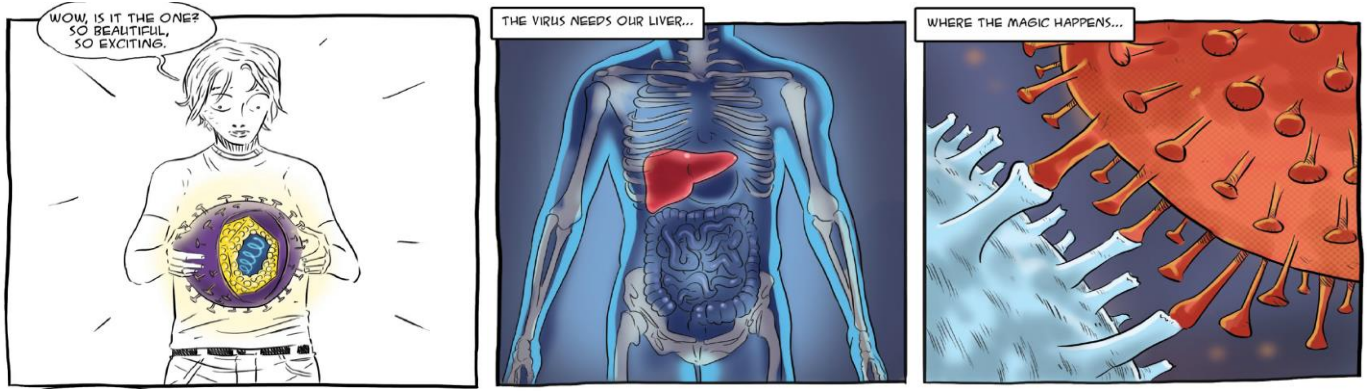
Hepatitis C reinfection among people who inject drugs: Should we worry?



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Disclosures

- Consultant/advisor and lecture fees from Abbvie, Gilead and MSD
- The low-threshold HCV clinic uses a mobile FibroScan donated from Abbvie

Starting point

- Scaled-up DAA treatment among people who inject drugs (PWID) is crucial to achieve the WHO viral hepatitis elimination goals[1]
- DAA treatment is effective across various PWID populations[2]
- Reinfection after successful treatment does occur and may compromise individual- and population-level benefits of cure[3]
- Strategies to address, prevent and manage reinfection are needed[4]

1 WHO GHS Strategy 2016; 2 Hajarizadeh et al. Lancet Gastroenterol Hepatol 2018; 3 Midgard et al. J Hepatology 2016; 4 Martinello et al. Infect Dis Clin North Am. 2018

Outline

- How often does reinfection occur?
  - Incidence rates, the effect of OAT, post-IFN vs. post-DAA
- Strategies to address, prevent and manage reinfection
  - Population- and individual level
- The extended HCV care continuum for individuals at risk
  - Post-SVR care in clinical practice

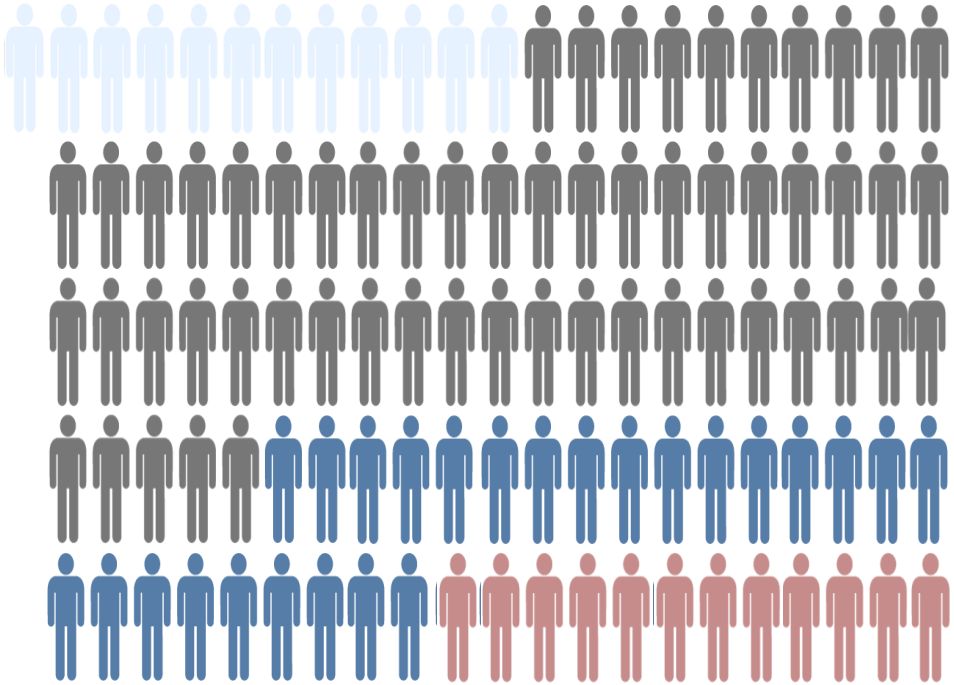
Proportion remaining HCV RNA neg 5 years after SVR:

