29 who injected drugs (PWID), recruited between 2014–2016 in NYC. This HCV prevalence is lower than the 42% in Lower East Side and 51% in Harlem reported by Diaz et al. among similar samples of street-recruited PWID ages 18–29 between 1997–1998 (43). The lower prevalence reported in this manuscript might indicate a decrease in the overall prevalence among young PWID in NYC. This possible overall trend is also presented in the NYC Hepatitis A, B, and C annual report, 2018, which indicates a 22% reduction in the number of HCV infections among those 29 or younger during the period 2009–2018 (44). The overall HCV incidence among the study sample was 10 per 100 person-years. This cross-sectional incidence was lower than 18 per 100 person-years reported by the DUIT prospective study (2002–2004), among a street recruited NYC sample of 18-30-year-old PWID and 19.5 per 100 person-years among a drug treatment sample of older PWID (mean age 41.2) recruited between 2006–2013 (29). These data suggest that a reduction in HCV prevalence and incidence among young PWID in NYC is perhaps the result of long sustained harm reduction efforts (needle exchange programs, medically assisted treatment, and HCV treatment) (45). It is worth noting that the overall prevalence for young PWID is less than half of the 67% HCV prevalence reported for older PWID during the 2006–2013 period (29).

Variables significantly associated with HCV Ab + in the present analysis are similar to those reported by other studies. HCV positive status was independently correlated with drug injection-related variables such as sharing cookers with two or more people and injecting drugs for 4 or more years consistent with multiple studies indicating the risk of sharing injection paraphernalia and length of drug injection period (11, 13–15, 46). HCV positive status was also independently correlated with structural factors such as lifetime homelessness and being incarcerated two or more times consistent with other studies reporting similar HCV risks (13, 14, 21, 43, 47). In conjunction, these results may indicate an overall positive impact of harm reduction efforts in reducing HCV prevalence among young PWID in NYC while injection risks and structural factors remain areas of key concern. If we are to reach HCV elimination among youth, both injection risk and structural factors will need to be addressed at the same time.

In an effort to better understand how these risk factors interact and what policies could be effective in reducing HCV infections, we resorted to system dynamics (SD) modeling. SD modeling is a systems science methodology that is well suited for population studies where multiple feedback effects, time delays, and nonlinearities are taken into account. SD has been increasingly applied to public health problems including chronic disease (48), epidemics (49), human immunodeficiency virus (HIV) (50), and drug abuse (51). Recent literature has applied SD to explore the impact of potential policy changes, including changes in opioid prescription dosage, drug diversion, OUD treatment, and naloxone distribution

on opioid-related outcomes (52–54). However, to our knowledge, no studies thus far have adopted SD modeling to better understand the spread of HCV among young opioid users, despite the interdependence and non-linearity of multiple underlying factors.

In this manuscript, we provide an example of how epidemiologic analysis and statistical associations can be the foundation for the development of SD modeling to better understand how multiple factors of different order (e.g. structural and injection risk) interact to increase rates of HCV infection among young PWID. SD is able to take basic epidemiological findings and create a visual model of how the interactions among variables could have a multiplicative effect in increasing HCV transmission. In this paper, we illustrate how the dynamic interactions among variables interact to increase the risk of HCV among young opioid users. We developed an SD model that depicts the interaction among *structural factors* (e.g. drug treatment, HCV treatment, harm reduction, criminal justice, and homelessness), *injection networks* (knowing opioid users older than 29), and *injection trajectories* among young adults (e.g. transition to drug injection and number of years of drug injection). Also, to further explore the interplay of these system components leading to HCV, we introduce the possible impact of potential policy changes affecting these key factors (e.g., housing assistance, HCV treatment, reducing incarceration).

For example, as more young PWID who are HCV-infected receive HCV treatment, an increasing number of them will clear the virus and flow back into the stock of 'HCV Susceptible – Young PWID' with less or equal to 1 year or multiple years of drug injection (Fig. 2). Thus, the HCV prevalence decreases, and the R1 – *HCV Spread among Young PWID with < 1 Year of drug injection* and R2 – *HCV Spread among Young PWID with > 1 Year of drug injection* feedback loops become virtuous and slow the spread of HCV at an increasing rate. However, as young PWID who are HCV positive continue to inject drugs, the baseline HCV prevalence within young injection networks increases, leading to a higher likelihood of infection per injection risk event among the uninfected. Consequently, the feedback loops R1 and R2, lead to an increasingly rapid spread of HCV among PWID. The feedback loop R2 has even a stronger impact on the spread of HCV due to the much higher HCV incidence among Young PWID with > 1 year IDU, indicating the need to prevent recently initiated injectors from becoming long-term injectors, further preventing the spread of HCV. Prevention efforts and HCV treatment focusing on recently initiated PWID could help prevent and eventually eliminate HCV among young PWID (34, 38).

