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Cohort Profile

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Cohort Profile: International Collaboration on Hepatitis C Elimination in HIV Cohorts (InCHEHC)

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Key Features

- The International Collaboration on Hepatitis C Elimination in HIV Cohorts (InCHEHC) is a multinational consortium of longitudinal cohorts of people with HIV who are at risk of hepatitis C virus (HCV) infection or infected with HCV. InCHEHC has been specifically designed to assess progress towards HCV elimination as a public health threat among people with HIV.
- The first data merge includes 104 740 participants from 11 cohorts in Australia ($n = 22\,033$), Canada ($n = 2070$), France ($n = 18\,387$), The Netherlands ($n = 24\,785$), Spain ($n = 16\,725$) and Switzerland ($n = 20\,740$), with data collected between 1987 and 2021. Participants include 86 132 males (81.4%), 19 514 females (18.4%) and 191 with unknown sex at birth (0.2%); 725 (1.0%) were known to be transgender across eight cohorts collecting data on this variable. At enrolment, the median age was 38 years (interquartile range: 30–46). Of the total 104 740 participants, 12 784 (12%) had an HCV antibody or RNA positive test at or up to 1 year prior to individual cohort enrolment; 32 360 (31%) did not have an HCV RNA or antibody test recorded at that time.
- Clinical data are collected on all participants and behavioural and mortality data on a subset of them. Clinical data include HIV-related markers, HCV testing and treatment, liver health-related markers and sexually transmitted and blood-borne virus co-infections. Behavioural data include sexual and injecting risk behaviours and alcohol and drug use. Mortality data are collected using the International Classification of Diseases 9th or 10th revision (ICD-9/10) or Coding Causes of Death in HIV (CoDE) classification.
- Data are available by request from the InCHEHC steering committee. Initial requests should be directed to Rachel Sacks-Davis (rachel.sacks-davis@burnet.edu.au).

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Why was the consortium set up?

Throughout the past decade, HCV treatment has been transformed by all-oral direct-acting antiviral (DAA) therapies. Whereas cure rates using previous 24–48-week treatment regimens including interferon were typically <50%, particularly for people with HIV (PHIV),[1] modern treatment with DAAs cures >95% of HCV infections in 8–12 weeks.[2] Prompted by the introduction of DAA therapies for HCV, in 2016 the World Health Organization (WHO) set ambitious targets to eliminate HCV as a public health threat which included reducing HCV incidence by 80% and HCV-related mortality by 65% by 2030[3]: a major undertaking, given the estimated 59 million people infected in 2020.[4] New targets to guide validating HCV elimination were added in 2021, specifying that countries should aim for an annual HCV incidence of ≤5 per 100 000 persons in the general population and ≤2 per 100 people who inject drugs.[3] The absolute HCV-related annual mortality rate target is ≤2 per 100 000 persons.[3]

PHIV are a key population for HCV elimination, as HCV infection is more common among PHIV and also liver disease progresses more rapidly than in individuals without HIV.[5–7] HIV/HCV co-infection results in higher rates of HCV-related mortality relative to those with HCV alone.[8–10] Moreover, regular clinic visits for HIV care provide opportunities for (early) HCV diagnosis and treatment in this group. Modelling suggests that if HCV treatment is scaled up, the resulting decline in HCV prevalence could drive a substantial decrease in HCV incidence.[11–13] In many high-income countries, DAA treatment uptake increased shortly after its introduction,[14–19] and some studies have demonstrated declines in primary HCV infection incidence rates[20–25] and mortality rates when DAAs became accessible.[26]

However, potentially high rates of post-treatment HCV reinfection are of concern.[11,27] Driven by ongoing HCV-related risk behaviour (e.g. sharing of needles, syringes and other injecting equipment and condomless anal intercourse), reinfection rates among PHIV have been estimated at 3–15 per 100 person-years (PY) for an individual's first reinfection, and up to 23 per 100 PY for subsequent reinfections prior to the availability of DAA therapies.[28–30] Reinfection rates reported by single-country studies after DAA introduction vary, depending on the populations engaged in certain behaviours associated with HCV and potentially on the methodology used.[27,28,31,32] For example, among people who inject drugs, a stable reinfection incidence was observed in Canada but increases were observed in Scotland.[28,32]

Whereas individual cohorts can assess progress toward HCV elimination targets set by the WHO, a large multinational consortium allows for cross-country comparisons using the same methodological approaches and can provide insight into the impact of policy differences. In addition, a large multinational collaboration is required to study uncommon events within individual cohorts, for example failure to reach HCV cure and behavioural drivers of HCV reinfection following successful treatment.

The International Collaboration of Hepatitis C Elimination in HIV Cohorts (InCHEHC) was established in 2017 to track progress and guide policy on elimination of HCV in PHIV. InCHEHC's first project examined the HCV care cascade among people living with HIV in five countries (Australia, Canada, France, The Netherlands and Switzerland). Since then, a cohort from Spain has joined the collaboration. The first data merge of individual-level data was conducted in 2020–21 and a new data merge is expected in 2023. Cohorts included in InCHEHC were chosen for the availability of broad access to DAA therapies in their respective country or jurisdiction while still having differences in HCV health care-related policies (e.g. HCV RNA testing), a large coverage of PHIV or a representative sample of PHIV in their setting (Table 1), longstanding cohort data among PHIV including HCV-related clinical data collection and/or detailed HCV-related behavioural data. Data from the first data merge are described in detail below.

Who is in the consortium?

Consortium design

InCHEHC is a consortium including prospective cohorts among PHIV with or without HCV co-infection from Australia, Canada, France, The Netherlands, Spain and Switzerland. This consortium includes three studies from Australia, three from France, two from The Netherlands, one from Switzerland, one from Spain and one from Canada (Table 1). Study designs include nationwide, multi- or single-site cohorts and clinical surveillance datasets (Table 1). Coverage of the PHIV in care may not be applicable and/or known for some cohorts, as their cohort was set up to answer specific research questions and not necessarily to represent the PHIV population in care in their country or jurisdiction. InCHEHC specifically recruited two types of cohorts for participation: large longstanding representative cohorts and smaller cohorts with detailed behavioural data.

Recruitment of participants and cohorts

Cohorts that recruited individuals with HIV with or without HCV and collected longitudinal HCV-related data such as HCV testing and treatment could be included. Participants were eligible for inclusion in the InCHEHC pooled dataset if they had a diagnosis of HIV and were at least 18 years of age.

Number entering the consortium

A total of 104 740 participants from 11 cohorts have been included in the pooled dataset. Table 2 presents participants sociodemographic and clinical characteristics at enrolment by cohort. The start of cohort enrolment ranges from 1987 to 2016, and six of 11 cohorts are open with ongoing recruitment. Five of 11 cohorts have enrolled individuals since the 1980s/90s, which explains differences in antiretroviral therapy (ART) uptake across cohorts. Median age ranged from 35 years in CoRIS to 49 years in the CEASE cohort. In all cohorts, most participants were male. Four cohorts included only individuals with HIV/HCV co-infection (i.e. CCC, CEASE, co-EC and HEPAVIH). The MOSAIC cohort included individuals with acute HCV and aimed to include at least one additional HIV-positive/HCV negative control. In the remaining cohorts, the proportion of individuals with a positive HCV antibody and/or RNA status ranged from 3.3% in SAIDCC to 14.4% in AQUITAINE (Table 2).

How often have they been followed up?

