



Hepatitis C virus reinfection following antiviral treatment among people who inject drugs: A systematic review and meta-analysis

Behzad Hajarizadeh¹, Evan B Cunningham¹, Heather Valerio¹, Marianne Martinello¹, Matthew Law¹, Julie Bruneau², Olav Dalgard³, John Dillon⁴, Matt Hickman⁵, Naveed Janjua^{6,7}, Håvard Midgard³, Gregory J Dore¹, Jason Grebely¹

1. The Kirby Institute, UNSW Sydney, Sydney, Australia; 2. Centre Hospitalier de l'Université de Montréal, QC, Canada; 3. Akershus University Hospital, Oslo, Norway; 4. Ninewells Hospital and Medical School, University of Dundee, Dundee, UK; 5. Population Health Sciences, University of Bristol, Bristol, UK; 6. British Columbia Centre for Disease Control, Vancouver, BC, Canada; 7. School of Population and Public Health, University of British Columbia, Vancouver, BC, Canada



Objectives

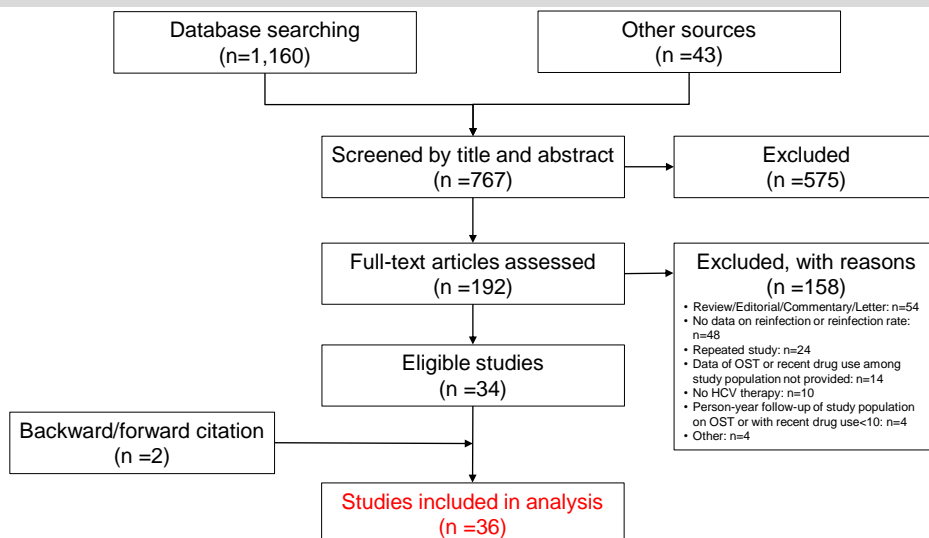
- To evaluate post-treatment HCV reinfection among overlapping populations of:
 - people with recent drug use (injecting or non-injecting),
 - people with recent injecting drug use,
 - people receiving opioid agonist therapy (OAT).
- To assess the factors explaining heterogeneity across studies.

Methods – Information sources

- Bibliographic databases:
 - MEDLINE (Pubmed)
 - Scopus
 - Web of Science
 - Cochrane Central Register of Controlled Trials (CENTRAL)
 - PsycINFO
- Conference presentations:
 - International Liver Congress™
 - The Liver Meeting®
 - Annual Conference on Retroviruses and Opportunistic Infections (CROI)
 - International Symposium on Hepatitis Care in Substance Users (INHSU)
- ClinicalTrials.gov was searched for registered clinical trials, including ongoing studies.
- Searches were performed in Oct 2018, and updated in June 2019.