Homelessness is another risk factor that has been shown to be associated with greater vulnerability to HCV infection for a variety of reasons, such as the increased likelihood of injecting in public spaces and limited ability to store sterile injection equipment (23–25). Thus, homelessness can make the reinforcing loops R1 and R2 become even more vicious and exponentially spread HCV. Since individuals who inject drugs for multiple years may be at increased risk of homelessness due to loss of social support and the economic burden of sustaining their drug use, there is an even further urgency to provide housing and prevent transition and continuation of injection drug use (e.g., by expanding and facilitating access to evidence-based drug treatment). As young PWID initiate drug treatment and flow out of the stock of 'HCV Susceptible' with less than 1 year or multiple years of drug injection, they are less vulnerable to becoming

HCV infected, which will slow down the spread of HCV by reducing the number of individuals who could potentially be exposed.

The model also includes the variable '*knowing opioid users older than 29*' and its impact on the spread of HCV among young PWID (Fig. 2). As we presented earlier, the large difference in prevalence among older and younger samples might be due to the tendency of young PWID to interact with drug users similar of age (38). This partial separation between older and younger PWID and reducing the chances of '*knowing opioid users older than 29*' could serve as a partial barrier to the spread of HCV from groups of older PWID who have higher HCV prevalence rates. Additionally, incarceration increases the likelihood of HCV infection according to our analysis and SD model. Other research also indicates the high prevalence of HCV among incarcerated populations (20–22).

In our SD model (Fig. 2) we have illustrated some potential leverage points by introducing policies (e.g. housing for PWID, reducing incarceration, harm reduction services, separation between older and younger PWID) that could counteract the multiplying effect of key variables (e.g. homelessness, incarceration, paraphernalia sharing). For clarity, in the model (Fig. 2), the text presenting policy/intervention leverage points is underlined and bolded. For example, by expanding harm reduction services such as syringe service programs, the risk of exposure to HCV through repeated sharing of needles and cookers could be reduced. Furthermore, in order to break the loop of contagion, strategies and interventions could focus on preventing young opioid users from transitioning to injection drug use by providing medication for opioid use disorder (MOUD) before they begin to inject drugs or early in their injection careers. Additionally, treating HCV-infected young PWID (causing them to exit the model's two lower stocks) could decrease the baseline HCV prevalence in the young PWID population, thereby reducing the spread of HCV. Furthermore, HCV treatment, if initiated in a timely manner, could assist with HCV elimination within injection networks (35).

A system dynamics approach extends our ability to study a complex problem from a linear traditional data analysis approach to a non-linear and operational thinking methodology, which is substantially needed to tackle the complexity of the HCV epidemic more effectively (32). SD modeling helps us to better understand interactions between variables, highlighting structural components beyond individual behaviors, and facilitates designing comprehensive prevention policies that would include addressing such structural factors. The SD model presented in this paper serves as the basis for developing a simulation model that captures the spread of HCV among young opioid users by mathematically quantifying the links. Once the model is validated towards historical time series data, we can then use the model to test what-if simulation scenarios and evaluate the effectiveness, sustainability, and unintended consequences of the aforementioned suggested intervention and policy strategies. In future research, this SD model may facilitate the generation of novel hypotheses and in silico evaluation of the combined effects of various intervention strategies over the short and long term, as well as the identification of potential unintended consequences of alternative interventions.

In our novel approach for this manuscript, we illustrate how SD modeling can facilitate the integration of different methodologies in social scientific and public health research: it graphically represents statistical findings while allowing researchers to incorporate their qualitative knowledge of how these variables interact. It also allows researchers to graphically represent areas of prevention and identify leverage points within the system where policy efforts could be most effective.

This study has some limitations. First, given that it is a cross-sectional study, our data only provides a snapshot of the prevalence of HCV status among young opioid users in NYC and cannot establish causation. Second, this study focuses exclusively on young adults in NYC who inject drugs. The results, therefore, may not be generalizable to drug users of other ages or in other areas, particularly those residing in non-urban areas. Third, the use of a non-random recruitment strategy – Respondent-Driven Sampling – may have also introduced bias into the sample that limits the generalizability of the findings. Lastly, the participants' ability to recall past exposures makes this study susceptible to recall bias.

