Poster #535

HCV Treatment as Prevention will Require Massive Scale up to See Prevention Benefits

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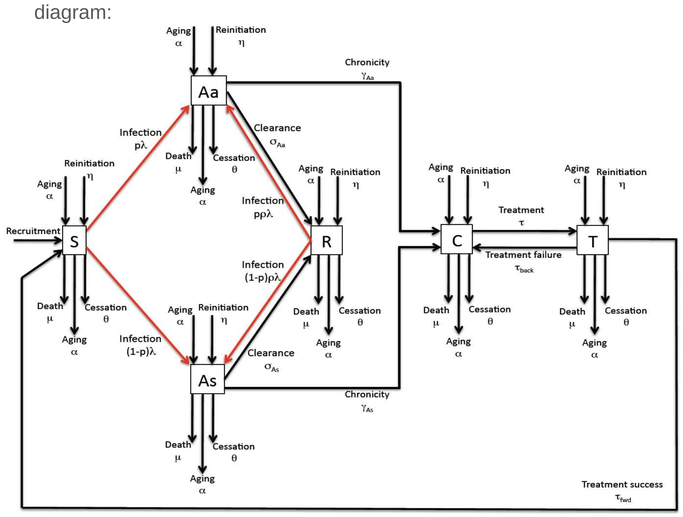
Modeling has suggested Hepatitis C virus (HCV) prevalence reductions of >50% with widespread treatment in people who inject drugs (PWID). However, there has been inadequate consideration of realistic treatment delays and patterns of injection cessation and relapse, age specific hazards and population-level mixing. We explore the impact of various treatment strategies on HCV incidence by building an age-specific compartmental model of HCV transmission in a community of current and former PWID, informed and parameterized by data from multi-decade studies of HCV transmission among PWID in Baltimore, Maryland. We compared strategies ranging from conservative to aggressive and estimated reductions in incidence and prevalence over 20 years for each program and per treatment course. Our model supports that widespread use of HCV treatment can have significant positive impact over 20 years. However, when treatment coverage is below ~90% of the PWID population over 20 years, almost all prevalence reduction was due to direct effects of curing infected individuals. Indirect effects were negligible due to the hazard of HCV infection being so high in this population, requiring extremely large amounts of treatment to reduce it. To greatly reduce HCV transmission among PWID, treatment programs need to be aggressive in treating large numbers of PWID almost immediately after acquisition of HCV and incorporate harm reduction strategies. Given the vast numbers of treatment needed to impact transmission, intervention programs should strongly prioritize clinical considerations and the relative impact of harm reduction strategies targeting primary infection.

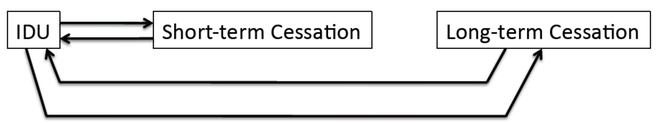
1) Age-Stratified Model of HCV Transmission

We model HCV transmission in a population of PWID using a compartmental model with the following characteristics:

- Total population of 44,000 current and past PWID (total size remains constant over time)
- Population stratified into yearly age classes from 18 to 70 (and older) years of age
- Individuals may be susceptible [S]; acute symptomatic [As] and asymptomatic [Aa]; spontaneously recovered [R]; chronically infected [C]; and undergoing treatment [T]. The possibility of cured individuals becoming re-infected is considered. Compartmental flow follows the diagram:



- In addition, the population is divided across 3 groups (below) in different injection drug use states: actively injecting (20,000), in short-term cessation (8,000) and long-term cessation (16,000). Sizes of these groups remain constant over time



Assumptions

- Parameters dictating disease progression and treatment response are age-independent; all other parameters are age-dependent
- Treatment efficacy is 90%
- Models assume varying levels of harm reduction scale-up which only reduces infection among individuals after treatment.
- Parameterization of cessation, hazards of infection and mixing matrices were fit to data from our cohort data.

