# Reinfection following successful direct-acting antiviral therapy for hepatitis C virus infection among people with recent injecting drug use: the SHARP-C study

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# Background/rationale

- There is a significant burden of hepatitis C virus infection among people who inject drugs globally
- Treatment is safe and effective in people who inject drugs
- Reinfection following therapy has been one of the major concerns around scale up of HCV DAA treatment among people who inject drugs
- Despite recent data from the scale up of HCV treatment in various settings, there remain important questions about reinfection

# Aims

1. Assess the incidence of HCV reinfection

2. Investigate predictors of time to HCV reinfection

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# SHARP-C study design

- Prospective observational cohort study designed to investigate HCV reinfection after successful DAA treatment
- 14 sites, 3 countries
- Study recruitment conducted through a network of drug and alcohol clinics and hospital clinics
- Study conducted from 2018-2020

# Participants

- ≥18 years of age
- Recent injecting drug use (within the last 6 months)

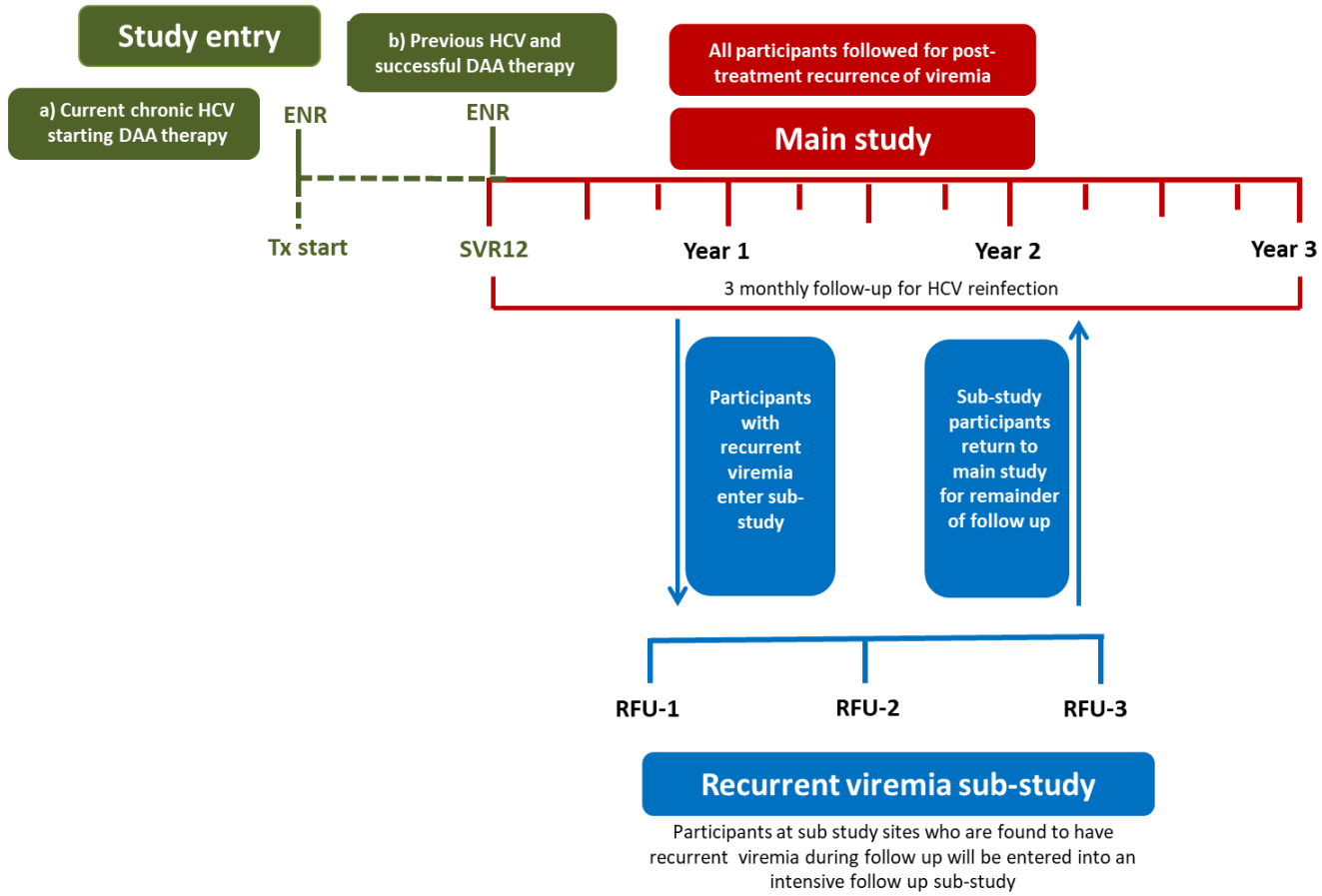
Two recruitment groups:

