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MAJOR ARTICLE

Microelimination of Hepatitis C Among People With Human Immunodeficiency Virus Coinfection: Declining Incidence and Prevalence Accompanying a Multicenter Treatment Scale-up Trial

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Background. Gay and bisexual men (GBM) are a key population affected by human immunodeficiency virus (HIV) and hepatitis C virus (HCV) coinfection. We aimed to measure HCV treatment effectiveness and to determine the population impact of treatment scale-up on HCV prevalence and incidence longitudinally among GBM.

Methods. The co-EC Study (Enhancing Care and Treatment Among HCV/HIV Coinfected Individuals to Eliminate Hepatitis C Transmission) was an implementation trial providing HCV direct-acting antiviral treatment in Melbourne, Australia, during 2016–2018. Individuals with HCV/HIV coinfection were prospectively enrolled from primary and tertiary care services. HCV viremic prevalence and HCV antibody/viremic incidence were measured using a statewide, linked, surveillance system.

Results. Among 200 participants recruited, 186 initiated treatment during the study period. Sustained virological response in primary care (98% [95% confidence interval {CI}, 93%–100%]) was not different to tertiary care (98% [95% CI, 86%–100%]). From 2012 to 2019, between 2434 and 3476 GBM with HIV infection attended our primary care sites annually, providing 13 801 person-years of follow-up; 50%–60% received an HCV test annually, and 10%–14% were anti-HCV positive. Among those anti-HCV positive, viremic prevalence declined 83% during the study (54% in 2016 to 9% in 2019). HCV incidence decreased 25% annually from 1.7/100 person-years in 2012 to 0.5/100 person-years in 2019 (incidence rate ratio, 0.75 [95% CI, .68–.83]; $P < .001$).

Conclusions. High treatment effectiveness by nonspecialists demonstrates the feasibility of treatment scale-up in this population. Substantial declines in HCV incidence and prevalence among GBM provides proof-of-concept for HCV microelimination.

Clinical Trials Registration. NCT02786758.

Keywords. hepatitis C; elimination; treatment; HIV coinfection.

Chronic hepatitis C virus (HCV) infection is a significant health problem globally for individuals living with human immunodeficiency virus (HIV) infection. There are estimated to be 2.3 million people living with HIV/HCV coinfection worldwide, and 37 million people living with HIV infection are at significantly greater risk of HCV acquisition compared to individuals not living with HIV [1]. HIV infection has been associated with more rapid progression to HCV-related liver disease and increased risk for liver fibrosis and cirrhosis [2, 3]. Since the early 2000s, increasing numbers of HCV infections among gay and bisexual men (GBM) living with HIV have been reported, including outbreaks in Europe [4–7], the United States [8], and Australia [9–12] that have been attributed to sexual transmission, and in particular, high-risk sexual practices. These outbreaks mostly occurred in a setting of increased access to antiretroviral therapy (ART) for HIV and reduced condom use prior to access to direct-acting antiviral (DAA) therapy for HCV.

In Australia, most jurisdictions reported increased diagnoses of HCV among people with HIV infection, mostly among GBM in the past decade [12, 13]. The state of Victoria has the second largest number of people living with HIV (PLWH) in

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Australia, with the majority in metropolitan Melbourne, and GBM account for >80% of this population. Due to enhanced efforts to scale up HIV care to meet the Fast Track City targets for HIV, >95% of PLWH in Victoria are engaged regularly with healthcare (www.fast-trackcities.org/cities/victoria, accessed 12 June 2019), in particular via primary care practitioners who provide the bulk of our HIV services. In similar settings globally, this key population could rapidly be engaged in HCV treatment [14, 15].

In an effort to eliminate HCV as a public health threat in line with the World Health Organization (WHO) 2030 targets, the Australian government made DAA therapy available to all people with chronic infection, including people with HIV coinfection and people who inject drugs, starting in March 2016 [16]. Despite primary care practitioners prescribing HIV treatment for many years, HCV treatment prescribing was uncommon in primary care, non–hepatitis specialist settings before then. Within the country-level targets set by WHO, the rapid reduction in HCV incidence in key populations or defined geography has been dubbed microelimination [15, 17–19]. A government-funded sentinel surveillance system (Australian Collaboration for Coordinated Enhanced Sentinel Surveillance [ACCESS] [20]) in place before DAA treatment access measures long-term trends in blood-borne virus prevalence and incidence in Australia, including HCV. Given the high degree of healthcare engagement of PLWH, publicly funded and community-based DAA prescribing, and surveillance systems to monitor impact, HIV/HCV microelimination became a realistic and measurable goal in our setting.

The Enhancing Care and Treatment Among HCV/HIV Coinfected Individuals to Eliminate Hepatitis C Transmission (co-EC) Study investigated HCV treatment effectiveness and population impact among PLWH in Melbourne. It had 2 co-primary aims: (1) to encourage HCV DAA treatment and determine treatment outcome to demonstrate treatment feasibility in real-world primary and tertiary care settings in PLWH; and (2) to report the population impact of HCV testing and treatment on prevalent and new HCV infections over time.

