Will HCV reinfection among PWID impede progress towards elimination

Oluwaseun Falade-Nwulia MBBS, MPH
Associate Professor
Division of Infectious Diseases
Johns Hopkins University School of Medicine

JOHNS HOPKINS
MEDICINE
SCHOOL OF MEDICINE

Disclosures

- Research grants paid to institution: Abbvie
- Advisory fees: Gilead

Background

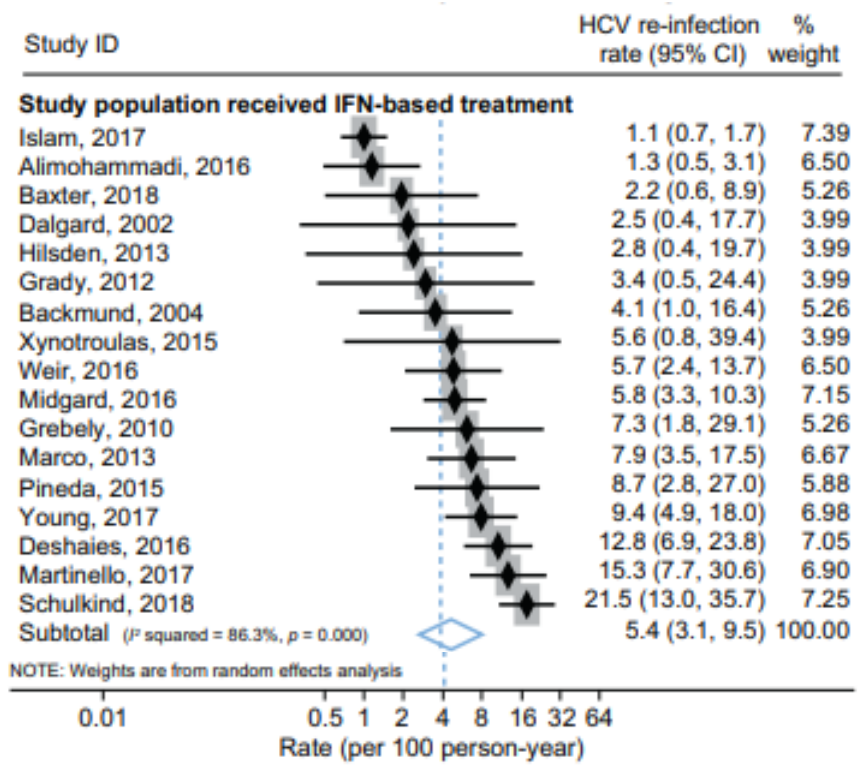
- Oral DAAs cure >95% of those treated
  - WHO call for HCV elimination by 2030
- Treatment does not confer protective immunity
  - Reinfection possible after spontaneous or treatment induced clearance
- Highest risk groups for reinfection
  - People who inject drugs (PWID)
  - HIV infected men who have sex with men

The what and why of reinfection

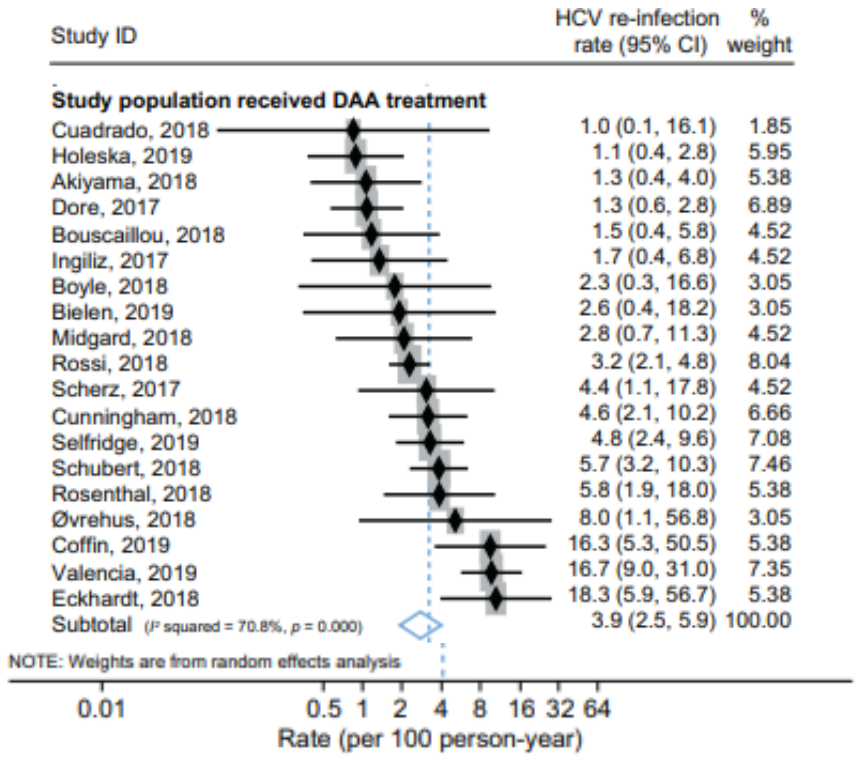
- What: Reinfection is the reoccurrence of HCV viremia after a previously cleared infection
- Why does reinfection matter
  - Patient level: Concern for reinfection is a major driver of provider and system level barriers to HCV treatment of PWID
  - Population level: Elimination dependent on reducing pool of individuals able to sustain epidemic through treatment and cure