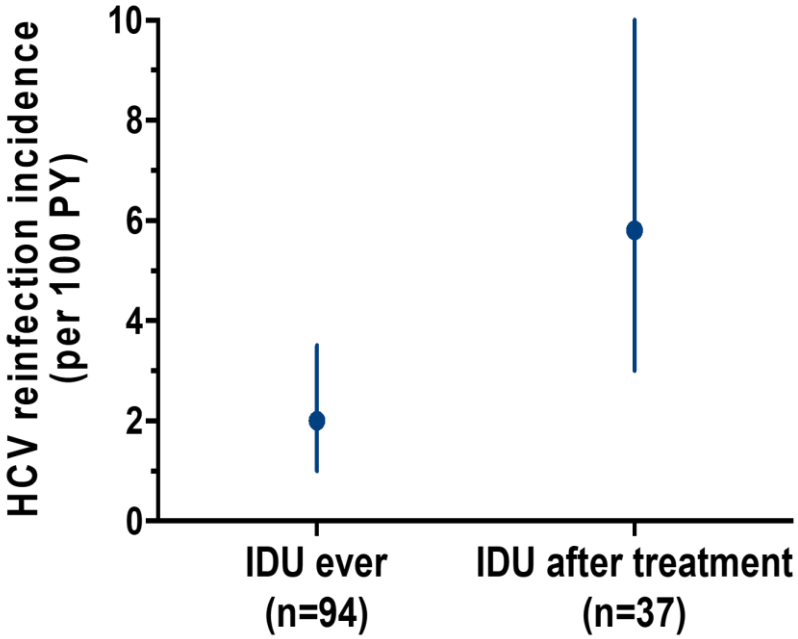
Worst case scenario - if no efforts are made

SVR	2%	4%	6%	8%	10%
95%	86%	77%	70%	63%	56%
90%	81%	73%	66%	59%	53%
85%	77%	69%	62%	56%	50%
80%	72%	65%	59%	53%	47%
75%	68%	61%	55%	49%	44%

Annual reinfection rate

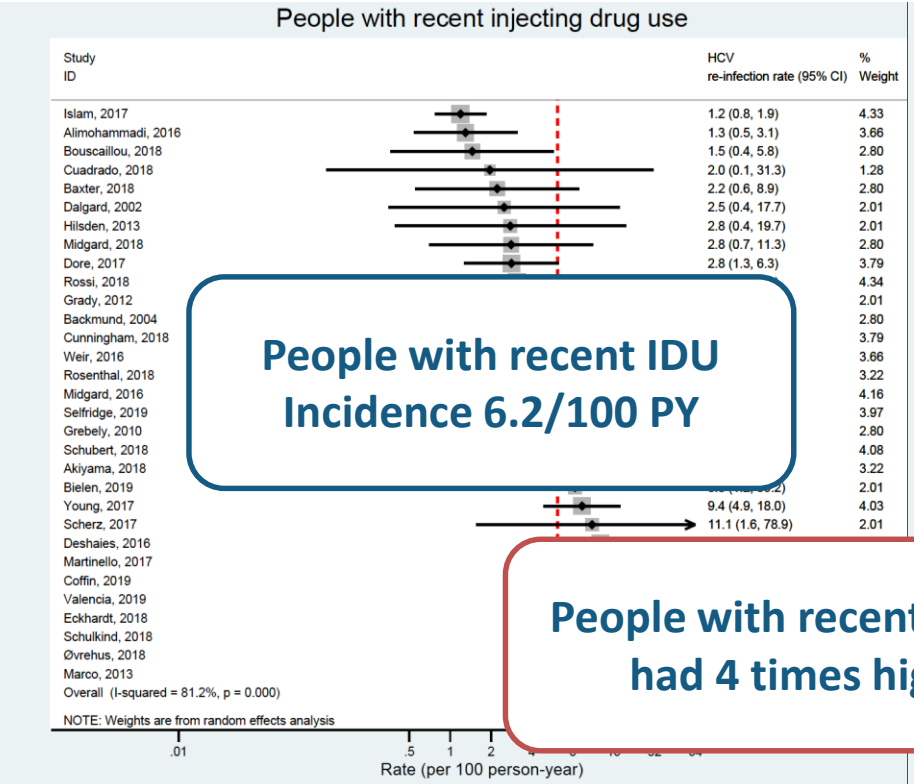
A historical look back: 7-year follow-up of PWID who achieved SVR in Norway 2004-06 (n=106)