The studies' enrolment periods range from 1981 to currently ongoing. Six cohorts started enrolling participants before 2005, three cohorts between 2005 and 2009, one cohort between 2010 and 2015 and one after 2015 (Table 2). The majority of cohorts are open cohorts with ongoing enrolment

Table 1. International Collaboration on Hepatitis C Elimination in HIV Cohorts (InCHEHC): participating cohort characteristics and data availability from the first merge, data submission 2020–21

Cohort (country)	Study design	Enrolment period/ database closure for Merge 1	Primary study population	Coverage of PHIV in care	Primary aims of the study	Cohort visit definition	Follow-up pre-HCV diagnosis/after treatment	Detailed longitudinal risk behaviour	Mortality availability and coding
ACCESS: Australian Collaboration for Coordinated Enhanced Sentinel Surveillance (Australia)	Nationwide linked database from primary care, community clinics, hospitals, and patholo laboratories	2009–ongoing/ July 2021	Individuals presenting to health services captured by ACCESS, primarily PWID and MSM	59% of PHIV in care in 2018	To provide indicator data against strategic targets set out in Australian blood-borne virus and sexually transmitted infection strategies, including those related to testing coverage, treatment coverage and diseases incidence	Primary care, sexual health clinics, and hospital clinics consultations	Annual/annual	✓ (Subset of patients)	
CEASE: Control and Elimination within AuStralia of HEpatitis C from people living with HIV (Australia)	Nationwide multisite observational study (majority Sydney inhabitants)	2014–18/July 2018	HIV-positive HCV antibody-positive	Unknown	To evaluate the feasibility of rapid scale-up of interferon-free DAA treatments and impact on the proportion with HCV viraemia within the HIV-HCV population of Australia	Primary or tertiary consultations	NA/6-monthly	✓	
Co-EC: Eliminating hepatitis C transmission by enhancing care and treatment among HIV co-infected individuals (Australia)	Melbourne-based multisite cohort recruiting mainly gay and bisexual men	2016–19/ January 2020	MSM living with HIV and HCV co-infection	50% of PHIV with HCV co-infection in care in Victoria[b]	Explore feasibility of primary care-based treatment of HCV for people with HIV compared with tertiary care, and measure population level impact of treatment scale up	Primary care, sexual health clinics and hospital clinic consultations	NA/6-monthly	✓	
AQUITAINE (France)	Multisite prospective hospital-based cohort (13 sites through South-Western France)	1987–ongoing/ July 2021	PHIV	85% of PHIV living in Nouvelle Aquitaine[c]	Explore clinical outcomes of participants with HIV/HCV co-infection compared with those with HIV monoinfection	Hospital consultations, day visits or hospitalizations in the infectious disease department	Annual/6–12 monthly[d]	✓ (Subset of patients)	✓ ICD-10

(continued)

Table 1. (continued)

Cohort (country)	Study design	Enrolment period/ database closure for Merge 1	Primary study population	Coverage of PHIV in care	Primary aims of the study	Cohort visit definition	Follow-up pre-HCV diagnosis/after treatment	Detailed longitudinal risk behaviour	Mortality availability and coding
SAIDCC: Saint-Antoine Infectious Disease Clinical Cohort (France)	Single-site (Paris) hospital and clinic-recruited prospective cohort	1992–2017/ December 2017	PHIV	35% in COREVIH Ile de France Centre[e]	Explore clinical outcomes of participants with HIV/HCV co-infection compared with those with HIV monoinfection	Hospital consultations day visits or hospitalizations in the infectious disease department	Annual/6–12 monthly[d]		✓ ICD-10
HEPAVIH: Clinical Centres Collaborations of Subjects co-infected with HIV and HCV (France)	Nationwide multisite prospective hospital-based cohort (29 sites)	2005–2015/ November 2019	PHIV with HCV co-infection	Unknown	To better define the natural history of HIV-HCV co-infection in terms of morbidity and mortality and its determinants, and to better understand the interactions between these two viruses and their treatments	The schedule of follow-up visits is based on clinical practice as recommended by the European consensus conferences on hepatitis C	NA/6–12 monthly[d]	✓ (Subset of patients)	✓ ICD-10
ATHENA: AIDS Therapy Evaluation in the Netherlands (Netherlands)	Nationwide prospective cohort	1998–ongoing/ February 2020	PHIV	98%	Initially (1998) study effect of triple cART. Subsequently, the HIV Monitoring Foundation was established to continue the registration and monitoring of all HIV-positive people as an integral part of HIV care in all 26 HIV treatment centres in The Netherlands	Scheduled standard of care visits to the outpatient clinic for PHIV in The Netherlands	Annual/varies by clinical signs		✓ CoDe[a]
MOSAIC: MSM Observational Study of Acute Infection with hepatitis C (Netherlands)	Multisite prospective comparative study with and without acute HCV	2009–18/ September 2018	MSM living with HIV[f]	Unknown	To study the sequelae of acute hepatitis C virus infection among HIV-infected individuals. Focus shifted to	Scheduled standard of care visits to the outpatient clinic for PHIV in The Netherlands	Six-monthly/ Six-monthly	✓	✓ CoDe[a]

(continued)

Table 1. (continued)

Cohort (country)	Study design	Enrolment period/ database closure for Merge 1	Primary study population	Coverage of PHIV in care	Primary aims of the study	Cohort visit definition	Follow-up pre-HCV diagnosis/after treatment	Detailed longitudinal risk behaviour	Mortality availability and coding
					study the interplay between HIV and acute HCV to understand the reasons for and consequences of HCV outbreak among MSM	(same as ATHENA)			
CoRIS: The cohort of Spanish HIV research network (Spain)	Nationwide multicentre prospective cohort	2004–ongoing/ December 2019	PHIV diagnosed with HIV from 2004 onwards and naive to ART at cohort enrolment	12% (~15 000 of ~130 000 in care)	To provide innovative procedures and reinforce structures that integrate epidemiological data, biological samples and data derived from medical care, to support public health actions to reduce mortality, morbidity and HIV transmissions	Scheduled standard of care visits to the outpatient clinic for PHIV in Spain	Annual/varies by clinical signs		✓ CoDe[a]
SHCS: Swiss HIV cohort study (Switzerland)	Nationwide prospective cohort	1988–ongoing/ January 2020	PHIV	71% patients on ART (59% estimated total PHIV population)	New focus—updated after 2009: co-medication and co-morbidities; impact of new HIV treatment strategies; STIs; immunological and human genome studies, HIV transmission and HIV cure; health economic assessments	Cohort visits scheduled every 6 months	6-monthly/ Six-monthly	✓	✓ CoDe[a]
CCC: Canadian Co-infection Cohort study (Canada)	Multisite prospective observational (18 clinical/community-based sites)	2003–ongoing/ August 2022	PHIV with HCV co-infection	15% of all co-infected patients in Canada	Initially to determine the effect of HAART progression to ESLD in HCV-HIV co-infection. Since	Visits are scheduled every 6 months (1 month) specifically for the study or incorporated into	NA/6-monthly	✓	✓ Modified CoDe[a]

(continued)

Table 1. (continued)

Cohort (country)	Study design	Enrolment period/ database closure for Merge 1	Primary study population	Coverage of PHIV in care	Primary aims of the study	Cohort visit definition	Follow-up pre-HCV diagnosis/after treatment	Detailed longitudinal risk behaviour	Mortality availability and coding
					2016, the primary focus has shifted to monitoring the scale-up and impacts of direct-acting antiviral (DAA) HCV treatment in co-infected Canadians	routine medical follow-up			

ART, antiretroviral therapy; cART, combination ART; COREVIH, Committee to coordinate the fight against sexually transmitted infections and HIV (the COREVIHs are governmental regional centres where PHIV are seen); DAA, direct-acting antivirals; ESLD, end-stage liver disease; HAART, highly-active antiretroviral therapy; HCV, hepatitis C virus; ICD-10, International Classification of Diseases 10th Revision; MSM, men who have sex with men; NA, not applicable; PHIV, people living with HIV; PWID, people who inject drugs; STI, sexually transmitted infection.

[a] Kowalska JD *et al*. The Coding causes Of Death in HIV (CoDe) Project. *Epidemiology* 2011; **22**:516–23.

[b] 66% of PHIV in care in the Australian State of Victoria in the ACCESS study who were diagnosed with HCV, and HCV RNA-positive at last test in March 2016, when DAA therapies became available. Estimated to be 50% of PHIV living with HCV in Victoria given ACCESS covers 75% of PHIV in Victoria.

[c] Cohort covers about 85% of PHIV in care in the Nouvelle Aquitaine region, i.e. patients from 18 of 23 hospitals/Corevih of the region—Corevih Nouvelle Aquitaine report 2021.

[d] Depending on level of risk.