HCV reinfection rate low overall among PWID

HCV reinfection rate in the IFN-era



HCV reinfection rate in the oral DAA-era



Overall HCV reinfection rate 4.6 (95% CI 3.2-6.5) /100 PYs

JOHNS HOPKINS MEDICINE SCHOOL OF MEDICINE

Hajarizadeh J. Hepatol 2020

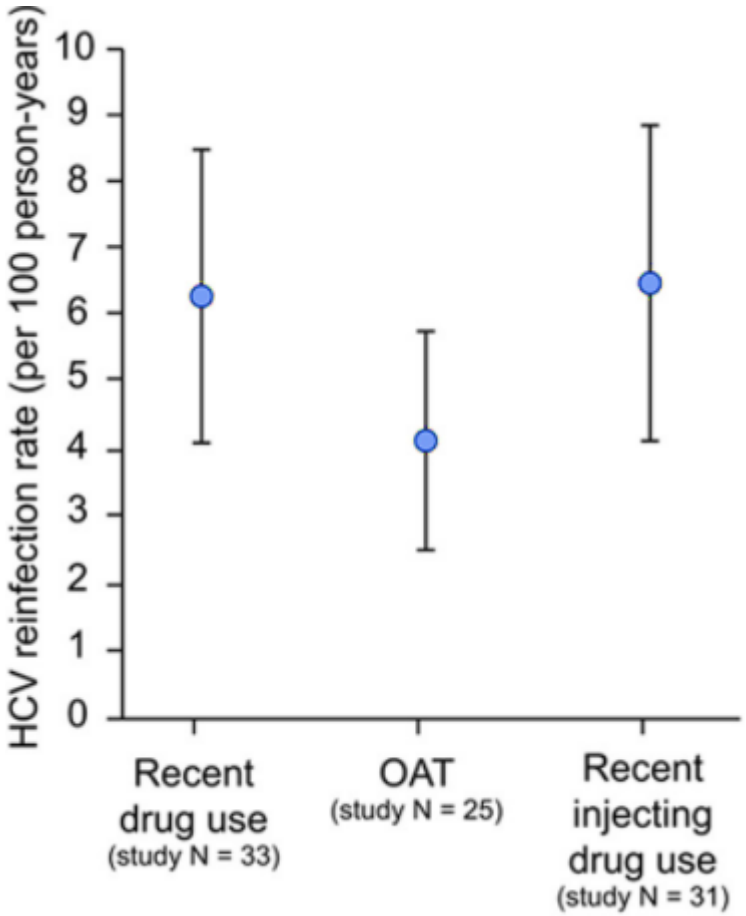
Factors associated with HCV reinfection

- Recent drug use
- Younger age
  - 6% decrease in reinfection risk for each additional year of mean/median age
- Shorter follow-up
  - 23% decrease in reinfection risk for each additional year of mean/median post treatment follow-up