METHODS

Study Design

The co-EC Study was a clinician-directed, open-label, nonrandomized study of HCV DAA implementation across 2 tertiary and 4 primary care clinics in Melbourne from 2016 to 2018. The study protocol and reporting followed the Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) statement [21] and was registered before commencement at ClinicalTrials.gov (identifier NCT02786758).

Study Setting

The study involved high-HIV and high-GBM caseload general practitioner–run clinics and the statewide sexual health service, and 2 major academic hospitals providing care for PLWH in Melbourne, Australia. More than 85% of all HIV-infected GBM in our jurisdiction are seen at the primary and tertiary health services involved in this project [22], making us well placed to scale up HCV treatment and measure potential microelimination of HCV/HIV coinfection.

Study Intervention

The co-EC study implemented a nurse-led, clinician-directed, model of care across all sites to increase complete HCV diagnosis (antibody and RNA) and prescription of HCV DAA treatment among PLWH. Trained nurses experienced in HCV care attended all primary care services to support primary care HIV practitioners; their role was to facilitate participant assessment and treatment commencement, and to increase capacity of local staff around management of HCV infection. Hepatitis specialist advice (for drug interactions or elevated aspartate aminotransferase-to-platelet ratio index) or formal referral (for cirrhosis or serious comorbidities) was protocolized. All participants received open-label HCV treatment selected by their treating clinicians, within national licensing and government funding rules. Clinicians could prescribe any combination and duration of HCV antiviral therapy approved for use in Australia.

Eligibility Criteria and Recruitment

Any individual living with HCV/HIV coinfection aged >18 years and attending 1 of the study sites for HIV care was eligible to participate and was screened. Participants required evidence of chronic HCV infection (HCV antibody or RNA positive for ≥6 months and HCV RNA positive at screening). Full eligibility and study assessments are outlined in the Supplementary Methods.

Study Assessments and Data Collection

To measure participant outcomes, assessments included clinical review, behavioral questionnaires, and blood samples at screening, on treatment, and posttreatment for 48 weeks, in keeping with standard of care at the time. To measure the impact of treatment scale-up on HCV transmission at a population level, we accessed HCV and HIV testing data from the ACCESS surveillance system [20], which uniquely captures and links primary care services and laboratory testing data across our jurisdiction, and captures positive and negative HCV test information.

Outcome and Analyses

Objective 1: Treatment Success

The primary treatment outcome was the proportion of participants with a sustained virological response >12 weeks after

treatment (SVR_{12+}) using any licensed HCV RNA test. Failure to achieve SVR_{12+} was categorized into treatment failure or reinfection using genotype and/or sequencing data. New HCV RNA positivity after SVR_{12+} was also evaluated for reinfection, and the reinfection rate was calculated using person-time among all people from end of treatment to last available HCV RNA–negative result (or first HCV RNA–positive result if reinfected).

Statistical Analyses. Descriptive proportions for SVR_{12+} using modified intention-to-treat (any participant receiving 1 DAA dose) and per-protocol methods are reported for the whole cohort. Comparison of SVR_{12+} proportion by primary or tertiary care site used χ^2 tests.

Objective 2: Population Impact

The primary population outcomes were HCV RNA prevalence (approximated by annual proportion positive) and HCV incidence among PLWH in Victoria.

HCV Prevalence and Testing Definitions. Using the ACCESS surveillance data from primary care services included in the co-EC Study, annual HCV antibody prevalence was calculated among all PLWH in care with at least 1 HCV test result during each year between 2012 and December 2019. Annual HCV RNA prevalence was calculated among HCV-antibody/HIV-positive individuals with at least 1 HCV RNA test result during each year. Additionally, we assessed the annual proportion of HCV-negative/unknown GBM receiving any kind of HCV test between 2012 and 2019. To assess differences in HCV testing over calendar years, logistic regression models were used accounting for repeated measurement of individuals using robust standard errors.

HCV Incidence Definition. HCV incidence was determined as the number of (1) newly detected HCV RNA or (2) HCV antibody–positive cases occurring among all HCV antibody–negative/HIV-positive individuals in care between 2012 until December 2019. The midpoint date between the last HCV antibody–negative and first HCV-positive results was used as the estimated date of HCV infection. Individuals were considered at risk of HCV infection from the time of their first HCV antibody–negative result. Follow-up continued until the estimated date of HCV infection or last recorded HCV antibody–negative result.

Statistical Analyses

Changes in HCV incidence over time were assessed using Poisson regression. We assessed whether calendar year had a linear association with HCV incidence by comparing the fit of a model including calendar year as a linear term, and a model that included a nonlinear term for calendar year using restricted cubic splines [23]. For illustration purposes, we plotted the predicted HCV incidence from the model using restricted cubic splines with 4 knots at 2-year intervals starting in 2012. The impact of DAA introduction on the HCV incidence trends was modeled as an interaction with calendar time.

