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MAJOR ARTICLE

Hepatitis C virus (HCV) micro-elimination among people with HIV in San Diego: Are we on track?

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***Background*:** Rising incidence of hepatitis C virus (HCV) among persons living with HIV (PLWH) in San Diego County (SDC) was reported. In 2018, UCSD launched a micro-elimination initiative among PLWH, and in 2020 SDC launched an initiative to reduce HCV incidence by 80% across 2015-2030. We model the impact of observed treatment scale-up on HCV micro-elimination among PLWH in SDC.

***Methods*:** A model of HCV transmission among people who inject drugs (PWID) and men who have sex with men (MSM) was calibrated to SDC. The model was additionally stratified by: age, gender, and HIV status. The model was calibrated to HCV viremia prevalence among PLWH in 2010, 2018, and 2021 (42.1%, 18.5%, 8.5%, respectively), and HCV seroprevalence among PWID aged 18-39, MSM, and MSM with HIV in 2015. We simulate treatment among PLWH, weighted by UCSD Owen Clinic (reaching 26% of HCV-infected PLWH) and non-UCSD

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treatment, calibrated to achieve the observed HCV viremia prevalence. We simulated HCV incidence with observed and further treatment scale-up (+/- risk reductions) among PLWH.

***Results*:** Observed treatment scale-up from 2018-2021 will reduce HCV incidence among PLWH in SDC from a mean 429 infections/year in 2015 to 159 infections/year in 2030. County-wide scale-up to the maximum treatment rate achieved at UCSD Owen Clinic (in 2021) will reduce incidence by 69%, missing the 80% incidence reduction target by 2030 unless accompanied by behavioral risk reductions.

***Conclusions*:** As SDC progresses towards HCV micro-elimination among PLWH, a comprehensive treatment and risk reduction approach is necessary to reach 2030 targets.

KEY POINTS

Question: What can infectious disease modeling inform us about the impact of hepatitis C (HCV) treatment scale-up in our progress to achieve HCV micro-elimination among PLWH in San Diego County?

Findings: The observed DAA scale-up from 2018-2021 will reduce HCV incidence among PLWH from a mean of 429 infections/year in 2015 to 159 infections/year in 2030 (63% reduction), missing the 80% reduction target.

Meaning: Further county-wide treatment scale-up and behavioral interventions to reduce risk are required to meet the 80% incidence reduction target by 2030.

INTRODUCTION

Hepatitis C virus (HCV) and HIV share common transmission routes [1]. Although the most common HCV transmission form in the United States occurs due to sharing injection equipment among people who inject drugs (PWID) [2], sexual transmission of HCV is significant among persons living with HIV (PLWH), especially among men who have sex with men (MSM) [3]. Hence, the co-infection of HCV among PLWH is a major public health concern. According to 2009 data from the Centers for Disease Control and Prevention (CDC), 21% of all PLWH were HCV seropositive [1]. As individuals co-infected with HIV and HCV experience accelerated liver disease progression [1], complications due to untreated HCV are a significant cause of morbidity and mortality among PLWH who are otherwise well-controlled on antiretroviral therapy [1].

In 2016, the World Health Organization (WHO) adopted its Global Health Sector Strategy (GHSS) and set the strategic goal to eliminate HCV as a public health threat [4]. The WHO targets include a 90% reduction in HCV and HBV incidence (with specific targets of 80% reduction for HCV and 95% reduction for HBV) and a 65% reduction in HCV mortality by 2030 compared to a 2015 baseline [4]. Because screening for HCV is part of the HIV standard of care and many PLWH already have access to health services through integrated models of care [5], many consider

that PLWH comprise a population where HCV elimination (micro-elimination) is feasible [5]. Indeed, some countries with universal healthcare systems have reported significant progress toward HCV micro-elimination among PLWH [6,7]. Similar programs exist nationally, statewide, and county-wide in the United States. Our 2018 study on HCV burden in San Diego County estimated that 55,354 individuals are HCV seropositive in San Diego County [8]. The Eliminate Hepatitis C San Diego County Initiative is a public-private joint endeavor between the San Diego County Health Department and the American Liver Foundation to support the achievement of the WHO HCV elimination goal [9].