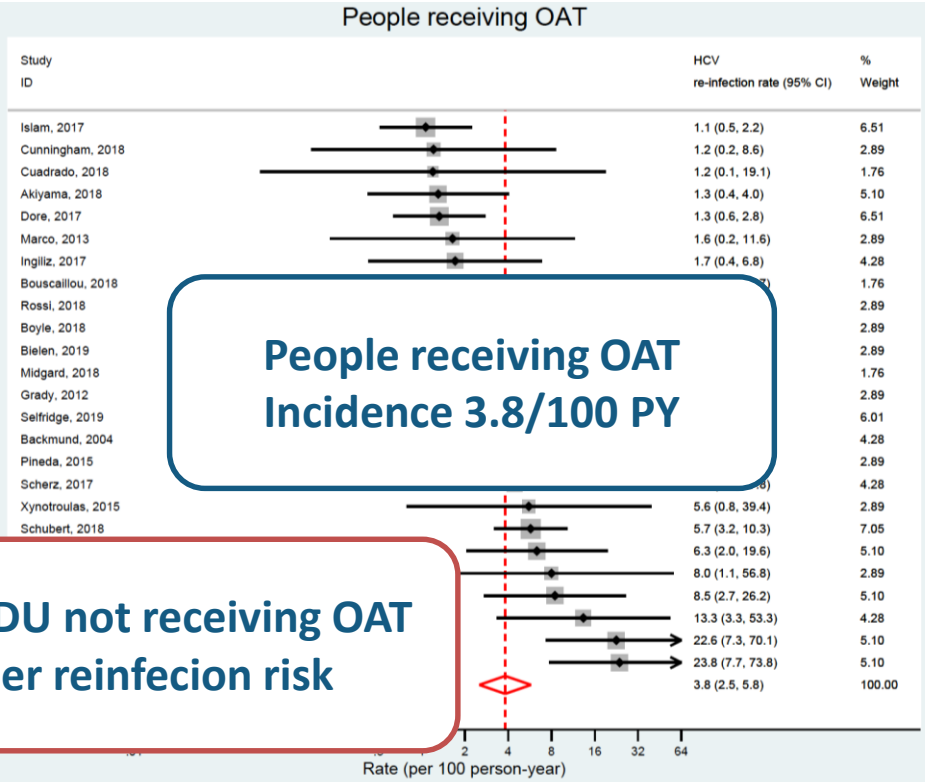


Midgard et al. J Hepatology 2016

Reinfection incidence: Recent IDU vs. OAT



People with recent IDU
Incidence 6.2/100 PY

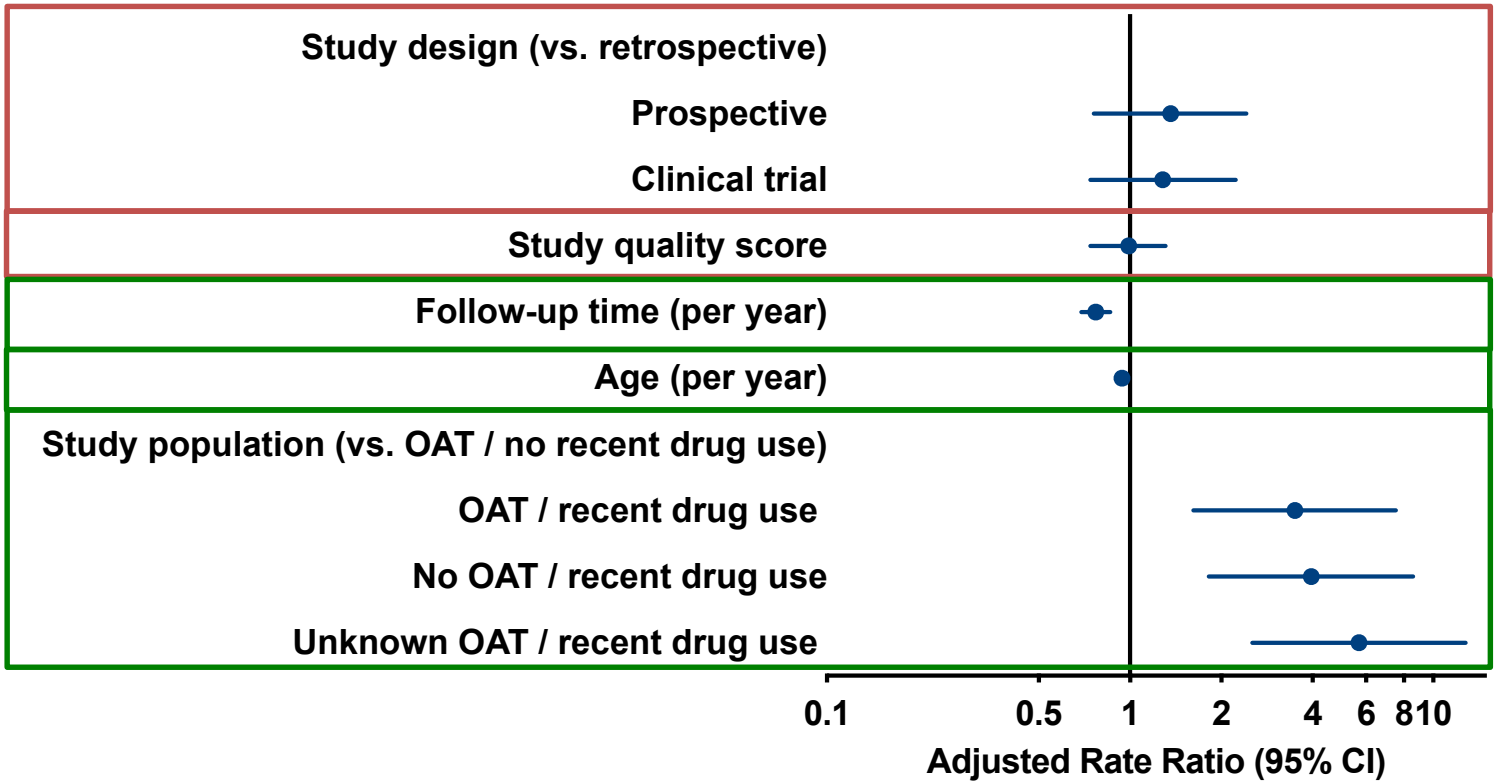


People receiving OAT
Incidence 3.8/100 PY

People with recent IDU not receiving OAT had 4 times higher reinfecion risk