Sample Size and Ethics

Our target sample size for the treatment intervention was based on the estimated number of HCV/HIV-coinfected GBM who attended the clinical sites involved in this study (see Supplementary Methods). The study was approved by the Alfred Health Human Research Ethics Committee (HREC 56/16), and all participants provided written informed consent.

RESULTS

Recruitment and Baseline Characteristics

Two hundred PLWH were enrolled in the co-EC Study, of whom 197 of 200 reported male sex at birth and 92% were GBM, with a median age of 47 years (interquartile range [IQR], 41–55 years) (Table 1). Of the 200 participants, 198 had confirmed HCV viremia (2 participants spontaneously cleared at treatment commencement; Figure 1). Almost all (98%) participants were on ART, and 91% had an undetectable HIV viral load for a median of 6.5 years (IQR, 2.3–11 years) at baseline.

At treatment commencement, 67% reported ever injecting drugs, of whom 33% had injected in the past month (all used methamphetamine use); 55% reported any substance use in the past month; and 40% reported ever sharing needles, syringes, or equipment (Table 1). Most participants (125/191 [65%]) reported sex with men in the previous 6 months, of whom 106 (83%) reported sex with at least 1 casual partner. Most men with casual sex partners reported inconsistent condom use 62 (76%), and 40 (49%) reported group sex.

Ninety-four percent of 186 HCV-viremic participants started treatment (67% genotype 1; 28% genotype 3; 16% peginterferon-based treatment experienced; Table 2). Prescribing choices reflected the drugs available through Australia's Pharmaceutical Benefit Scheme at the time of the study; ledipasvir/sofosbuvir (46%) and sofosbuvir plus daclatasvir (47%) were the most commonly prescribed regimens (Table 2). Overall treatment commencement (186/198) did not vary by site (93% in primary care vs 94% in tertiary care) (Table 3).

Objective 1: SVR_{12+} Outcome

Among 186 starting treatment, 173 had documented completion of therapy (7 individuals were lost to care, and 6 discontinued prematurely [1 discontinuation was clinician directed for adverse effects]). In an intention-to-treat analysis including all participants who were prescribed therapy in the denominator, SVR_{12+} was achieved in 156 of 186 (83.4% [95% confidence interval {CI}, 77.8%–88.9%]). Among participants completing treatment, attending the SVR_{12+} visit, and with HCV RNA data (per-protocol analysis, n = 163), 160 (98.2% [95% CI, 94.4%–99.6%]) achieved SVR_{12+}. There was no difference in primary care or tertiary care outcomes in either intention-to-treat (84%

Table 1. Baseline Sociodemographic, Clinical, and Behavioral Characteristics of 200 co-EC (Enhancing Care and Treatment Among HCV/HIV Coinfected Individuals to Eliminate Hepatitis C Transmission) Study Participants

Characteristic	No.	(%)
Sociodemographic characteristics		
Male sex	197	(98.5)
Age, y, median (IQR)	47	(41–55)
Higher education	101	(59.1)
Not employed	77	(45.0)
Behavioral characteristics[a]		
Substance use[b]		
Substance use in the past month	89	(54.6)
Ever injected drugs	113	(67.3)
Ever shared needles[c]	40	(40.0)
Injected drugs in the last month[c]	37	(33.0)
Alcohol consumption in the past 12 months		
Any alcohol consumption	132	(77.7)
Hazardous alcohol consumption[d,e]	16	(12.2)
Drinks ≥6 drinks at a time monthly or more[d]	30	(22.9)
Sexual risk in the past 6 months		
Men reporting sex with men	102	(65.0)
Inconsistent condom use with casual partners[f]	62	(76.5)
Involved in group sex[f]	40	(49.4)
HCV mode of infection		
Sexual contact with person of same sex	73	(36.5)
Injecting drug use	61	(30.5)
Blood transfusion and blood products	4	(2.0)
Tattoo and body piercing	3	(1.5)
Other	9	(4.5)
Not reported or unknown	50	(25.0)
Clinical characteristics		
Current psychiatric disorder	66	(33.0)
Current opiate substitution therapy use	5	(3.0)
HIV-related characteristics		
Current antiretroviral therapy use	195	(97.5)
Virologically suppressed	177	(91.2)
Time virally suppressed, y, median (IQR)	6.5	(2.3–11)
Current HBV infection[g]	5	(2.6)

Data are presented as no. (%) unless otherwise indicated.

Abbreviations: HBV, hepatitis B virus; HCV, hepatitis C virus; HIV, human immunodeficiency virus; IQR, interquartile range.

[a]Among participants who completed the enrollment behavioral survey (n = 175). Percentages do not include missing values.

[b]Substance use defined as any of the following: heroin, speed, ice, methadone, other opioids, ecstasy/MDMA, cannabis, cocaine, γ-hydroxybutyrate, ketamine, amyl/poppers, Suboxone, benzodiazepines, other drug.

[c]Among individuals reporting ever injection drug use.