[e] Based on 2017 governmental activity reports for the governmental regional centres where PHIV are seen (COREVIH) and from French Hospital Database on HIV.

[f] In addition to MSM, one woman was included in the MOSAIC cohort. All participants from MOSAIC are nested within the ATHENA cohort. Nine participants were included in both co-EC and CEASE cohorts. All participants from co-EC and 259 participants from CEASE are nested within the ACCESS study. Database closure date is last date the dataset was updated and/or last visit/laboratory measurement recorded in a cohort. References for the coverage of PHIV in care in each cohort: [23,33–38].

Table 2. Sociodemographic and clinical characteristics of 104 740 participants in the International Collaboration on Hepatitis C Elimination in HIV Cohorts (InCHEHC) at cohort enrolment

Characteristic	ACCESS ($n = 22\,033$)	AQUITAINE ($n = 9296$)	ATHENA ($n = 24\,785$)	CCC ($n = 2070$)	CEASE ($n = 402$)	Co-EC ($n = 200$)	CoRIS ($n = 16\,725$)	HEPAVIH ($n = 1723$)	MOSAIC ($n = 397$)	SAIDCC ($n = 7466$)	SHCS ($n = 20\,740$)
Age, years											
Median (IQR)	41 (32–49)	37 (30–46)	39 (32–47)	45 (39–52)	49 (43–55)	47 (41–55)	35 (29–43)	47 (43–52)	47 (41–54)	35 (30–42)	35 (29–43)
Missing	0	0	0	0	0	<5	0	0	0	767 (10.3%)	0
Age at HIV diagnosis, years											
Median (IQR)	41 (32–49)	32 (26–41)	36 (29–44)	34 (28–41)	32 (27–39)	33 (27–40)	34 (28–42)	28 (24–34)	37 (31–42)	32 (27–39)	32 (27–40)
Missing	0	0	69 (0.3%)	68 (3.3%)	21 (5.2%)	10 (5%)	0	7 (0.4%)	13 (3.3%)	206 (2.8%)	0
Sex at birth											
Female	1887 (9%)	2325 (25%)	4470 (18%)	585 (28%)	15 (4%)	<5	2460 (15%)	469 (27%)	<5	1717 (23%)	5582 (27%)
Male	20 016 (91%)	6971 (75%)	20 315 (82%)	1460 (71%)	382 (95%)	196 (98%)	14 265 (85%)	1252 (73%)	373 (94%)	5744 (77%)	15 158 (73%)
Unknown/missing	130 (1%)	0	0	25 (1%)	5 (1%)	<5	0	<5	23 (6%)	5 (<1%)	0
Key population[a]											
MSM	13 444 (61%)	3663 (39%)	15 072 (61%)	284 (14%)	162 (40%)	106 (53%)	10 346 (62%)	209 (12%)	384 (97%)	3999 (54%)	8350 (40%)
PWID	0	1838 (20%)	753 (3%)	1111 (54%)	42 (10%)	18 (9%)	1187 (7%)	1089 (63%)	<5	372 (5%)	3858 (19%)
MSM + PWID	0	116 (1%)	0	193 (9%)	175 (44%)	45 (22%)	0	65 (4%)	0	0	979 (5%)
Other/unknown	8589 (39%)	3679 (40%)	8960 (36%)	482 (23%)	23 (6%)	31 (16%)	5192 (31%)	360 (21%)	12 (3%)	3095 (41%)	7553 (36%)
Enrolment period											
Before 2005	0	5992 (64%)	8866 (36%)	136 (7%)	0	0	816 (5%)	0	0	3731 (50%)	13 390 (65%)
2005–09	10 091 (46%)	882 (9%)	5974 (24%)	794 (38%)	0	0	4883 (29%)	1175 (68%)	39 (10%)	1167 (16%)	2810 (14%)
2010–15	6801 (31%)	888 (10%)	5822 (23%)	501 (24%)	89 (22%)	0	5614 (34%)	220 (13%)	280 (71%)	1239 (17%)	2592 (12%)
2016–19	4427 (20%)	1329 (14%)	4113 (17%)	540 (26%)	313 (78%)	198 (99%)	5412 (32%)	328 (19%)	78 (20%)	562 (8%)	1947 (9%)
2020 onwards	714 (3%)	205 (2%)	10 (<1%)	99 (5%)	0	0	0	0	0	0	<5
Missing	0	0	0	0	0	<5	0	0	0	767 (10%)	0
HCV status[b]											
Negative	8677 (39%)	4893 (53%)	20 129 (81%)	0	0	0	13 891 (83%)	0	0	2680 (36%)	10 423 (50%)
Positive	823 (4%)	1341 (14%)	1716 (7%)	2070 (100%)	402 (100%)	200 (100%)	1615 (10%)	1723 (100%)	204 (51%)	246 (3%)	2444 (12%)
Unknown	12 533 (57%)	3062 (33%)	2940 (12%)	0	0	0	1219 (7%)	0	193 (49%)	4540 (61%)	7873 (38%)
CD4 T cell count, cells/mm^3[c]											
Median (IQR)	510 (349–703)	380 (192–597)	390 (218–580)	420 (260–610)	598 (449–812)	596 (438–782)	395 (214–590)	483 (323–684)	579 (440–744)	395 (238–563)	353 (180–560)
Missing	8303 (37.7%)	353 (3.8%)	305 (1.2%)	35 (1.7%)	30 (7.5%)	25 (12.5%)	141 (0.8%)	<5	9 (2.3%)	4266 (57.1%)	702 (3.4%)
Detectable HIV viral load[cd]											
No	2419 (11%)	2689 (29%)	7542 (30%)	1497 (72%)	345 (86%)	172 (86%)	879 (5%)	1465 (85%)	355 (89%)	664 (9%)	3974 (19%)
Yes	2179 (10%)	2686 (29%)	16 411 (66%)	476 (23%)	34 (8%)	14 (7%)	15 699 (94%)	255 (15%)	39 (10%)	1870 (25%)	9380 (45%)
Missing	17 435 (79%)	3921 (42%)	832 (3%)	97 (5%)	23 (6%)	14 (7%)	147 (1%)	<5	<5	4932 (66%)	7386 (36%)
ART experienced[e]											
No	0	5913 (64%)	24 305 (98%)	197 (10%)	25 (6%)	<5	2404 (14%)	49 (3%)	23 (6%)	521 (7%)	6698 (32%)
Yes	22 033 (100%)	3383 (36%)	480 (2%)	1848 (89%)	377 (94%)	191 (96%)	14 321 (86%)	1674 (97%)	374 (94%)	6414 (86%)	5013 (24%)
Missing	0	0	0	25 (1%)	0	6 (3%)	0	0	0	531 (7%)	9029 (44%)

ACCESS, Australian Collaboration for Coordinated Enhanced Sentinel Surveillance; AQUITAINE, ANRS CO3 AQUITAINE/AquiVIH-NA; ATHENA, AIDS Therapy Evaluation in the Netherlands; CCC, Canadian co-infection Cohort study; CD4 T-cell count, CD4 cluster of differentiation 4; CEASE, Control and Elimination within AuStralia of HEpatitis C from people living with HIV; co-EC, Eliminating hepatitis C transmission by enhancing care and treatment among HIV co-infected individuals; CoRIS, The cohort of Spanish HIV research network; HCV, hepatitis C virus; HEPAVIH, Clinical Centres Collaborations of Subjects co-infected with HIV and HCV; IQR, interquartile range; MOSAIC, MSM Observational Study of Acute Infection with hepatitis C; MSM, men who have sex with men; PWID, people who inject drugs (lifetime or active); SAIDCC, Saint-Antoine Infectious Disease Clinical Cohort; SHCS, Swiss HIV cohort study.

[a] To define key population, individuals were classified as MSM based on the recorded mode of HIV or HCV transmission or, for cohorts with available data, sexual orientation. Individuals were classified as PWID based on recorded mode of HIV or HCV transmission. Subsequently, individuals classified as both MSM and PWID were classified as MSM+PWID.