Our results suggest recommendations for further research and intervention strategies. Further research should investigate the relationship between HCV positive status and incarceration among young opioid users. Interventions that target the homeless population and those involved with criminal justice may also be an efficient way to identify young PWID at risk for HCV and treat those who are HCV-positive. Since young uninfected PWID are connected to young opioid users who are infected, these connections also provide a pathway for the transmission of HCV. Therefore, harm reduction efforts should teach young injectors skills and strategies to enable long-term risk avoidance and the implementation of healthy protective behaviors among injectors and their networks.

To conclude, young PWID are at considerable risk for HCV and thus, a key population for intervention. Despite the study's limitations, the current findings suggest that harm reduction services should make concerted efforts to reach young PWID with histories of incarceration and/or homelessness, and networks with older PWID.

# Abbreviations

Hepatitis C virus (HCV)

System dynamics (SD)

People who inject drugs (PWID)

New York City (NYC)

Injection drug use (IDU)

Pharmaceutical opioids (PO)

Opioid use disorder (OUD)

Respondent-driven sampling (RDS)

Antibody positive (Ab+)

Single room occupancy hotel (SRO)

Person-years of injection (PYI)

Human immunodeficiency virus (HIV)

Medication for opioid use disorder (MOUD)

## Declarations

# Ethics approval and consent to participate

The study was approved by NDRI's Institutional Review Board. All participants provided written consent to participate.

# Consent for publication

Not applicable

# Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

# Competing interests

The authors declare that they have no competing interests

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# Authors' contributions

PMG formulated the overarching research goals and aims, prepared the draft, and reviewed and edited the manuscript. NS formulated the system dynamics overarching research goals and aims, developed the system dynamics models, prepared the draft and reviewed and edited the manuscript. HG prepared the draft and reviewed and edited the manuscript. CC prepared the draft and reviewed and edited the manuscript. KJ prepared the draft. BE reviewed and edited the manuscript. CF scrubbed and maintained research data for use and applied statistical techniques to analyze data. TTKH reviewed and edited the manuscript.

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Not applicable

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# Tables

Table 1
HCV Antibody Status by Years of Injection: Prevalence and Incidence per 100-person years (n = 332)

| | | | | **Sample** | **Incidence** |
|---|---|---|---|---|---|
| Years of Injection | | HCV- | HCV+ | Prevalence | per 100 PY |
| < 1 year | (1–11 months) | 68 | 2 | 2.9% | 6 |
| 1 year | (12–18 months) | 7 | 1 | 12.5% | 13 |
| 2 years | (19–30 months) | 38 | 10 | 20.8% | 12 |
| 3 years | (31–42 months) | 27 | 11 | 28.9% | 11 |
| 4 years | (43–54 months) | 20 | 6 | 23.1% | 7 |
| 5 years | (55–66 months) | 19 | 14 | 42.4% | 11 |
| 6 years | (67–78 months) | 18 | 12 | 40.0% | 8 |
| 7 years | (79–90 months) | 9 | 8 | 47.1% | 9 |
| 8 yrs or more | ( > = 91 months) | 25 | 37 | 59.7% | |
| | Total | 231 | 101 | 30.4% | 10 |

Sample total is 332 instead of 337 because we could not ascertain years of injection for 5 participants

Table 2
Correlates of HCV antibody-positive serostatus among young PWID (n = 337)

| | HCV- | HCV+ | Unadjusted OR (95% CI) | OR p value | AOR (95% CI) | AOR p value |
|---|---|---|---|---|---|---|
| **N (%)** | 234 (69) | 103 (31) | – | – | – | – |
| **Gender** | | | | | | |
| Male | 152 (66) | 68 (67) | Ref | Ref | | |
| Female | 79 (34) | 34 (33) | 0.96 (0.59–1.58) | 0.878 | – | – |
| **Race/Ethnicity** | | | | | | |
| Latino/a | 43 (19) | 18 (17) | Ref | Ref | | |
| White | 171 (74) | 77 (75) | 1.08 (0.58–1.99) | 0.815 | – | – |
| Non-Latino/Non-white | 18 (8) | 8 (8) | 1.06 (0.39–2.88) | 0.906 | – | – |
| **Household income growing up (annual)*** | | | | | | |
| $0–50,000 | 85 (38) | 36 (42) | Ref | Ref | | |
| $51–100,000 | 73 (33) | 35 (41) | 1.13 (0.65–1.98) | 0.665 | – | – |
| > $100,000 | 64 (29) | 15 (17) | 0.55 (0.28–1.10) | 0.090 | – | – |
| **Homeless (lifetime)** | | | | | | |
| No | 91 (39) | 11 (11) | Ref | Ref | Ref | Ref |
| Yes | 143 (61) | 91 (89) | 5.26 (2.67–10.38) | **< 0.01** | 2.52 (1.19–5.36) | **0.016** |
| **Injected POs (lifetime)** | | | | | | |
| No | 106 (46) | 20 (20) | Ref | Ref | Ref | Ref |