Hajarizadeh et al. INHSU 2019

Study-level factors associated with reinfection:
Meta-regression analysis of 61 studies

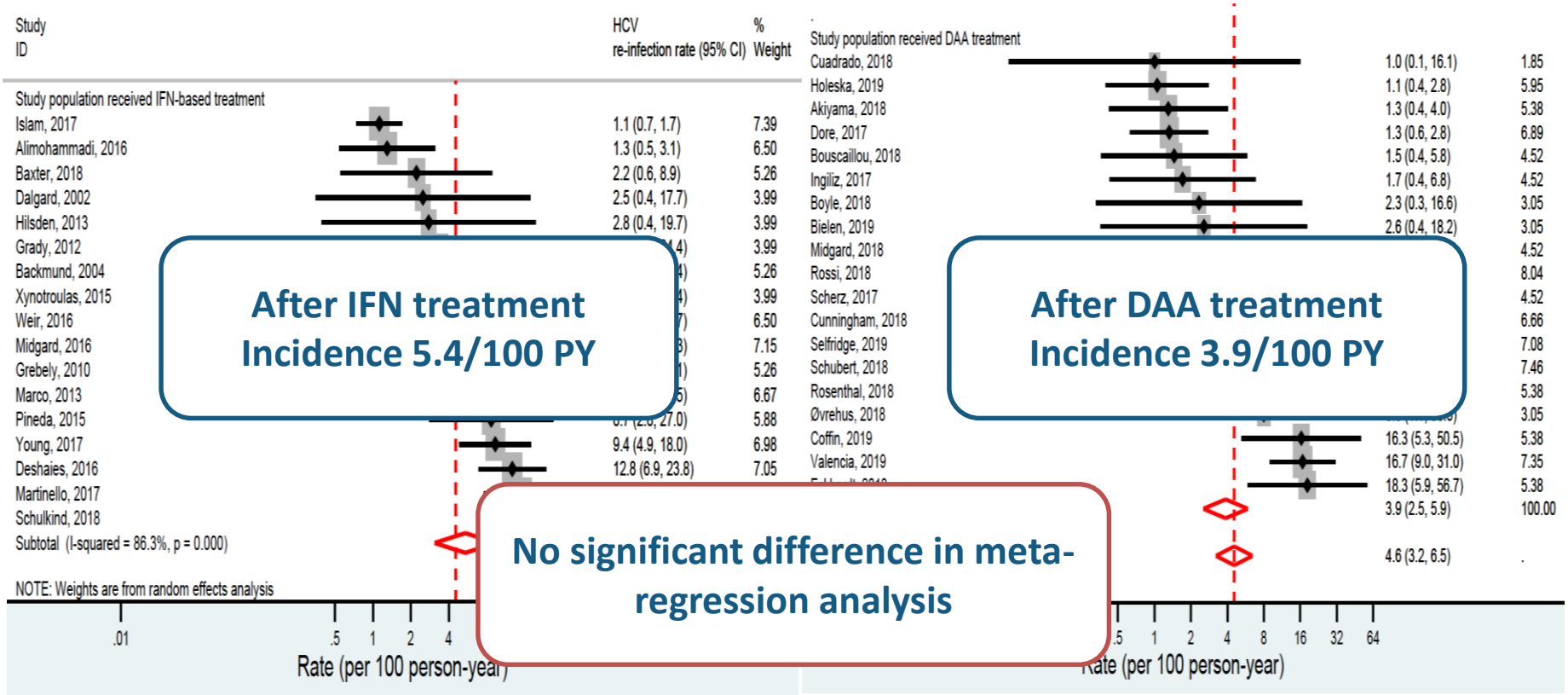


Modified from Hajarizadeh et al. INHSU 2019

Reinfection after DAA treatment: Concerns of increasing risk behaviours and reinfection rates?