JOHNS HOPKINS MEDICINE SCHOOL OF MEDICINE

Hajarizadeh J. Hepatol 2020

Differential HCV reinfection rate by OAT and drug use status



JOHNS HOPKINS MEDICINE SCHOOL OF MEDICINE

Hajarizadeh J. Hepatol 2020

Low HCV reinfection in PWID engaged in harm reduction

	Falcato 2021	Midgard 2021	Akiyama 2020
Study location/design	Low threshold SUD treatment services Zurich observational	Low threshold SUD clinic/Norway Observational	PWID on OAT in New York, USA Clinical trial
Sample Size	153 346 PY Median fu 2.1 y	297 308.2 PY Median fu 0.5 Y	114 246PY Median fu 1.6Y
Reinfection rate	1.2/100 PY Ongoing drug use 1.6/100 PY	2.6/100PY IDU: 3.74/100 PY	1.2/100 PY Ongoing IDU 7.4/100 PY

JOH
SCHOOL OF MEDICINE

Falcato IJDP 2021, Midgard IJDP 2021, Akiyama CID 2021

HCV reinfection in high risk PWID

	Cunningham 2021	Bhandari 2020	Valencia 2019
Study location/design	Clinical trials of recent PWID or receiving OAT 8 countries	North East England Prisons	Mobile harm reduction units in Australia
Sample Size	177 254 PY Median fu: 1.8 y	111 52 PY Median fu: 1Y	121 101 PY Median fu: 0.6 Y
Reinfection rate	Shared needles/syringes 17.9/100Py	40.6/100 PY	9.8/100 PY IDU in prior 30days 18.9/100PY

JOHNS HOPKINS
MEDICINE
SCHOOL OF MEDICINE

Cunningham CID 2021, Bhandari JVH 2020, Valencia IJDP 2019

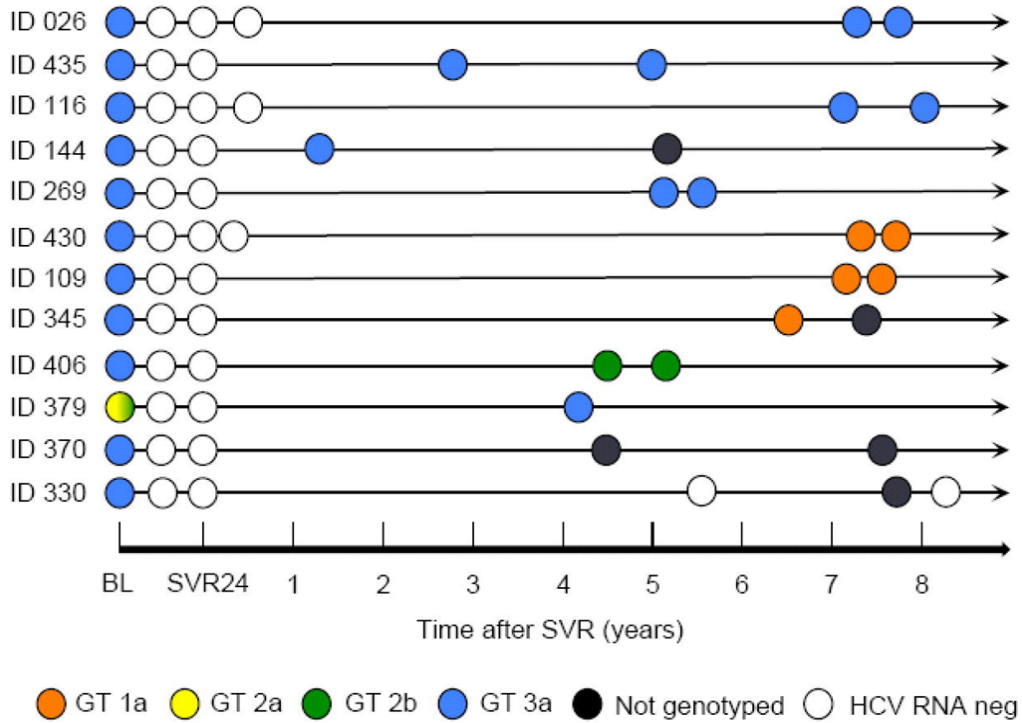
High rates of HCV reinfection in high risk PWID

- 94 PWID enrolled from NSP, Dundee, UK
- Peg/IFN + RBV +/- Simepravir/Telaprevir