[d]Among those reporting alcohol consumption in the last 12 months.

[e]Defined as >4 drinks for men and >2 drinks for women in a typical day when drinking.

[f]Among individuals reporting any casual partner in the last 6 months.

[g]Hepatitis B virus surface antigen positive; all individuals were receiving HIV treatment that included hepatitis B antiviral activity.

vs 83%, respectively; $P = .782$) or per-protocol analyses (98.2% vs 97.8%, respectively; $P = .862$) (Table 3). Three treatment failures were all due to early treatment discontinuation; only 1 was clinician directed.

Three individuals had a confirmed reinfection within 121.5 person-years (PY) of follow-up after end of treatment. Median follow-up after the end of treatment among 147 participants with an HCV-negative result at end of treatment was 10.8 months (IQR, 6.1–13.4 months). Three reinfected participants had detectable HCV RNA at or after SVR_{12} and were virologically confirmed (2 documented change in genotype; 1 through sequencing at NS3/5/core region). The observed reinfection rate was 2.5 (95% CI, .8–7.7) per 100 PY. All reinfection cases reported sexual or injecting risk behavior post-SVR_{12}, but there were insufficient events to explore predictors of reinfection.

Objective 2: Population Prevalence and Incidence Outcome

Testing data from the ACCESS surveillance system from 2012 to 2019 showed there were 4735 individual GBM living with HIV at the primary care sites in the co-EC study. Between 2434 and 3476 GBM living with HIV were engaged in care in each calendar year, of whom between 2218 and 3083 GBM living with HIV did not have confirmed HCV infection The proportion susceptible to HCV (ie, without detectable HCV RNA) receiving a test remained relatively stable over time, with a peak in testing in 2017 (Supplementary Figure 1). Between 50% and 60% GBM living with HIV attending our services received

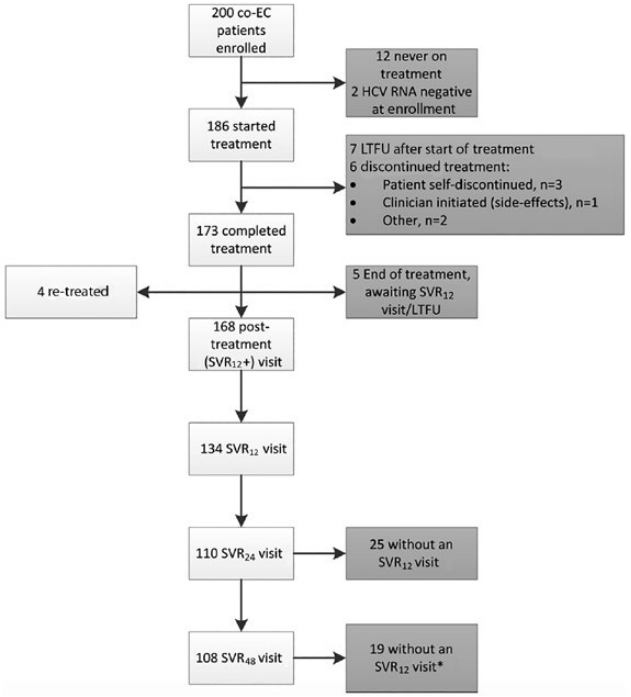


Figure 1. Flowchart of study participants. *Overlap between 10 patients with sustained virological response visits at both 24 weeks (of the 25 patients) and 48 weeks (of the 19 patients) and no sustained virological response visit at 12 weeks. Abbreviations: co-EC, Enhancing Care and Treatment Among HCV/HIV Coinfected Individuals to Eliminate Hepatitis C Transmission; HCV, hepatitis C virus; HIV, human immunodeficiency virus; LTFU, lost to follow-up; SVR_{12}, sustained virological response 12 weeks after treatment; SVR_{12+}, sustained virological response >12 weeks after treatment; SVR_{24}, sustained virological response 24 weeks after treatment; SVR_{48}, sustained virological response 48 weeks after treatment.

Table 2. Treatment Characteristics and Outcomes Among 198 co-EC (Enhancing Care and Treatment Among HCV/HIV Coinfected Individuals to Eliminate Hepatitis C Transmission) Study Participants With Chronic Hepatitis C Virus Infection

Characteristic	No.	(%)
HCV genotype		
1	132	(67.0)
2	4	(2.0)
3	55	(27.9)
4	4	(2.0)
6	2	(1.0)
Estimated years since HCV diagnosis, median (IQR)	6.0	(2–13)
Liver stiffness measurement, kPa, median (IQR)	5.6	(4.7–7.3)
Treatment site		
Tertiary care	62	(31.3)
Primary care, sexual health clinic	39	(19.7)
Primary care, general practice	97	(49.0)
Previous HCV therapy		
Yes	31	(15.8)
Type of treatment (n = 186)		
Ledipasvir/sofosbuvir	85	(46.5)
Sofosbuvir + daclatasvir	86	(47.0)
Sofosbuvir + ribavirin	2	(1.1)
Ombitasvir/paritaprevir/dasabuvir ± ribavirin	1	(0.6)
Sofosbuvir/velpatasvir	9	(4.9)
Treatment outcomes		
SVR_{12+} among patients who started treatment	156/186	(83.9)
SVR_{12+} among patients with an SVR_{12+} visit and HCV RNA data	160/163	(98.2)
SVR_{12+} among genotype 1	110/113	(97.3)
SVR_{12+} among genotype 3	43/44	(97.7)
SVR_{12+} among other genotypes	6/6	(100)