[b] HCV-positive status based on a (previous) positive HCV antibody or RNA test result within 1 year of enrolment or first visit date. HCV-negative status based on recorded HCV antibodies only. For the MOSAIC cohort, individuals categorized as 'Unknown' were the controls and known to be HCV RNA- or antibody-negative.

[c] Value at a maximum of 1 year before or after enrolment.

[d] Detectable viral load defined as >200 copies/mL.

[e] Ever on antiretroviral treatment before or at enrolment.

(*n* = 6/11). A total of 104 740 InCHEHC participants have been followed for over 791 884 person-years (PY) from cohort enrolment until their last recorded study visit. Median follow-up was 7 years [interquartile range (IQR) = 2, 12], ranging from 4.6 years in CoRIS to 6.8 years in the SHCS (Figure 1A).

The frequency of visits per individual differs per cohort, and predominantly follows the European or Australian standard of care guidelines for people with HIV (Table 1). Overall, the median number of study visits was 19 (IQR = 7, 39), ranging from 1.0 (IQR = 1.0, 16.0) in SAIDCC to 31.0 (IQR = 11.0, 63.0) in ACCESS (Figure 1B). ACCESS captures routine visits from multiple clinics and hospitals, including visits with the GP (general practitioner), outside HIV-related clinical visits. This is different from the other cohorts, and explains why there are more visits per person in ACCESS than other studies.

Loss to follow-up: drop-out and mortality

We used two approaches to define loss to follow-up (LTFU): one mainly based on each cohort's approach to define LTFU (called cohort classification), and a standardized definition across cohorts based on a participant not being seen for more than 2 years since their last study visit at the date of cohort-specific dataset closure (called 2-year gap classification). LTFU definitions are described in detail in the Supplementary Material (available as Supplementary data at *IJE* online). Figure 2 depicts the annual rate of loss to follow-up using the two approaches to calculate the number of events and follow-up time.

Based on the 2-year gap classification, a total of 17 554 individuals were considered LTFU, and an additional 13 310 were known to have died by the end of cohort data collection. When restricting data between 2010 and 2018—during which period all cohorts had started enrolment and sufficient follow-up was available considering the cohort's database closure date and our LTFU defintions–the rate of LTFU was 2.3 per 100 PY in 2010 [95% confidence interval (CI) = 2.1, 2.4] and 4.3 per 100 PY in 2018 (95% CI = 4.0, 5.9). Both approaches to classifying LTFU led to relatively similar rates of LTFU across all years, except for 2018 (Table 1), as using the cohort classification definition many participants were classified as LTFU in 2018 because of subsequent missed visits during the COVID-19 pandemic. LTFU rates per country are shown in Supplementary Figure S1 (available as Supplementary data at *IJE* online).

The crude mortality rate between 2010 and 2019 was 1.0 per 100 PY (95%CI = 0.9, 1.0), declining between 2010 and 2013 and remaining stable afterwards. Crude mortality rates were highest in Canada (i.e. the Canadian co-infection Cohort) in all calendar years compared with the other countries, which may be explained by the higher proportion of current or former people who inject drugs (PWID) than in other cohorts (Supplementary Figure S2, available as Supplementary data at *IJE* online, Table 2).

Differences among those lost to follow-up compared with those remaining in the cohort

Table 3 presents sociodemographic and clinical differences at enrolment between individuals LTFU and those known to have died combined (LTFU based on the 2-year gap classification) and those on active follow-up. Compared with those in active follow-up, those LTFU or who had died were more often PWID (20.9% vs 5.0%), from Switzerland (32.2%), enrolled before 2005 (53.0%), were antibody- and/or RNA-

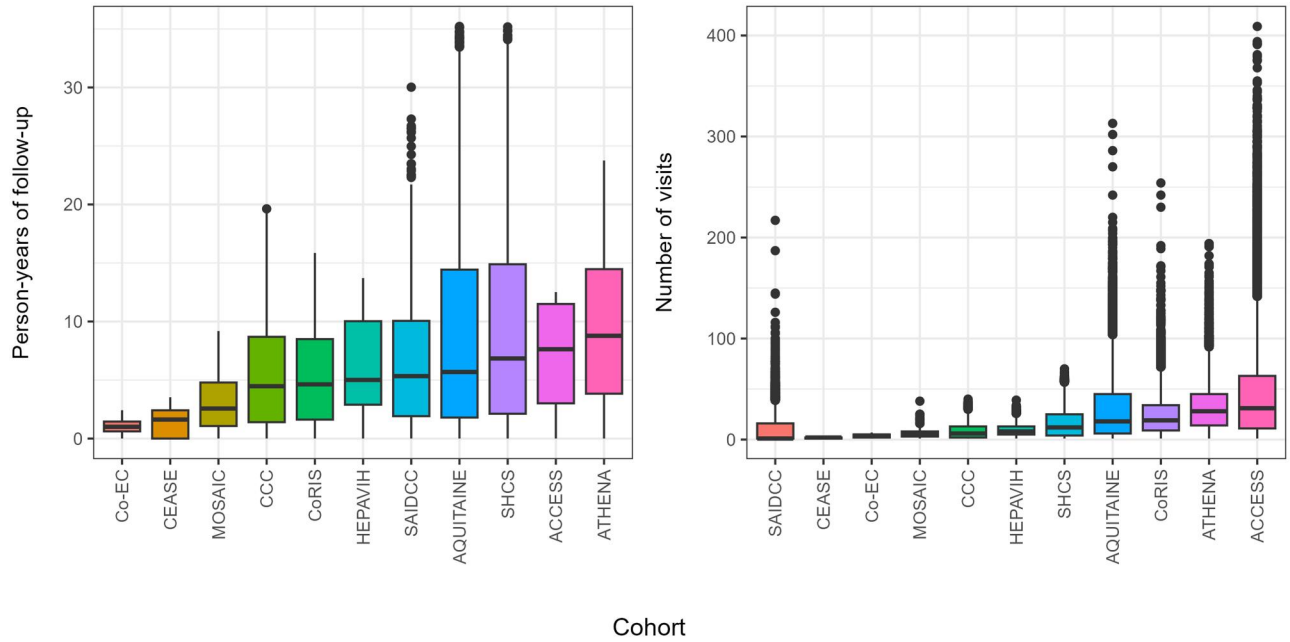

Figure 1. Distributions of person-years of follow-up and study visits in the International Collaboration on Hepatitis C Elimination in HIV Cohorts (InCHEHC), stratified by cohort. Box plots have been ordered in ascending order of the median follow-up time (Panel A) and median number of visits per individual (Panel B). Visits included those occurring from cohort enrolment onwards. ACCESS, Australian Collaboration for Coordinated Enhanced Sentinel Surveillance; co-EC, Eliminating hepatitis C transmission by enhancing care and treatment among HIV co-infected individuals; CEASE: Control and Elimination within AuStralia of HEpatitis C from people living with HIV; CCC, Canadian co-infection Cohort study; MOSAIC, MSM Observational Study of Acute Infection with hepatitis C; HEPAVIH, Clinical Centres Collaborations of Subjects co-infected with HIV and HCV; SHCS, Swiss HIV cohort study; ATHENA, AIDS Therapy Evaluation in the Netherlands; SAIDCC, Saint-Antoine Infectious Disease Clinical Cohort; CoRIS, the cohort of Spanish HIV research network; AQUITAINE, ANRS CO3 AQUITAINE/AquiVIH-NA