Characteristic	n (%)
Age, mean (range)	34 (21-49)y
Male	67 (71)
Homeless	20 (21)
Current Opiate use	93 (99)
Inject daily or more	51 (54)
Harm reduction	
100% needle and syringe	75 (82)
OST	55 (63)

- Reinfection rate of 21.5/100PYs

7 year follow up of HCV cured PWID

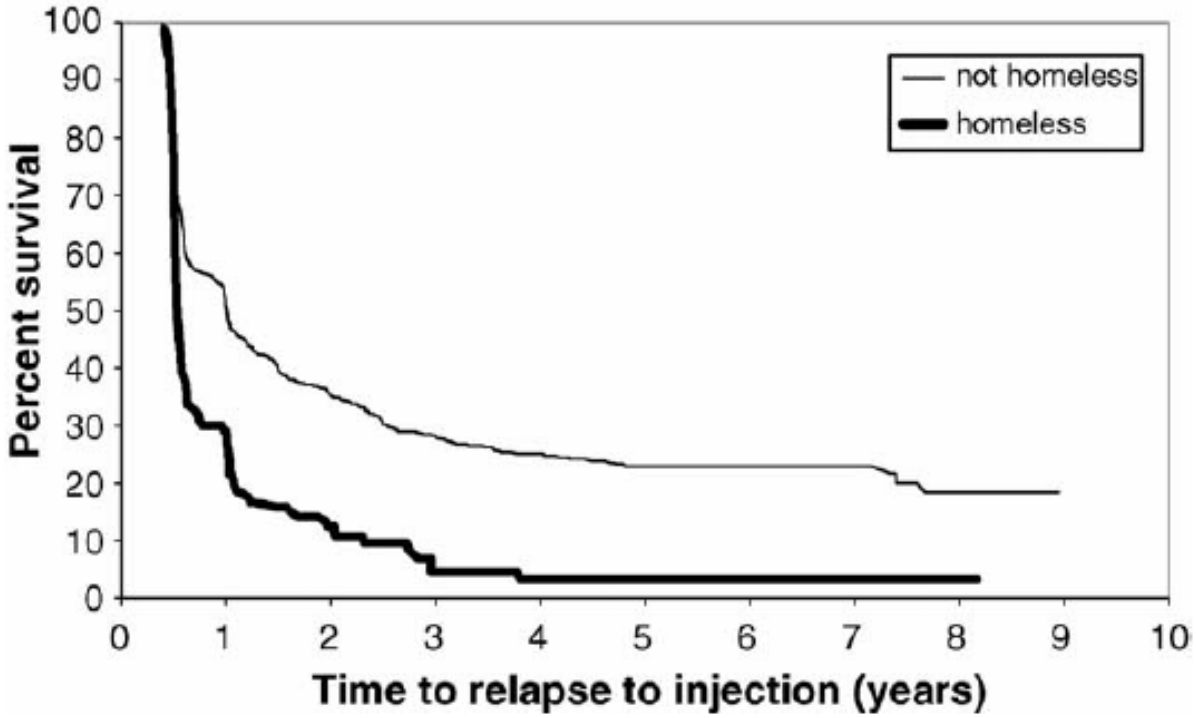


- 39% relapsed into IDU within 7 years
- Reinfection in 10 of 37 (27%) who relapsed vs 10 of 94 (11%) who did not
- Only predictor of reinfection was relapse

JOHNS HOPKINS MEDICINE SCHOOL OF MEDICINE

Schulkind et al JVH 2018, Midgard et al. J Hepatol 2016

Predictors of relapse into injection drug use



- Age <30 years
  - OR 7 compared to age >40
- Low education
  - OR 3.6 compared to higher education

