The potential prevention benefits of a treat-all hepatitis C treatment strategy at global, regional, and country levels: a modelling study

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Hepatitis C virus (HCV) epidemic

- Highly effective direct acting antivirals (DAAs) have been developed as treatment for hepatitis C virus (HCV) infection
- An estimated 71 million people are infected with HCV globally
- The WHO has set targets to eliminate HCV by 2030
  - Includes reducing incidence by 80% from 2015 levels

- Main modes of transmission: injecting drug use, unsafe medical injections and procedures, and vertical transmission
  - Injecting drug use important in many settings¹
  - Unsafe medical procedures important mostly in low- and middle-income settings²

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¹: The contribution of injection drug use to hepatitis C virus transmission globally, regionally, and at country level: a modelling study. Trickey et al, 2019
Treatment as prevention and aims

- Many countries are developing strategies to scale-up treatment
- **Some countries have treatment guidelines excluding people with substance use issues or limit treatment to those with advanced liver disease**
- How do we treat to prevent transmission?
  - Target high risk groups?
  - What prevention gains do we achieve from a treat all strategy?

- We **aimed** to estimate the number of infections averted by treating people with chronic HCV, for several strategies:
  - Treat all
  - Treat people who inject drugs (PWID)
  - Treat older age groups
  - Treat people with advanced liver disease
Model description

• A dynamic, deterministic model of HCV transmission for simulating country-level HCV epidemics among:
  • PWID
  • the general population

• Incorporates:
  • population growth
  • ageing
  • demographics
  • disease progression
  • injecting drug use
  • vertical HCV transmission
  • historical treatment numbers
Schematic of age and injecting status
Schematic of HCV infection, treatment and disease progression
Model parameterization

- Demographic information: UN datasets
- Key parameters and bounds from various systematic reviews:
  - HCV prevalence among general population¹
  - HCV prevalence among PWID²
  - Proportion of adults that are PWID²
- Countries included if data were available on all three key parameters
- Model accounted for uncertainty in parameters for each country

- Model uses historical country-level treatment data taken from a range of sources (mostly the Center for Disease Analysis: https://cdafound.org/polaris/)

1: Global prevalence and genotype distribution of hepatitis C virus infection in 2015: a modelling study. Blach et al, 2017
2: Global prevalence of injecting drug use and sociodemographic characteristics and prevalence of HIV, HBV, and HCV in people who inject drugs: a multistage systematic review. Degenhardt et al, 2017
Key model assumptions

• Decreasing HCV epidemics among general population (around 1% per year)
  - due to evidence from countries with 2 surveys
• Stable HCV epidemics among PWID
• Stable proportion of adults that are PWID
  • except in Eastern Europe and Sub-Saharan Africa: increasing

• Assumptions investigated in many sensitivity analyses

1: Global prevalence and genotype distribution of hepatitis C virus infection in 2015: a modelling study. Blach et al, 2017
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Mathematical model scenarios

• The model was run 2018-2038 (1000 model fits for each country)
• Firstly with that country’s baseline level of treatment (counterfactual)
• And then with **50 additional individuals being treated in 2018**
  • Treat all – individuals randomly selected from all infected individuals
  • Treat PWID – selected randomly from PWID
  • Treat older age groups – selected randomly from people ≥35 years
  • Treat people advanced liver disease – selected randomly from people with cirrhosis
  • Infected individuals can overlap between categories
• Track benefits to 2038 with baseline treatments from 2018 continued
• Low number of 50 treatments chosen to give an estimate of prevention benefit without altering each country’s epidemic trajectory
Determinants of infections averted

• To investigate the determinants of the number of infections averted per treatment we used **univariable and multivariable linear regression analyses** of country-level characteristics:
  • Current population growth rates
  • Population-attributable fraction of IDU to HCV transmission (from Trickey et al\(^1\))
  • Population proportion of PWID among adults\(^2\)
  • Average duration of IDU
  • HCV prevalence among IDU
  • HCV prevalence among PWID
  • HCV prevalence among the general population

• We did this for the infections averted in the treat all and PWID scenarios

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1: The contribution of injection drug use to hepatitis C virus transmission globally, regionally, and at country level: a modelling study. Trickey et al, 2019
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Countries included

