Modeling hepatitis C treatment scale-up in persons who inject drugs in metropolitan Chicago

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Background

- In the United States alone, about 4 million people are infected with the hepatitis C virus (HCV). An estimated 60% of all HCV infections in the United States are attributable to injection drug use.
- Less than 1% of persons who inject drugs (PWID) and are infected with HCV in Chicago are treated with IFN-based annually. This may change with wider availability of direct-acting antivirals (DAAs) that are expected to be interferon-free, all-oral and can cure about 90% of infected individuals within 12 weeks. However, there are several barriers restricting access to treatment, such as cost and poor treatment readiness due to a drug use lifestyle that may lead to re-exposure after treatment.
- Martin et al.[1,2] developed models of HCV infection for treatment scale-up predictions for PWID that determined the effectiveness of HCV antivirals; however, these studies have used data on PWID that reside outside of the United States and assumed that people who spontaneously clear HCV infection have very limited (or none) probability of acquiring immunity.
- We aim to predict the impact of DAA therapy on HCV prevalence among Chicago PWID, considering a higher immunity, rate, and its to project cost using a mathematical model.

Methods

To estimate the HCV antibody and RNA prevalence among the Chicago population, we relied on empirical Chicago-based data from **(i)** the CDC-sponsored National HIV Behavioral Surveillance System (NHBS) of 2009, **(ii)** the Third Collaborative Injection Drug Users (CIDUS III, 2002-2004) study and **(iii)** the Early Natural History of HCV Infection Among Injection Drug Users (NATHCV, 2002-2006) study. The model developed by Martin et al[1] was used here assuming that those who spontaneously clear the infection [δ] are protected against reinfection (immune).

Martin et al.[1] described the transition among five groups of PWID: (i) susceptible (including those who clear infection after antiviral treatment, termed sustained viral response (SVR), but are not immune), (ii) chronically infected who are naïve to treatment or re-infected, (iii) chronically infected who have failed treatment (non-SVR), (iv) currently in treatment, and (v) immune (Fig. 1 and Equation 1). We reproduced Martin et al.[1] predictions that treating 10 infections per 1000 IPWID would decrease baseline prevalence 20%, 40%, or 60% by 31%, 13%, or 7% respectively, after 10 years.

Methods Cont'd

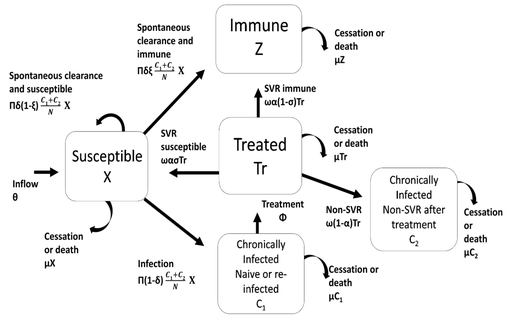

Figure 1. Schematic for mathematical model (Equation 1). N represents the total PWID population ($X+Tr+Z+C_1+C_2$). Model parameters are described in Table 1.

$$\frac{dX}{d\tau} = \theta - \pi(1-\delta+\delta\xi)\frac{C_1+C_2}{N}X + \omega\alpha\sigma Tr - \mu X$$
$$\frac{dC_1}{d\tau} = \pi(1-\delta)\frac{C_1+C_2}{N}X - f(C_1) - \mu C_1$$
$$\frac{dTr}{d\tau} = f(C_1) - \omega Tr - \mu Tr$$
$$\frac{dZ}{d\tau} = \pi\delta\xi\frac{C_1+C_2}{N}X + \omega\alpha(1-\sigma)Tr - \mu Z$$
$$\frac{dC_2}{d\tau} = \omega(1-\alpha)Tr - \mu C_2$$

Equation 1. Model equations. Variables and parameters are described in Fig. 1 and Table 1.