Participants enrolled before initiating HCV DAA treatment

Participants enrolled after completing HCV DAA treatment with documented SVR

# Participant follow-up

- Differed between those enrolled before or after DAA treatment
- Reinfection follow-up was the same for both groups:
  - 3 monthly for 10 visits (120 weeks)
  - Any viral recurrence was followed up more intensively
    - Weeks 2, 4, and 8 following recurrence



# Study procedures

- At baseline and at each visit participants:
  1. Completed a behavioural survey
  2. Received a POC HCV RNA test
  3. Provided a blood sample for laboratory testing

- Treatment conducted as per standard care for the treating clinic

# Reinfection

- Quantifiable HCV RNA distinct from the primary infecting strain following treatment.
  - Where possible, all recurrent cases were sequenced to distinguish relapse from reinfection
  - HCV RNA undetectable at SVR12 followed by a positive test during follow-up
  - The genotype at recurrence was distinct from the original infecting genotype
- Rate calculated using person-time (cases per 100 person-years)
- Factors associated with time to HCV reinfection assessed using unadjusted Cox proportional hazard models

# Participant characteristics

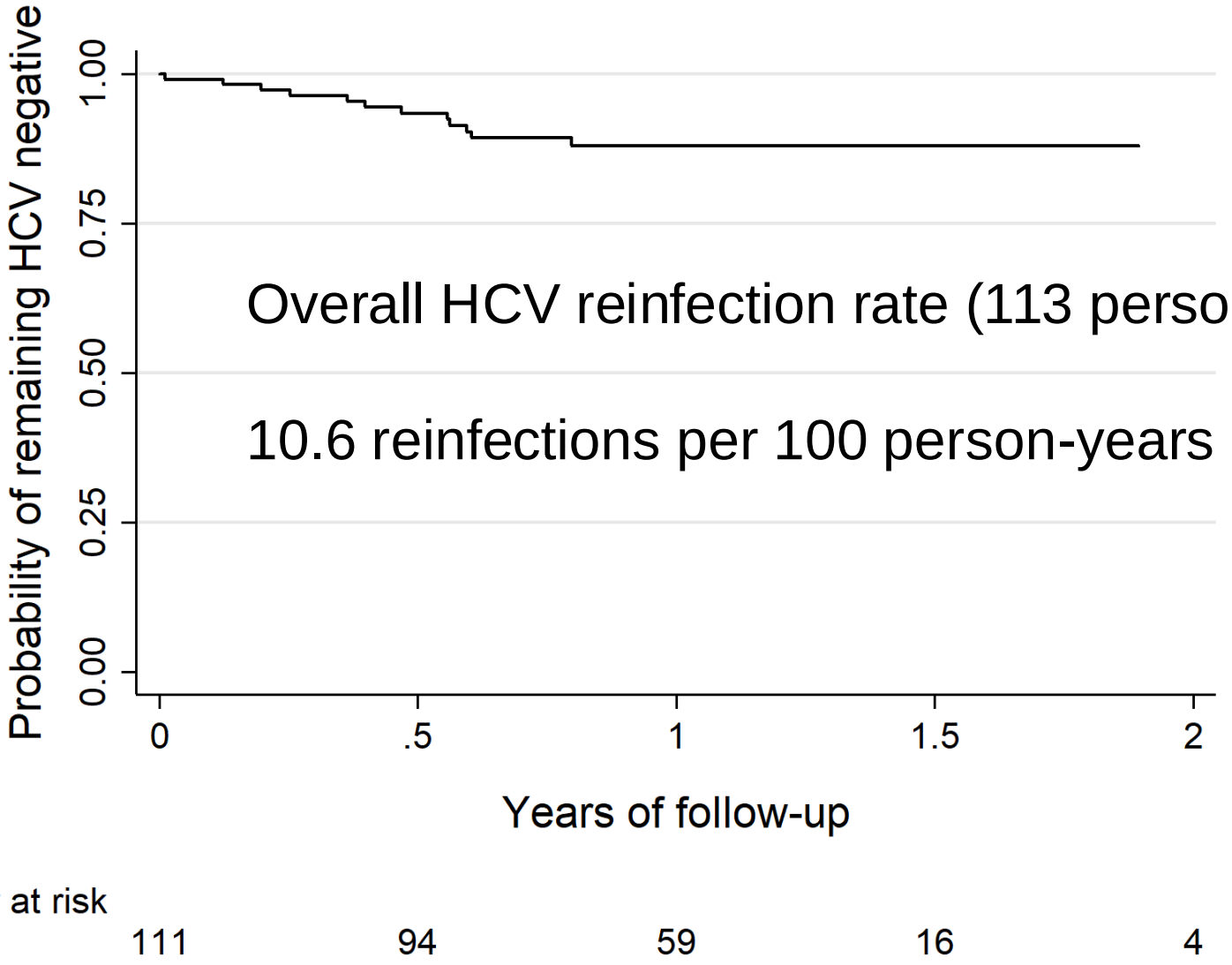
| Characteristics | At risk of reinfection (N=113) |
|---|---|
| **Age; median (IQR)** | 43 (37-49) |
| **Male** | 75 (66%) |
| **Aboriginal and/or Torres Strait Islander** | 40 (38%) |
| **High school completion or greater education** | 30 (29%) |
| **HIV** | 21 (19%) |
| **Cirrhosis** | 4 (4%) |
| **Currently on OAT** | 69 (61%) |
| **Injecting drug use** | |
| **Ever, not in the last 30 days** | 15 (14%) |
| **In the last 30 days** | 90 (86%) |
| **Drugs injected in the last 30 days** | |
| **Heroin** | 40 (38%) |
| **Cocaine** | 16 (15%) |
| **Amphetamine** | 54 (51%) |
| **Pharmaceutical opioids** | 16 (15%) |