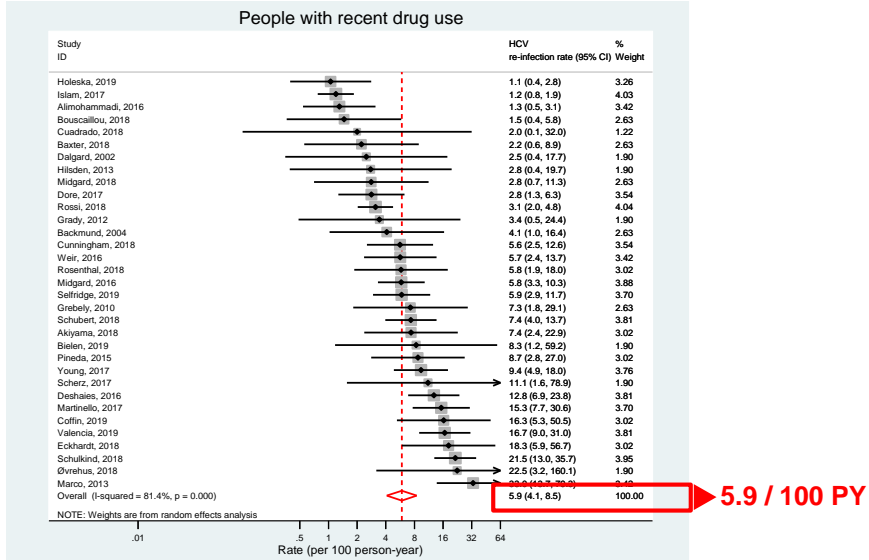
3

Results



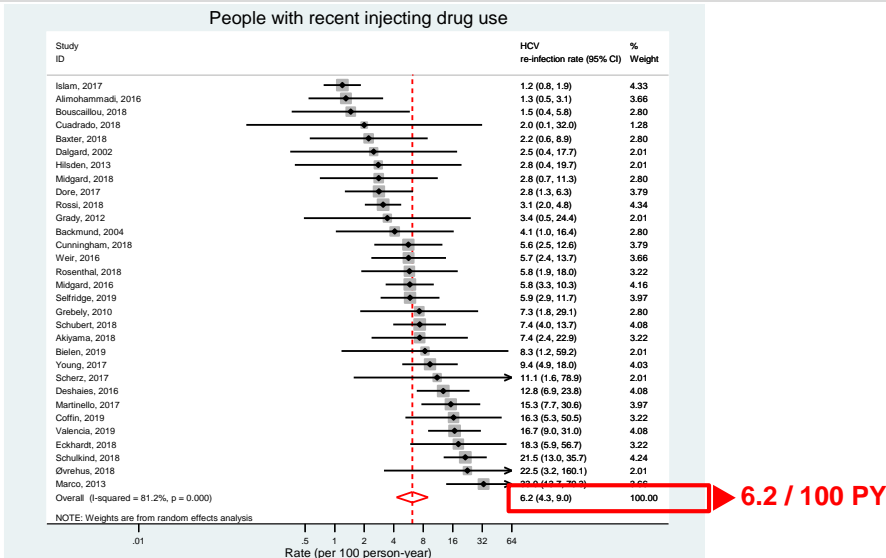
4

Results – Reinfection rate, individuals with recent drug use



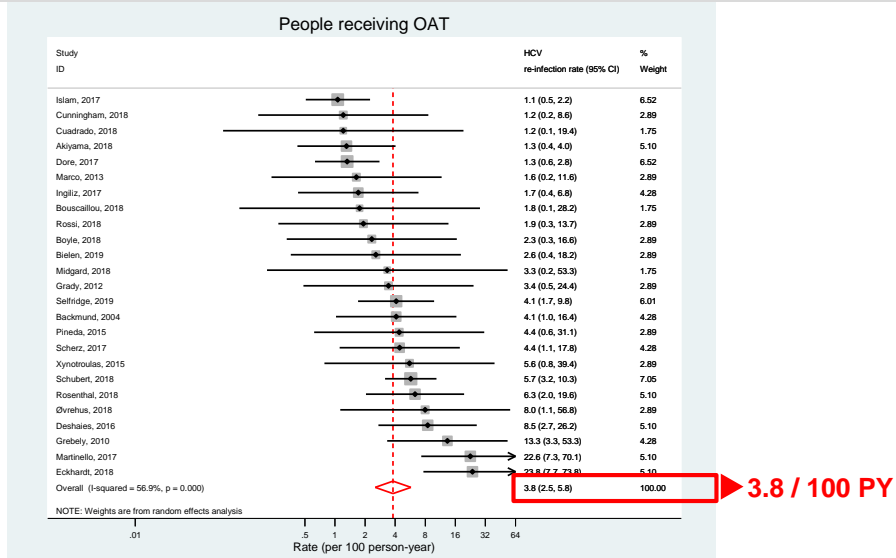
5

Results – Reinfection rate, individuals with recent IDU



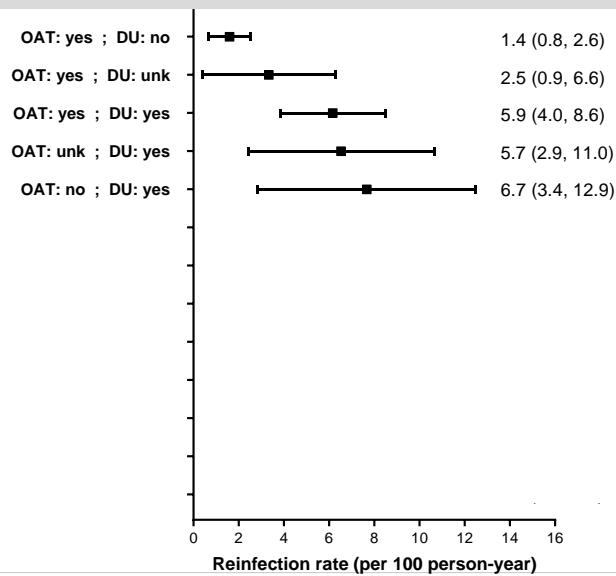
6

Results – Reinfection rate, individuals on OAT



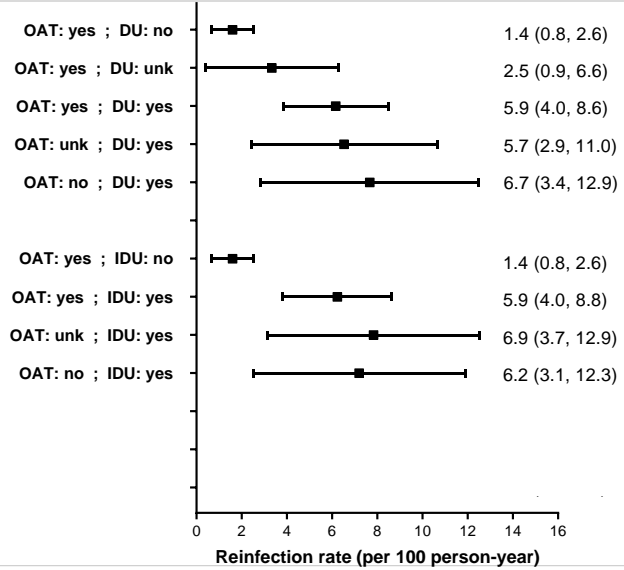
7

Results – Reinfection rate by OAT and DU status



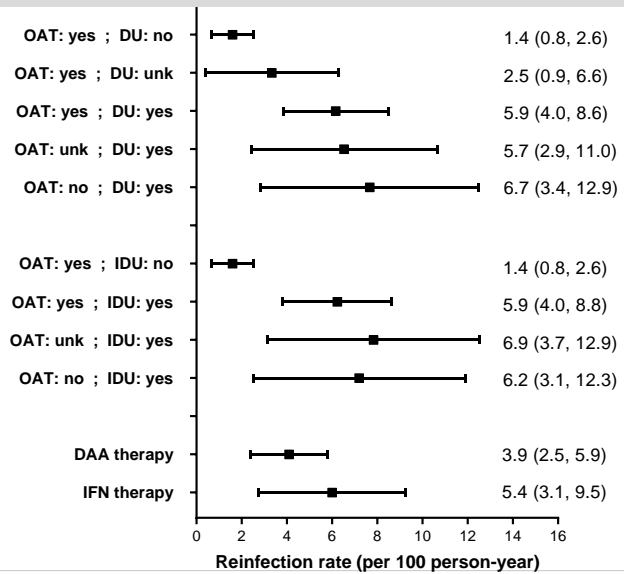
8

Results – Reinfection rate by OAT and DU status



9

Results – Reinfection rate by OAT and DU status



10

Results – Meta-regression

Unadjusted models		
	Rate Ratio (95% CI)	P
Proportion of men, per 10% increase	1.08 (0.84, 1.39)	0.524
Median/mean age, per year increase	0.95 (0.91, 0.98)	0.002
Proportion with HIV, per 10% increase	1.04 (0.93, 1.17)	0.465
Study design	Observational, retrospective	1.00
	Observational, prospective	2.62 (1.38, 4.99)
	Clinical trial	2.02 (1.06, 3.88)
Study setting	Tertiary, primary or community clinic	1.00
	Drug treatment service	1.74 (0.84, 3.63)
	Prison	1.74 (0.48, 6.29)
	Mixed setting	0.82 (0.39, 1.70)
HCV treatment	IFN-based therapy	1.00