Model parameter definition	Symbol	Value	Source
Population Dynamics		[min–max]*	
Average new injector rate*	θ	85 [50-200]	[1]
Average IDU leaving rate (cessation or death)*	μ	0.085 [0.05-0.2]	[1]
Infection Dynamics			
Average HCV infection rate per year	π	[0-0.95]	**
Average proportion of infections that spontaneously clear the infection	δ	0.26 [0.22-0.29]	[1,3]
Average proportion of spontaneously cleared infections resulting in immunity	ξ	1 [0-1]	[4-7]
Treatment Dynamics			
Average treatment rate	Φ	5-55	[1]
Average treatment duration	1/ω	0.23	[8]
Average proportion of cured infections due to treatment, resulting in immunity	1-σ	0 [0-0.25]	[1]
Average proportion of cured infections with SVR	α	0.9	[8]

Table 1. Martin et al. model parameters. θ and Φ units are per 1000 PWID annually; μ, π, and 1/ω units are per year; *ranges used for sensitivity analysis; ** Varied to produce a range of baseline prevalences.

$$H_{RNA}P_0 = H_{AB}P^*(1-\xi\delta)$$

Equation 2. Converting antibody prevalence to RNA prevalence. $H_{RNA}P_O$, HCV-RNA prevalence; $H_{AB}P$, antibody prevalence; ξ, protection against infection (Table 1); δ, spontaneous clearance from infection (Table 1).

References

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Results

Population	Approx. Pop. Size (n)	Median Age (IQR)	HCV AB+ prevalence (%)	HCV RNA+ prevalence (%)	Infection rate (π)	Scale up per 1000 to halve the baseline HCV RNA prevalence after 10 years of therapy [min–max]*	Estimated Cost ($M) per respective PWID population for 10 years [min–max]*
ALL	32,000[@]	44 (35-52)	59[A]	44[C]	.284	32 [29-43]	1024-1536 [928-2060]
HR	22,000	45 (35-52)	38[A]	28[C]	.185	17 [16-20]	374-561 [352-660]
NH-Black	15,000	51 (44-56)	66[A]	49[C]	.34	38 [33-55]	570-855 [495-1238]
NH-White	12,000	31 (26.75-42.25)	38[A]	28[C]	.185	17 [16-20]	204-306 [192-360]
Hispanic	4,000	41 (34-39)	64[A]	47[C]	.315	35 [32-51]	140-210 [128-306]
Young PWID	11,000	27 (24-28)	14[B]	9[D]	.149	5	55-83

Table 2. Prevalence and treatment scale up estimates. HR, PWID in harm reduction programs; NH, Non-Hispanic; @, includes ~1000 PWID from other ethnical groups; IQR, interquartile range; [A] , data from NHBS09 of 2009; [B] data from CIDUS III study; [C] was calculated using Eq.2 and δ=0.26 as in Martin et al; [D], was calculated using Eq. 2 and δ=0.34[2]; M, million; Cost was determined using expected DAA cost $100,000-$150,000 per person; *, based on one-way sensitivity analysis (Table 1).

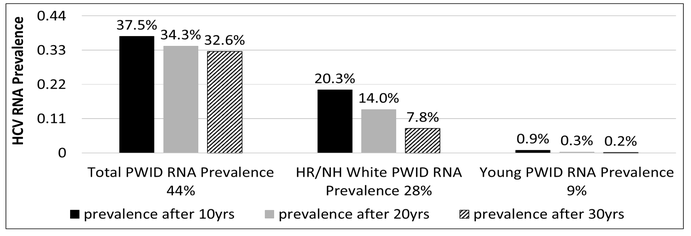

Fig. 2. Resulting $H_{RNA}P$ after 10, 20 and 30 years of treating 10 infections per 1000 PWID with 90% SVR rate, 12-week treatment duration and acquired immunity (ξ=1) from Chicago's subpopulation with high $H_{RNA}P_0$ (44%), moderate $H_{RNA}P_0$ (28%), and low $H_{RNA}P_0$ (9%).

Conclusion

- Treatment scale-up could dramatically reduce the prevalence of HCV RNA (within 10 years of treatment scale-up of 10 infected subjects per 1000) among PWID in Chicago, who serve as the major source of disease transmission.
- Focusing treatment on young PWID could have an important impact on HCV at an attainable projected cost of $5.5 to $8.3 million per years of treatment scale-up.
- Further modeling efforts (such as agent-based modeling) are needed to test and refine modeling predictions.