***** 29 (9%) participants did not respond to this household income question

| | HCV- | HCV+ | Unadjusted OR (95% CI) | OR p value | AOR (95% CI) | AOR p value |
|---|---|---|---|---|---|---|
| Yes | 126 (54) | 79 (80) | 3.32 (1.91–5.79) | **< 0.01** | 1.25 (0.63–2.48) | 0.517 |
| **Number of people shared syringes with (past 12 months)** | | | | | | |
| 0 | 156 (67) | 48 (47) | Ref | Ref | Ref | Ref |
| 1 | 59 (25) | 28 (27) | 1.54 (0.89–2.68) | 0.125 | 1.43 (0.71–2.86) | 0.317 |
| 2 or more | 18 (8) | 27 (26) | 4.88 (2.47–9.61) | **< 0.01** | 2.17 (0.91–5.16) | 0.080 |
| **Number of people shared cookers with (past 12 months)** | | | | | | |
| 0 | 109 (47) | 26 (25) | *Ref* | *Ref* | *Ref* | *Ref* |
| 1 | 53 (23) | 17 (17) | 1.32 (0.66–2.64) | 0.433 | 1.35 (0.57–3.18) | 0.491 |
| 2 or more | 70 (30) | 60 (58) | 3.59 (2.07–6.22) | **< 0.01** | 2.15 (1.05–4.37) | **0.035** |
| **Number of times incarcerated (lifetime)** | | | | | | |
| **None** | 108 (46) | 28 (27) | *Ref* | *Ref* | *Ref* | *Ref* |
| **1** | 53 (23) | 10 (10) | 0.73 (0.33–1.61) | 0.432 | 0.49 (0.19–1.22) | 0.128 |
| **2 or more** | 72 (31) | 64 (63) | 3.43 (2.01–5.85) | **< 0.01** | 1.99 (1.06–3.73) | **0.032** |
| **Number of years Injected drugs** | | | | | | |
| 0–3 | 140 (61) | 24 (24) | *Ref* | *Ref* | *Ref* | *Ref* |
| 4–6 | 57 (25) | 32 (32) | 3.27 (1.78–6.04) | **< 0.01** | 2.49 (1.22–5.09) | **0.012** |
| 7+ | 34 (15) | 45 (45) | 7.72 (4.15–14.37) | **< 0.01** | 4.95 (2.35–10.46) | **< 0.01** |
| **Know one or more opioid user(s) older than 29** | | | | | | |
| No | 127 (54) | 43 (42) | *Ref* | *Ref* | *Ref* | *Ref* |

***** 29 (9%) participants did not respond to this household income question

| | HCV- | HCV+ | Unadjusted OR (95% CI) | OR p value | AOR (95% CI) | AOR p value |
|---|---|---|---|---|---|---|
| Yes | 107 (46) | 60 (58) | 1.66 (1.04–2.65) | **0.035** | 1.04 (0.58–1.86) | 0.889 |
| ***** 29 (9%) participants did not respond to this household income question | | | | | | |

