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HCV Reinfection Risk following DAA Therapy in People Living with HIV in Australia

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Background:

- With unrestricted access to direct-acting antiviral (DAA) therapy from March 2016 in Australia, HCV elimination should be achievable among people living with HIV (PLWH).
- Increasing HCV risk behavior and HCV reinfection have the potential to compromise HCV elimination, even within the setting of high treatment uptake.

Methods:

- The Control and Elimination of HCV from HIV-infected individuals within Australia (CEASE) is an ongoing observational cohort study. HIV/HCV (antibody positive) co-infected individuals (≥18 years) were enrolled from 14 primary and tertiary clinics in Australia (n=402).
- Participants completed a behavioral questionnaire at enrolment (July 2014 - March 2017) and at follow-up (June 2017 - May 2018).
- Among participants who completed behavioral questionnaires at enrolment and follow up, we compared longitudinal injecting risk behaviors (n=272) and sexual risk behaviors (n=225; gay and bisexual men only [GBM]).
- Reinfection incidence was calculated using person-time of observation, with time at risk commencing at end of treatment (if SVR was achieved post enrolment) or enrolment (if HCV RNA negative) and follow up time censored at estimated date of reinfection, date of last follow up, or death.
- Analysis was performed using STATA (version 15.0).

Results:

- Between 2014 - 2017, 402 HIV/HCV antibody-positive participants were enrolled, of whom 288 (72%) had current HCV infection (**Table 1**).
- Of those enrolled, 272 (68%) completed behavioral questionnaires at enrolment and follow up. Median time between enrolment and follow-up was 2.1 years (IQR 1.6, 2.6 years; total follow up time: 582 person-years).

Table 1. Participant enrolment characteristics.

Demographic and clinical characteristics	All enrolled (N = 402)	Completed questionnaires at enrolment and follow up (N = 272)
Mean age (SD)	49 (10)	50 (9)
Male, n (%)	382 (95)	260 (96)
Gay and bisexual men, n (%)	322 (80)	225 (83)
White, n (%)	344 (86)	240 (88)
Completed higher education, n (%)	207 (52)	143 (53)
Full or part-time employment, n (%)	154 (38)	97 (36)
CD4 count (10^6/L), median (IQR)	596 (440, 810)	590 (404, 799)
HIV viral load <50 copies/mL, n (%)	346 (86)	233 (86)
On antiretroviral therapy, n (%)	377 (94)	256 (94)
Mode of HCV acquisition		
Injecting drug use	217 (54)	146 (54)
Sexual exposure	127 (32)	88 (32)
Other	58 (14)	38 (14)
Cirrhosis, n (%)	51 (13)	38 (14)
HCV treatment experienced, n (%)	126 (31)	83 (31)
HBsAg positive, n (%)	15 (4)	10 (4)
Injecting drug use ever	316 (79)	216 (79)

Treatment uptake and HCV prevalence

- HCV treatment uptake among those with current HCV infection increased from 7% in 2014 and 10% in 2015 to 80% in 2016 and 35% in 2017.
- This was accompanied by a substantial decline in the proportion with current HCV infection.
- Among the 272 participants in this analysis, the proportion with current HCV infection fell from 72% (95% CI 67%, 76%) at enrolment (2014 - 2017) to 6% (95% CI 4%, 10%) at follow-up (2017 - 2018) (**Figure 1**).

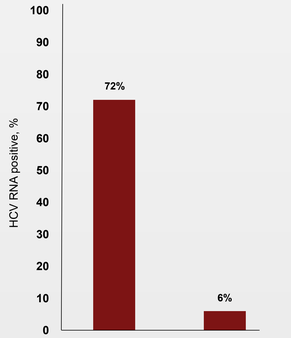

Figure 1. Proportion of CEASE cohort with current HCV infection at enrolment and follow up.

Injecting risk behaviors

- The proportion reporting injecting drug use (IDU) within the last six months (current) and the last month (recent) remained stable (**Figure 2**).
- Among people reporting recent IDU, the proportions reporting frequent injecting drug use (≥weekly), sharing of needles and/or syringes, and sharing of injecting equipment remained stable (**Figure 2**).
- Amphetamines were the predominant drug injected within the last six months (**Figure 3**).

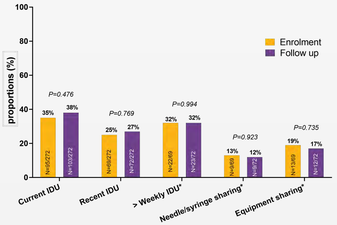

Figure 2. Injecting Risk behavior at enrolment and follow-up.

* Among people reporting recent IDU

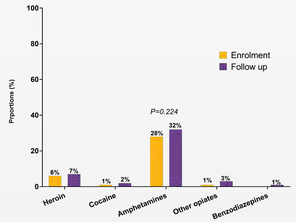

Figure 3. Injecting drug types at enrolment and follow-up.

Sexual risk behaviors among GBM

- Among GBM, the proportion reporting casual male partner/s (CMP) and condom-less anal intercourse (CLAI) in the last six months declined at follow-up compared to enrolment (**Figure 4**).
- However, the proportion reporting condom-less anal intercourse with casual male partners (CLAI with CMP) and group sex in the last six months remained stable (**Figure 4**).

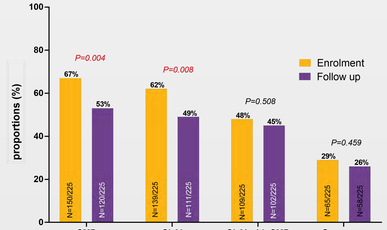

Figure 4. Sexual risk behavior among GBM at enrolment and follow-up.

Reinfection incidence and characteristics

- Reinfection was reported in five participants through follow-up who were all GBM (incidence 0.81 per 100 person years, 95% CI 0.34, 1.94) (**Table 2**).

Table 2. Demographic and behavioral characteristics of HCV reinfection cases.

Age	IDU (in the last 6 months)		CLAI with CMP (in the last 6 months)		Time between end of treatment* and reinfection (days)	Reinfection outcome
	Enrolment	Follow-up	Enrolment	Follow-up		
53	No	**Yes**	Yes	**Yes**	405	Persistence Retreatment with sofosbuvir/ledipasvir (SVR)
47	No	No	No	**Yes**	182	Persistence In follow up
55	No	**Yes**	Yes	**Yes**	72	Spontaneous clearance
33	Yes	**Yes**	Yes	**Yes**	103	Persistence In follow up
67	No	No	No	No	108	Persistence Retreatment with sofosbuvir/ledipasvir (SVR)

*Time at risk for reinfection was calculated from date of end of treatment or date of enrolment (for those who were HCV RNA negative)

Abbreviations: IDU, injecting drug use; CLAI with CMP, condom-less anal intercourse with CMP in last 6 months

Conclusions:

- A substantial reduction in HCV viraemic prevalence was observed among PLWH in Australia following unrestricted DAA access.
- In the early post DAA period, no evidence of increasing HCV risk behavior was observed, with injecting risk remaining stable and some reduction in indicators of sexual risk behaviour.
- HCV elimination should be achievable among PLWH in Australia providing high levels of treatment uptake are maintained, alongside prompt detection and treatment of re-infection cases.

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