Modelling the Impact of Interventions Targeting High-Risk Populations on the HCV Epidemic in Resource-Limited Settings

Pakistan as a Case Study

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Conflicts of Interest

- None.
HCV Epidemic in Pakistan
The Global HCV Epidemic is Concentrated

**Figure:** In terms of numbers, Pakistan has the world’s second-largest HCV burden.

Gower et al. J Hep (2014)
Global Hepatitis Report 2017
The Global HCV Epidemic is Concentrated

Estimated 71 million chronic HCV infections globally in 2015
- Pakistan: ~7.5 million infections
- >10% of global HCV burden

Figure: Updated global HCV estimates put Pakistan’s HCV epidemic into perspective.

Gower et al. J Hep (2014)
Global Hepatitis Report 2017
Characterising the HCV Epidemic in Pakistan

- Large, rapidly growing population
  - ~197 million in 2017 ➔ ~230–270 million by 2030
Characterising the HCV Epidemic in Pakistan

- Large, rapidly growing population
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- High chronic HCV prevalence which is increasing
  ✷ 3.6% overall (2007 National Survey data\(^1\))
  ✷ ~0.15-0.9% per decade (blood donor data)

\(^1\)Qureshi et al. EMHJ (2010)
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- High chronic HCV prevalence which is increasing
  - 3.6% overall (2007 National Survey data\(^1\))
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- Risk factors for transmission of HCV\(^1,2\)
  - **Injecting drug use:** ~430,000 in 2012, 62% Chronic Prev\(^3\)\(^-\)\(^4\)
  - Medical risk: e.g. blood transfusions, surgery, haemodialysis, medical injections
  - Community risk: e.g. barbering, ear/nose piercing, tattooing, acupuncture

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\(^1\)Qureshi et al. EMHJ (2010), \(^2\)Trickey et al., AJTMH (2017), \(^3\)UNODC Drug Use in Pakistan Report 2013, \(^4\)Nelson et al., Lancet (2011)
Characterising the HCV Epidemic in Pakistan

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  - Medical risk: e.g. blood transfusions, surgery, haemodialysis, medical injections
  - Community risk: e.g. barbering, ear/nose piercing, tattooing, acupuncture

- Historical treatment with non-DAAs from 2005-2015*
  - ~1-2% of chronic infections each year (public sector data)
  - Treatment level as of the end of 2015 was 150,000/yr

Determining The Way Forward

Objectives

① Project the likely trajectory of the HCV epidemic in Pakistan
Determining The Way Forward

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① Project the likely trajectory of the HCV epidemic in Pakistan

② Identify the impact of prevention and treatment interventions, especially those targeting high-risk persons, e.g. people who inject drugs (PWID)
Methods

- Stratified general population dynamic transmission model based on an Susceptible-Infected-Treatment (S-I-T) framework
  - Demographics (age, gender, population growth)
  - People who inject drugs (PWID)
  - Low and high medical + community risk
  - HCV transmission
  - Disease progression (pre-cirrhosis, cirrhosis, decompensation, HCC)
Methods

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- Calibrate the model to Pakistan-specific data

- Focus mainly on what has been happening since 2016
  - At baseline, assume no interventions from 2016
① Epidemic Projections
Figure: Model projections suggest ~3.9% chronic HCV prevalence in 2016 (7.5 million chronic prevalent infections), increasing to ~5.1% (12.6 million) by 2030.
**Figure:** Model projections suggest ~3.9% chronic HCV prevalence in 2016 (7.5 million chronic prevalent infections), increasing to ~5.1% (12.6 million) by 2030.
Figure: HCV incidence is also projected to increase: 700,000 new infections in 2016, up to 1.1 million new infections in 2030.
Figure: A disproportionate number of new infections will be attributable to PWID.
2 Impact of Interventions
Illustrative Intervention Scenarios

- Reducing HCV incidence is crucial to controlling the epidemic
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- Consider the following intervention scenarios from 2017:
  - No treatment & halve PWID-related HCV transmission
  - Treat 150,000 treatments/yr (‘Status Quo’) with DAAs
  - Treat 150,000 treatments/yr targeting 40% of PWID
  - Treat 300,000 patients/year with no targeting
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  - **Treat 300,000 patients/year targeting 40% of PWID and halving PWID transmission**
Without Intervention From 2016

- 1.1 million new infections in 2030

- Total HCV Incidence (per 1000 pyrs)

- Year: 2010, 2015, 2020, 2025, 2030

- Intervention Start 2017
No Treatment
Halve PWID Transmission Only

- Averts 860,000 new infections over 15 years
- Minimal reduction in incidence
- Treatment is needed to reduce prevalent infections

Intervention Start 2017

Total HCV Incidence (per 1000 pyrs)
‘Status Quo’: Treat 150,000/Yr With DAA

- Non-targeted and targeted treatment similar reductions in incidence
- Incidence rate is nearly stabilised
Non-Targeted Vs. Targeting PWID

- Targeting treatment to PWID has greater impact after treatment scale-up

Graph showing the impact of different treatment strategies on HCV incidence, with intervention start in 2017. The graph illustrates the reduction in incidence with targeted treatments compared to non-targeted treatments and the benefits of scaling up treatment.