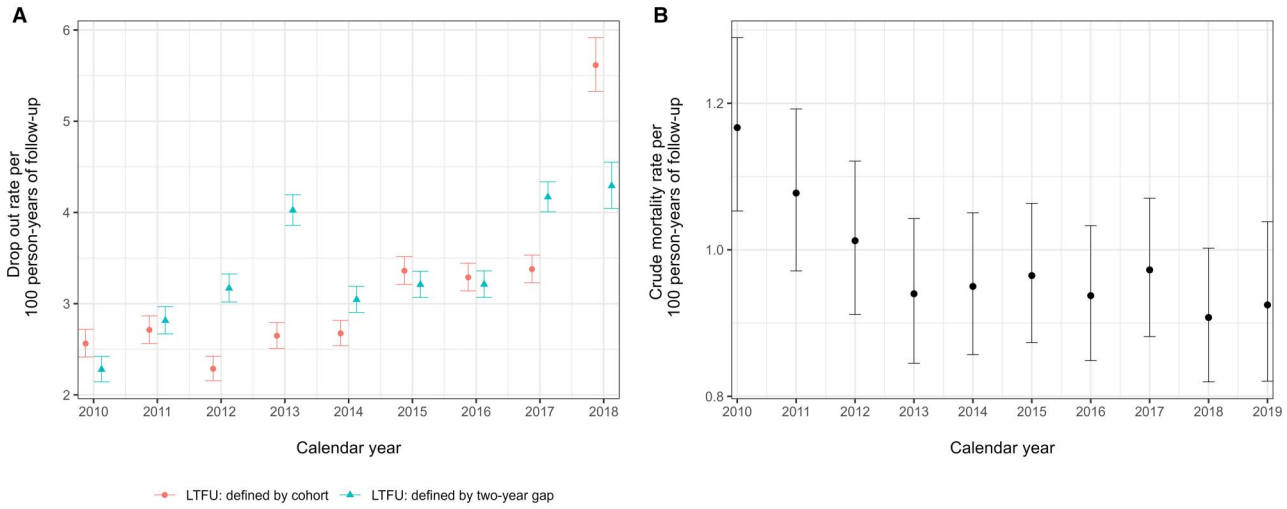

Figure 2. (A) Annual rate of loss to follow-up (LTFU) in the International Collaboration on Hepatitis C Elimination in HIV Cohorts (InCHEHC) using two approaches to calculate follow-up time and the number of events; and (B) annual crude mortality rate using data from cohorts systematically collecting mortality data. Panel A: Loss to follow up calculation based on two approaches to calculate the event and person-years. Panel B: Australia was excluded from this graph due to lack of systematic collection of mortality data. Follow-up started at study enrollment and ended at last known date to be alive or at death date for those who died. Data are shown until the year most cohorts provided data (i.e. 2019), except for SAIDCC providing data until the end of 2017. ACCESS, Australian Collaboration for Coordinated Enhanced Sentinel Surveillance; co-EC, Eliminating hepatitis C transmission by enhancing care and treatment among HIV co-infected individuals; CEASE, Control and Elimination within AuStralia of HEpatitis C from people living with HIV; CCC, Canadian co-infection Cohort study; MOSAIC, MSM Observational Study of Acute Infection with hepatitis C; HEPAVIH, Clinical Centres Collaborations of Subjects co-infected with HIV and HCV; SHCS, Swiss HIV cohort study; ATHENA, AIDS Therapy Evaluation in the Netherlands; SAIDCC, Saint-Antoine Infectious Disease Clinical Cohort; CoRIS, the cohort of Spanish HIV research network; AQUITAINE, ANRS CO3 AQUITAINE/AquiVIH-NA

positive (18.4% vs 9.1%) and had a lower median CD4 T cell count (340 vs 430 cells/mm^3).

Missing data

Missing data at enrolment on selected sociodemographic and clinical variables for all participants are described in Table 2. Of particular interest are variables relating to HCV antibody and RNA testing to determine current or past HCV status and to monitor changes in HCV prevalence and incidence.

Among those enrolled after 2004, the proportion without recorded HCV tests was 30.5% (n = 15 633/51 211) in 2005–09, 25.1% (n = 18 832/74 881) in 2010–14 and 26.6% (n = 24 839/93 538) in 2015–19. Of those previously HCV antibody-negative, 6.2% in 2010–14 and 10.8% in 2015–19 did not have a subsequent antibody test in the following calendar period (Figure 3).

Deaths are systematically recorded in a subset of studies (Table 1). LTFU may include deaths in other studies. LTFU was based on the 2-year gap classification as described in the LTFU section of this manuscript. Individuals from the Australian cohorts co-EC and CEASE and the Dutch cohort MOSAIC were excluded as they overlap with a nationwide dataset from Australia (ACCESS) and The Netherlands (ATHENA), respectively.

What has been measured?

InCHEHCs's data dictionary was developed to answer questions relating to HCV elimination. Our data harmonization tool is based on the well-established and longstanding HIV Cohorts Data Exchange Protocol (HICDEP) used previously by several HIV-related international collaborations and on a behavioural data harmonization process based on an international collaboration of injecting cohorts.[39] We used this tool to assess each cohort's data format, data quality, and consistency with the proposed InCHEHC format, while resolving any discrepancies. A subset of behavioural variables were asked similarly across the cohorts (e.g. alcohol use). Where methodological differences between cohorts exist (e.g. recall period), we collected cohort-level variables specifying these differences, to enable sensitivity analysis.

Each cohort study team prepared and submitted data to the coordinating centre (Burnet Institute) based on HICDEP for HIV collaborations (version 1.100). The following HICDEP data tables were collected for all studies: tblBAS, tblART, tblLAB, tblLAB_CD4, tblLAB_RNA, tblLAB_VIRO, tblLTFU and tblVIS. The HICDEP table tblOVERLAP was collected for the following overlapping cohorts: SAIDCC and HEPAVIH from France; ATHENA and MOSAIC from The Netherlands; and CEASE, co-EC and ACCESS from Australia. The HICDEP tool was adapted to meet InCHEHC data availability and format, to facilitate data management across cohorts and to collect only data necessary to answer the research questions in line with our ethics approvals. In addition to these HICDEP tables, we collected sociodemographic and behavioural data available from selected cohorts based on a behavioural data harmonization process from the international collaboration of injecting cohorts.[39] Time-updated data were collected on housing, alcohol use (AUDIT-C), drug use (including recent use, injecting and non-injecting drug use and frequency of use, needle and syringe sharing and specific data on the type of drug used or injected), and male-to-male sexual behaviour (including casual and steady partners, sex with people living with HIV and/or HCV, condomless anal sex and group sex). Behavioural variables were selected for inclusion in the consortium data request if they were available for at least three participating cohorts. We also created a table to collect transient elastography data (tblFIBRO) and added new variables in tblMED and tblVIS to obtain additional details (e.g.HCV medication completion). An overview of data collected is provided in Table 4.

Table 3. Characteristics at enrolment of participants in the International Collaboration on Hepatitis C Elimination in HIV Cohorts (InCHEHC) on active follow-up vs those lost to follow-up (LTFU) or known to have died.

Characteristic	Active follow-up ($n = 64\,017$)	LTFU or died ($n = 30\,833$)
Age, years		
Median (IQR)	38 (31–47)	36 (30–45)
Missing	0	0
Sex at birth		
Female	11 177 (17%)	6566 (21%)
Male	52 734 (82%)	24 231 (79%)
Unknown/missing	106 (<1%)	36 (<1%)
Key population[a]		
MSM	37 912 (59%)	11 938 (39%)
PWID	3195 (5%)	6431 (21%)
MSM + PWID	374 (1%)	952 (3%)
Other/unknown	22 536 (35%)	11 512 (37%)
Country		
Australia	15 839 (25%)	5052 (16%)
Canada	840 (1%)	1123 (4%)
France	7847 (12%)	6097 (20%)
Spain	10 710 (17%)	3957 (13%)
Switzerland	9935 (16%)	9938 (32%)
The Netherlands	18 846 (29%)	4666 (15%)
Enrolment period		
Before 2005	13 177 (21%)	16 339 (53%)
2005–09	19 436 (30%)	8139 (26%)
2010–15	18 086 (28%)	5288 (17%)
2016–19	13 296 (21%)	1062 (3%)
2020 onwards	22 (<1%)	5 (<1%)
Missing	0	0
HCV antibody status		
Negative	42 805 (67%)	13 307 (43%)
Positive	5830 (9%)	5673 (18%)
Unknown	15 382 (24%)	11 853 (38%)
CD4 T cell count, cells/mm^3		
Median (IQR)	430 (260–620)	340 (164–548)
Missing	6434 (10.1%)	3242 (10.5%)
Detectable HIV viral load[b]		
No	14 396 (22%)	5313 (17%)
Yes	33 585 (52%)	12 155 (39%)
Missing	16 036 (25%)	13 365 (43%)
ART-experienced[c]		
No	26 053 (41%)	11 623 (38%)
Yes	36 082 (56%)	12 277 (40%)
Missing	1882 (3%)	6933 (22%)

Individuals from the Australian cohort co-EC and CEASE and the Dutch cohort MOSAIC were excluded as they overlap with nationwide dataset from Australia (ACCESS) and The Netherlands (ATHENA).
CD4 T cell count: CD4 cluster of differentiation 4; IQR, interquartile range; MSM, men who have sex with men; PWID, people who inject drugs (lifetime or active).
[a] To define key population, individuals were classified as MSM based on recorded mode of HIV or HCV transmission, or sexual orientation. Individuals were classified as PWID based on recorded mode of HIV or HCV transmission. Subsequently, individuals classified as both MSM and PWID were classified as MSM + PWID.
[b] Detectable viral load defined as >200 copies/mL.
[c] Ever on antiretroviral treatment before or at enrolment.