We recently reported that the rising HCV incidence among MSM with HIV indicates an urgent need for interventions to control the expanding HCV epidemic [10], with a projected number of 3,500 PLWH co-infected with HCV in San Diego in 2017 [11]. In 2018, UCSD Owen Clinic launched a micro-elimination initiative to scale-up HCV treatment among PLWH. While this program has achieved significant progress in HCV treatment uptake among PLWH, the potential impact of the scale-up, particularly on meeting the 2030 elimination targets, is uncertain. Further, it is unclear whether San Diego is on track to achieve the HCV elimination goals among PLWH. We aim to address that knowledge gap by using dynamic epidemic modeling of HCV transmission to assess the potential impact of observed treatment scale-up on HCV micro-elimination among PLWH in San Diego County by 2030.

METHODS

Model description

We developed a dynamic, deterministic compartmental model of HCV transmission and progression, stratified by HIV infection, which was calibrated to San Diego County. The model was stratified by Hepatitis C infection and disease progression status (Figure 1a), age, gender, HIV status, and transmission risk, which included PWID or MSM (Figure 1b). The HCV infection and disease stages, represented by *n* are: (i) Susceptible, (ii) Spontaneous Clearance from no/mild liver disease, (iii) SVR from no/mild liver disease, (iv) SVR Moderate Liver Disease, (v) SVR Compensated Cirrhosis, (vi) SVR Decompensated Cirrhosis, (vii) SVR Hepatocellular Carcinoma, (viii) No/Mild Liver Disease, (ix) Moderate Liver Disease, (x) Compensated Cirrhosis, (xi) Decompensated Cirrhosis, (xii) Hepatocellular Carcinoma. The age stages are: 18-39, 40-54, 55-74, and 75+ years. The six population sub-types are: MSM HIV-, MSM HIV+, PWID HIV- Male, PWID HIV+ Male, PWID HIV- Female, and PWID HIV+ Female. The model assumes that individuals enter the adult population at 18 years old, susceptible to primary HCV infection, and in one of the population sub-type compartments stratified by gender, HIV status, PWID status, and MSM (Figure 1b). PWID enter the model in the first age stage (18-39 years), and progress through the age stages or discontinue injection drug use. The rate of permanent cessation of injecting was sampled widely with uncertainty using data on duration of injection among PWID from STAHR II [12]. We assume HIV status is a

fixed characteristic; the model does not simulate HIV transmission dynamically due to the stable HIV prevalence among PWID and MSM in San Diego County [13,14].

Individuals enter the model susceptible to primary HCV infection. HCV transmission is simulated among PWID and MSM groups separately (without transmission between these groups) because very few MSM report injecting drugs in San Diego (1% of HIV-negative and 3% of MSM diagnosed with acute HIV) [15,16], and based on phylogenetic analyses in other settings indicating that MSM-IDU and PWID epidemics are distinct [17]. Therefore, although a small fraction of MSM may inject drugs, we classify these individuals as MSM and assume they inject with other MSM. The model also assumes assortative mixing among MSM by HIV status.

Once acutely infected, individuals can either transition to the no/mild liver disease compartment, or they may spontaneously clear HCV infection and move to the spontaneous clearance from the no/mild liver disease compartment. The fraction of individuals spontaneously clear infection, which is reduced for those with HIV. From the no/mild liver disease compartment, individuals continue to progress through the disease stages as if they continue to have chronic persistent infection unless successfully treated. Individuals can be treated from all stages. Those who have been successfully treated move into the equivalent SVR stage and are susceptible to HCV reinfection. Successful treatment stops any HCV-related disease progression unless an individual has already reached the compensated cirrhosis stage or beyond, where disease progression occurs at a slower rate compared to those without SVR. HCV-related mortality occurs from the decompensated cirrhosis compartments and hepatocellular carcinoma compartments. All baseline model parameters, sampling distributions, and sources are listed in Table S1 (Supplement).

Model Parameterization and Calibration

The model was parameterized mainly from the published literature (see Table S1, Supplement). For model calibration and parameterization, we used data from our 2018 HCV burden estimation (population sizes and HCV seroprevalence) among adults over age 18 in San Diego County [8] and three time-points of HCV viremia prevalence among PLWH from UCSD Owen Clinic [18]. By varying seven pre-determined parameters (transmission rate among MSM, transmission rate among PWID, degree of assortative mixing among MSM by HIV status, county-wide annual treatment rates among HIV/HCV co-infected individuals treated from 1996-2010 and 2011-2017, non-UCSD treatment rates among HIV/HCV co-infected individuals from 2018-2021, and number of PWID at model initialization in 1955) the model was calibrated to: HCV seroprevalence estimates in 2015 among MSM (4.6% among all MSM, 16.5% among MSM with HIV) and PWID aged 18-39 years (49.5%) [8,12], HCV viremia prevalence among HCV seropositive PLWH of 42.1% (2010), 18.5% (2018) and 8.5% (2021) [18], and number of PWID in 2007 [19]. Calibrated parameters are listed in Table S2 (Supplement). The calibrated model was then validated against HCV seroprevalence among PWID aged 40-54 (68%) and 55-74 (88%) in 2015 (age stratified data unpublished, but overall prevalence published in [12]).