Data are presented as no. (%) unless otherwise indicated. Percentages do not include missing values. Missing values: HCV genotype, n = 1; estimated time since HCV diagnosis, n = 8; HCV RNA result at an SVR_{12+} visit, n = 3; liver stiffness measurement, n = 18.

Abbreviations: HCV, hepatitis C virus; HIV, human immunodeficiency virus; IQR, interquartile range; SVR_{12+}, sustained virological response >12 weeks after treatment.

an HCV antibody and/or HCV RNA test each calendar year (Figure 2A). Of the 4735 GBM living with HIV, 606 (12.8%) were never tested for HCV antibody or RNA.

Table 3. Treatment Outcomes in the co-EC (Enhancing Care and Treatment Among HCV/HIV Coinfected Individuals to Eliminate Hepatitis C Transmission) Study, by Site

Outcome	Primary Care	Tertiary Care
Treatment uptake, No. (%)	128/138 (92.8)	58/62 (93.5)
Specialist referral required, No. (%)[a]		
No specialist input needed	42 (31.3)	Not applicable
Specialist advice only	51 (38.1)	Not applicable
Specialist referral	41 (30.1)	Not applicable
SVR_{12+} (per protocol)[b]	114/116 (98.2)	46/47 (97.9)
SVR_{12+} (intention to treat)[c]	108/128 (84.4)	48/58 (82.8)

Abbreviations: HCV, hepatitis C virus; HIV, human immunodeficiency virus; SVR_{12+}, sustained virological response >12 weeks after treatment.

[a]Among 134 individuals with available data at enrollment.

[b]Per protocol: out of those participants who completed treatment, had an SVR_{12+} visit, and had HCV RNA data.

[c]Modified intention to treat: out of those participants who started treatment.

Among GBM living with HIV, the proportion who had an HCV antibody or RNA test over time also varied only slightly, with a peak in 2016 and 2017 coinciding with DAA availability (Figure 2B). Between 10% and 14% of GBM with HIV had detectable HCV antibodies and/or RNA (Figure 2A). However, of those with detectable HCV antibodies, the proportion that were HCV RNA positive declined dramatically from 60% in 2015 (prior to co-EC Study and DAA access) to 54% in 2016, 20% in 2017, and 9% in 2019 (Figure 2B). This corresponded to an 83% reduction in the proportion viremic from 2016 to 2018 in the full years after the co-EC Study commenced.

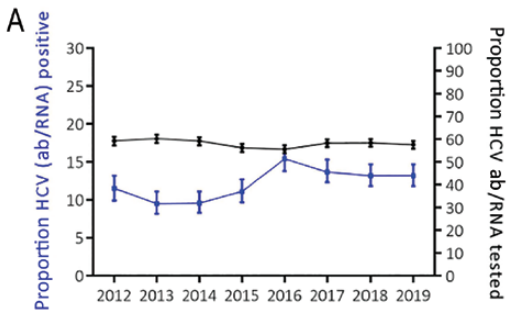
Among GBM with HIV infection at risk for HCV infection, 112 new HCV infections were observed over a total of 13 801 PY of follow-up. The overall incidence rate over the study period was 0.81 (95% CI, .67–.98) per 100 PY. Prior to co-EC Study and DAA access, incidence in primary care was 1.12 (95% CI, .84–1.84) per 100 PY in 2015, compared with 0.24 (95% CI, .06–.95) per 100 PY in 2019. Incident infection among those attending primary care sites from 2012 to 2019 declined significantly by 25% annually from 2012 until the end of 2019 (incidence rate ratio, 0.75 [95% CI, .68–.83]; $P < .001$) (Figure 3). The interaction term between calendar year and DAA availability was not significant ($P = .929$).

DISCUSSION

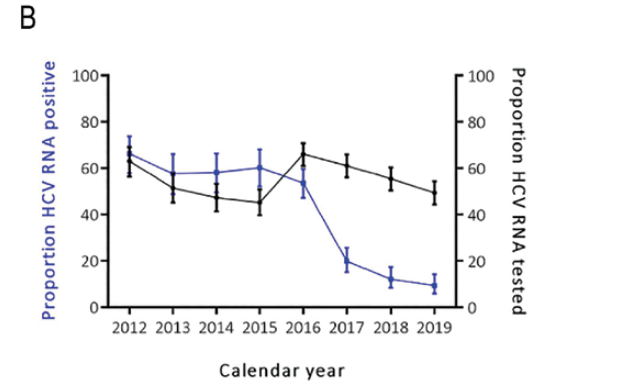
The co-EC Study showed that HCV treatment was safe and highly effective in a real-world cohort of PLWH. Treatment uptake and cure rates were substantial and equivalent in specialist and primary care settings. Despite HCV/HIV coinfection historically requiring specialist management, our findings add valuable evidence that most PLHW receiving DAA treatment for their HCV can be managed in primary care settings [24]. Furthermore, this study with longitudinal surveillance offers empirical evidence that scaling up treatment for HCV in individuals coinfected with HIV may reduce prevalent infection and new primary infections with the associated potential to eliminate HCV/HIV coinfection in GBM as a public health threat, consistent with WHO 2030 targets.

