University of BRISTOL

Modelling interventions to achieve HCV elimination among PWID in Haiphong, Vietnam

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Background and aims

- Modelling suggests ~50% of HCV infections in Vietnam are among PWID[1]
- Evidence suggests scaling up HCV treatment can majorly decrease HCV transmission among PWID[2-5]
  - But most evidence from high income countries
- DRIVE-C tested a strategy to increase testing and treatment for PWID in Haiphong:
  - Used a Respondent driven sampling study (2019)
  - DRIVE-C modified DRIVE which used 4 RDS to increase HIV testing and treatment (2016-2019)
  - Also improved referral on to opioid substitution therapy (OST)

AIMS: Use infectious disease modelling to

1. Estimate impact of existing DRIVE and DRIVE-C interventions
2. What extra future interventions are needed to reach WHO HCV incidence elimination targets:
   - Annual DRIVE-C RDS, and/or
   - Implement HCV testing and treatment in OST centres & ART centres
3. Investigate cost-effectiveness of existing and future interventions

WHO HCV elimination targets – 80% decrease in incidence versus 2016 or incidence ~2 per 100 person-years

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1. Trickey.. Vickerman Lancet Gast 2019; 2. Martin Hep 2013; 3. Palmateer addiction 2021; 4. Iversen Jhep 2019; 5. Iversen addiction 2023

Model structure and assumptions

- Compartmental deterministic model of HCV transmission and progression among PWID and ex-PWID
- Model stratified by:
  - Low and high-risk injecting status
  - Age (16-39; 40+)
  - Currently or temporary ceased injecting and whether on opioid agonist therapy (OAT)
  - Incarceration status
  - HCV infection status and Liver disease
  - Cascade of care from testing to treatment through different initiatives

Assumptions:

- Slow-down in people initiating injecting drug use over time
- Older PWID have lower HCV incidence (0.53-times if 40+ compared to younger)[1].
- High-risk state used to mimic PWID with HIV having 6 times higher HCV incidence[1]:
  - Don't model HIV because very few new HIV infections among PWID in Haiphong
  - Additional mortality which reduces over time due to scale-up of ART
- Incarceration - Recently released have higher HCV incidence risk (1.62 times)[2]

1. Analyses of DRIVE and DRIVE-C data; 2. Stone Lancet ID 2018

Parameterisation and calibration

- Model parameterised using data from various sources,
  - particularly DRIVE and DRIVE-C RDS surveys and linked cohort data:
  - Assign uncertainty bounds to each parameter
- Use Bayesian methods to calibrate model to the following data[0]:
  - Increasing Age distribution among PWID
  - Increasing OAT coverage from 12 to 49% over 2016-2020
  - Stable Antibody prevalence ~70%
  - Stable RNA prevalence among antibody positive - 83%
  - % diagnosed in 2016 – 22%
  - % ever incarcerated ~55%
- Validate model projections against:
  - Increase in % PWID ever tested for HCV from 41 to 60% over 2017-2020[0]
  - Primary HCV incidence – 19 per 100 person years[1]
  - Reinfection HCV incidence – 4 per 100 person years[2]
  - Mortality rate among PWID – 2.5 per 100 person years[3]

0. Analyses of RDS data or otherwise 1. Moles Sci Rep. 2020, 2. Nagot Lancet Reg Health 2023, 3. Vinh J Clin EPID 2021

Existing intervention assumptions

- **Background antibody testing** - low rate from 2008 onwards - fitted to % PWID Ab diagnosed in 2016 from 1st RDS – 22%
- **OAT** Starts in 2008.
  - Reduces HCV incidence (50% lower) and mortality (33% lower)
  - Increases background antibody testing by 2.3 times
- **DRIVE** survey interventions – DRIVE-IN and RDS 1, 2 and 4 over 2014 to 2019 – HCV antibody testing for ~1400 people for RDS and 600 for DRIVE-IN
- **DRIVE-C** (Last quarter of 2018) – HCV antibody and RNA testing and treatment:
  - 979 people treated in all
- RDS surveys also increase **linkage to OAT** over 2016-2020

Future intervention assumptions

Assumptions

- Background antibody testing continues as before
- OST recruitment – as before with it being increased in each new RDS
- All scenarios assume reinfection rate is 60% of primary infection rate
  - Halfway between reinfection rate in Nagot et al (20%) and modelled primary infection rates[1]

Main intervention scenarios:

