

INCIDENCE OF HCV REINFECTION AMONG PEOPLE WITH HIV PRIOR TO AND DURING PERIODS OF LIMITED AND BROAD ACCESS TO DIRECT-ACTING ANTIVIRAL THERAPIES FOR HCV IN SIX COUNTRIES

Rachel Sacks-Davis^{1,3}, Daniela K. van Santen^{1,2,3}, Anders Boyd^{2,5}, Jim Young¹², Tim Spelman¹, Ashleigh Stewart^{1,3}, Marc van der Valk^{4,5}, Andri Rauch⁶, Inmaculada Jarrin⁷, Karine Lacombe⁸, Linda Wittkop⁹, Gail Matthews¹⁰, Joseph Doyle^{11,12}, Marina Klein¹², Maria Prins^{2,4}, Mark Stoove^{1,3}, Margaret Hellard^{1,3,11} on behalf of the InCHEHC Collaboration
 1 Burnet Institute, 2 Public Health Service of Amsterdam, 3 Monash University, 4 Amsterdam University Medical Centers, Location AMC, 5 Stichting HIV Monitoring, 6 Inselspital, UKarinen University Hospital Bern, 7 Instituto de Salud Carlos III, 8 Sorbonne Universités, 9 University of Bordeaux, 10 Kirby Institute, 11 Alfred Hospital, 12 McGill University Health Centre

BACKGROUND

- Direct-acting antivirals (DAA) may reduce HCV incidence through a treatment-as-prevention effect.
- With increasing DAA availability, WHO has focused on achieving HCV elimination
 - By 2020, 30% reduction in new cases of HCV
 - By 2030, 80% reduction in new cases of HCV
- Evidence of decreased incidence after DAAs were introduced in individual cohorts, mainly driven by primary HCV incidence
- Reinfection incidence after successful treatment has been a major concern for HCV elimination, particularly among people with HIV (PHIV).
- Unclear whether trends in HCV reinfection incidence will follow the same pattern as trends in HCV primary infection incidence
- Large international datasets allow assessment of trends in HCV reinfection overtime and comparison between settings

Research question:

Are there differences in HCV reinfection incidence across periods of DAA availability among PHIV?

METHODS

Data:

Individual level data were from the **I**nternational **C**ollaboration on **H**epatitis **C** **E**limination in **H**IV **C**ohorts (InCHEHC)

- Eleven cohorts. Data from eight cohorts used for this analysis.
- Six countries: the Netherlands, Switzerland, Canada, Australia, Spain, and France
- Study period for this analysis: 2010-2019.
- Incidence of first reinfection per participant was measured.



Definitions:

Reinfection eligibility: An HCV positive test followed by spontaneous or treatment clearance (Table 1).

Reinfection incidence calculation:

- **Time zero:** first negative HCV RNA test indicating treatment or spontaneous clearance.
- **Censoring date:** last negative HCV RNA test or reinfection date
- **Reinfection date:** estimated as the midpoint between the last negative and first positive test dates.

Statistical analysis:

1. Trends in HCV reinfection incidence were visualized by aggregating incidence by calendar year and fitting cubic spline models to these aggregated data.
2. The rate of reinfection was compared between three periods: prior to DAA access, and during limited access, and broad access to DAA in each jurisdiction using a piecewise exponential survival model, with a fixed effect for risk group (men who have sex with men [MSM], people who inject drugs [PWID] vs. other/unknown) and a random intercept at the country level.

TABLE 1: Reinfection eligibility

HCV positive test	HCV clearance	Follow-up
HCV Ab or RNA positive test	Treatment-induced clearance: <ul style="list-style-type: none"> • Evidence of treatment initiation • HCV RNA negative test \geq 12 weeks after DAA treatment or 24 weeks after interferon treatment Spontaneous clearance: <ul style="list-style-type: none"> • Two consecutive HCV RNA negative tests \geq 12 weeks apart • No evidence of treatment initiation 	At least one HCV RNA test after HCV clearance

RESULTS

Of 104,702 participants in InCHEHC, 6,195 were eligible for the reinfection analysis (Figure 1)

Participants:

Eligible participants were:

- ♂ 81% male
- 👤 Median age 49 years
- 👫 4.6% MSM
- 💉 34% PWID

Reinfection rate by period:

- Incidence of reinfection was stable or decreased in all countries other than Spain (Figure 2).
- In Spain, the rate of reinfection increased over time (Figure 2).
- After adjusting for country and risk group, the incidence of reinfection was highest prior to DAA access (Table 2 & Figure 3A).
- The incidence of reinfection was approximately 20% lower in the limited and broad DAA availability periods compared to the pre-DAA period (Table 2 & Figure 3A).

Reinfection rate by risk group

- The rate of reinfection was approximately double in MSM compared to PWID and those with unknown risk factors (Table 2 & Figure 3B).