Legend:
- Without Intervention From 2016
- No Treat & Halve PWID Trans.
- Treat 150,000/Yr Non-Targeted
- Treat 150,000/Yr Target PWID
- Treat 300,000/Yr Non-Targeted
- Treat 300,000/Yr Target PWID
- Treat 300,000/Yr Target PWID & Halve PWID Trans.
Combining treatment with prevention of HCV transmission is crucial to halting the epidemic.
TasP & Treatment Efficacy

- Treatment-as-Prevention (TasP):
  - Targeting treatment to those with high risk of transmission can lead to onward prevention benefits
  - Treatment coverage must be sufficiently high

- Treatment efficacy:
  - E.g. # of new infections averted per treatment over the time period
  - Larger is better
Number of Infections Averted Per 1000 Treatments

- Treat 150,000/Yr Non-Targeted
- Treat 150,000/Yr Target PWID
- Treat 300,000/Yr Non-Targeted
- Treat 300,000/Yr Target PWID
- Treat 300,000/Yr Target PWID & Halve PWID Transmission

By Year End:
- 2020
- 2025
- 2030
Re-Infection Risk is High if Treatment is Insufficient

Between 2016-2030:
- 560 IA/1000Trt
- 540 IA/1000Trt

By Year End

- Treat 150,000/Yr Non-Targeted
- Treat 150,000/Yr Target PWID
- Treat 300,000/Yr Non-Targeted
- Treat 300,000/Yr Target PWID
- Treat 300,000/Yr Target PWID & Halve PWID Transmission
Targeting + More Treatment Accumulates Prevention Benefit

Between 2016-2030:
- Treat 150,000/Yr Non-Targeted
- Treat 150,000/Yr Target PWID
- Treat 300,000/Yr Non-Targeted
- Treat 300,000/Yr Target PWID
- Treat 300,000/Yr Target PWID & Halve PWID Transmission

By Year End:
- 2020: 570 IA/1000Trt
- 2025: 610 IA/1000Trt
- 2030: 630 IA/1000Trt

# of Infections Averted Per 1000 Treatments
Combining Treatment Scale-Up & Risk Reduction

Between 2016-2030:
➢ 880 IA/1000Trt
Conclusions
Conclusions: Model Projections

① The burden of HCV infection in Pakistan is likely to increase markedly in the near future

✧ Current levels of intervention are not enough to reduce the general HCV epidemic in Pakistan, even with new DAA treatments
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② Combining prevention & treatment has the greatest impact

✧ Risk reduction can prevent onward transmission, but alone is not enough to reduce the epidemic – treatment is needed

✧ High-coverage, targeted treatment to high-risk populations, such as PWID, can avert a greater number of new infections per treatment
Conclusions: Model Projections

① The burden of HCV infection in Pakistan is likely to increase markedly in the near future
   ✅ Current levels of intervention are not enough to reduce the general HCV epidemic in Pakistan, even with new DAA treatments

② Combining prevention & treatment has the greatest impact
   ✅ Risk reduction can prevent onward transmission, but alone is not enough to reduce the epidemic – treatment is needed
   ✅ High-coverage, targeted treatment to high-risk populations, such as PWID, can avert a greater number of new infections per treatment
   ✅ Even in general population HCV epidemics, as in Pakistan, such targeted treatment & prevention scale-up can play an important role in curbing the overall HCV burden
Acknowledgements

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Thank you!
Additional Slides
Global HCV Epidemic & WHO Targets
What is HCV?

- Hepatitis C virus (HCV) is a blood-borne virus
  - Can cause acute and chronic hepatitis C affecting the liver
- Globally, estimated 71 million chronic (viraemic) infections in 2015
  - ~1% of world’s population
- Approx. 700,000 HCV-related deaths annually
  - Cirrhosis, decompensation, and hepatocellular carcinoma
- Epidemic is concentrated in few countries
  - Low-middle income countries (LMIC) account for 80% of chronic infections and mortality
- There is a cure – treatment achieves “sustained virologic response (SVR)”
  - Conventional IFN-based treatment (e.g. IFN+RBV), SVR ~50%
  - From 2014, direct-acting antivirals (DAAs), up to ~90-95% SVR
WHO Targets for HCV “Elimination” by 2030

**Figure:** Specific targets for HCV are an 80% reduction in HCV incidence and a 65% reduction in HCV-related deaths by 2030 (95% and 65%, respectively, for HBV).