Historic (pre-2017) HCV treatment rates among PLWH were unknown in San Diego County and calibrated to observed HCV viremia prevalence trends among PLWH. To obtain the observed declines in viremic prevalence among PLWH, we simulated a piece-wise treatment function from 1996-2010, 2011-2017, and 2018-2021. The time period of 1996-2010 represents the pegylated interferon (IFN) plus ribavirin era. 2011-2017 represents the era of the first generation of direct-acting antiviral (DAA) therapy, such as Telaprevir (which still required IFN and was available in Feb 2011 at UCSD through compassionate access programs), along with the DAA era. The UCSD Owen Clinic cares for approximately 3,200 PLWH every year. As we had data from UCSD Owen Clinic on treatment rates from 2018 onwards, we simulated a weighted treatment rate during this period between UCSD and other (non-UCSD) clinics, with UCSD Owen Clinic providing care for an estimated 26% of PLWH in San Diego County in the last five years [11,20] and our model assumed a conservative estimate of a similar proportion of PLWH co-infected with HCV. At Owen clinic, a rapid scale-up of HCV treatment among PLWH occurred from 2018 onwards, achieving an average rate of 54% HCV-infected PLWH treated per year between 2018-2021, reaching a maximum treatment rate of 71% in 2021. HCV treatment rates among patients without HIV were obtained from studies in San Francisco and nationally [21,22]. As the model does not explicitly model diagnosis, the data informing our treatment rates are based on treatment among the entire population, and calibrated treatment rates among PLWH outside Owen Clinic implicitly incorporate undiagnosed individuals.

To capture uncertainty in input parameters, a sample of 500 parameter sets was drawn from uncertainty distributions for each parameter. These sampled parameter sets were then used to generate 500 model fits to the observed data. Calibration was achieved using a least-squares minimization solver, *lsqnonlin*, in MATLAB (Optimization Toolbox). The lsqnonlin function uses the Levenberg-Marquardt minimization algorithm, and we use the function *MultiStart* to start from multiple initial guess points within the parameter priors to ensure a global minimum is found. We assign wide prior bounds to the unknown parameters and assess our posterior estimates to ensure our priors were sufficiently wide (Table S2 shows priors and posteriors).

Calibrated model runs were then excluded if the fits fell outside the 95% CI of the calibration data for HCV seroprevalence in 2015 among (i) all MSM, (ii) PWID aged 18-39 years, (iii) MSM with HIV [8,12], generating a total of 182 model fits to the data.

Simulation scenarios

We simulated three scenarios of HCV treatment. For all of them, we assumed a treatment rate of 2%/year from 1996 to the end of 2012. It increased to 5%/year from 2013 onwards for all non-PLWH populations [21,22]. Among PLWH, our calibrated model fits generated estimates of mean treatment rates of 25.4%/year from 1996-2010 and 28.8%/year from 2011-2017. From 2018 onwards, the following scale-up among PLWH was simulated:

- **Scenario 1 (counterfactual, no scale-up from 2018 onwards):** continuation of pre-2018 treatment rates [mean 28.8% of chronically infected PLWH treated/year]
- **Scenario 2 (observed):** UCSD [53.7%/year], other sites [calibrated 60.6%/year]
- **Scenario 3 (enhanced scale-up from 2021):** As in scenario 2, then all scale-up to maximum UCSD treatment rate [in 2021, 71% chronically infected PWH treated/year] starting in 2021
- **Scenario 4 (enhanced scale up plus halved transmission risk from 2021 onwards):** As in scenario 3, with the addition of a halving of transmission risk starting in 2021.

We outputted the incidence of HCV infections among PLWH, HCV viremia prevalence among PLWH, and the percent reduction in HCV incidence among PLWH from 2015 to 2030.

Sensitivity analyses

We performed a partial rank coefficient correlation (PRCC) analysis to understand how sensitive the model prediction of HCV incidence reductions (2015-2030) was to uncertainty in the underlying parameters.

We perform several one-way sensitivity analyses to test the importance of model assumptions. First, we examine variations in assumptions of treatment among people without HIV. For our baseline analysis, we assume historic treatment rates, but we perform two additional sensitivity analyses assuming: (i) treatment scale-up at the same relative percent increase as HCV-infected PLWH compartments and (ii) 2-fold relative percent increase as compared to HCV infected PLWH compartments.