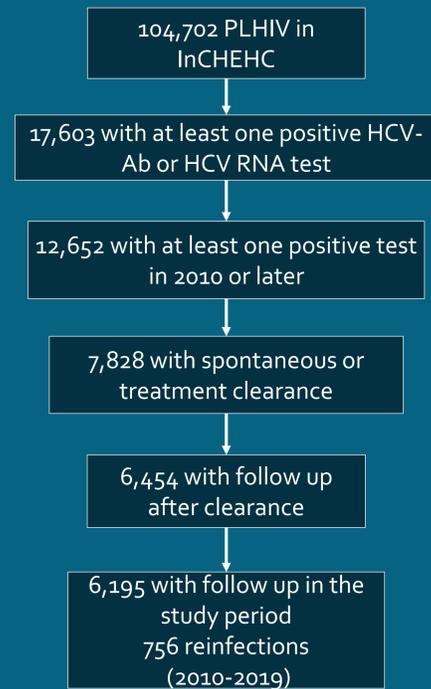


FIGURE 1: Flowchart of participation

FIGURE 2: Trends in HCV reinfection incidence in the InCHEHC collaboration 2010-19, by country

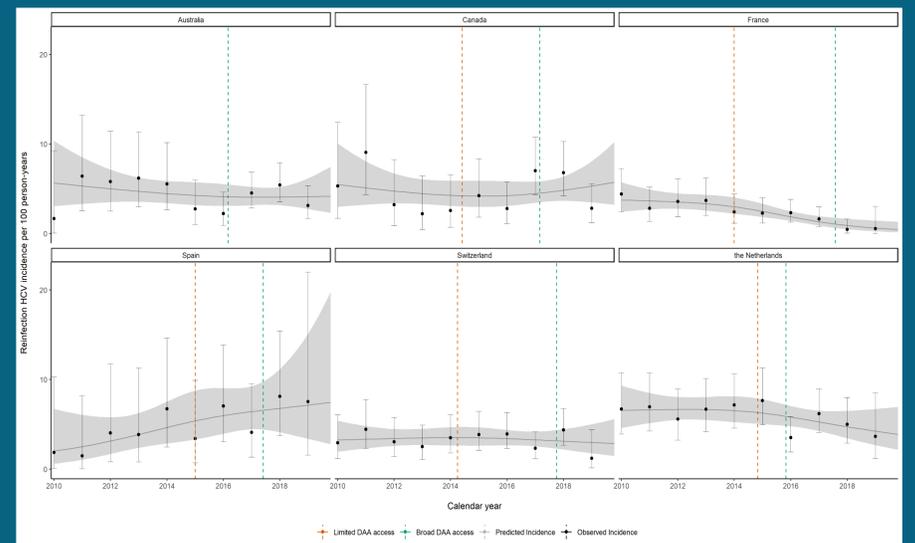


FIGURE 3: HCV reinfection incidence by DAA availability period (panel A) and risk group (panel B) in InCHEHC 2010-2019, piecewise exponential model

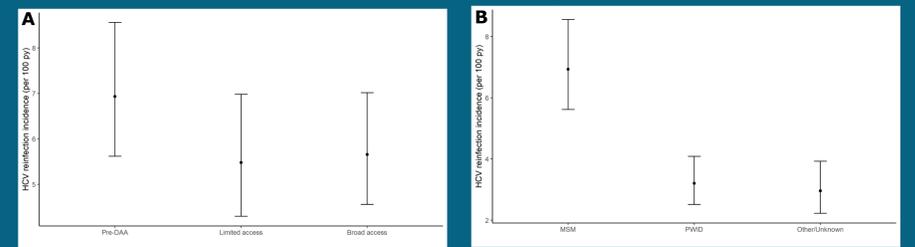


TABLE 2: Reinfection incidence rate ratios by DAA access period and risk group, piecewise exponential model

		IRR (95% CI)
DAA access period	Pre-DAA	REF
	Limited DAA access	0.79 (0.64-0.98)
	Broad DAA access	0.82 (0.68-0.98)
Risk group	MSM	REF
	PWID	0.46 (0.38-0.57)
	Other/Unknown	0.43 (0.33-0.54)
Intercept: IR(95% CI)		0.07 (0.06-0.09)
Intraclass correlation		0.01

LIMITATIONS

- No data on recent injecting or sexual risk behaviour included in this analysis.
- Testing data mainly from routine clinical tests and frequency of testing varied. However, testing increased slightly after DAA access so unlikely to explain observed reduction in reinfection incidence (data not shown).
- High treatment uptake resulted in large increases in the number of people at risk of reinfection in the limited and broad DAA access periods.
 - Characteristics of those at risk differed by period (data not shown): participants in the limited access period had characteristics associated with lower risk.
 - Nonetheless, rate of reinfection remained stable in the broad DAA access period, where participants had characteristics associated with relatively higher risk.

CONCLUSION

Hepatitis C reinfection incidence has declined or remained stable in most InCHEHC countries since the introduction of direct acting antivirals. Overall, reinfection incidence declined in the InCHEHC collaboration after DAA therapies became available. The decline started in the limited access period, and remained stable during the broad access period. This is reassuring for HCV elimination efforts, suggesting that reinfection is unlikely to be a major threat to HCV elimination.

