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A Test, Treat and Retain Combination Strategy for Elimination of HCV Transmission among Injection Drug Users: A Mathematical Model.

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Abstract

Background: The burden of HCV remains a major public health challenge, especially among injection drug users. Based on the success of the "HIV Treatment as Prevention" strategy, and in view of the imminent availability of new and more effective HCV treatments, we proposed to evaluate a parallel "HCV Treatment as Prevention" strategy within a continuum of care framework.
Methods: We built a deterministic compartmental model of HCV transmission. Clinical, behavioral and epidemiological data have been gathered to simulate the HCV epidemic in British Columbia (BC), Canada. We simulated the HCV infection from 2011 to 2025, and measured HCV incidence, prevalence, and all-cause mortality cases.
Results: Our results suggest that even moderate rates of testing and treatment, coupled to an aggressive engagement and retention of high-risk individuals into harm-reduction strategies, could have a dramatic effect by reducing incidence, prevalence and mortality. However, our model also shows that this strategy will fail if it is not coupled with effective harm-reduction initiatives.
Conclusion: Our model and the interventions that we tested provided unique insights on how to decrease the burden and on how to control the spread of the HCV epidemic. Our results suggest that failure to couple an effective seek and treat HCV program with a highly effective "prevention" package could potentially have a substantial negative impact on the HCV burden especially for individuals engaged in ongoing transmission risk activities.

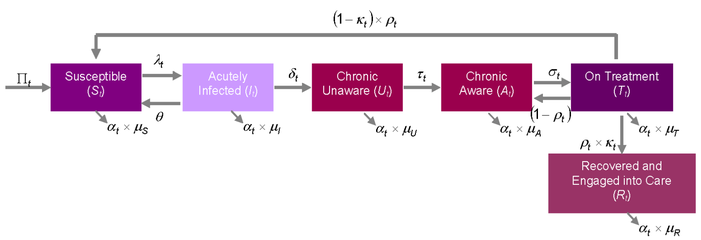
Background

- The burden of hepatitis C (HCV) infection, particularly among individuals who inject drugs (IDUs), remains a major public health challenge, with HCV prevalence in this population ranging from 15% to 90%.
- Timely diagnosis and treatment are potentially key to decreasing the HCV disease burden.
- The main goal of HCV treatment has been to achieve a sustained virological response (SVR).
- HCV treatment is undergoing significant evolution. Several new anti-HCV drugs have been shown to be associated with improved SVR rates in HCV mono-infected individuals. Ongoing and planned clinical trials will further evaluate the safety and efficacy of these therapies in HIV co-infected individuals and among IDUs, given that pegIFN-RBV remains a core component of the approved new antiviral agents in the near term.
- Recent mathematical models have assessed the impact of increasing HCV treatment coverage on both HCV incidence and prevalence, showing a dramatic effect, despite the limited efficacy of pegIFN–RBV.
- In view of the imminent availability of new and more effective HCV treatments, we conducted the present study to predict the potential impact of using a "HCV Treatment as Prevention" strategy within a continuum of care framework

Methods

- The model was designed to address the current state of the HCV epidemic among IDUs in British Columbia (BC), Canada.

Figure 1. Schematic for the HCV model.



Footnote: The parameters used are: Π (new injector birth rate), λ (force of infection), θ (proportion of acute infections that spontaneously clear), δ (rate of progression from acute to chronic unaware compartments), τ (testing rate), σ (proportion of individuals being offered HCV treatment), ρ (proportion of treated infections that achieve sustained virologic response), κ (proportion of individuals who after achieving sustained virologic response remain in the recovered and engaged into care compartment), α (ageing factor) and μ (all-cause mortality rate). The subscript indicates that the parameter changes over time.

Methods

- This model proposes to assess the feasibility of this new initiative by proposing realistic scenarios for testing, treatment coverage and engagement in harm-reduction initiatives.
- This is a deterministic mathematical model, which simulated the HCV epidemic from 2013 to 2025. The baseline scenario was based on the years 2011 and 2012. The model was updated yearly.
- The interventions were:
  - Increase testing from 5% (status quo) to 50% (parameter τ) during 2013-2025.
  - Increase treatment coverage from 3% (status quo) to 40% (parameter σ) during 2013-2025.
  - Increase treatment efficacy for genotype 1 from 50% (status quo) to 80% (parameter ρ_1). Because we are focusing on an IDU population, we performed a sensitivity analysis in which we lower the efficacy of this therapy to 60%, 70% and 75%.
  - Change the risk of being re-infected (ε). The pool of susceptibles is composed of individuals who experienced spontaneous virus clearance, individuals who experienced SVR and those who have ever been infected with HCV. Based on a few studies, we assumed that the risk of infection among those individuals not naïve to HCV infection will decrease by 30%, 50% and 80% in comparison to those naïve to HCV infection.
  - Change the proportion of individuals who achieved SVR and are engaged and retained into harm-reduction initiatives (parameter κ). This parameter ranged from 0% (status quo) to 100%. Basically, this addresses the question: What happens if "kappa%" of HCV-positive IDUs cease risky injection practices following HCV cure?