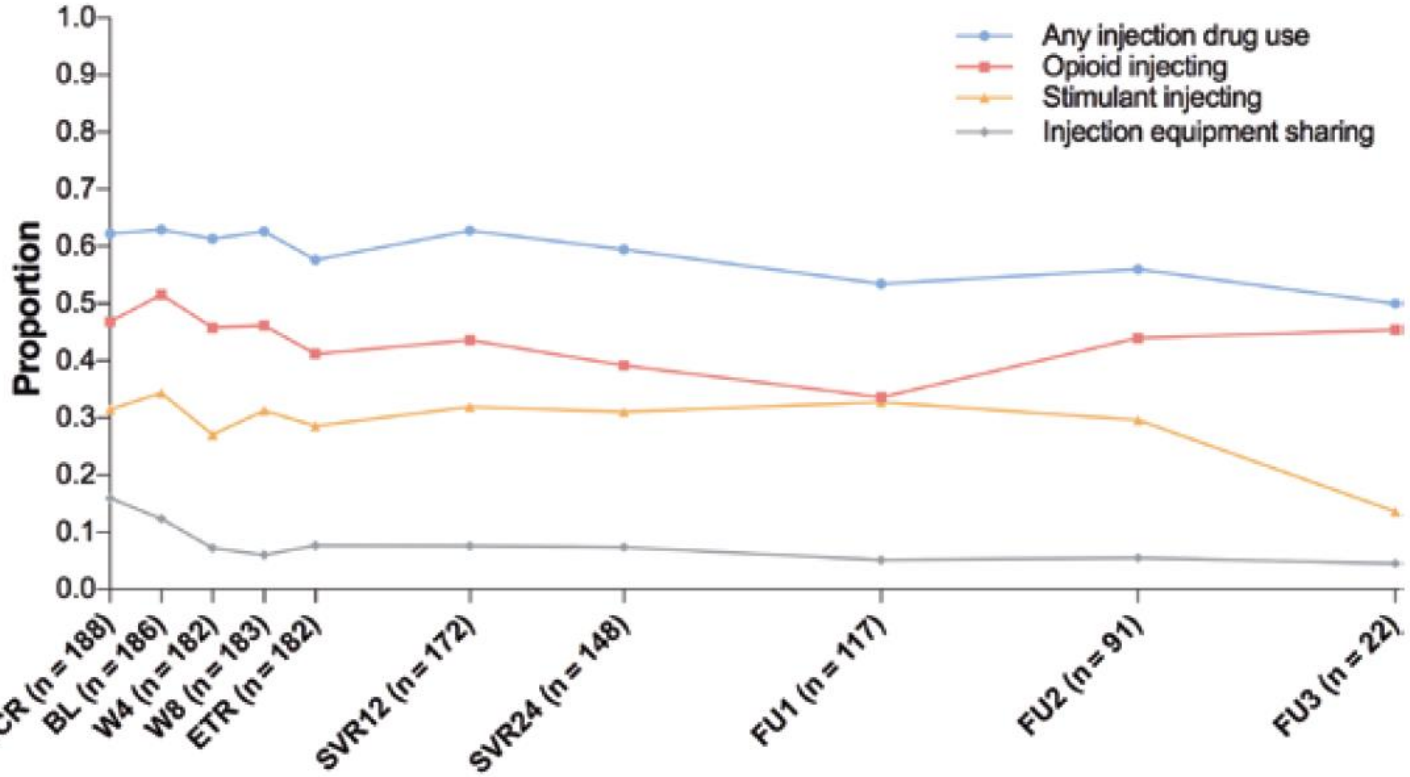
- Increased treatment uptake among more marginalized PWID
- Less interaction with health care providers
- Less fear of treatment side effects
- Loss of “cathartic” effect of interferon

Reinfection incidence: IFN vs. DAA treatment



Hajarizadeh et al. INHSU 2019

Changes in risk behaviours during and following DAA treatment: The SIMPLIFY & D3FEAT studies