JOHNS HOPKINS MEDICINE SCHOOL OF MEDICINE

Shah et al. Drug & alcohol dependence 2006, Midgard et al J. Hepatol 2006

Factors Associated with reinfection

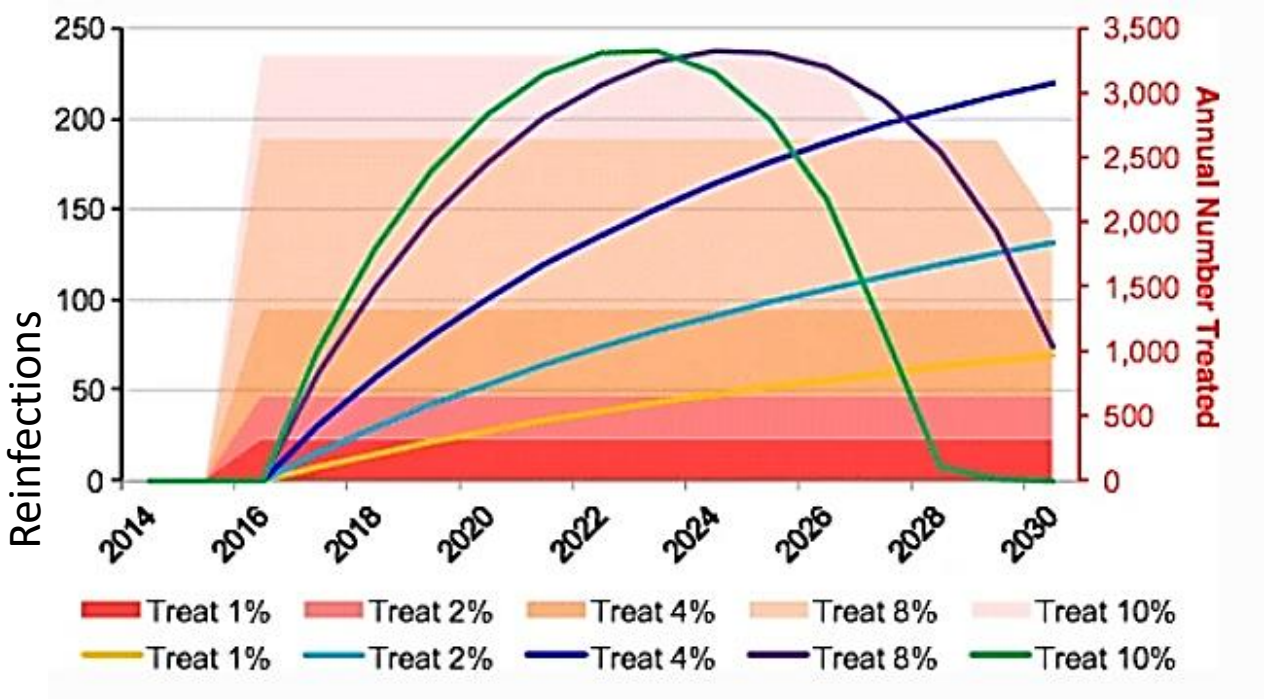
- Ongoing drug use[1, 2, 3]
- Younger age[1, 2, 5]
- Needle and syringe sharing[3]
- Mixed heroin/amphetamine injecting [2, 3]
- Low confidence in ability to avoid reinfection[2]
- Homeless[2,4]
- Low education, unemployment [5]
- Living with a PWID[6]
  - Transmission linkages within drug treatment center and in spousal and common-law relationship [5]

JOHNS HOPKINS
MEDICINE
SCHOOL OF MEDICINE

1. Hajarizadeh 2 Akiyama et al CID 2020 3 Midgard IJDP 2021, 4 Cunningham et al CID 2021 5. Midgard et al IJDP 2021 6 Akiyama JID 2020