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2) Fitting Model to Empirical Data from a Community-based Cohort of PWID in Baltimore

We fit our model to data from a long-standing cohorts of PWID in Baltimore Maryland; the ALIVE study (1988-present) and the STEP study to reproduce: *i*) age at which PWID initiate injection; *ii*) the age-dependent Injection drug use patterns; *iii*) HCV prevalence over time; *iv*) Cessation and relapse into injection drug use as a function of age and time.

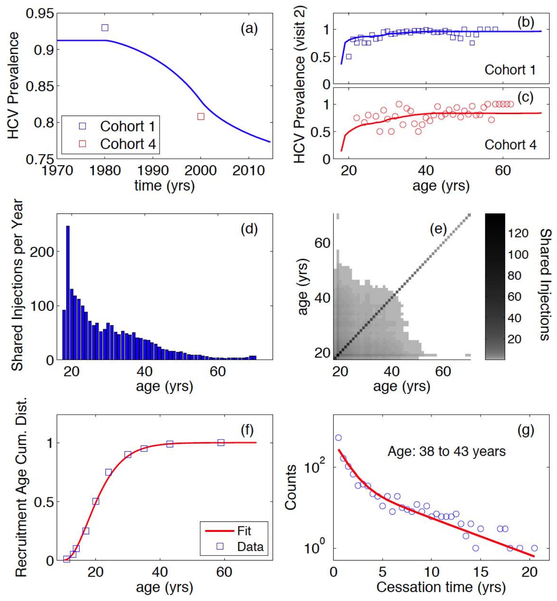

Figure 1: Empirical support for model. Parameterization of the model framework to a) Overall HCV antibody prevalence over four recruitment cohorts as measured in the ALIVE cohort; b-c) age specific HCV antibody prevalence in cohorts enrolled in b) 1988-89 (Cohort 1) and c) 2004 (Cohort 4); d) number of shared injections by PWID of different ages as measured in the STEP study; e) number of shared injections between people of age i (rows) with people of age j (columns); e) Age at initiation of drug injection; f) time to cessation since start of drug use for one age group in model (38-43 year olds).

3) Results

With our model, we explored a range of interventions using antivirals (0-40,000 PWID treated, 1-15 years after infection) and harm reduction scale-up (0-75% coverage) from 2015 to 2035, while targeting different groups of individuals according to their injection drug use state (actively injecting, cessation only, and everyone regardless of injection status).

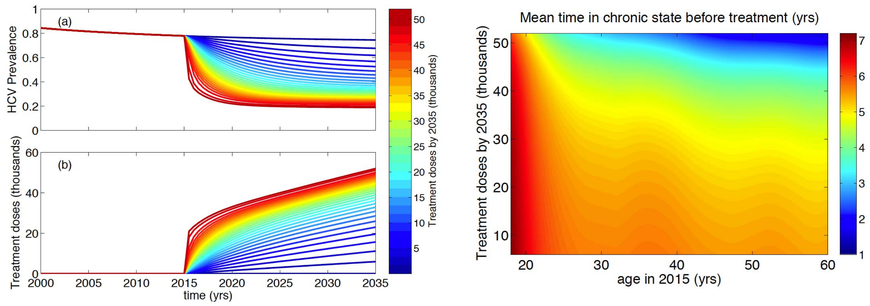

Figure 2: *Left*: HCV prevalence reduction (a) and treatment doses applied in time (b). *Right*: for individuals treated from 2015-2035, the heatmap shows the mean number of years spent in chronic infection before being treated, for various intervention intensities. In this scenario, only individuals who have ceased injection are treated and no harm reduction scale-up is assumed.