WHO Global Health Sector Strategy on Viral Hepatitis (2016)
Global HCV Epidemic is Concentrated

**Figure 1:** Approx. 80% of total viraemic infections lie in a handful of countries.

Gower et al. J Hep (2014)
Figure: Demographic structure.
Mathematical Model Structure – M/C Risk

Figure: Medical & community risk structure.
Figure: Epidemic and disease progression structure.
# Cumulative Burden of HCV Infection from 2016 to 2030

## Morbidity

<table>
<thead>
<tr>
<th>Metric</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of New Infections</td>
<td>13.4 [11.9–15.0] million</td>
</tr>
<tr>
<td>No. of New Disease Cases†</td>
<td>5.4 [4.6–6.6] million</td>
</tr>
<tr>
<td>No. of New Cirrhotic</td>
<td>3.5 [3.2–3.9] million</td>
</tr>
<tr>
<td>No. of New Decompensated</td>
<td>1.3 [0.8–1.7] million</td>
</tr>
<tr>
<td>No. of New HCC</td>
<td>560,000 [88,000–1,500,000]</td>
</tr>
</tbody>
</table>

## Mortality

<table>
<thead>
<tr>
<th>Metric</th>
<th>Value</th>
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<tbody>
<tr>
<td>No. of Deaths Due to ESLD</td>
<td>1.4 [1.0–2.0] million</td>
</tr>
<tr>
<td>No. of Deaths Due to Decompensation</td>
<td>0.9 [0.5–1.2] million</td>
</tr>
<tr>
<td>% Of All Deaths</td>
<td>1.3% [0.7–1.8%]</td>
</tr>
<tr>
<td>% Of All Non-Childhood‡ Deaths</td>
<td>2.1% [1.2–3.0%]</td>
</tr>
<tr>
<td>No. of Deaths Due to HCC</td>
<td>510,000 [80,000–1,400,000]</td>
</tr>
<tr>
<td>% Of All Deaths</td>
<td>0.8% [0.1–2.0%]</td>
</tr>
<tr>
<td>% Of All Non-Childhood‡ Deaths</td>
<td>1.2% [0.2–3.4%]</td>
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</tbody>
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†(Advanced) Disease Cases = Total Cirrhosis + Decompensation + HCC.
‡Non-childhood is defined here as 20 years of age and above.
Interventions
Status Quo Treatment (2%,~150,000/yr), Switch to DAAs

1. Reduction of transmission risk (prevention)
   ✦ Reduce all PWID, high medical, and high community risk by 50%
   ✦ Reduce overall transmission risk by 30%
   ✦ Reduce overall transmission risk by 50%

2. Non-targeted treatment at a per capita rate with DAAs
   ✦ **Treat 2.0% of chronic infections per year (~150,000 trts/yr)**
   ✦ Treat 5.0% of chronic infections per year (~370,000 trts/yr)

3. Combination of the above
   ✦ Reduce overall risk by 50% & treat 5.0% per year (~370,000 trts/yr)
Impact on Chronic HCV Prevalence

- Without Intervention From 2016
- Reduce High Risk (PWID, Medical & Community) By 50%
- Reduce Overall Risk By 30%
- Reduce Overall Risk By 50%
- Treat 2.0% Annually With DAA (Status Quo)
- Treat 5.0% Annually With DAA
- Reduce Overall Risk By 50% & Treat 5.0% Annually With DAA

Chronic HCV Prevalence is Stabilised at 2015 Levels
Impact on HCV Incidence

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HCV Incidence is Stabilised at 2015 Levels

Total HCV Incidence (per 1000 pyrs)
Impact on New HCV Disease Cases

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- Reduce High Risk (PWID, Medical & Community) By 50%
- Reduce Overall Risk By 30%
- Reduce Overall Risk By 50%
- Treat 2.0% Annually With DAA
- Treat 5.0% Annually With DAA
- Reduce Overall Risk By 50% & Treat 5.0% Annually With DAA

Number of New Disease Cases Continues to Rise
Impact on HCV-Related Mortality

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- Reduce Overall Risk By 30%
- Reduce Overall Risk By 50%
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Number of HCV-Related Deaths Continues to Rise
Risk Reduction Versus Treatment

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   ✷ Reduce overall transmission risk by 30%
   ✷ **Reduce overall transmission risk by 50%**

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Disease-Related Deaths (100,000s)

Year

2000 2010 2020 2030

Treatment Impacts HCV-Related Mortality
Achieving WHO Targets
Estimated Treatment Numbers for WHO Targets by 2030*

*WHO targets: 80% reduction in HCV incidence and 65% reduction in HCV-related mortality by 2030

(A) Non-targeted treatment (no HCV risk reduction)
(B) Targeted treatment of cirrhosis (no HCV risk reduction)
(C) Targeted treatment of cirrhosis & PWID (no HCV risk reduction)
(D) Targeted treatment of cirrhosis & PWID + halve PWID risk
(E) Targeted treatment of cirrhosis & PWID + halve PWID and high risk
(F) Targeted treatment of cirrhosis & PWID + halve all risks