A marked decline in chronic HCV prevalence was observed directly following the co-EC Study period. HCV incidence was declining before and continued to decline after this intervention. Some of this early incidence decline was likely due to increased HCV awareness among PLWH, prevention efforts around safer sex health promotion, and limited DAA treatment uptake via clinical trials and early access schemes preceding government subsidization. The observed fall in HCV incidence from 1.2/100 PY prior to the study in 2015 to 0.23/100 PY after the study in 2019 is highly encouraging. Broad treatment access from 2016 may have contributed to ongoing decline in HCV incidence and may help achieve and sustain microelimination.

The co-EC study population captured the majority of HCV/HIV-coinfected individuals in metropolitan Victoria, providing



	2012	2013	2014	2015	2016	2017	2018	2019
Total tested	1440	1605	1733	1690	1766	1947	2003	1997
Total positive	222	246	276	314	368	371	388	395
Total HIV+	2434	2668	2932	3008	3180	3345	3435	3476



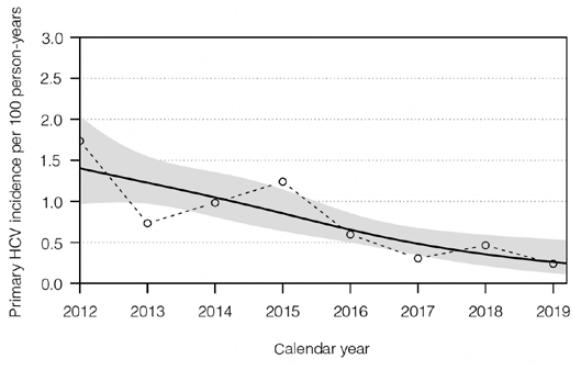
	2012	2013	2014	2015	2016	2017	2018	2019
Total tested	136	125	129	141	241	226	214	194
Total positive	90	72	75	85	129	45	26	18
Total HIV+ (Ab+)	1440	1605	1733	1690	1766	1947	2003	1997

Figure 2. Hepatitis C virus (HCV) testing and HCV exposure among all gay and bisexual men (GBM) living with human immunodeficiency virus (HIV) (*A*) and among hepatitis C virus (HCV) antibody (Ab)–positive GBM with HIV (*B*), by calendar year in primary care. *A*, HCV RNA and/or Ab testing among HIV-positive GBM (black bars/line) and HCV RNA–positive and/or Ab-positive HIV-positive GBM tested for HCV RNA (blue bars/line). Note that the scales in the right and left axis differ. *B*, HCV RNA testing among all HIV-positive GBM (black bars/line) and HCV RNA positive among those with HCV RNA tested (blue bars/line). *P* values for calendar year were obtained using logistic regression models accounting for repeated measurements; calendar year was included as a categorical variable. The overall *P* value for calendar year was $P < .001$ for all proportions related to testing shown above.

a unique opportunity to achieve microelimination of HCV among HIV-coinfected GBM. Because the study was conducted in conjunction with the expansion of ACCESS, a strength of the study was the ability to measure the impact of the treatment not only on individual participants, but also HCV incidence and proportion positive (which closely approximated prevalence) among the wider GBM HIV-infected population. ACCESS collects HIV and HCV testing and treatment data from all primary care sites involved in the study. A further strength of our study is that by using HCV test records linked at an individual patient level from ACCESS, it was possible to assess new (incident) HCV infection and avoid double-counting of positive test records across and within health services.

Microelimination of HCV/HIV coinfection has been identified as a feasible strategy to achieve HCV targets globally [17–19]. Many cities or jurisdictions with similar HCV/HIV epidemics are working toward similar goals [14, 25, 26]. High HCV treatment uptake and cure among PLWH is a key requirement for driving HCV treatment-as-prevention microelimination outcomes. Our finding that most people screened and testing HCV positive will go on to treatment in a real-world clinic setting confirms findings from other jurisdictions [27]. High-risk sexual and injecting behavior is common among GBM living with HIV and HCV in many, but not all, high-income settings [28]. Yet these behavioral risks did not appear to be a barrier to treatment commencement or treatment success. Moreover, modeling of sexual behavior in HCV/HIV populations suggests that, in situations of greater variability in risk behavior and clusters of very high-risk HCV transmission risk, there is even greater population health benefit from high levels of treatment [29].