Second, there is uncertainty regarding the effect of the COVID-19 pandemic on treatment rates in San Diego County, but national analyses showed a drop in treatment by 20% during 2020, which rebounded through the end of 2020 but did not achieve pre-COVID levels . We performed two sensitivity analyses where treatment rates were reduced by a relative 20% from (iii) 2020 to 2021 (then returning to pre-COVID levels in 2022), and (iv) 2020 to 2024 (returning to pre-COVID levels in 2025).

Lastly, our baseline analysis assumes similar SVR rates by risk, as a recent meta-analysis found SVR rates among PWID or people on opiate substation therapy are high (90%) and were not significantly different to patients without a history of injecting drugs [23]. However, we additionally performed a sensitivity analysis, where SVR rates among PWID are reduced by a relative 10% (re-calibrated parameters listed in Table S3, Supplement).

Statistical analysis

The model was created using MATLAB (version R2022b).

RESULTS

The model calibration resulted in 182 runs that fit the data. The calibrated model accurately matched 2015 HCV seroprevalence estimates for MSM and PWID aged 18-39 years and HCV viremia prevalence among PLWH for 2010, 2018, and 2021 (Table 1). The model was validated against HCV seroprevalence estimates among PWID aged 40-54 (model estimate 71.5% [95% CI: 61.9%, 77.9%] compared to 68% target) and PWID aged 55-74 (84.3% [95% CI: 75.7%, 89.4%] compared to 88% target) in 2015. In 2015, the model projects 429 [95% CI: 238, 777] incident HCV infections among PLWH (Figure 2), with an HCV incidence rate of 2.6 per 100 person-years (/100py) [95% CI: 1.4, 4.6]. HCV viremia prevalence among HCV seropositive PLWH was estimated at 27.2% [95% CI: 21.7%, 32.3%] (Figure 3). Details on HCV incident infections (total) among PLWH in San Diego County are provided in Table S4 (Supplement).

Without treatment scale-up in 2018 (scenario 1), incident HCV infections among PLWH were expected to decrease to 342 [95% CI: 183, 633] incident infections by 2018, with an HCV incidence rate of 2.0/100py [95% CI: 1.1, 3.7]. By 2030, incident infections decline to 347 [95% CI: 185, 636] but the HCV elimination target is not reached – with an estimated 43% [95% CI: 33%, 52%] reduction in HCV incidence from 2015-2030 (Figure 2). By 2030, HCV incidence rate declines to 1.4/100py [95% CI: 0.7, 3.0]. HCV viremia prevalence among PLWH declines to 18.8% [95% CI: 13.2%, 25.1%] in 2018 and 11.2% [95% CI: 8.1%, 17.4%] in 2030.

With observed treatment scale-up from 2018 onwards (scenario 2), the model projects a sharp decline in incident HCV infections and HCV viremia prevalence among PLWH that slowly tapers off as the model approaches 2030. By 2021, the number of incident infections drops to 211 [95% CI: 109, 421], HCV incidence rate drops to 1.2/100py [95% CI: 0.6, 2.4], and viremia prevalence among HCV seropositive PLWH drops to 8.6% [95% CI: 8.6%, 8.6%]. By 2030, the number of incident infections drops to 159 [95% CI: 78, 331], HCV incidence rate drops to 0.9/100py [95% CI: 0.4, 1.9], and viremia prevalence drops to 6.3% [95% CI: 5.2%, 7.3%]. Between 2015 and 2030, this would achieve a reduction in HCV incidence among PLWH of 63% [95% CI: 57%, 67%].

If non-UCSD sites scale-up to the *maximum* levels achieved at UCSD from 2021 onwards (scenario 3), the model predicts 132 [95% CI: 59, 309] incident HCV infections among PLWH in 2030, with an HCV incidence rate of 0.7/100py [95% CI: 0.3, 1.8], just falling short of the HCV elimination goal (achieving a decrease in HCV incidence among PLWH of 69% [95% CI: 60%, 75%]). If in addition to treatment scale-up to the maximum level, there is a reduction in the behavioral risk starting in 2021 (Scenario 4), the model predicts 28 [95% CI: 13, 68] incident infections among PLWH in 2030, with an HCV incidence rate of 0.002/100py [95% CI: 0, 0.004], meeting the HCV elimination goal (achieving a decrease in HCV incidence among PLWH of 94% [95% CI: 91%, 95%].