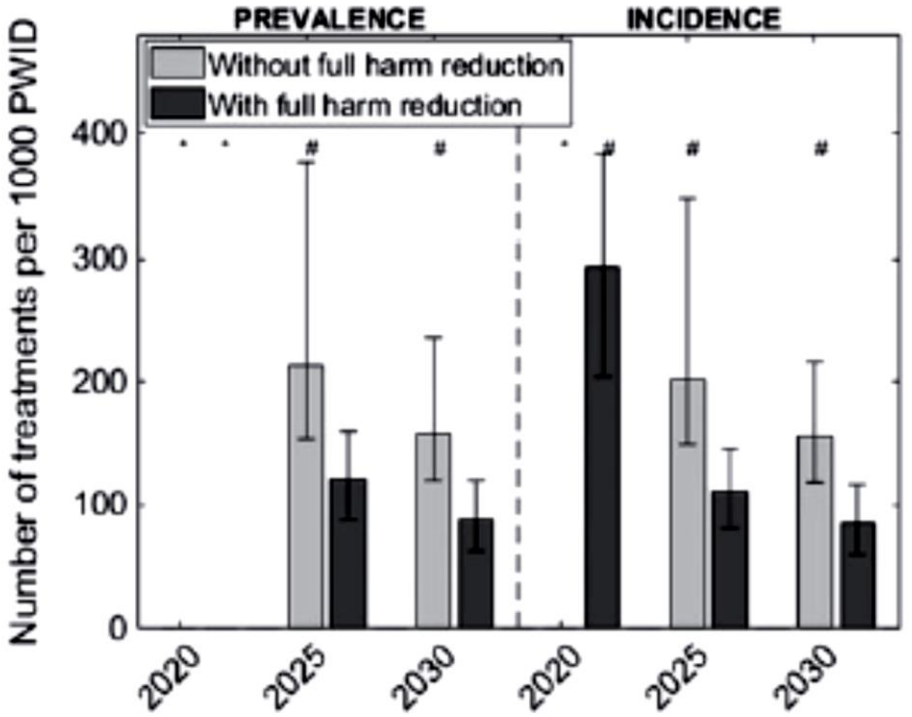
Modeling treatment as prevention and impact of reinfection in PWID

PWID in Australia



Rate of HCV reinfection following HCV treatment scale up assuming varying rates of HCV treatment

HCV Epidemic scenario in rural US



Required intervention to achieve 90% reduction in incidence

JOHNS HOPKINS MEDICINE SCHOOL OF MEDICINE

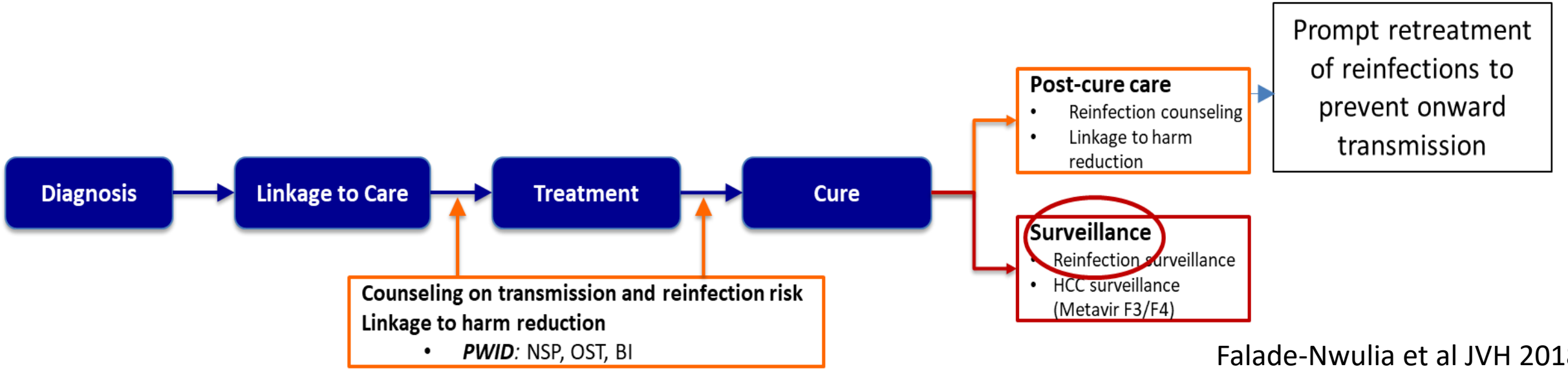
Martinello et al 2017 Cur HIV/AIDs report, Razavi INHSU 2015, Fraser et al Addiction 2018

PWID perception and concerns

- Participants in The Surveillance and Treatment of Prisoners living with hepatitis C (SToP-C) study
- “we'll do the treatment, but there's no use really doing the treatment, because we're just going to continue to shoot up” and you know there's no rehabilitation in this jail …. And you want help to get off whatever you're doing, but they won't put you on methadone or they won't put you on bupe or nothing like that. So if I myself was put on methadone or bupe, I wouldn't shoot up anymore, so that would save me from reinfecting myself every time, but they won't help..” [Mickey, Maximum Security, Current IDU, not prescribed OAT, HCV reinfection]