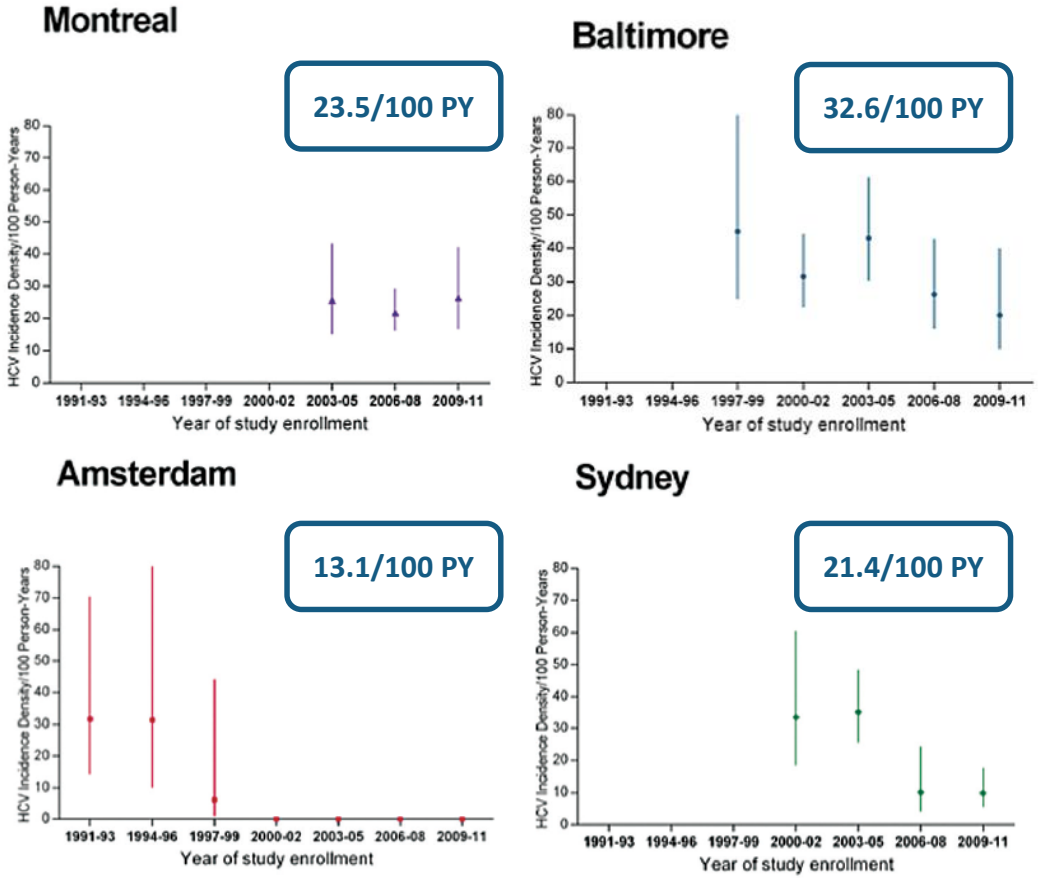


OR 0.95 per visit

OR 0.87 per visit

Artenie et al. Clin Infect Dis 2019

Reinfection incidence < primary infection incidence



Pooled incidence of primary infection 22.6/100 PY

Will reinfection incidence ≈ primary infection incidence?

Morris et al. Clin Infect Dis 2017

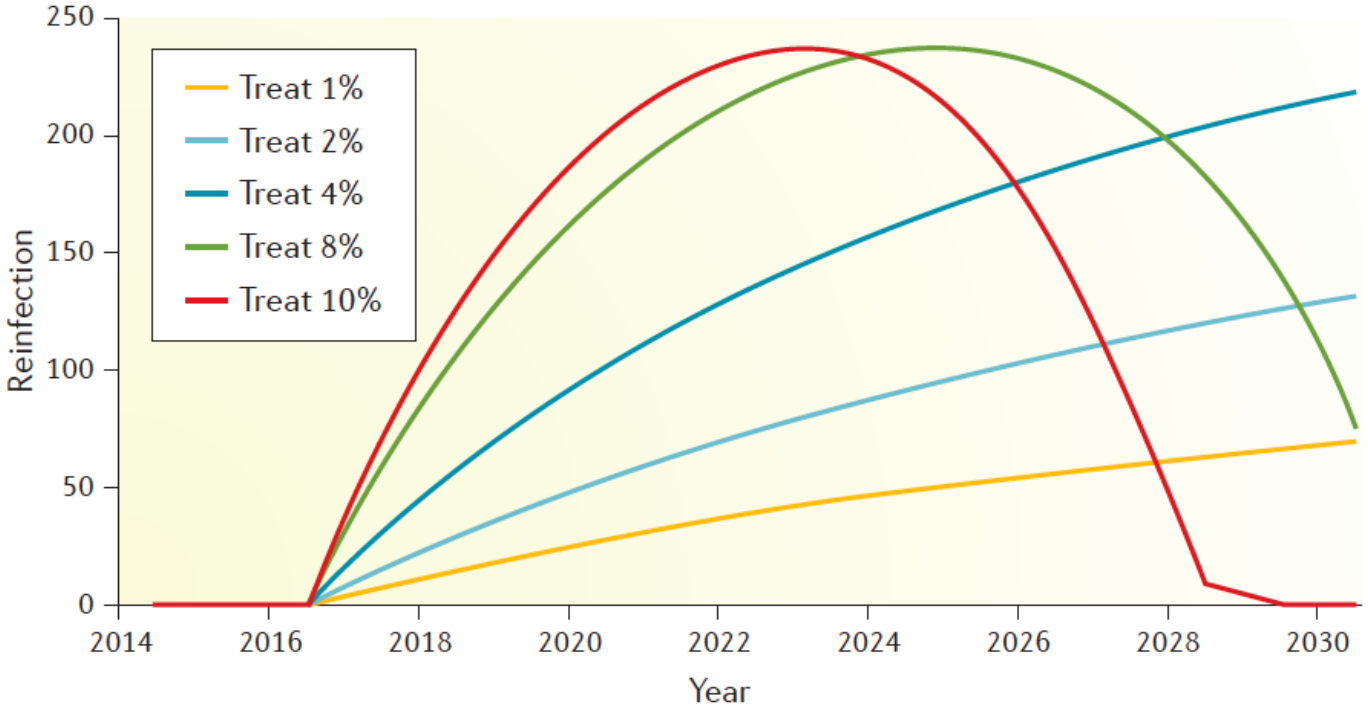
Constructive strategies: Address, prevent and manage