	DAA therapy	0.79 (0.44, 1.42)
Study population	OAT: yes, DU: no	1.00
	OAT: yes, DU: unknown	1.80 (0.37, 8.82)
	OAT: yes, DU: yes	4.00 (1.58, 10.15)
	OAT: unknown, DU: yes	3.96 (1.47, 10.66)
	OAT: no DU: yes	4.53 (1.72, 11.97)
Median/mean follow-up, per year increase		0.87 (0.76, 0.99)
Start point for reinfection assessment	SVR12 or later	1.00
	End of treatment	1.39 (0.78, 2.51)

Results – Meta-regression

Adjusted models		
	Rate Ratio (95% CI)	P
Median/mean age, per year increase	0.94 (0.91, 0.97)	<0.001
Study design	Observational, retrospective	1.00
	Observational, prospective	1.36 (0.77, 2.43)
	Clinical trial	1.29 (0.74, 2.25)
Study population	OAT: yes, DU: no	1.00
	OAT: yes, DU: unknown	1.15 (0.27, 4.88)
	OAT: yes, DU: yes	3.47 (1.61, 7.45)
	OAT: unknown, DU: yes	5.65 (2.52, 12.69)
	OAT: no DU: yes	3.95 (1.82, 8.58)
Median/mean follow-up, per year increase		0.77 (0.69, 0.86)

Residual I-square = 20.6%

Conclusion

- Post-treatment HCV reinfection rate was associated with recent drug use/OAT status, with the highest rate identified among people with recent drug use, not receiving OAT.