There are a few factors that may limit the generalizability of this study. First, the cohort was largely engaged with care, indicated by nearly the entire cohort being successfully virologically suppressed on HIV ART. While typical of GBM living with HIV in Australia [22], these attributes make our population easier to engage in HCV care and potentially harder to reproduce globally. That said, our results may be generalizable to other cities in high-income settings with access to highly subsidized healthcare and medications. Second, broad government- or insurance-funded DAA access is a key ingredient to achieve similar treatment uptake



	2012	2013	2014	2015	2016	2017	2018	2019
Primary infections	27	13	19	25	12	6	8	2
Person-years at risk	1554	1771	1931	2015	2012	1959	1722	834

Figure 3. Hepatitis C virus (HCV) incidence per calendar year (2012–2019) among gay and bisexual mean living with human immunodeficiency virus in primary care. Circles denote the observed incidence by calendar year; solid line represents primary HCV incidence trend by calendar year; and shaded area represents the 95% confidence interval.

in key populations. Fortunately, many high-income and some middle-income countries, along with insurance systems such as the United States Veterans Administration, now provide DAA access. A third limitation is that despite being a real-world cohort, the nursing support at each site to train staff and educate participants contributed to the high treatment uptake, cure, and relatively small losses to follow up (up to 15%). Nevertheless, task-shifting away from specialist-led to nurse-led care may add clinical benefits and cost-savings: it strengthens the case for feasibility and efficiency of nurse-led HCV care. Not all settings will have access to this resource; however, as our results suggest, if directed at targeted populations, such support might only be required for a short period.

In summary, the co-EC Study provides evidence that treatment scale-up in defined populations can rapidly lead to declines in HCV prevalence, and suggests that further declines in HCV incidence may follow, which are necessary precursors to achieve global HCV elimination targets. GBM living with HIV report high sexual and injecting risk behavior, making rapid treatment scale-up essential to avoid ongoing HCV transmission as part of comprehensive programs aimed at reducing drug use and sexual risk behavior along with frequent sexually transmitted infection and HCV testing. Furthermore, given risk behaviors observed and ongoing new infections, these data suggest that once HCV disease burden is lowered in any jurisdiction, ongoing vigilance will be required to ensure that HCV prevalence and incidence remain controlled in this key population.

Supplementary Data

Supplementary materials are available at *Clinical Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Notes

Author contributions. Guarantor: J. S. D. Study design and concept: J. S. D., D. I., J. S., M. O., J. R., M. E. H. Data collection: J. S. D., D. I., J. S., M. O., J. R., R. W., J. C. C., A. L. B., N. M., R. M., B. T., C. K. F., J. A., C. E., J. F. H., and M. E. H. Data analysis and interpretation: J. S. D., D. K. v. S., M. W. T., B. H., M. A. S., M. E. H. Manuscript preparation and critical revision: all authors. All authors approved the final submitted version.

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References

1. Platt L, Easterbrook P, Gower E, et al. Prevalence and burden of HCV co-infection in people living with HIV: a global systematic review and meta-analysis. Lancet Infect Dis **2016**; 16:797–808.
2. Farahani M, Mulinder H, Farahani A, Marlink R. Prevalence and distribution of non-AIDS causes of death among HIV-infected individuals receiving antiretroviral therapy: a systematic review and meta-analysis. Int J STD AIDS **2017**; 28:636–50.
3. de Ledinghen V, Barreiro P, Foucher J, et al. Liver fibrosis on account of chronic hepatitis C is more severe in HIV-positive than HIV-negative patients despite antiretroviral therapy. J Viral Hepat **2008**; 15:427–33.
4. Ghosn J, Deveau C, Goujard C, et al. Increase in hepatitis C virus incidence in HIV-1-infected patients followed up since primary infection. Sex Transm Infect **2006**; 82:458–60.
5. Rauch A, Rickenbach M, Weber R, et al; Swiss HIV Cohort Study. Unsafe sex and increased incidence of hepatitis C virus infection among HIV-infected men who have sex with men: the Swiss HIV Cohort Study. Clin Infect Dis **2005**; 41:395–402.
6. Danta M, Brown D, Bhagani S, et al; HIV and Acute HCV (HAAC) Group. Recent epidemic of acute hepatitis C virus in HIV-positive men who have sex with men linked to high-risk sexual behaviours. AIDS **2007**; 21:983–91.
7. van de Laar TJ, van der Bij AK, Prins M, et al. Increase in HCV incidence among men who have sex with men in Amsterdam most likely caused by sexual transmission. J Infect Dis **2007**; 196:230–8.
8. Centers for Disease Control and Prevention. Sexual transmission of hepatitis C virus among HIV-infected men who have sex with men—New York City, 2005–2010. Atlanta, GA: CDC, **2011**.
9. Gamage DG, Read TR, Bradshaw CS, et al. Incidence of hepatitis-C among HIV infected men who have sex with men (MSM) attending a sexual health service: a cohort study. BMC Infect Dis **2011**; 11:39.
10. Jin F, Prestage GP, Matthews G, et al. Prevalence, incidence and risk factors for hepatitis C in homosexual men: data from two cohorts of HIV-negative and HIV-positive men in Sydney, Australia. Sex Transm Infect **2010**; 86:25–8.
11. Matthews GV, Pham ST, Hellard M, et al; ATAHC Study Group. Patterns and characteristics of hepatitis C transmission clusters among HIV-positive and HIV-negative individuals in the Australian trial in acute hepatitis C. Clin Infect Dis **2011**; 52:803–11.
12. Mahony AA, Donnan EJ, Lester RA, et al. Beyond injecting drug use: investigation of a Victorian cluster of hepatitis C among HIV-infected men who have sex with men. Med J Australia **2013**; 198:210–4.
13. Hagan H, Jordan AE, Neurer J, Cleland CM. Incidence of sexually transmitted hepatitis C virus infection in HIV-positive men who have sex with men. AIDS **2015**; 29:2335–45.
14. Martinello M, Yee J, Bartlett SR, et al. Moving towards hepatitis C microelimination among people living with human immunodeficiency virus in Australia: the CEASE Study. Clin Infect Dis **2020**; 71:1502–10.
15. Sulkowski MS. The proof is in the patient: hepatitis C virus microelimination in the Swiss Human Immunodeficiency Virus Cohort Study. Clin Infect Dis **2019**; 68:577–9.
16. Douglass CH, Pedrana A, Lazarus JV, et al. Pathways to ensure universal and affordable access to hepatitis C treatment. BMC Med **2018**; 16:175.
17. Lazarus JV, Safreed-Harmon K, Thursz MR, et al. The micro-elimination approach to eliminating hepatitis C: strategic and operational considerations. Semin Liver Dis **2018**; 38:181–92.