1. **Acknowledgement without stigma**
   - Reinfection is a marker of successful treatment uptake

2. **Population-level (elimination efforts)**
   - Universal access to DAA (re)treatment and harm reduction
   - Rapid treatment scale-up (treatment as prevention)

3. **Individual-level (“secondary prophylaxis”)**
   - Pre-treatment risk assessment, education and counselling
   - Harm reduction optimization
   - Network-based treatment
   - Post-treatment HCV RNA surveillance and retreatment

Rapid treatment scale-up among PWID is required to reduce the incidence of HCV reinfection



Grebely et al. Nat Rev Gastroenterol Hepatol 2017, modified from Razavi et al. INHSU 2016

Cochrane Library

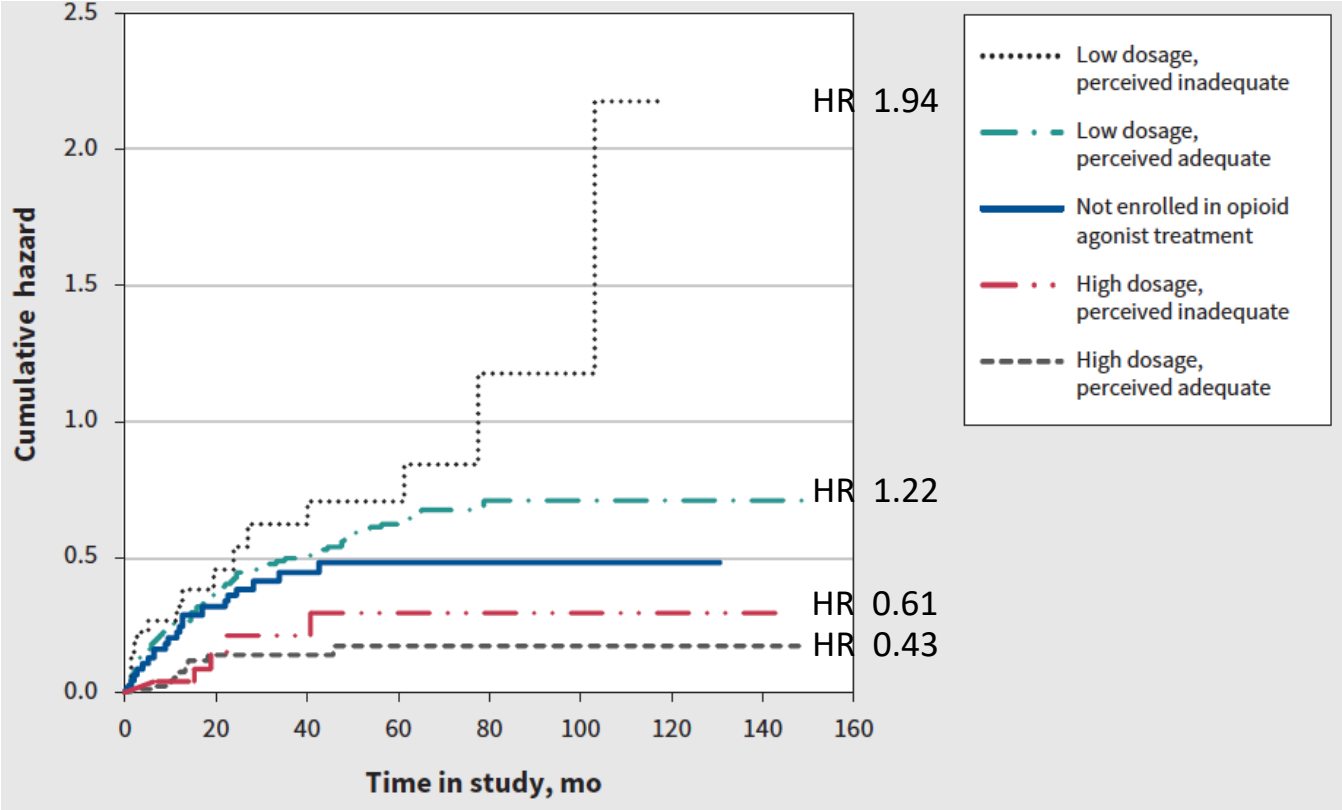
Cochrane Database of Systematic Reviews

Needle syringe programmes and opioid substitution therapy for preventing hepatitis C transmission in people who inject drugs (Review)

- **High-coverage needle and syringe provision (NSP)** (5 studies)
  - 76% risk reduction in Europe
- **Opioid agonist treatment (OAT)** (12 studies)
  - 49% risk reduction
- **Combined OAT and high-coverage NSP** (3 studies)
  - 74% risk reduction

Platt et al. Cochrane Database Syst Rev 2017

Risk of HCV infection is associated with OAT dosage



Artenie et al. CMAJ 2019

The extended HCV care continuum:
Post-SVR care for individuals at risk

Liver-related complications

- Counseling and education
- Harm reduction
  - Alcohol
  - Obesity
- HCC surveillance

Reinfection

- Counseling and education
- Harm reduction
  - Needle and syringe programs
  - Opioid agonist treatment
- HCV RNA surveillance