In Table 5, we characterize cohort participants according to HCV (i.e. RNA and genotype) and liver-related [e.g. Fibrosis-4 score (FIB-4)] testing outcomes at enrolment and during follow-up among 18 495 participants ever testing HCV antibody- or RNA-positive during follow-up. In all cohorts, 13 299 (71.9%) participants had at least one HCV RNA test result; median time between the closest positive RNA test result and enrolment was 1.1 year (IQR = 0.0, 4.9). From the first positive test onwards (i.e. during follow-up), the median number of HCV RNA tests since first HC-(antibody or RNA)-positive test and the last visit with a recorded HCV test was 5.0 (IQR = 0.0, 4.9), and was highest in MOSAIC, likely as this cohort included participants with acute HCV between 2009 and 2018 when DAAs became increasingly available and due to retrospective testing. The proportion of participants with at least one HCV genotype result varied per cohort and ranged from 27.1% in AQUITAINE to 99.0% in co-EC. A total of 12 339 (66.7%) had at least one FIB-4 score and 6816 (36.9%) at least one transient elastrography measurement by FibroScan after their first HCV-positive test. The French cohort AQUITAINE and the Australian cohort ACCESS did not collect FibroScan measurements. For the French cohort HEPAVIH and the Australian cohort CEASE, no FIB-4 scores could be calculated. Among cohorts collecting FIB-4 and FibroScan data, 75.4% of participants had at least one FIB-4 score and 41.4% of participants at least one FibroScan measurement.

What has been found? Key findings and publications

InCHEHC's first collaborative project was an overview of linkage and retention in care of HIV/HCV-co-infected groups in the early DAA era (i.e. 2014–17).[40] The study found HCV treatment uptake had increased after DAA treatment became available, but by 2017, approximately half of diagnosed patients remained untreated. Among those who had initiated treatment, 96% completed treatment and 93% achieved sustained virological response 12 or more weeks (SVR12+) following the end of DAA treatment.

Since then a data merge was conducted, enabling more detailed analyses of changes in HCV incidence associated with DAA introduction, failure to achieve HCV cure and understanding the characteristics of PHIV who remain untreated in the DAA era. Key findings include the following.

Primary infection and reinfection HCV incidence

Using data from six out of 11 cohorts, 45, 942 participants at risk of primary infection were followed over 248, 189 PY, with an overall primary infection incidence of 0.82 per 100 PY (95%CI = 0.78, 0.86) between 2010 and 2019.[41] Using data from eight of 11 cohorts to assess changes in HCV reinfection, 6,144 participants were followed for 17, 303 PY, with an overall incidence of reinfection of 3.7 per 100 PY (95%CI = 3.4, 4.0).[42] Both primary infection and reinfection incidences decreased over calendar years; broad and unrestricted access to DAA treatment was associated with a decline in primary HCV incidence, indicative of a treatment-as-prevention effect.

Unsuccessful direct-acting antiviral hepatitis C treatment

Using data from nine out of 11 cohorts from six countries, 4554 people had DAA treatment data. Failure to achieve HCV cure was observed among 5.5% (212/3844) of individuals who had initiated DAA treatment and had an SVR12+ RNA test.[43]

Reasons for not commencing direct-acting antivirals despite unrestricted access for people with HIV

Using data from nine out of 11 cohorts from six countries, a total of 4552 individuals who were HCV RNA-positive and

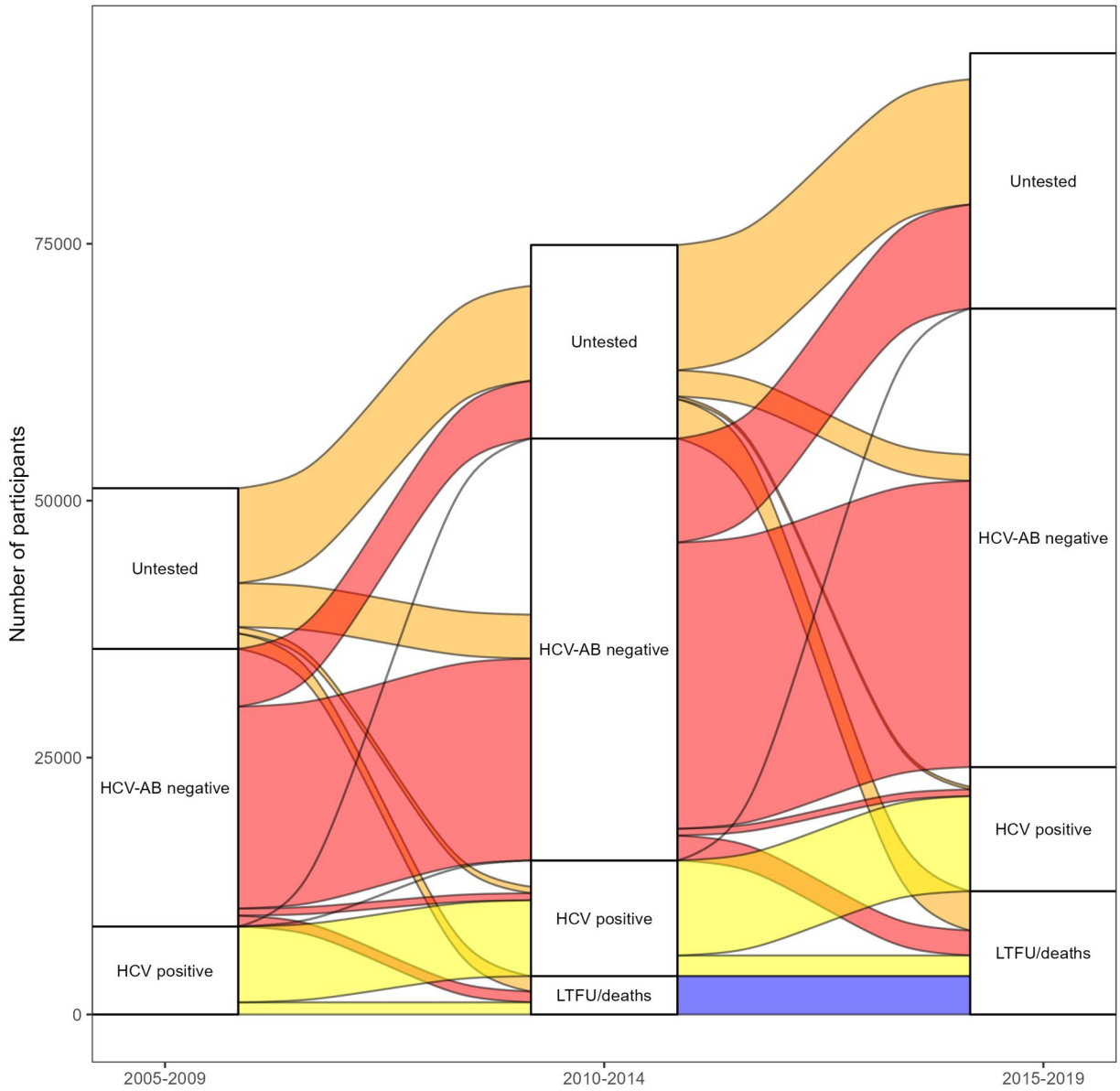

Figure 3. Flow diagram of HCV testing in the International Collaboration on Hepatitis C Elimination in HIV Cohorts (InCHEHC) between 2005 and 2019. The coloured streams represent changes over time in HCV testing/diagnosis status among individuals in follow-up in each calendar period, including those newly enrolled. The colour orange represents the change in HCV status in the subsequent calendar period among those classified as untested. The colour red represents the change in HCV status in the subsequent calendar period among those classified as HCV antibody-negative. The colour yellow represents the change in HCV status in the subsequent calendar period among those classified as HCV-positive. Lost to follow-up (LTFU)/death is represented in purple. HCV, hepatitis C virus; AB, antibody; HCV-positive, past or current HCV antibody or RNA positive test, HCV status, based on final HCV test within the study period; untested, no HCV test within the 5-year period and no previous HCV antibody-positive result; LTFU, lost to follow-up

had follow-up data during the period when DAA were broadly accessible were included. Despite unrestricted access to DAAs, 30% of individuals with HIV/HCV remained DAA-untreated during follow-up.[44]