18. Lazarus JV, Wiktor S, Colombo M, Thursz M; EASL International Liver Foundation. Micro-elimination—a path to global elimination of hepatitis C. J Hepatol **2017**; 67:665–6.
19. Martin NK, Boerekamps A, Hill AM, Rijnders BJA. Is hepatitis C virus elimination possible among people living with HIV and what will it take to achieve it? J Int AIDS Soc **2018**; 21(Suppl 2):e25062.
20. Callander D, Moreira C, El-Hayek C, et al. Monitoring the control of sexually transmissible infections and blood-borne viruses: protocol for the Australian Collaboration for Coordinated Enhanced Sentinel Surveillance (ACCESS). JMIR Res Protoc **2018**; 7:e11028.
21. Chan AW, Tetzlaff JM, Altman DG, et al. SPIRIT 2013 statement: defining standard protocol items for clinical trials. Ann Intern Med **2013**; 158:200–7.
22. McMahon JH, Moore R, Eu B, et al; Victorian Initiative for Patient Engagement and Retention VIPER Study Group. Clinic network collaboration and patient tracing to maximize retention in HIV care. PLoS One **2015**; 10:e0127726.
23. Shepherd BE, Rebeiro PF; Caribbean, Central and South America Network for HIV Epidemiology. Brief report: assessing and interpreting the association between continuous covariates and outcomes in observational studies of HIV using splines. J Acquir Immune Defic Syndr **2017**; 74:e60–3.
24. Kattakuzhy S, Gross C, Emmanuel B, et al; ASCEND Providers. Expansion of treatment for hepatitis C virus infection by task shifting to community-based nonspecialist providers: a nonrandomized clinical trial. Ann Intern Med **2017**; 167:311–8.
25. Sacks-Davis R, Doyle JS, Rauch A, et al. Linkage and retention in HCV care for HIV-infected populations: emerging implementation research. J Int AIDS Soc **2018**; 21:e25051.
26. Boerekamps A, van den Berk GE, Lauw FN, et al. Declining hepatitis C virus (HCV) incidence in Dutch human immunodeficiency virus-positive men who have sex with men after unrestricted access to HCV therapy. Clin Infect Dis **2018**; 66:1360–5.
27. Boerekamps A, Newsum AM, Smit C, et al; NVHB-SHM Hepatitis Working Group and the Netherlands ATHENA HIV Observational Cohort. High treatment uptake in human immunodeficiency virus/hepatitis C virus-coinfected patients after unrestricted access to direct-acting antivirals in the Netherlands. Clin Infect Dis **2018**; 66:1352–9.
28. Newsum AM, Stolte IG, van der Meer JT, et al. Development and validation of the HCV-MOSAIC risk score to assist testing for acute hepatitis C virus (HCV) infection in HIV-infected men who have sex with men (MSM). Euro Surveill **2017**; 22:30540.
29. Scott N, Stoove M, Wilson DP, et al. Eliminating hepatitis C virus as a public health threat among HIV-positive men who have sex with men: a multi-modelling approach to understand differences in sexual risk behaviour. J Int AIDS Soc **2018**; 21:e25059.