- 88 countries were modelled that had the required data (85% of world’s population)
Global results summary

• Similar numbers of infections averted per treatment for treat all, cirrhosis, and age ≥35 years strategies – much higher for PWID

<table>
<thead>
<tr>
<th>Strategy</th>
<th>Global average HCV infections averted 2018-2038 per treatment Median (95% credibility intervals)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treat all (random selection)</td>
<td>0.35 (0.16, 0.61)</td>
</tr>
<tr>
<td>People aged ≥35 years</td>
<td>0.30 (0.12, 0.53)</td>
</tr>
<tr>
<td>People with cirrhosis</td>
<td>0.28 (0.12, 0.49)</td>
</tr>
<tr>
<td>PWID</td>
<td>1.27 (0.68, 2.04)</td>
</tr>
</tbody>
</table>

• Extra analyses (with similar methods) suggest that from the 1.5 million HCV treatment globally in 2018, **525,764 (95%Crl: 243,948-980,523)** chronic HCV infections would be averted over the next 20 years
Regional variation

• Less infections averted in high-income countries (HICs) than low- and middle-income countries (LMICs)

• Eastern Europe appears to have the least benefit of treatment as prevention, followed by Latin America

• Sub Saharan Africa and South Asia see the biggest benefit
Determinants of infections averted

• For both the random allocation (treat all) strategy and the PWID strategy, the infections averted is associated with:
  • Increases ↑ with a country’s population growth-rate
  • Increases ↑ with the proportion of adults that are PWID
  • Decreases ↓ with HCV prevalence in the general population
  • Decreases ↓ with HCV prevalence in PWID
Treat all strategy

PWID strategy

\[ R^2 = 0.3592 \]

\[ R^2 = 0.2534 \]

\[ R^2 = 0.2702 \]

\[ R^2 = 0.6582 \]
Sensitivity analyses

- Each strategy averts more infections if the gen-pop HCV prevalence is stable instead of decreasing: 0.55 (95%CrI: 0.36-0.77) (vs 0.35)
- More infections averted if we assume regional epidemic trajectories differ based on CDA analyses¹: 0.65 (95%CrI: 0.30-1.10) (vs 0.35)
- Halving background treatment rates among PWID and doubling among people with cirrhosis produces a similar number of infections averted compared with the baseline projections
- Including only the countries with ≥2 key prevalence parameters scored as moderate or better quality, the IA per treatment was similar

¹: Global prevalence and genotype distribution of hepatitis C virus infection in 2015: a modelling study. Blach et al, 2017
Limitations

• Taking data from disparate sources can create imprecise results but overall trends should be robust

• **Data!**
  • Data unavailable for many countries (particularly Africa)
  • Not necessarily high quality data

• Migration not included – lack of data

• Different coverage rates of treatment may have different effects

• Assumes random mixing rather than actual networks among PWID – previous research suggests random mixing may overestimate treatment as prevention and that post-treatment behavioural changes are important¹

• Assumptions about directions of epidemics:
  • Only 3 countries had 2 robust, comparable general population estimates
  • Investigated in sensitivity analyses

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¹: Impact of Hepatitis C Treatment as Prevention for People Who Inject Drugs is sensitive to contact network structure. Metzig et al, 2017
Implications

• Prevention benefits can be achieved from a random treat all strategy

• Globally, more prevention benefits are achieved through targeting PWID (high incidence groups)

• High incidence groups drive the impact of treatment as prevention
  • Countries should not exclude people with substance use from HCV treatment

• Treating only those with advanced disease has less impact in terms of treatment as prevention than a treat-all strategy (however, other factors also important)

• Regardless of strategy, higher impact is achieved in countries with high population growth, more PWID, and lower HCV prevalence

• WHO now advocates a treat-all strategy, partially based on the impact of treatment as prevention¹

¹: Guidelines for the care and treatment of persons diagnosed with chronic hepatitis C virus infection. WHO, 2018
Published in the Journal of Viral Hepatitis: “Modelling the potential prevention benefits of a treat-all hepatitis C treatment strategy at global, regional and country levels: A modelling study” by Trickey et al, 2019

Also published as an annex to the 2018 WHO guidelines for the care and treatment of persons diagnosed with chronic hepatitis C virus infection

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