Summary of key findings

In summary, HCV incidence declined during broad access to DAA therapy, consistent with a treatment-as-prevention effect. Although HCV reinfection incidence did not decline as much as primary infection, with many additional people becoming at risk of reinfection following their treatment, combined HCV incidence (including primary and reinfection incidence) still declined during broad access to DAAs. Treatment uptake was initially high in InCHEHC countries but it has declined over time, and more research is required to determine whether this will lead to stabilized HCV incidence, thereby failing to meet WHO targets. Although the vast majority of PHIV treated were cured, approximately 5% were not cured and 30% remain untreated.

Key questions that are currently under investigation include the following

- Does the frequency of HCV antibody and RNA testing of those at risk of HCV infection differ between countries, and what is the impact on time to diagnosis of primary HCV infection and HCV reinfection?
- Has DAA introduction been associated with reductions in HCV-related mortality and how has this differed between countries?

Table 4. Overview of data collected by the International Collaboration on Hepatitis C Elimination in HIV Cohorts (InCHEHC) consortium, Merge 1

Broad category	Time point collected	Key variables collected
Demographics	Cohort enrolment	Age, sex, gender identity (including transgender), sexual orientation, route of HIV and HCV infections, country of birth, ethnicity, education
Clinical	Time updated	Hepatitis C treatment, cirrhosis diagnosis, HIV antiretroviral treatment, Fibroscan, opiate pharmacotherapy, BMI
Biological	Time updated	HCV antibodies and RNA, HCV genotype, HIV antibodies and RNA, CD4, ALT, AST, platelets, syphilis testing
Housing situation and behaviour[a]	Time updated	Housing situation, drug use and frequency (i.e. heroin, other opioids, methamphetamine, cocaine, Ecstasy/MDMA, amphetamine, benzodiazepine, cannabis and other), receptive syringe sharing, alcohol use (recent use, frequency and drinks per session and more than six drinks per session based on AUDIT-C), male-to-male sexual behaviour (recent and type, e.g. casual) number of sexual partners, known recent and type HCV and HIV sexual partners, recent condomless sex [CAS], type of partners related to recent CAS and group sex)

ALT, alanine transaminase; AST, aspartate aminotransferase; AUDIT-C, Alcohol Use Disorders Identification Test-Concise; BMI, body mass index; CD-4, cluster of differentiation 4; HCV, hepatitis C virus; MDMA, 3,4-methylenedioxymethamphetamine.

[a] The period to which behavioural variables refer to differs by cohort (e.g. since last visit, in the previous 6 months). Behavioural variables were collected by a subset of cohorts, with the level of detail varying between cohorts; each variable collected by the consortium was collected by at least three participating cohorts.

- Which sociodemographic, clinical and behavioural factors drive new HCV reinfections in the DAA era?
- Is DAA treatment associated with liver fibrosis regression, and how does this vary over time after cure?
- Has the prevalence of current HCV infections among individuals with HIV changed over calendar time?
- Does the proportion of current injection drug use among men who have sex with men living with HIV differ by country and has it changed over calendar time?

What are the main strengths and weaknesses?

Strengths

InCHEHC countries were selected because they have broad availability of DAA therapies and health systems facilitating broad testing, treatment, surveillance and research, and are able to examine the role of HCV diagnosis and DAA treatment on achieving HCV elimination targets. The large pooled dataset allows us to study uncommon outcomes (e.g. reinfection and failure to achieve HCV cure) which pose a threat to achieving HCV elimination, including disaggregation by participant characteristics and changes over time in these outcomes. In particular, cohorts collecting detailed HCV-related behavioural data are usually smaller cohorts, often lacking power to perform some analyses. Therefore, we have pooled behavioural data from a subset of cohorts to be able to perform analysis to understand the impact of HCV-related behaviours on hepatitis C reinfection and assess changes in behavioural trends over time, among other factors. Moreover, using two LTFU definitions, annual attrition (including loss-to-follow-up and mortality) is less than 5 per 100 PY per year between 2010 and 2018, which could be considered low.

Weaknesses

Currently we only collect data from cohorts following individuals in high-income countries and findings cannot be generalized to low- or middle-income countries. The study design and coverage of the PHIV population differ between cohorts; hence caution must be taken when comparing results across cohorts/countries and, in some instances, analyses may need to be restricted to selected cohorts/countries. For example, some cohorts include national data among most PHIV in care and others collect data within a smaller sample, including only individuals with HIV and HCV. Furthermore, most data are routinely collected clinical data. HIV- and HCV-related guidelines advise on regular and systematic testing and screening (although this may differ by HCV risk profile) but these guidelines may not be followed systematically across cohorts. A limited number of cohorts collect detailed behavioral data and most cohorts that do collect behavioural data are HIV/HCV co-infection cohorts; hence potential adjustments for confounding related to certain behaviours cannot be made for all analyses, nor can we assess their impact on certain outcomes (e.g. risk of HCV primary infection). Given that behavioural data are not available for all cohorts, classification of key populations is based on the mode of HIV and HCV transmission and, for cohorts with available data, data on sexual orientation. Hence, for cohorts without data on sexual orientation, mode of HCV and HIV transmission is used for key population classification, and we may be misclassifying individuals to either PWID or men who have sex with men rather than the combined group.

Can I get hold of the data? Where can I find out more?

Data requests are welcome subject to approval by the study steering committee. Requests and enquiries should be directed to the data coordinator: Rachel Sacks-Davis [rachel.sacks-davis@burnet.edu.au].

Ethics approval

All cohorts received approval from their regulatory or national ethics committees (Supplementary Material, available as Supplementary data at *IJE* online). The Alfred Hospital Ethics Committee (Melbourne, Australia) granted ethics approval for InCHEHC (reference number 662/18).

Data availability

See 'Can I get hold of the data?' above.