# Reinfections

- Overall there were 19 cases of viral recurrence
  - 12 reinfections

| Recruitment group | Sex, Age | Country | Injecting drug use frequency | Injection equipment sharing frequency | Estimated Time to Reinfection, wk | Visit of Detection | Reinfection Outcome |
|---|---|---|---|---|---|---|---|
| Prior to commencing DAA therapy | Male, 44 | Canada | ≥ daily | More than 5 times | 0.6 | ETR | Resolved |
| Prior to commencing DAA therapy | Male, 35 | Canada | ≥ daily | None | 19 | SVR 24 | Unknown |
| Prior to commencing DAA therapy | Female, 32 | Canada | <daily | None | 6 | SVR 12 | Persistent |
| Prior to commencing DAA therapy | Male, 32 | Canada | <daily | None | 32 | FU1 | Unknown |
| Prior to commencing DAA therapy | Female, 43 | Canada | ≥ daily | None | 29 | FU1 | Unknown |
| Prior to commencing DAA therapy | Male, 50 | Australia | <daily | None | 29 | SVR24 | Unknown |
| Prior to commencing DAA therapy | Male, 37 | Australia | ≥ daily | None | 24 | SVR24 | Unknown |
| Prior to commencing DAA therapy | Male, 39 | Australia | ≥ daily | One time | 42 | FU3 | Resolved |
| Prior to commencing DAA therapy | Male, 49 | Australia | <daily | 3 to 5 times | 13 | SVR 24 | Unknown |
| Prior to commencing DAA therapy | Male, 46 | Australia | ≥ daily | None | 31 | FU1 | Unknown |
| Prior to commencing DAA therapy | Female, 36 | Australia | ≥ daily | One time | 21 | FU1 | Unknown |
| Prior to commencing DAA therapy | Female, 26 | Australia | <daily | None | 10 | SVR 24 | Persistent |

# Participant characteristics




Overall HCV reinfection rate (113 person-years of follow-up)

10.6 reinfections per 100 person-years (95% CI 6.0-18.7)