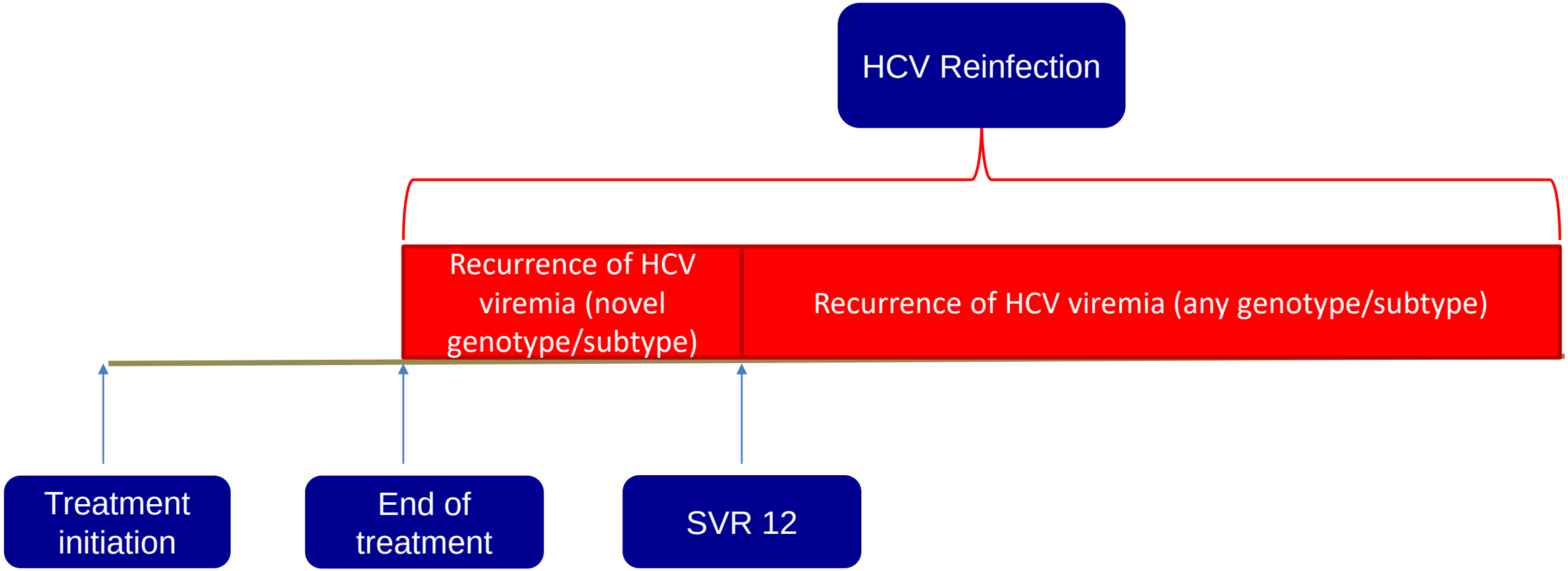
Addressing the challenge

- Reinfection should be viewed as a sign of HCV treatment engagement with PWID populations without which we cannot eliminate HCV
- In the absence of an effective HCV vaccine, the HCV care continuum does not end with cure
- Efforts to prevent, detect and promptly retreat reinfection a priority



Falade-Nwulia et al JVH 2018

Surveillance is key to early detection, retreatment & enhanced behavioral intervention