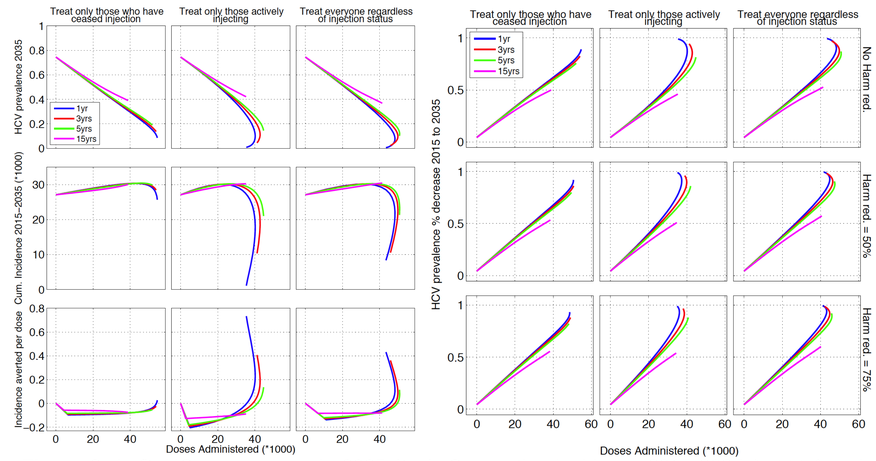

Figure 3: ***Left***: HCV prevalence in 2035 (*top*), Cumulative Incidence 2015-2035 (*middle*) and Incidence averted per treatment dose in the same time period (*bottom*), for different treatment intensities and that vary 1) number of total doses delivered (x-axis); the delay between infection and treatment (colored lines); and different states of injection from A) PWID who have ceased injection only (*left*); B) only actively injecting PWID (*middle*); and C) all PWID regardless of current injection (*right*) (columns). ***Right***: % decrease in HCV prevalence from 2015-2035 for different treatment and intensity of harm reduction scale up (none to coverage of 75% of cured PWID)

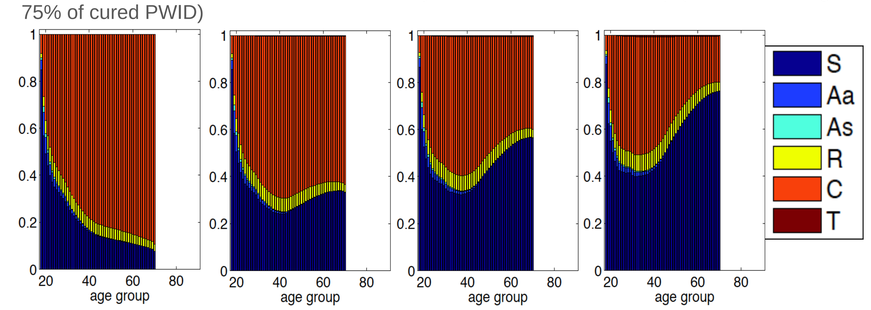

Figure 4: Population age-structure in 2035, for different intervention strategies (0, 10,000, 20,000, 30,000 treatment doses applied, left to right). In this scenario, only individuals not actively injecting are treated and no harm reduction scale up is assumed.

4) Conclusions

- Our model supports that widespread use of HCV treatment can have a significant positive impact – reduction in prevalence of 40% to 100% by applying 20,000 to 40,000 treatment courses over 20 years (PWID population in Baltimore~40,000).
- The impact of interventions varied little by who was treated (active vs. abstinent PWID) or when infected individuals received treatment (1-15 years after infection).
- At treatment levels below 90% of the PWID population over twenty years, almost all reduction in prevalence was due to direct effects of curing infected individuals. Indirect effects (protection of untreated individuals by treating those around them who could potentially infect them) were negligible because in this population the hazard of HCV is large enough that a massive amount of treatment is needed to reduce it substantially.
- Programs seeking to use antiviral treatment to reduce transmission of HCV at population scales should do so only in populations with measured hazards of HCV that are found to be low enough that these effects could be sizable.
- To impact transmission by indirect effects, treatment needs to be scaled to over 90% of the population targeted an average of 1 to 3 years after HCV infection with simultaneous scale up of harm reduction strategies.