Reductions in incidence can be tracked through corresponding reductions in HCV viremia prevalence among HCV seropositive PLWH (Figure 3) to monitor elimination progress, with scenarios 2 and 3 projecting between a 4% to 7% viremia prevalence among PLWH by 2030. The HCV reinfection rate among previously treated PLWH is projected to remain steady at around 4%, with treatment scale-up scenarios 2 and 3 projecting a slight increase from 3.4% in 2015 to above 4.5% by 2030. Only the scenario with behavioral risk reductions results in reduced reinfection incidence in 2030. Results on HCV reinfection rate among previously treated PLWH and HCV-infected PLWH under treatment in San Diego County are presented in Figure 4 and Figure S1 (Supplement), respectively.

Sensitivity and Uncertainty Analysis

There is uncertainty in treatment rates among HCV-infected persons without HIV, which we explored through sensitivity analysis (see Figures S2, S3, and S4, Supplement). Assuming an increase in background treatment among those without HIV, the model projects greater reductions in HCV incidence among PLWH (see Figure S5, Supplement, which looks at sensitivity analyses on relative reduction in HCV incidence among PLWH from 2015-2030 (%)). However, our models still predict that status quo treatment rates will not be able to achieve elimination with this level of scale-up, unless there was a two-fold relative increase in treatment rates among non-PLWH populations compared to PLWH populations (mean 82% reduction). In contrast, if treatment rates for PLWH were scaled-up among non-UCSD providers, and treatment rates for people infected with HCV mono-infection also increased (at the same relative rate or above), the HCV elimination targets could be met and even achieve a 90% reduction in incidence (see Figure S5, Supplement).

In additional scenario analyses assuming a 20% reduction in HCV treatment rates during the COVID-19 pandemic (from 2020-2021 or 2020-2025), the model projects more HCV incident cases during the reduced treatment rate period (see Figures S2, S3, and S4, Supplement). However, the relative reduction in HCV incidence among PLWH from 2015-2030 is similar to the baseline analysis (see Figure S5, Supplement).

The model findings were additionally insensitive to analyses assuming PWID have reduced SVR rates of a relative 10% lower than non-PWID (see Figures S2, S3, S4, and S5, Supplement).

The outcomes from the partial rank correlation coefficient uncertainty analysis found that the predicted relative reductions in HCV incidence among PLWH from 2015-2030 are most sensitive to the relative HCV susceptibility for PLWH compared to individuals without HIV, with greater susceptibility among PLWH resulting in lower incidence reductions (see Figure S6, Supplement)

DISCUSSION

Our analyses used epidemic modeling with available surveillance data from an HCV micro-elimination initiative among PLWH in San Diego County to determine whether we are on track to achieve 2030 HCV elimination targets. Our analysis indicates that despite a substantial increase in HCV treatment provided to PLWH at UCSD Owen Clinic, current levels of treatment are unlikely to achieve the HCV incidence elimination target of 80% reduction between 2015 and 2030 among PLWH in San Diego County. We found that achieving HCV micro-elimination among PLWH will likely require a scale-up of HCV treatment among both PLWH and reductions in transmission risk. In response to this observation, the Owen Clinic expanded services in 2022 to treat HCV in people who use drugs without HIV in conjunction with integrated substance use treatment and HIV prevention services. The expansion of evidence-based harm reduction interventions such as medications for opioid use disorder and syringe service programs (which together have been shown to reduce risk by 75% among PWID) [24], and the development of interventions to reduce HCV risk among MSM are both needed. Yet, there is insufficient evidence on effective interventions to mitigate the risk of sexual HCV transmission among MSM. Our Clinic protocol includes periodic STI testing during and after DAA treatment as a surrogate marker of ongoing condomless behaviors. This strategy provides us with opportunities for reinforcement counseling on sexual behaviors associated with HCV infection (such as condomless anal sex, fisting, and multiple partners) [25-27] to prevent HCV reacquisition and forwards transmission [28]. Additionally, our findings highlight that reinfection may be an important consideration among PLWH, with both modeling and observational studies showing a potential rise in reinfection rates with expanded treatment [28].

Strengths and Limitations

The Lancet Gastroenterology & Hepatology Commission on Accelerating the Elimination of Viral Hepatitis point out that HCV elimination data are limited [29]. Traditional surveillance data on new diagnoses is hampered by under-ascertainment and late diagnoses, so longitudinal data from at-risk populations may provide better insights regarding changes in reinfection incidence and chronic prevalence and treatment scale-up impacts [29]. This is one of the strengths of our analysis because it uses recent data on HCV treatment and chronic prevalence from a large cohort of PLWH at the UCSD Owen Clinic in San Diego.