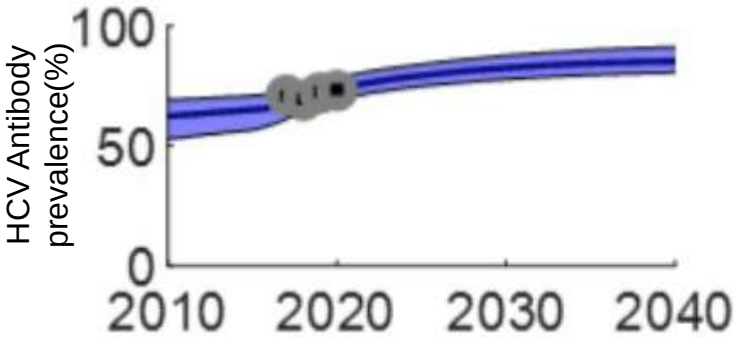
1. Status quo (SQ) – DRIVE and DRIVE-C BUT no future interventions from 2020
2. HCV testing and treatment at OST and ART centres from 2024
   - For both - 1250 people Ab and RNA tested, and a maximum of 250 treated, annually
3. Six Annual RDS interventions 2024-2029
   - 1000 people Ab and RNA tested each year and maximum of 800 treated in each RDS
4. Both testing at OST/ART centres and annual RDS interventions from 2024

Counterfactual:

- Counterfactual - No historical DRIVE-C survey intervention

1. Nagot Lancet Reg Health 2023,

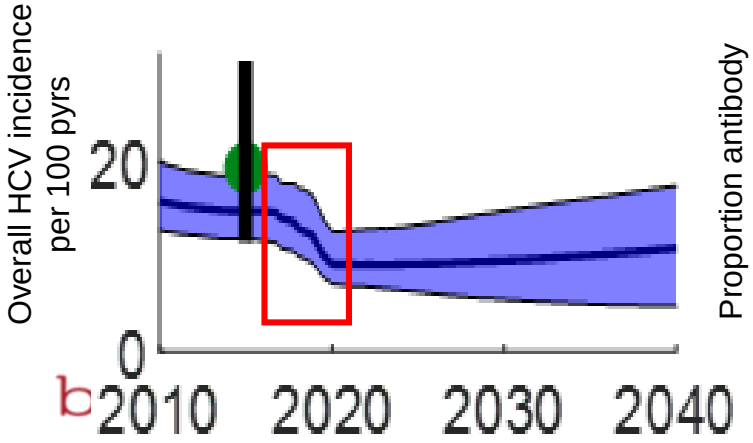
Model fitting and validation

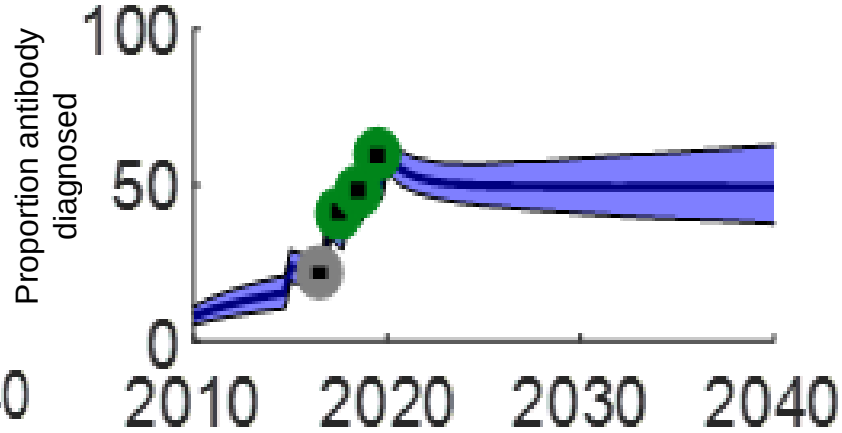


- Model fits to antibody and RNA prevalence
  - Slow increase in prevalence due to ageing cohort
- Model compares well to validation data:
  - increase in % diagnosed over time
  - Overall HCV incidence
- Suggests a high HCV prevalence and incidence epidemic
- DRIVE + DRIVE-C decreased incidence ~33%
  - Large role of OAT scale-up (12 to 49%); only one-sixth of HCV infections treated

Grey dots are calibration (model fitting)