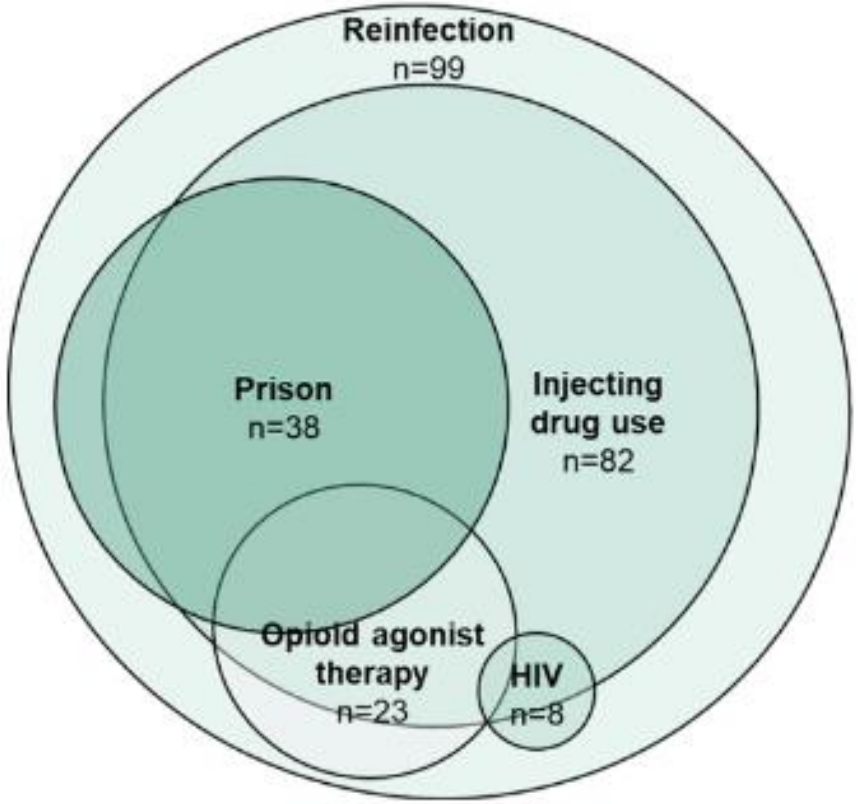
A proposed clinical definition for HCV reinfection when the gold standard of phylogenetic analysis of pre- and post-treatment HCV sequences are not available

JOHNS HOPKINS MEDICINE SCHOOL OF MEDICINE

Falade-Nwulia et al JVH 2018

Surveillance and retreatment is feasible and effective

HCV reinfection in REACH-C across
33 health services in Australia



- Observational cohort
- 10,843 (14%) of Australian population DAA treated March 2016-2019
- 99 reinfections (83% IDU)
- 88 treated for reinfection
  - primary care (42%)
  - prison (41%)
  - tertiary care (17%)
  - Median time to retreatment 1 year
- SVR 12 was 95% among 53 individuals with known treatment outcome

JOHNS HOPKINS
MEDICINE
SCHOOL OF MEDICINE

Carson et al IJDP 2020,

Feasibility of surveillance and retreatment

- Treatment as Prevention for Hepatitis C in Iceland
- Patients cured 2016 - 2018
- 617 treatments of 597 people
- 42 reinfections (reinfection rate 8.9/100PYs
- Homeless, age 20-24: reinfection rate 24/100 PYs
- Most successfully retreated

- PWID accessing low threshold SUD clinic in Oslo, Norway
- 363 people treated (90% SVR)
- 8 reinfections (reinfection rate 2.6/100PYs overall)
- Mixed heroin and amphetamine injection: reinfection rate 9.6/100PY
- All individuals with HCV recurrence were retreated as treatment naïve individuals and achieved cure.

JOHNS HOPKINS MEDICINE SCHOOL OF MEDICINE

Johannesson ILC 2020, Midgard et al IJDP 2021

Comprehensive holistic models are needed

- Combination interventions
  - Easy access to Opioid agonist therapy
  - High coverage NSP
- Integrated care
  - Mental health
  - Case management for linkage to housing, job programs etc
  - Peer based programs to support abstinence and safer injection
- Behavioral interventions for safer injection
- Education-Counseling and peer support
- Robust systems for routine post treatment surveillance (HCV RNA) and retreatment
- Unrestricted access to retreatment

Contextual

- Network based treatment e.g TAP trial, couples based treatment
- Destigmatization
- Effective HCV vaccine

JOHNS HOPKINS
MEDICINE
SCHOOL OF MEDICINE

Falade-Nwulia et al JVH 2018

Summary

- HCV treatment of PWID is critical to HCV control at the population level
- HCV reinfection is a challenge to HCV elimination that can be addressed
- Will require acceptance of reinfection as a marker of treatment of high risk populations
- The HCV care continuum needs to be extended beyond cure; counsel on, monitor for and promptly treat reinfection.
- Need for development and evaluation of strategies to optimize HCV treatment uptake, integrate harm-reduction strategies and other wrap around services for optimal health of PWUD