# Figures

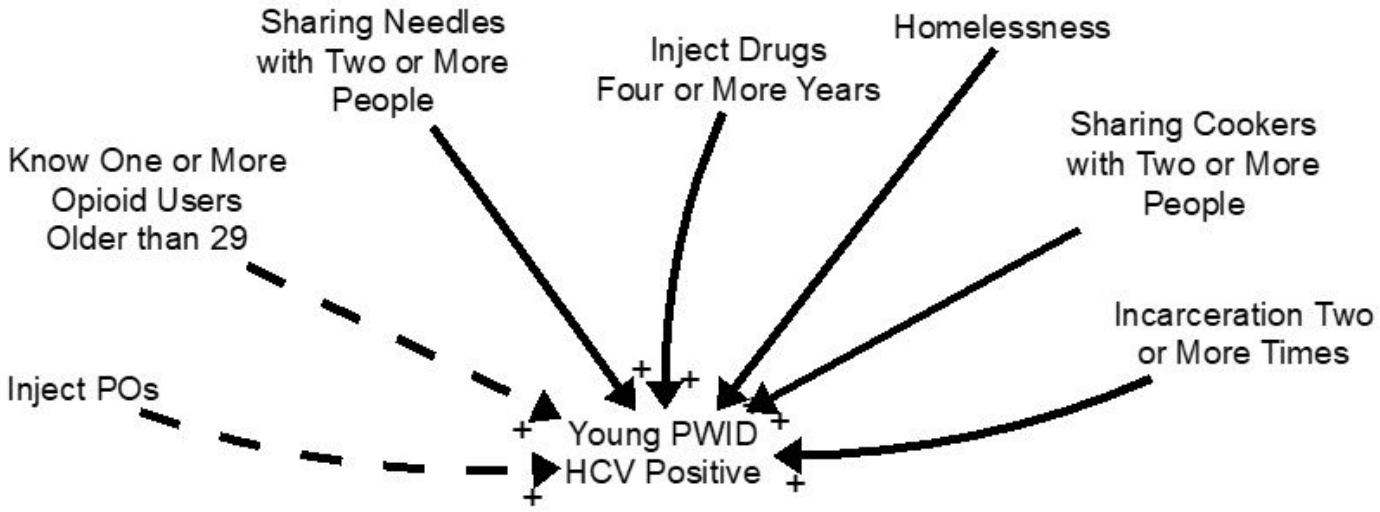
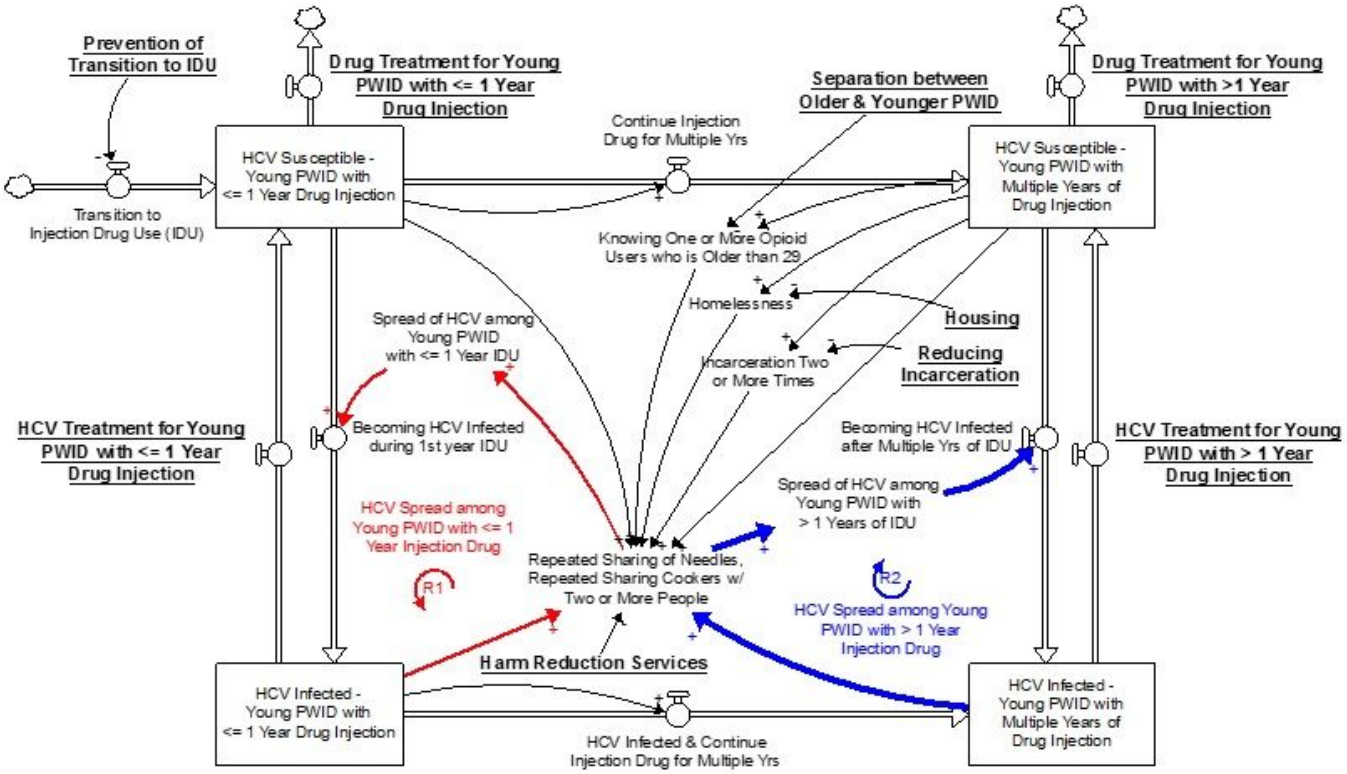



**Figure 1**

Identified Associations based on the Statistical Analysis




## Figure 2

Core System Dynamics Modeling Structure and Policy Analysis