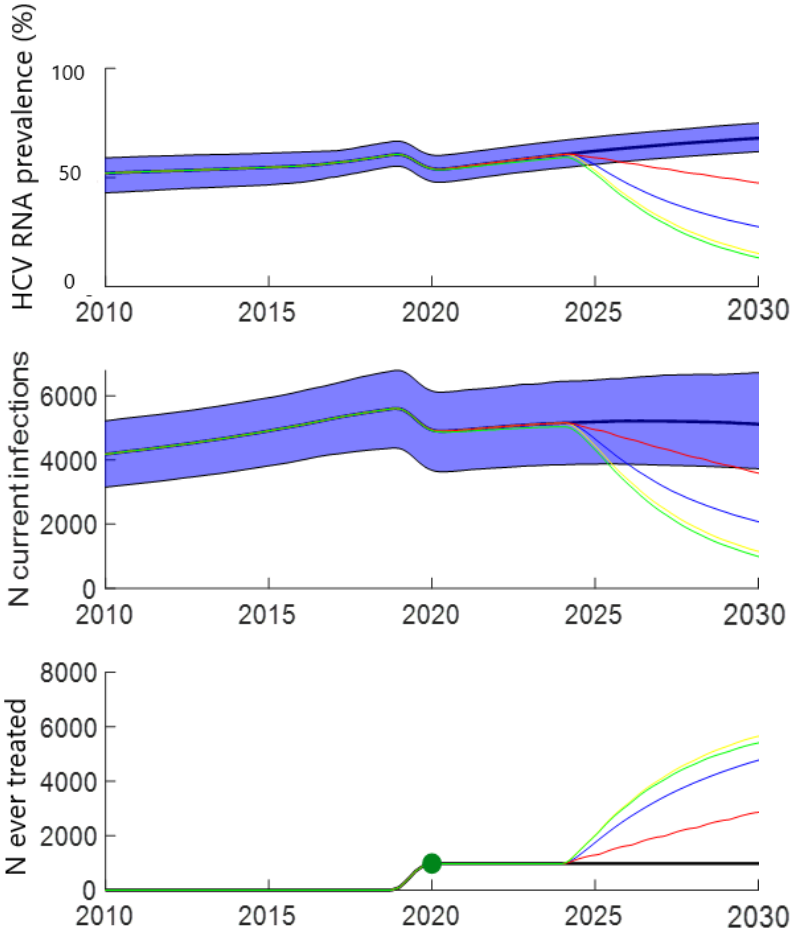
Green dots are for validation of results





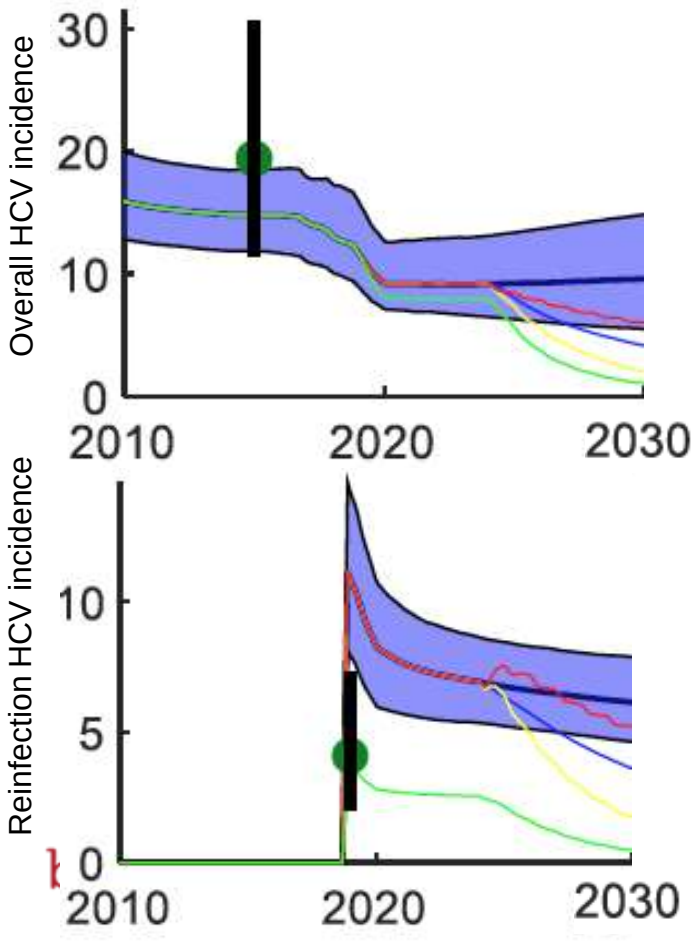
Impact on HCV RNA prevalence to 2030

Black – Status quo
Interventions from 2024:
Blue – OST and ART scale-up
Red – Annual RDS
Yellow – OST/ART+RDS
Green – OST/ART+RDS and reduced reinfection