Table 5. Selected characteristics and hepatitis C/liver related follow-up data among 18 495 HCV antibody- and/or RNA-positive participants in the International Collaboration on Hepatitis C Elimination in HIV Cohorts (InCHEHC)

	ACCESS ($n = 2109$)	AQUITAINE ($n = 2087$)	ATHENA ($n = 3013$)	CCC ($n = 2070$)	CEASE ($n = 402$)	Co-EC ($n = 198$)	CoRIS ($n = 2047$)	HEPAVIH ($n = 1723$)	MOSAIC ($n = 223$)	SAIDCC ($n = 495$)	SHCS ($n = 4128$)
Time point: at enrolment											
Age, years											
Median (IQR)	45 (37–51)	36 (31–43)	42 (36–48)	45 (39–52)	49 (43–55)	47 (41–56)	41 (35–46)	47 (43–52)	45 (40–51)	42 (36–48)	36 (31–41)
Missing	0	0	0	0	0	0	0	0	0	0	0
Sex at birth											
Female	101 (5%)	596 (29%)	448 (15%)	585 (28%)	15 (4%)	<5	417 (20%)	469 (27%)	<5	90 (18%)	1285 (31%)
Male	1992 (94%)	1491 (71%)	2565 (85%)	1460 (71%)	382 (95%)	194 (98%)	1630 (80%)	1252 (73%)	206 (92%)	405 (82%)	2843 (69%)
Unknown/missing	16 (1%)	0	0	25 (1%)	5 (1%)	<5	0	<5	16 (7%)	0	0
Key population[a]											
MSM	1419 (67%)	268 (13%)	1649 (55%)	284 (14%)	162 (40%)	106 (54%)	566 (28%)	209 (12%)	215 (96%)	261 (53%)	607 (15%)
PWID	0	1259 (60%)	704 (23%)	1111 (54%)	42 (10%)	18 (9%)	1000 (49%)	1089 (63%)	<5	100 (20%)	2184 (53%)
MSM + PWID	0	54 (3%)	0	193 (9%)	175 (44%)	45 (23%)	0	65 (4%)	0	0	573 (14%)
Other/unknown	690 (33%)	506 (24%)	660 (22%)	482 (23%)	23 (6%)	29 (15%)	481 (23%)	360 (21%)	7 (3%)	134 (27%)	764 (19%)
HCV RNA status											
Negative	326 (15%)	115 (6%)	300 (10%)	228 (11%)	19 (5%)	0	171 (8%)	294 (17%)	53 (24%)	42 (8%)	186 (5%)
Positive	1282 (61%)	400 (19%)	1525 (51%)	1153 (56%)	59 (15%)	198 (100%)	926 (45%)	1233 (72%)	146 (65%)	310 (63%)	860 (21%)
Missing	501 (24%)	1572 (75%)	1188 (39%)	689 (33%)	324 (81%)	0	950 (46%)	196 (11%)	24 (11%)	143 (29%)	3082 (75%)
Follow up since first HCV-positive test, years											
Median (IQR)	6 (2–9)	5 (1–14)	7 (3–12)	5 (2–9)	2 (0–2)	1 (1–2)	5 (1–9)	5 (3–10)	5 (3–7)	5 (2–9)	8 (3–17)
Missing	0	0	0	0	0	0	0	0	0	0	0
Time point: during follow-up since first positive test until last HCV-related measurement											
Any HCV RNA tests											
Yes	1827 (87%)	1170 (56%)	2562 (85%)	1882 (91%)	282 (70%)	179 (90%)	1620 (79%)	1689 (98%)	217 (97%)	327 (66%)	2828 (69%)
No	282 (13%)	917 (44%)	451 (15%)	188 (9%)	120 (30%)	19 (10%)	427 (21%)	34 (2%)	6 (3%)	168 (34%)	1300 (31%)
Number of RNA tests											
Median (IQR)	4 (2–7)	4 (2–10)	6 (3–11)	5 (2–11)	1 (1–2)	3 (2–4)	3 (1–7)	7 (4–11)	10 (5–17)	5 (2–10)	4 (2–9)
Missing	282 (13.4%)	917 (43.9%)	451 (15%)	188 (9.1%)	120 (29.9%)	19 (9.6%)	427 (20.9%)	34 (2%)	6 (2.7%)	168 (33.9%)	1300 (31.5%)
Any HCV genotype test											
Yes[b]	607 (29%)	566 (27%)	2041 (68%)	1699 (82%)	313 (78%)	196 (99%)	1133 (55%)	1701 (99%)	184 (83%)	190 (38%)	2105 (51%)
No	1502 (71%)	1521 (73%)	972 (32%)	371 (18%)	89 (22%)	<5	914 (45%)	22 (1%)	39 (17%)	305 (62%)	2023 (49%)
Number of HCV genotype tests											
Median (IQR)	1 (1–1)	1 (1–2)	1 (1–2)	1 (1–1)	1 (1–1)	1 (1–1)	1 (1–1)	1 (1–1)	1 (1–2)	1 (1–1)	1 (1–2)
Missing	1502 (71.2%)	1521 (72.9%)	972 (32.3%)	371 (17.9%)	89 (22.1%)	<5	914 (44.7%)	22 (1.3%)	39 (17.5%)	305 (61.6%)	2023 (49%)
Any FIB-4 scores[c]											
Yes	263 (12%)	2063 (99%)	2642 (88%)	2023 (98%)	0	189 (95%)	1701 (83%)	0	213 (96%)	370 (75%)	2875 (70%)
No	1846 (88%)	24 (1%)	371 (12%)	47 (2%)	402 (100%)	9 (5%)	346 (17%)	1723 (100%)	10 (4%)	125 (25%)	1253 (30%)
Number of FIB-4 scores[c]											
Median (IQR)	3 (1–5)	21 (6–46)	18 (7–37)	7 (3–14)	NA	4 (2–5)	11 (5–23)	NA	21 (13–28)	19 (7–34)	20 (9–28)
Missing	1846 (87.5%)	24 (1.1%)	371 (12.3%)	47 (2.3%)	402 (100%)	9 (4.5%)	346 (16.9%)	1723 (100%)	10 (4.5%)	125 (25.3%)	1253 (30.4%)
Any Fibroscans											
Yes	0	0	1093 (36%)	929 (45%)	370 (92%)	179 (90%)	970 (47%)	1606 (93%)	119 (53%)	174 (35%)	1376 (33%)
No	2109 (100%)	2087 (100%)	1920 (64%)	1141 (55%)	32 (8%)	19 (10%)	1077 (53%)	117 (7%)	104 (47%)	321 (65%)	2752 (67%)

In co-EC, the HCV RNA positive test at enrolment was not always recorded and 68 participants were retrospectively enrolled, hence although no RNA test was recorded, the HCV RNA status is assumed to be positive as this was an inclusion criterion. Moreover, two participants were/became HCV RNA-positive before between their first visit and the enrolment visit.
ACCESS, Australian Collaboration for Coordinated Enhanced Sentinel Surveillance; AQUITAINE, ANRS CO3 AQUITAINE/AquiVIH-NA; ATHENA, AIDS Therapy Evaluation in the Netherlands; CCC, Canadian co-infection Cohort study; CEASE, Control and Elimination within AuStralia of HEpatitis C from people living with HIV; co-EC, Eliminating hepatitis C transmission by enhancing care and treatment among HIV co-infected individuals; CoRIS, The cohort of Spanish HIV research network; FIB-4, Fibrosis 4; HEPAVIH, Clinical Centres Collaborations of Subjects co-infected with HIV and HCV; IQR, interquartile range; MOSAIC, MSM Observational Study of Acute Infection with hepatitis C; MSM, men who have sex with men; PWID, people who inject drugs (lifetime or active); SAIDCC, Saint-Antoine Infectious Disease Clinical Cohort; SHCS, Swiss HIV cohort study; any and number of tests, between first positive HCV test date or enrolment if HCV positive test prior to enrolment and last recorded laboratory measurement.

[a] To define key population, individuals were classified as MSM based on their recorded mode of HIV or HCV transmission, or sexual orientation. Individuals were classified as PWID based on their recorded mode of HIV or HCV transmission. Subsequently, individuals classified as both MSM and PWID were classified as MSM + PWID.

[b] First HCV RNA-positive test within 6 months on or after the first HCV-positive test or cohort enrolment in HIV/HCV co-infection cohorts and if first positive test was prior to cohort enrolment.

[c] FIB-4 scores were calculated based on available data provided by the cohorts on: age, aspartate transaminase (AST), platelet count and (alanine transaminase) ALT levels.

Supplementary data

Supplementary data are available at *IJE* online.

Author contributions

D.K.vS. and R.S-D.: Writing—original draft, conceptualization, visualization, data curation, project administration, methodology, software, formal analysis, funding acquisition. J.Y.: conceptualization, methodology, writing—review and editing. A.S.: project administration, data curation, writing—review and editing. J.A., C.S., A.B., M.vV., A.R., C.M., I.J., J.B., K.L., L.W., O.L., D.S., F.B., G.M., J.S.D., M.B.K., M.P., M.A.S.: conceptualization, resources, writing—review and editing. M.H.: conceptualization, resources, supervision, funding acquisition, writing—review and editing.

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Conflict of interest

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