However, the model does have several limitations. First, we lacked recent and robust data on HCV treatment rates among the population without HIV in San Diego. We explored the implications through sensitivity analyses, but this warrants further exploration. The COVID-19 pandemic led to reduced HCV testing and treatment, nationally [30] and it is possible that HCV treatment rates declined both among PLWH and overall in San Diego County, even though at the UCSD Owen Clinic, treatment rates increased in 2021. Nevertheless, even in our simulations with more pronounced disruptions until 2025, our key results were unchanged that scaled-up treatment is required to achieve HCV elimination. Although our modeling focuses on a single

county, to our knowledge, there are few funded projects explicitly aimed to facilitate larger-scale data accrual tracking HCV elimination among PLWH with a similar level of detail in the US. Investing in better surveillance systems for PLWH that track and routinely report data such as HCV diagnoses, treatment numbers, outcomes, and reinfections would facilitate more robust modeling, validation, and analytics to determine whether communities are on track for HCV elimination.

Second, our model only implicitly included the impact of harm reduction impact_in our calibrated transmission rates. We believe this is justifiable because there has been no evidence of a recent scale-up of harm reduction efforts in San Diego County. However, lifting the ban on syringe service programs in 2021 provided an important opportunity for the scale-up of these important prevention measures. If scaled-up, harm reduction could support HCV elimination efforts as explored in our behavior change scenario, prevent infection/reinfection among PWID, and have other benefits on preventing HIV and other health harms among PWID [31-33].

Third, our model neglects immigration and emigration as we lack data on migration into and out of San Diego county by HIV and HCV status. However, we note that the San Diego-Tijuana border is one of the busiest land border crossings in the world. While import of HCV infections could hamper elimination efforts, HCV treatment efforts in San Diego could aid in prevention of transmission from individuals who emigrate to other areas.

Fourth, our model assumes a stable PWID population size due to a lack of data to suggest otherwise, although we note the PWID population size estimate is old and uncertain. National data indicates an increase in PWID population size, mainly driven by increases in rural areas [34]. If the PWID population size is increasing in San Diego, it will likely further hamper elimination efforts.

Fifth, our work focuses on PLWH and therefore does not consider what is needed for HCV elimination more broadly, nor does it assess the cost implications of elimination. Future work should examine the most cost-effective HCV elimination strategies and the budgetary impact of achieving HCV elimination.

CONCLUSION

San Diego County is progressing towards HCV micro-elimination among PLWH, but increased HCV screening, treatment scale-up, and monitoring of HCV viremia among PLWH are required to reach the 2030 targets. To ensure treatment rates can be maintained, efforts to identify remaining treatment barriers among PLWH are necessary. Scale-up of harm reduction services, including medications for opioid use disorder, syringe exchange and supervised consumption sites among PWID both with and without HIV, are needed to reduce the risk of infection/reinfection.

TABLES

Table 1: HCV Calibration Data for San Diego County and Model Outputs

	Year	Observed Calibration Data [95% C.I.]	Calibrated Model Output [95% C.I.]	Reference
HCV seroprevalence among MSM with HIV	2015	0.165 [0.155, 0.176]	0.163 [0.156, 0.172]	Wynn et al. [8]
HCV seroprevalence among all MSM	2015	0.046 [0.030, 0.061]	0.054 [0.047, 0.061]	Wynn et al. [8]
HCV seroprevalence among PWID aged 18-39 years	2015	0.495 [0.428, 0.563]	0.494 [0.433, 0.552]	Horyniak et al. [12]
HCV viremia prevalence among HCV seropositive PWLH	2010	0.4211 [0.3791, 0.4643]	0.4212 [0.4128, 0.4444]	UCSD Owen Clinic [18]
	2018	0.1849 [0.1534, 0.2212]	0.1844 [0.1321, 0.2384]	UCSD Owen Clinic [18]
	2021	0.0857 [0.0636, 0.1146]	0.0857 [0.0857, 0.0857]	UCSD Owen Clinic [18]
Number of PWID (total)	2007	24,991 [3,751, 49,503]	24,996 [24,991, 25,031]	Tempalski et al.[19]

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Potential Conflicts of Interest: NM has received unrestricted research grants from Gilead and Merck. ERC has received unrestricted research grants from Gilead and Merck. He also participated in an advisory board to Theratechnologies for an unrelated topic.

Patient Consent Statement: Our study does not include factors necessitating patient consent

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FIGURE LEGENDS

Figure 1 : Model schematic of (a) HCV disease progression and (b) stratification by age, HIV status, and risk. PWID: people who inject drugs. MSM: men who have sex with men.