- Status quo – RNA prevalence increases after 2020
- Scale-up testing in OST and ART
  - large increase in treatment
  - 60% reduction in RNA prevalence compared to SQ
- 6 annual RDS interventions:
  - Less impact because less testing and fewer diagnosed
- Scale-up testing in OST and ART + RDS
  - 80% reduction in RNA prevalence versus SQ
- Not much added benefit of reduced reinfection following treatment

Impact on HCV incidence (per 100 person years)



Black – Status quo
Interventions from 2024:
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Yellow – OST/ART+RDS
Green – OST/ART+RDS and reduced reinfection

- Status quo – impact on HCV incidence is maintained after treatment scale-up finishes in 2020
  - Impact of OST scale-up
- HCV testing and treatment of people in OST and ART –
  - 50% decrease in incidence compared to SQ
- 6 annual RDS interventions:
  - 30% decrease in incidence compared to SQ
- Scale-up testing in OST and ART + RDS
  - 75% decrease in incidence compared to SQ
  - 90% decrease if reduced reinfection
- Reinfection incidence also decreases over time

Do we reach the WHO targets?

Incidence in 2030 ~2 per 100 pyrs or 80% decrease compared to 2016

Scenario	Incidence in 2030	% Reduction vs 2016*
Status quo – no future interventions	9.6 (5.5-14.8)	35
Counterfactual: No historical DRIVE-C RDS intervention	10.9 (5.7-16.9)	26
HCV testing and treatment at OST and ART centres	4.2 (2.5-7.4)	72
Annual RDS surveys 2024-2029	6.1 (3.8-9.8)	59
HCV testing and treatment at OST and ART centres and annual RDS surveys 2024-2029	**2.1 (1.2-4.1)**	**86**
As above, but with lower reinfection rates	**1.1 (0.5-2.5)**	**93**

* Relative reduction in HCV incidence compared to HCV incidence in 2016 for SQ - 14.8 per 100 PY

- To reach targets – need annual RDS plus scale-up of testing and treatment in OST and ART clinics
- Reduced chance of reinfection has important contribution to reaching the target

Cost-effectiveness analysis methods

Two cost-effectiveness analyses:

1. **Cost-effectiveness of existing DRIVE-C Status Quo**
   - DRIVE-C with no HCV testing and treatment after 2020 – Status Quo
   - Compared to counterfactual of no DRIVE-C
   - 26-year time horizon 2014 to 2040
2. **Cost-effectiveness of future interventions from 2024 to 2030**
   - Various scenarios of interventions 2024-2030 compared to counterfactual of Status Quo
   - 26-year time horizon 2024 to 2050

- **Costs included** – undertaking RDS surveys; HCV antibody and RNA testing in RDS survey, OST and ART clinics; HCV treatment costs
- **Impact** in terms of disability-adjusted life-years (DALYs) from Global Burden of Disease study
- 3% discount rate for costs and DALYs
- Calculate Incremental Cost-Effectiveness Ratio (**ICER**) – Incremental Cost per DALY averted
- Compared to willingness–to-pay threshold of 50% GDP (Euro 4095) for Vietnam- Euro 2047.5

Cost-effectiveness projections

- DRIVE-C highly cost-effective compared to willingness to pay threshold
  - Euro 1268 per DALY averted compared to threshold of Euro 2047

Historic scenario versus no DRIVE-C	Incremental total costs (Euros)	DALYs averted	ICER per DALY averted (Euros)
Status Quo intervention versus no DRIVE-C	883,694	697	1268

- All future interventions also highly cost-effective
  - Less than Euro 800 per DALY averted compared to threshold of Euro 2047

Future Scenarios versus Status Quo scenario	Incremental total costs (Euros)	DALYs averted	ICER per DALY averted (Euros)
HCV testing and treatment at OST and ART centres	2,000,858	2906	689
Annual RDS surveys 2024-2029	1,384,133	1726	802
HCV testing and treatment at OST and ART centres and annual RDS surveys 2024-2029	2,836,833	4162	682
As above (#11), but with lower reinfection rates	2,647,116	4478	591

DALYS: Disability adjusted life years
Lower costs per DALY averted are preferable
Cost-effectiveness thresholds are debated. 50% of the GDP per capita is commonly used (50% in Vietnam for 2023 = 2047.50 euros) as an upper threshold.

CONCLUSIONS

- HCV elimination can be reached among PWID by 2030 in Hai Phong, but need:
  - 6 annual RDS surveys 2024-2029
  - Scale-up of testing and treatment in OST and ART clinics
  - Reducing reinfection after treatment will help reach target

- These additional future interventions are cost-effective, but needs:
  - To treat nearly 6000 PWID over 2024-2029
  - Cost of 2.8 million euros

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