Midgard et al. J Hepatology 2016; Terrault et al. J Hepatology 2016

Post-SVR care in practice: A case for the social-hepatologist

LAP. RESECTION

HCC

35
30
25
20
15
10
5
0

TREATMENT

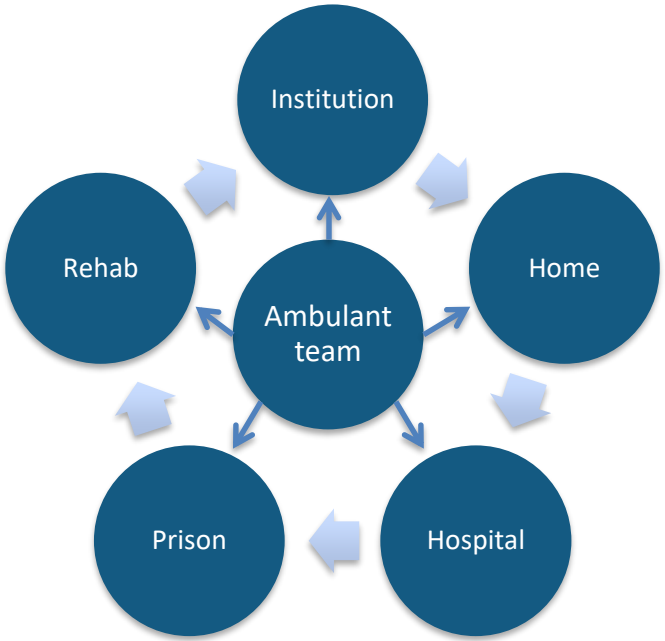
RETREATMENT

Baseline EOT SVR REINFECTION EOT

Nov-16 Feb-17 May-17 Dec-17 Feb-18 Jun-18 Dec-18 Aug-19

Liver stiffness (kPa) AFP (µg/L) HCV RNA (mill IU/ml)

HCV RNA surveillance and retreatment in practice:
A case for the committed nurse



- Low-threshold clinic in downtown Oslo
- HCV RNA surveillance at 3-6 months invervals as part of study protocol
- Reinfection incidence 4.2/100 PY

Midgard et al. EASL 2019

HCV RNA surveillance and retreatment in practice:
A case for the committed nurse

	Gender and age	OAT	IDU	Time to reinfection	Delay to retreatment	Retreatment status	Retreatment barriers	Solution
#1	female 45	+/-	+++	6 months	28 months	Completed	Unstable housing Frequent IDU Cancer	Ambulant work
#2	male 42	-	+	32 months	13 months	Completed	Fear of blood tests	Financial incentives
#3	male 46	+	+++	12 months	7 months	SVR	Delay in lab results	Ambulant work
#4	male 30	+	+	11 months	3 months	On treatment	None	Ambulant work

Conclusions

- Reinfection may challenge HCV elimination efforts unless strategies to address, prevent and manage reinfection are implemented
- Reinfection should be acknowledged without stigma or treatment restrictions
- Rapid treatment scale-up is necessary to curb the reservoir and reduce incidence
- OAT may be the strongest individual protective factor
- Post-SVR surveillance and retreatment options must be part of any elimination plan

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