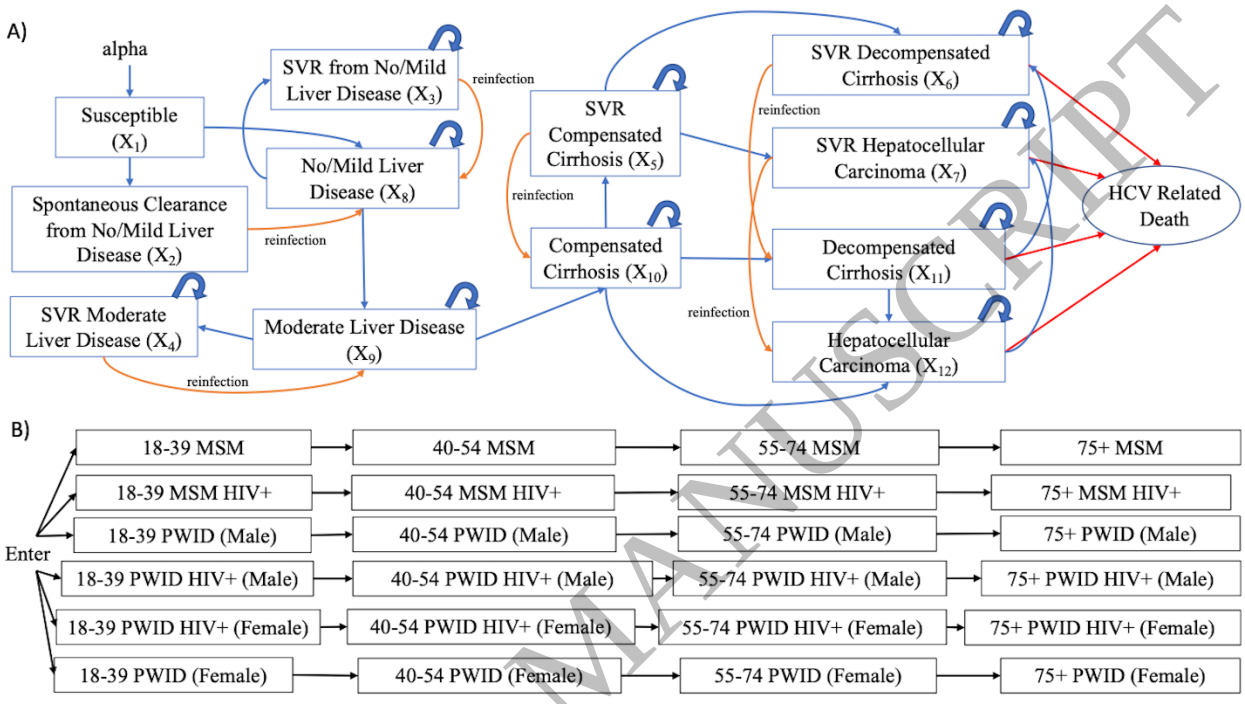

Figure 2: Annual number of new HCV infections among PLWH in San Diego County.

Scenarios shown are: (1) counterfactual continuation of pre-2018 treatment rates (29%/year, blue solid line); (2) observed scale-up from 2018 (to 54% at UCSD and 61%/year non-UCSD, green round dotted line); (3) county-wide scale-up to peak treatment achieved by UCSD (71%/year) from 2021 (71%/year, yellow square dotted line); (4) as in Scenario #3 plus halved transmission risk behavior from 2021 onwards (red dashed line). Mean model projections (lines), with shading denoting the 95% uncertainty interval around the observed scenario (Scenario 2).