# Factors associated with reinfection

| Characteristic | HCV Reinfection (n = 12) | Follow-up Time, person-years | Reinfection Incidence/100 person-years (95% CI) | HR (95% CI) | p-value |
|---|---|---|---|---|---|
| **Age (stratified by median)** | | | | | |
| 18-42 | 7 | 50.2 | 13.9 (6.6-29.3) | | |
| ≥43 | 5 | 62.9 | 8.0 (3.3-19.1) | 0.62 (0.20-1.95) | 0.411 |
| **Sex** | | | | | |
| Male | 8 | 72.2 | 11.1 (5.5-22.2) | | |
| Female | 4 | 40.9 | 9.8 (3.7-26.1) | 0.98 (0.29-3.25) | 0.973 |
| **Country** | | | | | |
| Canada | 5 | 48.5 | 10.3 (4.3-24.8) | | |
| Australia | 7 | 59.9 | 11.7 (5.6-24.5) | 1.20 (0.38-3.77) | 0.761 |
| New Zealand | 0 | 4.7 | - | | |
| **Currently receiving OAT at baseline** | | | | | |
| No | 5 | 45.0 | 11.1 (4.6-26.7) | | |
| Yes | 7 | 68.1 | 10.3 (4.9-21.6) | 0.84 (0.27-2.64) | 0.762 |
| **Recent injecting drug use (during study)** | | | | | |
| No | 0 | 10.9 | - | | |
| Yes | 12 | 98.3 | 12.2 (6.9-21.5) | NA | NA |
| **Recruitment category** | | | | | |
| Enrolled after treatment | 0 | 44.6 | - | | |
| Enrolled before treatment | 12 | 68.5 | 17.5 (9.9-30.8) | NA | NA |

# Factors associated with reinfection

| Characteristic | HCV Reinfection (n = 12), n | Follow-up Time, person-years | Reinfection Incidence/100 Person-years (95% CI) | HR (95% CI) | P-value |
|---|---|---|---|---|---|
| **Injection frequency** | | | | | |
| Less than daily | 7 | 54.7 | 12.8 (6.1-26.8) | | |
| Daily or more | 5 | 39.3 | 12.7 (5.3-30.5) | 1.11 (0.35-3.49) | 0.861 |
| | | | | | |
| **Shared needles/syringe** | | | | | |
| Injecting, no sharing | 8 | 81.7 | 9.8 (4.9-19.6) | | |
| Injecting and sharing | 4 | 12.4 | 32.3 (12.1-86.2) | 3.12 (0.94-10.36) | 0.064 |

# Discussion

- A high rate of HCV reinfection was observed among this population of people with recent injecting drug use
- All reinfections occurred among those with ongoing injecting
- Reinfections generally occurred quickly after treatment
- High rates of reinfection were observed in people who reported sharing needles/syringes
- Need to quickly identify and treat people who become reinfected
- Focus on enhancing harm reduction

# Acknowledgements

- SHARP-C study participants

**St Vincent's Hospital**
Principal Investigator: Greg Dore
Co-Principal Investigator: Gail Matthews
Study Coordinator/Research Nurse: Alison Sevehon
Additional Support: Mark Danta

**East Sydney Doctors**
Principal Investigator: David Baker
Co-Principal Investigator: Marilyn McMurchie
Study Coordinator/Research Nurse: Brit Johnson

**Kirketon Road Centre**
Principal Investigator: Phillip Read
Co-Principal Investigator: John Kearley
Study Coordinator/Research Nurse: Rosie Gilliver

**Hunter Drug and Alcohol Clinical Service**
Principal Investigator: Adrian Dunlop
Study Coordinator/Research Nurse: Susan Hazelwood

**Blacktown Hospital**
Principal Investigator: Marianne Martinello
Co-Principal Investigator: Golo Ahlenstiel
Study Coordinator/Research Nurse: Susan Holdaway

**Royal Adelaide Hospital**
Principal Investigator: Emily Rowe
Study Coordinator/Research Nurse: Catherine Ferguson

**Hastings Macleay Liver Clinic**
Principal Investigator: Alex Wade
Co-Principal Investigator: Sally Spruce
Study Coordinator/Research Nurse: Anita Hoskins
Additional Support: Jana Van der Jagt

**Vancouver Infectious Diseases Clinic**
Principal Investigator: Brian Conway
Co-Principal Investigator: David Truong
Study Coordinator/Research Nurse: Dorothee Rhee

**Cool Aid Community Health Clinic**
Principal Investigator: Chris Fraser
Study Coordinator/Research Nurse: Marian Selfridge

**Sherbourne Health Centre**
Principal Investigator: Jeff Powis
Study Coordinator/Research Nurse: Kate Mason

**Regina ID Clinic**
Principal Investigator: Alexander Wong
Co-Principal Investigator: Stephen Lee
Study Coordinator/Research Nurse: Sarah Craddock

**Calder Centre**
Principal Investigator: Richard Davies
Study Coordinator/Research Nurse: Victoria Oliver

**East St Needle Exchange**
Principal Investigator: Ed Gane
Study Coordinator/Research Nurse: Victoria Oliver

# Thank you

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