- Lower rate in studies with longer follow-up suggested higher risk of reinfection early post-treatment (or cohort effect?).
- Harm reduction services are required to reduce the reinfection risk while regular post-treatment HCV assessment is required to detect and treat reinfection early.

13

Acknowledgements

We would like to thank the individuals who responded to requests for additional data:

Matthew Akiyama, Alain Litwin (USA)
 Arshia Alimohammadi, Brian Conway (Canada)
 Markus Backmund (Germany)
 Joanne Baxter (UK)
 Tamar Kikvidze, Julie Bouscaillou, Niklas Luhmann (France)
 Philip Bruggman (Switzerland)
 Antonio Cuadrado, Javier Crespo (Spain)
 Lucie Deshaies (Canada)
 Heather Loryn Platt (USA)
 Benjamin Eckhardt (USA)
 Bart Grady (The Netherlands)
 Patrick Ingiliz, Heiner Wedemeyer, Florian Berger, Stefan Christensen, Stefan Mauss (Germany)
 Carmine Rossi (Canada)
 Andres Marco, Elisabet Turu (Spain)
 Anne Øvrehus (Denmark)
 Juan Pineda, Luis Real (Spain)

Elana Rosenthal, Sarah Kattakuzhy (USA)
 Raphael Schubert, Michael Gschwantler (Austria)
 Marion Selfridge (Canada)
 Jorge Valencia (Spain)
 John Xynotroulas (Greece)
 Rob Bielen, Geert Robaey (Belgium)
 Sharon Hutchinson, Allan Mcleod, Amanda Weir (UK)

14