Results

Table 1. Model outputs using as main parameters: τ = 5% (Status Quo) for testing coverage, σ = 3% (Status Quo) for treatment coverage, ρ_1 = 50% (Status Quo) for the proportion achieving SVR for genotype 1, κ = 0% (Status Quo) for the proportion of individuals moving and staying into the recovered and engaged into care compartment after achieving SVR, and ε = 0% (Status Quo), 30%, 50%, and 80% for the reduction in the probability of being re-infected.

Reduction in the probability of being re-infected	15 years			
	Status Quo	30%	50%	80%
Cumulative Incidence	18,431	17,788	17,367	16,748
Cumulative Mortality	10,032	9,990	9,962	9,921
Prevalence	58,096	57,499	57,109	56,534

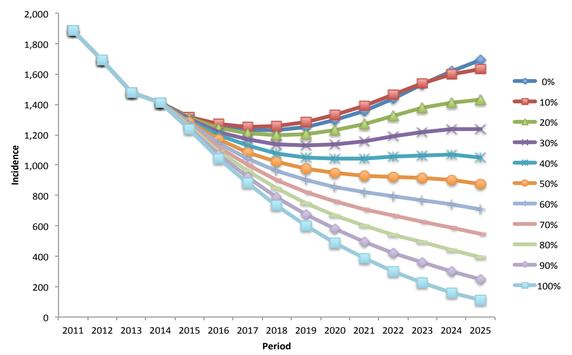
Table 2. Model outputs using as main parameters: τ = 5% (Status Quo*) to 50% for testing coverage (increased using an exponential growth), σ = 3% (Status Quo*) to 40% for treatment coverage (increased using an exponential growth), ρ_1 = 50% (Status Quo*) for the proportion achieving SVR for genotype 1, κ = 0% (Status Quo*) for the proportion of individuals moving and staying into the recovered and engaged into care compartment after achieving SVR, and ε = 50% (Status Quo*) for the reduction in the probability of being re-infected. **Note:** *Indicates what assumptions were made for the status quo scenario.

Interventions	15 years			
	Status Quo*	Testing Coverage	Treatment Coverage	Testing and Treatment Coverage
Cumulative Incidence	17,367	17,468	21,613	21,680
Cumulative Mortality	9,962	9,942	9,048	8,938
Prevalence	57,109	56,728	43,676	40,683

Table 3. Model outputs using as main parameters: τ = 5% (Status Quo*) for testing coverage, σ = 3% (Status Quo*) for treatment coverage, ρ_1 = 50% (Status Quo*) to 60%, 70%, 75% and 80% for the proportion achieving SVR for genotype 1 because of the new HCV treatment (using a duration of treatment of 24 weeks), κ = 0% (Status Quo*) for the proportion of individuals moving and staying into the recovered and engaged into care compartment after achieving SVR, and ε = 50% (Status Quo*) for the reduction in the probability of being re-infected. **Note:** *Indicates what assumptions were made for the status quo scenario.

Proportion achieving SVR - Genotype 1	15 years				
	Status Quo*	60%	70%	75%	80%
Cumulative Incidence	17,367	17,734	18,095	18,274	18,451
Cumulative Mortality	9,962	9,922	9,881	9,862	9,842
Prevalence	57,109	56,718	56,332	56,141	55,952

Figure 2. Projected incidence using as main parameters: τ = 5% to 50% for testing coverage, σ = 3% to 40% for treatment coverage, ρ_1 = 70% for the proportion achieving SVR for genotype 1 (using a duration of treatment of 24 weeks), κ = 0% (Status Quo) to 100% for the proportion of individuals moving and staying into the recovered and engaged into care compartment after achieving SVR, and ε = 50% for the reduction in the probability of being re-infected.



Conclusions

- Our results suggest that a proactive strategy aimed at seeking, testing, treating and retaining HCV infected IDUs into harm-reduction programs following HCV treatment could have a marked beneficial impact on HCV incidence, prevalence and mortality over time using conservative parameters.
- Studies have shown that if current IDUs are offered opioid substitution therapy, adherence to HCV treatment increases, premature mortality decreases, and consequently, they will be more likely to benefit from HCV treatment.
- Therefore, any seek, test and treat program should engage these individuals into innovative and effective harm-reduction initiatives, as these individuals are highly vulnerable to being re-infected after successful therapy, and to transmit their virus to other susceptible IDUs.
- Our model showed that for κ values higher than 50%, the number of incident cases decreased dramatically over time.

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