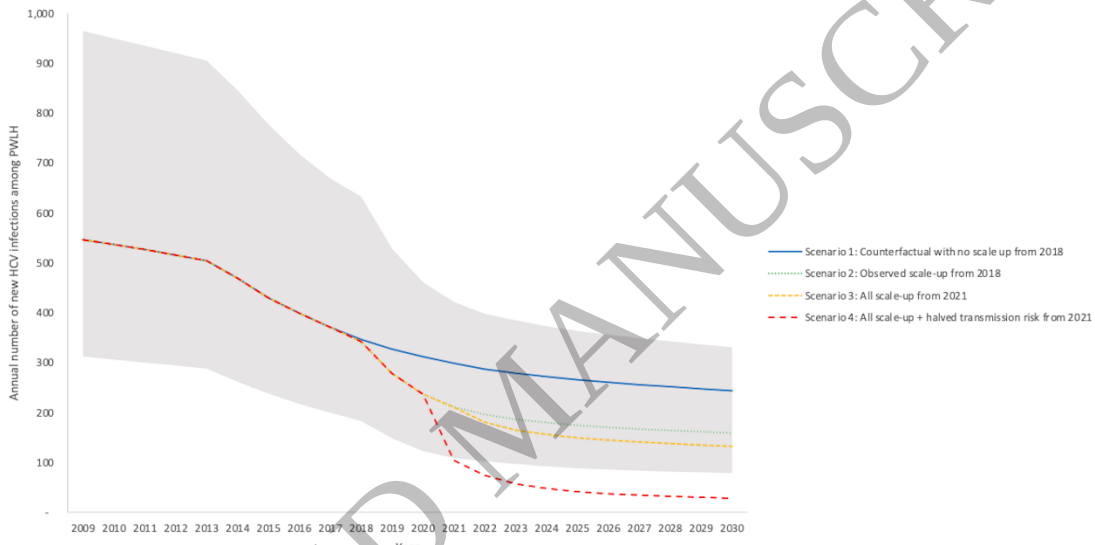

Figure 3: HCV viremia prevalence among HCV seropositive PLWH in San Diego County.

Scenarios shown are: (1) counterfactual continuation of pre-2018 treatment rates (29%/year, blue solid line); (2) observed scale-up from 2018 (to 54% at UCSD and 61%/year non-UCSD, green round dotted line); (3) county-wide scale-up to peak treatment achieved by UCSD (71%/year) from 2021 (71%/year, yellow square dotted line); (4) as in Scenario #3 plus halved transmission risk behavior from 2021 onwards (red dashed line). Mean model projections (lines), with shading denoting the 95% uncertainty interval around the observed scenario (Scenario 2).

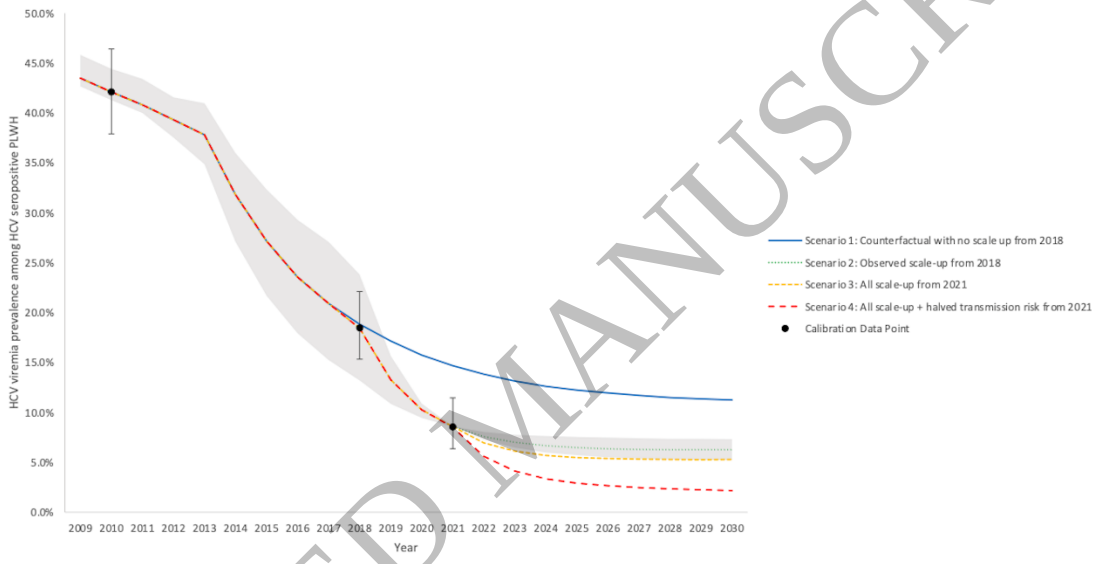

Figure 4: HCV reinfection rate among previously treated PLWH in San Diego County.

Mean model projections (lines) and observed data from UCSD Owen Clinic (dots and whiskers) to which the model was not calibrated. Shading denotes the 95% uncertainty interval around the observed scenario (Scenario 2). Scenarios shown are: (1) counterfactual continuation of pre-2018 treatment rates (29%/year, blue solid line); (2) observed scale-up from 2018 (to 54% at UCSD and 61%/year non-UCSD, green round dotted line); (3) county-wide scale-up to peak treatment achieved by UCSD (71%/year) from 2021 (71%/year, yellow square dotted line); (4) as in Scenario #3 plus halved transmission risk behavior from 2021 onwards (red dashed line).